Foot and ankle characteristics associated with falls and falls risk in adults with rheumatoid arthritis

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ABSTRACT

The thesis investigated whether foot and ankle characteristics are associated with falls or falls risk in adults with rheumatoid arthritis (RA). A systematic review of the incidence and risk factors for falls in people with RA found inconsistency in methods for collecting falls data and conflicting evidence about fall risk factors. The current study sought to extend our understanding of fall risk in people with RA through the inclusion of foot and ankle characteristics.

The thesis consisted of a cross-sectional study followed by a 12-month prospective study of 201 adults with established RA. In the cross-sectional study, falls experienced in the preceding year were recorded (12-month fall history) and a range of clinical and foot and ankle characteristics were measured. Participants were then followed for 12 months to record the occurrence of prospective falls following the Prevention of Falls Network Europe (ProFaNE) consensus guidelines for falls research. Data analysis involved both univariate and multivariate analysis.

Falls incidence for the cross-sectional study was 59%. The logistic regression analysis, controlling for age, identified (a) clinical and foot and ankle characteristics which were independently associated with falls in the preceding 12 months; and (b) clinical and foot and ankle characteristics that were independent predictors of prospective falls. Clinical and foot and ankle characteristics that were independently associated with falls in the preceding 12 months included cardiovascular disease (odds ratio (OR) 3.22, P=0.024), midfoot peak plantar pressure (OR 1.12 [for each 20 kPa increase], P=0.046) and foot-related disability and impairment (OR 1.17 [for each 3 point increase], P=0.005).

Falls incidence for the 12-month prospective study was 42%. Clinical and foot and ankle characteristics found to be independent predictors of prospective falls (not controlling for 12-month fall history) included psychotropic medication (OR 2.35, P=0.025) and presence of foot or ankle tender joints (OR 1.95, P=0.034). When 12-month fall history was included in the analysis, psychotropic medication (OR 2.34,

P=0.025) and 12-month fall history (OR 2.27, P=0.008) were independent predictors of falls.

Falls are complex, multi-system events with multifactorial aetiologies. Therefore, no single risk factor can be identified as the cause of any given fall event. As such, the thesis presented a synthesis of the findings relating to the foot and ankle fall risk factors, with a hypothetical model on how these risk factors might be interrelated. Further work is required to test the hypotheses relating to interrelationships between foot and ankle fall risk factors.

Clinical implications included a number of assessments that could be incorporated into routine clinical practice to identify or monitor fall risk in people with established RA. Future work is needed to confirm the study findings in people with early RA and to develop a tool to screen for falls risk, and predict falls, in people with RA. Future research could include dynamic tests of balance, 3D gait analysis of lower limb and foot function and assessment of lower leg muscle strength and ankle joint proprioception. In addition, further evaluation of the role of footwear in falls, in people with RA, is warranted. Qualitative research, exploring perceptions around falls and falls risk, and the development of expert consensus guidelines for participant grouping in falls data analysis, would benefit future RA falls research.

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AUTHORSHIP

I hereby declare that this submission is my own work and that, to the best of my knowledge and belief, it contains no material previously published or written by another person (except where explicitly defined in the acknowledgements), nor material which to a substantial extent has been submitted for the award of any other degree or diploma of a university or other institution of higher learning.

Angela Robyn Brenton-Rule

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DISSEMINATION

Peer-reviewed publications

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International presentations

Foot and ankle characteristics associated with falls in people with rheumatoid arthritis: a prospective longitudinal study. Oral presentation. 2015 American College of Rheumatology Annual Meeting. San Francisco, CA.

Foot and ankle characteristics associated with falls in adults with rheumatoid arthritis. Oral presentation. 2015 Australian Podiatry Council Conference. Gold Coast, Australia.

National presentations

Reliability of the TekScan MatScan® system for the measurement of postural stability in older people with rheumatoid arthritis. Oral presentation. 2012 Podiatry NZ Biennial Conference: Enhancing the Clinician. Auckland, New Zealand.

What are the key foot and ankle characteristics in falls related to rheumatoid arthritis? Invited speaker. 2013 APRSIG Biannual Podiatric Rheumatology Update. Auckland, New Zealand.

Are changes in foot structure and function associated with falls in people with rheumatoid arthritis? Invited speaker. 2015 APRSIG Biannual Podiatric Rheumatology Update. Auckland, New Zealand.

GLOSSARY OF ABBREVIATIONS

ACR	American College of Rheumatology
ADHB	Auckland District Health Board
AI	arch index
Anti-CCP	anti-cyclic citrullinated peptide
AP	antero-posterior
AUT	Auckland University of Technology
BMI	body mass index
CMDHB	Counties Manukau District Health Board
CNS	central nervous system
COF	centre-of-force
COM	centre-of-mass
CONSORT	Consolidated Standards of Reporting Trials
CRF	clinical research from
CRP	C-reactive protein
DAS	disease activity score
DMARD	disease-modifying anti-rheumatic drug
ESR	erythrocyte sedimentation rate
EULAR	European League Against Rheumatism
FIS	Foot Impact Scale
FIS_{AP}	Foot Impact Scale, activities/participation subscale
FIS_{IF}	Foot Impact Scale, impairments/footwear subscale
FIS_{TOTAL}	Foot Impact Scale, total score
FPS	foot problem score
HAQ	Health Assessment Questionnaire
HHD	hand-held dynamometry / hand-held dynamometer
kPa	kilopascal
MDT	multidisciplinary team
ML	medio-lateral
MTP	metatarsophalangeal
MRI	magnetic resonance imaging
NSAID	non-steroidal anti-inflammatory drug

OCP	oral contraceptive pill
OMERACT	Outcome Measures in Rheumatology
PGT	paper grip test
PPP	peak planter pressure
ProFaNE	Prevention of Falls Network Europe
PROM	patient-reported outcome measure
PTI	pressure-time integral
RA	rheumatoid arthritis
RF	rheumatoid factor
SAM	sway analysis module
FES-I	Falls Efficacy Scale - International
SJC	swollen joint count
TJC	tender joint count
TNF	tumour necrosis factor
VAS	visual analogue scale
VPT	vibration perception threshold

TERMINOLOGY

The following terminology has been used in the thesis.

Characteristics = features that were measured or assessed as potential fall risk factors at baseline and 12-months.

Fall risk factors = characteristics associated with increasing fall risk, independently associated with falls in the preceding 12 months or independent predictors of falls.

Characteristics associated with increasing fall risk = those characteristics identified as significantly different on univariate analysis in the cross-sectional or 12-month prospective study.

Characteristics independently associated with falls in the preceding 12 months = those characteristics found to be significant on multivariate analysis in the cross-sectional study.

Characteristics that are independent predictors of falls = those characteristics found to be significant on multivariate analysis in the 12-month prospective study.

CHAPTER 1: INTRODUCTION

1.1: Overview

Accidental falls are a common and potentially serious problem affecting the health and quality of life of older adults worldwide. In developed countries, approximately one-third of community-dwelling adults, aged over 65 years, fall each year (1). Falls incidence is even higher among adults in residential care, with over 40% falling each year (2). The consequences of falls include loss of confidence and independence, injury and death. Falls are the leading cause of injuries sustained by adults over 65 years old and account for two-thirds of accidental deaths (3). As such falls represent an important burden to healthcare resources with direct and indirect costs associated with falls totalling $75-100 billion in the USA annually (4). In 2013, approximately 325,000 New Zealanders were injured as a result of a fall in their home; costing the country $350 million (5). When considering the community-based costs associated with minor falls, not requiring hospitalisation, it is likely that the true economic impact is much greater. Therefore, in New Zealand, falls prevention is a major healthcare focus supported by legislation including the Health of Older People Strategy 2002 and Preventing Injury from Falls: The National Strategy 2005-2015 (6, 7).

The aetiology of falls is multifactorial and can result from complex interactions between intrinsic, behavioural or environmental factors (3, 8). As such, falls are not purely random events and can be predicted through assessment of known risk factors (9). Previous studies in older adults have identified a plethora of fall risk factors enabling clinicians to identify people at increased risk and implement strategies to prevent falls (3, 10). Risk factors consistently found to be associated with falls include history of a prior fall(s), general pain, impaired balance, gait problems, poor muscle strength, visual impairment, psychotropic and antiepileptic medications, multiple drug use, arthritis, diabetes mellitus, Parkinson's disease, vertigo, impaired cognition, urinary incontinence and walking aids (3).

The majority of population-based studies have examined fall risk factors in the general older adult population. However, in recent years, studies have emerged which have investigated falls in at-risk populations such as people with Parkinson's disease (11,

12), multiple sclerosis (13-15), diabetes mellitus (16, 17) and inflammatory arthritis (18-20). The current thesis is concerned with fall risk factors in people with rheumatoid arthritis (RA), an inflammatory disorder that primarily affects the joints. People with RA may be at greater risk of falling than the non-RA population (21). Falls in this already vulnerable group can be devastating. For example, the risk of fall-related hip fracture is threefold in people with RA due to disease-related reduced bone mass (22). Therefore, falls awareness and prevention of falls are important in the management of people with RA.

Several studies have suggested that age-related foot problems are associated with falls in older adults (23-26). The feet are commonly affected in RA (27-34) and RA-related foot problems may be risk factors for falls in this group. However, evidence is lacking. The current thesis investigated the relationship between a range of foot and ankle characteristics, and falls, in people with RA. This thesis is unique, as to date, no study in an RA population has specifically included a range of foot and ankle characteristics as potential fall risk factors. A recent randomised control trial, in 305 community-dwelling older people in Australia, found that a multifaceted intervention targeting the foot and ankle reduced the rate of falls by 36% (35). Similar foot and ankle interventions, such as footwear and foot orthoses, may prevent falls in people with RA. However, evidence specific to the rheumatoid foot and falls is needed to inform an intervention study. The current work will provide further evidence in relation to falls in people with RA.

1.2: Thesis structure

The thesis is structured to lead the reader through two stages of an observational study in which falls incidence and potential risk factors for falls were investigated in a cohort of adults with RA. The first stage was a cross-sectional study and the second stage was a prospective study over a 12-month period.

Chapter 2 provides an overview of RA and the effects of RA in the feet including; incidence and prevalence of foot disease, structural and functional changes and foot-related disability and impairment.

Chapter 3 presents a review of the current literature pertaining to the incidence and risk factors for falls in adults with RA.

Chapter 4 describes the aims of the thesis and the research questions.

Chapter 5 presents a literature review of foot and ankle characteristics and falls in older adults. This chapter identifies the foot and ankle characteristics of relevance to the observational study.

Chapter 6 describes the methodology for recruitment of study participants, collection of clinical and foot and ankle characteristics and procedures for data analysis.

Chapters 7 & 8 report the results of the cross-sectional study and discuss the findings in relation to people with RA with a 12-month history of falls. This study explores the differences between people with RA who have fallen and those who have not fallen, on a range of foot and ankle characteristics. Clinical characteristics associated with 12-month fall history are also explored.

Chapters 9 & 10 report the results of the 12-month prospective study and discuss the findings in relation to prospective falls. This study explores differences between people who fell during the 12-month prospective study period and those who did not fall, on baseline clinical and foot and ankle characteristics. The prospective study design allows for the identification of characteristics which are predictors of future falls.

Chapter 11 provides an overview of the thesis findings. The study limitations and strengths are presented as well as clinical implications and future directions.

Chapter 12 summarises the overall conclusions of the thesis.

CHAPTER 2: RHEUMATOID ARTHRITIS AND THE FOOT

2.1: Introduction

This chapter will provide an overview of RA, predisposing factors, diagnosis, monitoring of disease activity and treatment. Foot involvement in RA will then be described including the incidence, prevalence and progression of foot disease. The chapter will conclude with a discussion on foot-related impairments including range of motion, muscle strength, walking impairment, plantar pressure distribution and postural stability.

2.2: Search strategy

The literature review is focused on research and review articles published between 1980 and 2014 concerning RA and foot involvement in RA. A search was conducted using AMED, CINAHL, MEDLINE, Scopus and The Cochrane Library online databases; under the following terms, “rheumatoid arthritis”, “inflammatory arthritis”, “polyarthritis”, “rheumatic disease”, “foot”, “feet”, “foot characteristics”, “foot structure”, “foot change”, “postural stability” and “balance”. Citations from retrieved publications were examined to obtain further references and English text only hard copy journals were also searched for relevant articles.

2.3: Background to rheumatoid arthritis

RA is a chronic, inflammatory, autoimmune disease characterised by systemic inflammation, persistent synovitis and progressive articular destruction (36). The pathogenesis of RA is complex, involving innate and adaptive immune responses and several inflammatory cascades (36). Infiltration of inflammatory cells; including synviocytes, neutrophils, lymphocytes and macrophages, into the synovial cavity, coupled with an increase in blood vessels, results in an inflamed and thickened synovium, or pannus. The synovial pannus invades and erodes contiguous cartilage and bone leading to eventual joint destruction (36, 37). Any synovial joint can be affected however the peripheral joints are predominantly involved, most often the small joints of the hands and feet, and usually in a symmetrical distribution (27).

Symptoms of RA include severe pain, stiffness and loss of mobility (38). Profound fatigue, malaise and ongoing flu-like symptoms can also result from the systemic release of large concentrations of inflammatory proteins (39). The systemic nature of RA means that other organs and body systems can be affected. For example, inflammation of the inner lining of the blood vessels has potentially devastating effects on the organs supplied by the affected vessels. Other systemic features include interstitial lung disease, eye manifestations, rheumatoid nodules and distal polyneuropathy (40). Co-morbid conditions are common and can affect the prognosis and outcome of RA as well as the quality of life of the individual (41). Cardiovascular disease is the most significant; occurring earlier and at higher rates compared with the non-RA population (41). In addition, people with RA are two to three times more likely to suffer from depression (42). Other common co-morbidities include malignancies, bacterial infections, anaemia, gastrointestinal ulcers and osteoporosis (43). Mortality is increased in people with RA compared with the general population with the main causes of premature death being cardiovascular disease, infection and cancer (44).

RA is the most common form of inflammatory polyarticular arthritis affecting 0.5 to 1.0% of the world population (36) and up to 3.5% of the New Zealand population (45). There is currently no available data on the incidence of RA in New Zealand. However, the incidence is estimated to be 0.025 to 0.05% in the UK (46) and 0.04 to 0.08% in the USA (47). In terms of prevalence, RA affects women three times more than men (36). Peak age at onset is most commonly the fifth decade and prevalence increases with age (36). RA has a tendency to run in families. Twin studies have reported concordance of 15% in monozygotic twins and 5% in dizygotic twins (48). The risk of developing RA is doubled in individuals who have any relative with the disease (49). Overall, the incidence of RA, particularly in women, is declining (47). Suggested reasons for this decline include a protective effect of the oral contraceptive pill (OCP) (50) and a birth cohort effect, in which women of an earlier generation were more susceptible to developing the disease than women from a later generation (51). Further, the decline in RA incidence may reflect a fall in disease severity, since diagnostic criteria are based on severity markers such as erosions and acute phase reactants (47).

The direct and indirect costs of RA are substantial. In New Zealand, the costs associated with the diagnosis, assessment and treatment of people with RA were estimated at $20 million in 2010 (52). In the UK, annual costs of RA are estimated at £0.8 to £1.3 billion (53). The severity of complications associated with RA are declining due to earlier detection and targeted therapy (54). However, despite recent advances in disease-modifying drugs, total remission is not common. Progressive joint destruction eventually leads to varying degrees of physical disability affecting both paid employment and activities of daily living (55). Approximately 20% of people with RA report significant work disability within one year of diagnosis and one-third will leave the workforce within three years. Up to 60% report significant work disability within 10 years of initial diagnosis (53, 56).

2.4: Predisposing factors for RA

The exact cause of RA is unknown. Exposure to environmental risk factors are believed to trigger an immune response in individuals who are genetically predisposed to the disease (37). Once triggered, a self-limiting inflammatory arthritis can occur and resolve spontaneously. In other cases, persistent inflammation leads to established disease (47). The genetic contribution to RA susceptibility is estimated to be approximately 60% (37). More than 30 genetic regions have been found to be associated with RA (36). However, the most strongly associated genetic factor is differences in human leukocyte antigen (HLA)-DRB1 alleles which affect both disease susceptibility and severity (37). Environmental factors, accounting for 40% of risk, include age, gender, hormonal factors, cigarette smoking, diet, infection and stress (57, 58). In some genetically susceptible individuals, exposure to a single environmental risk factor may trigger RA. However, in the majority of cases, the threshold for development of the disease is gradually lowered through cumulative exposures to a combination of risk factors (47).

The most important predisposing factor is cigarette smoking which doubles the risk of developing RA (59, 60). The link between smoking and rheumatoid factor-positive RA, particularly in men, has long been established (47). However, more recent studies also showed a link between smoking and HLA-DRB1 alleles in patients with anti-cyclic citrullinated peptide antibodies-positive disease (61). The risk of developing RA

increases with age and the peak age of onset occurs around 10 years earlier in women than men (47). Hormonal factors may predispose women to RA. For example, the OCP has been linked to a decline in incidence of RA, in younger women, over the past 30 years. This could suggest that the OCP is protective for RA or reflect a delay in pregnancy, and subsequent breastfeeding, which is also associated with RA (47). The role of diet in the development of RA has been extensively studied (62). Low fruit and vitamin C intake was associated with a doubling in risk of RA in one study (63). Another study found that high red meat intake increased the risk of RA (64). Further, an intervention study showed that a Mediterranean diet, high in oily fish, reduced the risk of developing RA and improved disease outcomes (65). There is mixed evidence for the association of caffeinated coffee intake with RA (66, 67). However, tea consumption has been shown to be protective for development of the disease (67). Infections which have been implicated as risk factors for RA include the Epstein-Barr virus, parvovirus and some bacterial infections (37). A recent study also focused on people's perceptions of the cause of their RA and reported an association between family and/or work related stress and onset of the disease (57).

2.5: Diagnosis of RA

In order to evaluate people suspected of having RA a range of clinical investigations are required including; history taking, clinical examination, blood tests and imaging. History taking is important in confirming suspicion of inflammatory arthritis. Presence and duration of morning stiffness, as well as symptoms of fatigue and malaise, indicate active disease (39). Further, the identification of predisposing risk factors including age, gender, family history of RA and smoking is useful in forming a risk profile for RA (58). Clinical examination primarily involves physician assessment of tender and swollen joints (36). Blood tests identify the presence of autoantibodies and acute phase reactants. The classic autoantibody in RA is rheumatoid factor (RF), which is present in 60 to 90% of patients with established disease (68). However, RF is also present in other autoimmune and infectious diseases, and in three to five percent of healthy adults and 10 to 30% of older adults. Therefore, RF has low specificity for RA (69). Antibodies which are directed against citrullinated peptides (ACPA) are also diagnostic markers for RA. These are also known as anti-cyclic citrullinated peptide (anti-CCP) antibodies (68). Anti-CCP antibodies can be detected in up to 80% of people

with RA and are highly specific for the disease (69). Between 50-80% of people with RA have RF, Anti-CCP antibodies or both (36). People can also be classified as having seronegative disease when they are negative for RF and Anti-CCP antibodies but satisfy other diagnostic criteria for RA (36). Acute phase reactants are markers of disease activity and include erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP). Both are measures of inflammation, however CRP is more sensitive to change in inflammatory arthritis (70). Imaging is used to confirm joint and soft tissue damage associated with RA. Plain-film radiographic imaging (x-ray) is used to identify juxta-articular erosions typical of progressive established disease (36). Musculoskeletal ultrasound and magnetic resonance imaging (MRI) are also being increasingly used to identify soft tissue inflammation in early disease, before bone erosion has occurred (71).

2.6: Measuring disease activity

The prognosis of RA is related to the severity of disease and effectiveness of treatment. Clinical remission (absence of signs or symptoms of inflammation) occurs in up to 20% of people with RA, without ongoing treatment. In contrast, up to 75% of people with RA achieve clinical remission or low disease activity with continuing targeted pharmacological therapy (37). Measuring disease activity is important for monitoring response to treatment. This involves evaluation of tender and swollen joints to obtain a total joint count (36). Standard joint counts include 28 joints in the hands, upper limbs and knees (36). However, some rheumatologists prefer a more extensive 66 and 68 joint count which includes the feet (36). In addition, numerous disease activity measurement tools have been developed for routine office based monitoring. A recent review in conjunction with the American College of Rheumatology (ACR) recommended six indices for use in clinical practice (72). Recommended tools were the Clinical Disease Activity Index (CDAI) (73), Disease Activity Score with 28-joint count (DAS28) (74), Patient Activity Scale (PAS) (75), PAS-II (75), Routine Assessment of Patient Index Data with 3 measures (RAPID-3) (76), and Simplified Disease Activity Index (SDAI) (77). Of these assessment tools, the DAS28 (74) is the 'gold standard' tool endorsed by the ACR and European League Against Rheumatism (EULAR) for use in clinical trials (78). The DAS28 is a composite measure which combines single measures of disease activity into one continuous measure.

Calculation of the DAS28 includes tender and swollen 28 joint counts, ESR or CRP blood test result and patient-reported global health, using a visual analogue scale. The DAS28 provides a score ranging between 1 and 10. Scores greater than 3.7 are accepted to indicate high disease activity, 2.4 to 3.7 is moderate activity and below 2.4 is low disease activity. A score of <1.6 indicates disease remission (74). In addition, radiographic evaluation of bone erosion is a specific and useful way to determine disease progression.

2.7: Measuring functional ability and activity limitation

In people with RA, severity of disease and level of disease activity directly impact function and thus the ability to participate in the activities of daily living. Therefore, measuring functional ability and activity limitation is also important in monitoring disease progression and response to treatment. Functional ability can be assessed clinically, for example measuring grip strength, or through the use of patient-reported outcome measures (PROMs). These include global assessment of health, including pain, as well as disability and activity limitations. PROMs are increasingly used in healthcare settings to measure the effectiveness of care plans from the patient's perspective (79). PROMs provide an objective measure of subjective outcomes which can be used to monitor the efficacy of treatment plans, in addition to clinical measures of disease activity. A patient-centred approach is more common in rheumatology than other specialties with many instruments available for measuring the impact of living with a chronic and disabling condition (79). An example is the Stanford Health Assessment Questionnaire (HAQ) (80). The HAQ comprises 20 questions designed to measure difficulty during the past week in performing activities of daily living over 8 domains: dressing, grooming, rising, eating, walking, hygiene, reaching and gripping. Patients rate their difficulty on a 4-point scale from 0 (without any difficulty) to 3 (unable to perform). The total score is divided by the number of questions to arrive at a final score between 0 and 3. A score of 0-1 is considered to indicate mild to moderate difficulty, 1.1 to 2.0 indicates moderate to severe disability and 2.1 to 3.0 indicates severe to very severe disability (80). The HAQ is widely used in rheumatology and validated for use in people with RA (46). Several shortened versions have also been developed including the modified HAQ (MHAQ) (81), HAQ-disability index (HAQ-DI) (82) and revised HAQ (HAQ-II) (83).

2.8: Treatment of RA

Treatment of RA is primarily through the use of drugs to manage symptoms and modify or arrest disease activity (36, 84). Early pharmacological intervention and tight control, in which treatment is increased until remission or low disease activity is achieved, have been shown to be effective in clinical trials (85). Symptom relieving agents include analgesics and non-steroidal anti-inflammatory drugs (NSAIDs). Disease-modifying agents, collectively called disease-modifying anti-rheumatic drugs (DMARDs), are the mainstay of treatment for RA (84).

Conventional or traditional DMARDs include gold, methotrexate, D-penicillamine, sulfasalazine, azathioprine, antimalarials, ciclosporin-A and leflunomide. These DMARDs primarily act to reduce joint swelling and pain and decrease acute-phase reactants, thus limiting joint damage and improving function (36). Methotrexate is the most widely used conventional DMARD and usually the first DMARD administered at disease diagnosis (36, 84). When methotrexate is contraindicated, sulfasalazine and leflunomide are common alternatives. DMARDs can also be combined, e.g. methotrexate, sulfasalazine and hydroxychoroquine – termed triple therapy (36). Traditional DMARDs have a slow onset of action and a range of minor (e.g. nausea) and potentially serious (e.g. hepatotoxicity) adverse effects. As such, ongoing monitoring, including recording of blood counts and liver function tests, is usually required (36).

Biological agents are another form of DMARD which have been more recently developed. Biologics are protein-based DMARDs which interfere with specific inflammatory pathways, e.g. TNF inhibitors. Biologics are administered subcutaneously or via intravenous transfusion. Therefore, in some cases, the onset of action can be very rapid compared to traditional (non-biologic) DMARDs. Biologics can also be combined with non-biologic DMARDs including methotrexate and leflunomide to reduce antibody formation and increase efficacy. Adverse reactions for biologics include infections at infusion or injection sites. There is also an increased risk of tuberculosis with TNF inhibitors (36).

In addition to NSAIDs and DMARDs, glucocorticosteroids can be used to reduce synovitis in the short term. Glucocorticosteroids are also effective in decreasing joint

damage over time. However, long term use of glucocorticosteroids is associated with serious adverse events including infection and osteoporosis. Therefore, glucocorticosteroids are mostly used for treatment of individual active joints via intra-articular injection or for short-term use during a 'flare' to provide rapid improvement whilst allowing more slow acting DMARDs to take effect (36, 84).

Psychotropic medications including antidepressants, benzodiazepines and anticonvulsants are commonly used adjunct therapies for chronic pain conditions including RA (84). Use of additional drugs to treat co-morbid conditions and counteract medication side-effects is also common. This frequently results in polypharmacy, particularly in older people with long-standing RA (86).

Non-pharmacological management strategies including exercise programmes, joint support and protection, physiotherapy, podiatry and psychological support are also important for the health and well-being of people with RA (39). Treatment is targeted towards the reduction of symptoms, maintenance of function and improvement of quality of life for the individual (39). Exercise programmes can be on land or in water and include aerobic activities, muscle strengthening and balance rehabilitation (87). Psychological support involves cognitive and behavioural therapies and psychodynamic interventions to improve the person's perception of the disease and their ability to cope (88). The podiatrist's role specifically focuses on the management of foot health (39). Regular foot health assessment is important for all people with RA along with a tailored management programme which can include palliative care of skin and nails, footwear advice and orthotic therapy (89).

A multidisciplinary team (MDT), involving rheumatologists, rheumatology nurses, physiotherapists, podiatrists, nutritionists and other support services, is increasingly recognised as being the most effective approach to the overall management of people with RA (39, 90). In addition, patient education and self-management are vital and many people with RA are active members of the MDT involved in their care (39).

2.9: Classification criteria for RA

Classification criteria were designed to distinguish established RA from other types of inflammatory joint disease. The criteria ensure that researchers study homogenous patient groups, which is particularly important in clinical trials (36). Early attempts at developing classification criteria, in the 1950s and 1960s, were based on expert consensus opinion (91-93). Subsequent revised criteria were developed in 1987 using clinical data from patients with established RA (94). However, these criteria failed to identify RA patients with early disease. The most recent criteria, the 2010 rheumatoid arthritis classification criteria, were developed through collaboration between the ACR and EULAR (95). Figure 2.1 describes the 2010 criteria. To be classified as having definitive RA, patients must have confirmed synovitis in at least one joint that is not explained by a non-RA cause and a score of 6 or greater from the four classification domains. People can also be classified as having RA if they have typical erosions or longstanding disease which satisfied previous criteria.

1. Joint involvement
   - One medium to large joint (0)
   - Two to ten medium to large joints (1)
   - One to three small joints (large joints not counted) (2)
   - Four to ten small joints (large joints not counted) (3)
   - More than ten joints (at least one small joint) (5)

2. Serology
   - Negative RF *and* negative ACPA (0)
   - Low positive RF *or* low positive ACPA (2)
   - High positive RF *or* high positive ACPA (3)

3. Acute-phase reactants
   - Normal CRP *and* normal ESR (0)
   - Abnormal CRP *or* abnormal ESR (1)

4. Duration of symptoms
   - Less than 6 weeks (0)
   - 6 weeks or more (1)

Figure 2.1: ACR/EULAR 2010 Rheumatoid arthritis classification criteria
RF, rheumatoid factor; ACPA, anti-bodies against citrullinated antigens; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate

2.10: Foot involvement in RA

2.10.1: Epidemiology

Foot and ankle pathology is common in RA and foot symptoms, such as pain, are frequently present at initial diagnosis. Several studies have reported the incidence of foot disease, in early and established RA, as well as the distribution of joint involvement within the foot itself (27-34). Methods for collecting data included self-report questionnaires (27), clinical assessment (29-31, 33) and radiographic studies (28, 31-34). A large Swedish study investigated 1000 people with RA using a self-reported questionnaire relating to foot problems. Fifty-three percent (53%) of patients reported foot involvement at disease diagnosis. The forefoot (45%) was more frequently involved than the rearfoot/ankle (17%) and 9% reported both forefoot and rearfoot symptoms at diagnosis (27). This was in contrast to earlier work which reported rearfoot/ankle involvement to be more common than forefoot involvement (29, 96). Incidence of foot involvement increases as the disease progresses (29, 31) and up to 100% of patients experience foot problems at some stage of the disease course (27, 32). In a New Zealand study of 100 RA patients with established disease, 86% were found to have RA-related foot pathology including hallux valgus, lesser toes deformities, corns and pathological callus, on clinical examination (30). Similarly, a Turkish study of 40 RA patients and 40 control participants reported the frequency of deformity to be 79% (28) and 80% of patients in the large Swedish study reported current foot symptoms (27).

2.10.2: Foot pain

Foot pain is a common symptom in early RA and often the first indicator of synovitis in the feet (97). In a UK-based survey of 185 patients with early RA, 74% reported having experienced pain in the feet and 60% reported current foot pain (98). A further UK-based survey in patients with early disease found 90% experienced foot pain at some stage and 61% reported current foot pain (38). Prevalence increases with disease duration with foot pain occurring in up to 94% of patients with long-standing disease (29, 38). Foot pain in RA is not always associated with synovitis and may be attributable to mechanical causes associated with RA-related foot deformity, altered gait and increased plantar pressures (99-101). However, regardless of the underlying aetiology, foot pain is believed to have the strongest influence on functional ability in

RA, independent of disease duration (99). Instruments for measuring foot pain include one-item questionnaires, to determine presence of pain, and a 0-100mm visual analogue scale (VAS) to determine pain severity (102). The VAS is a well-established, valid, reliable and responsive measure to assess global pain and is included in the core set of outcome measures for rheumatology (102). However, the validity and reliability of a VAS specifically for foot pain have not been reported. Regardless, VAS foot pain is frequently reported in research (33, 103-105) with higher scores (80-100mm) generally related to inflammation in early disease and lower scores (40-60mm) related to altered structure in established disease. Assessment of foot pain is also included within multi-item questionnaires or patient-reported measures of functional status.

2.10.3: Detection of foot pathology

Synovitis in the metatarsophalangeal (MTP) joints is believed to be the main cause of foot pain in early RA (31). Inflammation in the MTP joints may cause widening of adjacent toes, commonly called the daylight sign, and is an easily recognisable sign of early RA (106). However, in the absence of the daylight sign, synovitis in the feet can be difficult to detect (107). A study using MRI reported the presence of synovitis, bone oedema and erosions in the MTP joints of people with early RA which were undetectable on plain x-ray (107). This study showed that irreversible damage can occur in very early disease when synovitis is clinically undetectable (107). A further study showed erosion and joint space narrowing in the MTP joints and first interphalangeal (IP) joints in 37% of patients at initial diagnosis (108). Early diagnosis of RA is necessary for effective treatment and prevention of foot deformity (54, 109). A ‘positive’ squeeze test in which pain is elicited through squeezing across the width of the forefoot, unresponsiveness to treatment of forefoot pain, and a history of morning stiffness of ≥30 minutes in three or more swollen joints, are grounds for referral for rheumatology assessment (110).

2.10.4: Progression of foot pathology

If left untreated, synovial inflammation will lead to bone erosion and joint deformity (37). The joints of the feet are particularly vulnerable to damage due to the constant demands of daily ambulation. The extent of the damage is thought to be governed by the loading at individual joints (46). For example, there is evidence to suggest that

larger joints, such as the ankle, are less susceptible to osteoarthritic erosion due to a greater surface-area-to-load ratio compared to smaller joints (111). Indeed, epidemiological studies report lower prevalence and later development of ankle joint involvement in RA (27, 112). In contrast, the talonavicular joint, in the midtarsal region, is commonly affected in early RA (113, 114) which may be attributable to low joint surface-area-to-load ratio.

Another factor in the progression of joint disease is the structure and function of the joint. The subtalar joint, for example, is particularly susceptible to damage due to its complex structure and pivotal role in locomotion (46). The subtalar joint enables triplanar motion to produce the movements of pronation and supination (115). Alteration in gait, due to foot pain, leads to altered load and abnormal forces. Laxity of the joint capsule, due to synovial effusion, and damage to intra-articular ligaments, caused by the advancing pannus, result in an unsupported joint. Normal joint space is lost and erosion of articular surfaces results in further damage (37). Compensation occurring at neighbouring joints can lead to further exacerbation of symptoms and progressive damage throughout the foot (46).

2.10.4.1: Forefoot pathology

In the forefoot, persistent synovitis and continuous loading of the MTP joints result in attenuation of the joint capsule and supporting ligaments. The integrity of the joint is compromised resulting in digital deformities including; hallux valgus, hammer and claw toes, splayed forefoot, subluxation and eventual dislocation of the joints (116). Distal shift of the fat pad, which usually sits beneath the MTP joints, exposes the metatarsal heads to increased pressure on weight-bearing. Plantar bursae form to protect the metatarsal heads and can cause a painful sensation described as “walking on pebbles” (46). Increased pressure beneath the metatarsal heads also causes the formation of corns and callus which can subsequently lead to skin breakdown and plantar ulcerations (117). Compression of the inter-digital nerves is a further complication of inflammation in the MTP joints, causing a sharp pain which radiates into the ipsilateral digit (46). Sesamoiditis, particularly in the sesamoids associated with the hallux, can also cause further symptoms of forefoot pain (118).

2.10.4.2: Rearfoot pathology

In the rearfoot, the talonavicular and subtalar joints, which are subject to greater mechanical stress, are the most frequently affected (119). Ankle joint involvement is less common and occurs later in the disease, as previously mentioned. Pes planovalgus (PPV) is the most common gross structural deformity, occurring in up to 80% of people with established disease (28, 34, 96). Shi (32) reported that the prevalence of PPV increases with disease severity and duration, as evidenced on serial X-rays. The development of PPV is associated with the gradual weakening of the ligamentous and tendinous structures which support the medial longitudinal arch (101, 120). Tenosynovitis and attenuation in the tibialis posterior tendon are believed to be major contributing factors, resulting in eventual arch collapse (121). Indeed, tibialis posterior tendon dysfunction is the most common cause of adult acquired flatfoot in non-RA populations (122). Tenosynovitis is frequently seen in the major tendons, which are encased in sheaths lined with a synovial membrane. Sustained inflammation of the tendon sheath leads to breakdown of the tendon itself and eventual rupture and loss of function. For example, ultrasound evaluation of the flexor hallucis longus tendon, in 30 RA patients with painful feet, found an association between tendon rupture and damage to the 1st MTP joint, decreased range of motion in the 1st MTP joint and PPV foot-type (123).

2.10.5: Foot-related impairment

Impairment can be defined as loss of function, or altered function, as a result of illness, injury or congenital condition (124). The predominant foot-related impairments in RA are reduced range of motion and decreased muscle strength. These factors, combined with foot pain, result in walking impairment, increased plantar pressures and decreased postural stability. Impairments can be measured clinically, from the physicians or researchers perspective, and via PROMs which include assessments of pain and disability.

2.10.5.1: Range of motion

Reduced range of motion is a prominent feature of RA closely associated with symptoms of joint stiffness and pain and directly impacting gait (125). Reduced range of motion can be attributed to synovitis and laxity within the joint capsule, in early

disease, and changes in articular structure and contracture of the muscles serving the tendons that cross the joints, in later disease (46). Clinical assessment, involving passive movement of the distal part of the joint in non-weight-bearing, provides a subjective measure useful for monitoring disease progression. In addition, assessment of gait provides valuable data on foot function (46). Due to the complex architecture of the foot, assessing dynamic joint motion is technically difficult and requires laboratory assessment of joint kinematics using 3D video-based motion analysis systems (125). Several studies have evaluated joint range of motion during gait in RA patients using 3D motion analysis (97, 99-101, 125-127). Khazzam (126) compared kinematic data for 22 people with RA-related forefoot pathology and 25 control participants and found that RA patients exhibited reduced range of motion in four foot segments (tibia, rearfoot, forefoot, hallux) affecting movement in the sagittal, coronal and transverse planes. In another study, Turner (100) compared 28 people with RA with severe forefoot and/or rearfoot deformity with 53 control participants and reported excessive subtalar joint eversion in mid-stance and reduced ankle plantarflexion and hallux dorsiflexion in terminal stance. Abnormal kinematic features have also been reported in people with early RA, without foot deformity, which may indicate early adaption to underlying inflammation and associated pain (97).

2.10.5.2: Muscle function

Coupled with pain and stiffness, muscle weakness is a significant feature in RA and symptoms of weakness are often reported from the onset of disease. People with RA are generally weaker and fatigue more easily than their non-RA counterparts (46). Localised muscle weakness and atrophy have been found to be associated with active disease in adults with RA and in children with juvenile arthritis (128, 129). One study assessed foot and ankle muscle strength in people with established RA and found a significant decrease in ankle plantarflexion, eversion and inversion compared to healthy controls (130). However, it was unclear whether the reduction in muscle strength preceded the onset of RA or was a consequence of the disease (130).

Muscle weakness in RA can result from inflammatory processes within the muscle itself as well as disruption to afferent signals from joint mechanoreceptors in damaged or inflamed joints (46). Decreased mobility, due to pain and functional impairment, is

also linked to muscle atrophy and decreased muscle strength in people with RA (131). A subjective measure of muscle strength can be obtained through manual muscle testing using grading scales such as the Oxford 0-5 scale. More objective methods used clinically and in research include the use of isokinetic machines (132) and hand-held dynamometers (133). Isokinetic machines have been shown to be highly reliable in measuring muscle strength in the lower limb (134) and foot (132) and are considered to be the criterion standard when measuring muscle strength (135). However, isokinetic machines are considered to be bulky, expensive and impractical for routine clinical examination (134, 136, 137). Hand-held dynamometry (HHD) is a convenient, non-invasive method for assessing muscle strength. HHD has been previously used to assess foot and ankle muscle strength in people with RA (130) and shown to be reliable for testing muscle strength in the older adult foot and ankle (133, 136). Wang (136) reported high test-retest reliability in older adults and suggested that HHD should be used for its simplicity, responsiveness and objectivity in measuring muscle strength changes in clinical practice.

2.10.5.3: Walking impairment

Walking impairment, or altered gait, is also a prominent feature of RA and is correlated with reduced joint range of motion, foot pain and foot deformity (97, 99-101). In a longitudinal study of 848 Dutch people with early disease, 57% reported walking disability at initial presentation decreasing to 40% after 8 years (31). In a study of 1000 Swedish people with RA, 71% reported difficulty in walking due to their feet (27) which was consistent with an earlier study in which the foot was reported to be the most important cause of walking difficultly in 76% of people with RA (138). A clinical approach to investigating the influence of foot involvement on walking ability has also been taken. One study evaluated the relationship between walking ability and talonavicular joint abnormality, using MRI, and found a positive correlation between increased severity of joint involvement and decreased walking ability (139). Other studies compared the temporal-spatial parameters of gait in people with RA and healthy control participants and demonstrated that people with RA have a significantly slower gait speed, shorter stride length and increased double-limb support time (97, 99, 100, 126, 140).

2.10.5.4: Plantar pressure distribution

A consequence of walking impairment in RA is alteration in plantar pressure distribution (100, 141). Measurement of plantar pressure distribution can be undertaken using a force plate, portable pressure mat or an in-shoe plantar pressure system (142). This technology measures the ground reaction force applied to the foot and calculates the peak pressure, defined as force per unit area and expressed in kilopascals (kPa). Plantar pressure analysis also provides information on structural foot deformity in RA. For example, increased forefoot pressures have been associated with bony erosion of the MTP joints (143, 144) as well as callosities overlying adventitious bursa which form to protect prominent metatarsal heads (145).

2.10.5.5: Postural stability

Postural stability can be defined as the maintenance of an upright position in quiet standing or the recovery of balance, associated with voluntary movement (146). People with RA have decreased postural stability and experience difficulty in maintaining postural control causing balance problems in everyday activities (140). Postural stability is controlled by the central nervous system (CNS). Afferent input from the somatosensory (tactile and proprioceptive), visual and vestibular systems combine with coordinated muscle activity to maintain balance in quiet standing and during gait (147). In healthy adults, balance control can flexibly and smoothly change between these systems in order to maintain a stable equilibrium (147). In order to maintain postural stability, the body's global centre-of-mass (COM) must remain inside the body's base of support. This requires active neural control of the COM position in space, resulting in tiny oscillatory movements around a single point, referred to as postural sway (148).

During static and dynamic activities, the body employs a variety of postural control strategies to restore and maintain balance. In quiet standing, the ankle strategy restores stability through tiny movements around the ankle joint. The ankle strategy is also effective during small perturbations. Where larger perturbations are experienced, the hip strategy is used with movement in the hip joint, and a stepping or hopping strategy is employed when the COM is displaced outside the base of support (149). Normal postural responses, such as the ankle strategy, may be compromised in people

with RA due to disease-related physiologic changes including muscle weakness, reduced joint range of motion and decreased plantar sensation (140, 150, 151).

2.10.6: Patient-reported foot-related disability and impairment

Patient-reported measures of impairment (functional status) are widely used in healthcare settings and research and are important in the assessment of treatment outcomes (102, 152). Many patient-reported measures also assess disability, which encompasses activity limitation and participation restriction, as a result of impairment. Numerous self-report tools have been developed for measuring the impact of foot pathology on foot function, foot pain and foot-related disability. However, there are a limited number of tools available that are specific for RA-related foot pathology. The current study utilised the Foot Impact Scale (FIS) (153) which was developed using a needs-based approach whereby semi-structured interviews are used to generate statements which best represent the issues of importance to the patient group (154). The FIS places emphasis on the bio-psychosocial experiences arising from RA-related foot problems as well as the qualitative aspects of pain, stiffness and the importance of footwear (152).

2.11: Summary

RA is a chronic, inflammatory, autoimmune disease and the most common form of polyarticular arthritis. The synovial joints are predominantly affected resulting in erosion of articular cartilage and bone, and eventual joint destruction. People with RA experience varying degrees of pain and physical disability which can profoundly affect their daily lives. Mortality is also increased due to life threatening co-morbidities associated with systemic inflammation. Foot involvement is common in RA with foot problems frequently reported at initial diagnosis. Foot pain and changes in foot structure and function lead to walking impairment, altered plantar pressures and decreased postural stability. These factors may be associated with falls and falls risk in people with RA.

