DEVELOPMENT AND EVALUATION OF EDUCATIONAL MATERIAL TO ADDRESS THE CARDIOVASCULAR ASPECTS OF RHEUMATOID DISEASE

by

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ABSTRACT

Rheumatoid arthritis (RA) is the most common inflammatory arthritis and patients require appropriate information and education. Cardiovascular disease (CVD) accounts for 50% of its mortality, due to both clustering of traditional risk factors and the novel role of systemic inflammation. However, there are no educational materials about CVD designed specifically for people with RA; existing generic resources are likely to be inadequate as their advice is not set in the context of the physical and psychosocial constraints of RA. Using a recommended framework for the design of complex interventions, qualitative stakeholder research was undertaken which informed the design of an eight week cognitive-behavioural education programme, underpinned by social cognition models and stages of change theory. An appropriate outcome questionnaire was developed and psychometrically validated. A randomised controlled trial of this programme showed that, compared to controls, patients achieved significant improvements in knowledge, which translated into changing their psychological views, particularly intentions, to make behaviour change and, in turn, an improvement in diastolic blood pressure was observed. The implications of this study are that patient education has a significant role to play in CVD risk factor modification for patients with RA and furthermore a theoretically-driven process of developing patient education materials is the approach most likely to yield dividends.

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LIST OF ABBREVIATIONS

ACR	American College of Rheumatology
ANA	Anti nuclear antibodies
Anti-CCP	Anti- cyclic citrullinated peptide antibodies
Anti-TNFα	Anti-tumour necrosis factor α therapy
ANCOVA	Analysis of covariance
ANOVA	Analysis of variance
AR-UK	Arthritis Research UK
BMI	Body mass index
BSR	British Society for Rheumatology
CHD	Coronary heart disease
CHF	Congestive heart failure
cIMT	Carotid intima media thickness
CKD	Chronic kidney disease
COX II	Cyclo-oxygenase II inhibitors
CVA	Cerebrovascular accident
CVD	Cardiovascular disease

DBP	Diastolic blood pressure
DM2	Type 2 diabetes mellitus
DMARD	Disease-modifying anti-rheumatic drug
ECG	Electrocardiogram
EDH	Ms Elizabeth Hale
EULAR	European League Against Rheumatism
GFR	Glomerular filtration rate
GJT	Dr Gareth Treharne
HAQ	Health Assessment Questionnaire
HDFQ	Heart Disease Fact Questionnaire
HDFQ-RA	Heart Disease Fact Questionnaire-Rheumatoid Arthritis
HDL	High density lipoprotein
HJ	Holly John
HLA	Human leucocyte antigen
hsCRP	High sensitivity C reactive protein
IHD	Ischaemic heart disease
IPA	Interpretative Phenomenological Analysis

LDL	Low density lipoprotein
MHC	Major histocompatibility complex
MI	Myocardial infarction
MRC	Medical Research Council
NRAS	National Rheumatoid Arthritis Society
NSAIDs	Non-steroidal anti-inflammatory drugs
RA	Rheumatoid arthritis
RhF	Rheumatoid factor
SBP	Systolic blood pressure
SD	Standard deviation
SMR	Standardized mortality ratio
TC	Total cholesterol

LIST OF PAPERS AND CONFERENCE PROCEEDINGS

This thesis incorporates the following ten papers:

1. **John H**, Hale ED, Treharne GJ, Kitas GD. Patient education on cardiovascular aspects of rheumatoid disease: An unmet need. Rheumatology 2007; 46: 1513-1516.

2. **John H**, Kitas G, Toms T, Goodson N. Cardiovascular Co-morbidity in Early Rheumatoid Arthritis. Best Pract Res Clin Rheumatol 2009; 23: 71-82.

3. **John H**, Hale ED, Treharne GJ, Carroll D, Kitas GD. "All singing from the same hymn sheet": Health professionals' perceptions of developing patient education material about the cardiovascular aspects of rheumatoid arthritis. Musculoskeletal Care 2009; 7: 272-87.

4. **John H**, Hale ED, Treharne GJ, Carroll D, Kitas GD. "Extra information a bit further down the line": Rheumatoid arthritis patients' perceptions of developing educational material about the cardiovascular disease risk. Musculoskeletal Care 2009;7:272-87.

5. **John H**, Treharne GJ, Hale ED, Panoulas V, Carroll D, Kitas GD. Development and initial validation of a heart disease knowledge questionnaire for people with rheumatoid arthritis. Pt Educ Couns 2009; 77: 136-43.

6. **John H**, Hale ED, Bennett P, Treharne GJ, Carroll D, Kitas GD. Translating patient education theory into practice: developing material to address the cardiovascular education needs of people with rheumatoid arthritis. Pt Educ and Couns 2011; 84: 123-7.

7. **John H**, Carroll D, Kitas GD. Cardiovascular education for people with rheumatoid arthritis; what can existing patient education programmes teach us? Rheum 2011; 50: 1751-9.

8. **John H**, Toms TE, Kitas GD. Rheumatoid arthritis: is it a coronary heart disease equivalent? Curr Opin Card 2011; 26: 327-33.

9. **John H**, Hale ED, Treharne GJ, Korontzis K, Obrenovic K, Carroll D, et al. Patient evaluation of a novel patient education leaflet about heart disease risk among people with rheumatoid arthritis. Musculoskeletal Care 2011; Epub ahead of print 06/05/2011

10. **John H**, Hale ED, Treharne GJ, Carroll D, Kitas GD. A randomised controlled trial of a cognitive behavioural patient education intervention versus a traditional information leaflet to address the cardiovascular aspects of rheumatoid disease. Submitted to Ann Rheum Dis 2011.

In addition, the following conference abstracts arose from presentations of material from this thesis:

1. Development and evaluation of patient educational material to address the cardiovascular aspects of rheumatoid disease. Presented at Arthritis Research UK 'Teach the Teachers', 2008 and British Society for Rheumatology/Arthritis Research UK Special Interest Group at British Society for Rheumatology Annual General Meeting 2008.

2. "All singing from the same hymn sheet": Health Professionals' perceptions of developing patient education material about the cardiovascular aspects of rheumatoid arthritis. Rheum 2008; 47(Suppl 2): ii105(359).

3. Knowledge of Heart Disease in Patients with Rheumatoid Arthritis. Midlands Rheumatology Society Spring Meeting, 2008

4. "Extra information a bit further down the line": Rheumatoid arthritis patients' perceptions of developing educational material about the cardiovascular disease risk. Rheum 2009; 48(Suppl 1): i149(372).

5. Development and validation of a heart disease knowledge questionnaire for people with rheumatoid arthritis. Rheum 2009; 48(Suppl 1): i135(351).

6. Translating patient education theory into practice: developing material to address the cardiovascular education needs of people with rheumatoid arthritis. Rheum 2011; 50(Suppl 3): iii81(102) and poster presentation Arthritis Research UK Annual Fellows Meeting 2011

In addition, the following papers were published during the period of postgraduate study at the University of Birmingham:

1. Panoulas V, **John H**, Kitas GD. Six step management of hypertension in patients with rheumatoid arthritis. Future Rheumatology 2008; 3: 21-35.

2. Panoulas VF, Metsios GS, Pace AV, **John H**, Treharne GJ, Banks MJ, et al. Hypertension in rheumatoid arthritis. Rheum 2008; 47: 1286-1298.

3. Daoussis D, Panoulas VF, Toms T, **John H**, Antonopoulos I, Nightingale P, et al. Uric acid is a strong independent predictor of renal dysfunction in patients with rheumatoid arthritis. Arthritis Res Ther 2009; 11: R116.

4. Toms TE, Panoulas VF, **John H**, Douglas KM, Kitas GD. Methotrexate therapy associates with reduced prevalence of the metabolic syndrome in rheumatoid arthritis patients over the age of 60 – more than just an anti-inflammatory effect? A cross sectional study. Arthritis Res Ther 2009; 11: R110.

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6. Metsios GS, Stavropoulos-Kalinoglou A, Sandoo A, van Zanten JJ, Toms TE, **John H**, et al. Vascular function and inflammation in rheumatoid arthritis: the role of physical activity. Open Cardiovasc Med J 2010; 23: 89-96.

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CHAPTER 1: GENERAL INTRODUCTION; RHEUMATOID ARTHRITIS

Rheumatoid arthritis (RA) is thought to have emerged as a condition in Europe in the early 19th century, although the disease had been prevalent for thousands of years in North America (1). Today, rheumatoid arthritis (RA) is the most common chronic inflammatory polyarthritis (1).

Epidemiology

Established in 1989, the Norfolk Arthritis Register recruited and followed up all adults presenting to primary care with recent onset inflammatory polyarthritis. This cohort, recruited from a well-defined population, revealed an annual incidence of RA of 36/100000 in women and 14/100000 in men. The peak age of onset in women was aged 65-74, whereas in men it was aged over 75 (2). A prevalence study, using the same cohort, showed the overall prevalence of RA in the adult population to be 0.8%; sex-specific prevalence estimates are 1.1% in women and 0.4% in men (3). Geographically, interesting variations in occurrence of RA have been observed: South European countries possibly have lower incidence rates of RA than north European and North American countries (1;4). Differences in genetic or environmental (for example, the Mediterranean diet) factors between these populations may explain these differences. In developing countries, a lower prevalence of RA has been observed; this may reflect the shorter life expectancy or poorer access to medical care in developing countries (4). Other studies have suggested that RA may be related to an industrialized lifestyle (1).

Clinical features

RA is an inflammatory arthritis, characterized by synovial inflammation which manifests clinically as joint swelling, tenderness, warmth and functional loss. The 1987 American Rheumatism Association (now the American College of Rheumatology (ACR)) classification criteria for RA require four or more of the following criteria: morning stiffness, arthritis of at least three or more joints for at least six weeks, arthritis of hand joints for at least six weeks, symmetrical involvement of joints, presence of rheumatoid nodules, positive rheumatoid factor, or typical radiographical changes (5). Uncontrolled articular inflammation will result in bony erosions and subsequent joint damage, deformity and disability (6). Furthermore, RA is a multisystem disease; extra articular manifestations include rheumatoid nodules or rheumatoid vasculitis as well as organ specific involvement; rheumatoid lung disease includes pulmonary effusions, fibrosis or nodules, cardiac involvement includes pericarditis or conduction defects, ocular involvement includes episcleritis and scleritis as well as sicca symptoms with secondary Sjogrens syndrome, neurological involvement includes peripheral nerve entrapment syndromes, mononeuritis multiplex, peripheral neuropathy or cord compression. Longstanding uncontrolled inflammation may cause renal amyloidosis (6).

Aetiology

The exact aetiology of RA is not clear but is likely to be multifactorial. Determinants of the onset of RA include both genetic and environmental, such that when a genetically predisposed individual is exposed to certain environmental/host antigens an immune response occurs (7).

Clinical observation reveals a tendency for RA to run in families and indeed genetic factors are thought to explain 60% of the susceptibility to RA (8). Multiple genetic factors are responsible. The major histocompatibility complex (MHC) is a large genomic region on chromosome 6 that encodes MHC molecules; class II MHC molecules are expressed on most immune system cells, specifically antigen presenting cells. The best known genes in this MHC region are the human leucocyte antigen (HLA) genes. Many alleles at the HLA locus DRB1 have been found to associate with the development and severity of RA, including HLA-DR4, the first allele to be associated with RA, discovered in 1978 (1). These alleles share an amino acid sequence in the third hypervariable region of their DRB1 chain, and this is referred to as the shared epitope hypothesis (7). In particular, the allele HLA-DRB1*0404 seems to be associated with the susceptibility of developing RA whereas only a modest association was found between the presence of other shared epitope alleles and recent onset inflammatory polyarthritis (9). The other major susceptibility locus is the PTPN22 gene (10). More recently other genetic loci have been implicated; a single nucleotide polymorphism in the STAT4 on chromosome 2 (11), the region of chromosome 9 containing TRAF1 and C5 genes (14) and a locus lying between the OLIG3 and TNFAIP3 genes on chromosome 6 (13) have been to found to associate with an increased risk of RA.

Many environmental factors have been shown to have an aetiological role, including hormonal factors, lifestyle factors and the role of infection (1). The incidence is higher in women; use of the oral contraceptive pill protects against the development of RA whereas subfertility and an adverse pregnancy outcome are associated with an increased risk of developing RA (14). Multiple studies have shown a positive association between cigarette smoking and RA (15;16),

and seropositive RA (15;17), including studies of recent onset inflammatory arthritis (18). Only moderate intensity smoking was required to confer such risk and this risk remained for many years after smoking cessation (15). An association between obesity and the development of RA has been observed (18). Diet may also play a role in the aetiology of RA (19). There is some evidence that those consuming a low daily intake of antioxidants, such as vitamin C (20) or carotenoids, particularly β cryptoxanthin (21), were at greater risk of subsequently developing inflammatory polyarthritis; synovial inflammation is mediated by free radical activity, hence antioxidants, which scavenge reactive oxygen radicals and protect against oxidative damage would have a protective effect. Red meat is a source of arachidonic acid, involved in the production of eicosanoids which can have proinflammatory activity (22). Oils, such as olive oil or oil-rich fish may also have a protective effect via their anti-inflammatory properties; certainly, RA is less common in Southern Mediterranean countries where the diet is characterized by high quantities of fruit and vegetables, olive oil and oil-rich fish (19).

Other environmental factors which may trigger the development of RA include a recent infection, with Epstein-Barr virus possibly implicated, (23) or immunization (24). A history of a blood transfusion associates with developing RA (18).

Predictors of severe rheumatoid disease

The clinical course of RA may vary across a wide spectrum from mild to severe disease.
As well as determining susceptibility, patients who are positive for the shared epitope are at high risk of severe RA (13;25). Environmental determinants of poor outcome include older age at

onset (26) and female gender as well as smoking. Smoking is associated with rheumatoid factor positivity and more severe rheumatoid disease (27) as well as a greater likelihood of developing extra-articular disease, such as rheumatoid nodules or vasculitis (28). Disease-specific factors and measures of inflammation which have been shown to associate with adverse radiological outcome include autoantibody status (anti- cyclic citrullinated peptide (CCP) antibodies are associated with the development and extent of erosions (29)) as well as combined measures such as swelling of at least two large joints, disease duration of more than three months and a positive rheumatoid factor (30) or Larsen erosion score and swollen joint score (31).

Treatment

Perhaps the greatest determinant of RA outcome is treatment. Historically, treatment was initially with non-steroidal anti-inflammatory drugs, progressing to sequential monotherapy with disease-modifying anti-rheumatic drugs (DMARDs), such as methotrexate or sulphasalazine, once erosions had developed (32). However, since the early 1990s, when it became apparent that erosions and damage developed early in the disease course, treatment strategies have radically changed; the emphasis is now on early and aggressive treatment to achieve tight control of RA (33;34) . Initial combination DMARD therapy, rather than sequential monotherapy (35) or step-up combination therapy (36) has been shown to result in significantly better outcomes. Corticosteroids are used to rapidly treat active disease, both early in the disease course, during a flare or as bridging therapy between DMARDs; occasionally corticosteroids are used long-term at a low dose if DMARDs are contraindicated (37). The advent of anti-tumour necrosis factor alpha therapy (infliximab, etanercept and adalimumab) further revolutionized outcomes being

effective in patients who had not responded to traditional DMARDs, both in terms of improving symptoms and signs of RA as well as inhibiting structural damage (34). Further biologic treatments have been licensed and the goal of treatment is remission.

Inevitably, treatments may be associated with side-effects. Non-steroidal anti-inflammatory drugs may cause upper gastrointestinal side-effects, and both these, as well as cyclo-oxygenase II inhibitors (coxibs) may induce or aggravate hypertension (38;39) as well as increase a person's risk of cardiovascular disease (CVD) (40). Furthermore, hypertension may also be a side-effect of the DMARDs leflunomide or ciclosporin or due to treatment with corticosteroids (38). Different DMARD treatments may also be associated with some of the following; rashes, nausea, diarrhoea, bone marrow suppression, renal or hepatic toxicity, pulmonary toxicity and others (41). Other side-effects of corticosteroids include increased appetite with consequent weight gain, diabetes, osteoporosis, thinning of the skin and easy bruising and cataracts (42). Biologic treatments associate with an increased risk of infection, demyelinating disorders, cardiac failure and although there is a theoretical risk of malignancy there is no evidence of an increased risk over that which would be expected of the general RA population (43).

Importantly, medical treatments for RA must be provided within a multidisciplinary team setting whereby nurse specialists provide drug counselling and monitoring, occupational therapists provide joint protection advice, splints, assistive equipment, podiatrists assess for biomechanical foot deformities and provide insoles and shoes and physiotherapists improve muscle strength, manage pain, improve function and promote exercise (37;40). Indeed exercise is particularly important for people with RA as it helps reduce RA-related inflammation and improves function,

pain, mobility and psychological well-being (44). All these health professionals may contribute to patient education programmes which can promote self-management, positive health behaviours and concordance between health professionals and patients (45).

Co-morbidity

Co-morbidities associated with RA include cardiovascular disease (CVD), infection, malignancy, depression, osteoporosis, lung disease and gastrointestinal ulceration (46). These are not only serious but also frequent conditions; on average, a person with established RA has two or more such co-morbidities and these may have a significant effect on quality of life (47), disability and mortality (46;48). Different comorbid conditions influence the different outcomes differently; for example, depression most commonly associates with work disability, whereas CVD and lung disease associate with mortality and hospitalization (46). Indeed CVD accounts for about 50% of the excess mortality in RA (49). Management of a patient with RA must therefore include screening, identifying, investigating and treating these comorbid conditions.

Prognosis

a) Function

The self-report Health Assessment Questionnaire is the primary measure of functional ability in RA (50). HAQ scores range from 0 (no disability) to 3 (severe disability). A score of greater than one suggests a person is functionally disabled. In a primary care based cohort, 29% of patients had a HAQ score greater than one, one year after presentation with inflammatory arthritis

(51). Five years after presentation, 47% of patients in the same cohort had a HAQ score greater than 1 (52). Thus, a conflict can be seen between the recommendation for people with RA to exercise and the practical issues involved. Other measures of functional disability include use of home adaptations and/or wheelchair use by 10% of patients at 5 years (53), 58% of RA patients reported some limitation on their driving ability (54) and a considerable number of men and women report trouble with their joints during sexual activities (55).

b) Employment

Work disability is an important outcome for people with RA of working age. Two English cohorts of patients with early RA have both shown that, at five year follow up, one third of (previously gainfully employed) people with RA had stopped working because of their RA (56) or ill health (57). Manual work (56) and high baseline Health Assessment Questionnaire (HAQ) scores (56;57) were predictors of work disability. Other studies in the USA and northern Europe have reported five year work disability rates between 29-50% (53).

c) Mortality

RA is associated with reduced life expectancy, and this has been noted in studies since the 1950's (58). A review of the main mortality studies since 1990 reveals a significant increase in mortality; this excess mortality is apparent within the first few years of the disease and increases with disease duration (58;59). Examining cause-specific mortality reveals that most of the excess deaths are attributable to infection, cardiovascular disease and respiratory disease. Non-Hodgkins lymphoma and lung cancer also explain some of the excess mortality (58).

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CHAPTER 2 (PART 1): GENERAL INTRODUCTION;

CARDIOVASCULAR DISEASE IN RHEUMATOID ARTHRITIS

Medical care of patients with rheumatoid arthritis (RA) involves managing their joint disease but also addressing the co-morbidities associated with RA, such as osteoporosis, depression, cardiovascular disease (CVD) and malignancy (1). Such co-morbidities may have a significant effect on quality of life, work disability or mortality (1). Indeed, the increased mortality of RA (2) is most commonly due to co-morbidities such as infection, CVD or respiratory disease (3); in particular, CVD accounts for almost 50% of the excess mortality (3;4). Given the frequency and impact of CVD co-morbidity in RA, this chapter focuses exclusively on this. We first summarise the epidemiological evidence for increased CVD morbidity and mortality in patients with established RA and discuss possible mechanisms for increased CVD risk in this group of patients. We then focus on the evidence for concurrent CVD co-morbidity early in the RA disease process: we consider cardiovascular risk prior to the onset of RA, examine shared risk factors or predictors for both RA and CVD and discuss an overall framework of incorporating these into the current drive for early diagnosis and management of RA.

Cardiovascular disease co-morbidity in established RA

Rheumatoid arthritis is associated with heart disease. Pericardial disease, including pericarditis and pericardial effusions, have long been identified as extra-articular manifestations of RA and were first described by Charcot in 1881 (5). The true prevalence of pericardial disease in association with RA is difficult to determine as it often remains clinically silent.

Echocardiographic studies in established cohorts of RA patients have reported prevalence rates of pericardial disease between 1-30%. Little is known about the prevalence of pericardial inflammation in the early years of RA. In addition myocardial and endocardial disease have been described in association with RA. Again, these cardiovascular complications rarely cause clinical symptoms and are often identified as coincidental finding on autopsy or imaging studies. Whilst extra-articular RA is associated with mortality (6), this does not appear to be due to haemodynamic consequences of structural rheumatoid cardiovascular disease.

Many epidemiological studies have examined cardiovascular mortality in longitudinal cohorts of RA patients (tabulated in (7) and (8), also (9;10)). Overall, the consensus is that CVD mortality is increased in RA, with standardized mortality rates (SMR) of between 1.13 and 5.15 (11). Studies that have explored cause-specific mortality in detail have highlighted that much of the excess CVD mortality is due to accelerated atherosclerotic CVD (12). As expected, there is also evidence for increased CVD morbidity, namely myocardial infarction (MI), congestive heart failure (CHF) and stroke, in patients with RA (13-15), with their risk for MI or CVA being at least double that of the general population (15). The relative risk for a CVD event is greatest in young adults, although in absolute terms the greatest difference in rates of CVD events was in older adults because CVD prevalence increases with age (15).