CHAPTER 3: FALLS IN ADULTS WITH RHEUMATOID ARTHRITIS

3.1: Introduction

This chapter will provide a detailed review of the current evidence surrounding the incidence and risk factors for falls in adults with RA. Methodological considerations will also be discussed in relation to the current RA falls research. The review was recently published in *Seminars in Arthritis and Rheumatism* (Appendix 11).

Brenton-Rule A, Dalbeth N, Menz HB, Bassett S, Rome K. The incidence and risk factors for falls in adults with rheumatoid arthritis: a systematic review. Semin Arthritis Rheum. 2015;44(4):389-398.

3.2: Search strategy

A primary literature search was conducted using electronic databases (from 1980 to 2013) such as AMED, CINAHL, MEDLINE, Scopus and The Cochrane Library under the following terms: “rheumatoid arthritis”, “inflammatory arthritis”, “polyarthritis”, “rheumatic disease”, “falls”, “fall risk” and “falls incidence”. Search terms were applied to title and/or abstract, and all studies were obtained from English-language peer-reviewed journals. Citations from retrieved publications were examined to obtain further references and English text only hard copy journals were also searched for relevant articles. Studies with a primary or secondary outcome measure of falls in the preceding 6-12 months and/or prospective falls over a 12-month period in adult participants with diagnosed RA were included. Studies that investigated fear of falling as a primary outcome, in addition to current falls or fall history, were also included in order to capture falls data. Studies that included participants with other forms of inflammatory arthritis were excluded.

3.3: Studies identified in the search

Nine studies were identified for inclusion in the review (Table 3.1). These included five cross-sectional studies (155-159), three prospective cohort studies (21, 160, 161) and one case-control study (162). Study size was varied with participant number ranging between 78 (156) and 4996 (158). Two studies included females only (160, 162) with the remainder including both males and females. The mean age of participants ranged from 54 (159) to 65 years old (157, 160).

Table 3.1: Summary of papers reviewed

Study	Country	Participants (Male: Female)	Age (years) Mean (SD)	Method of falls data attainment	Study design	Fall definition	Falls incidence results
Stanmore (21)	UK	559 (173: 386)	Male 62 (11) Female 62 (14)	Baseline - falls in preceding 12-month period recorded at baseline interview Follow-up falls recorded over 12 months via pre-addressed, prepaid daily falls calendars (posted monthly) and monthly follow-up telephone calls	Prospective	<u>Fall history:</u> During the past year, how often have you had any fall, including a slip or trip in which you lost balance and landed on the floor, ground or lower level? <u>Current falls:</u> An unexpected event in which participants come to rest on the ground, or other lower level.	<u>Fall history:</u> 43% fell at least once 22% multiple falls <u>Current falls:</u> 36.4% fell at least once 18.9% multiple falls Falls rate 1.11 falls/person year
Bohler (156)	Austria	78 (12:66)	59 (14)	Falls in preceding 12 months via interview assisted questionnaire	Cross-sectional	None	<u>Fall history:</u> 26.9% fell at least once 16.7% multiple falls
Duyur Cakit (162)	Turkey	84 cases 44 controls (All female)	Cases 56 (9) Controls 54 (5.2)	Falls in preceding 12 months via interview (cases only)	Case-control	None	<u>Fall history:</u> 14.3% fell at least once (cases only)
Hayashibara (160)	Japan	80 (All female)	65.2 (7)	Falls recorded over 12 months via falls calendar (posted monthly) and monthly follow-up telephone calls	Prospective	The subject unintentionally coming down on the floor or to a lower level.	<u>Current falls:</u> 50% fell at least once

Table 3.1: continued

Furuya (158)	Japan	4996 (765:4231)	Median age 60	Falls in preceding 6 months via questionnaire	Cross-sectional	None	Fall history: 10.1% fell at least once 2.2% multiple falls 8.0% males fell at least once, 1.3% multiple falls 10.5% females fell at least once, 2.4% multiple falls
Smulders (161)	The Nether-lands	84 (25:59)	59 (12)	Falls over 12 months using monthly falls registration cards	Prospective	None	Current falls: 42% fell at least once Falls rate .82 falls /person year
Armstrong (155)	UK	253 (72:181)	62 (11)	Falls in preceding 12 months via interview	Cross-sectional	None Exclusion of falls as a result of a road accident or act of violence.	Fall history: 33% fell at least once 52% multiple falls 26% males fell 36% females fell
Jamison (159)	USA	128 (22:106)	54 (9)	Falls in preceding 12 months via interview	Cross-sectional	An unplanned descent to the floor, ground, or other lower level. Falls could be from standing, sitting or lying position.	Fall history: 35.2% fell at least once Of the total fallers 53.3% had one fall 33.4% multiple falls 13.3% did not specify number of falls
Fessel (157)	USA	570 (138:432)	65 (9)	Falls in preceding 12 months via interview	Cross-sectional	Falling and landing on the floor or ground, or falling and hitting an object like a table or stair.	Fall history: 30.9% fell at least once 15.5% multiple falls

3.4: Falls incidence

Falls incidence refers to the number (%) of people who fell during the study period. In the current review, incidence of retrospective falls (i.e. fall history) ranged from 10% (158) to 43% (21) and prospective falls incidence ranged from 36% (21) to 50% (160). Falls data from all studies was self-reported. However, several studies did not include a fall definition (155, 156, 158, 161, 162) and there was inconsistency in fall definition across the remaining studies. There was also variation in the methodology for collecting falls data, including the use of questionnaires (158), interviews (21, 155, 157, 159, 162), interview-assisted questionnaires (156) and prospective monthly reporting via calendars or registration cards (21, 160, 161).

3.5: Fall risk factors

Seven studies investigated factors associated with falls in RA (21, 155, 158-162). Fall risk factors were classified into (1) physiological, (2) pharmacological, (3) extrinsic and (4) measures of RA disease activity. Multivariate logistic regression analysis was used to identify factors associated with fall history in cross-sectional studies (155, 158, 159) and to identify independent predictors of falls in prospective studies (21, 160, 161). In addition, one prospective study also used bivariate logistic regression analysis to identify risk factors associated with falls, not taking into account confounding variables. The case-control study analysed potential fall risk factors using multiple stepwise linear regression and reported *r* values (162).

3.5.1: Physiological risk factors

Age was assessed as a risk factor in all seven studies and found not to be associated with falls. This is important as studies in healthy older adults consistently report an increase in fall risk with increasing age (3, 163, 164). Countries with falls prevention provision such as the UK, Canada, USA, Germany and New Zealand focus on the over 65 age group. Therefore, it is possible that younger people with RA may be marginalised and not receive tailored appropriate treatment which addresses potential fall risk. Studies that assessed gender (21, 155, 158, 159, 161) and disease duration (158-162) as potential fall risk factors also found no difference between fallers and

non-fallers. In contrast, female gender is associated with increased fall risk in healthy older adults (3, 163, 164) and disability and impairment, in RA, is generally associated with increasing length of disease (36). Therefore, health professionals may also be unaware of the potential fall risk in males and individuals with early RA.

Increased body mass index (BMI) was found to be associated with a history of single and multiple falls, over 6 months, in a large Japanese study of men and women with RA (158). However, there was no association found between BMI and prospective falls in a smaller study of Japanese women (160). Similarly, an association between fall history and number of co-morbid conditions was reported by Jamison (159) but three subsequent prospective studies found no association between falls and co-morbid conditions (21, 160, 161). Jamison (159) reported that the odds of falling more than doubled with each additional co-morbid condition. Decreased general health was associated with a history of falling in one study (158). General health was self-reported using a 0-10 cm VAS (158).

Stanmore (21) reported significant associations between prospectively recorded falls and fall history, injury from a previous fall, history of fracture, dizziness and fatigue. Fatigue and history of single and multiple falls were also reported to be independent predictors of future falls (21). This was in agreement with an earlier study which reported that the odds of a fall in the coming year were almost 10 times higher in people with RA who had experienced a prior fall (161). Stanmore (21) found fear of falling to be associated with falls but not a predictor of future falls. Two previous studies reported no association between fear of falling and falls (161, 162).

One study assessed lower extremity muscle strength as a potential fall risk factor, using the Chair Stand Test (21). The authors concluded that, in the absence of other fall risk factors, every additional second taken to complete the test increased the risk of falling by 2% (21). No other studies assessed lower limb or foot muscle strength as a fall risk factor. Balance was assessed in four studies (21, 159, 160, 162). Measures of standing balance found to be associated with falls included, postural sway (160), one leg stand time (160) and inability to maintain double limb standing balance for 10

seconds (21). Duyur Cakit (162) assessed balance and gait using the Tinetti Balance Test (TBT) and Tinetti Gait Test (TGT). No associations were found between TBT or TGT and fall history in the participant group. However, the combined score for balance and gait, Tinetti Total Score, was found to be an independent risk factor for falls. Duyur Cakit (162) also assessed walking speed and 10m walk time and found no association with falls. No association was found between falls and other measures of dynamic balance; including functional reach, step-up step-down, walk speed and walk time, in two further studies (159, 160).

3.5.2: Pharmacological risk factors

Four studies evaluated medications as potential risk factors for falls (21, 155, 158, 160). Medications found to be associated with falls in a single study included psychotropics and steroids (21), concomitant use of methotrexate and active vitamin D3 (158), antidepressants (155) and antihypertensives/diuretics (160). Armstrong (155) reported that participants who fell in the previous year were twice as likely to be taking antidepressant medication as non-fallers. Stanmore (21) reported that taking psychotropic medications more than doubled the odds of falling, in the absence of other fall risk factors, but was not an independent predictor of falls. Hayashibara (160) found that people who were taking antihypertensive medication, including diuretics, were nine times more likely to fall. In contrast, Armstrong (155) found that antihypertensives were not associated with falls. The number of medications was assessed in two studies (21, 155). Armstrong (155) recorded medications which were considered to cause falls; including antihypertensives, diuretics, sedatives and antidepressants. The authors concluded that increasing number of medications (range 0-4) was associated with a significantly increased risk of falling (155). Stanmore (21) listed all current medications and found that taking four or more medications more than doubled the risk of falling.

3.5.3: Extrinsic risk factors

The use of a walking aid was assessed as a potential fall risk factor in one study and found not to be associated with falls (160). No other extrinsic or environmental fall risk factors have been assessed in an RA population.

3.5.4: Measures of RA disease activity

All studies included clinical measures of disease activity. Tender joint count (TJC) and swollen joint count (SJC) were included in four studies (21, 158-160). An association between falls and SJC was reported in two studies (158, 160). However, Stanmore (21) reported no association between SJC and falls. Similarly, TJC was associated with falls in one study (158), which was in disagreement with a further two studies (21, 160). Jamison (159) evaluated total joint count (TJC plus SJC) and found no association with falls. In contrast, Stanmore (21) found that the presence of any swollen or tender lower extremity joint doubled the odds of falling. Increased ESR was associated with risk of multiple falls in one study (158) and found not to be associated with falls in two later studies (160, 162). Stanmore (21) found that pain was associated with falls but not a predictor of future falls. In contrast, Smulders (161) found pain to a predictor of future falls and reported that the risk of falling increased nearly five-fold with increased pain intensity. However, a further two cross-sectional studies found no association between pain and fall history (158, 159). No studies reported the locality and nature of pain assessed. Two studies identified high HAQ scores to be associated with falls (21, 158). Armstrong (155) identified two of the eight HAQ domains (walking and rising from a chair) to be associated with fall history. In contrast, four studies found no associated between HAQ score and falls (155, 160-162). DAS28 was found to be associated with a history of falls, but not a predictor of future falls, in one study (21). A further two studies found no association between DAS28 score and falls (158, 160).

3.6: Methodological considerations in RA falls research

The review has highlighted a number of methodological issues in relation to the collecting of falls data and the measurement of fall risk factors. These issues may have impacted on the findings of the review.

3.6.1: Recording of falls data

The wide variation in falls incidence may be due to variation in the method for collecting falls data (165). Falls recall period has been identified as a substantial source of variation in falls reporting (165). Furuya (158) reported falls incidence of 10% which

was relatively low compared to previous studies. These findings were from falls incidence recorded for the preceding six-month period only, whereas all other studies recorded falls over 12 months. Fall recall within the previous three to six months has been reported to be less accurate than recall over a 12-month period (166). Therefore, the low falls incidence may be due to the shorter time period for recording falls, compared to other studies. Reporting periods in falls prevention trials in older adults range from one week to four years (165). There are currently no guidelines recommending the timeframe for the collection of falls data within falls studies.

Fall recall can be problematic in studies which use retrospective falls data (166-168). Forgetting a fall, particularly falls without injury, results in under-reporting of falls incidence (167, 168). To improve accuracy of falls recall, the Prevention of Falls Network Europe (ProFaNE) recommend prospective daily recording and notification of falls, with minimum monthly reporting (169). ProFaNE also recommend that a core set of outcome measures; including number of falls, number of fallers and fall rate are used to improve comparability of study results (169). Two prospective studies followed the ProFaNE recommendations (21, 161).

A definition of the term 'fall' is frequently missing from falls research (165). In the absence of a specific fall definition, falls can be interpreted differently by participants and researchers (170). In studies of older adult populations, differences in falls rates have been attributed to variation in the definition of a fall event (169). Consensus guidelines recommend that a fall be defined as, "an unexpected event in which participants come to rest on the ground, floor or other lower level" (169). Using a lay perspective of falls is also recommended when questioning study participants (169). Only one study in the current review followed these guidelines (21).

3.6.2: Measurement of fall risk factors

The review has shown conflicting evidence regarding a number of measures used to evaluate fall risk in people with RA. Whilst, there was consistency that fall history predicts future falls in people with RA, we are unable to draw any conclusions regarding other physiological risk factors. A recent systematic review of risk factors for

falls in community-dwelling older adults found that several potential fall risk factors could not be addressed as they were considered by too few studies (3). In the current review, many physiological factors were assessed in a single study only, therefore evidence to support positive findings is lacking. Inconsistency in measurement protocols has also been identified as an issue in falls research (3, 171) and may account for the lack of evidence for fall risk factors in people with RA. For example, fourteen different measures of balance in people with RA were reported across five studies (21, 159-162). A core set of outcome measures and consistent measurement protocols is currently lacking in falls research in RA populations.

3.7: Future directions

Inactivity and exercise intolerance, due to pain, fatigue and disease related impairment, have been reported in people with RA (150, 172). Jamison (159) suggested that inactivity and physical de-conditioning may increase fear of falling leading to further inactivity, deterioration of physical functioning and increased fall risk. A similar cycle of physical and psychological deterioration, known as post-fall syndrome, is recognised in older adult fallers (173) but has not been reported in falls-related RA studies. However, physiological fall risk factors may be fundamentally linked as part of a fall risk cycle.

RA-related physiological changes and functional impairment may affect the quality of sensory information and automatic postural responses required for the maintenance of static and dynamic balance (172). Impaired balance may in turn be associated with falls in RA, however, evidence to support impaired balance is lacking. Positive findings for fall risk factors relate to measures of static balance only (21, 160). In addition, specific measures of balance, which have been identified as fall risk factors, were not included in any other study. The Chair Stand Test, a proxy measure of lower extremity muscle strength and endurance, was the only intrinsic measure of functional change which may impact balance in RA. Decreased plantar sensation is linked to falls in older adults (25, 174). However, plantar sensation has not been assessed as a potential fall risk factor in people with RA.

In assessing dynamic postural stability in patients with RA, compared to healthy controls, Aydog (172) determined that dynamic balance was affected by functional status but not RA disease activity. Fall risk in RA may also be independent of disease activity. However, the available evidence is inconsistent and limits our ability to draw specific conclusions. Based on the current evidence, it is unclear as to whether pain is a risk factor for falls in RA. Smulders (161) suggested that pain may be an important predictor of future falls due to a decrease in physical activity and decline in physical functioning as a result of painful arthritic joints. Decreased physical functioning, leading to a decline in muscle strength, has been linked to a decrease in postural stability in people with RA, which may increase fall risk (150).

People with RA are at increased risk of developing co-morbid conditions including cardiac disease, bone disease and depression (36). Medications used to manage co-morbid conditions have been linked to falls in RA (21, 155, 160). The contribution of antihypertensive medication to fall risk in RA remains unclear. However, there is evidence linking antihypertensives to falls in older adult populations (3, 175). The findings from the review suggest that increasing number of medications is a risk factor for falls in RA. Polypharmacy, generally defined as four or more medications, is recognised as a fall risk factor in older adults and people with diabetes mellitus (3, 176, 177). One study found that taking four or more medications was a predictor of future falls in people with RA (21).

RA-related foot deformity and altered foot function may also affect balance and increase the risk of falls. Indeed, several studies in non-RA populations have suggested that foot and ankle characteristics, including structural and functional changes, may impair balance and increase the risk of falling in healthy older adults (23-26, 178-180). To date, one study has included foot specific measures as potential fall risk factors in people with RA (160). This prospective 1-year study investigated the risk factors associated with falls in 84 women with RA aged over 50 years (mean age 64.1 years). Baseline measures of postural stability, physical performance, disease activity, foot deformity, muscle volume and bone density were obtained. The study cohort were then followed for 12 months to record falls incidence. Foot deformity was assessed

using an 8-point scoring system with one point added for each occurrence of hallux valgus, hammer toe, pes planovalgus or callus on either foot. Postural stability was assessed with eyes open in quiet standing using a stabilometer. The authors found that standing balance at baseline was decreased in those who fell during the 12-month follow-up period. No association was found between baseline foot deformity and falls (160).

3.8: Summary

Studies of people with RA show large variation in falls incidence. This disparity likely reflects inconsistency in method for collecting falls data. In people with RA, falls appear to be independent of age, gender and RA disease duration. History of prior falls and increasing number of medications are the most significant predictive risk factors. Given the paucity of evidence for fall risk factors in people with RA, further prospective studies with larger sample sizes are warranted. Risk factors warranting further investigation include: fear of falling, postural stability, lower limb muscle strength, plantar sensation, RA disease activity, pain and medications. Considering the extent of foot involvement in RA, and associated functional impairment, the inclusion of foot and ankle characteristics found to be associated with falls in non-RA populations would also be warranted.

3.9: Additional studies

Since the review was submitted for publication three additional studies have been published relating to RA and falls (181-183). Bugdayci (181) reported retrospective falls incidence of 32% and prospective falls incidence of 19% in a 12-month prospective study of 185 people with RA. Falls were found to be correlated with age, pain intensity, previous falls, use of an assistive device, increasing number of medications and ability to do heel-toe walking. Use of an assistive device (OR 3.3) and fall history (OR 6.2) were predictors of falls (181). Marques (182) reported retrospective falls incidence of 30% in a cross-sectional study of 43 people with RA. Risk factors associated with falls were not assessed in this study. Guler (183) reported retrospective falls incidence of 10% in a cross-sectional study of 89 people with RA. Non-fallers and fallers were compared on foot pain and foot deformity with no significant differences found.

CHAPTER 4: AIMS OF THE THESIS

4.1: Introduction

The current thesis is concerned with determining whether specific measures of foot structure and function (described as foot and ankle characteristics) are associated with falls or falls risk in adults with RA. The thesis will explore differences in foot and ankle characteristics between RA fallers and non-fallers. Associations between foot and ankle characteristics and fall history will also be explored as well as associations between foot and ankle characteristics and prospectively recorded falls.

4.2: Research questions

1. Are there differences in the foot and ankle characteristics of people with RA who have a history of falls, compared to people with RA who have not fallen?
2. Are foot and ankle characteristics independently associated with a history of falls in people with RA?
3. Which foot and ankle characteristics are associated with increasing falls risk and predict the occurrence of falls in people with RA?

The research questions will be answered through the completion of a 12-month prospective observational study of adults with RA. The study was conducted in two stages.

Stage 1 is a cross-sectional study in which a range of clinical and foot and ankle characteristics and 12-month fall history were recorded at baseline. Cross-sectional data analysis compared fallers and non-fallers, on all characteristics, using retrospective falls data. The results of the cross-sectional analysis will answer research questions 1 and 2.

Stage 2 is a prospective study in which the cohort from stage 1 were followed for 12 months to obtain prospective falls data. Prospective data analysis compared fallers and non-fallers, on the clinical and foot and ankle characteristics recorded at baseline,

using prospective falls data. The results of the prospective analysis will answer research question 3.

4.3: Null hypotheses

1. There will be no significant difference in structural and functional foot and ankle characteristics in people with RA with a history of falls, compared to people with RA who have not fallen.
2. There will be no association between foot and ankle characteristics and falls history in people with RA.
3. Specific foot and ankle characteristics, in the rheumatoid foot, will not be associated with increasing falls risk or predict the occurrence of falls in people with RA.

CHAPTER 5: IDENTIFICATION OF FOOT AND ANKLE MEASURES

5.1: Introduction

This chapter will provide an overview of the current evidence regarding foot and ankle characteristics associated with falls, impaired balance and functional ability in healthy older adults. The purpose of the review was to identify relevant foot and ankle measures for inclusion in the study. The chapter concludes with a list of the foot and ankle measures to be included in the current study plus additional measures to form a comprehensive foot and ankle assessment.

5.2: Search strategy

A search was conducted using AMED, CINAHL, MEDLINE, Scopus and The Cochrane Library online databases; under the following terms, “foot”, “feet”, “foot characteristics”, “postural stability”, “balance”, “falls”, “falls risk” and “older adult”. Research and review papers published between 2000 and 2014 were included from peer-reviewed English text journals only. Citations from retrieved publications were examined to obtain further references. Foot and ankle characteristics were defined as specific measures of foot structure and/or function including; pain, range of motion, strength, sensation, postural stability and gait.

5.3: Foot and ankle characteristics associated with falls, impaired balance and functional ability in older adults

In a cross-sectional study of 135 men and women aged 79 to 93 years, Menz and Lord (178) compared participants, with and without foot deformity, on performance in clinical tests of balance and functional ability. Foot deformity was quantified using a scoring system, the ‘foot problem score’, which was developed by the researchers. Balance tests included measurement of postural sway and coordinated stability. Functional tests included stair ascent/descent, alternate step-up test and timed 6-metre walk test. The authors found that foot deformity and pain did not impair performance in postural sway but had significant detrimental effect on the coordinated stability and functional tests (178).

In a further paper, Menz and Lord (24) evaluated the association between 'foot problem score' and history of falls in the preceding 12 months. Subjects were divided into two groups, 1) non-fallers and single-fallers, and 2) multiple-fallers. The authors found that subjects with a history of multiple falls had significantly higher 'foot problem score' than those who did not fall or had experienced only one fall. The cumulative effect of multiple foot problems was also found to be more important in increasing fall risk than individual foot conditions (24).

Menz, Morris and Lord (179) assessed a range of foot and ankle characteristics in 176 older adults to determine the relative contribution of each foot and ankle characteristic to performance in balance and functional tests. Foot and ankle assessments included foot posture, 1st MTP and ankle joint range of motion, presence of hallux valgus, lesser toe deformity and callosities, toe plantarflexor strength and fine touch sensation at the 1st MTP joint. Balance assessment included postural sway, leaning balance and coordinated stability tests. Functional assessment included alternate stepping test, sit-to-stand and timed 6-metre walk. The authors found that plantar tactile sensitivity and ankle flexibility were strongly correlated to increased postural sway. Ankle flexibility and strength of toe plantarflexors were consistently associated with the leaning tests and functional measures. Toe deformity was significantly associated with decreased balance and functional ability (179).

In a prospective follow-up study, the 176 older adult participants recorded falls experienced over the next 12 months, using a monthly falls calendar (25). Falls were defined as, "events that resulted in a person coming to rest unintentionally on the ground or other lower level, not as a result of a major intrinsic event or overwhelming hazard". Participants were classified as 1) non-fallers or 2) fallers (one or more falls). Pain was also assessed using the Manchester Foot Pain and Disability Index (184). The authors reported that fallers demonstrated reduced ankle range of motion, more severe hallux valgus deformity, reduced tactile sensitivity and decreased toe strength. Fallers also experienced more disabling foot pain than non-fallers (25).

In agreement with Menz, Morris and Lord (25), Mickle (180) found that reduced toe plantarflexor strength and toe deformity were predictors of falls in a prospective study of 312 men and women aged 60 to 90 years. A subsequent paper from this study reported that fallers had a significantly higher prevalence of foot pain than non-fallers, thus further supporting the findings of earlier work. Fallers also generated significantly higher total peak plantar pressures and total pressure-time integral values than non-fallers. Increased dynamic plantar pressures were also associated with increased pain in all study participants (26).

The association between foot problems and falls was further confirmed by Chaiwanichsiri (23) who evaluated health status, foot problems, walking performance and falls history in 213 men and women aged 60 to 80 years. Foot characteristics assessed included hallux valgus and lesser toe deformities, callus formation, arch height, fine touch plantar sensation and foot pain. Walking performance was assessed by the Timed Get Up & Go test (185) and 6-metre walk speed. Falls history was obtained for the previous 6 months. Foot characteristics found to be related to falls included foot pain, plantar fasciitis, PPV foot-type and decreased plantar sensation. Walking performance did not differ between the falls and no-falls groups (23).

5.4: Foot and ankle measures identified for inclusion in the observational study

The review identified foot and ankle characteristics that are associated with falls, impaired balance and functional ability in healthy older adults. These characteristics were included as potential fall risk factors in the current study. Foot and ankle characteristics can be classified as structural or functional. Measures of foot structure included foot-type and foot deformity. Measures of foot function included sensation, muscle strength, range of motion, gait, postural stability and patient-reported measures. It could be argued that postural sway is not strictly a measure of foot and ankle function due to the involvement of the visual and vestibular systems in the maintenance of balance. However, impaired postural stability is widely recognised as a fall risk factor in older adults (10, 186, 187), as well as people with neuromuscular conditions such as Parkinson's disease (188, 189) and multiple sclerosis (190). Therefore, a measure of postural stability was considered to be important in the

current study. In addition, postural sway also provided an indirect measure of plantar sensation, proprioception and foot and ankle muscle strength. Table 5.1 summarises the foot and ankle measures identified in the literature for inclusion in the observational study. Additional measures, indicated by an asterisk in the table, were included to form a comprehensive foot and ankle assessment.

Table 5.1: Foot and ankle characteristics identified in the literature for inclusion in the observational study.

Foot structure	**Foot function**
Foot-type Pes planovalgus Deformity Foot problem score Presence of hallux valgus	Sensation Fine touch sensation Vibration perception threshold* Muscle strength Hallux and lesser toes Foot and ankle* Range of motion Ankle Gait and balance Walking speed Plantar pressure Postural sway Patient-reported measures Foot pain Foot-related disability and impairment* Footwear*

*additional measures not included in older adult studies

Vibration perception threshold provided an additional measure of plantar sensation. Foot and ankle muscle strength was included in the assessment as people with RA have been reported to have decreased plantarflexion and inversion strength, compared to healthy controls (130) which may impact strategies employed in the maintenance of balance, such as the ankle strategy. Footwear was included as an extrinsic fall risk factor as previous studies reported an association between footwear

and falls risk in older adults (191, 192). Foot-related disability and impairment was assessed using the Foot Impact Scale (153). This patient-reported measure of foot-related disability and impairment was included as a holistic, patient-centred measure of foot function.

CHAPTER 6: METHODOLOGY

6.1: Introduction

This chapter will describe the methods and procedures implemented during the study. Key areas will include recruitment of study participants, instrumentation, protocols for data collection, methodology for measurement of falls outcome and a summary of the cross-sectional and prospective statistical analysis. Data collection was conducted in two stages over a 20-month period between February 2013 and October 2014. Stage 1 was a cross-sectional study of 201 participants with diagnosed RA in which demographic, clinical, foot and ankle meaures, and PROMs were assessed at a baseline study visit. Fall history, for the 12 months preceding baseline, was recorded for cross-sectional analysis. Stage 2 was a 12-month prospective observational study of the 201 participants followed for 12 months to capture current falls data. A second study visit reassessed clinical measures, foot and ankle measures, and PROMs at the end of the follow-up period. Prospective analysis was based on falls reported during the study year.

6.2: Ethical approval

Ethical approval (Appendix 1) was granted by the Auckland University of Technology Ethics Committee (AUTEC, reference 12/47) and the Northern X Ethics Committee (reference NTX/11/12/114). Locality approvals (Appendix 1) were obtained from the Auckland District Health Board (ADHB, reference A+5364) and the Counties Manukau District Heath Board (CMDHB, reference 1220). The study was registered with the Australia New Zealand Clinical Trial Registry (trial ACTRN12612000597897). Verbal and written informed consent was obtained from all participants meeting the inclusion criteria (Appendix 2).

6.3: Recruitment and sampling

The study was conducted in Auckland, New Zealand. Participants were primarily recruited from ADHB and CMDHB rheumatology outpatient clinics, the AUT Podiatry School podiatric rheumatology clinic and Arthritis New Zealand Auckland database. All

eligible people were invited into the study via a letter (Appendix 3) and participant information sheet (Appendix 4) which provided detailed information on the study. Rheumatologists and rheumatology nurses at ADHB and CMDHB were informed of the study and invited to refer their patients. Recruitment posters (Appendix 5) were also placed in ADHB and CMDHB rheumatology outpatient clinic rooms and the AUT podiatry clinic reception. Potential participants were asked to contact the researcher via email or telephone to register their interest and/or ask further questions. Based on a previous falls study involving 176 older adults (25), an a priori sample size calculation, based on a 15% dropout rate, 80% power, and a significance level of 5%, indicated that 200 participants were needed.

6.4: Participant inclusion and exclusion criteria

To be eligible for the study participants were required to be English speaking, 18 years and older and have RA according to the 2010 ACR/EULAR classification criteria (95). Participants were excluded if they were non-ambulatory or unable to attend a study visit at a specified clinic or research facility. Participants were also excluded if they were unable to read and understand the information sheet or sign the consent form.

6.5: Research environment

In order to reduce travelling time for participants, study visits were conducted at three locations: AUT North campus, Greenlane Hospital (central Auckland) and AUT South campus. All tests were conducted in a single study room with the exception of a walking test which was conducted in the hallway directly outside the study room. The study room was private, well lit and at a temperature which was comfortable to the participant.

6.6: The researcher

All testing, recording of data and data analysis were undertaken by a single researcher, Angela Brenton-Rule. The researcher is a New Zealand registered podiatrist with five years of practice experience and postgraduate training. The current thesis forms part of the requirements for the researcher's degree of Doctor of Philosophy.

6.7: Demographics and clinical characteristics

Basic demographic data including age, gender, ethnicity, weight, height and BMI were collected for all participants. Medical records were accessed to confirm RA disease type (RF-positive, anti-CCP antibody-positive, seronegative), disease duration (years), presence of erosive foot disease (evidenced by radiographs), previous foot surgery (yes/no), most recent blood test for inflammation (ESR/CRP), medications and co-morbid conditions. Use of visual aids, assistive devices and self-reported hearing impairment were recorded. Participants were asked whether they had ever visited a podiatrist, and if so, the frequency of podiatric care received. All data were manually recorded, in hardcopy format, on a clinical research form (CRF) (Appendix 6).

6.8: RA disease activity

Patient self-reported general pain (over the past week) and patient global assessment of current health were recorded using a 100mm VAS. Pain and patient global assessment are part of the core set of outcome measures for RA clinical trials endorsed by OMERACT and ACR (193). A score of 0mm on the VAS pain scale indicated 'No Pain' and 100mm indicated 'Severe Pain'. On the patient global assessment scale, a score of 0mm indicated 'Very Well' and 100mm indicated 'Very Unwell'. Participants also completed the HAQ-II (83), a shortened version of the Stanford Arthritis Centre HAQ (80) which is included in the OMERACT core set of measures for longitudinal studies in rheumatology (194). The HAQ-II (83) is a self-reported measure of functional status and disability that is routinely used in rheumatology consultations.

Current RA disease activity was determined by assessment of joints for tenderness and swelling and calculation of the four variable DAS28 (74). The researcher was trained by a rheumatologist to assess 76 joints for tenderness (TJC) and 74 joints for swelling (SJC), including the ankles and 16 joints in each foot. Joint tenderness and swelling were assessed according to the EULAR guidelines for clinical assessments in RA (195). Tenderness was recorded as "pain in a joint under defined circumstances" which included pain at rest with pressure applied to the joint margins using the thumb and index finger, or pain on passive movement of the joint. Swelling was defined as "soft tissue swelling…detectable along the joint margins" (195). The number and location of

tender and swollen joints were recorded on a score sheet. Presence (yes/no) of any tender foot or ankle joint, and any swollen foot or ankle joint, was additionally recorded. A score of ≥1 tender foot or ankle joint was regarded as 'presence of foot or ankle tender joints' and a score of ≥1 swollen foot or ankle joint was regarded as 'presence of foot or ankle swollen joints'.

6.9: Fear of falling

Fear of falling has been found to be associated with falls in older adults (3) and adults with RA (21). Fear of falling was assessed in the current study through participant completion of the Short Falls Efficacy Scale-International (Short FES-I) (196). The Short FES-I is a 7-item questionnaire which assesses fear of falling related to a range of daily activities. Patients rate their level of concern on a 4-point scale from 1 (not at all concerned) to 4 (very concerned). The scores for each question are totalled arriving at a final score between 7 (no fear of falling) to 28 (very fearful of falling). The Short-FES-I has been used in a previous RA falls study (21) and the validity and test-retest reliability has been reported to be excellent (196).

6.10: Foot pain, impairment and disability

Patient-reported foot pain (over the past week) was recorded using a 100mm VAS. A score of 0mm on the pain scale indicated 'No Pain' and 100mm indicated 'Severe Pain'. Foot pain was also recorded as a dichotomous variable (present/absent) for either foot. Patient-reported foot-related disability and impairment was assessed using the Foot Impact Scale (FIS) which was designed specifically to assess the impact of RA disease-related foot involvement in terms of impairment, disability and quality of life of the patient (153). The FIS comprises 51 statements divided into two subscales; impairment/footwear (FIS_{IF}; range 0-21) and activities/participation (FIS_{AP}; range 0-30). The total FIS score (FIS_{TOTAL}; range 0-51) and subscale scores are calculated by agreement (1 point) or disagreement (0 points) with each statement based on the patient's current perceptions of their foot-related pain, function and disability. An elevated FIS_{IF} or FIS_{AP} score indicates greater foot impairment or activity limitation respectively (153). Scores of ≤6 were considered mild, from 7-13 were considered moderate, and ≥14 were considered severe for FIS_{IF}. For FIS_{AP}, scores ≤9 were

considered mild, 10-19 were considered moderate, and ≥20 were considered severe (197). The FIS has been validated in people with RA and has high test-retest reliability (153). A longitudinal change of 3 points in either direction for FIS_{IF} or FIS_{AP} has been reported to be clinically relevant (198).

6.11: Footwear

Footwear worn to the study visit was recorded using a list of 14 footwear styles adapted from a previous study (199) (Appendix 7). The footwear was matched to the closest style on the footwear list and recorded on the CRF. Footwear type was grouped into good, average and poor for reporting purposes according to a previous study (200). Participants were also asked to identify the type of footwear that they usually wear inside and outside from the footwear list, including bare feet and socks.

6.12: Procedures

6.12.1: Foot-type

Foot-type was determined through calculation of the arch index (AI) which represents the ratio of the area (mm^2) of the middle third of the foot relative to the total area of the foot, excluding the toes (201). Calculation of the AI is depicted in Figure 6.1. Foot-type was defined as high arch, normal and low arch. Higher AI value indicated a lower arch or flatter foot. Left and right digital footprints were captured by a TekScan MatScan® model 3150 (TekScan Inc, South Boston, USA) portable pressure mat with participants in quiet standing in their natural angle and base of gait. The MatScan® (Figure 6.2) is a low profile floor mat (5mm thick) consisting of 2288 resistive sensors (1.4 sensors/cm^2) with a sampling frequency of 40Hz. The MatScan® is commonly used in research and clinical settings and has previously been shown to have moderate to good intra-session reliability for the measurement of plantar forces and pressures during barefoot walking in healthy children (202), healthy adults (203) and adults with gout (204). Footprint area was determined using the TekScan F-Scan® research 6.33 software and the AI value was calculated by the researcher. In order to determine cut-off values for high, normal and low arch, all AI scores for left and right feet were pooled and the distribution was divided into quartiles. AI values below the first quartile

(0.17) indicated a high arch foot and values above the third quartile (0.25) indicated a low arch foot. AI values between 0.17 and 0.25 indicated a normal foot-type.

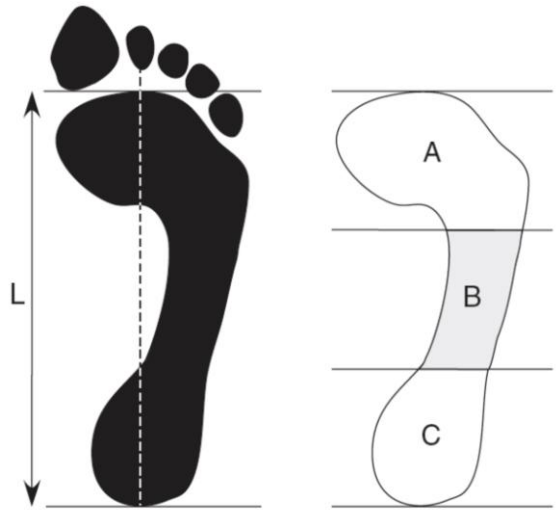

Figure 6.1: Calculation of the arch index (AI)
The length of the footprint excluding the toes (L) is divided into equal thirds. The AI is then calculated as the area of the middle third of the footprint divided by the area of the entire footprint (AI=B/A+B+C).

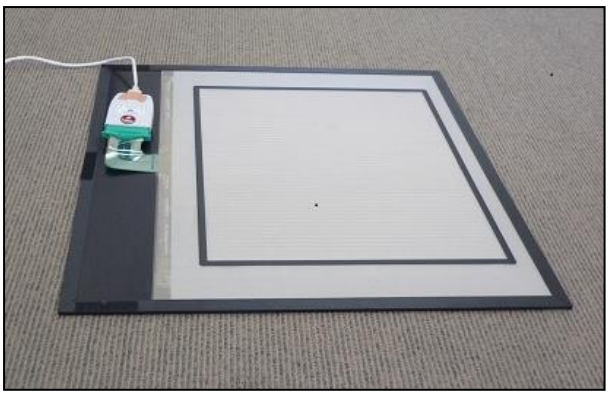

Figure 6.2: TekScan MatScan® pressure mat

6.12.2: Foot deformity

Foot deformity was assessed through calculation of the 'foot problem score' (FPS) (24). The FPS is a simple scoring system which involves observing and documenting the presence of hallux valgus (bunion), abnormal bony prominences, lesser toe deformities and hyperkeratotic lesions. Each bony prominence scored 1 point. Lesser toe deformities were scored according to the number of joints affected. For example, a claw toe was scored 2 points and a hammer toe was scored 1 point. Single hyperkeratotic lesions covering multiple joints were scored according to the number of joints covered. Hallux valgus severity (mild = 1 point, moderate = 2 points, severe = 3 points) was added to give a score for each foot (205). The feet were observed with the participant in a sitting position (hips flexed, knees extended) on an examination table or recliner chair. Each foot was assessed separately and then the total FPS for both feet was calculated. The FPS has been reported to have excellent inter-examiner reliability in older adults (24).

6.12.3: Neuropathy

Neuropathy was assessed as fine touch sensation, using a Semmes-Weinstein 5.07 nylon wire, and vibration perception threshold (VPT), using a biothesiometer (Bio-medical Instruments, Newbury, OH, USA) (206, 207). The Semmes-Weinstein 5.07 nylon wire (Figure 6.3), commonly called a 10g monofilament, exerts 10 grams of force when bowed to a C-shape against the skin. People who cannot detect the monofilament on the plantar surface of the foot are considered to have lost fine touch "protective" sensation (208). The monofilament has been reported to have very good test-retest reliability for the detection of peripheral neuropathy in people with RA (207).

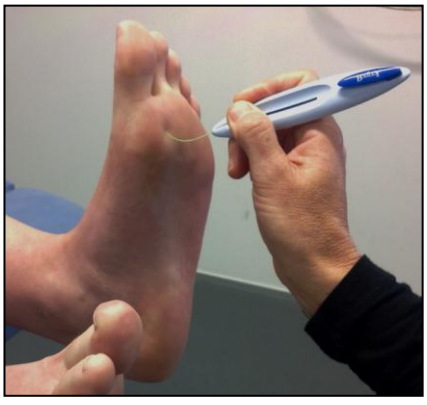

Figure 6.3: 10g Monofilament

The biothesiometer (Figure 6.4) is a hand-held device with a rubber probe of 13mm in diameter that produces a vibration stimulus at 120Hz and measures VPT. The vibration stimulus is detected when it is held to the skin. The vibration intensity is measured in mV ranging from 0-50mV. VPT above 25mV is considered to indicate presence of peripheral neuropathy (209, 210). The sensitivity of the biothesiometer for detecting peripheral neuropathy in diabetic patients has been reported to be 86% with specificity of 76% (210).

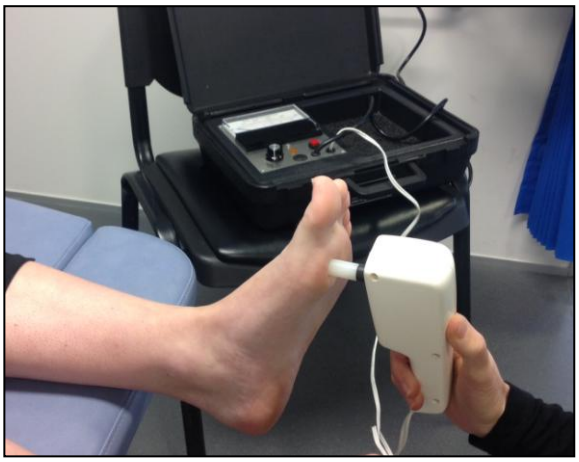

Figure 6.4: Biothesiometer

Participants were positioned on an examination table or reclining chair in a sitting position and instructed to close their eyes. Prior to testing, the instrument was tested on the participant's hand in order to familiarise them with the stimulus. For fine touch, the researcher applied the monofilament to the surface of the foot, at a pressure causing the nylon wire to buckle to a C-shape, and held it for 1 second. The participant was instructed to report "yes" whenever the monofilament was detected. For VPT, the researcher held the biothesiometer firmly at right angles to the surface of the foot and gradually increased the vibration output from 0mV to a maximum 50mV. The participant was instructed to report "yes" when they felt the initial vibration stimulus at each test site. Sensation was tested at the hallux, heel, arch, 1st, 3rd and 5th MTP joint, in a random order. Each site was assessed twice with the monofilament, to obtain a score out of 12, and once with the biothesiometer, to obtain an average measure (mV) across the six sites. Monofilament score was recorded as a continuous

variable (0-12) and VPT was recorded as a dichotomous variable (≤ 25mV or > 25mV) to indicate neuropathy (209, 210). Each foot was assessed and scored separately.