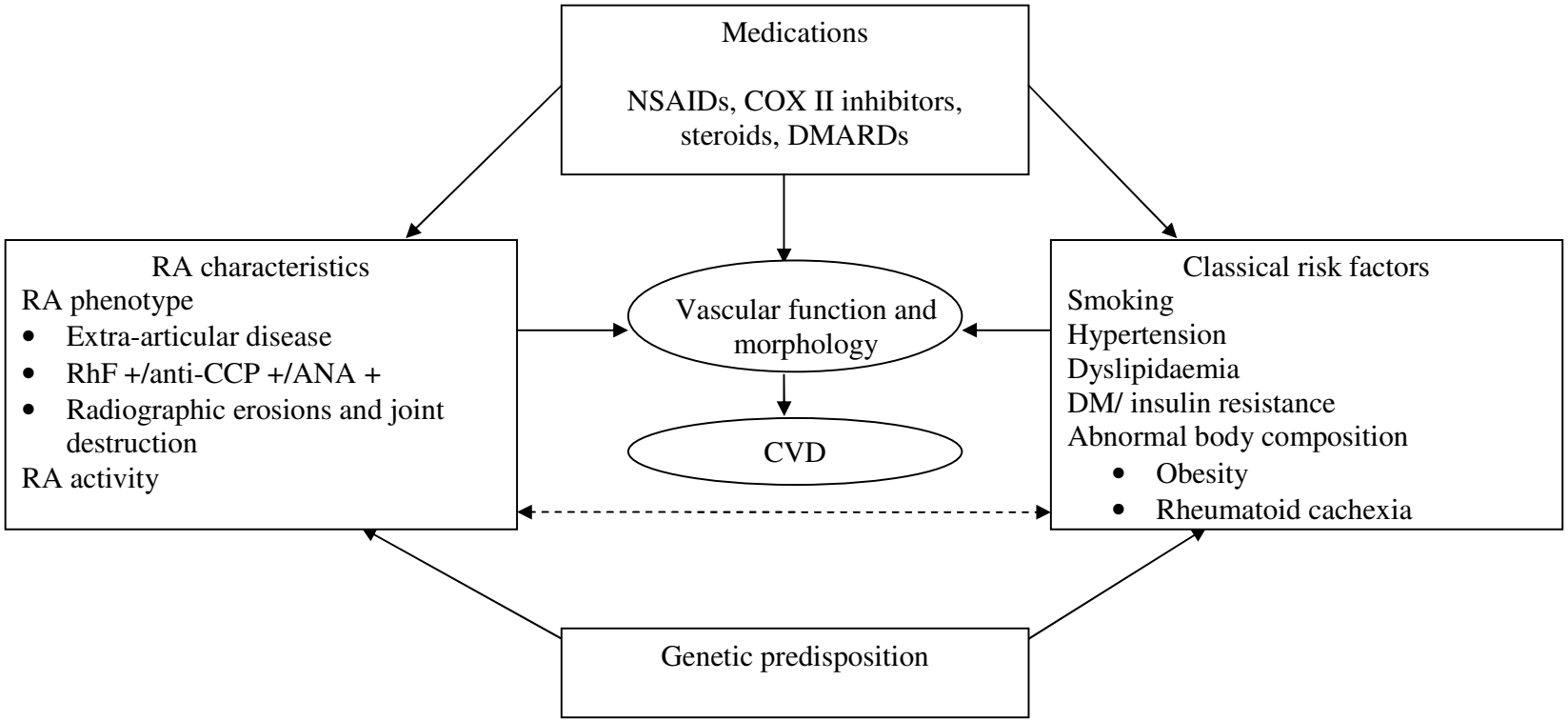
Not only is ischaemic heart disease (IHD) more prevalent in patients with RA, but also the clinical presentation of IHD appears to be different to that in the general population. Symptoms of IHD may be silent (16), or angina may be unrecognized medically (17). Patients with RA are less likely to report chest pain or symptoms of angina associated with ambulatory ECG evidence

of cardiac ischaemia, than patients without RA (18). Comparing clinical presentations in RA patients diagnosed with an acute coronary syndrome with age and sex matched non-rheumatoid controls showed that RA patients were less likely to present with chest pain and more likely to have an atypical presentation such as collapse or dyspnoea (19). Other studies have demonstrated that patients with RA are more likely to experience unrecognized MIs or sudden death than non-RA patients (14). The Stockport inception cohort study in England in the 1980s and 1990s supports this: although the SMR for CVD was increased in this RA cohort, admissions to hospital with a CVD event were not, suggesting RA patients were less likely to seek hospital care, due to any of the above reasons (9). After an index CVD event, Douglas et al. found that patients with RA were more likely to experience recurrent cardiac events or death (19). The Stockport inception cohort revealed that, of those RA patients admitted to hospital, 70% only had one admission with a CVD event during the period of follow up (9), which may also suggest that patients with RA were more likely to die during or after their first cardiovascular admission; others have also observed an increased 30-day mortality after a CVD event (including both MI and stroke) (15;20). Therefore, overall, not only is CVD more prevalent in RA but it also associates with a higher case fatality (20;21).

a) Why is cardiovascular disease increased in patients with RA?

Accelerated atherosclerosis in RA (8) is thought to be due to the interplay between classical risk factors for CVD, which may be adversely affected by RA, as well as novel risk factors, particularly systemic inflammation (11;22). This is summarized in Figure 1.

Figure 1; Pathways leading to CVD in RA showing the role of traditional and classical risk factors



RhF = rheumatoid factor; anti-CCP = anti-cyclic citrullinated peptide antibodies; NSAIDs = non steroidal anti-inflammatory drugs; COX II inhibitors = cyclo-oxygenase II inhibitors; DMARDs = disease modifying anti rheumatic drugs; DM = diabetes mellitus

i) Classical CVD risk factors

Classical risk factors, such as hypertension, dyslipidaemia, insulin resistance and obesity, appear to cluster in patients with RA and are highly prevalent (23). A systematic review of hypertension in RA suggests the prevalence lies between 51.7% and 73% and discusses how factors pertinent to RA, namely, systemic inflammation, physical inactivity, obesity and medications (non-steroidal anti-inflammatory drugs, cyclo-oxygenase II inhibitors, glucocorticoid and disease modifying drugs such as leflunomide or cyclosporin) may all contribute to the high rates and poor control of hypertension observed in RA (24).

Dyslipidaemia in RA seems to relate to the inflammatory disease activity; greater disease activity associates with lower total cholesterol levels and particularly depressed levels of high density lipoprotein (HDL) leading to an unfavourable atherogenic index (25;26). Pro-inflammatory cytokines, specifically tumour necrosis factor alpha (TNFα), may explain this finding (25). Treatment of inflammatory joint disease may therefore lead to a rise in total cholesterol, but the disproportionate rise in HDL cholesterol leads to improvement in the atherogenic index (27). The effects of anti-TNF medications on dyslipidaemia have been explored in several studies. These have reported varied effects with some studies demonstrating improvement in dyslipidaemia whilst others have reported a more atherogenic lipid profile after treatment with prolonged TNF blockade (28). Pro-inflammatory cytokines also mediate the development of rheumatoid cachexia (29), the involuntary loss of skeletal muscle with progressively increased fat mass. As a result, a patient with RA may have a higher percentage body fat when compared to a healthy control with the same body mass index; this increased body fat may contribute to the development of CVD (30). Whilst the literature examining the prevalence of diabetes in RA is

conflicting (31), there is certainly evidence of insulin resistance associated with RA (32;33), related to systemic inflammation or glucocorticoid therapy (31). Controlling systemic inflammation, using prednisolone or disease modifying drugs and dietary advice, has been shown to lead to improvements in insulin resistance (33).

Smoking is common in RA and whilst it does not seem to confer the same relative risk of CVD events when compared to the general population (34), cigarette smoking certainly associates with more severe RA and with rheumatoid factor positive status; both these factors independently associate with increased CVD mortality (34). Patients with RA may be at greater risk of physical inactivity if they have uncontrolled rheumatoid disease and/or chronic joint damage. Physical inactivity in the general population has been shown to associate with an increased prevalence of risk factors for CVD such as increased body mass index, central adiposity, systolic hypertension and dyslipidaemia (35); these risk factors can however be modified by regular exercise (36).

Despite the adverse effects that RA and systemic inflammation has on these classical CVD risk factors, analysis controlling for these risk factors still leaves RA patients with a twofold greater risk for IHD than controls (37). The Rochester, Minnesota, incidence cohort of RA patients demonstrated that the prevalence and incidence of traditional CVD risk factors was similar between RA patients and age and gender matched non-RA subjects. However, some traditional risk factors including male gender, smoking and prior cardiovascular disease, appear to have a weaker association with CVD events in patients with RA (38). Thus novel cardiovascular factors are thought to play a pivotal role in the CVD morbidity and mortality associated with RA. These novel risk factors relate to the vascular and metabolic effects of systemic inflammation.

ii) Novel CVD risk factors

Understanding the vascular effects of systemic inflammation requires an appreciation that atherosclerosis per se is an inflammatory disease (39). Factors such as free radicals from cigarette smoking, hypertension and diabetes mellitus, alongside high levels of low density lipoprotein cause endothelial cell dysfunction which sets up a chronic inflammatory process in the artery with procoagulant properties and migration of inflammatory cells . Fatty streaks, consisting of foam cells and T lymphocytes and migrated smooth muscle cells, progress to intermediate and advanced lesions, ultimately developing a fibrous cap walling off the lesion, which has the potential to occlude the arterial lumen (39). Local inflammatory phenomena not only drive this development of the atherosclerotic plaque but also their rupture and subsequent clot formation that causes the acute events (8). Further evidence supporting the central role that inflammation plays in the pathogenesis of atherosclerosis is provided from studies in the general population using high sensitivity assays of CRP (hsCRP); high hsCRP values have been shown to be a moderate predictor of future coronary heart disease (40). Such high hsCRP values would be considered normal by routine assays suggesting that low-grade systemic inflammation is sufficient to potentiate atherosclerosis (8). Thus it has been argued that high levels of systemic inflammation, as seen in RA, are pivotal to the accelerated atherosclerosis observed in RA (37;41). Potential mechanisms for inflammation induced vascular damage include, a) the development of endothelial dysfunction via excessive production of nitric oxide, b) activation of the coagulation cascade and c) induction of secondary dyslipidaemia with an atherogenic profile (42). In support of this hypothesis that systemic inflammation promotes atherosclerosis in RA are observational studies and reviews of the literature that show reduced CVD event rates with use of DMARDs (43;44) and anti TNF agents (45;46).

Other novel risk factors for atherosclerosis include hyperhomocystinaemia, as well as adversely effected thrombotic markers (7). Hyperhomocystinaemia has been shown to be an independent risk factor for atherosclerotic disease (7;11) with higher levels observed in patients with RA and significantly higher levels in patients with RA and CVD (7). Methotrexate may increase homocysteine levels but this needs to be balanced against its effectiveness in reducing systemic inflammation (11). Thrombotic markers, such as elevated fibrinogen or factors that impair fibrinolysis, are independent predictors of CVD mortality and higher levels have been found in patients with RA compared with healthy controls (7;47).

Cardiovascular disease in early RA

a) What is early RA?

The definition of early RA is not always easy as the 1987 ACR classification criteria were derived from study of patients with established disease (48) and have not been found to be discriminatory at symptom onset (49). For patients presenting with recent-onset inflammatory polyarthritis (IP) or undifferentiated inflammatory arthritis, it has been suggested that the patient should not be immediately classified but observed (50). Experience in early arthritis clinics, such as the Leiden early arthritis clinic where patients whose symptoms are for less than two years duration are intensively investigated and followed up (51), suggests that a third of such patients remit, a third of patients become diagnosed with RA and the others remain undifferentiated or develop other rheumatological diagnoses (52;53). Thus, while some disagree with the concept of 'early RA' (preferring either undifferentiated inflammatory arthritis or established RA) (50) others find it helpful to emphasise the need for speedy referral to secondary care, prompt

diagnosis and intervention to suppress inflammation (54). In practice, randomized clinical trials use a definition of disease duration of either less than two (55) or three (52) years to describe patients with early RA .

b) What is the evidence for CVD co-morbidity in patients with early RA?

In patients with early RA, there is both surrogate evidence for co-morbid CVD (for example, carotid intima media thickness studies) as well as evidence from cohort studies of patients with recent-onset inflammatory polyarthritis. This evidence is summarized in Tables 1 and 2.

Carotid intima media thickness (cIMT) measured using ultrasound shows early subclinical atherosclerosis and has been shown to predict CVD events in the general population (56). In patients with established RA, case-control cross sectional studies have also shown increased cIMT which independently associates with duration and severity of RA (57), and which is significantly reduced following anti-TNF therapy (58), although no long term studies exist to show whether cIMT can predict future CVD events in RA (56). Hannawi et al examined cIMT in 40 patients with early RA (less than 12 months disease duration) and in 40 control patients matched for age, sex and CVD risk factors (59). Patients presenting with early RA were found to have both increased cIMT as well as increased carotid arterial plaque indicating an increased atherosclerotic burden (59). Similarly, Georgiadis et al examined cIMT in 40 non-smoking patients with early RA (again, defining this as disease duration less than one year) and no past medical history of a CVD event. This case-control study involved age and sex matched controls with no history of CVD events. At baseline, patients with early RA had statistically significant

Table 1: Surrogate evidence for CVD in early RA

Author	Year published	Type of study	Number of subjects	Definition of early RA	Surrogate marker for CVD used	Result
Georgiadis et al (60)	2008	Case-control	40 ERA 45 controls	Disease duration < 1 year	cIMT carotid plaque	- cIMT statistically higher in ERA subjects than controls - No difference in prevalence of carotid plaque between groups
Hannawi et al (59)	2007	Case-control	40 ERA 40 controls	Disease duration < 1 year	cIMT carotid plaque	- cIMT statistically higher in ERA subjects than controls - Statistically increased prevalence of carotid atherosclerotic plaque in RA patients compared to controls
Park et al (61)	2002	Case-control	53 RA (unspecified how many had early RA) 53 controls	Disease duration < 1 year	cIMT	- cIMT greater in patients with RA than controls; those with ERA had greater cIMT than controls, but not as great as those with RA of a longer duration
Kumeda et a (57)	2002	Case control	138 RA 94 controls	Not specified	cIMT carotid and femoral artery plaque	- cIMT significantly higher in RA patients than controls; this associated with the duration of RA - No difference in the prevalence of carotid or femoral artery plaque between groups
Chung et al (62)	2005	Case-control	70 ERA 71 established RA 86 controls	Disease duration < 5 years	Electron beam CT to measure coronary calcification	- coronary calcification significantly increased in patients with established RA, compared to controls, but not in those with ERA
Bergholm et al (63)	2002	Case-control	10 ERA 33 controls	Disease duration < 18 months	Vasodilatory responses to intra-arterial endothelium-dependent and -independent vasodilators	- significantly impaired vasodilatory responses in ERA patients compared with controls

RA = rheumatoid arthritis; ERA = early rheumatoid arthritis; cIMT = carotid intima media thickness; CT = computed tomography

Table 2: Epidemiological evidence for CVD in early RA

Author	Year published	Country	Type of study	Criteria to enter cohort	Number of subjects in cohort	Length of follow up	Result
Goodson et al (64)	2002	Norfolk, England	Inception cohort	Inflammatory polyarthritis (2 or more swollen joints for four weeks or longer)	1,236	Median 6.9 years	Overall no increase in mortality; those seropositive RA patients however had an increased risk of death from all causes, and CVD was the most common cause of death (SMR for CVD was 1.34 for men and 2.02 for women)
Young et al (65)	2007	Multi-centre, England	Inception cohort	RA symptoms less than 2 years	1,429	Median 9.1 years	Survival was lower than expected in the first 7 years from diagnosis. IHD was the most common cause of death (SMR 1.49).
Maradit-kremers et al (66)	2008	Rochester, Minnesota, USA	Incidence and control cohort	First date of fulfilment of 4 out of 7 ACR criteria	553 RA subjects 574 control subjects	Median 14.7 years for RA patients. Median 16.1 years for non-RA subjects	Ten years after a diagnosis of RA, the absolute CVD risk in RA patients was similar to non-RA subjects 5-10 years older.

RA = rheumatoid arthritis; CVD = cardiovascular disease; IHD = ischaemic heart disease; ACR = American College of Rheumatology

greater cIMTs' than controls, although the prevalence of plaques in the carotid artery did not differ between the case and control groups. After one year of treatment with methotrexate and prednisolone the cIMT in the patients with early RA had significantly decreased. This change in cIMT was independently associated with changes in inflammatory markers and serum lipids (60).

Another surrogate measure of vascular disease is evidence of endothelial dysfunction, which predates the development of atherosclerotic plaques. Endothelial dysfunction has been shown in patients with cardiac risk factors as well as in patients with rheumatoid arthritis and systemic lupus erythematosus (67;68). In a small study of 10 patients with early RA (defined as disease duration less than 18 months) all disease modifying drug naïve, blunted vasodilatory responses were observed (both endothelial–dependent and endothelial–independent mechanisms) compared to control subjects without RA, suggesting early abnormalities in vascular function in patients with early RA (63). There is, therefore, some evidence that the pathophysiological processes of vascular injury are occurring early in RA. Not all studies, however, have shown this pattern (62) and clearly further research is required.

Epidemiological studies also provide evidence of CVD co-morbidity occurring early in the disease process. Between 1964 and 1978 a cohort of patients with established RA was developed and subjects were followed up until 1990. The proportion of excess deaths due to CVD was not related to length of disease duration (2). More recent epidemiological studies of patients with recent-onset inflammatory polyarthritis provide evidence of CVD co-morbidity occurring in early RA. The Norfolk Arthritis Register (NOAR) is a primary care inception cohort of all patients aged over 16 years living in what was the former Norwich Health Authority, with two or more

swollen joints lasting for four weeks or longer with an onset since January 1st 1989 (69). Between 1990 and 1994 1,236 patients were recruited, followed up and tracked for notification of death. It should be noted that this cohort therefore included patients subsequently diagnosed with RA, psoriatic arthritis, inflammatory polyarthritis or post-viral arthritis. After a median follow up of 6.9 years, although mortality was not increased in this group of patients compared to annual death rates for the Norfolk population, those patients with seropositive inflammatory polyarthritis had an increased risk of death from all causes; the majority of this excess mortality was due to CVD, with SMRs for CVD being 1.34 for men and 2.02 for women (64). Further analysis of this cohort has shown that this increased mortality from CVD in seropositive patients with early inflammatory arthritis was apparent after five years from symptom onset and was greatest in women younger than aged 55 years at symptom onset (70). CRP level at baseline (41) and Health Assessment Questionnaire (HAQ) score after 1 year (71) are important independent predictors of CVD death in patients with new onset inflammatory polyarthritis. Another multi-centre inception cohort which has studied mortality in patients with early RA is the Early Rheumatoid Arthritis Study (ERAS). Established in 1986, 1429 patients newly diagnosed with RA (less than 2 years of symptoms) were recruited. Mortality was greater than expected for the first seven years of follow up, and the main cause for this increased mortality was ischaemic heart disease (IHD) (65). In America, using the resources of the Rochester Epidemiology Project, newly diagnosed patients with RA were identified (defined as fulfilling 4 of the 7 ACR criteria). These patients, and non-RA matched controls, were followed longitudinally. After 10 years, the absolute risk of a CVD event in a RA person was the same as a non-RA subject 5 to 10 years older (66).

Not only has CVD mortality been shown to be increased in early RA, but also CVD morbidity. Since 1985, Kroot et al. recruited 186 patients with recent onset RA (diagnosed less than 1 year) to participate in a prospective longitudinal cohort study. After a mean period of follow up of 4.3 years, 27% of patients reported a co-morbid condition, the most common of which was a cardiovascular condition, particularly hypertension or angina (72).

These studies showing evidence of atherosclerosis or CVD mortality or morbidity in early RA support the hypothesis that atherosclerosis is part of the disease itself, exacerbated by adversely affected traditional CVD risk factors, rather than simply related to the cumulative side effects of medication and decreased physical mobility accrued with increasing disease duration (67). Therefore, interventions to address CVD risk factors should be implemented in patients with early RA. This should include not only traditional risk factors, as has been recommended by the British Society for Rheumatology (73), (and there are guidelines on the management of hypertension specific to patients with RA (24;74)) but theoretically also requires rapid and effective control of systemic inflammation (22). Trials of intensive disease modifying drug treatment and biologic therapy on CVD outcomes in early RA are required.

c) What is the evidence for CVD risk factors in early RA?

There is a growing body of evidence showing dyslipidaemia is present in early RA, likely related to the untreated systemic inflammatory burden in those with early disease (25). Georgiadis et al examined the lipid profile of 58 treatment naïve patients diagnosed with RA in the past year, and with no past history of CVD events or conditions or concomitant medications known to affect the lipid profile. Their mean disease activity score from 28 joints was 5.8 indicating active disease.

These patients had evidence of a mild dyslipidaemia with higher levels of total cholesterol, low density lipoprotein (LDL) and triglycerides (TG) and lower levels of HDL compared to healthy controls; the atherogenic index (TC/HDL) was therefore less favourable. After 1 year's treatment with methotrexate and prednisolone, levels of HDL were significantly higher, despite no dietary modification or weight change, hence the atherogenic index was reduced (75). This increase in HDL inversely correlated with improvements in the inflammatory indices CRP and ESR (erythrocyte sedimentation rate). Similar findings of low total cholesterol, low HDL but elevated atherogenic index have also been reported in patients with early, untreated, active RA from several early arthritis studies in The Netherlands. The atherogenic ratio improved with antirheumatic treatment (27). Of note, one of these studies was the COBRA study whereby patients with active RA and median disease duration of 4 months were randomized to combination treatment including corticosteroids versus sulphasalazine alone; the atherogenic index improved faster in those patients taking combination treatment. However, the authors acknowledge that longer term studies are required to evaluate the role of corticosteroids on the breadth of cardiovascular risk factors in the longer term (27).

The role of novel risk factors for CVD, particularly systemic inflammation, has also been explored in patients with recent onset inflammatory polyarthritis in the NOAR cohort. One hypothesis to explain why these rheumatoid factor positive patients have increased CVD mortality (64) is that they have more severe disease with increased levels of inflammation (34) contributing to accelerated atherosclerosis. The combination of other markers of severe disease, namely smoking, presence of anti-cyclic citrullinated peptide (anti-CCP) antibodies and possession of 2 copies of the shared epitope (SE) also associate with CVD mortality (76).

Risk of cardiovascular disease prior to the onset of RA

a) What is the evidence for CVD events or CVD risk factors prior to RA?

Retrospectively exploring medical records back to aged 18 years of all 603 patients in the Rochester RA incidence cohort revealed that in the two year period prior to fulfilling the diagnostic ACR criteria for RA, these participants were significantly more likely to have been hospitalized for an acute MI or to have experienced an unrecognized MI compared to non-RA subjects (14). The previously discussed study examining co-morbidities in patients with early RA also revealed that for many patients with RA their co-morbidities were present before the diagnosis of RA (72). These observations may be explained by studies that reveal the presence of several risk factors for CVD in the pre-RA period; specifically, there is evidence of dyslipidaemia, an acute phase response and the production of autoantibodies prior to a diagnosis of RA (42). van Leuven et al therefore suggest that the pathological processes initiating atherogenesis may initiate years before the diagnosis of RA is made (42).

Although there is evidence regarding dyslipidaemia prior to a diagnosis of RA (blood donors who subsequently developed RA have been shown to have a more atherogenic lipid profile up to 10 years before they developed RA (77)) there is also conflicting research; namely, a prospective case control study found no difference between blood pressure readings, cholesterol levels and obesity between participants who did, and those who did not, subsequently develop inflammatory arthritis (78). Additionally, as smoking is a shared risk factor for both RA and CVD (see below), this is another CVD risk factor present in the pre-RA period.

b) Are there any shared risk factors for the development of both CVD and RA?

Smoking is certainly a risk factor for the development of both RA (34;78) and CVD (79). Moreover, smoking is also associated with more severe RA, for example, more erosive disease or extra-articular features (53). Serologically, smokers are more likely to be RF positive as well as positive for anti-CCP antibodies. In non-RA smokers, smoking causes citrullination of cells; in patients with RA this citrullination of cells is particularly important as anti-CCP antibodies predict more aggressive RA (53).

There is evidence for diet also having an aetiological role in the development of RA (80) and CVD. Both atherosclerosis and synovial inflammation are mediated by free radical activity; hence antioxidants, which scavenge reactive oxygen radicals and protect against oxidative damage are thought to have a protective effect. Certainly, levels of CRP and oxidized LDL, both linked to the development of RA and CVD, are inversely related to serum concentrations of circulating antioxidants (81). In studies involving both a Norfolk population-based prospective study, which included baseline diet diaries, and the NOAR cohort, the pre-morbid diets of those who subsequently developed IP could be analysed. People with a lower daily intake of fruit and, particularly, foods containing the antioxidant vitamin C were at greater risk of subsequently developing IP (82) as were those whose diets were low in the antioxidant dietary carotenoids, particularly β cryptoxanthin, (81), and those who consumed high levels of red meat (83). Dietary red meat is a source of arachidonic acid, involved in the production of eicosanoids which can have proinflammatory activity (83). The Mediterranean diet, comprising a high intake of oily fish, white meat, olive oil, fruit and vegetables is advocated for primary and secondary prevention

of CVD, and as these studies suggest may also have a protective role in the development of RA, although further work is required (80).

As already discussed, dyslipidaemia has been observed many years prior to the onset of RA. However, the novel concept of dyslipidaemia as an aetiological agent for both RA and CVD has been considered by van Halm et al. (77). In their study, changes in CRP only explained a small part of the differences in the lipid profile between those who subsequently developed RA and controls. Therefore they postulate that either an unfavourable lipid profile renders a person more susceptible to inflammation, or, is related to the development of RA by a linked background, either genetic or socioeconomic.

There are also genetic predictors for both RA and CVD. The gene HLA-DRB1 is a susceptibility gene for RA and also is associated with severity of RA (84). However, there is evidence that this gene also appears to confer risk of CVD: using evidence of endothelial dysfunction as a surrogate marker for CVD, it has been shown that endothelial dysfunction was greater in RA patients with certain HLA-DRB1 genotypes (85). Mortality data also supports this finding. Carrying two copies of shared epitope alleles at the HLA-DRB1 gene, particularly certain genotype combinations such as HLA-DRB1*0101/*0401, gave an increased risk of CVD death in patients with IP, compared to patients with 0 or 1 copy of shared epitope alleles (76;86). Other gene polymorphisms relating to thrombotic factors and inflammation are also currently being explored with regard to increased frequency of CVD in RA patients (87;88).

Conclusion

In summary, there is well established evidence for CVD mortality and morbidity in patients with RA. The more recent evidence that CVD morbidity and mortality occurs early in the disease process, and the suggestion that pathogenic processes for atherosclerosis may be in place even before a diagnosis of RA, however, represents a new development in our understanding of CVD co-morbidity. Further research is required to explore CVD in early RA, particularly to elucidate the relative contributions of both traditional and novel CVD risk factors, as well as the effect of their modification early in the disease course, including the effect of early immunosuppressive treatment (including corticosteroids and biologic therapy) on CVD outcomes. Importantly, these findings will need to be translated into direct clinical practice with CVD risk management being an integral part of the care of every patient with RA, in both primary and secondary care, from the point of diagnosis. This will require including RA as a risk factor multiplier in CVD risk calculators as well as providing sufficient resources to support patients making necessary lifestyle changes to modify traditional CVD risk factors, such as prescribed physical activity, weight loss programmes and smoking cessation.

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CHAPTER 2 (PART 2): GENERAL INTRODUCTION;
IS RHEUMATOID ARTHRITIS A CORONARY HEART DISEASE EQUIVALENT?

The archetypal disease considered a coronary heart disease (CHD) equivalent is type 2 diabetes mellitus (DM2), as people with DM2 have the same risk for future CHD events as non-diabetic patients who have had a previous myocardial infarction (MI) (1). This review addresses the question whether rheumatoid arthritis (RA) is also a CHD equivalent and discusses the implications of this.

Epidemiology

RA is associated with an increased mortality with standardised mortality ratios (SMR) ranging from 1.3 to 3.0 (2). Cardiovascular disease (CVD) accounts for up to 50% of this excess mortality (3); several epidemiological studies and recent meta-analyses clearly show that RA patients have an SMR for CVD of 1.5-1.6 compared to the general population (2;4). The increased CVD risk of RA has specifically been compared with that of DM2 in both cross-sectional (5) and longitudinal (6) studies. Three groups of subjects were studied: i) patients with RA and normal fasting glucose levels from the Dutch Cardiovascular and Rheumatoid arthritis (CARRE) cohort; ii) patients with DM2; iii) non-diabetic controls; these latter two groups of patients were drawn from another Dutch cohort, the Hoorn cohort, (5;6). The prevalence of CVD was 12.9% in patients with RA (n = 294), 12.4% in patients with DM2 (n = 194) and 5.0% in control patients (n = 258), giving an age- and gender-adjusted prevalence odds ratio for CVD of

2.3 for patients with DM2 and 3.1 for patients with RA in comparison to the non-diabetic control group (5). These patients were followed longitudinally until the occurrence of a fatal or nonfatal CVD event, death of any cause or the cessation of the study. The mean follow-up period was nearly 3 years; age- and gender-adjusted hazard ratios of CVD events was 2.16 for non-diabetic RA patients and 2.04 for patients with DM2 compared to the non-diabetic control patients (6). Thus, both studies show a two-fold higher risk of CVD in patients with RA and the magnitude of this increased risk is comparable to the risk associated with DM2. Similar findings were seen in a, soon to be published, study of a Danish nationwide cohort comparing incident RA with incident DM2 (Lindhardsen J, personal communication).

Independently, another research group cross-sectionally compared a group of non-diabetic RA patients (n=48), with a disease-duration, age- and sex-matched group of patients with DM2 (n=48) and a matched control group (n=48). Assessments of vascular function and morphology were used to identify prevalent preclinical atherosclerosis. There was a significantly higher prevalence and severity of preclinical atherosclerosis in patients with RA compared to healthy controls, which was similarly found in the DM2 patients (1). Whether such vascular assessments are good surrogates of future CVD events in patients with RA remains unclear, however, this study again suggests that RA confers approximately the same risk for CVD as DM2 (1).

Mechanisms of atherosclerosis development

The development of atherosclerosis is thought to be related in part to the accumulation of "classical" risk factors for CVD. However, over the last 2 decades, it has emerged that atherosclerosis is an inflammatory disease *per se* (7) whereby systemic and local inflammatory phenomena drive the development of the atherosclerotic plaque, as well as its instability and rupture, with consequent clot formation causing an acute ischaemic event (3). There is also an appreciation of a complex interplay between "classical" and "novel" CVD risk factors, including inflammation (Figure 1, Chapter 2 (part 1)). Below, we consider both classical and novel risk factors and their interaction, and the relative contributions each group of risk factors plays in atherosclerosis development in DM2 and RA.

a) Classical CVD risk factors

Classical risk factors for CVD namely smoking, hypertension, insulin resistance, physical inactivity, dyslipidaemia and obesity are highly prevalent, tend to cluster and may frequently be undertreated in people with RA (3;8;9). Several of these risk factors may be affected by RA itself or its treatment: for example, joint pain or structural joint damage may contribute to physical inactivity (10), while non-steroidal anti-inflammatory drugs and cyclo-oxygenase II inhibitors, glucocorticoids, some disease-modifying anti-rheumatic drugs such as leflunomide or cyclosporine, and other factors such as obesity, physical inactivity or systemic inflammation *per se* can all contribute to hypertension in patients with RA (11). Some epidemiological studies suggest occasional paradoxical associations between RA and some CVD risk factors (12); body composition and dyslipidaemia are classical examples of this. Undesirable types of body composition in RA include obesity (which in cross-sectional studies associated with low levels of

physical activity or being an ex-smoker (13)) but also rheumatoid cachexia (a state of apparent normal or low weight, in which pro-inflammatory cytokines mediate the involuntary loss of lean body mass (muscle) which is progressively replaced by body fat, thus also representing a 'high fat' state (13-15)). Whilst obesity is widely appreciated as a risk factor for CVD in both the general population and people with RA (16), rheumatoid cachexia may provide an explanation for the paradoxical finding that a low body mass index (BMI) in people with RA associates with a threefold increase in CVD death (14). Further research also suggests the distribution (visceral or subcutaneous) of abdominal adiposity may be of relevance, with visceral adiposity associating with cardiometabolic risk factors and CVD in people with RA (17).

Lipid levels are another excellent example of paradoxical associations found in RA. Contrary to the general population, in RA, decreased lipid levels have been associated with increased CVD risk (12). This is thought to be because lipid levels are inversely associated with inflammation; specifically, pro-inflammatory cytokines, particularly tumour necrosis factor α (TNFα), associated with high levels of inflammation depress the total cholesterol (TC) level but particularly depress the high-density lipoprotein (HDL) cholesterol level leading to an unfavourable atherogenic index (TC:HDL ratio) (2;18;19). Using the CARRE cohort of patients described earlier, Peters and colleagues showed in 289 RA patients (not taking lipid-lowering medication) that indeed C reactive protein (CRP) correlated negatively with TC, more so with HDL and correlated positively with the TC:HDL ratio. These associations were predominant in patients whose CRP was greater than 10mg/l (20). These CARRE cohort patients were followed up prospectively as described above; TC:HDL ratio was positively related to risk of CVD event,

whereas TC alone was not (20). We have also observed that whereas individual lipid components (TC, low density lipoprotein, HDL, triglycerides) are influenced to a greater or lesser extent by inflammation, lipid ratios did not correlate with CRP (21); both studies therefore suggest that lipid ratios may be more robust and appropriate for CVD risk stratification in people with RA.

Insulin resistance has also been described in patients with RA (22) and appears to relate to systemic inflammation or glucocorticoid therapy (3). We have recently demonstrated that insulin resistance in RA has 2 main components: one that relates to active inflammation and appears to be reversible with its adequate control; and another that relates to adiposity and appears to remain unaltered with potent anti-inflammatory therapy, at least in the short and medium term. Furthermore, the risk (incidence ratio) of developing DM2 in a cohort of nearly 49 000 patients with RA has been calculated as 8.6 compared to 5.8 per 1000 person-years in non rheumatic controls (23).

It is clear that in terms of the classical CVD risk factor burden, there are several parallels between RA and DM2, including obesity, hypertension, dyslipidaemia and insulin resistance (1;24;25). However, it remains unknown whether these confer a proportionally similar CVD risk in the two disease groups, and whereas systematic screening and identification of such risk factors in routine clinical practice is now imperative in both conditions, it is not known whether primary prevention strategies applied successfully in DM2 would be equally easy to implement and demonstrate similar benefits in people with RA.

b) Novel CVD risk factors

Novel risk factors implicated in CVD risk in RA relate to both RA activity (ie level of inflammation) as well as other characteristics of the RA phenotype. In the general population, modest increases in circulating CRP (detected using high-sensitivity CRP (hsCRP) assays) have been associated with CHD risk (26). Thus high levels of inflammation observed in patients with RA are thought to contribute to accelerated atherosclerosis (12); potential mechanisms include the development of endothelial dysfunction, activation of the coagulation cascade and induction of secondary dyslipidaemia (27;28). Active RA disease has been shown to associate with an atheromatous plaque more vulnerable to rupture (1) as well as a greater prevalence and extent of coronary artery calcification (29). Having adjusted for classical risk factors and co-morbidities, RA characteristics which independently associate with an increased risk of CVD death include small and large joint swelling, destructive changes on joint radiographs, rheumatoid nodules, vasculitis, rheumatoid lung disease and corticosteroid use (30). Additionally, being positive for rheumatoid factor (RF) or anti-nuclear antibodies has been shown to be a significant predictor for CVD morbidity or mortality, supporting the theory that immune dysregulation may play a role in the aetiology of CVD in RA (31).

Comparing DM2 and RA with regard to novel risk factors reveals differences as patients with DM2 do not exhibit such high levels of systemic inflammation. However, patients with DM2 have "low grade" systemic inflammation; adiposity, insulin resistance, hyperglycaemia, hypertension and dyslipidaemia are some of the factors associated with low-grade systemic inflammation in the general population and these are prevalent in patients with DM2 (32).

Shared novel mechanisms have been proposed where the proinflammatory cytokine TNFα appears to be central. TNFα is the pivotal cytokine driving the inflammatory cascade in RA (33). However, TNFα also arises from adipose tissue and during chronic hyperglycaemia has harmful effects on insulin signalling, may cause insulin resistance and may impede the insulin-mediated disposal of glucose in the skeletal muscle (5).

A further consideration is the role that chronic kidney disease (CKD) is known to play in causing CVD. After adjusting for traditional CVD risk factors, patients with CKD have an increased risk of CVD death, and this risk extends to patients with mild CKD as well as those with end stage renal failure (34). Non-traditional risk factors have been implicated such as hyperactivity of the renin-angiotensin-aldosterone system, volume overload, dyslipidaemia other than LDL levels, inflammation, coagulopathy, oxidative stress and sympathetic hyperactivity, which lead to histomorphological alterations of the heart and vessels (34;35). CKD is a well known complication of DM2 (36) but is also prevalent in patients with RA; in our cohort of 400 RA patients, 67.75% of patients had a reduced glomerular filtration rate (GFR) of less than 90 ml/minute per 1.73m^2 and 12.75% had a GFR of less than 60ml/minute per 1.73m^2(37). The aetiology of renal impairment in RA has been hypothesised to include nephrotoxic medications, reactive amyloidosis, metabolic factors, levels of systemic inflammation or the role of serum uric acid (37). However, multivariate analysis in our cohort revealed renal dysfunction in RA associated with classic CVD risk factors such as advanced age and dyslipidaemia, levels of serum uric acid and the presence of extra-articular rheumatoid disease; RA duration and activity, disability and past or present use of nephrotoxic medications were not associated (37).

Interestingly serum uric acid has been shown to independently associate with hypertension (38), renal dysfunction (39) and CVD (40) in patients with RA and may be a common denominator/predictor for CVD and CKD in RA; indeed serum uric acid may be another novel risk factor, alongside systemic inflammation, for CVD in RA (41).

A comparison between the classical and novel risk factor burden in RA and DM2 is provided in Table 1.

Table 1: A comparison between "classical" and "novel" risk factors in RA and DM2

Risk factors		RA	DM2
Classical risk factors	• Smoking	Prevalent	Prevalent
	• Hypertension	prevalent; affected by RA and its medications	Prevalent
	• Insulin resistance	prevalent, related to RA or its medications (glucocorticoids)	100% prevalence
	• Physical inactivity	prevalent; affected by RA activity and previous damage	Prevalent
	• Dyslipidaemia	paradoxical association related to systemic inflammation	Prevalent
	• Abnormal body composition	both obesity and rheumatoid cachexia prevalent; related to RA or its medication (glucocorticoids)	obesity highly prevalent
Novel risk factors	• Systemic inflammation	high grade inflammation	low grade inflammation
	• Chronic kidney disease	prevalent, related to age, dylipidaemia, serum uric acid and extra-articular disease	Prevalent

c) Relative contribution of classical versus novel risk factors in RA and DM2

A population-based incidence cohort from Rochester, USA, of 603 patients with RA was compared to an age and gender matched control cohort of 603 people without RA; both groups

were followed up longitudinally for 15 and 17 years, respectively. The baseline prevalence of classical CVD risk factors was similar between groups, but the relative impact of several classical risk factors (male gender, current smoking and personal history of ischaemic heart disease) on CVD outcomes, appeared to be significantly less in those with RA compared to those without (42). These authors hypothesise this may be observed if a novel RA-specific risk factor results in a dilution effect making the relative contribution of classical risk factors appear smaller in RA (42). The same authors sought to estimate the proportion of CVD risk that could be attributed to classical risk factors. Using heart failure as the outcome measure, they identified that all classical CVD risk factors explained 80% of the risk for heart failure in non-RA subjects but only 40% of the heart failure risk among RA subjects, again suggesting that other, novel, risk factors make a significant contribution to the overall heart failure risk that RA patients have (30). Other groups have similarly concluded that in RA both classical and novel risk factors predict CVD outcomes. Solomon and colleagues examined baseline data from a prospective longitudinal cohort study of 10,156 patients with RA who were followed for a median of 22 months observing primary CVD events. Models predicting CVD events increased in accuracy when both classical and novel risk factors (markers of disease severity, namely, longer disease duration, radiographic joint erosions, subcutaneous nodules, prior total joint replacement, seropositivity, high Health Assessment Questionnaire score and a high clinical disease activity score) were included; increasing numbers of both types of factors were associated with greater risk (43).

The relative contribution both classical and novel risk factors play in CVD has been compared in patients with DM2 and RA using measurements of preclinical atherosclerosis (such as flow-

mediated dilatation, pulse wave velocity or ultrasound measures of carotid intima media thickness) as surrogate markers for CVD events (1). Different vascular assessments can be used to assess different aspects of the atherosclerotic process (44). Diabetic patients had a worse classical CVD risk factor profile compared to patients with RA, yet there were no differences in vascular assessments between both groups, suggesting other RA-specific novel risk factors played a significant role in atherosclerosis development in RA. Further analysis looked at individual vascular measurements; in DM2, endothelial dysfunction, an early indicator of atherosclerosis, appeared to be mediated via classical risk factors, whereas it was independent in RA. Early aggressive risk factor control may therefore be sufficient in DM2 but not in RA. In contrast, measurements of arterial stiffness, representing functional and structural deterioration in the vessel wall, were independent of classical risk factors in DM2, but not in RA (1).

Implications for practice

Patients considered at high risk for CVD should receive appropriate lifestyle advice and medication. High risk patients are defined as those who have had a previous CVD event, those whose 10 year risk of a CVD event is greater than 20% and those who have diabetes, as this is considered a CHD equivalent (45). If RA is a CHD equivalent, similar to DM2, then should similar preventative strategies be considered for patients with RA (5)? Whilst there is a strong evidence base for primary CVD prevention in DM2 (46), there is currently no evidence base to confirm/refute whether similar strategies should be applied in RA. RA patients have been excluded or reflect a very small number of the participants to all large primary (or secondary)

prevention trials performed to date. Large randomised controlled trials with hard CVD endpoints are urgently required specifically in RA, to inform clinical practice.

a) CVD risk management in RA

Education must underlie all strategies to decrease CVD risk. This includes not only patients, where education about relevant lifestyle modifications needs to be provided within the context of any physical and psychosocial constraints related to RA (47), but also of health professionals. The excess CVD risk conferred by RA has been shown to be under-recognised and under-assessed in primary care (48); appropriate education of both primary and secondary health care professionals is required so that a consistent message is given to the patient (49).

Recently the European League Against Rheumatism (EULAR) published recommendations for CVD risk management in patients with RA (50), stating that both classical and novel risk factors need to be addressed. Adequate treatment to control RA activity and systemic inflammation is essential and certainly effective treatment with disease modifying drugs, especially methotrexate has been suggested to decrease CVD risk (30) and the risk of mortality following an acute myocardial infarction (51). Anti-TNFα agents have also been shown to both improve lipid parameters and levels of inflammation, (52), measures of aortic stiffness (53), as well as actual CVD events (54-56). With regard to managing classical risk factors, pragmatic recommendations by EULAR include that all classical risk factors need to be regularly systematically screened for, as part of routine care, and included in a CVD risk score calculation. Using CVD risk calculators

to determine whether a patient falls over the 20% threshold to receive preventative treatment requires the calculation to be accurate and validated in the target patient population. Despite several risk calculators currently available (9), a specific calculator designed for and validated in the RA population does not exist, although a multiplier for RA is incorporated in QRISK2, a UK primary care CVD risk calculator (57). Current advice is therefore to use the nationally recommended risk calculator and apply a multiplication factor of 1.5 to the result, if 2 out of 3 of the following factors are present to take account of the novel risk factors likely increasing the risk; disease duration of more than 10 years, sero-positivity for RF or anti-cyclic citrullinated peptide antibodies, presence of severe extra-articular manifestations. Specific medical interventions should be implemented as per national guidelines (50). The impact of this approach remains unknown and needs to be prospectively evaluated.

Other guidelines have similarly recognised the importance of novel risk factors for CVD. Canadian guidelines list inflammatory biomarkers (alongside other classical risk factors) as a risk factor for CVD and emphasises the importance of screening for classical risk factors in patients with chronic autoimmune inflammatory diseases such as RA; more specific details are not provided as these guidelines are written by their Cardiovascular Society rather than from a rheumatologists perspective (58).

b) Future research

There are several key research questions needing answering to inform the ongoing debate about CVD risk management in RA. They include: (a) the development and validation of an RA-specific CVD risk calculator; (b) RA-specific prospective primary prevention trials of different interventions with hard clinical end points, such as the UK-based TRial of Atorvastatin for the primary prevention of Cardiovascular Events in Rheumatoid Arthritis (TRACE RA) trial (see www.dgoh.nhs.uk/tracera) (59). This study follows the promising results of a short-term smaller study in RA patients whereby atorvastatin effected a positive lipid-lowering effect of a magnitude in keeping with the findings in the non-RA population as well as mediating modest but clinically apparent anti-inflammatory effects, suggesting statins may attenuate both inflammatory and vascular risk parameters (60); (c) development and validation of imaging or biomarker techniques as surrogates of future CVD events specifically in patients with RA. Current imaging techniques such as carotid intima media thickness (cIMT) (61;62) or coronary arterial calcification measured by computed tomography (29) have been used in research settings in RA patients; however, as yet, they have not been validated as surrogates of CVD outcomes specifically in RA. Encouragingly, measures of carotid plaque using high-resolution ultrasound have recently been shown to strongly associate with future acute coronary syndromes in a RA cohort (63).

Conclusion

Current epidemiological evidence suggests that RA is a CHD equivalent similar to DM2. However, the mechanisms behind this increased risk of CVD may be different in the 2

conditions: classical CVD risk factors appear important in both cases but high-grade systemic inflammation may be particularly important in RA. Therefore, CVD risk management in RA may require effective management of systemic inflammation as well as classical CVD risk factors; the results of primary prevention trials in RA will hopefully provide definitive evidence to guide future recommendations.

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CHAPTER 3 (PART 1): GENERAL INTRODUCTION; CARDIOVASCULAR EDUCATION FOR PEOPLE WITH RHEUMATOID ARTHRITIS; WHAT CAN EXISTING PATIENT EDUCATION PROGRAMMES TEACH US?

Introduction

Rheumatoid arthritis (RA) is a chronic disabling inflammatory arthritis (1) and patients require long term patient-centred care; concordance between patients and health professionals will help the patient commit to necessary complex medication regimes, self-management and lifestyle behaviour modifications (2). Patient education, defined as 'any set of planned educational activities designed to improve patients' health behaviours and/or health status' (3), is at the heart of patient-centred care. Education can be provided verbally during the outpatient appointment, using leaflets, such as those by Arthritis Research UK (4), audio-visual material, or as specifically developed patient education programmes (5). The generic chronic disease self management programme (6) and arthritis specific version (7) are well known examples of patient education programmes and, additionally, a wealth of RA-specific programmes have been developed, published and reviewed (8;9). Broadly, these have aimed to improve bio-clinical features of arthritis such as pain or disability, self management skills or psychosocial status; 28 of the 37 studies (involving 9955 patients in total) reviewed by Albano et al reported positive results (9). Specifically, the Cochrane review found that RA patient education effected, when compared to no intervention at first follow up, a 10% improvement in functional disability, measured using the Health Assessment Questionnaire, a 12% improvement in the Arthritis Impact Measurement

Scales arthritis impact subscale and a 12% improvement in depression (8). Although depression has been included as a topic/outcome measure (8), other co-morbidities of RA have been largely neglected. This is particularly pertinent as these co-morbid conditions not only affect quality of life (10), but also account for the excess morbidity and mortality associated with RA (1).