6.12.4: Muscle strength

Foot and ankle muscle strength was determined by the maximum force generated during dorsiflexion, plantarflexion, inversion and eversion of the foot at the ankle joint. A hand-held dynamometer (HHD) was used to measure peak force using the make-test, in which the examiner resists the movement of the muscle (130). The HHD (CIT Technics, Groingen, the Netherlands) measures the peak force (N) produced by a muscle as it contracts while pushing against an object (Figure 6.5).

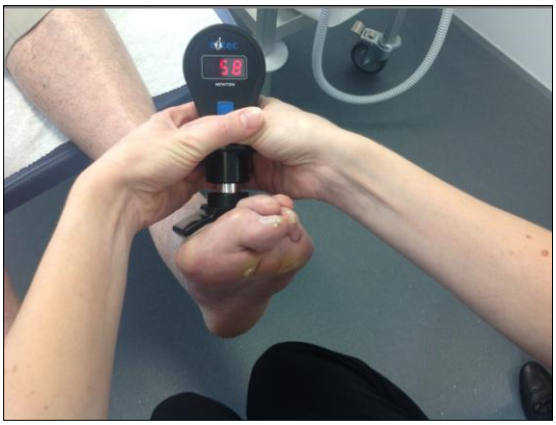

Figure 6.5: Hand-held dynamometer

Testing was conducted with the participant on an examination table in a sitting or supine position with feet extending over the edge of the table. For each muscle action the HHD was placed on the foot as follows: eversion, against the lateral border of the foot distal to the 5th metatarsal head; inversion, against the medial border of the foot near the base of the 1st metatarsal head; plantarflexion, against the heads of the metatarsals on the plantar aspect of the foot; dorsiflexion, on the dorsal surface of the foot proximal to the metatarsal heads. Participants were instructed to maximally contract the muscles by pushing against the HHD and hold the contraction for three seconds. Three repetitions were obtained for each muscle group with a minimum 10 second rest period between contractions. The average of three contractions was recorded.

Toe flexor strength was assessed by the paper grip test (PGT) (25) and measurement of the maximum force generated by the hallux and lesser toes while standing on a pressure mat (180). For the PGT, the participant was seated in a straight backed chair with bare feet resting on the floor. A business card was placed under either the hallux or lesser toes. Participants were instructed to grip the business card while the assessor attempted to pull it out from underneath the toe(s). The ability to hold onto the card for at least one attempt out of three counted as a pass. Maximum force (N) generated by the toe flexors was measured using the TekScan MatScan® pressure mat. Participants stood in bare feet on the pressure mat with their feet hip-width apart and were instructed to push down on the mat as hard as possible with all toes while looking straight ahead. Three trials were completed and data were analysed using the TekScan F-Scan® research 6.33 software whereby the hallux and lesser toes were masked and the peak force calculated and normalised to body weight (%BW).

6.12.5: Ankle range of motion

Ankle range of motion was assessed by a modified lunge test (211). Participants were tested in bare feet. The lateral malleolus and head of fibula were located and marked with a pen. Participants stood with the right foot placed alongside an upright acrylic sheet inscribed with 2◦ protractor markings. They were instructed to take a comfortable step forwards with the left foot and bend both knees as far as possible while keeping the trunk upright and both heels flat on the floor. The position of the fibula head was marked on the acrylic sheet and ankle range of motion was determined by the angle formed between the fibula head and the lateral malleolus in relation to the floor (Figure 6.6). Both ankles were tested three times and the average measure for each ankle was recorded.

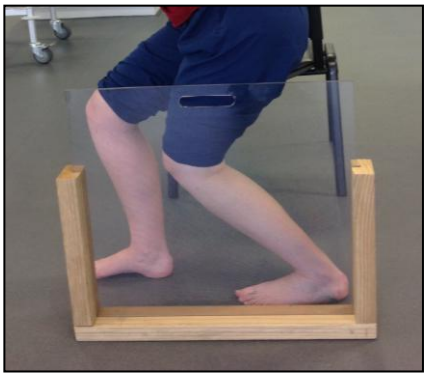

Figure 6.6: Modified lunge

6.12.6: Gait and balance

Walking speed was assessed using the 6-metre walk test (24). Participants were tested in the footwear which they wore to the study visit and instructed to walk at their usual speed using an assistive device (walking stick, crutch, walker) if required. The total time to complete a distance of 6 metres was recorded in seconds using a stopwatch. The test was repeated three times and the average gait speed (metres/second) was calculated.

Peak plantar pressure (PPP) and pressure-time integral (PTI) were recorded for both feet using a TekScan MatScan® pressure mat. PPP is the maximum force (kPa) in a defined region of the foot and PTI is the force (kPa) multiplied by the time taken (seconds) to complete propulsion through the foot region of interest (kPa.sec). Participants were tested in bare feet using a 2-step protocol, in which they walked across the mat at their normal self-selected pace, and scans were collected when the second step landed on the mat (212). For each foot, three trials were collected to obtain an average measure. PPP for the total plantar surface of the foot was recorded. In addition, PPP and PTI were calculated at the forefoot, midfoot and rearfoot using the TekScan F-Scan® research 6.33 software to manually mask each region of interest. The forefoot was defined as 50% of total foot length (including the toes), the midfoot was 19% and the rearfoot was 31%, according to a previous protocol (213, 214). Foot length was measured by the researcher by positioning the unshod foot on a piece of paper, in non-weight bearing, and drawing a line perpendicular to the longest toe and a second line, parallel to the first, at the base of the heel. The distance between the two lines was measured with a ruler to give the total foot length (mm) which was used to calculate forefoot, midfoot and rearfoot regions.

The MatScan® was also used to assess postural stability which was measured as postural sway in the antero-posterior (AP) and medio-lateral (ML) directions, during quiet standing (215). Postural sway (mm) was measured using the excursion of the centre of force (COF) in the AP and ML directions. We tested the reliability of the MatScan® for assessing postural stability in older people with RA and reported good to

excellent between-session reliability of COF based measures of postural control. The study was published in the *Journal of Foot and Ankle Research* (Appendix 12).

Brenton-Rule A, Carroll M, Dalbeth N, Bassett S, Mattock J, Menz HB, Rome K. Reliability of the TekScan MatScan ® system for the measurement of postural stability in older people with rheumatoid arthritis. J Foot Ankle Res. 2012;5:21.

During testing each participant was directed to step onto the pressure mat and stand in their natural angle and base of gait with their arms by their side and looking straight ahead. Foot position was standardised by placing a strip of tape on the surface of the pressure mat; just distal to the toes and along the lateral border of each foot. This enabled foot position to be replicated from trial to trial. In order to prevent vestibular disruption and head movement, head position was standardised by asking the participant to focus on a 10cm diameter solid black circle, positioned 1.5 metres in front of the pressure mat at eye level. The participant was asked to remain in this position for a period of 30 seconds while data was recorded. Three repetitions were taken to obtain a mean value. The participant stepped off the pressure mat and rested for 30 seconds between repetitions. Data were captured with eyes open and eyes closed. The Sway Analysis Module (SAM™) software was used to analyze the sway data.

6.13: Falls outcome

The primary outcome measures for the study were fall history over the 12 months preceding baseline (12-month fall history) and falls experienced during the 12-month study period (prospective falls). 12-month fall history and prospective falls were recorded as ‘no falls’, ‘single fall’ and ‘multiple falls’. The ProFaNE definition of “an event that results in a person coming to rest unintentionally on the ground or other lower level” (169) was used to identify falls. We did not include falls which were the result of syncope or an external force, such as being pushed or knocked over. In order to identify these types of falls we modified the fall definition by adding, “not as a result of a major intrinsic event or an overwhelming hazard”, as per a previous study (25).

To measure fall history at baseline participants were provided with the fall definition for the study and then asked the following question, “In the past 12 months, have you had any fall, including a slip or trip, in which you lost your balance and landed on the floor or ground or lower level?” To record prospective falls, which occurred during the 12-month study period, participants were issued with a Fall Calendar (Figure 6.7) at the baseline study visit. Fall calendars were completed and sent to the researcher every month for 12 months. If the participant experienced a fall during the month they were required to place a tick on the relevant calendar day and telephone the researcher to report the fall. The researcher recorded the fall and conducted a brief post-fall questionnaire (Appendix 8) in order to clarify that the fall was within the study definition and to capture other information. If the participant had no falls during the calendar month they still returned the calendar and ticked a box which said, “I had NO falls this month”. If a calendar was not received the researcher phoned the participant to follow up. This method for recording falls incidence is in accordance with the ProFaNE guidelines for falls research (169).

FALL CALENDAR

July, 2013

Your name: _____

Please place a tick (✓) for each fall in the appropriate date box below. Remember, a fall is "an unexpected event in which you come to rest on the ground, floor, or lower level"

SUN	MON	TUES	WED	THURS	FRI	SAT
	1	2	3	4	5	6
7	8	9	10	11	12	13
14	15	16	17	18	19	20
21	22	23	24	25	26	27
28	29	30	31			

❍ I had **NO** falls this month

Have you visited a health care provider this month? YES ❍ NO ❍
If you ticked YES please put a tick next to the relevant health care provider(s)
Rheumatologist❍ Rheumatology Nurse❍ Podiatrist❍ Physio❍ GP❍ Other _____

Please telephone Angela when you have a fall, even if it was a minor fall. The toll-free phone number is **0800 723255**

At the end of the month, please return this month's fall calendar sheet in the reply paid envelope.

Figure 6.7: Fall Calendar, sample calendar page

6.14: Statistical analysis

Statistical analysis was performed using Statistical Package for Social Sciences V22.0 (SPSS, IBM Corp., New York, USA). All data for left and right feet were entered into SPSS. However, analysis was undertaken using 1) the average measure for both feet for continuous variables e.g. ankle range of motion; and 2) the 'worst' foot measure for dichotomous measures e.g. presence or absence of a bunion.

6.14.1: Explanation of terms

Univariate analysis (comparing single variables) was used to compare groups (e.g. non-fallers or fallers) on individual clinical and foot and ankle characteristics measured in the study. The analysis was undertaken to address research questions 1 and 3.

Multivariate analysis (comparing multiple variables) was used to determine associations between multiple clinical and foot and ankle characteristics, and fall history, and to identify characteristics which are predictors of falls. The analysis was undertaken to address research questions 2 and 3.

6.14.2: Grouping of participants for univariate analysis

Participant grouping in falls research is varied and there is currently no 'gold standard' for analysis of fall risk factors. In determining the groupings for the analysis in the current study, the literature relating to fall risk factors in RA (Chapter 3) and the literature relating to foot and ankle characteristics and falls in older adults (Chapter 5) was reviewed. There were seven RA falls studies (21, 155, 158-162). Five studies classified participants into two groups (non-fallers, fallers) (155, 159-162) and two studies classified participants into three groups; (non-fallers, single-fallers, multiple-fallers) (21), (non-fallers, ≥1 fall, ≥2 falls) (158). Five studies assessed foot and ankle risk factors for falls in older adults (23-26, 180). The majority of studies classified participants into two groups (non-fallers, fallers) for analysis (23, 25, 26, 180). A further study defined two groups as non-fallers/single-fallers and multiple-fallers (24). The authors did not state the reason for grouping non-fallers and single-fallers together for analysis. However, falls data was collected retrospectively in which case fall recall may have been a factor, i.e. participants may be more likely to recall multiple

falls over a 12-month period than a single fall or no falls. Further, it could be argued that multiple-fallers are potentially more vulnerable to future falls than single-fallers. Therefore, the identification of risk factors for multiple falls may be of greater importance than single falls. Based on these findings, in the current study, participants were grouped as non-fallers or fallers for primary analysis at baseline and 12-months. Secondary analysis was then undertaken with participants grouped as the combination of non-fallers/single-fallers or multiple-fallers as well as non-fallers, single-fallers or multiple-fallers.

6.14.3: Grouping of variables for data analysis

A wide range of medications and co-morbid conditions were recorded for the participants resulting in very small numbers for some variables. Subsequent grouping of variables was required for data analysis. Table 6.1 lists the variables which were grouped together.

Table 6.1: Medications and co-morbid conditions grouped for analysis

Original variable	**New group name**
Anti-TNF Rituximab	Biologics
Methotrexate Leflunomide Sulfasalazine Hydroxychloroquine Other DMARDs	DMARD monotherapy OR Combination DMARD therapy
Benzodiazepine Antipsychotics Tricyclic antidepressants Anticonvulsants Selective serotonin reuptake inhibitors (SSRIs)	Psychotropic medication
Antihypertensives Diuretics	Antihypertensives
Oral hypoglycemics Insulin	Hypoglycemics
Stroke / Trans-ischemic attack Congestive heart failure Ischemic heart disease Arrhythmia Peripheral vascular disease	Cardiovascular disease
Depression Bipolar disorder	Depression or bipolar disorder

6.14.4: Cross-sectional analysis

Cross-sectional analysis was undertaken at baseline, to answer research questions 1 and 2, using the 12-month fall history to determine participant grouping and baseline measures of clinical and foot and ankle characteristics.

6.14.4.1: Primary univariate analysis

Participants were initially grouped as non-fallers or fallers based on the 12-month fall history. The distribution of all variables was checked for normality using visual inspection of histograms. Comparisons between groups were made using independent samples student's t tests for normally distributed variables and Mann-Whitney U tests for skewed data. Chi-square tests of trend were used as appropriate to examine differences between groups on categorical variables.

6.14.4.2: Primary multivariate analysis

To identify factors independently associated with a history of falls, a series of logistic regression models were created using falls in the preceding 12 months as the dependent variable. A limited number of predictor variables were selected based on statistical significance of $P<0.15$ on univariate analysis of non-fallers and fallers. Age was also included, as a controlling variable, to take into account the possible confounding effects of age-related foot changes plus age-related increased fall risk. Where multicollinearity ($r>0.5$) was present the variable with the lowest P value, or of greatest clinical relevance, was retained. Multivariate binary logistic regression analyses were conducted including the selected predictor variables and controlling for age. Backward elimination method was used to remove the variable with the highest P value, in a stepwise approach, until all remaining variables were significant at $P<0.05$.

6.14.4.3: Secondary univariate analysis

Participants were grouped as non-fallers, single-fallers or multiple-fallers. Comparisons between the three groups were made using one-way between-groups analysis of variance (ANOVA) for normally distributed variables and Kruskal-Wallis tests for skewed data. Where significant differences between the three groups was demonstrated ($P<0.05$) pair-wise comparisons were conducted to determine where

the differences lay. Chi-square tests of trend were used as appropriate to examine differences between groups on categorical variables. Participants were then regrouped as the combination of non-fallers/single-fallers or multiple-fallers and the analysis in 6.14.4.1 was repeated.

6.14.4.4: Secondary multivariate analysis

To identify factors independently associated with a history of multiple falls, the analysis in section 6.14.4.2 was repeated using multiple falls in the preceding 12 months as the dependent variable for the logistic regression models. Predictor variables were selected based on statistical significance of $P<0.15$ on univariate analysis of non-fallers/single-fallers and multiple-fallers plus age as a controlling variable.

6.14.5: Prospective analysis

Prospective analysis was undertaken after the 12-month falls follow-up period to answer research question 3.

6.14.5.1: Primary and secondary prospective analysis

Univariate and multivariate analyses, described in section 6.14.4, were repeated using prospective falls, to determine participant grouping, and baseline measures of clinical and foot and ankle characteristics. The 12-month prospective study included one additional variable, 12-month fall history, which is essentially a combination of fall risk factors. For this reason, 12-month fall history was excluded as a predictor variable in the initial logistic regression modelling due to the likelihood that it would be highly correlated with other variables in the model. 12-month fall history was then added into the final model to generate an odds ratio (OR) for 12-month fall history, to determine the effect of 12-month fall history on the other variables in the model and to determine the effect of 12-month fall history on the predictive power of the model.

6.14.5.2: Falls as a continuous dependent variable

In addition, negative binomial regression analysis was conducted using the number of falls experienced during the 12-month falls follow-up period as the dependent variable

(35, 216). The predictor variables which were selected for the logistic regression modelling were used for the negative binomial regression modelling, with age included as a controlling variable. Backward elimination method was used to remove the variable with the highest P value, in a stepwise approach, until all remaining variables were significant at $P<0.05$.

6.14.6: Subsequent analysis

Subsequent analysis was undertaken to; 1) explore potential interrelationships among foot and ankle characteristics and PROMs, 2) confirm the 12-month prospective study findings, and 3) assess the stability of the foot and ankle characteristics over the 12-month study period.

6.14.6.1: Correlations between foot and ankle characteristics and PROMs

Relationships among the baseline foot and ankle measures and PROMs, that were significantly different on primary and secondary univariate analysis, were investigated. Pearson's product-moment correlation coefficients were used for normally distributed data and Spearman Rank Order Correlations were used for skewed data. This analysis was undertaken to identify potential associations among the foot and ankle characteristics and PROMs that may underlie the potential mechanisms for falls.

6.14.6.2: Analysis of foot and ankle characteristics measured at 12-months

Non-fallers and fallers, grouped according to prospective falls, were compared on all foot and ankle measures recorded at 12-months using the analyses described in section 6.14.4.1. The analysis was then repeated comparing the combined group of non-fallers/single-fallers with multiple-fallers. The purpose of this analysis was to confirm the findings of the primary and secondary prospective analysis.

6.14.6.3: Comparing foot and ankle measures at baseline and 12-months

All foot and ankle measures recorded at 12-months were compared with the foot and ankle measures recorded at baseline using paired-samples t-tests for normally distributed variables and Wilcoxon Signed Rank Test for skewed data. McNemar's Tests were used as appropriate to examine differences between 12-months and

baseline on categorical variables. The purpose of this analysis was to determine if there were clinically significant changes in the foot and ankle characteristics over the 12-month study period.

CHAPTER 7: CROSS-SECTIONAL STUDY RESULTS

7.1: Introduction

In the cross-sectional study, a range of clinical and foot and ankle characteristics were assessed at a single baseline study visit. Participants were grouped for analysis according to their 12-month fall history which was recorded as 'no falls', 'single fall' or 'multiple falls'. Data were analysed following completion of all baseline study visits.

Univariate analysis was performed to answer research question 1) Are there differences in the foot and ankle characteristics of people with RA who have a history of falls, compared to people with RA who have not fallen? Multivariate analysis was performed to answer research question 2) Are foot and ankle characteristics independently associated with a history of falls in people with RA?

This chapter will begin with an overview of the participants recruited into the study including demographics, clinical characteristics and foot and ankle characteristics. The results of the primary univariate and multivariate analyses will be reported followed by the findings from secondary analyses. The chapter will conclude with a summary of the findings with respect to the research questions.

7.2: Recruitment

A convenience sample of 1827 people with RA were invited to participate in the study. Two hundred and twenty-nine people (13%) expressed interest in the study and booked a study appointment. Twenty-eight people did not attend the scheduled study visit (or subsequent rescheduled visits) resulting in a final sample of 201 participants. The sources of participants and reasons for non-attendance to the study appointment are illustrated in the Consolidated Standards of Reporting Trials (CONSORT) (217) flow diagram (Figure 7.1).

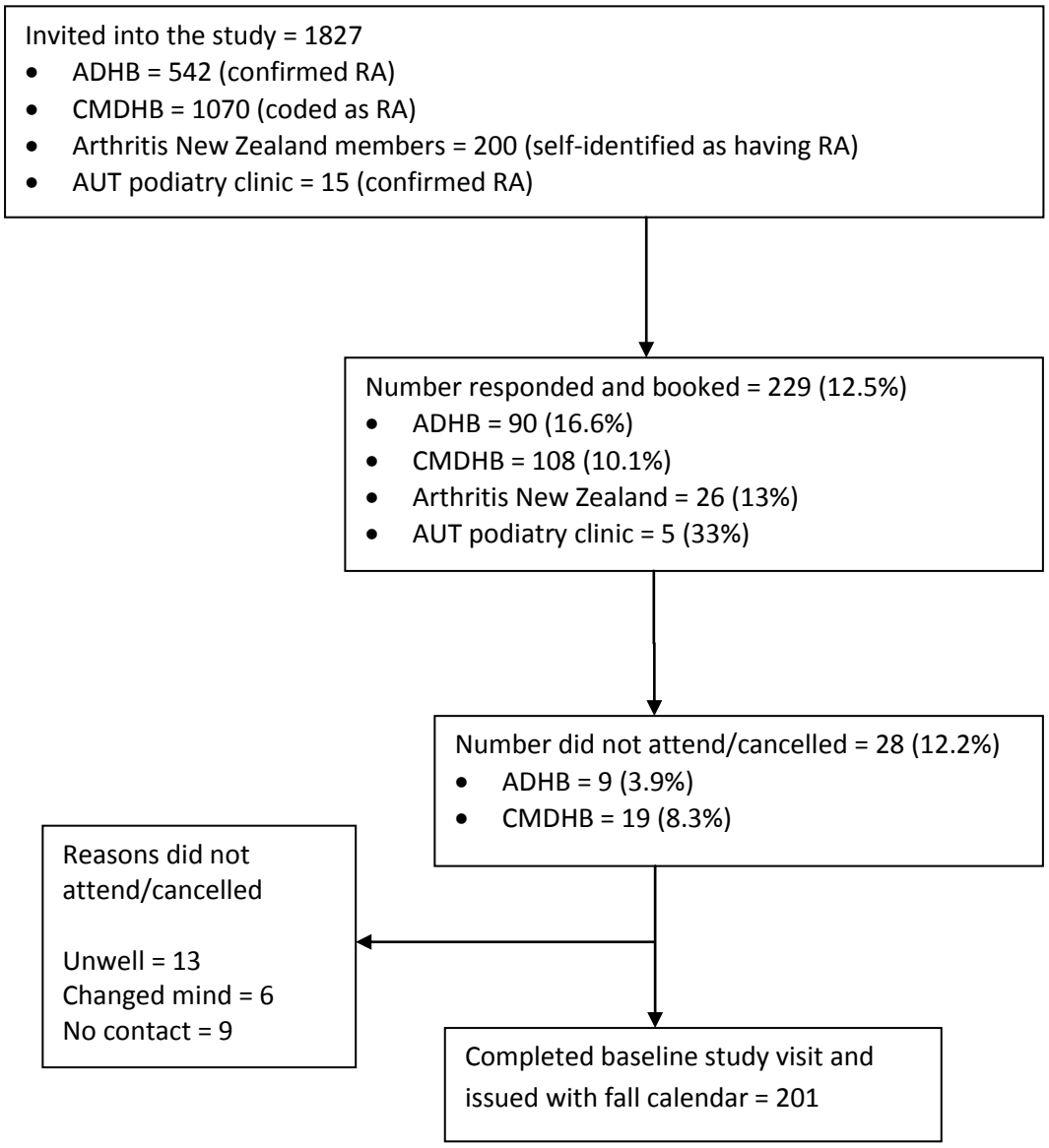

Figure 7.1: CONSORT flow diagram for baseline participant recruitment and reasons for non-attendance

7.3: Participant characteristics

Baseline clinical characteristics for the 201 participants are presented in Table 7.1. Participants were predominantly female (n=150, 75%). The mean (SD) age of female participants was 63 (11) years and male participants was 68 (10) years. Most of the participants (n=161, 80%) identified as European and had well-established RA, with mean (SD) disease duration 16 (14) years. Mean age (SD) of RA diagnosis was 49 (15) years. Sixty-nine percent had co-morbid conditions with hypertension (n=73, 36%) and osteoporosis (n=39, 19%) being the most common. Most participants (n=175, 87%) were taking non-biologic DMARDs and over one third (n=74, 37%) were taking prednisone. Antihypertensive medication (n=91, 45%) was also common. On the day of the study visit, participants had moderate disease activity and reported mild to moderate disability, with mean (SD) scores: DAS28-CRP 3.38 (1.26) and HAQ-II 0.89 (0.62).

Table 7.2 describes the foot and ankle characteristics in the entire group. Foot disease was frequently observed; 85% (n=170) presented with foot problems, 62% (n=112) had radiographic erosions in the feet, bunion deformity was present in 65% (n=130) and 34% (n=68) had pes planovalgus foot-type. Half of the participants failed the paper grip test for the hallux (n=101, 50%) and lesser digits (n=102, 51%) and 43% (n=85) had a vibration perception threshold greater than 26mV, indicating presence of neuropathy. Seventy-three percent (n=147) of participants reported foot pain experienced in the past week, with a mean (SD) pain score of 32 (29) using a 100mm VAS. On examination, 63% (n=125) presented with tender foot or ankle joints and 29% (n=58) presented with swollen foot or ankle joints. On the day of the study visit, participants reported moderate levels of foot impairment and disability, with mean (SD) score of 10 (5) for FIS_{IF} and 15 (9) for FIS_{AP}. Just over half of the participants (n=102, 51%) wore footwear classified as ‘good’ to the study visit and 57% (n=115) reported that they usually wear ‘good’ footwear outdoors. However, only 5% (n=10) of footwear identified as usually worn indoors was classified as ‘good’ with 64% (n=128) wearing ‘poor’ footwear indoors, 7% (n=14) wearing socks and 40% (n=81) reporting that they usually go barefoot indoors. Just over half of the participants (n=107, 53%) had previously visited a podiatrist but only 16% (n=32) received regular podiatry treatment.

Table 7.1: Baseline clinical characteristics (n=201). Data are presented as mean (SD) unless specified.

Age	64.7 (11)
Women, n (%)	150 (75)
European, n (%)	161 (80)
Body mass index, kg/m^2	27.8 (5.3)
Disease duration, years	16 (14)
Disease type, n (%)	
Rheumatoid factor positive	162 (81)
Anti-CCP antibody positive	105 (76)
Seronegative	26 (13)
Number of co-morbidities	1.2 (1.0)
Co-morbid conditions, n (%)	
Hypertension	73 (36)
Cardiovascular disease	29 (14)
Diabetes mellitus	18 (9)
Parkinson's disease	2 (1)
Osteoporosis	39 (19)
Depression or bipolar disorder	16 (8)
Number of medications	4.1 (2.0)
Taking 4 or more medications, n (%)	117 (58)
RA medications, n (%)	
DMARD monotherapy	71 (35)
Combination DMARD therapy (≥2 DMARDs)	104 (52)
Biologics	33 (16)
Prednisone	74 (37)
Other medications, n (%)	
Opiates	18 (9)
Antiplatelets	44 (22)
Anticoagulants	11 (6)
Antihypertensive	91 (45)
Hypoglycemics	16 (8)
Psychotropic medication	37 (18)
Patient self-reported pain (VAS 0-100), mm	39 (27)
Patient global (VAS 0-100), mm	36 (26)
Tender joint count	11 (12)
Swollen joint count	5 (7)
DAS28-CRP score	3.38 (1.26)
HAQ-II score	0.89 (0.62)
Short FES-I score (7-28)	12 (5)
Wears glasses or contact lenses, n (%)	181 (90)
Use of an assistive device, n (%)	57 (28)

DMARD, Disease-modifying anti-rheumatic drugs; VAS, Visual Analogue Scale; DAS, Disease Activity Score; FES-I, Falls Efficacy Scale-International; HAQ, Health Assessment Questionnaire

Table 7.2: Foot and ankle characteristics measured at baseline (n=201). Data are presented as mean (SD) unless specified.

Foot erosion on radiograph, n (%)	112 (62)
Previous foot surgery, n (%)	29 (21)
Presence of foot pain, n (%)	147 (73)
Foot pain (VAS 0-100), mm	32 (29)
Presence of foot or ankle tender joints, n (%)	125 (63)
Presence of foot or ankle swollen joints, n (%)	58 (29)
Foot problem score	15 (8)
Presence of at least one foot problem, n (%)	170 (85)
Pes planovalgus foot-type, n (%)	68 (34)
Presence of bunion deformity, n (%)	130 (65)
Monofilament sites felt (0-12)	10 (3)
Vibration perception threshold ≥ 26mV, n (%)	85 (43)
Foot muscle strength, N	
Dorsiflexion	63 (33)
Plantarflexion	69 (29)
Inversion	33 (17)
Eversion	30 (15)
Ankle range of motion, degrees	58 (7)
Gait speed, m/s	1.07 (0.3)
Peak plantar pressure, kPa	
Total-foot	330 (64)
Forefoot	310 (66)
Midfoot	113 (62)
Rearfoot	243 (69)
Pressure-time integral, kPa.sec	
Forefoot	84 (23)
Midfoot	44 (29)
Rearfoot	86 (39)
Failed paper grip test, n (%)	
Hallux	101 (50)
Lesser toes	102 (51)
Toe strength, N (%BW)	
Hallux	4.5 (2.5)
Lesser toes	2.1 (1.2)
Eyes-open postural sway, mm	
Antero-posterior direction	20.9 (9.7)
Medio-lateral direction	14.2 (8.7)
Eyes-closed postural sway, mm	
Antero-posterior direction	29.4 (12.9)
Medio-lateral direction	17.4 (9.7)
Has seen a podiatrist before, n (%)	107 (53)
Receives regular podiatry treatment, n (%)	32 (16)
FIS_{TOTAL} score (0-51)	25 (12)
FIS_{IF} subscale score (0-21)	10 (5)
FIS_{AP} subscale score (0-30)	15 (9)

Table 7.2: (continued)

FIS_{IF} subscale score, n (%)	
Mild	44 (22)
Moderate	105 (52)
Severe	52 (26)
FIS_{AP} subscale score, n (%)	
Mild	56 (28)
Moderate	81 (40)
Severe	64 (32)
Footwear type worn to study visit, n (%)	
Good	102 (51)
Average	18 (9)
Poor	81 (40)
Usual footwear worn indoors, n (%)	
Good	12 (6)
Poor	128 (64)
Socks	14 (7)
Bare feet	47 (23)
Usual footwear worn outdoors, n (%)	
Good	115 (57)
Average	14 (7)
Poor	72 (36)

VAS, Visual Analogue Scale; FIS_{TOTAL}, Foot Impact Scale total score; FIS_{IF}, Foot Impact Scale impairment/footwear subscale; FIS_{AP}, Foot Impact Scale activities/participation subscale

7.4: Primary univariate analysis comparing non-fallers and fallers

Of the 201 participants with RA, 119 (59%) reported one or more falls in the preceding 12 months. Of those who fell, 46 (39%) fell once (single-fallers) and 73 (61%) fell more than once (multiple-fallers). The results of univariate analysis comparing non-fallers and fallers at baseline are presented in Table 7.3. Results shown are for comparisons with P<0.15. Fallers had significantly longer mean disease duration (P=0.030), more co-morbid conditions (P=0.020) and higher midfoot peak plantar pressure (PPP) (P=0.007) and pressure-time integral (PTI) (P=0.002). There was a significant difference in HAQ-II score between the groups with fallers reporting greater difficulty with the activities of daily living, compared to non-fallers (P=0.014). Fallers also reported greater fear of falling with significantly higher short FES-I scores (P=0.002) than non-fallers. Foot-related disability and impairment was also greater in fallers compared to non-fallers with significantly higher scores recorded for the activities/participation subscale (FIS_{AP}) of the Foot Impact Scale (P=0.001). Compared to non-fallers, those who fell were more likely to have presence of tender (P=0.021) or swollen (P=0.047) foot or ankle joints, a history of cardiovascular disease including stroke, ischemic heart disease, congestive heart failure, arrhythmia and peripheral vascular disease (P=0.029) with a similar trend for osteoporosis (P=0.050).

Table 7.3: Univariate analysis of non-fallers and fallers at baseline. Comparisons with P<0.15 are shown. Data are presented as mean (SD) unless specified.

	Non-fallers n=82	**Fallers n=119**	**P value**
Clinical characteristics			
Disease duration	13.6 (12.8)	17.4 (13.9)	0.030*
Number of co-morbid conditions	0.96 (0.92)	1.33 (1.11)	0.020*
Cardiovascular disease, n (%)	6 (7)	23 (19)	0.029*
Osteoporosis, n (%)	10 (12)	29 (24)	0.050
Number of medications	3.8 (2.3)	4.3 (2.2)	0.081
DMARD monotherapy, n (%)	35 (43)	36 (30)	0.097
Combination DMARD therapy, n (%)	36 (44)	68 (57)	0.089
Tender joint count	10 (13)	12 (12)	0.095
DAS28-CRP	3.22 (1.24)	3.48 (1.26)	0.123
HAQ-II	0.76 (0.60)	0.98 (0.62)	0.014*
Fear of falling (short FES-I)	11 (5)	13 (5)	0.002*
Foot and ankle characteristics			
Presence of foot or ankle tender joints, n (%)	43 (52)	82 (69)	0.021*
Presence of foot or ankle swollen joints, n (%)	17 (21)	41 (35)	0.047*
Foot problem score	14 (7)	16 (9)	0.057
Pes planovalgus foot-type, n (%)	22 (27)	46 (39)	0.085
Ankle range of motion, degrees	57 (6)	59 (8)	0.110
Gait speed, m/s	1.12 (0.27)	1.04 (0.3)	0.063
Total-foot peak plantar pressure, kPa	319 (59)	337 (67)	0.055
Midfoot peak plantar pressure, kPa	100 (44)	122 (71)	0.007*
Midfoot pressure-time integral, kPa.sec	38 (20)	50 (34)	0.002*
Hallux strength, N (%BW)	5.0 (2.2)	4.5 (2.7)	0.148
Eyes-closed AP sway, mm	27.5 (9.7)	31.7 (13.7)	0.063
Patient-reported foot-related disability and impairment (FIS_{AP})	12 (9)	16 (8)	0.001*

* significant at P<0.05

DMARD, Disease-modifying anti-rheumatic drug; DAS, Disease Activity Score; HAQ, Health Assessment Questionnaire; FES-I, Falls Efficacy Scale-International; AP, antero-posterior; FIS_{AP}, Foot Impact Scale activities/participation subscale

7.5: Primary multivariate analysis of predictive risk factors comparing non-fallers and fallers

Multivariate logistic regression analysis identified associations between potential fall risk factors and falls in the preceding 12 months. The results comparing all non-fallers with fallers using logistic regression analyses are shown in Table 7.4. Nineteen variables, plus age, were entered into the original model including: disease duration, DAS28-CRP, DMARD monotherapy, combination DMARD therapy, number of medications, number of co-morbid conditions, cardiovascular disease, osteoporosis, tender joint count, pes planovalgus foot-type, presence of foot or ankle tender joints, presence of foot or ankle swollen joints, gait speed, foot problem score, hallux strength, ankle range of motion, midfoot PPP, eyes-closed AP sway and FIS_{AP} subscale score. To avoid multicollinearity, HAQ-II and FES-I were excluded from the model as they were both highly correlated ($r>0.5$) with FIS_{AP}. In addition, total-foot PPP and midfoot PTI were excluded as they were highly correlated with midfoot PPP ($r>0.5$). The final model contained three variables which were independently associated with a fall in the preceding 12 months ($P<0.05$): cardiovascular disease (OR 3.22, P=0.024), midfoot PPP (OR 1.12 [for each 20kPa increase], P=0.046) and foot-related disability and impairment (OR 1.17 [for each 3 point increase FIS_{AP}], P=0.005). The final model explained 13% (Nagelkerke R squared) of the variance in falls status and correctly predicted 66% of falls.

Table 7.4: Results from backwards stepwise logistic regression analyses comparing non-fallers (n=82) and fallers (n=119) on all predictor variables and controlling for age. Associations with P<0.05 are shown.

	Odds ratio (95% confidence interval)	**P value**
Cardiovascular disease	3.22 (1.17-8.88)	0.024
Midfoot peak plantar pressure (for each 20kPa increase)	1.12 (1.00-1.25)	0.046
Foot-related disability and impairment (for each 3 point increase FIS_{AP})	1.17 (1.05-1.31)	0.005

kPa, kilopascals; $FIS_{AP,}$ Foot Impact Scale activities/participation subscale

Variables included in the model: age, disease duration, DAS28-CRP, DMARD monotherapy, combination DMARD therapy, number of medications, number of co-morbid conditions, cardiovascular disease, osteoporosis, tender joint count, pes planovalgus foot-type, presence of foot or ankle tender joints, presence of foot or ankle swollen joints, gait speed, foot problem score, hallux strength, ankle range of motion, midfoot peak plantar pressure, eyes-closed AP sway and FIS_{AP} subscale score.

7.6: Secondary univariate analysis

7.6.1: Comparing non-fallers, single-fallers and multiple-fallers

The results of univariate analysis comparing non-fallers, single-fallers and multiple-fallers at baseline are presented in Table 7.5. Results shown are for comparisons with P<0.15 and overall P values are reported. When comparing the three groups, there were no significant differences between single-fallers and non-fallers on any of the continuous variables except for midfoot PPP (P=0.023) and midfoot PTI (P=0.014). However, significant differences were found between multiple-fallers and non-fallers and multiple-fallers and single-fallers on a number of other variables.

Multiple-fallers had more co-morbid conditions than non-fallers (P=0.002) and single-fallers (P=0.027), were more likely to have a history of cardiovascular disease (P=0.007), and took more medications than non-fallers (P=0.007) and single-fallers (P=0.013). Multiple-fallers also reported significantly higher foot pain (VAS) than non-fallers (P=0.018) and single-fallers (P=0.009) and greater foot-related disability and impairment, as indicated by FIS_{TOTAL}, than non-fallers (P=0.004) plus higher FIS_{AP} subscale score (P<0.001). In terms of disability, multiple-fallers reported increased fear of falling (FES-I) compared to non-fallers (P<0.001) and single-fallers (P=0.010) and greater difficulty with the activities of daily living (HAQ-II) than non-fallers (P=0.002) and single-fallers (P=0.027). Multiple-fallers were more likely to have tender foot or ankle joints (P=0.037) than non-fallers and single-fallers. Multiple-fallers also had greater midfoot PTI (P=0.022) than non-fallers.

Table 7.5: Univariate analysis of non-fallers, single-fallers and multiple-fallers at baseline. Comparisons with P<0.15 are shown. Data are presented as mean (SD) unless specified.

	Non-fallers n=82	**Single-fallers n=46**	**Multiple-fallers n=73**	**Overall P value**
Clinical characteristics				
Disease duration	13.6 (12.8)	18.2 (14.5)	17.0 (13.6)	0.091
Number of co-morbid conditions	0.96 (0.92)	1.04 (1.00)	1.51 (1.13)	0.005*
Osteoporosis, n (%)	10 (12)	12 (26)	17 (23)	0.093
Cardiovascular disease, n (%)	6 (7)	5 (11)	18 (25)	0.007*
Number of medications	3.8 (2.3)	3.7 (1.9)	4.7 (2.3)	0.010*
DMARD monotherapy, n (%)	35 (43)	17 (37)	19 (26)	0.093
Combination DMARD therapy, n (%)	36 (44)	24 (52)	44 (60)	0.126
Opiates, n (%)	7 (9)	1 (2)	10 (14)	0.099
Patient self-reported pain (VAS 0-100), mm	40 (26)	31 (26)	42 (28)	0.060
Patient global (VAS 0-100), mm	34 (24)	31 (26)	41 (27)	0.068
Tender joint count	10 (13)	10 (12)	13 (13)	0.089
HAQ-II	0.76 (0.60)	0.82 (0.58)	1.08 (0.63)	0.005*
Short FES-I	11 (5)	12 (4)	14 (5)	<0.001*
Foot and ankle characteristics				
Foot pain (VAS 0-100), mm	28 (26)	25 (27)	40 (31)	0.012*
Presence of foot or ankle tender joints, n (%)	43 (52)	30 (65)	52 (72)	0.037*
Presence of foot or ankle swollen joints, n (%)	17 (21)	14 (30)	27 (38)	0.071
Gait speed	1.12 (0.27)	1.08 (0.26)	1.02 (0.31)	0.078
Midfoot peak plantar pressure, kPa	100 (44)	127 (73)	120 (71)	0.035*
Midfoot pressure-time integral, kPa.sec	38 (20)	51 (30)	48 (37)	0.018*
Patient-reported foot-related disability and impairment				
FIS_{TOTAL}	22 (13)	24 (12)	29 (11)	0.004*
FIS_{IF}	10 (5)	10 (5)	11 (4)	0.133
FIS_{AP}	12 (9)	14 (8)	17 (8)	<0.001*

* significant at P<0.05

DMARD, Disease-modifying anti-rheumatic drug; VAS, Visual Analogue Scale; HAQ, Health Assessment Questionnaire, FES-I, Falls Efficacy Scale International: FIS_{TOTAL}, Foot Impact Scale total score; FIS_{IF}, Foot Impact Scale impairment/footwear subscale; FIS_{AP}, Foot Impact Scale activities/participation subscale

7.6.2: Comparing the combination of non-fallers/single-fallers with multiple-fallers

The results of univariate analysis comparing the combination of non-fallers/single-fallers with multiple-fallers at baseline are presented in Table 7.6. Results shown are for comparisons with P<0.15. Multiple-fallers had significantly worse patient global score (P=0.027), more co-morbid conditions (P=0.001), took more medications (P=0.002) and had a higher tender joint count (P=0.031). Multiple-fallers also had significantly higher foot pain VAS score (P=0.004), slower gait speed (P=0.030) and were more likely to have presence of foot or ankle tender joints (P=0.048) compared to the combination of non-fallers/single-fallers. There was a significant difference in HAQ-II score between groups with multiple-fallers reporting greater difficulty with the activities of daily living, compared to the combination of non-fallers/single-fallers (P=0.001). Multiple-fallers also reported greater fear of falling with significantly higher short FES-I scores (P<0.001). Foot-related disability and impairment was greater in multiple-fallers with significantly higher FIS_{TOTAL} score (P=0.001), and subscale scores; FIS_{IF} (P=0.044) and FIS_{AP} (P=0.001), compared to the combination of non-fallers/single-fallers. Multiple-fallers were also more likely to have a history of cardiovascular disease including stroke, ischemic heart disease, congestive heart failure, arrhythmia and peripheral vascular disease (P=0.004).

Table 7.6: Univariate analysis of non-fallers/single-fallers and multiple-fallers at baseline. Comparisons with P<0.15 are shown. Data are presented as mean (SD) unless specified.