CVD accounts for about 50% of the excess mortality in RA (11). This is thought to be due to accelerated atherosclerosis occurring due to "classical" CVD risk factors, such as hypertension (12), dyslipidaemia (13), obesity (14) and physical inactivity (15), which may be adversely affected by RA or its medications (16;17), as well as more recently implicated risk factors, particularly high-grade systemic inflammation (18-20). Guidelines, therefore, suggest that patients with RA should have an annual cardiovascular risk assessment (21;22). A shared care approach to CVD risk management seems sensible; when surveyed, only 5% of general practitioners (GPs) felt CVD risk management in people with RA should occur in secondary care suggesting their perceived ownership (23). Local protocols defining explicit but integrated roles for primary and secondary physicians will be important. Education for people with RA is required to compliment these clinical consultations about CVD. However, no patient education about CVD exists specifically designed for people with RA, and this has been identified as an unmet need (24). Experience from CVD education initiatives for the general population and other high risk patient groups is valuable, but may not be wholly transferable to the RA population. For example, advice about increasing exercise or achieving a normal weight must be provided within the context of any physical and psychosocial constraints from having RA. Fear of causing joint damage or the requirement for some medications, especially corticosteroids, may affect a patient's perceptions of these as realistic goals (24). These patient beliefs need to be

acknowledged and explored before patients are receptive to current medical evidence emphasising the contrary, and committing themselves to substantial lifestyle changes.

In this review we appraise existing patient education programmes for patients with RA and identify which specific features are characteristic of successful interventions. Similarly, we examine patient education programmes used in primary and secondary prevention of CVD. We then integrate the findings to provide a theoretical framework on how novel patient education addressing CVD in RA could be constructed.

Patient education in rheumatoid arthritis

There have been four systematic reviews/meta-analyses (8;25-27) of the RA patient education literature, (summarised by Christie et al (28)), which relate to studies published up until 2002. In addition, we have identified a further ten randomised controlled trials (RCTs) of RA patient education programmes published since 2002; 5 were self management programmes (29-33), one aimed to improve drug adherence (34) and four were therapeutic education programmes(35-38). We review these programmes in order to identify common patterns of structure and delivery as well as which aspects are most effective (39).

a) Fundamental design

The Cochrane systematic review (8) compared the results of information-only (9 studies; 687 patients), counselling (5 studies; 430 patients) or behavioural interventions (24 studies; 2493 patients) versus control groups. Pooled analysis revealed no significant effects for information

and counselling interventions, whereas behavioural interventions did show significant effects for scores on functional disability, patient global assessment and depression. Similarly, Niedermann and colleagues observed that purely educational programmes were not associated with improvements in health status whereas some psychoeducational programmes benefited both physical and psychological health (27). This concurs with the principle that the aims and content of an education programme must be congruent with the intended outcome: if the aim is to improve knowledge then information may suffice; if it is to change behaviours, which may subsequently confer clinical benefits, then the programme needs to include a behavioural component.

b) Robust theoretical underpinning

Psychoeducational programmes are more likely to be successful if they also address the psychology behind why we adopt or maintain certain behaviours (40). Indeed, a theoretical underpinning is thought to be instrumental to an intervention's success (41;42). RA patient education programmes, particularly in the last decade, do tend to be based upon theories of human behaviour, most notably Social Cognition Theory (29;32-36). This has, as a central tenet, the concept of self-efficacy (the belief in one's own ability to succeed in a certain situation) (43). Such interventions have aimed to enhance a patients' self-efficacy, e.g., using motivational interviewing, and have included specific skills-training in relation to encouraging behaviour change, e.g. goal-setting. As inaccurate health beliefs may undermine health professional efforts to encourage behaviour change, another theoretical consideration is to provide the opportunity to explore patients' beliefs about RA or its management (44).

c) Structure

A variety of formats of patient education programmes have been described, such as group sessions (29-33;35;37;38), one-to-one sessions (34) or a combination (36); it has been suggested that group formats are more successful (45). Telephone calls have been used to support participants (33); others have included subsequent booster sessions (29;32), although Riemsma and colleagues concluded that their booster sessions had little effect (29). Previous programmes have been facilitated by various members of multidisciplinary care teams but nurses have been the most common educators (9); none of the programmes were lay-led. Programmes ranged in duration from several consecutive days (37), to weekly sessions over several weeks (29-33;35;38), to a year-long programme (36). Programmes lasting more than six weeks are considered to be more effective (26;41), although it must be remembered that increased programme length may affect attrition (46). Shorter programmes have also produced successful outcomes, for example, Abourazzak described an intensive course which delivered 18 hours of education and group workshops over 3 days to 39 patients who were compared to a control group of 38 patients (37). Several programmes involved partners; one study was designed to analyse the effect of partner participation by comparing two groups receiving the same group self-management intervention, one group attending with a partner and the other without; contrary to expectation, partner participation was found to decrease self-efficacy (29).

d) Efficacy

A wide range of outcome measures have been employed to assess the efficacy of these programmes. The measures chosen should be congruent with the aims and content of the programme (47). Measures of knowledge, such as the Patient Knowledge Questionnaire, have

been used (38). However, if the education programme is seeking to encourage behaviour change, measures that reflect successful behaviour modification are essential, as well as consequential clinical outcome measures, for example, pain scores, tender and swollen joint counts or measures of disability (36).

Outcome measures have usually been assessed immediately after completing an educational intervention and also after a follow up period, ranging from 6 months (30;35) to 3 years (37). The Cochrane review showed a beneficial effect on clinical outcomes immediately post intervention, but these benefits were not maintained at the final follow up visit (8). Some studies have, however, been able to demonstrate longer term clinical benefits. For example, 43 patients were recruited to a study comparing a 1-year programme designed to improve self-reported disability using active learning strategies focusing on real life situations against a control group. The programme involved individual education sessions every three months, as well as two group sessions with full written information provided. After 18 months, 59% of participants in the intervention group achieved an ACR20 response (48) compared to 10% of the control group (36). Another successful study randomized 85 patients with moderate to severe RA treated with infliximab to either a 9-week programme or a control group. The programme comprised four three-hour group sessions aiming to improve pain, disability and health status. Activities included a detailed home-exercise programme, written programme brochure and home guide, as well as monthly supportive telephone calls. Seventy patients completed the trial and were included in the analysis. Significant benefits on pain and disability in the intervention group persisted up to the final follow up visit at eight months compared to the control group (33). The intensive three day course discussed earlier (37) followed up its intervention participants for three

years. Disease activity was significantly lower in the intervention group 3 years later, but no benefit on functional impairment or quality of life could be demonstrated; however, the control participants were not followed up at 3 years so between groups analysis was not performed.

Patient education in cardiovascular disease

The majority of modifiable "classical" CVD risk factors are over-represented in people with RA (14;18;49). We reviewed the literature specifically to identify studies using a multifactorial educational approach ('Healthy Heart Programmes') including both primary and secondary prevention programmes.

a) Fundamental design

Most CVD education programmes are behaviour-based. Primary prevention programmes include techniques, such as goal-setting or motivational interviewing (50). Most secondary prevention programmes comprise a comprehensive lifestyle programme to address health risk behaviours via behaviour change techniques, lifestyle coaching and psychosocial support; there is usually a particular emphasis on exercise (51).

b) Robust theoretical underpinning

Although few secondary prevention programmes indicate an underpinning theoretical model, some primary prevention programmes do; the Stages of Change Model is the most common model used (52-54). Some studies describe preceding research to explore patients' expectations

of CVD patient education (53) or health beliefs (55) in order to inform their subsequent CVD education programme; this approach is advocated by the literature (56).

c) Structure

CVD prevention programmes vary in terms of group or individual sessions and several included follow up telephone calls (50;57-59) or booster sessions (54;60). They were facilitated by various members of the multidisciplinary team rather than lay-led. Interestingly, some secondary prevention programmes relied entirely on telephone calls (61) or were delivered via the internet (including e-mail communication with a case manager) (62). Primary prevention programmes vary in duration from a few hours (63) to, for example, a programme involving 28 two-hour meetings over a ten month period (58). Most secondary prevention programmes lasted several weeks or months; for example, the Vestfold Heartcare Study Group lifestyle intervention programme involved six weeks of 'heart school' including supervised physical exercise and twice weekly group meetings (addressing dietary advice, smoking cessation, physical activity counselling, risk factor management, psychosocial management, medication and reduction of mental stress) followed by nine weeks of twice weekly supervised gym exercise with group meetings every three months (64). The value of longer programmes is unclear; distributing a 3-month programme over a year was found to make no difference to its impact (65). Further, a 2-year programme was associated with fewer clinical events (66), whereas a 3-year programme was not (51).

d) Efficacy

Outcome measures did not usually include measures of knowledge but instead were behavioural (smoking status, physical activity, weight) and clinical, including changes in individual risk factors. Framingham 10-year CVD risk, or subsequent rate of CVD events.

Both primary and secondary CVD prevention programmes showed improvements in CVD behaviours ((50;54;63) and (51;64) respectively) as well as CVD risk factors ((53;57;60) and (59;66;67) respectively). Some primary prevention programmes showed reductions in 10-year CVD risk (57;58). In terms of translating risk factor modification into hard clinical endpoints, primary CVD prevention programmes have had mixed success. The large multiple risk factor intervention trial (MRFIT) involving 12 966 patients was successful in modifying diastolic blood pressure, serum cholesterol levels and smoking status, and maintaining this over a 6 year period; the effect on coronary heart disease mortality rate was favourable although not significantly different from a usual care control group (68). Similarly, the Cochrane review (reviewing the literature up until 2001) found modest improvements in risk factors following counselling and education programmes but no significant impact on mortality (10 trials reported CVD event data comprising 903 000 patient years of observation; for total mortality there was a pooled odds ratio of 0.96 (95% CI 0.92 to 1.01) favouring intervention) (69). However, Rachmani and colleagues were able to demonstrate a significant reduction in CVD events over an eight-year follow up period in 165 patients with diabetes, hypertension and dyslipidaemia (70). A key feature of this particular programme (70) was that, as well as lifestyle advice and a fitness programme, patients were given their risk factor measurements as well as defined target values and were encouraged to urge their general practitioner to change their medication if target values were not met. Participants in this intervention programme had 52 CVD events compared to 80 CVD events in

the control group; the relative risk, over 8 years, for the combined CVD event index in the intervention compared to the control group was 0.65. This strategy whereby patients are empowered to request to be 'treated to target' by their doctors highlights the successful results that can be achieved when concordance in the patient-health professional partnership is achieved. A similar strategy was used as part of the COACH (Coaching patients On Achieving Cardiovascular Health) programme which aimed to improve CVD risk factors in people with coronary heart disease (61).

Secondary CVD prevention programmes have also shown an improvement in clinical events (62;66). For example, Giallauria and colleagues recruited 52 post-infarction patients, who had just completed a standard 3-month cardiac rehabilitation programme, and randomised them either to a further 2-year multifactorial educational and behavioural programme or a control group. The programme entailed monthly hospital visits providing dietary advice, lifestyle reinforcement and exercise; families were invited to help sustain the patient long term. Supportive written material was provided. This study observed CVD events in 27% of patients in the control group compared to 11% in the intervention group, although the study was not powered to detect CVD morbidity and mortality. Furthermore, the Cochrane systematic review of exercise-based cardiac [secondary] rehabilitation (involving 8440 patients) observed that cardiac mortality was reduced by 31% in exercise-only interventions and 26% in comprehensive cardiac rehabilitation schemes when compared to usual care (71). The pooled effect estimate of secondary cardiac rehabilitation on combined mortality, non-fatal myocardial infarctions and revascularisation procedures was 0.81 (71). Can specific features be identified to explain this improvement in clinical status in secondary prevention programmes? Most obviously, these programmes involve patients who

have had a cardiac event or procedure. For them, CVD is a 'real' rather than a potential event; this is likely to considerably increase motivation to engage in preventative behaviours, which will translate into increased self-efficacy (72;73). To similarly enhance motivation in primary prevention schemes will require skilful communication about the seriousness and implications of future risk (74). Alternatively or additionally, it may be the prominent role that exercise plays in secondary prevention schemes, which contributes to their greater general effectiveness. Certainly, exercise has a major beneficial effect on the likelihood to develop, become symptomatic or die from CVD, through ameliorating multiple risk factors including obesity, dyslipidaemia, hypertension and diabetes mellitus (15).

A comparison of the successful components of patient education programmes in RA and CVD is provided in Table 1.

Table 1: Successful components of patient education programmes

Component	**RA patient education programmes**	**CVD patient education programmes**
Fundamental design	Behavioural based	Behavioural based
Theoretical underpinning	Social Cognition Theory	Stages of Change Theory
Structure	• Group meetings • Participants attend individually • Duration of more than 6 weeks • Written information provided • Supportive follow up telephone calls	• Duration of several weeks/months with frequent meetings
Content	• Skills training in behaviour change techniques	• Skills training in behaviour change techniques • Compulsory exercise • Accurate and skilful communication of CVD risk to enhance motivation • Empowering participants to urge doctors to 'treat to target' their risk factors
Outcome measures	Measures of behaviour and clinical outcomes	Measures of behavioural and clinical outcomes, including hard clinical endpoints if follow up is long enough

Conclusion: Developing novel patient education to address CVD in RA; what have existing programmes taught us?

The principle of specifically designing patient education programmes to address a significant co-morbidity is novel in itself; this design process may be transferable, both to other RA co-morbidities but also other chronic diseases, with specific adjustments on a case by case basis.

There is significant common ground between successful RA and CVD education programmes (Table 1), which can be integrated to provide a framework for designing education for RA patients about CVD.

a) Fundamental design

A behavioural approach, rather than solely the provision of information, should be provided by the intervention.

b) Robust theoretical underpinning

Research will be required to ascertain which health psychology models may be pertinent, but the existing literature suggests that Social Cognition Theory is likely to be particularly important, combined with the Stages of Change model (75). Preceding research is also required to identify patients' expectations of the intervention.

c) Structure

The evidence suggests that a programme lasting several weeks or months would confer greatest benefit, providing the time for participants to learn and implement skills in behaviour change. A group format is recommended; the use of follow-up telephone calls could be a possible strategy. A relationship between the nature of the facilitator and the outcome of the programme was not observed; the facilitator should therefore be the person most suitable for the role who is adequately trained and educated. As this programme is providing cross-disciplinary education, training the facilitator will be particularly important; for example, the DESMOND (Diabetes Education and Self Management for Ongoing and Newly Diagnosed) primary prevention education programme in people with diabetes (63) describes providing two days of multidisciplinary training for the programme educators (55).

The actual content of the CVD education programme for people with RA will require appropriate modification to suit a rheumatoid population. Inaccurate health beliefs about CVD need to be corrected and skilful communication of the magnitude of the risk of CVD and its relevance to them must be included at the outset to enhance motivation for behaviour change (76;77). Cognitive-behavioural strategies (such as counselling, motivational interviewing (78) or lifestyle coaching) need to be deployed to change maladaptive ways of thinking and feeling about CVD and enhance participants' perceived control over CVD lifestyle behaviours (79), combined with specific skills in how to actually implement a desired behaviour change (80), such as smoking cessation, eating a low fat diet, weight control or increasing exercise. The benefits of corticosteroids and non-steroidal anti-inflammatory medications for a person with RA need to be provided alongside their potential adverse effects on weight or blood pressure; it should be emphasised however that these adverse effects are not inevitable or fixed and may be modified

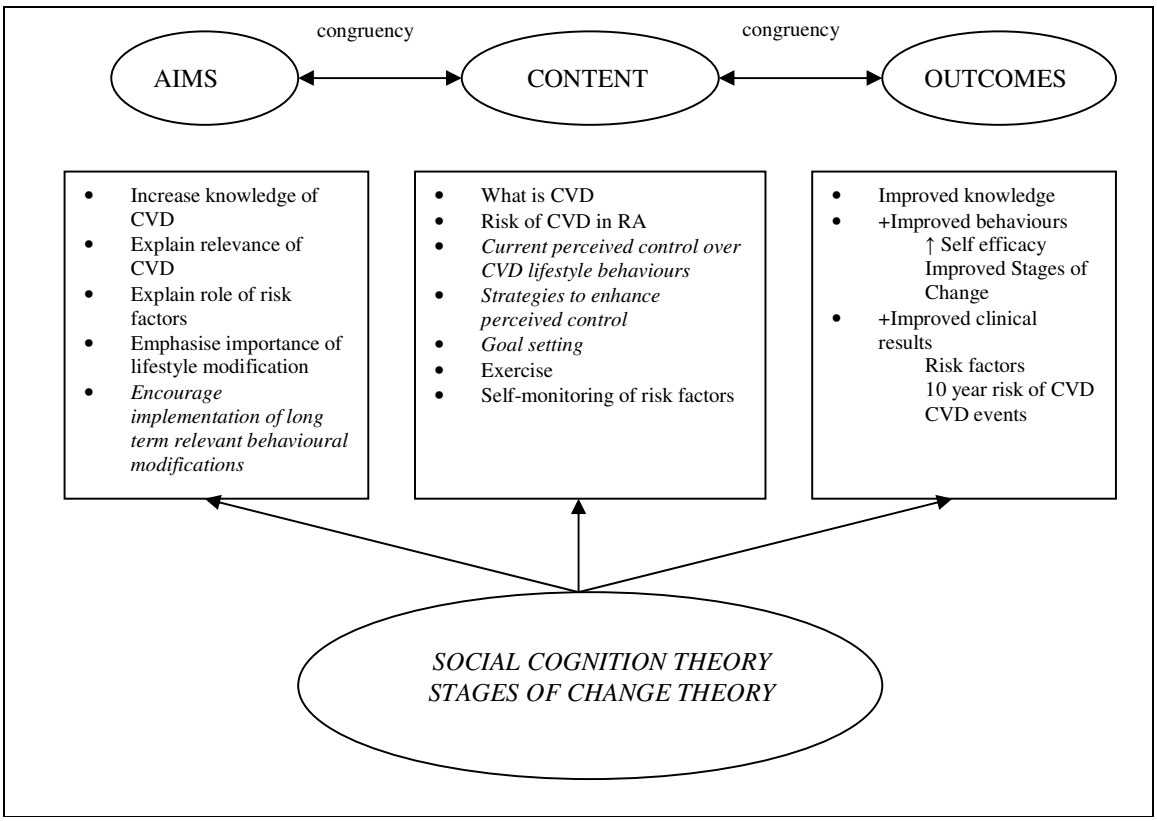
through dietary control and exercise. Empowering patients with the skills to monitor their own progress with CVD risk factor reduction, and seek further advice or treatment if they fail to reach target values has been shown to be a useful strategy. Existing shared care booklets for blood test monitoring related to drug therapy could be modified to incorporate RA patients' CVD risk factor results as well as target values for body mass index, smoking status, blood pressure or lipid profile (81). Exercise should be a core component. Both physical (pain, mobility) and psychological (low levels of self efficacy) factors are reported by RA patients as barriers to exercise (82). Therefore, advice is required to reassure patients that exercise will not only improve their cardiovascular risk (15) but may also reduce RA-related inflammation and improve function, pain and mobility (82;83) without damaging their joints (84). Strategies that foster self-efficacy and improve intrinsic motivation (85), and tailored advice from a healthcare professional (86), have been recommended to promote exercise participation.

d) Efficacy

Evaluation of the efficacy of a new intervention is essential. Knowledge of CVD can be measured using a questionnaire specifically designed and validated for people with RA (87). Alongside measuring actual behaviours, self efficacy measures (88-91) and Stages of Change measures for the different lifestyle behaviours could be used (92). Clinical outcomes could include risk factors, 10 year CVD Framingham risk or other risk algorithms (22), and, if follow up is long enough, rates of CVD events.

These suggestions for developing a successful CVD education programme are summarised in Figure 1.

Figure 1: Schematic representation of a theoretically-informed CVD education programme in people with RA, making explicit how recommended theoretical models relate to the content and outcomes of the programme.



+ represents enhanced results expected due to interventions theoretically driven

e) Other considerations

There are other practical factors that need to be considered in delivering CVD education to patients with RA (9;93) (Table 2).

Table 2: Additional factors to consider in designing CVD education for people with RA

• When is the appropriate time, in relation to participants' disease duration, to deliver such an intervention?
• Is the written material suitable for the reading age of the target audience (many RA patients have limited health literacy (94))?
• Is the reading material available in large text, Braille and appropriate ethnic languages?
• Would it be helpful to have the written material available in an on-line format?
• Does the intervention take into account potential cultural barriers?
• Is the educational intervention held in a convenient venue for participants, that is accessible by the disabled?
• Is the intervention available at different times of the day to be convenient for those in employment/ those who are retired/ those with small children?
• Have financial costs to the participants attending been minimised?

When would be the optimum time to deliver this intervention? Patients interviewed suggested once initial control of RA had been established, rather than at diagnosis (44). However, behavioural and cognitive-emotional adaptations have been shown to manifest early in RA (95), so education is required early enough to ensure appropriate behaviours are implemented and/or maintained. Inclusion of patients from ethnic minorities is particularly important as South Asians are at increased risk of CVD (96). How these barriers could be overcome will be an important component in the design of the intervention (93).

Only future implementation and evaluation of an education programme underpinned by these recommendations will allow us to judge how effective this process has been in providing a theoretical framework on which a novel education intervention may be constructed.

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CHAPTER 3 (PART 2): GENERAL INTRODUCTION; PATIENT EDUCATION ON CARDIOVASCULAR ASPECTS OF RHEUMATOID DISEASE: AN UNMET NEED

Rheumatoid arthritis (RA) is the most common form of inflammatory arthritis affecting nearly 1 in 100 adults (1). Cardiovascular disease (CVD) occurs at rates higher than expected in the general population, is the most prevalent co-morbidity and most common cause of death in RA patients (2-5). The exact reasons remain unclear, but both classical CVD risk factors (such as hypertension and dyslipidaemia) and novel mechanisms (such as systemic inflammation), and their interplay, appear to be important (6;7). Classical risk factors may be fixed (e.g. age, sex, family history) or modifiable (e.g. smoking, hypertension, dyslipidaemia, obesity, sedentarity). The latter are an obvious target for identification and intervention (7;8), neither of which appears to be happening systematically in the current rheumatology health care environment (3;9). This is partly due to lack of sufficient awareness of health professionals and information/education of patients on this aspect of their disease. Interestingly, many of the medications used for the management of RA may have a significant impact upon these factors, with the clearest example being the potential cardiovascular effects of the commonly used non-steroidal anti-inflammatory drugs (NSAIDs) and coxibs (10), the hypertensive effects of some disease-modifying anti-rheumatic drugs (DMARDs) such as cyclosporine and leflunomide, or potential beneficial lipid effects of others, such as hydroxychloroquine (7). Non-pharmacological interventions are of equal, if not more, importance: for example, there is excellent quality evidence to suggest that exercise provides significant functional benefits in RA patients, together, of course, with important cardiovascular benefits, such as improvements in lipid profile and insulin sensitivity,

reduction of prothrombotic states and body fat content, and diminished risk of death from CVD in the general population and high risk groups therein (11). The importance of systemic inflammation is more controversial: there is clear evidence that atherosclerosis is an inflammatory disease (12) and that RA appears to associate with premature peripheral atherosclerotic changes (13); there is also evidence that better control of systemic inflammation leads to survival benefits in RA (14-17). However, it remains unclear whether this is a direct effect or whether it operates through amelioration of the multiple metabolic and vascular effects of inflammation (18;19). Uncertainties also remain as to the best way to achieve sufficient control of high-grade inflammation without adverse effects to the vasculature.