	Non-fallers/ single-fallers n=128	**Multiple-fallers n=73**	**P value**
Clinical characteristics			
Number of co-morbid conditions	1.02 (0.94)	1.51 (1.16)	0.001*
Cardiovascular disease, n (%)	11 (9)	18 (25)	0.004*
Depression or bipolar disorder, n (%)	7 (5)	9 (12)	0.145
Number of medications	3.8 (2.1)	4.7 (2.2)	0.002*
Taking 4 or more medications, n (%)	68 (53)	49 (67)	0.074
DMARD monotherapy, n (%)	52 (41)	19 (26)	0.054
Combination DMARD therapy, n (%)	60 (47)	44 (60)	0.093
Psychotropic medication, n (%)	19 (15)	18 (25)	0.124
Opiates, n (%)	8 (6)	10 (14)	0.128
Patient self-reported pain (VAS 0-100), mm	37 (26)	42 (28)	0.112
Patient global (VAS 0-100), mm	33 (25)	41 (27)	0.027*
Tender joint count	10 (12)	13 (13)	0.031*
DAS28-CRP	3.26 (1.23)	3.58 (1.28)	0.099
HAQ-II	0.76 (0.58)	1.04 (0.62)	0.001*
Fear of falling (short FES-I)	11 (5)	14 (5)	<0.001*
Use of an assistive device, n (%)	30 (23)	27 (37)	0.059
Foot and ankle characteristics			
Foot pain (VAS 0-100), mm	27 (27)	40 (31)	0.004*
Presence of foot or ankle tender joints, n (%)	73 (57)	52 (72)	0.048*
Presence of foot or ankle swollen joints, n (%)	31 (24)	27 (38)	0.068
Gait speed, m/s	1.11 (0.27)	1.02 (0.31)	0.030*
Patient-reported foot-related disability and impairment			
FIS_{TOTAL}	22 (12)	28 (11)	0.001*
FIS_{IF}	9 (5)	11 (4)	0.044*
FIS_{AP}	13 (9)	17 (8)	0.001*

* significant at P<0.05

DMARD, Disease-modifying anti-rheumatic drug; VAS, Visual Analogue Scale; DAS, Disease Activity Score; HAQ, Health Assessment Questionnaire; FES-I, Falls Efficacy Scale-International; FIS_{TOTAL}, Foot Impact Scale total score; FIS_{IF}, Foot Impact Scale impairment/footwear subscale; FIS_{AP}, Foot Impact Scale activities/participation subscale

7.7: Secondary multivariate analysis of predictive risk factors comparing the combination of non-fallers/single-fallers with multiple-fallers

Multivariate logistic regression analysis identified associations between potential fall risk factors and multiple falls in the preceding 12 months. The results comparing non-fallers/single-fallers with multiple-fallers using logistic regression analyses are shown in Table 7.7. Fifteen variables, plus age, were entered into the original model including: foot pain (VAS), presence of foot or ankle tender joints, presence of foot or ankle swollen joints, gait speed, FIS_{AP} subscale score, use of an assistive device, patient global (VAS), DAS28-CRP, DMARD monotherapy, combination DMARD therapy, number of medications, number of co-morbid conditions, cardiovascular disease, psychotropic medication and opiates. To avoid multicollinearity, HAQ-II, short FES-I , FIS_{TOTAL}, FIS_{IF}, patient self-reported pain (VAS) and tender joint count were excluded from the model as they were highly correlated ($r>0.5$) with FIS_{AP} and foot pain (VAS). The final model contained three variables; combination DMARD therapy (OR 1.91; $P=0.043$), cardiovascular disease (OR 4.58, $P=0.001$) and patient-reported foot-related disability and impairment (OR 1.23 [for each 3 point increase FIS_{AP}], $P<0.001$), which were independently associated with a fall in the preceding 12 months. The final model explained 17% (Nagelkerke R squared) of the variance in falls status and correctly predicted 68% of falls.

Table 7.7: Results from backwards stepwise logistic regression analyses comparing non-fallers/single-fallers (n=128) and multiple-fallers (n=73) on all predictor variables and controlling for age. Associations with P<0.05 are shown.

	Odds ratio (95% confidence interval)	**P value**
Combination DMARD therapy	1.91 (1.02-3.58)	0.043
Cardiovascular disease	4.58 (1.87-11.2)	0.001
Foot-related disability and impairment (for every 3 point increase FIS_{AP})	1.23 (1.09-1.37)	<0.001

DMARD, Disease-modifying anti-rheumatic drug; $FIS_{AP,}$ Foot Impact Scale activities/participation subscale

Variables included in the model: age, foot pain (VAS), presence of foot or ankle tender joints, presence of foot or ankle swollen joints, gait speed, FIS_{AP} subscale score, use of an assistive device, patient global (VAS), DAS28-CRP, DMARD monotherapy, combination DMARD therapy, number of medications, number of co-morbid conditions, cardiovascular disease, psychotropic medication and opiates.

7.8: Correlations between foot and ankle variables and PROMs

Investigation of the linear relationship between all baseline foot and ankle characteristics and PROMs, which were significantly different ($P<0.05$) on primary and secondary univariate analysis, demonstrated a number of significant correlations. Table 7.8 details all correlations. Of note is midfoot PPP which was strongly correlated with midfoot PTI ($r=0.784$, $P<0.01$) and arch index score ($r=0.531$, $P<0.01$) but was not significantly associated with any other foot or ankle measure or PROM. There were significant negative correlations between gait speed and all other foot and ankle measures and PROMs, except midfoot PPP. The strongest associations were between gait speed and the measures of self-reported disability and impairment (HAQ-II, FES-I, FIS_{TOTAL}, FIS_{AP}). Medium to large correlations were demonstrated between all PROMs of disability and impairment.

Table 7.8: Correlations for all baseline foot and ankle measures and PROMs significant on primary and secondary univariate analysis *

	Foot pain	Gait speed	MF PPP	MF PTI	Arch index	EC AP sway	EC ML sway	FIS_{TOTAL}	FIS_{AP}	FIS_{IF}	HAQ-II	FES-I	General Pain	Patient global
Foot pain														
Gait speed	-0.221													
MF PPP	-0.030	-0.114												
MF PTI	0.019	-0.382	0.784											
Arch index	0.034	-0.293	0.531	0.495										
EC AP sway	0.057	-0.220	0.040	0.148	0.182									
EC ML sway	0.089	-0.333	-0.020	0.122	0.113	0.579								
FIS_{TOTAL}	0.543	-0.503	0.120	0.302	0.256	0.276	0.319							
FIS_{AP}	0.455	-0.560	0.130	0.310	0.248	0.294	0.331	0.956						
FIS_{IF}	0.593	-0.296	0.080	0.224	0.220	0.184	0.229	0.856	0.667					
HAQ-II	0.398	-0.553	-0.009	0.234	0.097	0.239	0.314	0.708	0.727	0.519				
FES-I	0.351	-0.442	0.068	0.280	0.148	0.181	0.264	0.660	0.684	0.475	0.762			
General pain	0.419	-0.360	-0.042	0.074	0.061	0.147	0.190	0.494	0.445	0.469	0.533	0.403		
Patient global	0.372	-0.378	0.071	0.130	0.060	0.167	0.188	0.547	0.552	0.437	0.606	0.472	0.668	

*r/rho ≤0.139 is not significant; r/rho 0.140-0.183 significant at P <0.05; r/rho ≥0.184 significant at P<0.01

MF PPP, midfoot peak plantar pressure; MF PTI, midfoot pressure-time integral; EC AP sway, eyes-closed antero-posterior sway; EC ML sway, eyes-closed medio-lateral sway; FIS_{TOTAL}, Foot Impact Scale total score; FIS_{AP}, Foot Impact Scale, activities/participation subscale; FIS_{IF}, Foot Impact Scale impairments/footwear subscale; HAQ, Health Assessment Questionnaire; FES-I, Fall Efficacy Scale-International

7.9: Summary of the cross-sectional findings

7.9.1: Findings for clinical characteristics

Primary univariate analysis demonstrated disease duration, HAQ-II score, number of co-morbid conditions, presence of cardiovascular disease and fear of falling to be significantly different between non-fallers and fallers. Additional variables found to be different between the combined group of non-fallers/single-fallers and multiple-fallers included patient global (VAS), number of medications and tender joint count. Multivariate analysis identified history of cardiovascular disease to be independently associated with one or more falls and multiple (≥2) falls in the preceding 12 months. Combination DMARD therapy was independently associated with multiple falls in the preceding 12 months.

7.9.2: Findings for research question 1

Are there differences in the foot and ankle characteristics of people with RA who have a history of falls, compared to people with RA who have not fallen?

Primary univariate analysis demonstrated a number of foot and ankle variables which were significantly different between non-fallers and fallers. These included presence of foot or ankle tender joints, presence of foot or ankle swollen joints, midfoot peak plantar pressure, midfoot pressure-time integral and patient-reported foot-related disability and impairment (FIS_{AP} subscale score). Secondary univariate analysis comparing the combination of non-fallers/single-fallers with multiple-fallers demonstrated two additional foot and ankle variables; foot pain (VAS) and gait speed, as being significantly different between the groups. Comparison of three groups (non-fallers, single-fallers and multiple-fallers) provided no additional findings. Therefore, based on the current results, we can reject the null hypothesis and state that there is a significant difference in structural and functional foot and ankle characteristics in people with RA with a history of falls, compared to people with RA who have not fallen.

7.9.3: Findings for research question 2

Are foot and ankle characteristics independently associated with a history of falls in people with RA?

Primary multivariate analysis identified two foot and ankle variables; midfoot peak plantar pressure and patient-reported foot-related disability and impairment (FIS_{AP} subscale score), to be independently associated with one or more falls in the preceding 12 months. FIS_{AP} subscale score was also independently associated with multiple (≥2) falls in the preceding 12 months. Therefore, based on the current results, we can reject the null hypothesis and state that foot and ankle characteristics are independently associated with a history of falls in people with RA.

CHAPTER 8: CROSS-SECTIONAL STUDY DISCUSSION

8.1: Introduction

This chapter will begin by evaluating the representativeness of the study sample with respect to the wider population of adults with RA. Falls incidence will be discussed and the key findings for the cross-sectional study will be compared with previous research. In order to further our understanding of fall risk in people with RA, the discussion explores the potential relationships between a range of intrinsic and extrinsic fall risk factors, incorporating the findings related to the foot and ankle and clinical features associated with a history of falling. The chapter will conclude with a summary of the findings for the cross-sectional study.

8.2: Discussion

The sample of 201 participants was representative of an older adult population with established RA. Seventy-five percent of participants were female which reflects the expected ratio of 3:1 females to males with RA. Mean disease duration was 16 years with a mean age at diagnosis of 49 years old. Foot disease was prevalent with 85% of participants presenting with at least one foot problem including; bunions, lesser toe deformities, decreased muscle strength, pes planovalgus, reduced peripheral sensation and disabling foot pain. The current findings are reflective of a study of 100 people with RA in Auckland, New Zealand (30) as well as several previous studies conducted in Columbia (218), Turkey (28, 33) and the UK (98). Therefore, in terms of age, gender, disease duration and foot disease, the cohort in the current study could be considered to be representative of the wider older adult population with established RA in New Zealand.

In this study, 59% of participants reported at least one fall during the 12 months preceding the baseline assessment. This is higher than the 30% reported for community-dwelling older adults (173) and is consistent with reports that adults with RA are at increased risk of falling compared to the non-RA population (21, 160, 161). However, the recruitment strategy, in which clinic patients were invited to participate in a study of fall risk, meant that people who had recently experienced a fall may have

been attracted to the study. Hence it should be noted that the number of fallers at baseline is likely to be an over-estimate of all people with RA.

8.2.1: Clinical characteristics

We found fallers to have a longer RA disease duration than non-fallers which was in agreement with a large Japanese study in adults with RA (158). However, two previous cross-sectional studies found no association between disease duration and falls (159, 162). As falls are generally associated with older adults, clinicians may not identify younger people with established RA who are at increased fall risk. The number of co-morbid conditions was also associated with increased fall risk, as observed in previous studies in RA (159), diabetes mellitus (17) and older adults (3). Given the prevalence of co-morbidities in people with RA (43), an association between fall risk and co-morbid conditions, in particular cardiovascular disease, is an important finding. Cardiovascular disease (not including hypertension) was the only clinical characteristic found to be independently associated with a fall in the preceding 12 months. This result is likely due to the inclusion of stroke in the variable 'cardiovascular disease'. At baseline, nine participants had a history of stroke; all of whom had experienced one or more falls in the preceding 12 months. Several studies have identified 'history of stroke' as a fall risk factor in older adults (3). In addition, having a history of stroke greatly increases the risk of falling, compared to the general older adult population, with a fall rate of up to 73% reported in community-dwelling stroke survivors (219).

The finding with respect to increasing number of medications and fall risk supports one previous cross-sectional study in adults with RA (155). However, this study only recorded the use of four medications, all of which were considered to increase the risk of falls (155). In contrast, 22 individual medications, or classes of medication, were recorded in the current study. Increasing number of medications and use of multiple medications, termed polypharmacy, are well recognised fall risk factors in community-dwelling older adults (3, 220). Polypharmacy is common in people with RA and is associated with increasing age, RA disease duration and co-morbid conditions (86). Therefore, based upon previous studies, we can hypothesise that the current findings

relating to RA disease duration, number of co-morbid conditions, increasing number of medications and increasing fall risk, are likely to be linked.

The inclusion of combination DMARD therapy (≥2 DMARDs), as a potential fall risk factor, was unique to the current study. One previous study assessed methotrexate as a potential risk factor for falls in adults with RA (158). In this cross-sectional study of 4996 Japanese men and women, Furuya (158) found that methotrexate use was negatively associated with a 6-month history of falling; that is methotrexate use was protective for falls. In the current study, taking combination DMARD therapy nearly doubled the risk of experiencing multiple falls. Combination DMARD therapy has been previously linked to polypharmacy in older people with established RA (86). Ongoing active or more severe RA, necessitating combination DMARD therapy, frequently requires other medications to target specific symptoms and mitigate potential drug side-effects (86). We observed 52% of participants were on combination DMARD therapy at baseline. Of the 73 participants who experienced multiple falls during the preceding 12-month period, 44 (60%) were on combination DMARD therapy and of those, 37 (84%) were also taking four or more medications. Therefore, the association between combination DMARD therapy and falls in the current study may be due to polypharmacy, or increasing number of medications, as the underlying mechanism for falls.

The manifestations of RA, and response to treatment, can be markedly different between individuals (221). Likewise, the impact of RA on a person's functional ability, and their ability to engage in the activities of daily living, varies between individuals (79). It is important then to consider the holistic view of the patient in the management of the disease (79). The same could be true of fall risk in this population. In agreement with several previous cross-sectional studies (155, 158, 162), poor functional ability (as assessed by the HAQ-II) was significantly associated with increasing fall risk. In addition, patient-reported global health was associated with increasing risk of multiple falls, which supports previous findings in RA (158). The current results suggest that an individual's perception of the impact of RA, in terms of their general health, functional ability and ability to participate in everyday activities,

may also indicate an increased vulnerability to falls. Therefore, a psychosocial as well as a medical approach to fall risk is important.

Fear of falling (short FES-I score) was significantly associated with increasing fall risk which is in agreement with previous cross-sectional studies in adults with RA (157, 162). Up to 50% of people with RA report a fear of falling (157) and fear of falling has been reported as a risk factor for falls in several older adult studies (3). Previous authors have suggested that inactivity, as a result of fear of falling, may in turn lead to decreased physical conditioning, muscle weakness and impaired balance, thus further increasing the risk of falling (159). In addition, we found fear of falling (FES-I) to be highly correlated with poor functional ability (HAQ-II) and reduced general health (patient global) (Table 7.8) which were also associated with increasing falls risk. Therefore, fear of falling may be a causative factor in future falls in people with RA.

Falls were not associated with age or female sex which is in agreement with several other cross-sectional studies in people with RA (155, 158, 159, 162). In the general population, older adults (over 65 years) and women experience significantly more falls than younger adults and men, and falls rate increases with increasing age (3). It is possible that age related fall risk factors, such as impaired general health, co-morbid conditions, fatigue and history of prior falls, may occur in adults of all ages with RA, thus mitigating age-related differences.

We found no association between BMI and falls, which is similar to a previous UK-based study in 316 women with inflammatory polyarthritis (IP); including RA, undifferentiated IP, psoriatic arthritis and post-viral arthritis (20). However, a large Japanese study reported an association between increasing BMI and 6-month fall history in men and women with RA (158). Increased BMI has also been identified as a risk factor for falls in older women with diabetes mellitus (222) and older adults with diffuse polyneuropathy (223). Therefore, the association between BMI and falls may be complex, with differences between ethnicities and long-term chronic conditions.

The current study demonstrated mixed results for measures of RA disease activity and falls. We found no association between general pain or DAS28-CRP score and falls, which supports two previous cross-sectional studies (158, 159). However, in agreement with one previous RA study (158), increasing tender joint count was associated with increasing fall risk. Conflicting evidence for measures of RA disease activity and falls was also reported in our recently published systematic review (224). The current findings suggest that joint tenderness, associated with active RA, is a more sensitive indicator of fall risk than other general measures of RA disease activity.

8.2.2: Foot and ankle characteristics

We found a range of foot and ankle features that were associated with increasing fall risk. However, midfoot peak plantar pressure was the only foot-specific measure that was independently associated with a fall in the preceding 12 months. The findings relating to increased plantar pressure variables, including peak plantar pressure and pressure-time integral, are similar to a previous study in community-dwelling older adults (26). Mickle (26) reported an association between elevated peak plantar pressure and pressure-time integral and falls, which were prospectively recorded over a 12-month period. However, the previous findings related to peak plantar pressure and pressure-time integral across the whole plantar surface of the foot, whereas the current results relate to peak plantar pressure and pressure-time integral in the midfoot region only. Total-foot peak plantar pressure was assessed in the current study and found to be higher in fallers compared to non-fallers. However, the mean difference did not reach significance. Mickle (26) also found an association between presence of foot pain and elevated peak plantar pressure and pressure-time integral and concluded that increased pressures during gait may contribute to foot pain and discomfort, leading to altered gait and increased fall risk in older adults. In the current study, foot pain intensity and increasing plantar pressures were not significantly correlated (Table 7.8). Therefore, the mechanism underlying the association between increased plantar pressures and falls in people with RA may be different from the general older adult population.

People with RA have been reported to have altered peak plantar pressures and pressure-time integrals compared to control participants (97, 99-101, 143, 144). Alterations in peak plantar pressure and pressure-time integral occur due to changes in foot structure (100, 144). Increased midfoot peak plantar pressure and pressure-time integral have been reported in people with RA with pes planovalgus deformity, compared to healthy controls (101). Pes planovalgus deformity is common in established RA, with prevalence of pes planovalgus increasing with disease duration (32). The gradual collapse of the medial longitudinal arch results in a stiffer, flatter foot that is less able to adapt to changes in the terrain thus compromising stability (225). Pes planovalgus is associated with changes in gait and foot function, in people with RA, which may compromise stability and increase fall risk (101). Pes planovalgus has also been associated with falls in healthy older adults (23, 226). The method for identifying pes planovalgus foot-type varies between studies and ranges from subjective clinical assessment (23, 101) to mathematical calculation of the arch index from digitally captured footprints (23, 226). In studies which use the arch index to determine foot-type, the cut-off values for high, normal and low arch vary according to the population sampled. Therefore, the interpretation of a pes planovalgus foot-type may also vary between studies. In the current study, there was no difference in pes planovalgus foot-type (defined as arch index value > 0.25) between non-fallers and fallers. However, there was a high positive correlation between increasing midfoot peak plantar pressure and pressure-time integral and increasing arch index value (Table 7.8). Therefore, the association between increased midfoot peak plantar pressure and pressure-time integral and falls, in the current study, may be related to the gradual collapse of the medial longitudinal arch, resulting in an increasingly flatter foot, in people with established RA.

Increases in midfoot peak plantar pressure and pressure-time integral can also occur due to delayed propulsion, which is an offloading strategy employed by people with RA to avoid painful joints associated with synovitis in the forefoot (141). We found fallers were more likely to have the presence of foot or ankle tender joints, and foot or ankle swollen joints, than non-fallers. In addition, a higher tender joint count, including the foot and ankle joints, was associated with increased risk of multiple falls. A previous

cross-sectional study also reported that increasing number of tender and swollen joints, including the ankles and metatarsophalangeal joints of the feet, was independently associated with a 6-month history of multiple falls in people with RA (158). Joint tenderness and swelling is generally indicative of synovitis associated with active RA (46). Therefore, based upon the current findings and previous studies we can hypothesise that altered gait, due to synovitis in the foot and ankle, may be a factor in falls in adults with RA. This finding is important as synovitis in the feet may go unnoticed by clinicians who routinely use the DAS28, which does not include the foot and ankle joints, to assess disease activity. In addition, synovitis in the feet could be treated, thus potentially mitigating future fall risk.

In the current study, multiple-fallers had greater foot pain intensity compared to the combined group of non-fallers/single-fallers. One previous cross-sectional study found no association between pain intensity and falls in adults with RA (159). However, pain intensity was assessed for the whole body, not specifically the feet. In addition, the previous study compared non-fallers and fallers only (159). Presence (yes/no) of foot pain was assessed in addition to foot pain intensity, in the current study, with no difference found between fallers and non-fallers. This finding likely reflects the high percentage of participants who reported foot pain at baseline, which we would expect to find in people with established RA (98, 104). Therefore, the current findings suggest that presence of foot pain is not an indicator of fall risk in people with RA. However, increasing foot pain intensity may be an indicator of increased fall risk.

Multiple-fallers also had a slower gait speed than non-fallers/single-fallers. It has been reported that the walking speed requirement for safe and independent ambulation in the community is 1.4 m/s (227). In the current study, 90% of fallers had a gait speed of less than 1.4 m/s which may support an association between decreased gait speed and fall risk. One previous study found no association between gait speed and falls in people with RA (159). The study did not compare multiple-fallers with non-fallers/single-fallers so direct comparison with the current results cannot be made. An association between reduced gait speed and falls has been reported in non-RA populations (228-231). Reduced gait speed may not be the cause of falls but the result

of fear of falling due to prior falls. Fallers with a pre-existing fear of falling tend to adopt a more cautious gait pattern including decreased stride length, increased double support time and decreased walking velocity, in order to increase walking stability (232). However, it is well documented that people with RA generally walk at a slower pace than the non-RA population (97, 99-101, 140) and in the current study the majority of non-fallers (84%) also had a gait speed of less than 1.4 m/s. Therefore, clinical assessment of gait speed alone may not be a reliable indicator of fall risk in this group. An association between delayed propulsion, increased midfoot contact area and decreased gait speed has been reported in people with RA (97). These factors may also be interrelated in terms of the mechanisms for falls and increasing fall risk in the current study.

Foot-related disability and impairment may also be an important indicator of falls risk in people with RA. In the current study, foot-related disability and impairment was independently associated with a fall in the preceding 12 months, with the odds of falling increasing by 17% for each 3 point increase on the Foot Impact Scale activities/participation subscale. One study reported an association between a high score on the Foot Impact Scale activities/participation subscale (>10 points) and a high number of tender, swollen and painful foot joints in people with early disease (97). Painful foot joints and decreased walking speed were found to be predictors of increased Foot Impact Scale activities/participation subscale score (99), and a high Foot Impact Scale activities/participation subscale score was associated with severely deformed feet (100), in people with established RA. Decreased gait speed, foot pain intensity and tender and swollen foot joints were associated with increasing falls risk in the current study, which may indicate a link between these risk factors, increased Foot Impact Scale activities/participation subscale score and falls in people with RA.

People with RA who have previously experienced a fall restrict their activities such as walking, climbing stairs and participating in outings, due to fear of experiencing another fall (157). Therefore, it is possible that an increased score on the Foot Impact Scale activities/participation subscale is also indicative of an increased fear of falling. Analysis of the relationship between the patient-reported outcome measures assessed

in the current study demonstrated medium to high correlations between the Foot Impact Scale, short FES-I, HAQ-II, patient global health and self-report foot pain (Table 7.8). This suggests that self-report questionnaires reflect similar findings with respect to level of disability and impairment in people with RA. As such, the finding relating to the Foot Impact Scale activities/participation subscale score and falls is to be expected in light of the current and previous findings relating to the HAQ-II, fear of falling, foot pain and falls in people with RA.

A number of foot and ankle characteristics assessed in the current study were not associated with falls or falls risk. These included foot problem score, pes planovalgus foot-type, bunion deformity, fine touch sensation (monofilament), ankle range of motion, hallux and lesser toe strength, postural sway, vibration perception threshold and foot muscle strength. However, whilst the differences were not statistically significant, fallers demonstrated worse scores on all foot and ankle measures compared to non-fallers. With the exception of foot muscle strength and vibration perception threshold, all the foot and ankle measures included in the current study were previously identified as fall risk factors in older adults or adults with diabetes mellitus (23, 25, 26, 180, 231). One explanation for the non-significant findings in the current study could be the prevalence and severity of foot problems in the cohort studied compared to the general older adult population. That is, the presence and severity of age-related foot problems that are associated with falls in older adults is greater in adults with established RA. Hence, there may not have been enough variation in the measures of foot and ankle function, in the current study, to discriminate fallers from non-fallers. An analogous scenario would be cognitive impairment, which is a major risk factor for falls in otherwise healthy older people (3). However, a measure of cognitive impairment might not be predictive of falls in a study on people with Alzheimer's disease. Therefore, certain foot and ankle characteristics may be risk factors for falls but not predictive of falls in older adults with established RA.

We found no association between fall risk and footwear in the current study. Footwear can improve postural stability through facilitating somatosensory feedback and

providing mechanical support to the foot (103, 233-235). In contrast, poor footwear type and characteristics can cause postural instability (103, 191, 236). Several epidemiological studies have suggested that inappropriate footwear including ill-fitting shoes (237, 238) and slippers (191, 192), plus going barefoot (239, 240) or wearing socks (239) in the home, contributes to falls in older adults. Structural foot changes associated with RA make it difficult for people to find appropriate shoes that are comfortable, aesthetically acceptable and can accommodate foot deformities (105). Previous studies in RA populations reported that many people wore inappropriate footwear including sandals, jandals, moccasins, slippers and socks (105, 241). In the current study, 49% of participants wore footwear that was classified as 'average' or 'poor' to the study visit. In addition, only 5% of participants reported footwear usually worn indoors that was classified as 'good'; with 72% wearing 'poor' footwear or socks and 23% usually going barefoot. It is possible that, similar to other foot and ankle measures in the current study, footwear may be a factor in falls in people with RA. However, the high prevalence of inappropriate footwear worn by the study cohort meant that footwear type was not associated with falls. In addition, the study only recorded the 'usual' footwear worn, which may not necessarily be the footwear worn at the time of a fall.

8.3: Summary

In summary, cross-sectional analysis revealed a number of clinical characteristics which were associated with increasing fall risk in people with RA. Cardiovascular disease (not including hypertension) was the only clinical feature that was independently associated with a fall in the preceding 12 months; which is likely due to the inclusion of participants with a history of stroke. The findings relating to falls risk and the number of co-morbid conditions and increasing number of medications are of importance with respect to the prevalence of co-morbid conditions and polypharmacy in older people with established RA. Patient-reported outcome measures are important in measuring response to treatment and may also be useful for identifying people with RA at increased fall risk. A range of foot and ankle characteristics were associated with increasing fall risk and may be linked in terms of the underlying mechanisms for falls. However, only one foot-specific measure, midfoot peak plantar pressure, was

independently associated with a fall in the preceding 12 months. A number of foot and ankle features plus footwear were found not to be associated with falls or falls risk. The non-significant results may be due to the high prevalence of foot problems and inappropriate footwear observed in the study cohort, compared to the general older adult population.

CHAPTER 9: PROSPECTIVE STUDY RESULTS

9.1: Introduction

In the 12-month prospective study, participants from the cross-sectional study were followed for 12 months to record their falls. Participants were grouped according to their prospective fall history and compared on all baseline clinical and foot and ankle characteristics. Univariate and multivariate analyses were performed at the end of the 12-month follow-up period in order to answer research question 3) Which foot and ankle characteristics are associated with increasing falls risk and predict the occurrence of falls in people with RA? This chapter will present the results from the 12-month prospective study. Falls incidence for the 12-month follow-up period (prospective falls) will be reported. Participant retention in the study and reasons for loss to follow-up will be described. The results of the primary univariate and multivariate analyses will be reported followed by findings from the secondary and subsequent analyses. The chapter will conclude with a summary of the findings with respect to the research question.

9.2: Participant 12-month retention in the study for falls data and second study visit

Falls data were prospectively collected from 200 participants, with only one participant declining to continue with the 12-month prospective study following the baseline study visit. One hundred and ninety-nine participants took the Fall Calendar. One participant declined to take the calendar but undertook to report any falls to the researcher and agreed to monthly telephone follow-up. One hundred and ninety-six participants completed the full 12-month reporting period. Four participants died during the study year. One participant died at the end of the study year and before the second study visit. One-hundred and eighty-two participants attended a second study visit after 12 months. Reasons for non-attendance to a second study visit included: died (n=5), unwell (n=8), moved away (n=3) and refused (n=2).

9.3: Falls incidence

Falls incidence is reported in accordance with the ProFaNE guidelines for falls research (169). In total 177 falls were reported over 198.7 person-years, with a falls rate of 891 per thousand person-years or 0.89 falls per person. Figure 9.1 shows how the person-years were calculated.

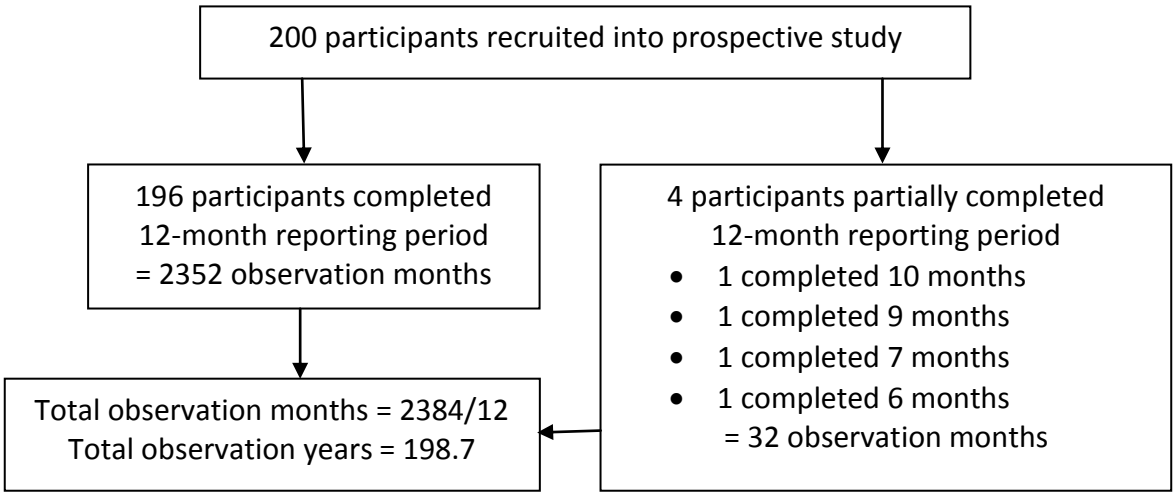

Figure 9.1: Flow diagram showing how person-years were calculated

Of the 200 participants who were prospectively followed, 84 (42%) fell at least once and 39 (20%) experienced more than one fall. One hundred and sixteen (58%) participants did not fall during the 12-month follow-up period. The frequency of falls is displayed in Table 9.1.

Table 9.1: Frequency of prospectively recorded falls, n=177 total falls

Number of falls	Number of participants
0	116
1	45
2	19
3	5
4	9
5	3
6	1
9	1
13	1

9.4: Primary univariate analysis comparing non-fallers and fallers

The results of univariate analysis comparing the baseline characteristics of non-fallers and fallers over 12 months are presented in Table 9.2. Results shown are for comparisons with P<0.15. Compared to non-fallers, those who fell had higher tender joint count (P=0.005), took more medications (P=0.039) and were more likely to receive anticoagulant (P=0.009) and psychotropic (P=0.028) medication. Fallers were also more likely to use an assistive device (P=0.007) than non-fallers. The probability of a 1-year follow-up fall significantly increased if the participant had a history of falling (P=0.009) or had experienced multiple falls (P=0.014) during the preceding 12 months. Specifically, of those with a 1-year history of falls preceding the baseline study visit, 59 (50%) reported a 1-year follow-up fall, whereas of those with no 1-year history of falls, only 25 (30%) reported a 1-year follow-up fall. Likewise, of those participants who reported a 1-year history of multiple falls preceding the baseline study visit, 39 (53%) reported a 1-year follow-up fall and of those with no 1-year history of multiple falls, 45 (35%) reported a 1-year follow-up fall. In terms of foot and ankle characteristics, fallers were more likely to have the presence of foot or ankle tender joints (P=0.028) and increased antero-posterior (AP) sway (P=0.040) and medio-lateral (ML) sway (P=0.042) in eyes-closed conditions. No other foot and ankle characteristics were significantly different between the two groups.

Table 9.2: Univariate analysis of non-fallers and fallers over 12 months. Comparisons with P<0.15 are shown. Data are presented as mean (SD) unless specified.

	Non-fallers n=116	**Fallers n=84**	**P value**
Clinical characteristics			
Number of medications	3.8 (2.1)	4.5 (2.3)	0.039*
Taking 4 or more medications, n (%)	62 (53)	55 (65)	0.119
Cardiovascular disease, n (%)	12 (10)	17 (20)	0.079
Diabetes mellitus, n (%)	14 (12)	4 (5)	0.126
Depression or bipolar disorder, n (%)	6 (5)	10 (12)	0.142
Opiates, n (%)	6 (5)	11 (13)	0.084
Anticoagulants, n (%)	2 (2)	9 (11)	0.009*
Psychotropic medication, n (%)	15 (13)	22 (26)	0.028*
Patient self-reported pain (VAS 0-100), mm	36.1 (26.5)	42.4 (27.0)	0.086
Tender joint count	9 (11)	14 (14)	0.005*
Fear of falling (short FES-I)	12 (5)	13 (5)	0.143
Use of an assistive device, n (%)	24 (21)	33 (39)	0.007*
12-month fall history, n (%)	59 (51)	59 (70)	0.009*
12-month multiple fall history, n (%)	33 (28)	39 (46)	0.014*
Foot and ankle characteristics			
Presence of foot or ankle tender joints, n (%)	65 (56)	60 (72)	0.028*
Eyes-open ML sway, mm	13.4 (7.8)	15.4 (8.2)	0.113
Eyes-closed AP sway, mm	27.7 (10.6)	31.8 (15.5)	0.040*
Eyes-closed ML sway, mm	16.1 (7.6)	19.2 (11.9)	0.042*

* significant at P<0.05

VAS, Visual analogue scale; FES-I, Falls efficacy scale international; ML, medio-lateral; AP, antero-posterior

9.5: Primary multivariate analysis of predictive risk factors comparing non-fallers and fallers

Multivariate logistic regression analysis identified associations between potential fall risk factors assessed at baseline and falls during the 12-month follow-up period. The results comparing all fallers with non-fallers using logistic regression analyses are shown in Table 9.3. Ten variables, plus age, were entered into the original model including: number of medications, opiates, psychotropic medication, cardiovascular disease, patient self-reported pain (VAS), use of an assistive device, FES-I, presence of foot or ankle tender joints, presence of foot or ankle swollen joints and eyes-closed AP sway. To avoid an underpowered model, anticoagulants and diabetes mellitus variables were excluded due to small numbers. To avoid multicollinearity, taking four or more medications, depression or bipolar disorder, tender joint count, eyes-open and eyes-closed ML sway and 12-month fall history, were excluded from the model. The final model contained two variables; psychotropic medication (OR 2.35, P=0.025) and presence of foot or ankle tender joints (OR 1.95, P=0.034) which were independent predictors of prospective falls (P<0.05). The final model explained 9% (Nagelkerke R squared) of the variance in falls status and correctly predicted 66% of falls.

Table 9.3: Results from backwards stepwise logistic regression analyses comparing non-fallers (n=116) and fallers (n=84) on all predictor variables and controlling for age. Associations with P<0.05 are shown.

	Odds ratio (95% confidence interval)	**P value**
Psychotropic medication	2.35 (1.11-4.95)	0.025
Presence of foot or ankle tender joints	1.95 (1.05-3.62)	0.034

Variables included in the model: age, number of medications, opiates, psychotropic medication, cardiovascular disease, patient self-reported pain (VAS), assistive device, FES-I, presence of foot or ankle tender joints, presence of foot or ankle swollen joints and eyes-closed AP sway.

The logistic regression analysis was then repeated including 12-month fall history (defined as one or more falls experienced in the 12 months preceding baseline) as a predictor variable. The results are shown in Table 9.4. The inclusion of 12-month fall history into the logistic regression modelling resulted in the variable 'presence of foot or ankle tender joints' being removed from the model, as it was no longer statistically significant at P<0.05. The final model contained two variables; psychotropic medication (OR 2.34; P=0.025) and 12-month fall history (OR 2.27; P=0.008), which were independent predictors of prospective falls. The final model explained 10% (Nagelkerke R squared) of the variance in falls status and correctly predicted 61% of falls.

Table 9.4: Results from backwards stepwise logistic regression analyses comparing non-fallers (n=116) and fallers (n=84) on all predictor variables, including 12-month fall history, and controlling for age. Associations with P<0.05 are shown.

	Odds ratio (95% confidence interval)	**P value**
Psychotropic medication	2.34 (1.11-4.94)	0.025
12-month fall history	2.27 (1.24-4.16)	0.008

Variables included in the model: age, number of medications, opiates, psychotropic medication, cardiovascular disease, patient self-reported pain (VAS), use of an assistive device, FES-I, presence of foot or ankle tender joints, presence of foot or ankle swollen joints, eyes-closed AP sway and 12-month fall history.

9.6: Secondary univariate analysis

9.6.1: Comparing non-fallers, single-fallers and multiple-fallers

The results of univariate analysis comparing non-fallers, single-fallers and multiple-fallers, at 12-months, are presented in Table 9.5. Results shown are for comparisons with P<0.15 and overall P values are reported. When comparing the three groups, there were no significant differences between non-fallers and single-fallers, or single-fallers and multiple-fallers on any of the continuous variables (P>0.05). However, significant differences were found between multiple-fallers and non-fallers on some variables. Compared to non-fallers and single-fallers at 12-months, at baseline, those experiencing multiple falls were more likely to use an assistive device (P=0.003) and have a 12-month fall history (P=0.003) or 12-month multiple fall history (P<0.001). Multiple-fallers also had significantly higher mean tender joint count (P=0.001) than non-fallers. There were also significant differences between the three groups on presence of foot or ankle tender joints (P=0.008) and use of anticoagulants (P=0.012).

Table 9.5: Univariate analysis of non-fallers, single-fallers and multiple-fallers. Comparisons with P<0.15 are shown. Data are presented as mean (SD) unless specified.

	Non-fallers n=116	**Single-fallers n=45**	**Multiple-fallers n=39**	**Overall P value**
Clinical characteristics				
Cardiovascular disease, n (%)	12 (10)	9 (20)	8 (21)	0.146
Number of medications	3.8 (2.1)	4.7 (2.3)	4.2 (2.2)	0.080
Opiates, n (%)	6 (5)	7 (16)	4 (10)	0.096
Anticoagulants, n (%)	2 (2)	6 (13)	3 (8)	0.012*
Psychotropic medication, n (%)	15 (13)	11 (24)	11 (28)	0.053
Tender joint count	9 (11)	12 (14)	17 (14)	0.003*
Use of an assistive device, n (%)	24 (21)	14 (31)	19 (49)	0.003*
12-month fall history, n (%)	59 (51)	27 (60)	32 (82)	0.003*
12-month multiple fall history, n (%)	33 (28)	14 (31)	25 (64)	<0.001*
Foot and ankle characteristics				
Presence of foot or ankle tender joints, n (%)	65 (56)	28 (62)	32 (84)	0.008*
Monofilament sites felt, (0-12)	10 (3)	11 (3)	9 (4)	0.147
Foot inversion strength, N	33.0 (17.6)	29.0 (13.6)	37.7 (19.1)	0.113
Eyes-closed AP sway, mm	27.7 (10.6)	31.2 (13.7)	32.6 (17.5)	0.080
Eyes-closed ML sway, mm	16.1 (7.6)	18.9 (10.8)	19.5 (13.3)	0.086
Patient-reported foot-related disability and impairment ($FIS_{IF)}$	10 (5)	10 (5)	12 (5)	0.124

* significant at P<0.05

AP, antero-posterior; ML, medio-lateral; FIS_{IF}, Foot Impact Scale impairment/footwear subscale

9.6.2: Comparing the combination of non-fallers/single-fallers with multiple-fallers

The results of univariate analysis comparing the combination of non-fallers/single-fallers with multiple-fallers, at 12-months, are presented in Table 9.6. Results shown are for comparisons with P<0.15. Multiple-fallers were more likely to use an assistive device (P=0.004) and have a 12-month fall history (P=0.002) or 12-month multiple-fall history (P<0.001), compared to the combination of non-fallers/single-fallers. Multiple-fallers also had a greater mean tender joint count (P=0.002) and were more likely to present with foot or ankle tender joints (P=0.004) compared to the non-fallers/single-fallers group. Multiple-fallers also scored worse on the FIS_{IF} subscale (P=0.041) indicating greater foot-related disability and impairment.

Table 9.6: Univariate analysis of non-fallers/single-fallers and multiple-fallers. Comparisons with P<0.15 are shown. Data are presented as mean (SD) unless specified.

	Non-fallers/ single-fallers=161	**Multiple-fallers=39**	**P value**
Clinical characteristics			
Number of co-morbid conditions	1.12 (1.04)	1.41 (1.12)	0.110
Psychotropic medication, n (%)	26 (16)	11 (28)	0.131
Patient self-reported pain (VAS 0-100), mm	37.1 (26.9)	43.5 (25.6)	0.081
Tender joint count	10 (12)	17 (14)	0.002*
HAQ-II score	0.85 (0.61)	0.97 (0.63)	0.134
Fear of falling (short FES-I)	12 (5)	13 (5)	0.080
Use of an assistive device, n (%)	38 (24)	19 (49)	0.004*
12-month fall history, n (%)	86 (53)	32 (82)	0.002*
12-month multiple fall history, n (%)	47 (29)	25 (64)	<0.001*
Foot and ankle characteristics			
Presence of foot or ankle tender joints, n (%)	93 (58)	32 (84)	0.004*
Monofilament sites felt, (0-10)	10.4 (2.7)	9.3 (3.5)	0.056
Inversion strength, N	32 (17)	38 (19)	0.081
Patient-reported foot-related disability and impairment			
FIS_{TOTAL}	24 (12)	28 (12)	0.081
FIS_{IF}	10 (5)	12 (5)	0.041*

* significant at P<0.05

VAS, visual analogue scale; HAQ-II, Health Assessment Questionnaire-II, FES-I, Falls Efficacy Scale International; FIS_{TOTAL}, Foot Impact Scale total score; FIS_{IF}, Foot Impact Scale impairment/footwear subscale

9.7: Secondary multivariate analysis of predictive risk factors comparing the combination of non-fallers/single-fallers with multiple-fallers

Multivariate logistic regression analysis identified associations between potential fall risk factors, assessed at baseline, and multiple falls during the 12-month follow-up period. The results comparing all non-fallers/single-fallers with multiple-fallers using logistic regression analyses are shown in Table 9.7. Eight variables, plus age, were entered into the original model including: number of co-morbid conditions, psychotropic medication, patient self-reported pain (VAS), use of an assistive device, presence of foot or ankle tender joints, presence of foot or ankle swollen joints, monofilament score and FIS_{IF} subscale score. To avoid multicollinearity (r>0.5), 12-month fall history, HAQ-II, short FES-I, FIS_{TOTAL} and tender joint count were excluded from the model. The final model contained one variable; presence of foot or ankle tender joints (OR 3.79, P=0.005) which was a predictor of prospective multiple falls (P< 0.05). The model explained 9% (Nagelkerke R squared) of the variance in falls status and correctly predicted 81% of falls.

Table 9.7: Results from backwards stepwise logistic regression analyses comparing non-fallers/single-fallers (n=161) with multiple-fallers (n=39) on all predictor variables and controlling for age. Associations with P<0.05 are shown.

	Odds ratio (95% confidence interval)	**P value**
Presence of foot or ankle tender joints	3.79 (1.50-9.60)	0.005

Variables included in the model: age, number of co-morbid conditions, psychotropic medication, patient self-reported pain (VAS), use of an assistive device, presence of foot or ankle tender joints, presence of foot or ankle swollen joints, monofilament score and FIS_{IF} subscale score.

The logistic regression analysis comparing the combination of non-fallers/single-fallers with multiple-fallers was then repeated including 12-month fall history as a predictor variable. The results are shown in Table 9.8. With the inclusion of 12-month fall history in the model, presence of foot or ankle tender joints (OR 3.26; P=0.014) and 12-month fall history (OR 3.33; P=0.008) were found to be independent predictors of falls. The final model explained 15% (Nagelkerke R squared) of the variance in falls status and correctly predicted 81% of falls.

Table 9.8: Results from backwards stepwise logistic regression analyses comparing non-fallers/single-fallers (n=161) with multiple-fallers (n=39) on all predictor variables, including 12-month fall history, and controlling for age. Associations with P<0.05 are shown.

	Odds ratio (95% confidence interval)	**P value**
Presence of foot or ankle tender joints	3.26 (1.27-8.40)	0.014
12-month fall history	3.33 (1.36-8.13)	0.008

Variables included in the model: age, number of co-morbid conditions, psychotropic medication, patient self-reported pain (VAS), assistive device, presence of foot or ankle tender joints, presence of foot or ankle swollen joints, monofilament score, FIS_{IF} subscale score and 12-month fall history.

9.8: Negative binomial regression modelling

Multivariate analysis was repeated using negative binomial regression modelling, with the number of falls experienced during the 12-month follow-up period as a continuous dependent variable. Predictors included all variables significant at P<0.15 on univariate analysis, excluding 12-month fall history. The final model contained presence of foot or ankle tender joints (P=0.019) and use of an assistive device (P=0.008) as being significantly associated with increasing number of falls. The analysis was then repeated with the inclusion of 12-month fall history as a predictor variable. The final model contained 12-month fall history (P<0.001), presence of foot or ankle tender joints (P=0.019) and use of an assistive device (P<0.001) as being significantly associated with increasing number of falls.

9.9: Subsequent analysis

9.9.1: Analysis of foot and ankle characteristics measured at 12-months

Participants were grouped according to falls experienced during the 12-month prospective study period. Univariate analysis comparing non-fallers and fallers on all foot and ankle characteristics, measured at the second study visit at 12-months, identified presence of foot or ankle tender joints as the only variable to be significantly different between the groups (P=0.014). Univariate analysis comparing the combined group of non-fallers/single-fallers with multiple-fallers on all foot and ankle characteristics, measured at 12-months, found no significant differences between the two groups. Appendix 9 shows the results for comparisons with P<0.15.

9.9.2: Comparing foot and ankle characteristics at baseline and 12-months

Univariate analysis compared all foot and ankle characteristics measured at baseline with foot and ankle characteristics measured at 12-months. The results demonstrated several foot and ankle characteristics that were significantly different at P<0.05. These included presence of foot or ankle swollen joints, foot problem score, ankle range of motion, inversion strength, rearfoot peak plantar pressure, monofilament score and FIS_{IF} subscale score. However, with the exception of presence of foot or ankle swollen joints, the mean difference between each foot and ankle characteristic at baseline and 12-months was not clinically significant. Appendix 10 shows the results of the analysis.

9.10: Summary of prospective findings

9.10.1: Findings for clinical characteristics

Clinical characteristics found to be significantly different between non-fallers and fallers on univariate analysis were; number of medications, anticoagulants, psychotropic medication, tender joint count, use of an assistive device and 12-month fall history. Secondary univariate analysis did not provide any further findings. Multivariate analysis, using logistic regression modelling, identified use of psychotropic medication as an independent predictor of one or more falls. 12-month fall history was also an independent predictor of one or more falls and multiple (≥2) falls.

9.10.2: Findings for research question 3

Which foot and ankle characteristics are associated with increasing falls risk and predict the occurrence of falls in people with RA?

In comparing baseline measures for participants who fell during the 12-month prospective study period with those who did not fall, the foot and ankle variables that were significantly different included presence of foot or ankle tender joints and eyes-closed AP and ML postural sway. Secondary univariate analysis comparing the combined group of non-faller/single-fallers with multiple-fallers demonstrated one additional foot and ankle variable; patient-reported foot-related disability and impairment (FIS_{IF} subscale score), as being significantly different between the two groups. Multivariate analysis, using logistic regression modelling, identified presence of foot or ankle tender joints to be the only foot and ankle variable which was an independent predictor of one or more falls; when controlling for age but excluding 12-month fall history. Presence of foot or ankle tender joints was also an independent predictor of multiple (≥2) falls and the variable remained significant with the subsequent inclusion of 12-month fall history into the model. Negative binomial regression modelling also identified presence of foot or ankle tender joints as being significantly associated with an increasing number of falls. Therefore, based on the current results, we can reject the null hypothesis and state that specific foot and ankle characteristics, in the rheumatoid foot, are associated with increasing falls risk and predict the occurrence of falls in people with RA.

CHAPTER 10: PROSPECTIVE STUDY DISCUSSION

10.1: Introduction

This chapter will discuss the findings for the 12-month prospective study. Falls incidence will be discussed in addition to the findings relating to fall history as a predictor of falls. Key findings relating to clinical and foot and ankle characteristics associated with falls and falls risk will be compared with the cross-sectional study and previous prospective falls studies in people with RA. The chapter will conclude with a summary of the 12-month prospective study findings.

10.2: Discussion

In this study, 42% of participants fell at least once during the 12-month follow-up period. However, as acknowledged in Chapter 8, the recruitment strategy at baseline may have been biased towards participants with a history of falls. The consequences of a fall, such as injury or fear of falling, increase the risk of experiencing another fall (3, 21). Therefore, if a recruitment bias existed at baseline, it would flow onto the 12-month prospective study thus affecting the results for falls incidence due to the number of past fallers who would have been predisposed to future falls. In order to avoid recruitment bias, the participants would have to be blinded to the study outcomes.

Findings for increased fall risk have been reported in adults with other long-term chronic conditions including Parkinson's disease (242-244), diabetes mellitus (16, 17, 231), multiple sclerosis (14, 15), stroke (219) and other forms of inflammatory arthritis (18-20). Previous studies have identified disease-specific complications; such as distal sensory neuropathy in people with diabetes mellitus (245), and gait disturbances in people with Parkinson's disease (242), as risk factors for falls. Similarly, disease-related impairments and reduced functioning may contribute to falls risk in adults with RA. However, our recently published systematic review reported a dearth of evidence to support RA-disease specific fall risk factors (224). The current study adds to existing evidence for fall risk factors in older adults with established RA.

In the current study, 12-month fall history was a significant predictor of prospective falls. This finding was expected and is in agreement with several previous prospective studies in RA cohorts (21, 161, 181) as well as studies in older adults (3) and other at-risk populations (14, 231, 243). Having a history of falls is considered to be the most powerful predictor of future falls, over and above all other potential fall risk factors (246). However, fall history as a predictor of future falls will not identify an individual who has not previously fallen but may still be at increased fall risk. In addition, fall history cannot be modified or mitigated in order to prevent future falls.

10.2.1: Clinical characteristics

We found increasing number of medications (polypharmacy) to be associated with increasing falls risk. The finding is in agreement with the cross-sectional study and supported by one previous prospective study in people with RA in which Stanmore (21) reported taking four or more medications more than doubled the risk of falling. The mechanisms underlying polypharmacy and falls in older adults have been reported to include cognitive impairment, urinary incontinence, adverse drug-drug interactions, inappropriate medication use and non-adherence due to complex drug regimes (220, 247). Of particular importance is the current finding for psychotropic medication which was the only variable to remain in the logistic regression model, comparing non-fallers and fallers, when 12-month fall history was included as a predictor variable. Our findings are in agreement with two previous studies in people with RA (21, 155). Stanmore (21) found psychotropic medications to be associated with prospective falls and Armstrong (155) found antidepressants to be independently associated with falls in the preceding 12 months. Psychotropics are commonly prescribed as an adjunct therapy for chronic arthritic pain as well as depression (84). In the current study, 18% of participants were taking psychotropic medication and, of those, 59% experienced one or more falls during the prospective 12-month study period. This is similar to the study by Stanmore (21) in which 19% of the cohort were taking psychotropic medication with 55% experiencing at least one fall during the 12-month follow-up period. Psychotropic medications have been found to be associated with falls in several older adult studies (175, 248-250). The current findings confirm that use of psychotropic medication also increases the risk of falls in adults with RA.

The finding for increasing tender joint count as a risk factor for falls is in agreement with the cross-sectional study findings but conflicts with two previous prospective studies that found no association between tender joint count and falls in people with RA (21, 160). This disparity may be due to differences between the studies in the joints assessed. In the current study, 34 joints in the foot and ankle were included in the total joint count. The two previous studies did not include any foot or ankle joints in the assessment (21, 160). Joint counts are used as a measure of disease activity in people with RA (36). Other measures of RA disease activity that were assessed in the current study, including the HAQ-II, DAS28-CRP and patient self-reported pain, were not associated with falls or falls risk. In contrast, presence of foot or ankle tender joints was an independent predictor of falls. Therefore, the current finding for increasing tender joint count and falls risk could be due to the inclusion of the foot and ankle in the total joint count.

Tenderness in the foot and ankle is generally indicative of synovitis associated with active RA (46). However, synovitis can be present in the joints of the feet in the absence of more global disease activity (31, 251-253). A previous study reported presence of synovitis in the forefoot of patients classified as being in clinical remission according to the DAS28; which does not include the joints of the feet (251). Another study reported tender and swollen joints, including the foot and ankle, in people with RA with a zero score for the 28-joint count (252). It is unclear why active foot synovitis can persist in the absence of generalised inflammation. However, previous studies included patients with early RA which may reflect a tendency for greater foot involvement in the early stages of the disease (251-253).

In the current study of older people with established RA, it is possible that foot and ankle joint tenderness may be indicative of chronic inflammation due to increased mechanical loading on deformed and prominent joints in addition to synovitis associated with active RA (99). Forefoot bursae, detectable on musculoskeletal ultrasound, are common in people with established RA and significantly associated with foot pain, disability and impairment (197, 254, 255). Bursae can be anatomic or adventitious. Anatomic bursae form between the metatarsals, have a synovial lining,

and are associated with inflammation in active RA (255). Conversely, adventitious bursae have no synovial lining and form in the plantar fat pad in response to mechanical irritation (255). Regardless of type, forefoot bursae contribute to foot symptoms in people with RA and may be a contributory factor in the findings relating to foot and ankle joint tenderness in the current study.

We found that fallers were more likely to use an assistive device than non-fallers which is in agreement with a previous RA study (181) and several older adult studies (3). Assistive devices included walking sticks, crutches and walkers. In contrast, Hayashibara (160) found no association between falls and ambulatory ability, with and without aids, in people with RA. The disparity in findings may be due to differences in methodology. In the current study, 'use of an assistive device' did not necessarily mean that the participant could not ambulate without the device. However, Hayashibara (160) differentiated between people who could only ambulate if they had an assistive device from those who could walk without an assistive device. Therefore, direct comparison between the study findings cannot be made. The findings of the current study and previous older adult studies likely reflect an increased level of walking disability in fallers compared to non-fallers. In addition, the increased risk of falls demonstrated in the current study may be due to a past history of falls, and subsequent fear of falling, rather than the assistive device per se.

A number of clinical characteristics, assessed in the current study, were not associated with falls or falls risk. We found no association between falls and increasing disease duration or number of co-morbid conditions. The findings support previous prospective studies in people with RA (21, 160, 161) but conflict with our cross-sectional study. Similar to the cross-sectional study, falls were independent of age, female sex, BMI, general pain and DAS28-CRP score. The non-significant findings for age, female sex and BMI are in agreement with previous prospective studies in RA (21, 160, 161). In contrast, general pain was a predictor of falls in two prospective studies (21, 161) and correlated with falls in a further study (181), and increased DAS28 score was associated with increased fall risk in one prospective study (21). In addition, there was no association between falls and functional ability (HAQ-II), in the current study,

which is in agreement with two previous studies (160, 161) but conflicts with another study (21). Falls were also independent of swollen joint count in the current study, which is in agreement with one study (21) and conflicts with another (160). General pain, DAS28, HAQ-II and swollen joint count are all measures of RA disease activity. The conflicting evidence demonstrated in the current study, as well as the cross-sectional study and the systematic review, suggests that measures of RA disease activity may be unreliable as indicators of fall risk in this population.

10.2.2: Foot and ankle characteristics

During the 12-month follow-up period there were no clinically significant changes in the measures of foot and ankle structure and function (Appendix 10). This finding was expected and reflects the chronic and stable nature of foot disease in people with established RA. Joint tenderness in the feet or ankles was the only foot and ankle characteristic to be an independent predictor of falls. This supports the cross-sectional study findings which found an association between presence of foot or ankle tender joints and increasing falls risk. One previous prospective falls study in an RA population reported findings related to tenderness in the lower extremity joints as a risk factor for falls (21). However, lower extremity joints included the hips, knees and ankles only, and tender and swollen joints were reported as a combined variable (21). Therefore, the findings cannot be directly compared with the current results.

The finding relating to increased postural sway (eyes-closed) and increasing falls risk was similar to a previous prospective study in 84 Japanese women with RA (160). However, the previous study assessed postural sway in the eyes-open condition only (160). Our findings suggest that the added challenge of maintaining postural stability, in the absence of visual stimuli, may increase fall risk in some people with RA. Several studies have found postural sway to be significantly increased in people with RA compared to healthy controls (140, 150, 151). Visual dependency for postural control has also been found to be greater in people with RA compared to control participants (140, 151). In particular, people with RA appear to be more markedly dependent on visual information to maintain balance in the AP direction; which may be a compensation for deficits in afferent sensory information from the lower limbs (151).

The maintenance of balance relies on input from the somatosensory (tactile and proprioceptive), visual and vestibular systems (147). In the current study, plantar afferent sensory function was assessed as fine touch sensation (monofilament) and vibration perception (biothesiometer). There was no association found between these measures of sensory function and falls. However, we did not assess proprioceptive function which is also important in the maintenance of balance. Proprioception can be decreased in people with RA (256, 257) leading to difficulties in maintaining postural control (172). Chronic inflammatory processes lead to proprioceptive impairments which consequently affect the afferent signals generated by the mechanoreceptors in weight-bearing joints (256). Disruption to proprioceptive feedback and automatic postural responses can also occur due to decreased muscle strength, muscle atrophy and contracture, decreased range of motion, instability of weight-bearing joints and impaired mobility associated with RA (257). Therefore, in addition to visual deficits, impaired proprioception may be a causative factor in increased postural sway leading to falls in people with RA.

The finding relating to multiple falls and increased Foot Impact Scale (impairment/footwear subscale score) provides further evidence that foot-related disability and impairment is an important indicator of fall risk in people with RA. Multiple-fallers also had a higher Foot Impact Scale total score than the combined group of non-fallers/single-fallers. The mean difference in the Foot Impact Scale total score of 4 points was not statistically significant. However, a change in Foot Impact Scale score of ≥3 points is considered to be clinically relevant (198). The findings from the cross-sectional and prospective analyses suggest that there is a relationship between fall risk and an individual's perception of their foot-related disability and impairment in people with established RA.

Similar to the cross-sectional study, we found no association between falls and a number of foot and ankle characteristics including: foot problem score, pes planovalgus foot-type, bunion deformity, fine touch sensation, vibration perception threshold, ankle range of motion, hallux and lesser toe strength, foot muscle strength, foot pain intensity, gait speed, presence of foot or ankle swollen joints, plantar

pressure variables and footwear. Fallers demonstrated worse scores for all foot and ankle measures, with the exception of gait speed and foot dorsiflexion strength. However, the differences in mean scores between non-fallers and fallers were not statistically significant. Of note are the non-significant findings for foot pain intensity, gait speed, presence of foot or ankle swollen joints and midfoot plantar pressure variables; which were all associated with falls in the cross-sectional study. The disparity in findings relating to the foot and ankle, between the cross-sectional and prospective studies, is likely due to differences in the falls outcome measure. Two previous prospective studies also found no association between foot pain and falls in adults with RA (21, 181) and one previous study found no association between gait speed and falls (160). Foot joint swelling and plantar pressure variables have not been previously assessed in a prospective RA falls study so comparisons cannot be made.

10.3: Summary

In summary, the 12-month prospective study supported previous reports of increased falls risk in adults with RA. 12-month fall history was a significant predictor of falls. However, fall history cannot predict future falls in people who have not previously fallen, nor can fall history be mitigated to reduce the risk of falls. The prospective analysis confirmed the findings of the cross-sectional study with respect to increasing number of medications and tender joint count, which were associated with increasing falls risk. In addition, psychotropic medication was an independent predictor of falls which supported previous studies in people with RA and older adults. Presence of foot or ankle tender joints was the only foot-specific measure found to be an independent predictor of falls. However, patient-reported foot-related disability and impairment may be an important indicator of increased fall risk. Eyes-closed postural sway was also associated with increasing falls risk and may indicate a greater visual dependency for postural control in fallers compared to non-fallers. A number of foot and ankle characteristics were not associated with falls, which was similar to the cross-sectional study.

CHAPTER 11: THESIS OVERVIEW AND CLINICAL IMPLICATIONS

11.1: Introduction

This chapter will provide an overview of the findings for the cross-sectional and prospective studies. In addition, a synthesis diagram will be presented which draws together the findings for both studies and explores the potential interrelationships between the foot and ankle fall risk factors identified in the current study. The study limitations and strengths will be described followed by a discussion on clinical implications and future work.

11.2: Aims of the thesis

The thesis was concerned with investigating whether foot and ankle characteristics are associated with falls or falls risk in adults with RA. In Chapter 3, the systematic review pertaining to falls in RA identified a number of clinical and RA-related fall risk factors. The review also identified wide variation in methodology for collecting falls data and a significant lack of evidence relating to specific foot and ankle measures and fall risk in people with RA. Therefore, the primary objective of the current thesis was to evaluate a range of foot and ankle characteristics, as fall risk factors, in a group of adults with RA.

The thesis consisted of two observational studies. Stage 1 was a cross-sectional study that identified foot and ankle characteristics associated with falls in the preceding 12 months. Stage 2 was a 12-month prospective study that identified foot and ankle characteristics which predict falls. ProFaNE consensus guidelines (169) for falls research were followed to ensure a valid and reliable methodology for the collection of falls data. Foot and ankle measures that have been validated for use in people with RA, or older adults, were used in the study. All assessments were able to be performed in a clinical environment.

11.3: Overview of thesis findings

The thesis reported retrospective falls incidence of 59% and prospective falls incidence of 42%. The findings were consistent with previous reports in people with RA. However, the falls data may not be a true representation of the general population of people with RA. The thesis investigated differences in clinical and foot and ankle characteristics between fallers and non-fallers using univariate analysis. In addition, characteristics that were associated with a history of falls, or predictors of falls, were identified using multivariate analysis. The complexity of falls is such that no one factor can be identified as the cause of any given fall event. In addition, fall risk factors are likely to be interrelated and hence strongly correlated. Therefore, the identification of factors which are independently associated with falls, or predictors of falls, is limited by multicollinearity. However, it can be argued that risk factors that are potential causes of falls, but not predictors of falls, are of equal clinical importance when considering falls prevention.

Fall history was a significant predictor of future falls which was in agreement with previous studies in RA (21, 161, 181), diabetes mellitus (231), Parkinson's disease (243), multiple sclerosis (14) and healthy older adults (3). In addition, the thesis provides novel evidence for clinical and foot and ankle characteristics that are predictors of falls, associated with falls or associated with increasing falls risk. Table 11.1 summarises the significant findings for the cross-sectional study and Table 11.2 summarises the significant findings for the 12-month prospective study. Non-significant findings were also of importance including age, gender, BMI and measures of RA disease activity. A number of foot and ankle characterises, that are associated with falls in older adults, were found not to be associated with falls in the current study. The non-significant findings relating to the foot and ankle may be due to the high prevalence and severity of foot disease in the cohort studied compared to the general older adult population.

Table 11.1: Summary of significant findings from the cross-sectional study

Clinical characteristics	**Association with falls or falls risk**	**Comparison with existing evidence in RA (ref)**
RA disease duration	Associated with increasing falls risk	Supports (158) Conflicts (159, 162)
Co-morbid conditions	Associated with increasing falls risk	Supports (159)
Cardiovascular disease	Independently associated with falls in the preceding 12 months	Novel finding
Medications (increasing number)	Associated with increasing risk of multiple falls	Supports (155)
Combination DMARD therapy	Independently associated with multiple falls in the preceding 12 months	Novel finding
Tender joint count	Associated with increasing risk of multiple falls	Supports (158)
HAQ-II score	Associated with increasing falls risk	Supports (155, 158, 162)
Patient global assessment of health (100mm VAS)	Associated with increasing risk of multiple falls	Supports (158)
Fear of falling (short FES-I score)	Associated with increasing falls risk	Supports (157, 162)
Foot and ankle characteristics		
Midfoot peak plantar pressure	Independently associated with falls in the preceding 12 months	Novel finding
Midfoot pressure-time integral	Associated with increasing falls risk	Novel finding
Presence of foot or ankle tender joints	Associated with increasing falls risk	Novel finding
Presence of foot or ankle swollen joints	Associated with increasing falls risk	Novel finding
Foot pain intensity (100mm VAS)	Associated with increasing risk of multiple falls	Novel finding
Gait speed	Associated with increasing risk of multiple falls	Conflicts (159)
Patient-reported foot-related disability and impairment (FIS_{AP})	Independently associated with falls in the preceding 12 months	Novel finding

Table 11.2: Summary of significant findings from the 12-month prospective study

Clinical characteristics	**Association with falls or falls risk**	**Comparison with existing evidence in RA (ref)**
Medications (increasing number)	Associated with increasing falls risk	Supports (21)
Psychotropic medication	Independent predictor of falls	Supports (21, 155)
Tender joint count	Associated with increasing falls risk	Conflicts (21, 160)
Use of an assistive device	Associated with increasing falls risk	Supports (181) Conflicts (160)
Foot and ankle characteristics		
Presence of foot or ankle tender joints	Independent predictor of falls	Novel finding
Eyes-closed postural sway	Associated with increasing falls risk	Novel finding
Patient-reported foot-related disability and impairment (FIS_{IF})	Associated with increasing risk of multiple falls	Novel finding

11.4: Synthesis of thesis findings

Figure 11.1 provides a synthesis of the current findings from the cross-sectional and 12-month prospective studies. The synthesis diagram serves to graphically depict the complex, multifactorial causes of falls in people with RA and proposes hypothetical interrelationships between the foot and ankle characteristics found to be associated with falls and fall risk. In addition to foot and ankle fall risk factors, we found a number of clinical characteristics that were associated with falls. Clinical characteristics may also impact on the foot and ankle, and hence contribute to falls and fall risk. For example, there is a relationship between RA disease activity (DAS28) and patient-reported measures of foot-related disability and impairment (197), and fear of falling is associated with decreased gait speed, in people with RA (159). The synthesis diagram includes the clinical characteristics found to be significant in the current study, to acknowledge their role in falls in RA.

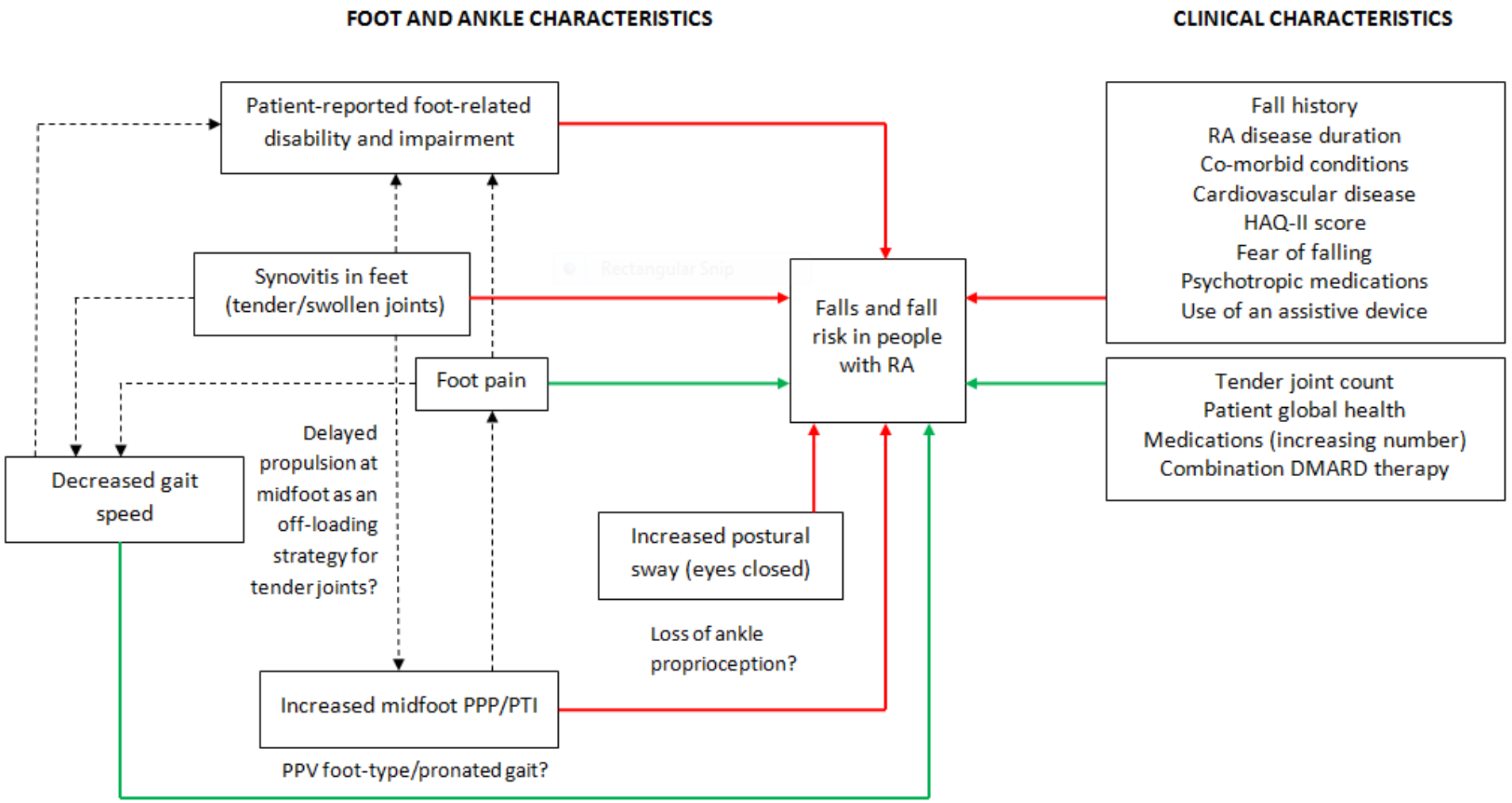

Figure 11.1: Synthesis of findings for the cross-sectional and prospective studies

Red line indicates association with falls (≥1). Green line indicates association with multiple falls (≥2)
Broken line indicates possible interrelationships between foot and ankle fall risk factors

It is currently unknown whether interrelationships between foot and ankle characteristics contribute to falls. Similarly, the mechanisms underlying the associations between foot and ankle characteristics and falls are unclear. Lower extremity function during weight-bearing activities occurs in a closed kinematic chain and clinical studies indicate that foot and ankle mechanics may be related (258). Therefore, interdependence between foot and ankle characteristics, particularly relating to foot function, is possible. In Chapter 8 we speculated based on the current evidence for foot function in people with RA. The following summarises the hypothetical interrelationships depicted in Figure 11.1.

- Increased midfoot peak plantar pressure and pressure-time integral may be a result of altered foot function during gait in which there is delayed propulsion through the midfoot as a strategy to avoid weight-bearing on tender forefoot joints.
- Increased midfoot peak plantar pressure and pressure-time integral may be due to a pes planovalgus foot-type in which the midfoot has completely collapsed and is in contact with the supporting surface for longer during the stance phase of gait.
- General foot pain may be due to increased plantar pressures, in addition to synovitis in the feet, resulting in a decreased gait speed.
- Increased foot-related disability and impairment could reflect joint tenderness and general foot pain, as well as altered gait.
- Increased postural sway, when the eyes are closed, could indicate a loss of ankle joint proprioception which may further compromise stability.

The findings of the thesis suggest that the foot and ankle may have a role to play in falls in people with RA. However, when considering the inflammatory nature of RA and the significant mechanical and systemic effects of RA on the entire body, the mechanisms underlying falls are likely to be far more complex than currently described. Further work is required to test the hypotheses relating to

interrelationships between foot and ankle fall risk factors and to further develop a model for fall risk in people with RA.

11.5: Study limitations

As the study was conducted by a single researcher, there was potential for researcher bias in recruitment and data collection. In addition, in the cross-sectional study, the retrospective recording of falls may be subject to recall bias (167, 168). For example, forgetting a fall has been identified as an issue in older adult falls studies (167). Likewise, it is possible that falls which preceded the timeframe of interest may have been reported particularly if the participant had a fear of falling or experienced a significant injury as a result of a fall. Therefore, falls frequency at baseline may also have been over-reported by the study participants.

We included foot and ankle characteristics that are associated with falls in older adults as potential fall risk factors in adults with RA. However, foot problems associated with RA may differ to age-related foot changes. For example, plantar heel pain is frequently experienced in older adults and is related to soft tissue changes in the heel pad and plantar fascia (225), whereas people with RA commonly experience forefoot pain associated with synovitis in the MTP joints (31) and distal migration of the forefoot plantar fat pad (46). In addition, the study design did not allow for changes in foot and ankle characteristics, that can occur over time, to be assessed as potential fall risk factors. A longitudinal study, capturing falls data over a three year period with foot and ankle measures assessed at baseline, 12 months and 24 months, would have provided additional data of relevance to the study population. In particular, the analysis of stable verses deteriorating foot impairment in relation to falls risk.

The statistical analysis has some limitations. The sample size calculation was based on a study of older adults in an aged-care facility and therefore may not have been representative of a community-dwelling population. There was no adjustment applied for multiple comparisons in the univariate analysis, e.g. Bonferroni adjustment, therefore the probability of a Type 1 error was increased. We used backwards stepwise logistic regression modelling and negative binomial regression modelling for

the primary and secondary multivariate analyses. However, other multivariate statistical techniques could have been applied, e.g. discriminant function analysis, which may have produced different results. Additionally, clinicians may lack the expertise to correctly interpret the findings from logistic regression modelling, e.g. odds ratios, percentage of falls correctly predicted, the predictive power of the model and the variance in falls status explained by the model.

A number of characteristics important in the maintenance of balance were not measured, including lower extremity muscle strength, hip or knee function and ankle joint proprioception. Dynamic arch lowering (pronation) during gait has been associated with falls in older adults (226) and the current thesis suggested that pronation, as an offloading strategy for tender forefoot joints, may be a mechanism for falls in people with RA. However, assessment of foot kinematics were not included in the current study. Further, people with RA have been reported to have decreased dynamic postural control leading to problems maintaining balance during everyday activities (140, 172). However, with the exception of gait speed, dynamic balance was not assessed in the current study.

People with RA experience difficulty in finding appropriate footwear (105, 241). Footwear has a role to play in postural stability (103, 191, 236) and inappropriate footwear has been identified as a risk for falls in older adults (191, 192, 237, 238). We found no association between footwear type and falls. However, we only recorded the footwear worn at the time of the study visit, and usual footwear worn indoors and outdoors, which may not represent the footwear type worn at the time of a fall.

11.6: Study strengths

The thesis presents a robustly designed prospective study, using rigorous methodologies and statistical modelling to provide novel and clinically important findings which will inform future research. The sample size of 201 participants is relatively large in proportion to the population of New Zealanders with RA. A range of foot and ankle measures were assessed as potential fall risk factors based on previous studies in older adult populations. Foot and ankle testing included measures of

structure and function as well as several PROMs. In this way, fall risk was considered from a patient-centred view as well as from a clinical perspective. All testing procedures followed previously published protocols using measurement tools which were valid and reliable in either an older adult or RA population. All foot and ankle assessments were repeatable, able to be undertaken in a clinical environment and were relatively simple to perform.

The inclusion of a second study visit was unique. To our knowledge, no previous prospective longitudinal falls study, in an RA population, has reassessed baseline measures at the end of the falls follow-up period. It is acknowledged that, in terms of the study design, a second study visit was not required to answer the research questions. However, re-measurement of the baseline variables after 12 months enabled; 1) comparison of baseline and 12-month foot and ankle measures to observe clinically significant changes over 12 months, and 2) confirmation of the prospective findings through comparing fallers and non-fallers, during the 12-month follow-up period, on all foot and ankle measures assessed at the second study visit. In addition, the inclusion of a second study visit meant that the participants were more engaged in the study. Most participants were interested in their foot and ankle measures and the researcher allowed additional time to explain each test, and the results, during the study visits. The researcher also ensured that participants fully understood the importance of remaining in the study and completing the 12-month falls follow-up. In this way a relationship was formed between the researcher and the participants which positively facilitated the longitudinal collection of falls data, with only one participant refusing to continue in the study after the baseline study visit. In turn, the participants benefited through having the opportunity to share their concerns regarding their feet in two face-to-face meetings, in addition to receiving two comprehensive foot assessments. Only two participants declined to attend a second study visit. The remainder who were lost to follow-up either died, were too sick to attend or had moved away.

The attainment of falls data, in accordance with the ProFaNE consensus guidelines for falls research (169), was an additional study strength. In the cross-sectional study, a fall

definition was provided and an interviewer-assisted question was used for recording 12-month fall history. Interview-assisted meant that the researcher read out the question and recorded the participant's answer. In the 12-month prospective study, the fall definition was provided to the participant as part of their fall calendar and a post-fall interview was carried out immediately after a fall was reported. The concept of a fall is intuitively understood but often difficult to articulate (170). A fall event can be described in terms of antecedents such as frailty, loss of balance or slippery surface, and consequences such as change of body position, injury or landing point. In essence, falls mean different things to different people and the interpretation of a fall event can differ greatly between fallers, healthcare professionals and researchers (170). For example, the terms slip, trip and fall are often used interchangeably even though a slip or trip may or may not result in a fall event (170). The inclusion of an operational definition of a fall, using language from a lay perspective, is therefore vital to ensure consistency of falls reporting and comparison of study findings relating to interventions to prevent falls or risk factors for falls. In addition, directly involving the researcher in the attainment of falls data enabled the researcher to clarify to the participant the exact study definition for a fall and decide whether a particular fall incident should be counted in the study.

In addition to identifying factors associated with the occurrence of one or more (≥1) falls, the current thesis evaluated risk factors for multiple (≥2) falls. It could be argued that multiple-fallers are potentially more vulnerable to future falls than single-fallers. Further, a single fall may be the result of a one-off random event whereas multiple falls suggest a pattern of behaviour or intrinsic risk. The identification of risk factors for multiple falls may then be of greater importance than risk factors for single a fall. However, any single fall event can be devastating thus the identification of risk factors for any fall is warranted. Only one study in an RA population has previously evaluated factors associated with multiple falls (158). In this cross-sectional study of 4996 Japanese people with RA, BMI, Japanese-HAQ score and tender joint count were associated with a 6-month history of multiple falls. The study did not include any foot and ankle measures of fall risk. Currently there are no consensus guidelines for the grouping of participants for analysis in falls studies. However, participant numbers may

prohibit analysis of multiple falls when small group size would affect statistical power. In the current study, the sample size of 201 participants was considered large enough to allow for analysis of multiple falls. A recent systematic review of risk factors for falls in community-dwelling older adults identified numerous studies which reported risk factors for multiple falls (3). Inclusion criteria included studies with samples greater than 200 participants. In the current study, the analysis of multiple-fallers included three groups (non-fallers, single-fallers, multiple-fallers) and two groups (non-faller/single-fallers and multiple-fallers). The results comparing the two groups (non-faller/single-fallers and multiple-fallers) were of most value.

11.7: Clinical implications

Having a history of a previous fall is one of the strongest predictors of future falls in community-dwelling older adults (3, 8). The current study, and previous falls studies in RA populations (224), reported similar findings with respect to fall history as a risk factor for future falls. Consensus guidelines for falls prevention recommend that all older adults who are in contact with a health professional should be routinely asked whether they have fallen in the past year (9, 259). A question regarding recent falls needs to be considered for inclusion into the routine assessment of all people with RA. Asking the patient whether they have fallen not only enables the clinician to assess potential fall risk but also provides an opportunity for patient education regarding fall risk. It is recommended that a simple fall definition is provided and basic details for any fall occurrence are recorded. This will enable the immediate identification of modifiable risk factors, such as poor footwear, as well as alert the patient and clinician to any adverse intrinsic event, such as syncope or suspected stroke, which may require further investigation.

We found that psychotropics increase the risk of falls in people with RA and are an independent predictor of future falls. Psychotropic medications cross the blood-brain barrier and act directly on the CNS causing impairments in dynamic and static postural control (260). This is in addition to the known adverse effects of cognition impairment and muscle relaxation which are likely to be a mediating factor in falls (260). Withdrawal from psychotropics has been shown to decrease the risk of falls in older

adults (261-264). Therefore, identification of people with RA who are taking psychotropics, and consideration of reduction or withdrawal of psychotropic medication, is warranted.

Assessment of tenderness and swelling in the foot and ankle joints may be important in identifying people with RA at increased fall risk. In addition, pharmacological management of RA, and the use of therapeutic footwear and orthoses (89, 214, 265) to support the foot and offload painful joints, may mitigate fall risk. The thesis findings highlight the importance of differentiating between joint tenderness, associated with active foot disease, and general foot pain associated with structural and functional foot changes. The majority of people with established RA, who seek podiatric care, will describe foot pain. Establishing the aetiology of foot pain (inflammatory or mechanical) will not only guide the management strategy or treatment plan but may also alert the clinician to an increased risk of falls associated with synovitis in the feet. Non-specialist clinicians, such as podiatrists, are not generally trained to assess joints for synovitis associated with inflammatory joint disease. In addition, synovitis in the small joints of the feet can be difficult to detect clinically without the use of musculoskeletal ultrasound or MRI (107). Tender joints can also be difficult to distinguish from other painful foot conditions such as plantar plate rupture, neuritis or pathologic plantar callus (266). Increasing evidence for the importance of early detection of foot disease in RA has highlighted the need for podiatrists to be able to recognise synovitis in the feet (109). Recommendations have been suggested for non-specialist clinicians to conduct a simple metatarsal squeeze test as part of an early referral algorithm for RA (110). The metatarsal squeeze test may also be useful for identifying joint tenderness associated with increased fall risk in people with RA.

Our results suggest that measurement of plantar pressures, at the midfoot, may also be useful in identifying people with RA at increased fall risk. Plantar pressure systems are available in some clinical practices and are used to identify areas of high pressure which may compromise tissue viability in patients with high-risk foot conditions (203). Such equipment could also be utilised to identify increased pressures at the midfoot, as part of a fall risk assessment in patients with RA. In clinical settings where pressure

analysis equipment is unavailable, the identification of a pes planovalgus foot-type may suffice as an indicator of increased midfoot pressures in people with established RA, particularly in the presence of callosities at the talonavicular joint (101).

People with RA need to be aware of visual deficits, such as impaired vision or poor lighting, which may further compound their risk of falling. Clinical assessment of standing balance, with eyes closed, may be useful for assessing fall risk in people with RA. The Romberg's test is a widely used and reliable assessment of standing balance in older adults (267, 268). The test is based on the premise that a person requires at least two of three senses; proprioception, vestibular function and vision, to maintain balance while standing (268). A positive Romberg's indicates proprioceptive loss by demonstrating loss of postural control in the absence of visual input (269). The Romberg's test may be useful for identifying people with RA at increased fall risk.

Despite significant advances in the clinical understanding of RA over the past decade, the impact of RA in the feet is still poorly understood (109). However, there is increasing recognition of the importance of foot care and foot health interventions for people with RA (39). Measurement of changes in foot health is required to monitor the effectiveness of treatment from an economic (cost-benefit) and person-centred perspective (152). This includes clinical measures of structure and function as well as patient-reported outcome measures which specifically focus on foot-related disability and impairment (152). The current findings suggest that a patient-reported measure of foot-related pain, disability and impairment may also be useful in identifying and monitoring fall risk in people with RA.

11.8: Future directions

11.8.1: Clinician education

Podiatry has a role to play in falls prevention. Chapter 5 detailed the evidence for foot and ankle features associated with falls in older adults. Guidelines for fall prevention recommend older adults seek podiatry care for foot problems and footwear advice (259, 270). In addition to treating foot problems, which may cause falls, podiatrists are well placed to identify patients at increased fall risk, undertake a fall risk assessment

and refer as appropriate. In New Zealand, undergraduate trainee podiatrists are taught basic fall risk assessment techniques and encouraged to question all older patients on their recent fall history. Indeed, in general podiatry practice, falls assessment is considered to be routine for older adult patients. However, because falls are generally associated with older adults, it is possible that other at-risk populations such as people with RA may not be monitored for fall risk. Given the current evidence, it is proposed that undergraduate podiatry students and clinicians are routinely taught to include a basic fall risk assessment for all people with RA. In addition, it is recommended that key messages, regarding fall risk in people with RA, are disseminated to all registered podiatrists through professional bodies.

The feet are often overlooked during rheumatology consultations (33, 271). The DAS28, which is commonly used by rheumatologists, excludes the joints of the feet (74). As such, the feet may not be assessed, or assessed infrequently, during routine rheumatology appointments (33). It has been shown that people with RA in clinical remission, according to the DAS28 (score <2.4), may suffer from active foot disease (31, 251). Indeed, previous authors have challenged the validity of the DAS28 for assessing clinical remission due to the exclusion of the lower extremity joints (252, 253). Synovitis in the feet may also be undetected by podiatrists who specialise in foot care but are not generally trained to assess joint tenderness and swelling in patients with rheumatic conditions. The current findings highlight the need for the feet to be included in the routine assessment of all people with RA. In addition, all podiatrists should be trained to clinically assess for synovitis in the feet.