Within the general population it is possible to estimate an individual's likelihood to sustain an acute CVD event in the next 10 years, using validated risk algorithms based on the presence and severity of classical CVD risk factors (20). On the basis of this, informed decisions can be taken, as to whether this individual would be suitable for primary prevention therapy, according to existing accepted guidelines (20). Communicating *future risk* and the need for therapy to *prevent* it (as opposed to the need for treatment to control symptoms or problems that a patient is already experiencing), is one of the most challenging education/communication tasks in the patient/health professional interaction (21). Despite such difficulties, patient education has been placed right at the heart of prevention strategies in cardiovascular medicine, and has been shown to be effective. Important examples include the PREMIER trial, where behavioural interventions improved multiple lifestyle factors and resulted in significant improvements of blood pressure control (22). Further studies in high-risk groups with diabetes and (for secondary prevention) in patients with confirmed previous cardiovascular events have shown that increased knowledge of CVD risk

factors correlated with improved adherence to medication, successful and sustained lifestyle modification, and improvement in individual CVD risk factors (23;24). More importantly, participation in education programmes has been shown to result in improved clinical outcomes, including statistically significant reduction in 10-year CVD risk (25) as well as actual CVD events in the long term (8 year follow up) (26).

Research in the cardiovascular aspects of rheumatic disease is increasingly being translated into clinical practice. Management of cardiovascular risk is becoming an integral component of the long term care of patients with RA. Every day practice indicates, and British Society for Rheumatology (BSR) guidelines state, that controlling co-morbidities such as ischaemic heart disease (IHD), hypertension and dyslipidaemia are already important aspects of rheumatology care provision (27). This has been operationalised in the "Arthritis and Musculoskeletal Alliance" (ARMA) standards of care for patients with inflammatory arthritis in the inclusion of an updated cardiovascular health check in the annual specialist review appointments (28). A recent Arthritis Research Campaign (arc) report also states that all patients with RA should be screened annually for CVD risk factors (29). However, a patient survey of the ARMA standards in 2006 by the National Rheumatoid Arthritis Society (NRAS) has revealed that monitoring of cardiovascular health was infrequent (30). Even with increasing awareness amongst health professionals about CVD risk identification and management in RA, effective implementation of such an important and ambitious change of practice requires appropriate and timely education of the patients themselves, in order to achieve concordance. Concordance, the informed interaction in the decision making process in the patient-professional partnership, promotes shared responsibility for care (31) and is particularly important for lifestyle modification interventions

and for prevention therapy. A survey of more than 2000 patients with diabetes in 2002 revealed that two thirds of respondents did not consider CVD a serious complication of diabetes, suggesting that their education on, and communication of, CVD risk had been inadequate (32). Such shortcomings are likely to be more pronounced in RA patients, where research evidence has only recently started to reach the medical, let alone the patient, communities. Indeed, previous work in our unit has shown that only a quarter of patients with RA and *confirmed CVD* recorded the latter as a co-morbidity when listing their other illnesses (33). Therefore, a combination of research findings, management imperatives, observations and experience from other conditions and from RA, as well as common sense, place patient education on the cardiovascular aspects of rheumatoid disease right at the centre of any successful prevention strategy.

In general, patient education is defined as "any set of planned educational activities designed to improve patients' health behaviours and/or health status" (34) and has a vital role to play particularly in the management of chronic disease. Its main purpose is to facilitate desired health outcomes (35), which can be achieved by increasing self-efficacy, decreasing helplessness and thus increasing the ability to make health-related decisions (36). Written information (such as the multiple *arc*-funded leaflets), when used to complement verbal information, has been shown to improve patient satisfaction (37) and disease knowledge (38). However, it has been suggested that knowledge alone, whilst it may be a pre-requisite, is rarely sufficient for behaviour change (39-41). Social cognition theory, developed by Bandura (42), examines the different factors that contribute to behaviour change. Several models have been developed, including the Theory of Planned Behaviour, developed by Ajzen and colleagues: this proposes that behaviours are a result of a persons attitude towards a behaviour (both beliefs and evaluation of the outcome, which may

be affected by gaining knowledge), but social norms and perceived behavioural control (self-efficacy) are also very important (43). Thus educational interventions developed to include knowledge, behavioural and psychosocial components have been found to be the most effective in behaviour modification (39). In patients with RA, such cognitive-behavioural educational interventions addressing articular symptoms have shown improvement in knowledge, self-efficacy to cope with chronic arthritis (44), exercise and joint protection, disability and pain (45). A systematic review of RA patient education analysed the effectiveness of different types of educational intervention, namely information only, counselling or behavioural treatments (46). Only studies involving behavioural interventions showed significant effects (improving outcomes for functional disability, patient global assessment and depression) but this was limited to immediately after the intervention. Perhaps the best known example of such a multifaceted education programme is the Arthritis Self-Management Programme (ASMP), pioneered by Lorig in the late 70s in the USA (47) and successfully run in Australia (48) and Europe (49) for many years. In the UK the ASMP is delivered through Arthritis Care under the name Challenging Arthritis (50), and significant improvements in self-efficacy, health behaviours and health status have been shown (51). A generic chronic disease self-management programme (CDSMP) is also established. In patients with heart disease, lung disease, stroke or arthritis, participation in the CDSMP reduced hospital visits and health distress and improved self-efficacy (52).

However, the systematic review of rheumatoid arthritis patient education mentioned above failed to show long-term benefit from patient education interventions (46). This may be because many of the existing interventions failed to explore the patient's previous level of knowledge (which may be low), or the patient's own model of illness and its management. More specifically, the

interventions may not have assessed the patient's needs beforehand (we have found through work in the Birmingham Arthritis Resource Centre (BARC) that, despite the ever-increasing availability of both educational material and format, formal 'needs assessments' continue to identify unmet needs (53)) or the intervention may have failed to explore the divergence of opinions between healthcare professionals and patients regarding the importance of various aspects of disease or management (41;54). For example, we have previously shown that, compared to health professionals, patients are more interested in information pertaining to medication side effects, diet and alternative treatments (53). This suggests that the quality of the analysis prior to designing an educational intervention will determine its subsequent effectiveness (55). Specifically in relation to CVD risk, research has also shown that patients' recall of blood test results may be susceptible to self-enhancement bias, wherein people with high cholesterol recall a lower figure (56): this may explain the lack of change in health behaviours even after personally relevant risk information. Overall, these observations would suggest that educational material and interventions are more likely to be successful if they are developed specifically for the purpose and evaluated for their effectiveness prior to application.

Patients' preferences for educational interventions are also important to consider, as this is central to their design. Qualitative research in RA patients has shown they found a one-to-one format helpful for learning about very specific information such as medications, whereas a group format was better for learning about self-management techniques and exercise due to the motivation factor a small group can offer (57). This will be particularly pertinent if one wants to promote lifestyle changes for cardiovascular benefit. Leaflets were viewed as helpful and a useful memory aid, but insufficient alone to address the breadth of concerns there may be, e.g.,

surrounding the value and safety of exercise (57). A comparison of group education with supporting self-help guide versus supporting self-help guide alone showed improvement in self-efficacy in the former group, whereas no changes from baseline were observed in the latter group, or, interestingly, in those participating in the group education session with their partner (58). Conversely, questionnaire research has shown the preferred format for learning about arthritis was in writing (59).

There has been a small pilot study in Glasgow of 22 RA patients who also attended a nurse-led clinic to address CVD lifestyle factors with modest (but promising) benefit as a result (60). Other than that, to the best of our knowledge, no educational interventions have been developed and evaluated for communicating the increased CVD risk and relevant requirements for pharmacological prevention therapy and lifestyle modification to people with RA. Our anecdotal, but significant, experience from the first combined rheumatology/cardiology clinic in the UK that has been running in Dudley for the last 3 years, is that there is a thirst and need for such material, which has to be developed specifically for the purpose. The approaches used in the general population or other high-risk groups, e.g. diabetics, may not be sufficient for people with RA, because they present several additional challenges. Some of these challenges relate to the healthcare community, for example the lack of consensus about the exact magnitude of additional CVD risk conferred by having RA, because this cannot yet be accurately calculated (as it can be for other conditions, such as diabetes or hypertension). Other challenges are of more personal nature. The RA patient presents with disabling joint symptoms yet rheumatologists also discuss cardiovascular disease, which may seem to the patient unrelated, unimportant if it is

currently asymptomatic or even overwhelming as we 'break bad news' twice about both RA and CVD. Potential adverse cardiovascular effects of medications needed for sufficient relief of RA symptoms, the possible need for even further medications on an already significant background of polypharmacy (61) and the potential drug interactions need to be outlined and put in perspective. Lifestyle changes, e.g. exercise, may seem daunting in the presence of significant joint discomfort. There are currently no "off the shelf" resources to address sufficiently this specific need.

In summary, patient-focused education on the cardiovascular aspects of rheumatoid disease is a very important yet neglected area of current RA patient education programmes. There is an urgent requirement to address this unmet need and develop properly designed and evaluated educational interventions, which will specifically address the complex lifestyle and pharmacological measures required to optimise the cardiovascular health of every person with RA. It is likely that a combination of appropriate written information with a psycho-educational behavioural approach will be the most effective means for this. Such programmes could be delivered through already existing infrastructure, for example the excellent network of rheumatology clinical nurse specialists (62), possibly with initial help by health psychologists (63), where available. It is now up to us, the wider rheumatology clinical and scientific community, to rise to this challenge.

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OVERVIEW OF THESIS

Having identified CVD education for patients with RA as a currently neglected area of patient education, this thesis describes the development and evaluation of an educational programme designed to meet this need. The Medical Research Council provides a framework on how complex non-pharmacological interventions should be developed and evaluated (1). The pre-clinical or theoretical phase has been provided in the Introduction, where both the scientific rationale for focussing on CVD co-morbidity in RA (Chapter 2), as well as existing patient education interventions in both RA and CVD (Chapter 3), are discussed.

Phase I, or the modelling phase, aims to identify or improve understanding of the various components of the proposed intervention and qualitative research is recommended as a useful tool in this setting. In order to develop patient education about CVD in RA it is important to seek the views of key stakeholders, namely relevant health professionals and patients. Chapter 4 describes a qualitative exploration of the perceptions of health professionals and how these could influence the subsequent content, timing and delivery of a programme whereas Chapter 5 similarly explores RA patients' existing health beliefs and perceived needs from a future intervention.

Phase II, or the exploratory phase, defines components of the proposed trial, including outcome measures to be used, the nature of the control arm of the intervention and the precise nature of the trial itself. As there was no extant measures of RA patients' knowledge of CVD in RA, a new questionnaire had to be both constructed and psychometrically validated. This is described in

Chapter 6. The proposed complex education intervention will need to be compared to a control arm, whereby patients are provided with basic knowledge about CVD in RA, akin to existing leaflets about RA or its other co-morbidities. The development of this leaflet, as well as its evaluation is described in Chapter 7. Chapter 8 describes the exact nature of the complex education intervention developed, explaining how information gained from Chapters 4 and 5 was integrated to inform the design, structure, and duration of the programme.

Phase III is the randomised controlled trial of the education intervention and is described in Chapter 9. The final MRC framework phase IV explores the practicalities of long term implementation. Chapter 10 discusses the issues that emerge from this thesis, as well as considering its possible limitations and future research directions.

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CHAPTER 4: "ALL SINGING FROM THE SAME HYMN SHEET": HEALTHCARE PROFESSIONALS' PERCEPTIONS OF DEVELOPING EDUCATIONAL MATERIAL ABOUT THE CARDIOVASCULAR ASPECTS OF RHEUMATOID DISEASE

Abstract

Objective: Cardiovascular disease (CVD) is the leading cause of death in Britain and its prevention is a priority. Rheumatoid arthritis (RA) patients have an increased risk of CVD and management of modifiable classical risk factors requires a programme with patient education at its heart. Before a programme for RA patients is implemented it is important to explore the perceptions of patients and relevant healthcare professionals and consider how these could influence the subsequent content, timing and delivery of such education. Here, we assess healthcare professionals' perceptions.

Methods: Qualitative focus group methodology was adopted. Four group meetings of healthcare professionals were held using a semi-structured interview schedule. The focus group transcripts were analysed using Interpretative Phenomenological Analysis.

Results: Three superordinate themes emerged: professional determinations about people with RA, including their perceptions about patients' priorities and motivations; communication about CVD risk, including what should be communicated, how, to whom and when; and responsibility for CVD management, referring to patients and the healthcare community.

Conclusions: Although healthcare professionals agree it is important to convey the increased CVD risk to patients with RA, there is concern they may be less proactive in promoting risk management strategies. There was uncertainty about the best time to discuss CVD with RA

patients. Maintaining a close relationship between primary and secondary care was thought to be important, with all healthcare professionals 'singing from the same hymn sheet'. These findings can inform the development of novel education material to fulfil a currently unmet clinical need.

Introduction

This paper describes the first in a pair of studies addressing opinions on the development of patient education to address knowledge and management of cardiovascular disease (CVD) risk among people with rheumatoid arthritis (RA). CVD is the leading cause of death in Europe (1), and its prevention, diagnosis, treatment and rehabilitation is a priority (2). Rheumatoid arthritis (RA) is a chronic inflammatory disease associated with an increased risk of CVD, which predominantly accounts for the excess mortality in patients with RA (3;4). Comprehensive care of the person with RA therefore needs to focus not only on management of articular symptoms and prevention of joint damage but also on managing their cardiovascular risk.

The increased risk of CVD in RA is attributed to accelerated atherosclerosis due to both classical risk factors for CVD and novel mechanisms such as systemic inflammation, and their interplay (5-7). Classical risk factors may be fixed (e.g., older age, male sex, positive family history) or modifiable (e.g., smoking, hypertension, dyslipidaemia, sedentarity, obesity) and appear to be highly prevalent in patients with RA (8). Although further research is required to elucidate the relative contributions these different factors make to overall CVD risk, management of modifiable classical cardiovascular risk factors is an obvious target. This requires active identification and proactive intervention (5), which does not currently appear to be happening

systematically (8;9). Recommendations by the British Society for Rheumatology suggest that all individuals with RA should have an annual assessment of all co-morbid conditions (10) and the Arthritis and Musculoskeletal Alliance standards of care for people with inflammatory arthritis specifically suggest an annual cardiovascular health check (11). A similar approach is advocated in France (12). To implement such a cardiovascular screening and intervention programme requires patient education to be at its heart in order to address such integral issues as patient-professional concordance with both lifestyle and behavioural modifications as well as polypharmacy and primary prevention therapy (13). Patient education programmes are well established in rheumatology (14). However, no cardiovascular educational material or programme exists, designed specifically for patients with RA. This has been recognised as a clinical oversight that should be addressed (13). The present paper is the first of a pair of manuscripts considering the design of such a novel educational programme; this endeavour will require input from both patients and healthcare professionals. Patients needs and health beliefs must be explored and reacted to (15-17) and this is addressed in the accompanying paper (18). However, it is also important to explore the perceptions of healthcare professionals and consider how these could influence the subsequent content, timing and delivery of a CVD risk education programme for patients with RA. It is these healthcare professionals who will be the source of referral to such programmes. Understanding the assumptions that healthcare professionals may bring to the design or structure of any patient education material is as crucial as understanding those of patients, especially as many education programmes include little or no patient involvement in the planning stages (15).

In order to fully explore healthcare professionals' perceptions of CVD education for RA, a variety of opinions needs to be canvassed and explored in-depth providing the opportunity for ideas, not initially anticipated, to emerge. Accordingly, a qualitative approach was adopted (19). Focus group methodology harnesses group interaction and allows discussion of each other's experiences and should prove an appropriate and effective technique for exploring healthcare professionals' attitudes (20). The aim of the present study, therefore, was to explore, qualitatively, healthcare professionals' perceptions of how to develop patient education regarding CVD risk for patients with RA.

Methods

a) Participants

Participants consisted of 12 healthcare professionals who were considered to have relevant experience, including doctors and nurses from both primary and secondary care, specialising in rheumatology, cardiology and management of cardiovascular risk factors (Table 1). Purposive sampling was used to recruit participants, from the pool of local healthcare professionals, with international, national and local expertise and to ensure a broad mix of participants in the sample.

b) Procedure

Local research ethics committee approval was granted and all participants provided informed written consent. Four focus groups were held with, on average, 3 healthcare professionals attending each (range 2-5); the number of participants in each group was related to the pragmatics of convening clinical staff at mutually convenient times. A semi-structured interview schedule

Table 1: Composition of the health professional focus groups

Profession	Focus group number	Sex	Age	Specialty	Special interest	Years of relevant experience
Medical doctor	1	Male	47	Rheumatology	Cardiovascular disease	20
Medical doctor	1	Male	56	Chemical Pathology	Obesity and dyslipidaemia	20
Director of Action Heart	1	Male	45	Cardiac Rehabilitation		15
Clinical nurse specialist	1	Female	52	Community Cardiology	Community Cardiac Liaison Nurse	20
Clinical nurse specialist	1	Female	48	Cardiology	Patient education and cardiac rehabilitation	27
Medical doctor	2	Female	57	Cardiology	Patient education nationally	28
Medical doctor	2	Male	41	Cardiology	Cardiac disease in rheumatoid arthritis	12
Clinical nurse specialist	3	Female	45	Rheumatology	Annual review clinics (including CVD risk assessment)	21
General practitioner	3	Male	52	Primary Care	CVD risk assessment	23
Medical doctor	4	Male	42	Rheumatology	Medical education	13
Medical doctor	4	Male	47	Diabetes	CVD primary prevention	18
Clinical nurse specialist	4	Female	43	Diabetes	Patient education	5

was created (by HJ) based on a review of the existing literature (13) and discussed among all authors, who include rheumatology clinicians and qualitative researchers, prior to the interviews. The schedule contained core open-ended questions (Table 2), which were employed, along with probes and prompts, in all four focus groups in no set order. The questions were non-directional and designed to stimulate in-depth discussion among participants. Opinions that emerged but were not anticipated were followed up with more probing questions. The focus groups were led

by HJ and facilitated by EDH. Each group discussion was audio-recorded and transcribed verbatim by a sole professional typist.

Table 2: Semi-structured interview schedule for all focus groups

Core open-ended questions	Relevant probes and prompts
Could you please introduce yourself to the group, what job you do and the relevant experience you have for this focus group?	
What are your thoughts about cardiovascular education for patients with RA?	• Is it the same as other patients with CVD? • Is it different to other CVD patients? • Are there different approaches to management of CVD risk factors if a patient has RA? • When should such education be given?
What do you think are the important messages to convey to patients with RA about the increased risk of CVD?	• Increasing awareness of associated CVD risk • Generic education on CVD • Discussion of risk factors • Lifestyle advice
What do you think should be a priority for the doctor in managing cardiovascular risk for a patient with RA?	• Primary prevention • Managing individual risk factors • Explaining relevance • Assessing compliance • Referrals to services that can support lifestyle modifications e.g., smoking cessation
What do you perceive are the priorities of a patient with RA?	• Managing arthritic pain • Optimising analgesia • Polypharmacy • Medications interacting • Worrying they may make their arthritis worse if they exercise • Needing a support group to motivate them for lifestyle modification • Do doctor and patient priorities clash and/or where do they match? • Do you perceive a patient wants to take responsibility for managing their disease themselves or do they want the doctor to take responsibility and treat everything with tablets?
What are your experiences of suggesting medication or lifestyle changes to patients at risk of CVD?	• Which do you feel most comfortable suggesting? • Which is easiest to suggest? • Which are patients most interested in? • What resources do you use to support lifestyle changes?
How successful do you perceive we are currently in educating patients about CVD risk?	• Primary prevention • Post MI • In high risk groups e.g. diabetics • How effective are we at supporting patients in lifestyle modification?
What educational methods have you found helpful for patient education on CVD risk management?	• Behaviour-orientated programmes • Written information • How do we engage people who don't want to know?

c) Qualitative analysis

Focus group transcripts were subjected to Interpretative Phenomenological Analysis (IPA). IPA is a method of qualitative analysis that has become established in health research as an effective approach for exploring participants' experiences. IPA follows established yet flexible methodology (21;22) with two levels of analysis; the descriptive (phenomenological), which explores the participants' personal perception of an event, and the explanatory (interpretative), whereby the researcher interprets the data in order to make sense of the personal experience of participants. These interpretations were subsequently presented to participants to check that their views were not being misrepresented. Thus, IPA can facilitate understanding of how individuals perceive illness and healthcare services (23), and may be used to learn from both the healthcare professional (24;25) and patient perspective (26). The transcripts were primarily analysed by HJ. Subsequently EDH and GJT read the transcripts to confirm that the interpretation was reflective of the content of the original discussions. Transcripts were analysed ideographically (individually) and returned to in an iterative process as later focus group discussions informed the analysis. Superordinate (overarching) themes were identified that represented a cohesive interpretation of the healthcare professionals' opinions across all focus groups.

Results

Three superordinate themes emerged from the analysis: (i) professional determinations about people with RA; (ii) communication about CVD risk; and (iii) responsibility for CVD management. Verbatim quotations are used to illustrate these three themes and square brackets are employed, where required, to provide context for the quotes.

The first theme describes the suppositions that the participants held about patients with RA. These healthcare professionals perceived that CVD risk would not be high on their agenda; rather, patients would be more concerned with management of their painful joints. Furthermore, symptom relieving drugs were considered to be more of a priority than cardiovascular prevention medication:

> "Because the rheumatoid is painful and disabling, they're not going to see the coronary disease side at all." (focus group 2, participant 1)

Healthcare professionals presumed that patients with RA would find various aspects of CVD risk management more difficult than patients without RA, particularly implementing lifestyle changes, such as exercise or coping with increasing polypharmacy. It was also assumed that patients with RA, who may not yet have had a cardiac event, would be less motivated to engage in preventative healthy behaviours:

> "They're not going to give up smoking, they're not going to eat properly, they're not going to do anything until we've got their disease under control." (focus group 3, participant 1)

> "Patients do not have the motivation because they don't feel the ill effect – you're trying to prevent something in the future." (focus group 1, participant 2)

The second superordinate theme concerned communication about CVD risk. When considering the design of a patient education programme, issues such as what, how, when and with whom should these healthcare professionals communicate emerged as important considerations. Essentially, any education programme must convey the increased risk of CVD in patients with RA:

> "… putting on the agenda that arthritis is more than just the joints…" (focus group 4, participant 1)

Participants also discussed how to convey the, sometimes difficult, concept of future risk:

> "They [patients] are saying 'What is he talking about? I am feeling well'." (focus group 4, participant 2)

An important sub-theme that emerged unprompted in all focus groups was the importance of conveying adequate information to allow patients to make informed choices; participants discussed how patients should be given the opportunity to negotiate their specific priorities with a healthcare professional. For the participants, the dual benefits of lifestyle modification for RA and CVD were regarded as an important message to get across:

> "... lifestyle modifications… make sense from both the rheumatoid point of view and the cardiovascular point of view." (focus group 1, participant 1)

How information should be communicated to patients was also viewed as critical to such an education programme. Participants perceived that raising the issue of increased CVD risk to patients with RA was akin to breaking further bad news:

> "… when you're dealing with people with rheumatoid arthritis I guess you also have to break the news to them that they're potentially at added risk of cardiovascular disease…" (focus group 1, participant 3)

> "… it's not a very palatable conversation to have though, is it…" (focus group 2, participant 2)

The matter of who multidisciplinary rheumatology teams should communicate with emerged. Beyond communication with patients, dialogue between healthcare professionals in primary and secondary care was considered essential. Primary care professionals regularly calculate CVD risk scores; good communication with general practitioners could prompt sharing of this information and avoid duplication. Importantly, educating general practitioners about the CVD risk associated with RA will mean a consistent message is given to patients by all healthcare professionals:

> "If they've [the patient] got all groups [of healthcare professionals] saying the same thing, we're all singing from the same hymn sheet… then they might actually think, well, maybe I should…" (focus group 3, participant 1)

The timing of an educational intervention provoked mixed opinions from the healthcare professionals; their dilemma was that:

> "… what we need to do is get over to them [patients] the priority of this [CVD] as an important issue… or do we do that once we've got them [i.e. their disease] under control?" (focus group 3, participant 1)

Some participants felt that education about CVD should be included in all interactions with patients from the moment of diagnosis because:

> "… the new diagnosis of rheumatoid arthritis is one of those golden opportunities for people to stand back and look at their lifestyle and be at a motivated stage where they can take control of their health condition." (focus group 1, participant 3)

This was considered to be because:

> "If you leave it too long… they will say 'Oh, what's he doing? I've been fine for the last year and now he's telling me about cholesterol, he's telling me about blood pressure.'" (focus group 4, participant 2)

Other participants stated they would delay patient education:

> "If you tell them too much in one go, you'll either frighten them to death and they won't come back or they'll switch off." (focus group 4, participant 3)

Further, patients' priorities were judged to change over time:

> "… in the beginning it is the rheumatoid arthritis [that patients are most concerned with] and probably this may not be the best time to tackle everything… after you've controlled the pain… then they are probably more receptive to other areas." (focus group 1, participant 2)

This issue of priorities links into the third superordinate theme: responsibility for CVD management. Participants judged that patients themselves have a responsibility to take advantage of the opportunities offered and to engage with services available:

> "I think as long as patients, all of them, are equally informed… each person has to take responsibility for their own actions." (focus group 1, participant 2)

The responsibilities that healthcare professionals identified for themselves included both provision of resources and further research to answer clinical questions. To support patients implementing lifestyle changes, adequate resources were deemed to be required and should be accessible to all cultural and other minority groups, as well as being available in different formats, and facilitated by different types of professionals and the patients themselves:

> "It's easy to give out information and to give booklets but what really is needed is some support to carry through those messages." (focus group 1, participant 3)

Equally important is that such resources should remain available for patients to access, even if initially they do not feel able or ready to participate:

> "… they [patients] should know that the offer is still there if they want to engage at any time..." (focus group 1, participant 1)

Participants identified a clear need and responsibility to increase research in certain areas. Issues such as being able to include RA as a risk factor in cardiovascular risk calculators to help more accurately determine CVD risk was highlighted:

> "I'd want to be able to quantify the risk." (focus group 3, participant 2)

> "The difficult bit is can you fit your rheumatoid patients into those risk registers… because they're [the risk registers] rather crude… they don't look at other risk groups." (focus group 2, participant 2)

Further, participants wanted a set of targets for risk factor management agreed with primary care and long term studies on both adherence to primary prevention and the effects of lifestyle modifications:

"Do we begin to set targets for patients that they can work with us together on?" (focus group 3, participant 2)

Discussion

Exploring healthcare professionals' perceptions of developing novel education material has identified assumptions currently held. This will inform how CVD risk messages are delivered. There was a clear presumption that patients with RA would not view CVD as a priority. Unfortunately this may afford a rationale for failing to inform patients about the clear association between RA and unfavourable CVD outcomes. Healthcare professionals have been reported to find 'breaking bad news' stressful (27), and so may unwittingly exploit the presumption of patients' priorities as a reason for not informing or delaying informing patients of CVD risk. This potential 'gatekeeping' of information may deny the patient the opportunity to make informed decisions about their lifestyle and could be considered to reflect a type of medical paternalism that constrains patients opportunities to act with autonomy; in developing novel education material, this defensiveness will necessarily have to be both acknowledged and challenged.

Healthcare professionals interviewed also presumed that implementing lifestyle changes would be harder for patients with RA than for others. As a consequence, they might be reluctant to encourage patients to initiate beneficial lifestyle changes. For example, some healthcare professionals stated that those in pain may find it more difficult to stop smoking. However, people in pain report that they are just as likely to feel ready to quit smoking than those without

pain (28) and, indeed, some of patient participants, in the accompanying paper, describe the motivation they had to quit smoking (18). Accordingly, it would seem important to actively encourage smoking cessation, despite the scepticism of professionals. In addition, healthcare professionals may 'excuse' patients from undertaking behaviour change. Some doctors believe that they need to empathise with overweight patients to maintain a good patient-professional relationship (25). However, empathising or excusing a patient from addressing unhealthy behaviours may inadvertently be giving the patient permission to persist with their current behaviours, which the patient could interpret as tacit approval. The assumption that patients will be less motivated to engage in healthy lifestyle behaviours prior to a cardiac event may similarly result in healthcare professionals not promoting lifestyle modifications with sufficient vigour. Motivation for behaviour change is complex, and is not simply a function of a previous adverse health event. It has been shown that women are more motivated than men, whereas perceiving oneself to be too old or too young, as well as finding medical advice conflicting at times, undermines motivation to change (29). The Theory of Planned Behaviour proposes that behaviour depends on a person's attitudes, based on beliefs of risk and evaluation of the outcome, toward the behaviour (30). It also posits that social norms and perceived behavioural control, i.e. self-efficacy, are very important. Indeed, perceived behavioural control has been shown to be the most influential component of the theory when it comes to predicting future lifestyle changes after a diagnosis of coronary heart disease (31). Therefore, instead of assuming that patients with RA will be poorly motivated to modify their lifestyle, healthcare professionals could consider how they can enhance and support their patients' self-efficacy for changing unhealthy behaviours. This should be an intrinsic component of any new education material. This is discussed further in our accompanying patient-centred analysis (18).

Given the preconceptions that healthcare professionals appear to hold about CVD risk-related behaviour change among RA patients, the development of education programmes is a challenging task (32;33). Nevertheless, it is an important pre-requisite for patient participation in an informed decision-making process, as part of the patient-professional partnership. This concordance is particularly critical for lifestyle modifications (34). Indeed, the concept of shared responsibility was addressed again in the third superordinate theme on responsibilities. Discussions surrounding the timing of a patient education programme proved interesting. There was consensus about identifying a 'golden moment', i.e., that point in time when a patient will objectively self-assess their health status and lifestyle and commit themselves to a specific behaviour change. Healthcare professionals need to capitalise on this moment. The Transtheoretical Model of behaviour change describes pre-contemplation, contemplation, preparation, action and maintenance as five stages through which patients pass (and may relapse and cycle through) to achieve permanent behaviour change (35). The preparation stage is when patients take preliminary steps towards making a specific change (36) which could be considered analogous to the 'golden moment'. Clearly, this point will be reached by different patients at different times, and by some it will not be reached in time. The challenge for healthcare professionals is not only to identify this point in different individuals but also to use this opportunity to encourage definitive action to modify behaviour and to provide adequate resources to support this commitment to change. The arthritis-specific and generic self-management programmes that have been set up and tested over the past decades (37;38) provide several important lessons about locally and individually tailored delivery of such education.

A salient finding from the present study is the perceived importance of maintaining and improving a close relationship between primary and secondary care. Mutual guidelines, electronic patient records, and transfer of information across the primary/secondary care interface will help to develop seamless care (39). This not only prevents duplication (e.g., cardiovascular risk scores) but, importantly, also allows all health professionals to be "singing from the same hymn sheet". Conflicting information from a general practitioner and consultant could prevent a patient from making progress and decrease the patient's confidence in the healthcare system (40). We would argue that the responsibility lies with secondary care, as well as the research community, to disseminate guidance to primary care highlighting the relationship between CVD and RA. As the present study revealed, this guidance will inevitably need to include specific information, such as how to 'fit' patients with RA into existing CVD risk calculators, as well as identifying specific targets for risk factor management that both primary and secondary care can work towards co-operatively. Cardiovascular risk charts based on the Framingham risk algorithms do not include some CVD risk factors, such as family history, being of South Asian origin, or having RA (41). Further research is clearly needed here and it is pertinent that this was identified as a priority in this study.

Strengths of the present study are that it addresses a currently neglected clinical issue, and that it highlights preconceptions and presumptions which, when challenged and addressed, will impact directly on the quality of patient care. A broad range of people with relevant expertise were recruited from primary and secondary care and a robust qualitative analytical methodology was employed. The sample size was necessarily small but it conformed to the norms for IPA research

(21). In qualitative research, the sample is selected primarily to illuminate the phenomena of interest (42), and it is "not the amount of data but rather the richness of the data" which is important (43). Purposive sampling of participants who could provide detailed narratives allowed the generation of an in-depth analysis to enable the phenomena to be understood; simply selecting more participants would have diluted the interpretation of the phenomena (44). The participants recruited have been involved in the first combined rheumatology/cardiology clinic in the UK; hence their narratives offered the necessary excellent insight. The views expressed here reflect those of a specific group of healthcare professionals from one region of the UK rather than those of the worldwide community of relevant rheumatology and cardiology healthcare professionals. Generalization is a secondary concern with all qualitative research (42), although this does not mean that it is not possible to theoretically or conceptually generalize from such research (45). It is suggested that as long as the clinical problem is the same, then the theoretical findings will also probably apply, even in different settings (44) thus comparisons can be made between similar people in similar circumstances (46;47). It is more than likely that the emergent themes from the present interviews will have international resonance. Future studies, however, could involve healthcare professionals from other regions and also involve other members of the multidisciplinary team, such as physiotherapists and occupational therapists, to broaden knowledge of the wider team input.

In summary, this study has revealed that currently healthcare professionals may be less proactive in promoting CVD risk management strategies to patients with RA than to patients without RA. In terms of timing, there was some uncertainty as to when CVD risk strategies should be

incorporated into patient education programmes but the need to maintain close relationships with primary care was evident. These findings, complemented by an examination of RA patients' perspectives in our accompanying paper (18), can be directly translated into clinical practice by informing the design of novel health educational material. This material needs to address the CVD co-morbidity associated with RA, actively encourage necessary lifestyle modifications, support patients' self-efficacy to implement behaviour change and signpost patients to helpful resources. Ultimately, this should improve the quality and length of RA patients' lives.

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CHAPTER 5: "EXTRA INFORMATION A BIT FURTHER DOWN THE LINE": RHEUMATOID ARTHRITIS PATIENTS' PERCEPTIONS OF DEVELOPING EDUCATIONAL MATERIAL ABOUT THE CARDIOVASCULAR DISEASE RISK

Abstract

Objective: There are no patient education programmes addressing the increased risk of cardiovascular disease (CVD) associated with rheumatoid arthritis (RA). This is the second in a pair of studies exploring stakeholder perceptions of developing such educational material. Healthcare professionals' perceptions were explored in the first study; here we explore the perceptions of people with RA.

Methods: Semi-structured interviews were held individually with 18 people with RA, purposively sampled to include participants with no co-morbid history of CVD, those with CVD risk factors, and those who had experienced a CVD event. The interview transcripts were analysed using Interpretative Phenomenological Analysis.

Results: Four superordinate themes were identified: experiences of living with RA; reactions to learning about co-morbid CVD; implementing lifestyle changes; and expectations of education. Participants found being diagnosed with RA a devastating experience and were mostly unaware of their increased risk of CVD co-morbidity. They explained how information about CVD would be overwhelming and irrelevant at diagnosis, but they would have coped with "extra information a bit further down the line."

Conclusion: There is a need to develop educational material or programmes. Their design must consider factors which facilitate lifestyle change, such as motivation or receiving personalised

advice, and factors that inhibit change, such as depression or fatalism. Emphasizing the positive effects that some CVD lifestyle changes may have on RA symptom control may be particularly persuasive. Group education would be a popular format. These findings can be directly translated into clinical practice.

Introduction

This paper describes the second of a pair of studies addressing the important and pressing requirement to provide patient education designed specifically for people with rheumatoid arthritis (RA) that addresses their risk for co-morbid cardiovascular disease (CVD). CVD mainly accounts for the excess mortality in RA patients (1). New CVD screening programmes for patients with RA have been advocated recently (2;3) and patient education is an important corollary (4).

In the general population, controlled studies of CVD patient education programmes versus usual care have shown relative improvements in behaviours, risk factors and actual cardiac events in both primary (5;6) and secondary (7;8) prevention settings. The only published study of CVD patient education intervention in patients with RA was a small non-controlled trial where participants attended an additional nurse specialist clinic to identify and address CVD lifestyle factors; the intervention led to modest improvements (9). The authors acknowledged the challenge in trying to change these patients' behaviours. An approach to developing new educational material in this context takes as its starting point the involvement of the key stakeholders. In our accompanying paper we explore the perceptions of healthcare professionals

(10); the other stakeholder group is the patients themselves. Any educational intervention must address both patients' health needs and health beliefs (11;12).

Patients' needs may not be the same as those presumed by healthcare professionals (13-15). In addition, patients' beliefs about illness or disability, which are likely to underpin their behaviour, may not be congruent with a healthcare professionals' medical model of disease (11;16). Educational interventions that do not take account of any divergence of opinion may be less than optimally effective. The evidence also supports the involvement of patients in designing services and resources. Patient information leaflets developed by healthcare professionals in conjunction with consumers compared to those developed by healthcare professionals alone were judged more relevant, understandable and readable to patients (17). Patient involvement in service development highlighted their specific health needs and suggested strategies to address them (18;19). Certainly, the benefits of consumer involvement in the NHS has ensured that it is now a prominent feature of government health policy and its importance at all levels of the health service is widely recognized (20).

There has been a call for more qualitative research with patients in order to understand their health needs and to inform the development of educational material (21). A qualitative approach allows the researcher to explore the full breadth of patient experiences and may reveal concepts that were not predicted, but may be central to understanding the patient perspective (22). Group dynamics may constrain personal disclosure and discussion of the full breadth of an individual patient's experiences. Thus, individual interviews, which maintain confidentiality, were considered the most effective manner to explore patients' perceptions (23). The aim of this paper

is therefore to explore qualitatively RA patients' perceptions about developing novel educational material to address their associated CVD risk.

Methods

a) Participants

Eighteen participants with a diagnosis of RA were recruited. Purposive sampling was used to include participants from three groups; those with no co-morbid history of CVD or CVD risk factors, those with CVD risk factors, and those who have had a CVD event. Both men and women were recruited and the age range was deliberately broad (Table 1). All participants had to be able to read, understand and speak English. Patients with severe mental illness or terminal physical illness were excluded.

Table 1: Demographic details of the participants interviewed

Participant	Sex	Age	CVD co-morbidity or risk factors
HG	Female	45	-
EB	Female	56	-
MR	Male	70	-
AB	Male	33	-
KW	Female	31	-
AH	Male	51	-
MD	Male	67	Hypertension; Hypercholesterolaemia
SE	Male	62	Hypertension; Obesity
EC	Female	31	Obesity; Smoker
EL	Female	54	Diabetes; Hypercholesterolaemia; Obesity
MH	Female	67	Diabetes; Hypercholesterolaemia
FB	Male	67	Angina
MW	Male	59	Coronary artery bypass graft
TH	Male	66	Myocardial infarction
IP	Male	58	Angina
PH	Female	68	Angina; Coronary stents inserted
BC	Male	64	Myocardial infarction
PC	Female	72	Angina

b) Procedure

Ethical approval was obtained and written informed consent was gained from all participants. A semi-structured interview schedule was created by HJ and its content and probes were agreed by all authors (Table 2).

Table 2: Semi-structured interview schedule used in the individual patient interviews

Core open-ended questions	Relevant probes and prompts
Would you please introduce yourself describing where you live, how old you are and how long you have had rheumatoid arthritis?	
Could you tell me what you understand by the expression 'heart attack'?	
Could you tell me what you understand by the term 'stroke'?	
Have you any experience, either yourself or a friend or family member, of heart attacks or strokes?	
Have you heard about any link between rheumatoid arthritis and heart attacks and strokes?	
If I confirm that there is a link and that patients with RA are more likely to have heart attacks and strokes, would you like to ask me any questions?	
Is there any other information you would want to know?	• Why are these associated? • How much more likely is a patient with RA to have a heart attack or stroke? • What can be done to decrease this risk of a heart attack or stroke? • Is this due to the medications a patient with RA takes?
Would you want to try and decrease this chance of heart attacks and strokes?	• By making changes yourself? • Would you prefer the doctor to treat you with tablets?
Stopping smoking, controlling your weight, lowering your cholesterol and exercising are important things that help to decrease the likelihood of heart attacks and strokes. How easy would you find it to do these things?	
What do you think might it take to persuade or motivate you to start to do more of these healthy lifestyle activities?	• Understanding why or how doing these healthy activities actually makes a difference • Having an actual heart attack or stroke • Partner or close family member asking them to make healthy changes to their lifestyle • Partner or close family member doing it with them • Believing in themselves that they really can do it • Tried doing these healthy lifestyle changes previously and they felt better for it • Joining a group to help 'kick-start' a new healthy lifestyle

Many people know that stopping smoking, taking more exercise etc is good for their health, but they still don't do it. What reasons might stop you from taking more exercise or improving your diet for example?	• Not believing these things really makes a difference to their health • Doing it on their own • Would be hard to do because the rest of the family smoke, for example • Having close family who wouldn't support them • Have tried stopping smoking before but failed and don't think they can do it again • Too busy/ too stressed/ not a 'convenient' time to make these changes • Don't believe they have the inner strength to make these changes • Worried that there may be consequences of taking up a healthy lifestyle e.g., exercise may make their arthritis worse.
What things might help you maintain this healthier lifestyle?	• Ongoing support of family • A partner who does it with you and to whom you are accountable • Local support group • Facilities available to help e.g. with exercise
What facilities would you find most helpful to support you making these changes to a healthier lifestyle	• Written information • Internet resources • Opportunity to attend a talk about why you need to make these changes • Attending a small group session to discuss practical advice in how to make these changes • Availability of smoking cessation group/ nicotine replacement therapy • Having a 'buddy' scheme to support you with these changes • Availability of exercise facilities to use • Advice from their doctor and nurse to make these healthy lifestyle changes

The ethos and approach of the semi-structured interview has been described elsewhere (10). Initial interviewees were happy with the interview schedule and process and so the interview schedule was not amended following this patient-involvement. All interviews were conducted by one author (HJ); they were held in a private room in the hospital and lasted between 32 and 63 minutes each. The interviews were audio-recorded and the recordings transcribed verbatim by a sole professional typist.

c) Qualitative analysis

Interview transcripts were analysed using Interpretative Phenomenological Analysis (IPA) (24). The theoretical basis and practical application of IPA to generate superordinate themes has been described in our accompanying paper (10) and in detail elsewhere (25). Transcripts were initially analysed by HJ; GJT and EDH also read the transcripts to confirm the representativeness of the resultant themes. Interpretation was also confirmed with the participants individually by telephone; all participants were happy with our interpretation of their interview.

Results

Four superordinate themes were identified from the analysis: (i) experiences of living with RA; (ii) reactions to learning about co-morbid CVD; (iii) implementing lifestyle changes; (iv) expectations of education. Verbatim quotations illustrate these themes. Square brackets are employed, where necessary, to provide context for the quotes.

The theme highlighting experiences of living with RA includes patients' reactions to being diagnosed with RA. For most participants this was a devastating experience, for some because it represented the onset of ill-health whereas for others it was the disabling effects of RA that were so worrying:

> "… when you're younger, you think you're invincible... and you're never going to get ill, but then when you actually think it might happen to me…" (HG)

> "It felt as though my life was virtually ended. Everything I loved to do was stopped and then what have I got in life? What's life worth living for? I can't do anything…" (MH)

Controlling their joint pain, unsurprisingly, emerged as the most important consideration for participants and any lifestyle changes initiated were with the aim of controlling their RA symptoms:

> "I know it's [smoking] not good for the rheumatoid… so that's why I decided I wanted to cut down and that's what I have done." (EB)

For many participants, living with RA involved taking personal responsibility for their health:

> "Part of the rehabilitation of having rheumatoid arthritis, along with the brilliant drugs… is you've got to help yourself. " (AB)

This was often motivated by wanting to minimise the risk of further adverse functional health outcomes in the future and to allow them to fulfil future roles:

> "I don't want to be…incapacitated in any way when I'm older" (AB)
> "… my grandson… I want to be here to see him." (MW)

Conversely, other participants described taking much less personal responsibility for their health and had a more fatalistic outlook of the future:

> "Why shouldn't I enjoy it [smoking] now when potentially in 20 years I'm stuck in a wheelchair… and I don't really care if I have a heart attack and drop down dead."(EC)

The second theme concerned participants' awareness of co-morbid CVD. Essentially, the vast majority were unaware of the association between RA and CVD:

> "… rheumatoid to me, it's all in the bones… I didn't think that would have affected your heart." (BC)

This generated several questions from the patients. Firstly, why is RA associated with CVD?

> "Is it the arthritis or... the drugs?"(EC)

Exploring participants' beliefs about the aetiology of CVD revealed that some attributed CVD to powerful external factors, rather than their own lifestyle:

> "… if [the government] do a full survey on all the nitrates and phosphates and everything else that's thrown on the land in order to grow stuff, they'll find out that all them chemicals have a lot to do with heart attacks… But… that ain't never going to happen. So they come up with a theory that… smoking is a big contributor…" (TH)

Such views were in the minority, however, and most participants listed some of the classical risk factors when describing their understanding of a heart attack and stroke.

Patients were also interested in what could be done to address cardiovascular risk:

> "Is there anything you can do to prevent it? I'm very keen on prevention." (HG)

When would patients with RA feel most receptive to education about CVD? Patients with established RA felt, retrospectively, that discussing CVD risk at the same time as making a diagnosis of RA would not only have been overwhelming, but also irrelevant:

> "I'd have topped myself… Do they need to know all the information in one go?" (EB)

> "I'd have thought, yeah and? I think I've got bigger things to worry about at the moment." (EC)

Interestingly, patients felt that, given time to adapt to their diagnosis of RA, they would then feel ready and able to cope with information about co-morbid CVD:

> "Maybe when it's [RA] got controlled a bit more, so you stop having the tunnel vision of arthritis, arthritis, arthritis, my joints hurt, my joints hurt. Once it's controlled… I think I certainly would have been better able to deal with extra information a bit further down the line." (EC)

The theme that centred on implementing lifestyle changes describes both reasons why participants have, or have not, made behavioural changes already. They articulated a number of

factors to explain why they had changed their behaviour, including being proactive and taking the initiative, being personally motivated to make changes, being inspired by seeing the benefits of lifestyle modification, receiving personal advice and having an actual cardiac event:

> "I think with smoking I think it's got to come from within. It's no good just saying… we've got to give up smoking. It don't work like that, it never will work for a smoker. It's got to come from within here – you really want to give up." (TH)

> Researcher: "How easy did you find it to stop smoking?"
> MW: "Quite easy when somebody tells you it's a warning, you're going to have a heart attack if you don't stop smoking – I just stopped."