11.8.2: Review of clinical guidelines

Several evidence-based guidelines currently exist for the management of people with early (272, 273) and established (39, 274) RA. These guidelines were developed by consensus groups and provide recommendations for treatment as well as standards of care and referral pathways. All guidelines recognise and recommend a MDT approach to patient management in terms of treatment and education. The MDT can include the general practitioner, rheumatologist, rheumatology nurse specialist, psychologist, nutritionist, physiotherapist, occupational therapist and podiatrist. Evidence-based

treatment modalities and expert consensus recommendations (where evidence is lacking) are provided for the management of RA within each supporting discipline. However, currently none of the guidelines describe fall risk, or make specific recommendations for the assessment of balance or fall risk, in the management of people with RA.

Consensus guidelines also acknowledge the role of the podiatrist as the primary provider of foot health services and recommend specialist podiatry services in the management of foot health in people with RA (39, 272). Despite these recommendations, studies in the UK (275-277), Turkey (33), Australia (278) and New Zealand (271, 279) reported that the foot care needs of people with RA are not being met. A lack of specialist rheumatology podiatry services is believed to be a major reason for this unmet need (89). In response, a UK-based guideline development group developed guidelines for non-specialist podiatrists in the assessment and management of foot health problems in people with RA (89). These comprehensive guidelines provide essential and 'gold standard' requirements for the assessment and treatment of RA-related foot problems. This includes a Foot Screening Pathway for foot assessment and referral to other branches of the MDT. Within the Foot Screening Pathway, 'Lack of stability' and 'Falls' are included as bullet point items. However, specific reference to, or recommendation for, the assessment of fall risk is not included within the detailed guideline document.

The consequences of falls in this potentially vulnerable group can be severe and include injury, reduced quality of life and death. For example, the risk of osteoporotic hip fracture, due to corticosteroid use and disease-related reduced bone mass (280), has been reported as threefold in people with RA (22). The collective evidence strongly supports the notion that people with RA are at increased risk of falling compared to the non-RA population (224). RA-related fall risk factors have been identified in several studies and the current thesis provides additional evidence for fall risk factors related to the foot and ankle. Falls assessment and education are vital in the prevention of falls. All people with RA should be asked whether they have fallen in the past year. In addition, it is proposed that an evidence-based recommendation for fall risk

assessment should be included in the consensus guidelines for the management of people with RA.

11.8.3: Falls education

Falls education is widely acknowledged as a key component in the prevention of falls in older adults. Likewise, patient education is an important aspect of the management of RA. Support organisations such as Arthritis New Zealand (www.arthritis.org.nz), Arthritis Australia (www.arthritisaustralia.com.au) and Arthritis Care (arthritiscare.org.uk) provide excellent educational material for people with all forms of arthritis. This includes brochures, videos, seminars, newsletters, support groups and links through social media, such as Facebook. These existing resources and communication pathways could be utilised to educate people with RA about potential falls risk. Future work, in collaboration with arthritis support organisations and other key stakeholders, is warranted to investigate the opportunities for falls education targeted to people with RA.

11.8.4: Further research

The systematic review pertaining to falls in RA (Chapter 3) found inconsistencies in fall risk measures and methodology for collecting falls data. A further prospective study using the same foot and ankle measures and methodology for falls data ascertainment would be valuable to confirm the current findings. In addition, this thesis presented several novel findings relating to foot and ankle characteristics and falls in people with established RA. Whilst the inclusion criteria for the study was all adults with a diagnosis of RA, there were relatively few participants with early RA. Confirmation of the current findings in a sample of participants with early RA would be of benefit.

In the current study, multivariate analyses explained only 9% to 15% of the variance in falls status. Therefore, further studies are required to identify additional predictors of fall risk in people with RA. Previous falls studies in RA cohorts have included tests of dynamic balance including step-up step-down (160), heel-toe walking (181), functional reach (160) and gait speed (159, 160, 162); with conflicting findings. Inclusion of additional measures of dynamic balance, such as the Timed Get Up and Go test (185)

that is used to predict falls in older adults (267), would be of value in future RA falls research. In addition, an accelerometer could be used to record gait parameters, including gait speed and dynamic balance (281), as well as to remotely record physical activity over a 7-day period (282). Evaluation of lower limb and foot function, using 3D gait analysis (125), would also be useful and could be combined with the assessment of lower leg muscle strength and ankle joint proprioception.

We found no association between fall risk and footwear in the current study. However, several studies have reported an association between footwear and falls in older adults (191, 192, 237, 238). Footwear is important in the maintenance of balance (233, 234). Motion control features such as heel-counter stiffness, midfoot rigidity and adequate fixation (e.g. laces, straps or buckles), are considered important in the prevention of falls (283). In contrast, footwear with poor structural features including excessively flexible heel counter, an excessively soft sole and inadequate fixation have been identified as contributing to falls risk (191, 236). In a previous study, our team evaluated the effect of sandals on postural stability in older women with established RA and found that sandals were detrimental to the maintenance of standing balance, in eyes-closed conditions (103). We also conducted a survey of the footwear habits of people with inflammatory arthritis, in New Zealand, and found that many people frequently wore footwear with poor structural characteristics including moccasins, sandals and slippers (105). In addition, a qualitative component of the survey revealed that difficulty in finding footwear to fit the shape of the foot, or good quality footwear that was aesthetically acceptable, contributed to poor footwear choices (284).

Given the existing evidence concerning footwear and falls in older adults, footwear features and falls, and footwear difficulties experienced by people with established RA, further investigation of the potential role of footwear in falls in people with RA is warranted. In the current study we assessed the type of footwear worn by the study participants and classified as ‘good’, ‘average’ or ‘poor’. A comprehensive assessment of the structural characteristics of the participant’s usual footwear, using a validated footwear assessment tool (199), is required to provide specific information on the

footwear properties which may contribute to falls risk. An evaluation of the actual footwear worn at the time of a fall should also be included (239).

The current findings relating to foot or ankle tenderness as a predictor of falls warrants further investigation. Foot and ankle tenderness is the only foot-related fall risk factor that is potentially modifiable. However, the underlying cause of foot tenderness in people with established RA, e.g. synovitis associated with active RA or increased mechanical loading associated with deformity, is unclear. A large cross-sectional study using ultrasound, x-ray and clinical assessment of disease activity and structural deformity in the feet of adults with established RA may inform the development of foot and ankle intervention which prevent falls.

The majority of participants attended two study visits of between 1-2 hours duration, dependent on the participant. Many participants openly shared their experiences of living with RA and the researcher allowed them to talk without being rushed. During this time, the researcher was able to establish a level of trust and confidence as a sound basis for an ongoing research relationship. The researcher also interviewed participants following each reported fall event and intermittently contacted participants by phone over the study year to 'keep in touch'. During these interactions, the researcher gained valuable insight into the disparity between the research definition of a fall and participant interpretation of falls. For example, when asked about their fall history, several participants stated that they would not have considered a trip or slip to be a fall even when it resulted in a descent to the ground or lower level. Additionally, tripping and landing on a step when going up stairs was considered not to be a 'real' fall by some participants and yet falling down stairs was. Further, it was noted that many participants were reluctant to report falls which they believed were their own fault, suggesting that true falls were the result of events outside of one's control. During the study year, reaction to falls ranged from amusement to anger. Some participants, who had not experienced a prior fall, were surprised or shocked and blamed the researcher for 'jinxing' them into falling. Such insights and anecdotal findings could be valuable for future falls studies. However, as

the project used a quantitative methodology, none of these insights were formally captured.

A qualitative study investigating attitudes towards falls, perceived risk and causes of falls would be of benefit for future falls research. The post-fall questionnaires used in the current study (Appendix 8) could be analysed as an initial step. The primary reason for conducting the post-fall interview was to ensure that the fall was within the study definition and to check that the participant was not badly injured, therefore reinforcing the researcher-participant relationship. However, it was also recognised that further information obtained regarding the fall event would be useful for future analysis. Information obtained included day and time of fall, location of fall, cause of fall, injuries suffered, medical attention required, whether the participant was wearing glasses and what they had on their feet at the time of the fall. In addition, in-depth interviews with a sample of participants who fell during the study year would provide valuable information on perceptions of falls in relation to the whole experience of RA as well as the consequences of falls from a physical and psychological perspective.

The study produced a rich data set which can be analysed to answer future research questions. For example, fear of falling (short FES-I score) was assessed as a potential risk factor (independent variable) for falls in the current study. Fear of falling could also be analysed as an outcome measure (dependent variable) for a future study which evaluated the association between the fear of falling and foot and ankle characteristics in people with RA. Likewise, foot-related pain, disability and impairment could be the primary outcome in a study evaluating associations between patient-reported measures and clinical measures of RA disease activity.

In Chapter 6, the literature pertaining to fall risk factors in RA, and foot and ankle characteristics and falls in older adults, was reviewed to determine participant grouping for univariate analysis. We found that participant grouping was varied and that there is currently no ‘gold standard’ for analysis of fall risk factors in falls research. As a result we compared non-fallers and fallers as a primary analysis. Secondary univariate analysis compared the combined group of non-fallers/single-fallers with

multiple-fallers. In addition, three groups were compared; non-fallers, single-fallers and multiple-fallers. The development of a discussion paper on the effect of different participant grouping on study findings in falls research would be valuable; using the dataset from the current study as an example. Further, the use of a Delphi technique involving experts in the field of falls research, would be of value, to provide a consensus opinion and recommendations for participant grouping for future falls research.

Based on the findings of the current thesis, an evaluation of fall risk should be incorporated into the routine clinical assessment of all people with RA. A number of techniques are currently available for assessing fall risk in older adults (285, 286), as well as other vulnerable populations such as people with Parkinson's disease (287), osteoporosis (288) and stroke patients (289). These range from basic falls screening tools (287, 290) to more comprehensive, multifactorial fall risk assessments (291) and algorithms for assessment and referral (259). It is acknowledged that a comprehensive assessment of fall risk can be time consuming and is not necessary or practical for all patients. Clinicians may also lack the knowledge, skills, confidence or space to conduct tests of balance, gait and mobility. This thesis provides additional evidence for fall risk factors of relevance to older people with established RA. The current findings could inform the development of a simple assessment tool to screen for falls risk in people with RA. Further, a tool to predict the occurrence of falls would be valuable and may contribute to future falls prevention in adults with RA. Ultimately, the development of an intervention to prevent falls in people with RA is the goal of future research. Collaboration with international researchers, with access to very large datasets such as the Framingham Foot Study and Johnston County Osteoarthritis Project, would be beneficial to extend the findings of the current work.

CHAPTER 12: OVERALL CONCLUSION

The aim of this thesis was to investigate whether foot and ankle characteristics are associated with falls or falls risk in adults with RA. We conducted a systematic review concerning falls in people with RA to determine the incidence and risk factors for falls. The review identified large variation in falls incidence and inconsistency in method for collecting falls data. History of prior falls and increasing number of medications were the most significant predictive risk factors. There was a paucity of evidence for other fall risk factors warranting a further prospective observational study. The current study sought to extend our understanding of fall risk in people with RA through the inclusion of foot and ankle characteristics previously reported to be associated with falls in older adults.

The study involved a cross-sectional study followed by a 12-month prospective study of 201 people with RA. In the cross-sectional study, participants reported falls experienced in the preceding year (12-month fall history) and a range of clinical and foot and ankle characteristics were measured at baseline. Participants were then followed for 12 months, in a prospective study, to record the occurrence of prospective falls following the ProFaNE consensus guidelines for falls research.

Falls incidence results for the cross-sectional study (59%) and the 12-month prospective study (42%) were consistent with previous reports in people with RA. Twelve-month fall history was a significant predictor of prospective falls which was in agreement with previous studies in people with RA, other long-term chronic conditions and older adults.

The cross-sectional study demonstrated a number of clinical characteristics that were associated with increasing risk of falls in the preceding 12 months. These included RA disease duration, number of co-morbid conditions, cardiovascular disease (not including hypertension), number of medications, combination DMARD therapy, tender joint count, HAQ-II score, patient global health and short FES-I score. Cardiovascular

disease and combination DMARD therapy were also independently associated with falls, or multiple falls, in the preceding 12 months. The cross-sectional study also identified foot and ankle characteristics associated with increasing risk of falls in the preceding 12 months. These included midfoot peak plantar pressure, midfoot pressure-time integral, presence of foot or ankle tender and swollen joints, foot pain intensity, decreased gait speed and foot-related disability and impairment. Midfoot peak plantar pressure and foot-related disability and impairment were also independently associated with falls, or multiple falls, in the preceding 12 months.

The 12-month prospective study demonstrated clinical characteristics associated with increasing risk of prospective falls. These included increasing number of medications, psychotropic medication, tender joint count and use of an assistive device. Psychotropic medication was also an independent predictor of falls. Foot and ankle characteristics associated with increasing risk of prospective falls included presence of foot or ankle tender joints, eyes-closed postural sway and foot-related disability and impairment. Presence of foot or ankle tender joints was also an independent predictor of falls.

A number of foot and ankle characteristics, indentified in previous studies as fall risk factors in older adults, were not associated with falls in the current work. These included foot problem score (i.e. the number of foot lesions), pes planovalgus foot-type, bunion deformity, fine touch sensation, ankle range of motion, hallux and lesser toe strength, vibration perception threshold, foot muscle strength and current footwear. The non-significant findings may have been due to the high prevalence and severity of foot problems in the cohort studied compared to the general older adult population.

Falls are complex, multi-system events with multifactorial aetiologies. Therefore, no single risk factor can be identified as the cause of any given fall event. A number of intrinsic, extrinsic and environmental risk factors may be present and combine in one instance with potentially devastating consequences. As such, a synthesis of the findings relating to the foot and ankle fall risk factors was presented, with a

hypothetical model on how these risk factors might be interrelated. Further work is required to test the hypotheses relating to interrelationships between foot and ankle fall risk factors.

Clinical implications resulting from this thesis included a number of assessments that could be incorporated into routine clinical practice and may be useful in identifying or monitoring fall risk in people with RA. Future work is needed to develop a tool to screen for falls risk, and predict falls, in people with RA. This thesis provided evidence to inform healthcare professionals involved in the care and management of people with RA, of foot-related fall risk factors. This evidence could also inform the future development of a foot-related intervention which prevents falls in people with RA.

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APPENDICES

Appendix 1: Ethics and locality approvals

Auckland University of Technology Ethics Committee approval dated 3 April 2012

Northern X Regional Ethics Committee approval dated 7 February 2012

Auckland District Health Board institutional approval dated 8 February 2012

Counties Manukau District Health Board locality approval 13 February 2012

MEMORANDUM

Auckland University of Technology Ethics Committee (AUTEC)

To: Keith Rome
From: **Dr Rosemary Godbold** Executive Secretary, AUTEC
Date: 3 April 2012
Subject: Ethics Application Number 12/47 **Foot and anklecharacteristic with falls and falls risk in people with rheumatoid arthritis.**

Dear Keith

Thank you for providing written evidence as requested. I am pleased to advise that it satisfies the points raised by a subcommittee of the Auckland University of Technology Ethics Committee (AUTEC) and the Acting Chair of AUTEC and I have approved your ethics application. This delegated approval is made in accordance with section 5.3.2.3 of AUTEC's *Applying for Ethics Approval: Guidelines and Procedures* and is subject to endorsement at AUTEC's meeting on .

Your ethics application is approved for a period of three years until 3 April 2015.

I advise that as part of the ethics approval process, you are required to submit the following to AUTEC:

- A brief annual progress report using form EA2, which is available online through http://www.aut.ac.nz/research/research-ethics/ethics. When necessary this form may also be used to request an extension of the approval at least one month prior to its expiry on 3 April 2015;
- A brief report on the status of the project using form EA3, which is available online through http://www.aut.ac.nz/research/research-ethics/ethics. This report is to be submitted either when the approval expires on 3 April 2015 or on completion of the project, whichever comes sooner;

It is a condition of approval that AUTEC is notified of any adverse events or if the research does not commence. AUTEC approval needs to be sought for any alteration to the research, including any alteration of or addition to any documents that are provided to participants. You are reminded that, as applicant, you are responsible for ensuring that research undertaken under this approval occurs within the parameters outlined in the approved application.

Please note that AUTEC grants ethical approval only. If you require management approval from an institution or organisation for your research, then you will need to make the arrangements necessary to obtain this.

To enable us to provide you with efficient service, we ask that you use the application number and study title in all written and verbal correspondence with us. Should you have any further enquiries regarding this matter, you are welcome to contact me by email at ethics@aut.ac.nz or by telephone on 921 9999 at extension 6902. Alternatively you may contact your AUTEC Faculty Representative (a list with contact details may be found in the Ethics Knowledge Base at http://www.aut.ac.nz/research/research-ethics/ethics).

On behalf of AUTEC and myself, I wish you success with your research and look forward to reading about it in your reports.

Yours sincerely

Dr Rosemary Godbold
Executive Secretary
Auckland University of Technology Ethics Committee

Cc: Angela Brenton-Rule abrenton@aut.ac.nz, Sandra Bassett

From the desk of ...
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Health and Disability Ethics Committees

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7 February 2012

Professor Keith Rome
School of Podiatry, Dept of Rehabilitation and Occupation Studies
AUT University, Northshore Campus
Akoranga Drive, Northcote
Auckland 0627

Dear Keith

Re:	Ethics ref:	**NTX/11/12/114** (please quote in all correspondence)
	Study title:	Foot and ankle characteristics associated with falls and falls risk in people with rheumatoid arthritis. Protocol, V#1, 1/10/11; PIS/Cons V#2, 20/1/12
	Investigators:	Professor Keith Rome (Principal), Associate Professor Nicola Dalbeth, Ms Angela Brenton-Rule
	Localities:	Auckland DHB, Counties ManukaU DHB

Thank you for your response and updated documents received 31 January 2012. This study has been given ethical approval by the Northern X Regional Ethics Committee. A list of members of the Committee is attached.

Approved Documents

- Protocol number [version 1, dated 1 October 2011]
- Information sheet/Consent Form version [2, dated 20 January 2012]
- Recruitment letter version [2, dated 20 January 2012]
- Data collection sheets [version 1, dated 18 October 2011]

This approval is valid until 30 May 2016, provided that Annual Progress Reports are submitted (see below).

The following documents were received and reviewed:

- Locality assessments from Auckland DHB and Counties ManukaU DHB
- Letter of Maori support from CMDHB MRRC dated 03/11/2011
- AUT letter dated 10 November 2011 signed by Martin Wilson

Access to ACC

For the purposes of section 32 of the Accident Compensation Act 2001, the Committee is satisfied that this study is not being conducted principally for the benefit of the manufacturer or distributor of the medicine or item in respect of which the trial is being carried out. Participants injured as a result of treatment received in this trial will therefore be eligible to be considered for compensation in respect of those injuries under the ACC scheme.

Amendments and Protocol Deviations

All significant amendments to this proposal must receive prior approval from the Committee. Significant amendments include (but are not limited to) changes to:

- the researcher responsible for the conduct of the study at a study site
- the addition of an extra study site
- the design or duration of the study
- the method of recruitment

— information sheets and informed consent procedures.

Significant deviations from the approved protocol must be reported to the Committee as soon as possible.

Annual Progress Reports and Final Reports
The first Annual Progress Report for this study is due to the Committee by **7 February 2013**. The Annual Report Form that should be used is available at www.ethicscommittees.health.govt.nz. Please note that if you do not provide a progress report by this date, ethical approval may be withdrawn.

A Final Report is also required at the conclusion of the study. The Final Report Form is also available at www.ethicscommittees.health.govt.nz.

Requirements for the Reporting of Serious Adverse Events (SAEs)
SAEs occurring in this study must be individually reported to the Committee within 7-15 days only where they:

— are *unexpected* because they are not outlined in the investigator's brochure, and
— are not defined study end-points (e.g. death or hospitalisation), and
— occur in patients located in New Zealand, and
— if the study involves blinding, result in a decision to break the study code.

There is no requirement for the individual reporting to ethics committees of SAEs that do not meet all of these criteria. However, if your study is overseen by a data monitoring committee, copies of its letters of recommendation to the Principal Investigator should be forwarded to the Committee as soon as possible.

Please see www.ethicscommittees.health.govt.nz for more information on the reporting of SAEs, and to download the SAE Report Form.

Statement of compliance
The committee is constituted in accordance with its Terms of Reference. It complies with the *Operational Standard for Ethics Committees* and the principles of international good clinical practice.

The committee is approved by the Health Research Council's Ethics Committee for the purposes of section 25(1)(c) of the Health Research Council Act 1990.

We wish you all the best with your study.

Yours sincerely

Cheh Chua
Administrator
Northern X Regional Ethics Committee

cc: Ms Angela Brenton-Rule
ADHB Research Office A+5364
Ms Alison Robertson, CMDHB Research Office

AUCKLAND
DISTRICT HEALTH BOARD
Te Toka Tumai

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Date 8 February 2012

Institutional Approval

Professor Keith Rome
School of Podiatry
Division of Rehabilitation & Occupational Studies
AUT University
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Auckland

Dear Keith

Re: Research project A+5364 (Ethics NTX/11/12/114) Foot and ankle characteristics associated with falls and falls risk in people with rheumatoid arthritis

The Auckland DHB Research Review Committee (ADHB-RRC) would like to thank you for the opportunity to review your study and has given approval for your research project.

Your Institutional approval is dependant on the Research Office having up-to-date information and documentation relating to your research and being kept informed of any changes to your study. It is your responsibility to ensure you have kept Ethics and the Research Office up to date and have the appropriate approvals. ADHB approval may be withdrawn for your study if you do not keep the Research Office informed of the following:

- Any communication from Ethics Committees, including confirmation of annual ethics renewal
- Any amendment to study documentation
- Study completion, suspension or cancellation

More detailed information is included on the following page. If you have any questions please do not hesitate to contact the Research Office.

Yours sincerely

On behalf of the ADHB Research Review Committee
Dr Mary-Anne Woodnorth
Manager, Research Office
ADHB

c.c. Julia Martin

..../continued next page

MAINTAINING YOUR RESEARCH APPROVAL

Your Ethical and Institutional approval is dependant on the Research Office having up-to-date information and documentation relating to your research and being kept informed of any changes to your study. While the RO endeavours to send reminders for annual approvals and missing documents, it is **your responsibility** to ensure you have kept Ethics and the Research office up to date and have the appropriate approvals.

Please note, when missing or updated document reminders are sent, if the RO receives no response from you after **3 reminders** it will be assumed that your research has been completed and we will notify the relevant Department CD, the RRC and Ethics Committee that your **Locality Assessment Approval has been withdrawn**. This will not be reinstated until all issues have been resolved.

All documents / communications must be referenced with the **ADHB project number**. For simplicity when sending information to the Ethics Committees, please cc the RO. When receiving letters from Ethics, please copy and send to RO for our records.

TOPIC	REQUIREMENT	ACTION
ETHICS		
All Ethics Correspondence	All formal Ethics Committee communications to you	o send a copy to RO immediately
Annual Ethics Renewal	Use Ethics form, complete and submit **BEFORE** anniversary date of original research approval	o copy to Ethics o copy to RO (e-copy) o send copy of Ethics approval letter to RO when received
Changes to Research (design, PI, protocol etc)	Write letter detailing changes, Mark up changes in relevant documents. Ethics approval must be received **BEFORE** implementing	o copy of changes to Ethics o copy changes to RO o send copy of Ethics approval letter to RO when received
Stopping Study or Study Complete	If the study is stopped for any reason or study is complete	o notify Ethics and attach relevant documents (final report etc) o notify RO and attach relevant documents
Final Report	Complete Ethics template for final report	o Send to Ethics and RO o Inform RO if all finance elements also complete
LEGAL		
Contracts, Indemnities, Agreements, insurance certificates	All legal must be reviewed and approved before signing	o Send all legal documents to RO
Amendments – Non-financial	As above	o Send all legal documents to RO
Amendments - financial	As above and revise Budget	o Send all legal documents to RO o Send revised budget using template to RO
FINANCIAL		
Budget Changes i.e. change in visits or tests or proposed income	Liaise with accountant and adjust budget accordingly	o Send revised budget using template to RO
Budget maintenance	it is recommended that you review and update budgets at least quarterly	o Liaise with accountant and forward update to RO

All documents must be referenced with the ADHB project number and can be sent via email to: RDOAdmin@adhb.govt.nz. All paper copies can be faxed to: 09 307 8913 or by post to: Research Office, Level 14, Support Building, Auckland City Hospital, Private Bag 92024, Auckland, New Zealand.

For further information go to www.adhb.govt.nz/researchoffice/

COUNTIES MANUKAU DISTRICT HEALTH BOARD

Middlemore Hospital
Private Bag 93311, Otahuhu
Manukau 1640
Auckland, New Zealand
Telephone: 64-9-276-0000

CMDHB Research Office
Ground Floor Room 56
Clinical Support Building
Middlemore Hospital

13-Feb-12

Dear Angela Brenton-Rule

Thank you for the information you supplied to the Research Committee regarding your research proposal:

Ethics Reference Number: NTX/11/12/114
Research Registration Number: 1220

Research Project Title: Foot and ankle characteristics associated with falls and falls risk in people with rheumatoid arthritis

I am pleased to inform you that the Counties Manukau District Health Board Research Committee has approved this research with you as CMDHB investigator.

We wish you well in your project and require an update on how it is progressing. A copy of the progress report that is required by the Ethics Committee is sufficient, and should be submitted to the Research Officer by 13 Feb 2013

Please note failure to submit the progress report may result in the withdrawal of ethical approval.

Yours Sincerely

Alison Robertson
Research Officer
Counties Manukau District Health Board
DDI: 09 276 0279 Ext: 8279
MB: 021 943 784
Email: amroberts@middlemore.co.nz

THE UNIVERSITY OF AUCKLAND
NEW ZEALAND

A tertiary teaching and research institution dedicated to excellence in the pursuit of knowledge

Appendix 2: Participant consent form

Professor Keith Rome
Department of Podiatry
School of Rehabilitation & Occupation Studies
Telephone: 64 9 921 9999 extn 7688
Facsimile: 64 9 921 9839
Email: krome@aut.ac.nz

20 January 2012

Participant Consent Form

THE RHEUMATOID FOOT AND FALLS

English	I wish to have an interpreter	Yes	No
Deaf	I wish to have a NZ sign language interpreter	Yes	No
Māori	E hiahia ana ahau ki tetahi kaiwhaka Māori/kaiwhaka pakeha korero	Ae	Kao
Cook Island Māori	Ka inangaro au i tetai tangata uri reo	Ae	Kare
Fijian	Au gadreva me dua e vakadewa vosa vei au	Io	Sega
Niuean	Fia manako au ke fakaaoga e taha tagata fakahokohoko kupu	E	Nakai
Sāmoan	Ou te mana'o ia i ai se fa'amatala upu	Ioe	Leai
Tokelaun	Ko au e fofou ki he tino ke fakaliliu te gagana Peletania ki na gagana o na motu o te Pahefika	Ioe	Leai
Tongan	Oku ou fiema'u ha fakatonulea	Io	Ikai

	Please tick box
I have read and I understand the information sheet dated 20January 2012 for volunteers taking part in the study which will investigate the rheumatoid foot and falls.	☐
I have had the opportunity to discuss the study and ask questions and I am satisfied with the answers I have been given.	☐
I have had the opportunity to use whanau support or a friend to help me ask questions and understand the study.	☐
I understand that taking part in this study is voluntary (my choice). If I change my mind after I have attended a study visit, I understand that I can withdraw my data up to one month after this visit, without having to give a reason for withdrawing and without affecting my future medical care.	☐
I understand that my participation in this study is confidential and that no material which could identify me will be used in any reports on this study.	☐
I have received enough information about the study and have had enough time to think about it.	☐
I know who to contact if I have any questions about the study.	☐
I agree to take part in this study.	☐
I wish to receive a copy of the study results.	Yes / No
I agree to my GP or rheumatologist being informed of the results of my participation in this study.	Yes / No

Signed……Date……

(NAME IN BLOCK CAPITALS)……

Investigator's signature……Date: ……

(NAME AND ROLE IN BLOCK CAPITALS)……

Appendix 3: Recruitment letters

Letter sent to Auckland District Health Board RA patients

Letter sent to Counties Manukau District Health Board RA patients

Letter sent to AUT Podiatry School outpatients clinic RA patients

AUCKLAND DISTRICT HEALTH BOARD
Te Toka Tumai

Greenlane Clinical Centre
Private Bag 92-189
Auckland Mail Centre
Auckland 1142
New Zealand

Rheumatology Department
Ph: 6380370 (DDI) or
3074949 Ext: 26670

1 February 2013

Mr M Kenny
200 Westview Rd
Remuera 1025

Dear Mr Kenny,

Re: New research project in rheumatoid arthritis

I am writing to tell you about a new research project and to introduce the researcher, Angela Brenton-Rule. Angela is interested in foot problems caused by rheumatoid arthritis, and how these problems might lead to falls in people with rheumatoid arthritis. Angela is undertaking research as part of her PhD degree. Angela is also a registered podiatrist (foot specialist) and educator at the AUT Podiatry School.

For the study Angela will be recruiting patients with rheumatoid arthritis from Auckland District Health Board and assessing their feet. She will ask questions about how arthritis affects their feet and also whether they have suffered any falls in the past year. Research participants will then keep a record of any falls experienced over the next 12 months and at the end of 12 months she will repeat the foot assessment. A Participant Information Sheet is enclosed which provides more detail about what the study involves.

Involvement in the study is completely voluntary (your choice) and participants can withdraw from the study at any time. If you do not wish to participate, this will not affect your clinical care in anyway.

If you would like to volunteer for the study or have any questions please contact Angela on 0800 RA FALL (0800 723 255) or abrenton@aut.ac.nz. She will be happy to answer any questions you may have about the study without any obligation to participate. The study has been approved by Auckland District Health Board and the Northern X Ethics Committee. Thank you for taking the time to read the enclosed information.

Kind regards,

Dr Nicola Dalbeth
Acting Clinical Director and Rheumatologist
Department of Rheumatology, Auckland District Health Board

1 May 2013

Ms Lisa Luke
27B Loius Drive
Manurewa Central 2102

Dear Ms Luke,

Re: New research project in rheumatoid arthritis

I am writing to tell you, as a person who has attended the rheumatology clinic, about a new research project and to introduce the researcher, Angela Brenton-Rule. Angela is interested in foot problems caused by rheumatoid arthritis, and how these problems might lead to falls in people with rheumatoid arthritis. Angela is undertaking research as part of her PhD degree. Angela is also a registered podiatrist (foot specialist) and educator at the AUT Podiatry School.

For the study Angela will be recruiting patients with rheumatoid arthritis from Counties Manukau District Health Board and assessing their feet. She will ask questions about how arthritis affects their feet and also whether they have suffered any falls in the past year. Research participants will then keep a record of any falls experienced over the next 12 months and at the end of 12 months she will repeat the foot assessment. A Participant Information Sheet is enclosed which provides more detail about what the study involves.

Involvement in the study is completely voluntary (your choice) and participants can withdraw from the study at any time. If you do not wish to participate, this will not affect your clinical care in any way.

If you would like to volunteer for the study or have any questions please contact Angela on **0800 RA FALL (0800 723 255)** or **abrenton@aut.ac.nz**. She will be happy to answer any questions you may have about the study without any obligation to participate. The study has been approved by Counties Manukau District Health Board and the Northern X Ethics Committee. Thank you for taking the time to read the enclosed information.

Kind regards,

Clinical Associate Professor Peter Gow
Clinical Head
Rheumatology Department
Counties Manukau District Health Board

Hazra Sahid
Rheumatology Nurse Specialist
Counties Manukau District Health board

Health & Rehabilitation Research Institute

Health & Rehabilitation Research Institute,
School of Podiatry
AUT University
Auckland 1142, New Zealand

1 February 2013

Mr M Kenny
200 West view Road
Remuera 1025

Dear Mr Kenny

Re: New research project in rheumatoid arthritis

I am writing to tell you about a research project which I am undertaking as part of my PhD degree and to invite you to be involved. My name is Angela Brenton-Rule and I am a registered podiatrist (foot specialist) and educator at the AUT Podiatry School. I am interested in foot problems caused by rheumatoid arthritis, and how these problems might lead to falls in people with rheumatoid arthritis.

For the study I will be recruiting patients with rheumatoid arthritis and assessing their feet. I will ask questions about how arthritis affects their feet and also whether they have suffered any falls in the past year. Research participants will then keep a record of any falls experienced over the next 12 months and at the end of 12 months I will repeat the foot assessment. A Participant Information Sheet is enclosed which provides more detail about what the study involves.

Involvement in the study is completely voluntary (your choice) and participants can withdraw from the study at any time. If you do not wish to participate, this will not affect your clinical care in any way.

If you would like to volunteer for the study or have any questions please contact me 0800 RA FALL (0800 723 255) or abrenton@aut.ac.nz. I am happy to answer any questions you may have about the study without any obligation to participate. The study has been approved by the AUT Ethics Committee and Northern X Ethics Committee. Thank you for taking the time to read the enclosed information.

Kind regards,

Angela Brenton-Rule
Health & Rehabilitation Research Institute
AUT University

Appendix 4: Participant information sheet

Professor Keith Rome
Department of Podiatry
Faculty of Rehabilitation & Occupation Studies
Telephone: 64 9 921 9999 extn 7688
Facsimile: 64 9 921 9839Email: krome@aut.ac.nz

20 January 2012

Participant Information Sheet

The rheumatoid foot and falls

An invitation

You are invited to take part in a research study. Before you decide, it is important for you to understand why the research is being done and what it will involve. My name is Angela Brenton-Rule and I will be conducting the research. I am a qualified podiatrist and teacher at the AUT Podiatry School. The research is part of my PhD degree. Participation in the study is voluntary (your choice) so you can chose not to be involved. You can also withdraw from the study at any time without giving a reason or being disadvantaged.

What is the purpose of this research?

I am interested in foot deformity caused by rheumatoid arthritis (RA) and whether this foot deformity causes people to fall. There have been a lot of studies done which show that people with RA fall more often than people without RA. Falls have lots of causes. Changes in the shape and function of the feet may be one of the causes of falls in people with RA but this has not been studied.

What will happen in this research?

The study involves asking you questions about your arthritis and how it affects your feet. I will assess your feet and take measurements which tell me about how your feet are functioning. I will then ask you if you have fallen in the past 12 months and give you a calendar to keep a record of any falls that you have over the next 12 months. If you have a fall, I will phone you to ask a few questions about the fall. At the end of 12 months I will assess your feet again to see if there have been any changes.

What happens if I change my mind about being in the study?

Your participation is entirely your choice. If you change your mind about participating after your first study visit, you can withdraw your data up to one month after the study visit without giving a reason. If you wish to withdraw your data, please contact Professor Rome (contact details above). You do not have to take part in this research study, and if you decide not to take part or withdraw from the study, this will not affect your normal medical care in any way.

What will happen at the study visit?

There will be two study visits. The first is at the start of the study and the second is one year later. Each study visit will take about 30 minutes and will be conducted in the Rheumatology Department at Counties Manuaku and Auckland District Health Board.

During the study visit I will do the following things:

1. Ask you questions about your arthritis and your general health.
2. Ask you to fill in forms to understand how RA affects your life and your feet.

3. Examine the main joints in the body affected by RA.
4. Look at your feet to note any changes in shape.
5. Take foot measurements to see how your feet are functioning.
6. Look at your footwear.
7. Ask you if you have had any falls in the past 12 months.
8. Give you a calendar to record any falls in the next 12 months.

If you have a fall during the 12 months following your first study visit I will phone you to ask some questions about your fall. I will then invite you back 12 months after the first study visit to repeat the assessments. This will enable me to compare the shape and function of your feet to see if anything has changed which may have caused a fall.

What are the benefits?

I will be happy to give you information about the progress of the project and about future projects at your request. I will keep you informed of the results of the study. Please note that there may be a delay between your study visit and when the results are made public.

What are the costs of participating in this research?

Participation in the study will not cost you anything. I will give you petrol vouchers to cover your travel costs. No payments are being made to any doctors or researchers for including patients in this study.

Will I receive feedback on the results of this research?

I plan to publish the results from this study in scientific journals so that the information is freely available to other doctors, scientists and the public. Participants will not be identified in any report or publication and indeed all information about your identity will be kept strictly confidential. Although no names will be used in the publication, age, sex, ethnicity, diagnosis and medications will be reported. If you agree, I will tell your GP and rheumatologist that you are involved in the study and provide them with the results of your tests.

What do I do if I have concerns about this research?

If you have any questions or medical problems during this study you can call the study doctor Professor Keith Rome who is in charge of this research or me (Angela Brenton-Rule). Professor Rome or I will also answer any questions you have about this research study or your participation in the study. You have the right to ask questions about this study at any time.

Study Doctor: Professor Keith Rome
Telephone Number: 921 9999 extension 7688

Researcher: Angela Brenton-Rule
Telephone Number: 921 9999 extension 7215

If you have any questions or concerns regarding your rights as a participant in this study you may wish to contact an independent Health and Disability Advocate.

Telephone: 0800 555 050

Free Fax: 0800 2787 7678 (0800 2 SUPPORT)

Email: advocacy@hdc.org.nz

For Auckland District Health Board Maori health support, please contact Mata Forbes, RGON; Coordinator / Advisor, Maori Health Services, Auckland Hospital, Grafton, Mobile 021 348432, Tel: (09) 307 4949 extension 7292.

For Counties Manukau District Health Board Maori health supoort, please contact the Maori cultural support team at Middlemore Hospital Tel: (09) 276 0044 extension 8138.

How do I agree to participate in this research?

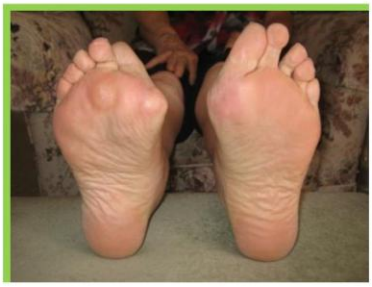
If you choose to help me with my research I will ask you to sign a consent form to show that you agree to the above. Thank you for reading this information sheet.

This study has ethical approval from the Northern X Regional Ethics Committee.

Appendix 5: Recruitment poster

The Rheumatoid Foot & Falls

AUT
AUCKLAND UNIVERSITY OF TECHNOLOGY
TE WĀNANGA ARONUI O TAMAKI MAKAU RAU



We are carrying out a study to evaluate the link between foot problems and falls in people with rheumatoid arthritis.

We are looking for volunteers with rheumatoid arthritis, aged 18 years and older, to participate in the study.

If you are interested, we need you to attend TWICE. The first study visit is to take measurements of your feet and the second visit is 12 months later. Each visit will take about 90 minutes.

If you require further information or would like to take part please contact the researcher, Angela, or the project leader, Professor Keith Rome.

Angela Brenton-Rule (PhD student)
Phone: 0800 RA FALL or 0800 723255
Email: abrenton@aut.ac.nz

Professor Keith Rome
Phone: 921-9999 extn 7688
Email: krome@aut.ac.nz

Appendix 6: Clinical research form

Demographics

Medical history and medications

Patient general pain (VAS)

Patient general health (VAS)

Podiatric foot care

Health assessment questionnaire

Fear of falling questionnaire

Leeds Foot Impact Scale

Joint evaluation sheet

Foot specific measures

Footwear

Visual aids

Assistive devices

Hearing impairment

Falls history

Contact details

Subject Number:
Date:
Study Visit: 1 or 2

CHECKLIST for RA participants:

Demographics and Clinical Measures

1. PIS, Inclusion / Exclusion criteria	Yes ☐	No ☐
2. Informed consent obtained	Yes ☐	No ☐
3. Demographics / Medical history	Yes ☐	No ☐
4. Medication details	Yes ☐	No ☐
5. VAS pain / Patient Global score	Yes ☐	No ☐
6. HAQ-II, LFIS, FOF	Yes ☐	No ☐
7. Tender / Swollen Joint count	Yes ☐	No ☐
8. DAS 28	Yes ☐	No ☐
9. CRP	Yes ☐	No ☐
10. Erosive disease in feet	Yes ☐	No ☐

Foot Measures

1. Gait speed	Yes ☐	No ☐
2. Foot problem score	Yes ☐	No ☐
3. HAV (Manchester)	Yes ☐	No ☐
4. Foot pain (VAS)	Yes ☐	No ☐
5. Foot and ankle strength	Yes ☐	No ☐
6. Plantar sensation (monofilament / biothes)	Yes ☐	No ☐
7. Ankle ROM	Yes ☐	No ☐
8. Toe strength (paper grip / pressure mat)	Yes ☐	No ☐
9. Foot length	Yes ☐	No ☐
10. PPP & PTI	Yes ☐	No ☐
11. Postural sway	Yes ☐	No ☐

Footwear

1. At study visit	Yes ☐	No ☐
2. Usual footwear	Yes ☐	No ☐

Falls History (study visit 1)	Yes ☐	No ☐
Current falls (study visit 2)	Yes ☐	No ☐
Falls Diary issued	Yes ☐	No ☐
Contact details obtained for falls follow-up (sep sheet)	Yes ☐	No ☐

Subject Number:
Date:
Study Visit: 1 or 2

Demographics

1. Patient hospital label/NHI number:

2. Rheumatologist: _____

3. GP/Phone Number: _____

4. Ethnicity: _____

5. Age / DOB: _____

6. Weight (kg): _____

7. Height (cm): _____

8. Gender: Male ☐ Female ☐

Rheumatoid arthritis and other Medical History:

1. Disease type: (file) RhF positive ☐ anti-CCP positive ☐ Seronegative ☐

2. Erosive foot disease (file) YES ☐ NO ☐

3. Age at diagnosis: (file/pt) _____

4. Disease duration: (file/pt) _____(years)

5. CRP: (file) _____

(file/pt)

Other Medical Conditions	Year Diagnosed	Active?
		Yes ☐ No ☐
		Yes ☐ No ☐
		Yes ☐ No ☐
		Yes ☐ No ☐
		Yes ☐ No ☐
		Yes ☐ No ☐

MEDICATIONS

Drug	YES= 1	NO=2	Other names or drugs in this category
No medications			
Methotrexate			
Leflunomide			Arava
Sulphasalazine			Salazopyrin
Hydroxychloroquine			Plaquenil
Other DMARDs (state)			azathioprine Cyclosporine im gold
Anti-TNF			Adalimumab (Humira) Infliximab (Remicade) Etanercept (Enbrel)
Rituximab			Mabthera
Prednisone			
NSAIDs			Naproxen (Naprosyn) Indomethacin Nurofen (brufen, ibuprofen) Voltaren (diclofenac) Celecoxib Meloxicam Etoricoxib Tenoxicam Tilcotil
Other analgesic			Panadol
Opiates			Codeine Morphine Tramadol Oxycontin
Aspirin			Cartia
Anti-platelet			Clopidogrel
Anti-thrombotic			Dipyridomole
Warfarin			
Benzodiazapines			Midazolam Diazepam Triazolam Zopiclone (Imovane)
Anti-psychotics			Risperdone Haloperidol Chlorpromazine Clozapin
Tricyclic antidepressants			Amitriptyline Nortriptyline Dothiepin
Anti-convulsant			Gabapentin
SSRIs			Venlafaxine Paroxetine Fluoxetine (Prozac) Cetalopram
Diuretics			Bendrofluazide Hydrochlorothiazide Frusemide Amiloride Spironolactine

Angiotensin II receptor antagonist			Cardesartan (Atacand) Cazaar (Losarten)
Betablockers			Atenolol Propanolol Carvedilol Metoprolol (Betaloc)
ACE Inhibitors			Quinapril Enalapril Captopril Acupril Cilazapri Inhibace
Calcium Channel Blockers			Felodopine (plendil) Nifedipine Diltiazem
Alpha blockers			Doxazosin
Insulin			
Sulfonylurea			Glipazide Gliclazide
Biguanides			Metformin
Bisphosphonates			Alendronate (Fosamax) Zoledronate (record if ever given)
Other medications (list)			Simvastatin Lipex Omeprazole Calciferol Inhalers Pantoprazole Atorvastin (Lipitor)

CO-MORBIDITIES

HT			
Diabetes			
OA			
Ischemic Heart Disease			MI, Angina, congestive heart failure
Arrhythmia			
PVD			
CVA / TIA			
Parkinson's Disease			
Bipolar disorder			
Dementia			
Other neurological dz (state)			
Osteoporosis			
Depression			
Other co-morbid conditions (state)			Cancer Coeliacs Dz Fibromyalgia Bronchiectasis Hyperlipidemia / dyslipidemia Asthma COPD

Subject Number:
Date:
Study Visit: 1 or 2

(file/pt)

Medication	Dosage	Route	Frequency	Reason

Patient Pain Evaluation Scale

How much pain have you had because of your illness **in the past week**?
Please indicate the amount of pain by placing a vertical mark on the line:

No Pain (0) (100) Severe Pain

(_____ mm)

Patient Wellbeing (General health) Evaluation Scale

Considering all the ways that your arthritis affects you, rate how you are doing on the following scale by placing a vertical mark on the line:

Very Well (0) (100) Very Poor

(_____ mm)

Podiatric Foot Care

Have you ever visited a Podiatrist to assess or care for your feet? Yes ☐ No ☐

How often do you visit the Podiatrist?
Once only ☐ 6-8 weeks ☐ 8-12 weeks ☐ Twice a year ☐ Yearly ☐

Do 6-meter walk test here and record in foot measures:

Subject Number:
Date:
Study Visit: 1 or 2

HAQ-II questionnaire

We are interested in learning how your illness affects your ability to function in daily life.