Conversely, some participants had felt unable so far to implement lifestyle changes. Reasons here included denial, depression, feeling self-conscious (about their weight or disability), lack of motivation or underestimating their cardiac risk:

> "I've thought about it [joining a gym] for months and months and I keep thinking I ought to really try and join… I think it's just the thought of starting… it's like the unknown and just sort of thinking, well, I'd really like to have a go but what would it be like?" (EL)

> "… if I had a serious heart attack, then I would probably change my ways a lot but touch wood, I haven't really had a serious one." (BC)

The final theme on expectations of education reflects what patients asked for, namely, common sense advice that addresses their uncertainties:

> "I don't know what sort of exercise to do. So like some sort of exercises which could help my heart but not hinder the rheumatoid arthritis. Because it's no good me doing the exercise to help my heart if it's going to make my arthritis worse because that's a vicious circle isn't it really?" (EL)

How healthcare professionals communicate information was considered important by all patients:

> "… a leaflet just sometimes poses questions that they can't often have answered. I think talks are the way forward… people begin to have more of an understanding and they're not alone really." (MH)

The idea of group education was popular, particularly because participants valued the opportunity to meet others with the same condition and to learn from their experiences:

> "…you feel so isolated - when you're on your own… but talking in a group and you suddenly realise there's other people in the same situation as you and you can talk things over… so in a group session I think it's far better." (PC)

Importantly, there was a plea from patients for staff to not only communicate information to them but also to listen to their concerns:

"…[healthcare professionals] don't really show any interest because they listen but they don't hear." (MR)

Such clear expectations of an education programme will guide the healthcare professional when developing novel patient education.

Discussion

This study offers rheumatology healthcare professionals a valuable insight into the perceptions that people with RA hold about developing a novel CVD education programme. Gaining a deeper understanding of a patients' personal experience of living with RA allows us to appreciate the context in which further decisions about their health will be made. The emotional impact of a diagnosis of RA has, similarly, been described in other studies (19;26). This study adds that potential improved control of their RA is the primary reason why patients have implemented behaviour change. Addressing patients' symptom control must be achieved before other health-related interventions, such as CVD risk education, could seem personally relevant; this is again reflected in the quotes relating to the timing of an educational intervention. Some lifestyle measures intrinsic to cardiovascular risk management, such as smoking cessation, also benefit management of RA (27). Such dual benefits were also identified by the healthcare professionals (10). These patient interviews suggest that emphasizing the positive effects such lifestyle measures may have on the management of RA may be more persuasive.

Patients with RA appear to be unaware of their risk of CVD co-morbidity. This most likely reflects the lack of current patient education (4). Poor levels of awareness of CVD co-morbidity have also been found in other at-risk patient groups, such as people with diabetes (28). Leventhal's Common-Sense Model suggests that how a person will react and cope when confronted with an(other) illness will depend on their beliefs or cognitions about that illness (informed by considering the identity/label, the perceived cause, the time-line, the consequences and the curability/controllability of the illness) as well as their emotional response (29). The model then proposes that an individual will develop coping strategies, either 'approach coping' techniques such as taking necessary medication or making relevant behavioural changes, or 'avoidance coping' techniques, such as denial (29). In this study, participants did describe being able to take on board the realisation they were at added risk of CVD provided they were informed about CVD at an appropriate time. The role of healthcare professionals is to then encourage the adoption of helpful 'approach coping' techniques.

Given the lack of awareness, it was not surprising to discover that few patients appear to have a good knowledge about CVD, with some participants describing quite complex, but incorrect, aetiological models of disease (30). Lack of relevant knowledge has been documented not only in patients undergoing primary prevention (31) but also secondary prevention of CVD (32). Additionally, it is not uncommon to uncover patients' health beliefs incongruent with those of healthcare professionals; such health beliefs may be formed from a wide variety of sources (including political or economic factors or the wider natural or man-made environment) and link ill-health to surrounding circumstances to generate personal theories of disease causation or 'lay epidemiology' (33). The implication, however, of misconceptions about CVD is that they will

inform illness cognitions which may then afford a rationale for poor motivation to make long-term lifestyle changes. An example is regarding myocardial infarction as an acute event, rather than as a symptom of chronic atherosclerotic disease (34). Conversely, improving knowledge and understanding about the aetiology of CVD, by exposing patients to educational material, should theoretically provide the framework for patients to understand why specific lifestyle changes or pharmacological interventions are required (32;34). In practice, however, knowledge alone does not always result in behaviour change (35;36). Other social cognitive factors need to be invoked to explain why behaviour change is, or is not, implemented. An individuals attitude to a behaviour, social norms and their self-efficacy for that behaviour, are examples of such factors proposed by the Theory of Planned Behaviour (37). Many of the quotes from this patient-focused study illustrate the importance of these factors and are worthy of further discussion to help inform a CVD risk education programme.

Patients' inaccurate perception of risk may act as a barrier to implementing behaviour change. Understanding the concept of 10 year cardiac risk is difficult and, instead, patients tend to base their risk perception on emotions related to experiences of friends or family (31). This may explain why many patients perceive their own CVD risk inaccurately. Research has shown the majority of RA patients were incorrectly optimistic about their risk, and this could limit their motivation for behavioural change (38). Although communicating risk is identified as a challenging task for healthcare professionals (39), effective risk communication will need to be an integral component of a CVD education programme for people with RA.

Depression may have a moderating effect on the impact of self-management training on patients' self-efficacy (40), which in turn may affect their intentions to implement behaviour change. Unfortunately, patients with RA and co-morbid CVD show higher depression scores than RA patients without CVD (41), perhaps mediated through venting of emotions (42). Thus, an important part of any educational programme addressing CVD risk in patients with RA should include the opportunity to screen for depression, and to refer for appropriate treatment where detected (43).

A striking finding from this study was the variation in levels of personal responsibility that different individuals held. Whereas some participants felt personally responsible for their health and were enthusiastic to engage in disease prevention, other participants took a more fatalistic view. This is not uncommon (36). Lay epidemiology includes personal theories whereby ill health is thought to be due to either luck or fate, factors beyond a persons control, or is unavoidable because of previous experiences, which could make personal behaviour change seem irrelevant (31;34;36). Addressing such lay beliefs must, therefore, be a pre-requisite imperative; tailored patient education could achieve this.

Lay beliefs may further affect behaviour through patients' conception of 'coronary candidacy'. Coronary candidacy describes the lay perception of 'the type of person who gets heart trouble' (44). Such a perception will be informed by society, the media or anecdotal experiences of friends and family and may have a very powerful effect in terms of informing social norms and motivating people to implement behaviour change. If a person does not believe that they fit the

description of a coronary candidate, even in the presence of several risk factors for CVD, they may not be motivated to make behavioural changes.

Encouragingly, the participants were able to identify several factors that had facilitated appropriate behaviour changes. Participant TH described stopping smoking having finally made a personal commitment to change, analogous to the preparation and action stages of the Transtheoretical Model of behaviour change (45). For participant MW, simply receiving personal advice from a healthcare professional about the consequences of smoking was enough to make him stop smoking. This is contrary to healthcare professionals' perceptions that people with RA would not consider CVD a priority or would find it harder to implement lifestyle changes (10). This should serve to remind healthcare professionals that their perceptions may be inaccurate and that they may underestimate the power and influence of their own advice to patients.

Participants who had achieved behavioural change frequently referred to personal motivation, being proactive or taking the initiative as being key. How does such motivation translate into action? And what can we learn to help motivate others? 'Wellness motivation' conceptions of the self are thought to be particularly important (46). A study into the role of self knowledge and the modification of cardiovascular risk suggested the following useful framework to consider in future cognitive behavioural programmes: representing the issue (how do I desire myself to be? how would friends and family want me to be? what am I afraid of becoming?), evaluating the issue (creating short and long term goals and expectations for behavioural outcomes, gauging my

personal efficacy) and implementing behavioural action (creating behavioural strategies, negotiating the social context and creating self monitoring strategies) (46).

These interviews generated a rich account of the factors that either motivated patients to undertake or inhibited them from undertaking lifestyle modification. In contrast, healthcare professionals articulated far fewer reasons why patients may, or may not, modify their lifestyle (10). This suggests that we, as healthcare professionals, have a lot to learn from patients, and the effectiveness of future education programmes may be less than optimal unless patients are truly 'heard' as well as 'listened' to.

With regard to the practicalities of designing a novel education programme, the timing of intervention appears to be critical. There was uncertainty among healthcare professionals (10), a finding that has also been reported in designing lifestyle programmes for cancer survivors (47). On the other hand, patients were clear that optimal time for CVD risk intervention was once they had learned to cope with their RA diagnosis. The form that such novel patient education should take was suggested by most participants to be small group work, with a small minority (often those in full-time employment) requesting internet or written material. This is consistent with previous research (48). The value that patients placed on learning from each other would also support a group intervention. A group approach is integral to the ethos of the Arthritis Self-Management Programme (49) and, indeed, was a key feature appreciated by patients when the Chronic Disease Self Management programme was qualitatively investigated (50).

In summary, the present study revealed a lack of awareness of increased CVD risk among patients with RA. This reinforces the need to develop appropriate educational material and programmes to bring about relevant lifestyle modifications, which must be designed following careful consideration of the multitude of pertinent factors discussed above. This study complements, and is complemented by, our accompanying paper addressing healthcare professionals' perceptions (10). Involving all stakeholders in a detailed examination of educational needs at the outset will result in the development of optimally effective patient education material.

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CHAPTER 6: DEVELOPMENT AND INITIAL VALIDATION OF A HEART DISEASE KNOWLEDGE QUESTIONNAIRE FOR PEOPLE WITH RHEUMATOID ARTHRITIS

Abstract

Objective: To develop and validate two parallel versions of the Heart Disease Fact Questionnaire-Rheumatoid Arthritis (HDFQ-RA), a modified and RA-specific version of the HDFQ.

Methods: The questionnaire was composed of generic questions from the original HDFQ with additional RA-specific questions added. Cognitive interviewing was performed and the questionnaire piloted to generate two parallel questionnaires. For psychometric validation, 130 patients with RA completed the questionnaires at baseline and two weeks later.

Results: Parallel form reliability of both questionnaires was established; the median score for both questionnaires was 9/13 with no statistical difference in scores. Kuder-Richardson-20 formula was 0.65 and 0.67 for both questionnaires. Test-retest stability showed constant median scores of 9/13 and no statistical difference in scores between baseline and follow-up. Known groups comparison revealed that patients who had self-educated themselves about heart disease, or who were taking CVD medications, had significantly higher scores on the questionnaires.

Conclusion: The two parallel forms of the HDFQ-RA have been shown to be equivalent measures of CVD knowledge and evidence supporting their reliability and validity is presented. The HDFQ-RA is an appropriate tool for application in clinical and research settings, e.g.,

assessing novel educational interventions or tracking participants' progress on an education course.

Introduction

The most common cause of mortality in the western world is cardiovascular disease (CVD), and its prevention and management is a national health priority (1;2). Identification and intensive management of risk factors for CVD is important, particularly in high risk groups of people such as those with diabetes mellitus. People with rheumatoid arthritis (RA) are also at increased risk of CVD (3), thought to be due to both clustering of traditional risk factors as well as novel risk factors such as inflammation (4;5). Traditional risk factors may be affected by both the disease itself and/or its treatments, for example, dyslipidaemia may relate to uncontrolled systemic inflammation (5), or hypertension may relate to ongoing use of non-steroidal anti-inflammatory drugs (6) or coxibs (7). The screening for CVD and its management (both relevant lifestyle changes and necessary pharmacological treatment) is therefore an important component of long term care of all patients with RA (5;8;9). Underpinning such a CVD screening programme must be patient education; improving patients' knowledge is fundamental to all treatment programmes (10) and is often a pre-requisite for initiating desired behaviour changes (11).

Before implementing patient education programmes it is prudent to show their efficacy (12); the availability of a relevant valid knowledge questionnaire is an essential tool to evaluate a novel educational intervention. In addition, such a questionnaire would also be useful in clinical practice to identify both patients who know little about CVD in general as well as to help tailor

educational opportunities to meet a patient's specific needs within this vast field of knowledge (13).

Validated knowledge questionnaires exist for use among patients with RA, but these are concerned with general knowledge about RA, signs and symptoms, as well as pharmacological management of joint pain and self-management techniques (14-17). Use of these questionnaires has revealed a lack of knowledge among patients with RA, particularly about the aetiology of RA and its drug treatment (14), and that patient knowledge increases following a group educational intervention (15;17). Currently available questionnaires, however, do not include questions about the CVD comorbidity associated with RA. There is therefore a pressing need to construct a psychometrically sound questionnaire to measure heart disease knowledge in patients with RA, both to evaluate necessary cardiovascular patient education programmes and to identify patients' particularly requiring education.

Existing patient knowledge questionnaires about CVD and its risk factors have been validated in male patients with diagnosed coronary heart disease (18) as well as in high risk patients with diabetes (13). This latter psychometrically validated questionnaire, the Heart Disease Fact Questionnaire (HDFQ), has 25 items; 15 questions concern the well-established risk factors of family history, age, gender, smoking, physical activity, lipids, blood pressure, weight and whether a person necessarily knows if heart disease is present; a further 10 questions address diabetes-related coronary heart disease risk factors. The HDFQ employs closed questions with a dichotomous response format, supplemented by an 'I don't know' option. Dichotomous answers are suitable for factual questions, whereas scaled response formats may be less so (15).

Questions are worded to try to minimize acquiescence, which is appropriate (19). Validation studies of the HDFQ showed a spectrum of item difficulty scores; it is important to have a balance and broad range of item-difficulty scores (17). The HDFQ demonstrated adequate internal consistency, good content and face validity and criterion related validity in a sample of people with diabetes, and has been recommended for both clinical and research applications (13). Indeed, use of this questionnaire has not only highlighted groups of patients in greatest need of patient education but also identified timely opportunities where further education is required (20). This excellent patient knowledge questionnaire is therefore a very valuable resource but it is specific to patients with diabetes. Patients with RA require disease-specific education to also address additional issues as exercise despite joint pain, (where they may have previously received conflicting advice (21)), the novel role of systemic inflammation as a risk factor for CVD, and the complex adverse effects on the vasculature of some medication used in RA such as non-steroidal anti-inflammatory drugs or steroid medication. It is therefore appropriate to modify the HDFQ to develop a RA-specific version, the Heart Disease Fact Questionnaire – Rheumatoid Arthritis (HDFQ-RA). This will require re-validation among patients with RA. Validation of the HDFQ did not include measuring test-retest reliability in a large sample and the authors propose this should be performed in the future (13). To use a questionnaire as a tool to evaluate an educational intervention requires its stability over time (in the absence of intervention) to be shown (19). Moreover, repeat administration of the same questionnaire may result in a respondent only 'learning' the answers to the questionnaire during the intervention in an artefactual nature. It would therefore be optimal to develop parallel forms of the questionnaire (HDFQ-RA-1 and HDFQ-RA-2) to be used in a pre- and post-intervention fashion (17;22); these

must show parallel form reliability and both must be validated and shown to be stable over time in the absence of intervention.

The purpose of this study was to develop and validate two parallel versions of the HDFQ-RA questionnaire which can be used clinically and in a research setting to measure knowledge of heart disease in patients with RA.

Methods

The present study used a multi-stage questionnaire development and validation process for which local research ethics committee approval was given.

a) Questionnaire design

The initial questions collected demographic data on the respondents, including sex, age, marital status, highest level of educational qualification, ethnicity and job/role. Self-reported diagnoses of CVD and CVD risk factors, medication and attendance at different health education opportunities were also requested.

Two domains of questions were generated; generic risk factors for CVD and risk factors for CVD specific to patients with RA. Questions in the first domain were the initial 15 questions from the original HDFQ, including the transfer of the question on diabetes as a risk factor for CVD, which was originally in the diabetes-specific subscale. Subsequent diabetes-specific questions in the HDFQ were not retained. Nine questions in the second domain addressing CVD risk factors for a

person with RA were generated on the basis of face validity following group discussion amongst the authors (HJ, GJT, EDH). A focus group of 5 consultant rheumatologists was next convened to discuss the questionnaire for content validity. The panel felt the questions addressed the full spectrum of CVD risk factors for a patient with RA, both novel risk factors and traditional risk factors that may be adversely modified by systemic inflammation or the medications use to treat RA. The panel did, however, suggest amending the language of the generic CVD risk factor questions into more lay language by changing "…you are at risk for developing heart disease…" to "…you are more likely to develop heart disease…" Additionally, the language used in the questions collecting demographic data was simplified and any medical jargon minimized.

This version of the questionnaire was then used for individual cognitive interviewing ('think-aloud' interviewing). This technique allows the interviewer to gain an understanding of how a participant perceives and interprets the questions and so is a valuable method of pre-testing a questionnaire (23). Four patients with RA (two men and two women) gave informed consent for an audio-recorded individual cognitive interview, all of which lasted around 1 hour. The participants both 'read aloud' the questions and 'thought aloud' their response. Appropriate probing by the interviewer (HJ) was used to clarify any hesitancies in answering a question as well as identifying any ambiguities or omissions with the wording or problems with the layout of the questionnaire. These interviews were used to identify questions that worked well (24) and a list of recommendations to improve the questionnaire was compiled and implemented (Table 1).

Table 1: Amendments to HDFQ-RA 1 and 2 following patient interviews

	Clarifications	Simplifications	Additions	Formatting
Amendments to demographic questions	'Divorced' clarified to mean 'Divorced/Separated'	'Caucasian' changed to 'White'	'Other' added as an option to question about level of qualifications obtained	Font size increased
	Clarified that the questionnaire wanted to know whether certain medications were taken, *both* prescribed by their GP or over the counter	Statins described as 'cholesterol lowering tablets'	Instructions added for respondent to tick the boxes as appropriate	Spacing between rows increased
	'Employed' changed to 'Work' (so to include the self employed)		Added a question 'Has anyone close to you, such as a relative or friend, ever had heart disease?'	Tick boxes aligned
	Educational opportunities explained more clearly			
Amendments to HDFQ-RA-1 and 2		'Undesirable' used instead of 'unfavourable' in HDFQ-RA-2	'Confidential' added to the title	
			Examples of anti-inflammatory medications added to the relevant question in HDFQ-RA-1	

This modified 24-item questionnaire was then piloted on 50 consecutive patients with RA attending an outpatient clinic. Data analysis was performed using SPSS for windows version 13.0. Each response to each question was coded as correct or incorrect ('I don't know' was coded as incorrect in reflection of the individual not knowing the correct answer). The responses of one respondent gave an overall score more than three standard deviations away from the mean; this respondent was treated as an outlier and their answers removed from analyses. Two further questions were added after this initial pilot; one question on generic risk factors for CVD and one question on RA-specific risk factors for CVD (see Table 3). Within each of the two domains of questions, responses to items were compared (using percentage of respondents to score the

correct answer) to identify concordant pairs of questions, with similar levels of difficulty for the parallel forms of the HDFQ-RA. Two parallel questionnaires were then developed by splitting the paired questions into two sets of questions, ensuring the question pairs were divided to ensure a sensible balance in question content between the two questionnaires; HDFQ-RA-1 and HDFQ-RA-2. Thus each questionnaire comprised 13 questions; eight questions from the original HDFQ on generic risk factors for CVD and five on CVD risk factors specific to a patient with RA.

b) Psychometric validation of HDFQ-RA-1 and HDFQ-RA-2 questionnaires

i) Participants

Participants were recruited from a secondary care setting in a single rheumatology department. The inclusion criteria were a diagnosis of RA, being able to read and write English and consenting to complete two questionnaires 2 weeks apart.

ii) Procedure

Participants were consecutively recruited and each assigned a participant identification number for this study; the first group of participants completed the demographic questions, then HDFQ-RA-1 and then finally HDFQ-RA-2. A second group of participants completed the demographic questions, followed by HDFQ-RA-2 and then finally HDFQ-RA-1. All participants were unaided in the completion of the questionnaires. Two weeks after completing the questions for the first time each participant was posted out the same questionnaires, but in the alternate order, i.e. a participant from the first group completed HDFQ-RA-2 then HDFQ-RA-1 in their second questionnaire pack and vice versa. The questionnaires were returned in stamped addressed envelopes enclosed. Repeat mailings were used to improve the response rate, until each group comprised 65 respondents with complete test/retest questionnaire results (130 respondents in

total); 100 has been suggested as a minimum sample size to validate a test (22) although others have advocated at least five participants are required per question being validated (25). Data collection was conducted by one of the authors (HJ). The questionnaires were produced in a scannable format using 'Snap' software; scanned results were entered into Microsoft Excel and transferred into SPSS for Windows version 13.0 for statistical analysis.

iii) Statistical analysis

The demographic data of the participants in the two groups were compared using two sample t-tests for differences in means (or Mann-Whitney U tests for differences in medians) and chi-squared tests or Fisher's exact test for differences in proportions.

The item ease scores for each question were calculated, that is, the percentage of participants who correctly answered that question, both for the pilot sample of people with RA, and the larger group of participants whose results were used for the psychometric validation (at baseline and at two-week follow-up). A factor analysis of all 26 questions was carried out separately at the two time-points.

Parallel form reliability was assessed by comparing descriptive statistics relating to HDFQ-RA-1 and HDFQ-RA-2 (22), using Wilcoxon signed ranks tests to calculate the significance of the difference in the scores for each individual at one point in time, and using Spearman's correlation to compare each individual's scores on HDFQ-RA-1 with HDFQ-RA-2. Internal consistency of the HDFQ-RA-1 and HDFQ-RA-2 (for the total scores of each questionnaire as well as separate domain scores at both baseline and follow-up) were tested using the Kuder-Richardson Formula 20 for dichotomously scored questions (26). The test-retest stability for the

HDFQ-RA-1 and HDFQ-RA-2 was measured by comparing descriptive statistics for each form of the questionnaire when repeated two weeks later to the baseline descriptive statistics. Also, Wilcoxon signed ranks test was used to calculate the significance of the difference in the scores at test and retest and Spearman's correlation was used to compare test and retest scores. Validity of the HDFQ-RA-1 and HDFQ-RA-2 was assessed in several ways. As described above, face and content validity were subjectively established in the process of developing and revising items. In addition, we conducted a known-groups analysis, using Mann-Whitney U tests, to examine discriminant validity; specifically by comparing scores among people who had self-educated themselves by reading about CVD to those who had not, as well as people who self-reported taking CVD medication versus those who did not. We hypothesised that patients who had received some form of CVD education or whom were taking medications for CVD or CVD risk factors would have more knowledge about CVD than those without those characteristics. There are currently no other measures of the same concept available for us to test convergent validity of the HDFQ-RA.