Place an X in the box which best describes your usual abilities **over the past week.**

Are you able to:	**Without any difficulty** 0	**With some difficulty** 1	**With much difficulty** 2	**Unable to perform** 3
Get on and off the toilet?				
Open car doors?				
Stand up from a straight chair?				
Walk outdoors on flat ground?				
Wait in a line for 15 minutes?				
Reach and get down a 5-pound object (such as a bag of sugar) from just above your head?				
Go up 2 or more flights of stairs?				
Do outside work (such as yard work)?				
Lift heavy objects?				
Move heavy objects?				

To calculate HAQ score add up numbers and divide by 10.

HAQ score _____

Subject Number:
Date:
Study Visit: 1 or 2

Fear of Falling questionnaire

The Short FES-1: Kempen et al. 2008

Now we would like to ask some questions about how concerned you are about the possibility of falling. Please reply thinking about how you usually do the activity. If you currently do not do the activity, please answer to show whether you think you would be concerned about falling IF you did the activity.

For each of the following activities, please tick the box which is closest to your own opinion to show how concerned you are that you might fall if you did this activity.

	Not at all concerned 1	Somewhat concerned 2	Fairly concerned 3	Very concerned 4
1. Getting dressed or undressed				
2. Taking a bath or shower				
3. Getting in or out of a chair				
4. Going up or down stairs				
5. Reaching for something above your head or on the ground				
6. Walking up or down a slope				
7. Going out to a social event (e.g. religious service, family gathering or club meeting)				

Handling Short FES-I sum scores:
To obtain a total score for the Short FES-I simply add the scores on all the items together, to give a total that will range from 7 (no concern about falling) to 28 (severe concern about falling).

Handling Short FES-I missing data:
If data is missing on more than one item then that questionnaire cannot be used. If data is missing on no more than one of the seven items then calculate the sum score of the six items that have been completed (i.e. add together the responses to each item on the scale), divide by six, and multiply by seven. The new sum score should be rounded up to the nearest whole number to give the score for an individual.

FES-1: Score _____

Insert LFIS & Joint Counts here:

LFIS-RA

Date:

Name:_____ Age:_____ Sex:_____

On the following pages you will find some statements which have been made by people who have Arthritis in their feet

Instructions: This questionnaire consists of 51 statements. Please read each statement carefully, and then pick out the **one statement** that best describes the way you have been feeling. Choose **True** if the statement applies to you and choose **Not True** if it does not apply to you **at the moment**. Circle the number beside the statement you have picked.

1. **My feet get painful when I'm standing**
   1 True
   0 Not True

2. **My feet hurt me**
   1 True
   0 Not True

3. **I find the pain in my feet frustrating**
   1 True
   0 Not True

4. **The pain is worse when I've been on my feet all day**
   1 True
   0 Not True

5. **At the end of the day there is pain and tension in my feet**
   1 True
   0 Not True

6. **I never get rid of the stiffness in the background**
   1 True
   0 Not True

7. **My feet throb at night**
   1 True
   0 Not True

8. **My feet wake me up at night**
   1 True
   0 Not True

9. **I feel as though I've got pebbles in my shoes**
   1 True
   0 Not True

10. **I get pain every time I put my foot down**
    1 True
    0 Not True

11. **I get a burning sensation all the time**
    1 True
    0 Not True

____ Subtotal Page 1

Continue on Back

12. **I cry with pain**
    1 True
    0 Not True

13. **I can only walk in certain shoes**
    1 True
    0 Not True

14. **I need shoes with plenty of room in them**
    1 True
    0 Not True

15. **I am limited in my choice of shoes**
    1 True
    0 Not True

16. **I need a wider fit of shoes**
    1 True
    0 Not True

17. **I feel I need a lot of padding under my feet**
    1 True
    0 Not True

18. **My footwear always feels heavy**
    1 True
    0 Not True

19. **I have to keep swapping and changing my shoes**
    1 True
    0 Not True

20. **I can't get any shoes on**
    1 True
    0 Not True

21. **I walk barefoot all the time**
    1 True
    0 Not True

22. **I feel unsafe on my feet**
    1. True
    2. Not True

23. **I have to walk for a bit and sit for a bit**
    1 True
    0 Not True

24. **I can't run**
    1 True
    0 Not True

25. **I find I shuffle around**
    1 True
    0 Not True

____ Subtotal Page 2

Continue on Page 3

26. **I am limping about all the time**
    1 True
    0 Not True

27. **I have to use a walking stick or walking frame**
    1 True
    0 Not True

28. **It takes me all my time to climb the stairs**
    1 True
    0 Not True

29. **I need help to climb stairs**
    1 True
    0 Not True

30. **I can't walk on cobbles**
    1 True
    0 Not True

31. **I am unsteady on uneven surfaces**
    1. True
    2. Not True

32. **I can't walk as far as I would like to**
    1 True
    0 Not True

33. **It takes me longer to do things**
    1 True
    0 Not True

34. **My whole life has been adapted**
    1 True
    0 Not True

35. **My feet restrict my movement**
    1 True
    0 Not True

36. **I get annoyed because I'm slower**
    1 True
    0 Not True

37. **I get frustrated because I can't do things So quickly**
    1 True
    0 Not True

38. **My whole life has slowed down**
    1 True
    0 Not True

39. **It's reduced the range of things I can do**
    1 True
    0 Not True

____ Subtotal Page 3

Continue on Back

40. **I have to plan everything out**
    1. True
    2. Not True

41. **I can't keep up like I used to**
    1 True
    0 Not True

42. **Socially it's affected my a lot**
    1 True
    0 Not True

43. **I am ashamed of how I walk**
    1 True
    0 Not True

44. **I'm nervous of missing a curb edge**
    1 True
    0 Not True

45. **I feel isolated because I can't go very far**
    1 True
    0 Not True

46. **I feel I slow other people down**
    1 True
    0 Not True

47. **I can't do some of the things I take for granted**
    1 True
    0 Not True

48. **I can't go for walks with the people close to me**
    1 True
    0 Not True

49. **I'm finding it difficult to be independent**
    1 True
    0 Not True

50. **I dread finishing up in a wheelchair**
    1 True
    0 Not True

51. **I get frustrated because I can't do things for myself**
    1 True
    0 Not True

Subtotal Page 4 _____

Subtotal Page 3 _____

Subtotal Page 2 _____

Subtotal Page 1 _____

Total Score _____

Joint Evaluation – Upper Extremities

RIGHT SIDE	LEFT SIDE

Not Evaluable	Tenderness		Swelling		JOINTS	Not Evaluable	Tenderness		Swelling	
Yes	Yes	No	Yes	No		Yes	Yes	No	Yes	No
☐	☐	☐	☐	☐	Tempromandibular	☐	☐	☐	☐	☐
☐	☐	☐	☐	☐	Sternoclavicular	☐	☐	☐	☐	☐
☐	☐	☐	☐	☐	Acromioclavicular	☐	☐	☐	☐	☐
☐	☐	☐	☐	☐	Shoulder	☐	☐	☐	☐	☐
☐	☐	☐	☐	☐	Elbow	☐	☐	☐	☐	☐
☐	☐	☐	☐	☐	Wrist	☐	☐	☐	☐	☐
☐	☐	☐	☐	☐	MCP1	☐	☐	☐	☐	☐
☐	☐	☐	☐	☐	MCP2	☐	☐	☐	☐	☐
☐	☐	☐	☐	☐	MCP3	☐	☐	☐	☐	☐
☐	☐	☐	☐	☐	MCP4	☐	☐	☐	☐	☐
☐	☐	☐	☐	☐	MCP5	☐	☐	☐	☐	☐
☐	☐	☐	☐	☐	IP1	☐	☐	☐	☐	☐
☐	☐	☐	☐	☐	PIP2	☐	☐	☐	☐	☐
☐	☐	☐	☐	☐	PIP3	☐	☐	☐	☐	☐
☐	☐	☐	☐	☐	PIP4	☐	☐	☐	☐	☐
☐	☐	☐	☐	☐	PIP5	☐	☐	☐	☐	☐
☐	☐	☐	☐	☐	DIP2	☐	☐	☐	☐	☐
☐	☐	☐	☐	☐	DIP3	☐	☐	☐	☐	☐
☐	☐	☐	☐	☐	DIP4	☐	☐	☐	☐	☐
☐	☐	☐	☐	☐	DIP5	☐	☐	☐	☐	☐

Joint Evaluation – Lower Extremities

RIGHT SIDE	LEFT SIDE

Not Evaluable	Tenderness		Swelling		JOINTS	Not Evaluable	Tenderness		Swelling	
Yes	Yes	No	Yes	No		Yes	Yes	No	Yes	No
☐	☐	☐			Hip	☐	☐	☐		
☐	☐	☐	☐	☐	Knee	☐	☐	☐	☐	☐
☐	☐	☐	☐	☐	Ankle	☐	☐	☐	☐	☐
☐	☐	☐	☐	☐	Subtalar	☐	☐	☐	☐	☐
☐	☐	☐	☐	☐	Mid tarsal	☐	☐	☐	☐	☐
☐	☐	☐	☐	☐	MTP1	☐	☐	☐	☐	☐
☐	☐	☐	☐	☐	MTP2	☐	☐	☐	☐	☐
☐	☐	☐	☐	☐	MTP3	☐	☐	☐	☐	☐
☐	☐	☐	☐	☐	MTP4	☐	☐	☐	☐	☐
☐	☐	☐	☐	☐	MTP5	☐	☐	☐	☐	☐
☐	☐	☐	☐	☐	PIP1	☐	☐	☐	☐	☐
☐	☐	☐	☐	☐	PIP2	☐	☐	☐	☐	☐
☐	☐	☐	☐	☐	PIP3	☐	☐	☐	☐	☐
☐	☐	☐	☐	☐	PIP4	☐	☐	☐	☐	☐
☐	☐	☐	☐	☐	PIP5	☐	☐	☐	☐	☐
☐	☐	☐	☐	☐	DIP2	☐	☐	☐	☐	☐
☐	☐	☐	☐	☐	DIP3	☐	☐	☐	☐	☐
☐	☐	☐	☐	☐	DIP4	☐	☐	☐	☐	☐
☐	☐	☐	☐	☐	DIP5	☐	☐	☐	☐	☐

Subject Number:
Date:
Study Visit: 1 or 2

Foot Specific Measures

6-meter walk test X 3 (with shoes)

Time to complete (s)		value
Gait speed (m/s)		value

Foot Problem Score (Menz, 2001)

	Left		Right
HV (graded 1,2,3)		value (1,2,3)	
Lesser toe deformity (1 pt each)		value	
HK lesions (1 pt each)		value	
Abnormal bony prominences (1 pt each)		value	
Pain (0 = no pain, 5 = pain)		value (0,5)	
		Total	

Total FPS both feet =

HAV (Manchester Scale)

Grade 1		tick	
Grade 2		tick	
Grade 3		tick	
Grade 4		tick	

Foot Pain

How much foot pain have you had because of your illness **in the past week**?
Please indicate the amount of pain by placing a vertical mark on the line:

No Pain (0) (100) Severe Pain

(_____ mm)

Subject Number:
Date:
Study Visit: 1 or 2

Monofilament (10 g)

	L X 2	tick / cross	R X 2
plantar hallux			
plantar heel			
1st MPJ			
3rd MPJ			
5th MPJ			
Arch			

(Total / 12)
L = **R=**

Biothesiometer (mV)

	LEFT	RIGHT
plantar hallux		
plantar heel		
1st MPJ		
3rd MPJ		
5th MPJ		
Arch		

(Average of 6 measures = VPT)
L= **R=**

Foot & ankle strength (N)

	LEFT				RIGHT			
Dorsiflexion								
Plantarflexion								
Inversion								
Eversion								

Ankle ROM (degrees)

	LEFT				RIGHT			
DF								
PF								

Subject Number:
Date:
Study Visit: 1 or 2

Foot Length:
Record on notes page

Plantar pressure
(bare feet)

Peak Plantar Pressure (PPP) Kpa	LEFT x 3	L. AVE	RIGHT X 3	R. AVE
TF				
FF				
MF				
RF				
Pressure Time Integrals (PTI) Kpa/s				
TF				
FF				
MF				
RF				

Toe strength

paper grip test
pass / fail

Pass L/R	Fail L/R

MatScan (Kpa)	LEFT				RIGHT			
Lesser toes								
Hallux								

Postural sway (mm) (bare feet)

				AVERAGE
AP EO				
ML EO				
AP EC				
ML EC				

Subject Number:
Date:
Study Visit: 1 or 2

NOTES & FOOT LENGTH MEASURE

Subject Number:
Date:
Study Visit: 1 or 2

Footwear (identified from footwear chart)

Type worn to study visit: _____

Usual footwear worn indoors: _____ Usual footwear worn outside: _____

Visual aids

Do you usually wear visual aids Yes ☐ No ☐

Distance glasses ☐ Bifocals ☐
Reading glasses ☐ Multifocals (progressives) ☐
Contact lenses ☐

Assistive devices

Do you use an assistive device Yes ☐ No ☐
Walker ☐ Cane ☐ Other_____

When do you use your assistive device?

All the time ☐
Only in your home ☐
Only when out and about ☐
Other_____

Hearing impairment

Do you have hearing impairment? Yes ☐ No ☐

If you have a hearing impairment do you wear a hearing aid? Yes ☐ No ☐

Do you have a hearing aid, apart from when you are asleep, do you use it

All the time ☐ Most of the time ☐ Not often ☐ Never ☐

Subject Number:
Date:
Study Visit: 1 or 2

Falls History (study visit 1 only)

In the past 12 months have you experienced any falls?

A fall is defined as:

"An event that results in a person coming to rest unintentionally on the ground or other lower level not as a result of a major intrinsic event or an overwhelming hazard"

0 falls ☐
1 fall ☐
2 or more falls ☐

Falls diary explained and issued (study visit 1 only)

Start month:

End month:

Current falls (study visit 2 only)

In the past 12 months did you experienced any falls?

A fall is defined as:

"An event that results in a person coming to rest unintentionally on the ground or other lower level not as a result of a major intrinsic event or an overwhelming hazard"

0 falls ☐
1 fall ☐
2 or more falls ☐

Subject Number:
Date:
Study Visit: 1 or 2

Contact details for falls follow-up (to be stored separately to data)

Study number: _____

Name: _____

Address:

Email address:

Phone number: (please * preferred number)

Day time:

Evening:

Mobile:

Best time to phone:

Appendix 7: Footwear chart

Adapted from:

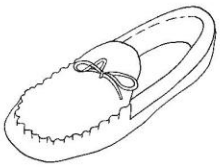
Menz HB, Sherrington C. The footwear assessment form: a reliable clinical tool to assess footwear characteristics of relevance to postural stability in older adults. Clin Rehabil. 2000;14(6):657-64.

Walking shoe

Athletic shoe / Runner

Oxford shoe

Moccassin

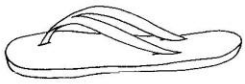


Boot

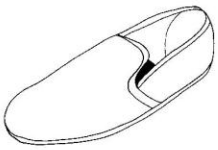
Ugg boot

High heel / Stiletto

Thong / Flip flop

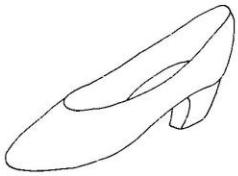


Slipper

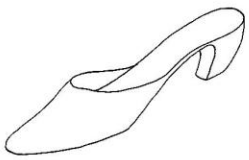


Backless slipper

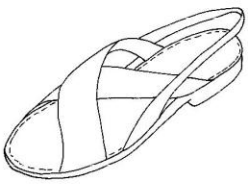
Court shoe



Mule



Sandal



Surgical / Bespoke footwear

Appendix 8: Post-fall questionnaire

FALLS FOLLOW-UP TELEPHONE INTERVIEW

Name: ID Number: Date:

1. What day did you fall this month?

Date: _____

2. What time of day did your fall?

Morning (6am-12pm) ☐ Afternoon (12pm-6pm) ☐

Evening (6pm-12am) ☐ Overnight Night (12am-6am) ☐

3. Where did you fall?

Inside own home ☐ On the one level ☐ Accessing the shower/bath ☐ Getting out of bed ☐ Getting out of a chair ☐ Walking up or down stairs ☐ Accessing the toilet **Outside own home** Walking up or down stairs On the one level (e.g. footpath) **Inside but NOT own home** ☐ On the one level ☐ Accessing the shower/bath ☐ Getting out of bed ☐ Getting out of a chair ☐ Walking up or down stairs ☐ Accessing the toilet	**Outside** ☐ Crossing a street ☐ On a bus or train ☐ Garden/park/grassed area ☐ Carpark/driveway ☐ On a step/escalator ☐ On a footpath ☐ On a kerb ☐ Getting into or out of a vehicle ☐ On the one level **Other area (please specify)**

4. Do you know what caused the fall?

5. Did you suffer any injuries as a result of the fall (even if minor?)

6. Did you injuries require you to seek medical attention?

7. Were you wearing glasses at the time of the fall?

I do not wear glasses		☐
No I was not wearing my glasses		☐
Yes, I was wearing:	distance glasses	☐
	reading glasses	☐
	bifocals	☐
	multifocals	☐
	contact lenses	☐

8. What were you wearing on your feet at the time of the fall (please refer to the footwear sheet in your falls calendar folder)

Appendix 9: Subsequent prospective analysis

Univariate analysis of non-fallers and fallers on foot and ankle characteristics measured at 12-months. Comparisons with P<0.15 are shown. Data are presented as mean (SD) unless specified.

Foot and ankle characteristics	Non-fallers n=107	Fallers n=75	P value
Presence of foot or ankle tender joints, n (%)	57 (53)	55 (72)	0.014
Foot problem score	12 (8)	14 (9)	0.135
Inversion strength, N	35 (17)	40 (26)	0.128
FIS_{TOTAL}	22 (12)	25 (13)	0.135
FIS_{AP}	13 (8)	15 (9)	0.130

FIS_{TOTAL}, Foot Impact Scale total score; FIS_{AP}, Foot Impact Scale activities/participation subscale score

Univariate analysis of non-fallers/single-fallers and multiple-fallers on foot and ankle characteristics measured at 12-months. Comparisons with P<0.15 are shown. Data are presented as mean (SD) unless specified.

Foot and ankle characteristics	Non-fallers/ single-fallers =146	Multiple-fallers = 36	P value
Presence of foot or ankle tender joints, n (%)	85 (58)	27 (75)	0.088
Foot problem score	12 (8)	15 (8)	0.055
Plantarflexion strength, N	70 (31)	80 (34)	0.101
FIS_{TOTAL}	23 (12)	26 (11)	0.086
FIS_{AP}	13 (9)	16 (8)	0.075

FIS_{TOTAL}, Foot Impact Scale total score; FIS_{AP}, Foot Impact Scale activities/participation subscale score

Appendix 10: Comparison of foot and ankle characteristics at baseline and 12-months

Univariate analysis comparing foot and ankle characteristics at baseline and 12-months. Comparisons with P<0.05 are shown. Data are presented as mean (SD) unless specified.

Foot and ankle characteristics	Baseline	12-months	P value
Presence of foot or ankle swollen joints, n (%)	49 (27)	21 (12)	<0.001
Foot problem score	14.96 (8.42)	12.52 (8.08)	<0.001
Monofilament	10.15 (2.90)	10.50 (2.80)	0.039
Ankle range of motion, degrees	57.51 (6.99)	58.79 (6.52)	0.002
Inversion strength, N	33.51 (17.39)	37.07 (21.15)	0.006
Rearfoot peak plantar pressure, kPa	247.43 (69.86)	260.02 (83.16)	0.001
FIS_{IF}	10.18 (4.87)	9.59 (4.70)	0.027

FIS_{IF}, Foot Impact Scale impairment/footwear subscale

Appendix 11: Systematic review

Brenton-Rule A, Dalbeth N, Menz HB, Bassett S, Rome K. The incidence and risk factors for falls in adults with rheumatoid arthritis: a systematic review. Semin Arthritis Rheum. 2014;44(4):389-98.

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The incidence and risk factors for falls in adults with rheumatoid arthritis: A systematic review

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Balance
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ABSTRACT

Objective: To conduct a systematic review of the incidence and risk factors for falls in people with rheumatoid arthritis (RA).
Methods: A search was conducted of the electronic databases AMED, CINAHL, MEDLINE, Scopus and The Cochrane Library. Study participants were adults with RA. Outcome measures were falls experienced in the preceding 6–12 months or prospective falls over a 12-month period. Articles were scored for quality using a modified version of the Downs and Black Quality Index Tool.
Results: Nine articles were included with mean (range) quality scores 72% (43–93%). The quality assessment revealed inconsistency in falls data attainment. Falls incidence ranged from 10% to 50% and was independent of age, gender or RA disease duration. History of a prior fall (odds ratio (OR) = 3.6 and 9.8) and increasing number of medications (OR = 1.4 and 2.1) were consistently associated with falls in RA. Number of co-morbid conditions, swollen and tender lower extremity joints, anti-depressants, anti-hypertensives, psychotropics, pain intensity and static balance were also identified as significant fall risk factors in at least one study. However, the evidence was limited to a single study or conflicted with other studies.
Conclusion: In studies of falls in people with RA, there is a wide range in reported falls incidence, which may be due to inconsistency in falls data attainment. Numerous potential fall risk factors have been evaluated, producing limited or conflicting evidence. It is recommended that future studies follow previous consensus guidelines for collecting and reporting falls data.

Introduction

Falls represent an important burden to healthcare resources worldwide [1]. The aetiology of falls is multifactorial and can result from a complex interaction of intrinsic, behavioural or environmental risk factors [2]. The consequences of falls include loss of confidence, injury and death. People with rheumatoid arthritis (RA) may be at greater risk of falling than the non-RA population [3]. This increased falls risk may be due to RA disease-related impairments including pain, deformity and decreased muscle strength, as well as reduced functioning such as altered gait and a decline in postural stability. The risk of hip fractures, as a result of a fall, is threefold in people with RA and may be due to disease-related reduced bone mass [4]. Therefore, falls awareness and the prevention of falls are important to guide management of people with RA. The aim of this review was to determine the incidence and risk factors for falls in people with RA.

Materials and methods

Search strategy for identification of articles

To identify studies concerning falls in people with RA, a primary literature search was conducted using electronic databases (from 1980 to 2013) such as AMED, CINAHL, MEDLINE, Scopus and The Cochrane Library online databases under the following terms: "rheumatoid arthritis," "inflammatory arthritis," "polyarthritis," "rheumatic disease," "falls," "falls risk" and "falls incidence." Search terms were applied to title and/or abstract, and

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http://dx.doi.org/10.1016/j.semarthrit.2014.08.001
0049-0172/

all studies were obtained from English-language peer-reviewed journals. Citations from retrieved publications were examined to obtain further references, and English text-only hard copy journals were also searched for relevant articles.

We included studies with a primary or secondary outcome measure of falls in the preceding 6–12 months and/or prospective falls over a 12-month period in adult participants (18 years or older) with diagnosed RA. Studies that investigated fear of falling as a primary outcome, in addition to current falls or fall history, were also included in order to capture falls data. Studies that included participants with other forms of inflammatory arthritis, such as undifferentiated polyarthritis, were excluded. Where two articles were published from the same study, only one was selected for inclusion in the review to avoid duplication of results. One reviewer undertook the searches and assessed potential studies against the inclusion criteria (A.B.R.). The review was conducted with reference to the PRISMA statement [5].

Data extraction

The following data were extracted from the articles reviewed: study design, participant characteristics (sample size, geographic location, mean age and gender), method of falls attainment, fall definition and falls incidence. Odds ratios (ORs), 95% confidence intervals (95% CIs) and *P* values were also extracted for potential fall risk factors.

Assessment of methodological quality

The Quality Index Tool, developed by Downs and Black [6], was used to assess the methodological quality of each article and has been reported to have high internal consistency, good test–retest reliability and good inter-rater reliability [6]. Clear guidelines are provided for use, enabling the tool to be applied and interpreted in a standardised manner [6]. The Quality Index Tool consists of 27 items that allow for the assessment of internal and external validity, reporting and power [6]. The quality index was modified to meet the aims of the study, with 10 items excluded from the analysis (items 4, 8, 13–15, 17, 19, 23, 24 and 27) as they relate specifically to intervention studies. The first eight items relate to reporting and include the aims, outcome measures and results of the study. Items 11 and 12 relate to external validity and assess the representativeness of the study findings and whether they could be generalised to the wider population of interest. The last seven items relate to internal validity (bias and confounding). Items 9 and 26 were applied to prospective studies only. Item 10 was applied only to studies that reported probability values, and items 5, 21 and 22 were applied only to case–control studies. Item 20 relates to validity and reliability of outcome measures. To score positively on this item, a study must describe the main outcome measures of interest or reference other work. As "falls" was the primary focus of the review, item 20 was scored "yes" only if a fall definition was provided and method of falls data attainment was described. Each item was scored as yes = 1 and no/unable to determine = 0, with the exception of item 5, which was scored as yes = 2, partially = 1 and no/unable to determine = 0. To take into account the varying number of Quality Index Tool items used for the assessments of articles, quality assessment results are presented as percentages. Methodological quality was assessed by two reviewers (A.B.R. and K.R.).

Results

A total of 124 articles were retrieved and nine met the inclusion criteria for the analysis (Fig. 1). The nine articles represented five cross-sectional studies, three prospective cohort studies and one case–control study. There was wide variation in study size, with number of participants ranging between 78 [7] and 4996 [8]. Two studies included females only [9,10], with the remainder including both males and females. The mean age of participants ranged from 54 [11] to 65 years [10,12]. Articles reviewed are summarised in Table 1.

Study quality

Table 2 presents the results of the methodological quality assessment. Quality assessment scores ranged from 43% to 93% (mean = 72%). Reporting within studies was generally consistent, although three studies did not clearly describe the study aim/objective/hypothesis [8,10,13] and four studies did not include a clear description of patient characteristics and/or inclusion/exclusion criteria [7,12–14]. External validity was varied, with two-thirds of the studies identifying the source population and methods of patient selection [3,7,8,10–12] but only one study demonstrating that the patients who agreed to participate were representative of the source population [12]. Internal validity was inconsistent across the studies. While all studies outlined the statistical analysis for the main outcomes, adjustment for confounding factors was not evident in three studies [7,9,13] and the case–control study did not report on patient source or time frame for recruitment [9]. All prospective studies accounted for losses of patients to follow-up [3,10,13], but only four studies included a fall definition and reported the methodology for determining and recording falls incidence [3,10–12]. When interpreting the results of this review, the quality and rigour of included studies should be taken into account. It should also be noted that the lowest scoring article was published as a letter [13].

Falls incidence

In this review, falls incidence refers to the number (%) of people who fell during the study period. Retrospective falls (i.e., fall history) incidence ranged from 10% to 43% and prospective falls incidence ranged from 35% to 50%. Methodology for collecting falls data varied between studies and included the use of questionnaires [8], interviews [3,9,11,12,14], interview-assisted questionnaires [7] and prospective monthly reporting via calendars or registration cards [3,10,13]. Falls data from all studies was "self-reported." However, five studies did not include a fall definition [7–9,13,14] and there was inconsistency in fall definition across the remaining studies [3,10–12].

Risk factors

Seven studies investigated factors associated with falls in RA [3,8–11,13,14]. Risk factors were classified into (1) physiological, (2) pharmacological, (3) extrinsic and (4) measures of RA disease activity. Multivariate logistic regression analysis was used to identify factors associated with falls history in cross-sectional studies [8,11,14] and to identify independent predictors of falls in prospective studies [3,10,13]. In addition, one prospective study [3] also used bivariate logistic regression analysis to identify risk factors associated with falls, not taking into account confounding variables. The case–control study analysed potential falls risk factors using multiple stepwise linear regression and reported *R* values [9]. Results are summarised in Table 3.

Physiological risk factors

All studies assessed age as a risk factor for falls and found no significant association between age and falls frequency. There was no gender difference between fallers and non-fallers in five studies

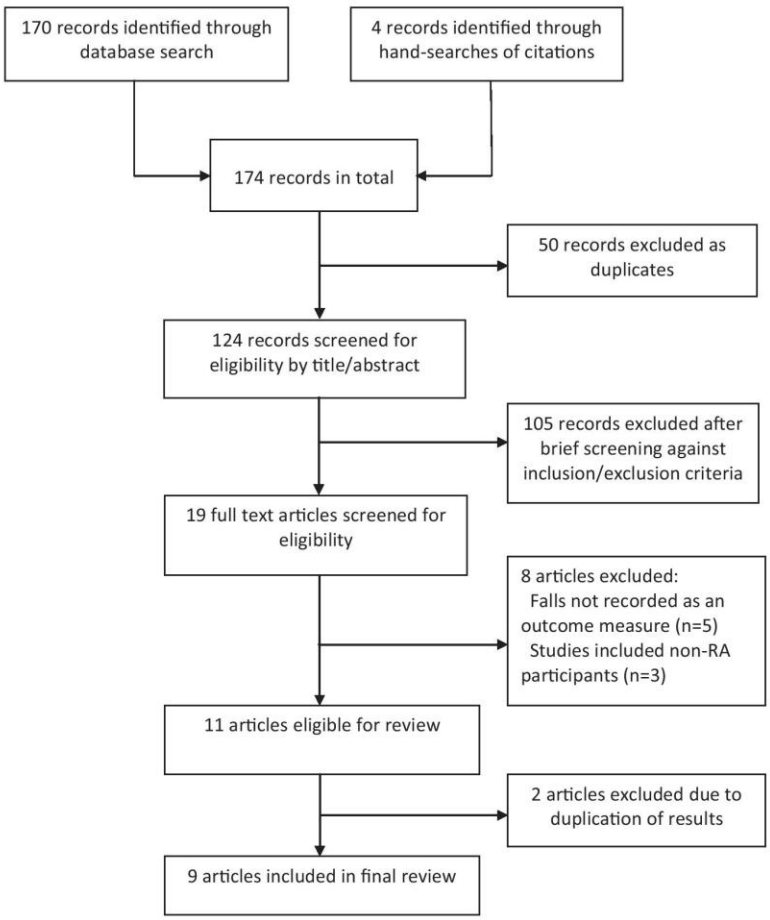

Fig. 1. Flowchart of literature search for incidence and risk factors for falls in RA.

[3,8,11,13,14], and two studies included female participants only [9,10]. Five studies assessed RA disease duration as a falls risk factor and found no association [8–11,13].

Increased body mass index (BMI) was found to be associated with a history of single and multiple falls, over six months, in a large Japanese study of men and women [8]. However, there was no association found between BMI and prospective falls in a smaller study of Japanese women [10]. Similarly, an association between fall history and number of co-morbid conditions was reported by Jamison et al. [11], but three subsequent prospective studies found no association between falls and co-morbid conditions [3,10,13]. Jamison et al. [11] reported that the odds of falling more than doubled with each additional co-morbid condition.

Decreased general health was associated with a history of falling in one study [8]. General health was "self-reported" using a visual analogue scale (VAS) of 0–10 cm [8]. Stanmore et al. [3] reported significant associations between prospectively recorded falls and fall history, injury from a previous fall, history of fracture, dizziness and fatigue. Fatigue and history of single and multiple falls were also reported to be independent predictors of future falls [3]. This was in agreement with an earlier study that reported that the odds of a fall in the coming year were almost 10 times higher in RA patients who had experienced a prior fall [13]. Stanmore et al. [3] found fear of falling to be associated with falls but not a predictor of future falls. Two previous studies reported no association between fear of falling and falls [9,13].

One study assessed lower extremity muscle strength as a potential fall risk factor, using the Chair Stand Test [3]. The authors concluded that, in the absence of other falls risk factors, every additional second taken to complete the test increased the risk of falling by 2% [3]. No other studies assessed lower limb or foot muscle strength as a fall risk factor. Balance was assessed in four studies [3,9–11]. Measures of standing balance found to be associated with falls included postural sway [10], one-leg stand time [10] and inability to maintain double limb standing balance for 10 seconds [3]. Duyur Cakit et al. [9] assessed balance and gait using the Tinetti Balance Test (TBT) and Tinetti Gait Test (TGT). No associations were found between TBT or TGT and fall history in the patient group. However, the combined score for balance and gait, Tinetti Total Score, was found to be an independent risk factor for falls. Duyur Cakit et al. [9] also assessed walking speed and 10-m walk time and found no association with falls. No association was found between falls and other measures of dynamic balance, including functional reach, step-up step-down, walk speed and walk time, in two further studies [10,11].

Pharmacological risk factors

Four studies evaluated medications as potential risk factors for falls [3,8,10,14]. Medications found to be associated with falls in a single study included psychotropics and steroids [3], concomitant use of methotrexate and active vitamin D_3 [8], anti-depressants

Table 1
Summary of articles reviewed

Study	Country	Participants (male: female)	Age (years) [mean (SD)]	Method of falls data attainment	Study design	Fall definition	Fall incidence results
Stanmore et al. [3]	UK	559 (173: 386)	Male: 62 (11) Female: 62 (14)	Baseline—falls in preceding 12-month period recorded at baseline interview	Prospective	*Fall history*: During the past year, how often have you had any fall, including a slip or trip in which you lost balance and landed on the floor, ground or lower level?	*Fall history*: 43% fell at least once; 22% multiple falls
				Follow-up falls recorded over 12 months via pre-addressed, prepaid daily falls calendars (posted monthly) and monthly follow-up telephone calls		*Current falls*: An unexpected event in which participants come to rest on the ground, or other lower level	*Current falls*: 36.4% fell at least once; 18.9% multiple falls *Falls rate*: 1.11 falls/person year
Bohler et al. [7]	Austria	78 (12: 66)	59 (14)	Falls in preceding 12 months via interview-assisted questionnaire	Cross-sectional	None	*Fall history*: 26.9% fell at least once 16.7% Multiple falls
Duyur Cakit et al. [9]	Turkey	84 Cases, 44 controls (all female)	Cases: 56 (9) Controls: 54 (5.2)	Falls in preceding 12 months via interview (cases only)	Case–control	None	*Fall history*: 14.3% fell at least once (cases only)
Hayashibara et al. [10]	Japan	80 (All female)	65.2 (7)	Falls recorded over 12 months via falls calendar (posted monthly) and monthly follow-up telephone calls	Prospective	The subject unintentionally came down on the floor or to a lower level.	*Current falls*: 50% fell at least once
Furuya et al. [8]	Japan	4996 (765: 4231)	Median age 60	Falls in preceding six months via questionnaire	Cross-sectional	None	*Fall history*: 10.1% Fell at least once 2.2% Multiple falls 8.0% Males fell at least once 1.3% Multiple falls 10.5% Females fell at least once 2.4% Multiple falls
Smulders et al. [13]	The Netherlands	84 (25: 59)	59 (12)	Falls over 12 months using monthly falls registration cards	Prospective	None	*Current falls*: 42% fell at least once *Falls rate*: 0.082 falls/person year
Armstrong et al. [14]	UK	253 (72: 181)	62 (11)	Falls in preceding 12 months via interview	Cross-sectional	None	*Fall history*: 33% fell at least once 52% Multiple falls
						Exclusion of falls as a result of a road accident or act of violence	26% Males fell 36% Females fell
Jamison et al. [11]	USA	128 (22: 106)	54 (9)	Falls in preceding 12 months via interview	Cross-sectional	An unplanned descent to the floor, ground or other lower level	*Fall history*: 35.2% fell at least once
						Falls could be from standing, sitting or lying position	Of the total fallers: 53.3% Had one fall 33.4% Had multiple falls 13.3% Did not specify number of falls
Fessel and Nevitt [12]	USA	570 (138: 432)	65 (9)	Falls in preceding 12 months via interview	Cross-sectional	Falling and landing on the floor or ground, or falling and hitting an object like a table or stair	*Fall history*: 30.9% fell at least once 15.5% Multiple falls

Table 2
Quality assessment scores (from modified Downs and Black Quality Index)

References	Item 1: Study objectives clearly described?	Item 2: Main outcome measures described in introduction and methods?	Item 3: Patient characteristics clearly described?	Item 5: Distribution of confounders described?	Item 6: Main study findings clearly described?	Item 7: Estimates of random variability in data for main outcomes described?	Item 9: Characteristics of patients lost to follow-up described?	Item 10: Confidence intervals and/or actual *P* values reported?	Item 11: Subject asked to participate representative of entire population?	Item 12: Subject who agreed to participate representative of entire population?	Item 16: Results based on data dredging made clear?	Item 18: Statistical tests for main outcomes appropriate?	Item 20: Main outcome measures accurate (valid and reliable)?	Item 21: Cases and controls recruited from the same population?	Item 22: Cases and controls recruited over the same period of time?	Item 25: Adequate adjustment for confounding?	Item 26: Loses of patients to follow-up taken into account?	% Score
Stanmore et al. [3]	1	1	1	[a]	1	1	1	1	1	0	1	1	1	[a]	[a]	1	1	93
Bohler et al. [7]	1	1	0	[a]	1	1	[a]	1	1	0	1	1	0	[a]	[a]	0	[a]	67
Duyur Cakit et al. [9]	1	1	1	0	1	1	[a]	1	0	0	1	1	0	0	0	0	[a]	53
Hayashibara et al. [10]	0	1	1	[a]	1	1	1	1	1	0	1	1	1	[a]	[a]	0	1	79
Furuya et al. [8]	0	1	1	[a]	1	1	[a]	1	1	0	1	1	0	[a]	[a]	0	[a]	67
Smulders et al. [13]	0	1	0	[a]	0	0	1	1	0	0	1	1	0	[a]	[a]	0	1	43
Armstrong et al. [14]	1	1	0	[a]	1	1	[a]	[a]	0	0	1	1	0	[a]	[a]	1	[a]	64
Jamison et al. [11]	1	1	1	[a]	1	1	[a]	0	1	0	1	1	1	[a]	[a]	0	[a]	75
Fessel and Nevitt [12]	1	1	0	[a]	1	1	[a]	0	1	1	1	1	1	[a]	[a]	1	[a]	83

All items scored using the following scale: yes = 1, unable to determine/no = 0.

[a] Item not applicable to article.

Table 3
Summary of fall risk factors

Factor of interest	References	Was factor significantly associated with or a predictor of falls?	Odds ratio (95% CI)	*P* value
Physiological risk factors				
Increasing age	Stanmore et al. [3]	No	1.0 (1.0–1.0)[a]	> 0.05
	Furuya et al. [8]	No	1.0 (1.0–1.0)	> 0.05
	Hayashibara et al. [10]	No	NR	0.22
	Duyur Cakit et al. [9]	No	NR	0.1
	Smulders et al. [13]	No	NR	NR
	Jamison et al. [11]	No	NR	> 0.05
Age range	Armstrong et al. [14]			
35–45 years		–	Referent	–
45–55 years		No	1.2 (0.4–3.7)	NR
55–65 years		No	0.9 (0.3–2.6)	NR
65–75 years		No	0.9 (0.3–2.8)	NR
75+ years		No	0.9 (0.3–3.1)	NR
Female gender	Smulders et al. [13]	No	NR	NR
	Stanmore et al. [3]	No	1.1 (0.7–1.6)[a]	> 0.05
	Furuya et al. [8]	No	1.8 (0.9–4.1)[b]	> 0.05
	Jamison et al. [11]	No	NR	> 0.05
	Armstrong et al. [14]	No	1.6 (0.9–2.9)	NR
Disease duration	Jamison et al. [11]	No	NR	> 0.05
	Furuya et al. [8]	No	NR	> 0.05
	Smulders et al. [13]	No	NR	NR
	Hayashibara et al. [10]	No	NR	0.22
	Duyur Cakit et al. [9]	No	NR	0.07
Body mass index	Furuya et al. [8]	Yes	1.1 (1.0–1.1)	0.002
			1.1 (1.0–1.2)[b]	0.005[b]
	Hayashibara et al. [10]	No	NR	0.89
Number of co-morbid conditions	Jamison et al. [11]	Yes	2.2 (1.1–4.1)	< 0.05
	Stanmore et al. [3]	No	1.0 (1.0–1.2)[a]	> 0.05
Presence of co-morbid conditions	Smulders et al. [13]	No	NR	> 0.05
Co-morbidities				
Cardiac disease	Hayashibara et al. [10]	No	NR	0.24
Diabetes		No	NR	0.36
Thyroid disease		No	NR	0.99
Pulmonary disease		No	NR	0.99
Urinary incontinence		No	NR	0.24
Collagen disease		No	NR	0.49
Cancer		No	NR	0.99
Parkinson's disease	Stanmore et al. [3]	No	1.8 (0.9–3.6)[a]	> 0.05
Visual impairment	Smulders et al. [13]	No	NR	NR
	Stanmore et al. [3]	No	NR	0.87
History of fracture	Stanmore et al. [3]	Yes	1.5 (1.0–2.1)[a]	< 0.05
		No	1.3 (0.8–1.9)	> 0.05
Injury from previous fall	Stanmore et al. [3]	Yes	1.3 (1.1–1.6) [a]	< 0.05
		No	0.8 (0.6–1.1)	> 0.05
History of previous surgery	Stanmore et al. [3]	No	NR	0.63
Joint replacement	Stanmore et al. [3]	No	NR	0.74
Impaired general health (VAS)	Furuya et al. [8]	Yes	1.1 (1.0–1.1)	0.002
			1.2 (1.0–1.3)[b]	0.048[b]
Physician-assessed general health (VAS)	Furuya et al. [8]	No	NR	NR
Fatigue (VAS)	Stanmore et al. [3]	Yes	1.2 (1.1–1.2)[a]	< 0.05
		Yes	1.2 (1.1–1.3)	< 0.05
Dizziness/unsteadiness	Stanmore et al. [3]	Yes	1.8 (1.2–2.6)[a]	< 0.05
		No	0.9 (0.5–1.5)	> 0.05
Health status (AIMS)	Smulders et al. [13]	No	NR	0.062
Fear of falling	Stanmore et al. [3]	Yes	1.1 (1.0–1.1)[a]	< 0.05
		No	1.0 (0.9–1.0)	
	Smulders et al. [13]	No	NR	0.054
	Duyur Cakit et al. [9]	No	NR	NR
Emotional status (POMS short form; anger, epression, fatigue and tension)	Jamison et al. [11]	No	NR	*P* > 0.05
Becks depression score	Duyur Cakit et al. [9]	No	NR	0.123
Hesitation to go out	Furuya et al. [8]	No	NR	NR
Fall history	Smulders et al. [13]	Yes	9.8 (NR)	< 0.05
History of single fall	Stanmore et al. [3]	Yes	3.6 (1.8–7.3)	< 0.001
History of multiple falls	Stanmore et al. [3]	Yes	5.3 (2.3–12.3)	< 0.001
Lower extremity muscle strength	Stanmore et al. [3]	Yes	1.02 (1.01–1.04)[a]	< 0.05
		No	0.99 (0.98–1.02)	> 0.05

Table 3 (*continued*)

Factor of interest	References	Was factor significantly associated with or a predictor of falls?	Odds ratio (95% CI)	*P* value
Balance				
One-leg stand time	Hayashibara et al. [10]	Yes	0.2 (0.0–0.9)	0.03
Standing balance	Hayashibara et al. [10]	Yes	1.8 (1.2–2.8)	0.01
Four-test balance scale (unsuccessful)	Stanmore et al. [3]	Yes	2.3 (1.1–4.7)	< 0.05
		No	1.0 (0.8–1.3)	> 0.05
Balance confidence	Smulders et al. [13]	No	NR	NR
Walk speed	Duyur Cakit et al. [9]	No	NR	NR
50-ft walk time	Jamison et al. [11]	No	NR	> 0.05
5-m walk time	Hayashibara et al. [10]	No	NR	0.14
10-m walk time	Duyur Cakit et al. [9]	No	NR	NR
Maximum step length	Hayashibara et al. [10]	No	NR	0.09
Step-up step-down	Hayashibara et al. [10]	No	0.2 (0.5–9.1)	0.31
Functional reach	Hayashibara et al. [10]	No	NR	0.06
Tinetti balance test	Duyur Cakit et al. [9]	No	NR	NR
Tinetti gait test	Duyur Cakit et al. [9]	No	NR	NR
Tinetti balance and gait	Duyur Cakit et al. [9]	Yes	$R^2 = 0.22$[c]	NR
Hand grip strength	Jamison et al. [11]	No	NR	> 0.05
	Hayashibara et al. [10]	No	NR	0.07
	Duyur Cakit et al. [9]	No	NR	NR
Functional class	Hayashibara et al. [10]	No	2.3 (0.6–9.2)	0.26
	Duyur Cakit et al. [9]	No	NR	NR
Functional stage	Hayashibaraet al. [10]	No	NR	0.64
Physical activity	Hayashibara et al. [10]	No	NR	0.81
Foot deformity	Hayashibara et al. [10]	No	NR	0.69
Bone mineral density	Hayashibara et al. [10]	No	NR	0.63
Muscle and fat volume (paravertebral)	Hayashibara et al. [10]	No	NR	0.72
Atlantoaxial subluxation	Duyur Cakit et al. [9]	No	NR	0.178
Pharmacological risk factors				
Psychotrophics	Stanmore et al. [3]	Yes	2.4 (1.5–3.7)[a]	< 0.05
		No	1.6 (0.9–2.9)	> 0.05
Steroids	Stanmore et al. [3]	Yes	1.5 (1.0–1.24)[a]	< 0.05
		No	1.3 (0.8–2.3)	> 0.05
Methotrexate	Furuya et al. [8]	Yes	0.5 (0.4-0.8)[b]	0.0024[b]
Active vitamin D_3	Furuya et al. [8]	Yes	1.4 (1.1–1.8)	0.0016
			1.7 (1.0–2.7)[b]	0.035[b]
Diuretics or	Hayashibara et al. [10]	Yes	9.2 (1.9–45.4)	< 0.01
Anti-hypertensives	Armstrong et al. [14]	No	1.0 (0.6–1.8)	NR
Anti-depressants	Armstrong et al. [14]	Yes	2.1 (1.0–4.2)	NR
Increased number of medications	Stanmore et al. [3]	Yes	2.1 (1.3–3.3)[a]	< 0.05
	Stanmore et al. [3]	Yes	1.8 (1.5–3.1)	< 0.05
	Armstrong et al. [14]	Yes	1.4 (1.0–2.0)	NR
Extrinsic risk factors				
Walking aids	Hayashibara et al. [10]	No	NR	0.52
Measures of RA disease activity				
DAS28 score	Stanmore et al. [3]	Yes	1.2 (1.1–1.3)	< 0.05
	Stanmore et al. [3]	No	0.9 (0.8–1.1)	> 0.05
	Furuya et al. [8]	No	NR	NR
	Hayashibara et al. [10]	No	NR	0.64
HAQ score	Stanmore et al. [3]	Yes	1.7 (1.4–2.1)[a]	< 0.05
		No	1.2 (0.7–2.0)	> 0.05
	Smulders et al. [13]	No	NR	NR
	Armstrong et al. [14]	No	1.3 (0.9–1.9)	NR
Japanese HAQ	Duyur Cakit et al. [9]	No	NR	NR
	Furuya et al. [8]	Yes	1.5 (1.3–1.8)	< 0.001
			2.5 (1.8–3.4)[b]	< 0.001[b]
Modified HAQ	Hayashibara et al. [10]	No	NR	0.08
HAQ-impaired rising	Armstrong et al. [14]	Yes	1.4 (1.1–1.9)	NR
HAQ-impaired walking	Armstrong et al. [14]	Yes	1.4 (1.0–1.8)	NR
Joint count				
Swollen joint count	Furuya et al. [8]	Yes	0.6 (0.4–0.9)	0.02
	Hayashibara et al. [10]	Yes	1.3 (1.1–1.5)	0.01
Tender joint count	Stanmore et al. [3]	No	NR	0.09
	Furuya et al. [8]	Yes	1.4 (1.1–1.7)	0.0011
			1.7 (1.3–2.3)[b]	0.0004[b]
	Hayashibara et al. [10]	No	NR	0.41
	Stanmore et al. [3]	No	1.0 (1.0–1.0)[a]	> 0.05
Total tender and swollen joint count	Jamison et al. [11]	No	NR	> 0.05
Swollen and tender lower extremity joints	Stanmore et al. [3]	Yes	2.0 (1.3–2.8)[a]	< 0.05
	Stanmore et al. [3]	Yes	1.7 (1.1–2.8)	< 0.05

Table 3 (*continued*)

Factor of interest	References	Was factor significantly associated with or a predictor of falls?	Odds ratio (95% CI)	*P* value
ESR	Furuya et al. [8]	Yes	0.9 (0.9–0.9)	0.0027
	Hayashibara et al. [10]	No	NR	0.56
	Duyur Cakit et al. [9]	No	NR	NR
CRP	Hayashibara et al. [10]	No	NR	0.64
	Duyur Cakit et al. [9]	No	NR	NR
Rheumatoid factor	Furuya et al. [8]	No	NR	NR
Morning stiffness	Jamison et al. [11]	No	NR	> 0.05
Painful feet	Stanmore et al. [3]	No	NR	0.17
Pain intensity	Smulders et al. [13]	Yes	4.8 (NR)	< 0.05
	Stanmore et al. [3]	Yes	1.2 (1.1–1.2)[a]	< 0.05
		No	1.02 (0.9–1.1)	> 0.05
	Furuya et al. [8]	No	0.9 (0.8–1.1)[b]	> 0.05
	Jamison et al. [11]	No	NR	> 0.05
Ritchie articular index	Duyur Cakit et al. [9]	No	NR	0.056
Chronic arthritis systemic index	Duyur Cakit et al. [9]	No	NR	NR

CI: confidence interval, NR: not reported, VAS: visual analogue scale, AIMS: arthritis impact measurement scale, POMS: profile of mood states, DAS28: disease activity score using 28 joint count, HAQ: Health Assessment Questionnaire, ESR: erythrocyte sedimentation rate, CRP: C-reactive protein.

[a] Associations evaluated by bivariate logistic regression.

[b] Multiple falls.

[c] Associations evaluated by multiple stepwise linear regression.

[14] and anti-hypertensives/diuretics [10]. Armstrong et al. [14] reported that patients who fell in the previous year were twice as likely to be taking anti-depressant medication as non-fallers. Stanmore et al. [3] reported that taking psychotropic medications more than doubled the odds of falling, in the absence of other risk factors, but was not an independent predictor of falls. Hayashibara et al. [10] found that patients taking anti-hypertensive medication, including diuretics, were nine times more likely to fall. In contrast, Armstrong et al. [14] found that anti-hypertensives were not associated with falls. The number of medications was assessed in two studies [3,14]. Armstrong et al. [14] recorded medications that were considered to cause falls, including anti-hypertensives, diuretics, sedatives and anti-depressants. The authors concluded that increasing number of medications (range: 0–4) was associated with a significantly increased risk of falling [14]. Stanmore et al. [3] listed all current medications and found that taking four or more medications more than doubled the risk of falling.

Extrinsic risk factors

The use of a walking aid was assessed as a potential falls risk factor in one study and found not to be associated with falls [10]. No other extrinsic or environmental fall risk factors have been assessed in an RA population.

Measures of RA disease activity

All studies included clinical measures of disease activity. Tender joint count (TJC) and swollen joint count (SJC) were included in four studies [3,8,10,11]. An association between falls and SJC was reported in two studies [8,10]. However, Stanmore et al. [3] reported no association between SJC and falls [3]. Similarly, TJC was associated with falls in one study [8], which was in disagreement with further two studies [3,10]. Jamison et al. [11] evaluated total joint count (TJC plus SJC) and found no association with falls [11]. In contrast, Stanmore et al. [3] found that the presence of any swollen or tender lower extremity joint doubled the odds of falling [3].

Increased erythrocyte sedimentation rate (ESR) was associated with risk of multiple falls in one study [8] and found not to be associated with falls in two later studies [9,10]. Stanmore et al. [3] found that pain was associated with falls but not a predictor of future falls. In contrast, Smulders et al. [13] found pain to be a predictor of future falls and reported that the risk of falling increased nearly five-fold with increased pain intensity [13]. However, further two retrospective studies found no association between pain and fall history [8,11]. No studies reported the locality and nature of pain assessed. Two studies identified high health assessment questionnaire (HAQ) scores to be associated with falls [3,8]. Armstrong et al. [14] identified two of the eight HAQ domains (walking and rising from a chair) to be associated with fall history [14]. In contrast, four studies found no associated between HAQ score and falls [9,10,13,14]. Disease Activity Score (DAS28) was found to be associated with a history of falls, but not a predictor of future falls, in one study [3]. Further two studies found no association between DAS28 score and falls [8,10].

Discussion

The aim of this review was to determine the incidence and risk factors for falls in people with RA. Based on the quality assessment, it is our opinion that overall the quality of the studies was good. However, several studies failed to report information such as participant representation of the recruitment population and methodology for attaining falls data. A falls definition was missing in several studies and there was inconsistency in falls definition across the remaining studies.

We found that falls incidence varied considerably across the studies and this may be due to the variation in the method for collecting falls data [15]. Falls recall period has been identified as a substantial source of variation in falls reporting [15]. Furuya et al. [8] reported fall incidence of 10%, which was relatively low compared to previous studies. These findings were from falls incidence recorded for the preceding six-month period only, whereas all other studies recorded falls over 12 months. Fall recall within the previous three to six months has been reported to be less accurate than recall over a 12-month period [16]. Therefore, the low falls incidence may be due to the shorter time period for recording falls, compared to other studies. Reporting periods in falls prevention trials in older adults range from one week to four years [15]. There are currently no guidelines recommending the time frame for the collection of falls data within falls studies.

Fall recall can be problematic in studies that use retrospective falls data [16–18]. Forgetting a fall, particularly falls without injury, results in under-reporting of falls incidence [17,18]. To improve

accuracy of falls recall, the Prevention of Falls Network Europe (ProFaNE) recommends prospective daily recording and notification of falls, with minimum monthly reporting [1]. ProFaNE also recommend that a core set of outcome measures, including number of falls, number of fallers and fall rate, be used to improve comparability of study results [1]. Two prospective studies followed the ProFaNE recommendations [3,13].

A definition of the term "fall" is frequently missing from falls research [15]. In the absence of a specific fall definition, falls can be interpreted differently by participants and researchers [19]. In studies of older adult populations, differences in falls rates have been attributed to variation in the definition of a fall event [1]. Consensus guidelines recommend that a fall be defined as, "an unexpected event in which participants come to rest on the ground, floor or other lower level" [1]. Using a lay perspective of falls is also recommended when questioning study participants [1]. Only one study in the current review followed these guidelines [3].

Our analysis of the literature suggests that falls incidence is independent of age. This is an important finding as studies in healthy older adults consistently report an increase in falls risk with increasing age [2,20,21]. Countries with falls prevention provision such as the UK, Canada, USA, Germany and New Zealand focus on the over 65 years age group. Therefore, it is possible that younger patients with RA may be marginalised and not receive tailored appropriate treatment, which addresses potential falls risk. The literature also suggests that falls incidence is independent of gender and RA disease duration. In contrast, female gender is associated with increased falls risk in healthy older adults [2,20,21], and disability and impairment, in RA, are generally associated with increasing length of disease [22]. Therefore, health professionals may also be unaware of the potential falls risk in males and individuals with early RA.

This systematic review has shown conflicting evidence regarding a number of measures used to evaluate falls risk in people with RA. There was consistency that fall history predicts future falls in people with RA. However, we are unable to draw any conclusions regarding other physiological risk factors. A recent systematic review of risk factors for falls in community-dwelling older adults found that several potential fall risk factors could not be addressed as they were considered by too few studies [2]. In the current review, many physiological factors were assessed in a single study only; therefore, evidence to support positive findings is lacking. Inconsistency in measurement protocols has also been identified as an issue in falls research [2,23] and may account for the lack of evidence for falls risk factors in people with RA. For example, 14 different measures of balance in people with RA were reported across five studies [3,9–11,13]. A core set of outcome measures and consistent measurement protocols are currently lacking in falls research in RA populations.

Inactivity and exercise intolerance, due to pain, fatigue and disease-related impairment, have been reported in patients with RA [24,25]. Jamison et al. [11] suggested that inactivity and physical de-conditioning may increase fear of falling, leading to further inactivity, deterioration of physical functioning and increased falls risk. A similar cycle of physical and psychological deterioration, known as post-fall syndrome, is recognised in older adult fallers [26], but has not been reported in falls-related RA studies. However, physiological fall risk factors may be fundamentally linked as part of a falls risk cycle.

Physiological changes, as a result of RA, are widely reported and include decreased muscle strength, limited joint range of motion, impaired gait and mobility and decreased plantar sensation [24,25,27]. These factors result in functional impairment, which may affect the quality of sensory information and automatic postural responses required for the maintenance of static and dynamic balance [24]. Previous studies have found that balance is significantly decreased in the RA population compared to healthy controls [25,28,29]. Impaired balance may be associated with falls in RA. However, evidence to support impaired balance is lacking. Positive findings for fall risk factors relate to measures of static balance only. In addition, specific measures of balance, which have been identified as falls risk factors, were not included in any other study. The Chair Stand Test, a proxy measure of lower extremity muscle strength and endurance, was the only intrinsic measure of functional change that may impact balance in RA. Decreased plantar sensation is linked to falls in older adults [30,31]. However, plantar sensation has not been assessed as a potential fall risk factor in people with RA.

In assessing dynamic postural stability in patients with RA, compared to healthy controls, Aydoğ et al. [24] determined that dynamic balance was affected by functional status but not RA disease activity. Falls risk in RA may also be independent of disease activity. However, the available evidence is inconsistent and limits our ability to draw specific conclusions. Based on the current evidence, it is unclear as to whether pain is a risk factor for falls in RA. Smulders et al. [13] suggested that pain may be an important predictor of future falls due to a decrease in physical activity and decline in physical functioning as a result of painful arthritic joints. Decreased physical functioning, leading to a decline in muscle strength, has been linked to a decrease in postural stability in people with RA, which may increase fall risk [25].

The foot is a common site of pathology in the early stages of RA, and foot involvement becomes greater with disease progression [32]. Foot deformity and altered foot function may also affect balance and increase the risk of falls. Only one study included foot-specific measures as potential falls risk factors in people with RA [10]. However, several studies in non-RA populations have suggested that foot and ankle characteristics, including structural and functional changes, may impair balance and increase the risk of falling in healthy older adults [30,33–38].

People with RA are at an increased risk of developing co-morbid conditions, including cardiac disease, bone disease and depression [22]. Medications used to manage co-morbid conditions have been linked to falls in RA [3,10,14]. The contribution of anti-hypertensive medication to falls risk in RA remains unclear. However, there is evidence linking anti-hypertensives to falls in older adult populations [2,39]. The findings from the review suggest that increasing the number of medications is a risk factor for falls in RA. Polypharmacy, generally defined as four or more medications, is recognised as a falls risk in older adults and patients with diabetes [2,40,41]. One study found that taking four or more medications was a predictor of future falls in people with RA [3].

There are limitations to this systematic review. A meta-analysis was not conducted due to heterogeneity across the studies. We also excluded studies not written in English. However, strengths of this systematic review are the use of a validated quality assessment tool [6] and the systematic approach used to assess the risk factors for falls in people with RA. Fall risk factors identified in this review, such as prior fall history and polypharmacy, are also common to non-RA populations. Therefore, the review did not identify RA disease-specific falls risk factors over and above other older populations.

Given the paucity of evidence for fall risk factors in people with RA, further prospective studies with larger sample sizes and longer time frames for prospective falls follow-up are warranted. Considering the extent of foot disease in RA, and the impact of RA on foot function, foot and ankle characteristics could be considered for future falls studies. Future studies may also consider the combined effect of physiological fall risk factors as predictors of falls. Consensus of outcome measures and consistent measurement protocols would also be valuable in future falls research in RA populations.

Summary

Studies of people with RA show large variation in falls incidence. This disparity likely reflects inconsistency in method for collecting falls data. In people with RA, falls appear to be independent of age, gender and RA disease duration. History of a prior fall and increasing number of medications are the most significant predictive risk factors. There is a dearth of evidence to support other fall risk factors in RA, in particular, RA disease-specific risk factors. Further studies would be valuable to supplement the existing body of knowledge and should include outcome measures and measurement protocols consistent with previous work. Future studies should also follow previously published consensus guidelines for collecting and reporting falls data.

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Appendix 12: TekScan MatScan® reliability study

Brenton-Rule A, Mattock J, Carroll M, Dalbeth N, Bassett S, Menz HB, et al. Reliability of the TekScan MatScan ® system for the measurement of postural stability in older people with rheumatoid arthritis. J Foot Ankle Res. 2012;5:21.

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METHODOLOGY Open Access

Reliability of the TekScan MatScan® system for the measurement of postural stability in older people with rheumatoid arthritis

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Abstract

Background: Postural stability can be measured in clinical and research settings using portable plantar pressure systems. People with rheumatoid arthritis (RA) have decreased postural stability compared to non-RA populations and impaired postural stability is associated with falls in people with RA. The purpose of this study was therefore to investigate the reliability of the TekScan MatScan® system in assessing postural stability in people with RA.

Methods: Twenty three participants with RA, mean (SD) age 69.74 (10.1) years, were assessed in barefoot double-limb quiet standing, with eyes open and eyes closed, for antero-posterior and medio-lateral postural sway values. Three repetitions, at a sampling frequency of 40 Hz, were recorded for each test condition to obtain a mean value. Measurements were repeated one hour later. Intraclass correlation coefficients (ICC) with 95% confidence intervals (CI) were calculated to determine between-session reliability. Measurement error was assessed through the calculation of the standard error of the measurement (SEM) and the smallest real difference (SRD).

Results: The system displayed good to excellent reliability for antero-posterior and medio-lateral sway, with eyes open and closed, as indicated by ICC values ranging from 0.84 to 0.92. Measurement error, as evidenced by the SEM, ranged from 1.27 to 2.35 mm. The degree of change required to exceed the expected trial to trial variability was relatively high, compared to mean values, with SRD ranging from 3.08 to 5.71 mm.

Conclusions: The portability and ease of use of the TekScan MatScan® makes it a useful tool for the measurement of postural stability in clinical and research settings. The TekScan MatScan® system can reliably measure double-limb quiet standing in older people, aged 60 to 80 years, with RA.

Keywords: Postural sway, Balance, Falls, Rheumatoid arthritis, Pressure system

Background

Postural stability can be defined as the maintenance of an upright position in quiet standing or the recovery of balance, associated with voluntary movement [1]. In order to maintain postural stability the body's global centre-of-mass (COM) must remain inside the body's base of support; as defined by the outer borders of the feet. This requires active neural control, whereby the central nervous system maintains the COM position in space, resulting in tiny oscillatory movements referred to as postural sway [2]. Postural sway can be measured using portable plantar pressure systems, such as the TekScan MatScan®, which records sway parameters as centre of pressure (COP) excursions in an antero-posterior (AP) and medio-lateral (ML) direction.

Rheumatoid arthritis (RA) is a chronic inflammatory disease characterized by synovial inflammation and progressive articular destruction [3]. Foot deformity is common in RA, with 75% of patients reporting foot involvement within four years of diagnosis, increasing to 90% as the disease progresses [4]. An association between foot deformity and foot function in people with RA has been shown in previous studies [3,5-9]. Functional changes, such as muscle weakness, painful joints,

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altered gait and decreased postural stability can impair balance and affect everyday activities requiring postural control [10-12].

A high incidence of falls in people with RA has been reported in the literature [13,14]. In a study of 253 people with RA, Armstrong et al. [13] found that 33% reported falls in the previous year, with 52% of these falling more than once. Similarly, Fessel and Nevitt [14] reported that 31% of their sample of 570 RA participants fell once per year and 16% fell twice or more. Postural sway has been found to be increased in RA [15] and associated with falls in people with RA [16]. Rome et al. [15] conducted an exploratory study of 19 RA participants and age matched non-RA controls. AP and ML postural sway was measured for 30 seconds, with eyes open and closed, using a force plate. The results showed that RA participants displayed a significantly larger COP excursion in the AP direction during quiet standing, when compared to the non-RA group, suggesting that postural control mechanisms such as ankle strategies are impeded by the RA process. In a one year prospective study of 84 women with RA, Hayashibara et al. [16] reported that 50% of participants fell and increased postural sway was significantly associated with falls in the study group.

The TekScan MatScan® is commonly used in research and clinical settings and has previously been shown to have moderate to good reliability for the measurement of plantar forces and pressures during barefoot walking in healthy children (ICCs 0.58 to 0.99) [17] and adults (ICCs 0.44 to 0.95) [18]. In both studies, interpretation of the ICCs was in accordance with Portney and Watkins [19] whereby values of > 0.75 indicate good reliability, values ranging from 0.5 to 0.75 imply moderate reliability and values < 0.5 suggest poor reliability.

However the reliability of the TekScan MatScan® for assessing postural sway in double-limb quiet standing has not been evaluated. Previous studies have demonstrated postural stability changes in RA and an association between increased postural sway and falls in an RA population [15,16]. Further investigation into the relationship between postural stability and falls in RA is warranted and there is a need to ensure the equipment used to measure postural sway variables is reliable in this population. Therefore, the primary objective of this study is to determine the between-session reliability of COP based measures of postural control in RA participants using the TekScan MatScan® system.

Methods

Participants

Twenty three participants with RA, all meeting the American College of Rheumatology diagnostic criteria [20], were recruited from an outpatient clinic based at AUT University, Auckland, New Zealand. Participants were excluded from the study if they were younger than 18 years, were diagnosed with a neurological condition which could impair balance; such as multiple sclerosis, Parkinson's disease and history of stroke; lower limb amputation and diabetes with previously diagnosed peripheral neuropathy.

Clinical characteristics

Clinical characteristics including age, ethnicity, gender, body mass index (BMI), disease duration, co-morbidities, revised Health Assessment Questionnaire (HAQ-II) [21] and pharmacological management, were recorded for each participant. Pharmaceuticals included non-steroidal anti-inflammatory drugs (NSAIDs), Methotrexate, other disease modifying anti-rheumatic drugs (DMARDs), prednisone and biologic therapies.

Equipment

The TekScan MatScan® pressure mat model 3150 (TekScan Inc, South Boston, USA) was used to capture postural sway values over two sessions. The TekScan MatScan® is a low profile floor mat (5 mm thick) consisting of 2288 resistive sensors (1.4 sensors/cm^2) with a sampling frequency of 40 Hz. The mat provides measures of AP and ML sway parameters described as; area and direction of sway, distance and direction travelled by the COP and variability of distance travelled by the COP [22]. In the current study, AP and ML sway were measured using the excursion (mm) of the COP in the AP and ML directions. The Sway Analysis Module (SAM™) software was used in conjunction with the TekScan MatScan® to analyze the sway data. One examiner (JM) assessed all the participants. Prior to the commencement of the study, the examiner underwent training in the use of the TekScan MatScan® and interpretation of data using the TekScan SAM™ software.

Procedure

The AUT University Ethics Committee approved the study. Written informed consent was given by all participants prior to testing. Participants were tested in barefoot double-limb quiet standing on two separate occasions approximately one hour apart. A one hour interval was chosen for practical purposes to enable data collection to occur during the participant's scheduled podiatry appointment. The one hour interval also ensured that the clinical characteristics of the participants remained consistent. During the period between sessions, participants were provided with a podiatry assessment and treatment as required. To avoid fatigue, the podiatry appointment was conducted in an adjoining room. During testing each participant was directed to step onto the TekScan MatScan® pressure mat and

stand in their natural angle and base of gait with their arms by their sides looking straight ahead. To enable the foot position to be replicated from trial to trial, a template was created for each individual according to their preferred barefoot quiet standing position [23]. In order to prevent vestibular disruption and head movement, head position was standardized by asking each participant to focus on the centre of a visual target. The visual target, a 2 cm diameter white spot, was positioned on a screen 2 m in front of the pressure mat at eye level [24]. Participants were asked to remain in this position for a period of 30 seconds while postural sway data was recorded. Participants were tested with eyes open (EO) then eyes closed (EC). Trials were repeated three times for each eye condition to obtain a mean value. Each participant was asked to step backwards off the pressure mat and sit for 30 seconds between repetitions to avoid fatigue. The testing protocol was in accordance with a previous study which used the TekScan MatScan® system to evaluate postural sway in healthy older adults [24].

Data analysis

Data were analyzed using SPSS V18. Alpha was set at 0.05. All continuous data were screened for normality using the K-S (Kolmogorov-Smirnov) one-sample test. The mean (SD) was obtained for all continuous data. Intraclass Correlation Coefficients (ICC, 2,1) with 95% confidence intervals (CI) were applied to determine between-session reliability of mean sway measurements using a two way mixed effects model with consistency definition [25]. Reliability findings were interpreted by arbitrary benchmarks initially proposed by Fleiss [26]. The strength of the agreement was deemed poor if the correlation ranged from 0 to 0.40; fair to moderate if the correlation ranged from 0.40 to 0.75 and excellent if the correlation ranged from 0.75 to 1.00. Standard error of the measurement (SEM) and SEM% were calculated to assess the difference between the actual measured score and the estimated true scores [27]. The smallest real difference (SRD) was calculated from the SEM to indicate the degree of change that would exceed the expected trial to trial variability [28]. The SEM, SEM% and SRD were calculated as follows: SEM = SD$\sqrt{1}$-ICC, SEM% = (SEM/mean) x100, SRD = SEM $\times \sqrt{2} \times 1.717$ (where 1.717 represents the t value of distribution for a 95% CI ($df = 22$). Bland-Altman plots were calculated to demonstrate graphical representation of key reliability findings. The Bland and Altman method calculates the range within which the difference between the two sessions will lie within a probability of 95% [29]. The use of ICC's and Bland-Altman plots provide complementary information, as shown by Rankin and Stokes [30].

Results

All participants completed the trials. No outliers were identified. Participant characteristics are presented in Table 1. All participants were European and most were female. Descriptive statistics for postural sway values are presented in Table 2. The data were normally distributed.

The relative reliability between sessions, when using the mean measurement for AP and ML sway with eyes open and closed, was good to excellent, as evidenced by ICCs ranging from 0.84 to 0.92 (Table 3). The SEM, SEM% and SRD values consistently showed a moderate level of measurement error, SEM 1.27 to 2.35 mm, SEM % 12.13 to 14.51%, SRD 3.08 to 5.71 mm (Table 3).

Figure 1 illustrates the Bland-Altman plot for AP EO measurement in session 1 and 2, with 95% limits of agreement, bias of -0.17 mm (lower limit -7.19 mm, upper limit 6.85 mm). Figure 2 illustrates the Bland-Altman plot for AP EC measurement in session 1 and 2, with 95% limits of agreement, bias of -0.48 mm (lower limit -9.69 mm, upper limit 8.75 mm). Figure 3 illustrates the Bland-Altman plot for ML EO measurement in session 1 and 2, with 95% limits of agreement, bias of -1.39 mm (lower limit -6.59 mm, upper limit 3.81 mm). Figure 4 illustrates the Bland-Altman plot for ML EC measurement in session 1 and 2, with 95% limits of agreement, bias of 0.34 mm (lower limit -4.65 mm, upper limit 5.32 mm).

Table 1 Demographic and clinical characteristics

Variable	Value
Age, years, mean (SD), range	69.74 (10.14) 36
Female sex, n (%)	21 (91%)
Ethnicity, n (%)	
European	23 (100%)
Disease duration, years, mean (SD), range	24.24 (12.6) 54
BMI, kg/m^2, mean (SD), range	26.7 (5.7) 24.1
Revised Health Assessment Questionnaire, mean (SD), range	1.14 (0.56) 1.8
Co-morbidities	
Diabetes, n(%)	3 (13%)
Hypertension	7 (30%)
Other cardiovascular disease, n(%)	4 (17%)
Osteoporosis, n(%)	2 (9%)
Anaemia, n(%)	2 (9%)
Medications	
Methotrexate, n(%)	15 (65%)
Other DMARD, n(%)	8 (35%)
NSAID, n(%)	12 (52%)
Biologics, n(%)	3 (13%)
Corticosteroids, n(%)	9 (39%)

Table 2 Descriptive statistics for AP and ML sway (between sessions)

Sway direction	Eye condition	Session 1 mean(SD) mm	Session 1 range mm	Session 2 mean(SD) mm	Session 2 range mm
AP	EO	14.45 (5.44)	5.52-25.20	14.63 (6.10)	6.62-29.97
	EC	18.24 (7.07)	6.81-33.51	18.72 (7.71)	6.73-39.97
ML	EO	8.47 (2.82)	4.71-15.39	9.86 (4.27)	4.60-22.61
	EC	10.62 (4.48)	4.08-24.35	10.29 (4.83)	5.18-22.91

AP: antero-posterior; *ML*: medio-lateral; *EO*: eyes open, *EC*: eyes closed.

Discussion

The reliability of a measurement system used clinically, or in research, must be established in order to be confident in achieving reproducible and meaningful results on different testing occasions. In the current study, the system showed good to excellent between-session reliability in assessing barefoot postural control in double-limb quiet standing, in a sample of older people with RA, as evidenced by ICCs ranging from 0.84 to 0.92. However, measurement error, as expressed by the SEM, SEM% and SRD was relatively high compared to mean values.

The reproducibility of the measures may be attributed to the accuracy of the TekScan MatScan® system in capturing the variables of interest. Indeed the system was found to be highly accurate in an independent study which compared several commonly used plantar pressure measurement systems [31]. Further, due to postural sway values being captured by the measuring system and not the examiner, rater error and bias which may be present in non-computerized tools, such as the sway-meter [32], was minimized.

Measurement error can be due to the precision of the instrument, systematic error introduced by the rater, or the variation in the population being measured [33]. In the current study, measurement error may have occurred as a result of the inherent variability of postural control parameters in the study sample. The wide range in recorded sway values, resulting in a large SD of the mean, supports this possibility. Variation in postural stability parameters within an RA population is to be expected and may be associated with the differing demographic and clinical characteristics of the sample. For example, in a study of 61 patients with RA, Ekdahl [11] found that age, sex and high C-reactive protein level were related to decreased postural control in quiet standing. Given the relatively broad inclusion criteria in the current study it would be expected that this population would display a broad range of demographic and clinical characteristics and therefore a potentially wide range of postural sway values. Therefore, in the current study, the relatively high SEM, SEM% and SRD values may be indicative of the variability of the population tested rather than the reliability of the equipment used to test the population.

It can be further argued that SEM and SRD values are of more relevance in the analysis of within-subject variability. Indeed in a clinical setting measures of postural stability would be undertaken on individuals not populations and the ability to detect a real change in the variables measured over time is essential. As the study aim was to assess between-session reliability over 1 hour, within-subject variability was not analyzed however it is acknowledged that such analysis would be valuable in

Table 3 Between-session reliability

Sway	ICC	95% CI	SEM (mm)	SEM%	SRD (mm)
AP sway EO	0.89	0.75-0.96	1.79	12.30	4.35
AP sway EC	0.89	0.74-0.95	2.35	12.70	5.71
ML sway EO	0.84	0.63-0.93	1.33	14.51	3.23
ML sway EC	0.92	0.81-0.97	1.27	12.13	3.08

AP: antero-posterior; *ML*: medio-lateral; *EO*: eyes open, *EC*: eyes closed.

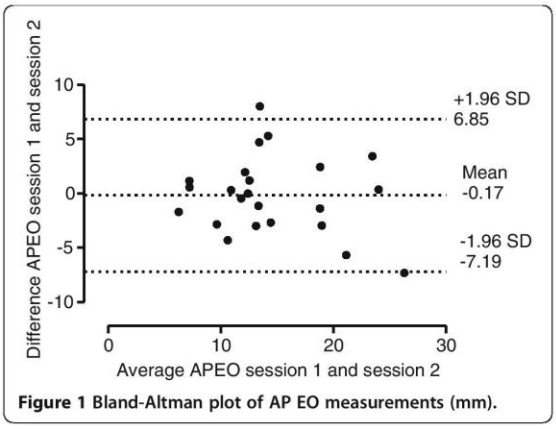

Figure 1 Bland-Altman plot of AP EO measurements (mm).

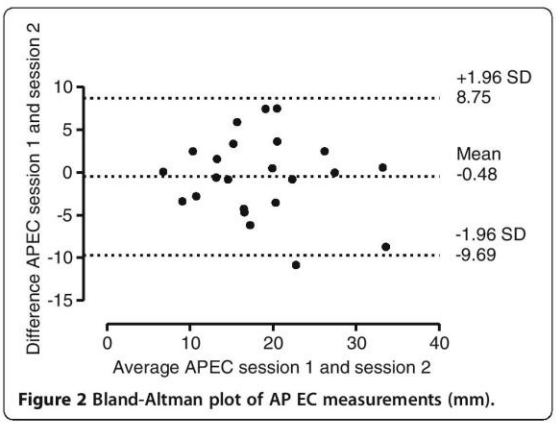

Figure 2 Bland-Altman plot of AP EC measurements (mm).

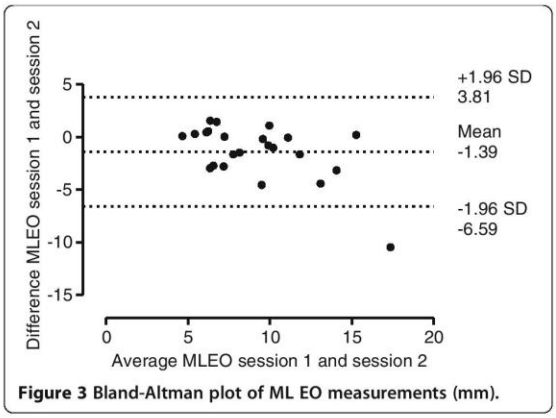

Figure 3 Bland-Altman plot of ML EO measurements (mm).

determining the potential measurement error of the system in a clinical setting.

Postural stability is controlled by the central nervous system. Afferent input from the somatosensory, visual and vestibular systems combine with coordinated muscle activity to maintain balance in quiet standing. In healthy adults, postural control is maintained through flexible and smooth interaction between these systems in order to maintain a stable equilibrium [34]. This may not be the case in an RA population as the ability to maintain balance in quiet standing has been shown to be decreased compared to healthy controls [15]. Variability in postural control between participants was found in the current study as demonstrated by the relatively high degree of measurement error. For this reason, it was necessary to assess the reliability of the TekScan MatScan® system in measuring postural control in an RA group specifically, as this is a population of particular interest to the researchers.

Postural control is a dynamic phenomenon that changes over time. As such, variability in COP values can be expected within individuals and should be

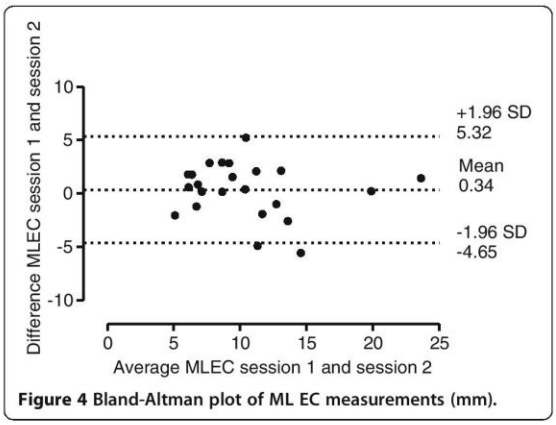

Figure 4 Bland-Altman plot of ML EC measurements (mm).

accounted for through repetition of test measurements to obtain a mean value [35]. In the current study, the mean of three test measurements of 30 seconds was taken. This was in accordance with a previous study which found that three measurements were sufficient for obtaining a consistent average for dynamic plantar pressure measurements in patients with foot problems associated with chronic arthritis [36]. Due to the variability of COP variables, comparison of individual measurements, i.e. within-session reliability, was not undertaken in the current study.

The role of vision in postural control is well documented and is of particular importance in older adults [34]. Previous studies have demonstrated that removing visual feedback increases postural sway compared to EO test conditions [32,37]. Whilst the current study was interested in adults with RA aged 18 years and older, the cohort age range was 60 to 80 years and hence can be defined as older adult. Our results showed an increase in AP and ML postural sway with the eyes closed condition compared to eyes open condition, which is in agreement with previous studies [24,32,37,38]. Further, when assessing AP and ML sway in an RA population compared with healthy controls, Rome et al. [15] found that, while both groups demonstrated greater sway in eye closed conditions compared to eyes open, the effect was more marked in the RA group. It is important therefore that postural stability in an RA population is assessed with eyes open and eyes closed and hence eyes open and eyes closed test conditions were used to assess the reliability of the equipment in the current study.

The TekScan MatScan® is a portable pressure system commonly used in research and clinical settings to capture and reproduce plantar pressure measures of dynamic foot function. The reliability of the system to accurately and consistently capture dynamic measures has been previously shown [17,18]. The results of the current study suggest that the TekScan MatScan® is reliable for assessing postural control in double-limb quiet standing in older adults with RA. Research implications include the ability to gain a better understanding of the changes in postural stability that occur with age [2] and diseases that affect the feet, such as diabetes and RA. Clinical implications include the ability to identify and manage, through podiatric intervention, patients who are at increased risk of falling. The system may also be useful in evaluating the efficacy of clinical interventions, such as pathological callus debridement, foot orthoses and therapeutic footwear, in reducing postural sway in RA patients.

We acknowledge the limitations of this study. The study cohort was not representative of the general RA population, as all participants were over the age of 60 years. RA affects women three times more than men

and peak age at onset is most commonly the fifth decade, although a shift towards older age at onset has been seen in recent studies [39]. A sampling frequency of 40 Hz is relatively low, compared to laboratory based force plate technology, however we believe it is acceptable for measuring the postural sway parameters of interest. Inflammatory disease activity was not assessed as part of the study protocol, and therefore it is not possible to assess the impact of disease activity on variability of the instrument. The study does not address the validity of the TekScan MatScan® in assessing postural control in quiet standing. The validity of a measurement tool can be described as its ability to measure what it is supposed to measure [40]. The validity of the TekScan MatScan® system has been reported by the manufacturer [18] however independent assessment comparing the TekScan MatScan® to force-platform technology would be valuable.

The reliability of the TekScan MatScan® for assessing double-limb quiet standing in healthy adults would be useful. Future investigations should also explore the reliability of the system during more complex dynamic balance tests, in people with RA, as well as other populations of interest such as patients with diabetes or older adults with a history of falls. Testing of the reliability of postural control measures in participants' usual footwear will also be of interest.

Conclusion

The portability and ease of use of the TekScan MatScan® makes it a useful tool for use in research and clinical practice. The results of the current study demonstrated good to excellent between-session reliability of postural control measures in older people with RA using the TekScan MatScan® pressure mat.

Competing interests

ABR, JM, MC, ND, SB and KR have no competing interests to declare. HBM is Editor-in-Chief of the Journal of Foot and Ankle Research. It is journal policy that editors are removed from the peer review and editorial decision-making processes for papers they have authored or co-authored.

Authors' contributions

ABR and KR designed the study. JM collected and inputted the data. ABR and MC conducted the statistical analysis. ABR drafted the manuscript with assistance from KR, ND, MC, SB and HBM. All authors approved the final manuscript.

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