Results

In order to have 130 participants in total with complete test/retest results, 151 participants were approached; all accepted to take part but 21 participants did not return the second questionnaire and so were excluded from analysis

a) *Demographic characteristics of respondents*

The demographic details of the two groups of patients with RA who completed both questionnaires are listed in Table 2. Overall, 78% of respondents were female and the mean age was 64 years. This is representative of a typical sample of people with RA, which is three times more prevalent among women and shows greater incidence and prevalence among older adults (27). No formal qualifications were held by 60% of respondents. The mean duration of RA was 16 years; in addition, 15% of the participants reported a previous CVD event and 42%, although they had not had a CVD event, reported risk factors for CVD. The two groups of respondents were matched for all demographic variables.

b) The questionnaires

The two questionnaires (HDFQ-RA-1 and HDFQ-RA-2), each composed of 13 questions, are in Table 3. The item ease score is given for each question as are factor loadings of the individual questions. Factor analysis showed the questions generally load onto factors representing generic knowledge of CVD and RA-specific CVD risk knowledge, as predicted. This factor analysis produces a fairly good fit, although a few questions did not load as expected; in particular, two RA-specific CVD questions from HDFQ-RA-1 (10 and 11) had consistently stronger loadings on the same factor that most of the generic knowledge questions also load most strongly on.

Table 2: Demographic features of respondents to questionnaire (N = 130)

Demographic factor	Group 1 n = 65	Group 2 n = 65	p
Age, years (mean ±sd)	64.45 ± 11.3	63.3 ± 11.2	0.564
Sex; number of females	52	50	0.67
Marital status			0.614
Married:	38	43	
Living with a partner:	4	3	
Single:	3	5	
Divorced/separated:	7	3	
Widow(er):	13	11	
Highest qualification attained			0.454
No qualifications:	35	43	
School qualifications gained at age 16:	9	8	
School qualifications gained at age 18:	10	6	
University degree:	1	2	
Other:	8	3	
Blank:	2	3	
Ethnicity; number Caucasian	64	64	1.0
Self-reported co-morbid CVD			0.532
CVD event:	12	8	
Risk factors alone for CVD:	27	27	
None:	24	29	
Blank:	2	1	
Duration of RA, years (median ± IQ range)	14.5 (5.25 – 24.75)	13.5 (4.0 – 23.0)	0.665
Smoking status			0.733
Current smoker:	12	11	
Ex smoker:	24	27	
Never smoked:	29	24	
Blank:	0	3	
Self reported medications taken†			
For CVD or risk factors:	36	34	0.412
Non steroidal anti-inflammatories:	31	23	0.228
Steroids:	25	18	0.401
Attendance at the following educational opportunities			
Heart clinic at GP:	6	3	0.492
Well man / well woman clinic at GP:	8	17	0.045*
Hospital cardiology appointment:	11	17	0.201
Combined rheumatology/cardiology clinic:	9	8	0.795
Rheumatology nurse:	48	48	1.0
Cardiac rehabilitation:	2	3	1.0
Expert Patient Programme:	1	0	1.0
Events about heart disease in the community:	1	0	1.0
Read articles/leaflets about heart disease:	15	16	0.837
Looked up information on heart disease on the internet:	2	3	1.0

IQ range = interquartile range

*indicates $p<0.05$

† patients were asked to self-report if they specifically took “aspirin, cholesterol lowering tablets, blood pressure tablets, tablets or insulin for diabetes, anti-inflammatories, such as ibuprofen or diclofenac, or steroids ie prednisolone”. We classified aspirin, cholesterol lowering tablets, blood pressure tablets and diabetes medication into ‘medications for CVD or its risk factors’.

Table 3: The HDFQ-RA-1 and HDFQ-RA-2 questionnaires with their question ease scores and factor loadings.

Form	Risk focus	Question	Item ease (% getting it correct)			Factor loadings[1] for N = 130			
			N = 49	N = 130		Baseline		2 week follow-up	
			Pilot	Baseline	2 week follow-up	Factor 1	Factor 2	Factor 1	Factor 2
HDFQ-RA-1	General	1.1: A person always knows when they have heart disease	75.5	73.8	86.9	**0.31**	**-0.33**	0.07	0.00
	General	1.2: A person who smokes is more likely to develop heart disease	--[2]	86.9	93.1	**0.71**	0.04	**0.58**	-0.06
	General	1.3: Keeping blood pressure under control will reduce a person's chance of developing heart disease	89.8	89.2	91.5	**0.36**	**0.29**	**0.38**	**0.22**
	General	1.4: A person with high cholesterol is more likely to develop heart disease	87.8	90.8	83.1	**0.69**	**0.22**	**0.71**	0.18
	General	1.5: If your 'good' cholesterol (HDL) is high you are more likely to develop heart disease	51.0	33.1	38.5	**0.29**	-0.03	**0.37**	0.18
	General	1.6: Only exercising in a gym or in an exercise class will lower a person's chance of developing heart disease	81.6	80.8	86.9	**0.41**	0.08	**0.35**	0.06
	General	1.7: Eating fatty foods does not affect blood cholesterol levels	81.6	82.3	84.6	**0.46**	-0.13	**0.52**	0.16
	General	1.8: A person with diabetes is more likely to develop heart disease	61.2	45.4	47.7	**0.22**	**0.43**	0.04	**0.60**
	RA-specific	1.9: A person with rheumatoid arthritis can reduce their chance of heart disease by keeping their weight under control	87.8	89.2	86.9	0.13	**0.28**	**0.47**	0.09
	RA-specific	1.10: A person with rheumatoid arthritis can reduce their chance of heart disease by stopping smoking	95.9	90.8	93.8	**0.66**	0.20	**0.49**	0.11
	RA-specific	1.11: People with rheumatoid arthritis should not exercise because it can damage their joints	83.7	84.6	87.7	**0.32**	-0.06	**0.25**	-0.02
	RA-specific	1.12: Anti-inflammatory medications, such as diclofenac or ibuprofen, taken by patients with rheumatoid arthritis may increase the chance of heart disease	12.2	12.3	13.8	-0.01	**0.48**	0.08	**0.52**
	RA-specific	1.13: Having lots of inflammation ('flares') of rheumatoid arthritis adds to the increased chance of heart disease	18.4	23.1	22.3	0.03	**0.63**	0.11	**0.68**

Continued over

Table 3 continued

Form	Risk focus	Question	Item ease (% getting it correct)			Factor loadings[1] for N = 130			
			N = 49	N = 130		Baseline		2 week follow-up	
			Pilot	Baseline	2 week follow-up	Factor 1	Factor 2	Factor 1	Factor 2
HDFQ-RA-2	General	2.1: If you have a family history of heart disease, you are more likely to develop heart disease	75.5	71.5	80.8	**0.49**	0.15	0.13	**0.27**
	General	2.2: Regular exercise will lower a person's chance of getting heart disease	91.8	90.8	92.3	**0.42**	0.01	**0.40**	-0.03
	General	2.3: A person who stops smoking will lower their chance of developing heart disease	83.7	93.1	96.2	**0.73**	0.04	**0.57**	-0.12
	General	2.4: A person with high blood pressure is more likely to develop heart disease	75.5	86.9	89.2	**0.64**	0.20	**0.71**	0.20
	General	2.5: If your 'bad' cholesterol (LDL) is high you are more likely to develop heart disease	65.3	80.8	75.4	**0.38**	**0.40**	**0.50**	**0.22**
	General	2.6: Being overweight increases a person's chance of developing heart disease	98.0	95.4	96.9	**0.25**	0.12	0.09	0.09
	General	2.7: The older a person is, the more likely they are to develop heart disease	44.9	33.8	40.8	0.04	**0.53**	**0.24**	**0.31**
	General	2.8: Walking and gardening are considered exercise that will help lower a person's chance of developing heart disease	87.8	86.9	90.0	**0.24**	**0.24**	0.19	-0.07
	RA-specific	2.9: Patients with rheumatoid arthritis are more likely to develop heart disease	32.7	30.8	36.2	0.04	**0.59**	0.08	**0.66**
	RA-specific	2.10: Rheumatoid arthritis affects the balance of 'good' and 'bad' cholesterol in the blood in an undesirable way	14.3	16.2	12.3	**-0.23**	**0.60**	-0.05	**0.57**
	RA-specific	2.11: Long term or high dose steroids taken by a person with rheumatoid arthritis may cause diabetes	--[2]	26.2	27.7	-0.02	**0.36**	-0.23	**0.57**
	RA-specific	2.12: A person with rheumatoid arthritis can reduce their chance of heart disease by keeping their cholesterol under control	77.6	82.3	86.9	**0.22**	**0.44**	**0.50**	**0.21**
	RA-specific	2.13: A person with rheumatoid arthritis can reduce their chance of heart disease by keeping their blood pressure under control	77.6	84.6	90.0	**0.40**	**0.43**	**0.54**	0.17
Proportion of the variance explained						16.0%	11.6%	15.4%	10.4%

[1] Principal components extraction of two factors with varimax rotation across all 26 questions; loadings in bold are > 0.20.

[2] Question added after pilot phase.

c) Psychometric validation of the questionnaires

Parallel form reliability was established: For HDFQ-RA-1, the median score was 9 (interquartile range 8 – 10). For HDFQ-RA-2, the median score was also 9 (interquartile range 7 – 10). Wilcoxon signed ranks test confirmed that there were no significant differences in scores between parallel forms ($z = -0.313$, $p = 0.754$). Spearman's correlation between scores to HDFQ-RA-1 and HDFQ-RA-2 showed $r = 0.50$.

The internal consistency of the parallel questionnaires was adequate with a Kuder-Richardson-20 formula of 0.65 for HDFQ-RA-1 and 0.67 for HDFQ-RA-2 (between 0.5 and 0.7 is considered the minimum acceptable level for internal consistency (19)) (Table 4).

Table 4: Internal consistency results (with 95% confidence intervals) of the two versions of the HDFQ-RA, including subscales, at baseline and follow up (N = 130).

Questionnaire	Questions	Number of questions	Baseline questionnaire internal consistency (and 95% confidence interval)	Two-week follow up questionnaire internal consistency (and 95% confidence interval)
HDFQ-RA-1	All questions	13	0.65 (0.56 – 0.73)	0.66 (0.57 – 0.74)
	Generic CVD questions	8	0.61 (0.50 – 0.70)	0.57 (0.45 – 0.67)
	RA-specific CVD questions	5	0.34 (0.14 – 0.50)	0.37 (0.18 – 0.53)
HDFQ-RA-2	All questions	13	0.67 (0.58 – 0.75)	0.58 (0.46 – 0.68)
	Generic CVD questions	8	0.63 (0.52 - 0.72)	0.44 (0.28 – 0.57)
	RA-specific CVD questions	5	0.51 (0.36 – 0.63)	0.41 (0.24 – 0.56)

In terms of test-retest, the median scores remained constant at 9 (HDFQ-RA-1 interquartile range 8 – 11; HDFQ-RA-2 interquartile range 8 – 10). In addition, Wilcoxon signed ranks test confirmed that there were no significant differences in scores between baseline and two weeks later (HDFQ-RA-1; z=-1.78, p=0.08: HDFQ-RA-2; z=-1.74, p=0.08). Spearman's correlation for test-retest showed r = 0.54 for HDFQ-RA-1 and r = 0.41 for HDFQ-RA-2.

The parallel forms of the questionnaire demonstrated face and content validity in expert and patient investigations. The investigators and patients involved in cognitive interviewing agreed the questionnaire was well presented and the questions were relevant and clear. The content was appropriate and addressed the full scope of the domains being tested. Known groups comparison revealed that patients who had specifically received education about CVD (by virtue of reporting self-educating themselves by reading about CVD, both leaflets and on the internet, or attending community events on CVD) or who self-reported taking medication for CVD or CVD risk factors had statistically significantly higher scores in both questionnaires (Table 5). There was no relationship between scores on both HDFQ-RA questionnaires and level of qualifications obtained, reflective of years in formal education.

Table 5: Discriminant validity of the HDFQ-RA-1 and HDFQ-RA-2; participants who had self-educated themselves, or who took medications for CVD or CVD risk factors scored higher on both questionnaires.

Groups		HDFQ-RA-1			HDFQ-RA-2		
		Median score	U value	p value	Median score	U value	p value
Self educated about heart disease	Yes n=32	9.5	1215.0	0.05	10	1117.0	0.01
	No n=98	9			9		
Taking medications for CVD or CVD risk factor	Yes n=70	9.5	1302.0	0.03	9	1312.5	0.04
	No n=48	9			8		

Discussion

The HDFQ-RA was developed in response to the clinical need to address the CVD risk associated with RA. It is based on a well validated pre-existing questionnaire addressing the same issue in diabetic patients. The present questionnaire will have applications in both clinical and research settings; the two parallel versions are appropriate to be used in a before-after fashion when assessing either a novel educational intervention or a participants' progress on a patient education course. Both parallel questionnaires have been shown to be an equivalent measure of CVD knowledge, and evidence supporting the reliability and validity of the scales has been shown in this sample.

Psychometric validation was performed in a suitably large sample of patients with RA following appropriate cognitive interviewing to address its readability and acceptability. The reliability of a

questionnaire is related to the variability between items and the length of the questionnaire (22). This questionnaire was designed to test knowledge about several issues, both classical risk factors for CVD as well as novel risk factors, and yet remain brief and convenient to use in practice. The factor analyses revealed that the questions do indeed generally load onto these two factors, although some apparently RA-specific elements of knowledge (focusing on applied generic issues, such as exercise being important for managing CVD risk among people with RA) may relate more closely to other elements of generic CVD knowledge. The internal consistency was satisfactory, and certainly better than an existing RA patient knowledge questionnaire (15). Increasing the length of the questionnaire, i.e. using all 26 questions, rather than two parallel questionnaires, yielded an internal consistency of 0.78 at baseline, identical to the original HDFQ (13). However, there is a finite set of established CVD risk factors to write questions about and we did not want to expand the questionnaire with essentially repeated questions; indeed the two parallel shorter versions are more suitable for cross-over application to avoid artefactual learning. Based on the present study these two questionnaires should be used as described, not broken down into their two domains of questions as the internal consistency results of the individual domains of questions on each version of the questionnaires was sometimes less than adequate. Overall, one would not expect perfect factor structure or internal consistency for such factual knowledge questions because people will tend to only know certain facts (rather than knowing absolutely all or none of them), and the aim is to get a reasonable assessment of a complex aspect of patient knowledge. Moreover, it is important to have a sensible balance of questions between the two questionnaires, which we achieved during the questionnaire design process, rather than react to the factor loadings and produce unbalanced questionnaires. Similarly, during the development of the original HDFQ, the authors acknowledged they were seeking to measure

knowledge of a factorially complex set of items and so expected considerable variability between items and a lower internal consistency; they too declined to increase the number of items in their questionnaire (which would produce a more homogenous test) in order to keep the questionnaire user-friendly (13).

Reproducibility was not included in the validation of the original HDFQ (13). Test-retest stability with both the HDFQ-RA questionnaires was good with the median scores staying constant. Again, there are factors which may affect test-retest stability; physical or emotional problems may lower test-retest reliability (22). Our participants were recruited when attending a hospital appointment which may be relevant, but despite this the test-retest stability was maintained. The spectrum of difficulty of the questions employed will also affect the test-retest correlation, for example, questions that are very easy should always be answered correctly leading to a high test-retest correlation (22). However, for a knowledge questionnaire to be a useful tool requires it should be composed of questions of different levels of difficulty (17). This was demonstrated by the HDFQ-RA, such that it can identify patients in need of further education or show progress following an education course. Both HDFQ-RA questionnaires showed discriminant ability whereby meaningful groups of people scored differently on the scale as expected; specifically, respondents who had, or were more likely to have been educated about CVD (by virtue of having been commenced on relevant medications), scored higher scores on the HDFQ-RA than those who had not received CVD education. A similar finding was observed with the original HDFQ; taking medications for CVD did predict heart disease knowledge in a sample of patients with diabetes, whereas having risk factors for CVD did not predict knowledge (20). The lack of a relationship between respondents' level of qualifications (reflective of their

years of formal education) and their scores on the HDFQ-RA may be influenced by the fact that many of respondents were elderly and so left school early, and that knowledge about CVD specifically pertaining to people with RA is comparatively 'new'. The important implication is that patient education addressing CVD in RA is required by all patients, regardless of how long they have been diagnosed.

There are some limitations of this questionnaire. The patients were recruited from one regional expert unit where annual review clinics to address co-morbidities, including CVD, are in place as recommended by the Arthritis and Musculoskeletal Alliance Standards of Care (28). As such, the levels of heart disease knowledge may be higher in these respondents than in the general population of patients with RA. It would be ideal to use the HDFQ-RA in a much larger national survey of patients' knowledge which would both increase the geographical spread of respondents, as well as the number of respondents, although an adequate sample was recruited in the present study (25). Another limitation is that the questionnaire has been validated only in English. People of South Asian origins are at increased risk of CVD compared to the general population (29) and patient education and supporting resources should be provided in relevant languages (30) It would therefore be valuable for this questionnaire to be translated into other languages, which may require small adjustments to ensure it is culturally appropriate, and then re-validated.

Other future studies with the HDFQ-RA could involve its use in a survey of health professionals' knowledge about RA and CVD. The results might be used to help inform local educational initiatives. Having shown the HDFQ-RA is stable in the absence of an intervention, research is required to assess its sensitivity to change consequent on an education intervention.

In summary, the availability of a psychometrically validated questionnaire addressing knowledge of heart disease in patients with RA is a necessary and timely development, especially given the emphasis on managing CVD co-morbidity in RA (5). Not only will the HDFQ-RA have important applications in current clinical practice, discussed below, but it will also be a particularly important measure to use in forthcoming research studies, including both educational and clinical research. Current clinical research strategies are addressing the role of pharmacological therapies (31) on CVD risk in patients with RA but also need to address other non-pharmacological lifestyle measures such as regular exercise (21) and optimizing diet. A valid score of heart disease knowledge will be an important measure in these trials, for example, to see if it affects adherence to the intervention.

However, it is also important to consider, as with all health knowledge questionnaires, how these new gains in knowledge can be translated into behavioural change. Therefore, we would emphasise the importance of using this questionnaire within the context of developing and delivering a CVD patient education programme whereby knowledge is conveyed to explain and underpin the rationale for implementing lifestyle modifications alongside the provision of appropriate resources to support such lifestyle changes.

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CHAPTER 7: PATIENT EVALUATION OF A NOVEL PATIENT EDUCATION LEAFLET ABOUT HEART DISEASE RISK AMONG PEOPLE WITH RHEUMATOID ARTHRITIS

Abstract

Objective: People with rheumatoid arthritis require access to clear and consistent information about their condition and Arthritis Research UK produce a wide range of leaflets to meet this need. There is no patient information leaflet about CVD in the context of having RA, despite the fact that CVD accounts for 50% of the mortality in RA. A leaflet was developed; this paper describes the patient evaluation of this novel education resource.

Methods: A questionnaire was developed to evaluate the leaflets' content, literacy, graphics, layout and ability to stimulate learning. It was distributed, with the leaflet, to 500 NRAS members.

Results: There was a 72.8% response rate. Of the respondents: 96% agreed the purpose of the leaflet was clear; 78% agreed the leaflet was relevant to them; 96% agreed they understood the leaflet; 53% agreed the leaflet cover was appealing; 81% agreed that the size of the typing was suitable; 71% agreed the advice was appropriate for their lifestyle. Omissions included adequately describing any risks associated with its advice, what sources of information were used to compile the leaflet and when this information was produced. 84% of respondents would recommend this leaflet to other people with RA. Qualitatively, many people felt more empowered as a result of reading the leaflet.

Conclusions: Patient evaluation of new educational resources is important and ensures materials meet patients' needs and are presented in a user-friendly style. Ultimately, the test of the effectiveness of the leaflet will be if patients change their behaviour appropriately.

Introduction

For people with a chronic disease, the provision of information and education should help them feel empowered to self-manage their condition, as well as make any necessary lifestyle changes that they wish based on professional advice and patients perceptions. Specifically, providing appropriate and desired health-related information is a right all patients can expect under the UK Patient's Charter (1).

For people with rheumatoid arthritis (RA), the most common inflammatory arthritis, European guidelines consider patient information about the disease, its treatments and its outcome is important (2). The Arthritis and Musculoskeletal Alliance Standards of Care state patients should have access to clear and consistent information presented in a variety of formats (3). Educational preferences may vary from a one-to-one format to group work but certainly written material has been shown to be preferred by patients with arthritis for learning new information (4). Certainly, to compliment the traditional clinical (verbal) consultation, written information is often provided for RA patients, including leaflets about specific medical conditions and medications, for example those produced by Arthritis Research UK (AR-UK). Increased knowledge has been demonstrated in patients having read the AR-UK RA disease-specific leaflet (5;6) as well as a drug information leaflet (7). The AR-UK leaflet range includes leaflets about

several co-morbidities associated with RA. However, it is co-morbid cardiovascular disease (CVD) that accounts for 50% of the mortality in patients with RA (8) and there is currently no patient information leaflet available that discusses CVD in the context of having RA (9). CVD risk management involves people making lifestyle changes such as increasing the amount of exercise they do or stopping smoking. In order for patients to instigate such behaviour changes, they may need to be informed about the risk of CVD with RA and the rationale and practicalities associated with making behaviour change. There is therefore a need to develop a patient education leaflet to address the cardiovascular co-morbidity that associates with RA.

Mindful that the literature reports a potential incongruence between the information provided by health professionals and the information patients request (10), it was felt important to have patient input both in the development of the leaflet and in its evaluation. Hence, qualitative research with stakeholders was performed, namely individual interviews with patients with RA and focus groups with relevant healthcare professionals (11;12). This revealed patients were mostly unaware of the association between RA and CVD, but were interested in learning what could be done to address their risk, requesting "common sense" advice taking into account their RA (11). A leaflet was therefore developed by a steering committee of rheumatologists and psychologists. It describes why there is an increased risk of CVD associated with RA and includes practical lifestyle advice on what patients can do to reduce their risk with specific examples. User involvement was sought; the UK National Rheumatoid Arthritis Society (NRAS) distributed it to selected members for feedback which informed further iterations of the leaflet. The reading age of the leaflet was calculated using the Flesch-Kincaid readability test. This

measure of comprehension difficulty can be calculated using a readability calculator available at: http://www.editcentral.com/gwt/com.editcentral.EC/EC.html. The Flesch reading ease score was 68.1%, that is, it is easily readable by someone with a reading age of an average 13 year old, a level which 89% of a sample of English RA patients achieved (7). Permission was sought to reproduce graphics in the leaflet and copyright for the overall leaflet was obtained. The leaflet was laid out in a style similar to the current AR-UK leaflets that are familiar to patients with RA, paying attention to checklists of factors suggested to enhance the quality of written patient information (13). These include accuracy and reliability of material, acceptability, readability, style and attractiveness of presentation, references to sources of further information, and cultural appropriateness (13). The leaflet was formatted by a professional web developer and professionally printed; it is available on written request to our departmental secretary (Jaclyn.Griffiths@dgoh.nhs.uk).

Patient feedback on resources is highly desirable (10;13) and so it was felt important to seek formal evaluation by patients on this new leaflet. This paper describes the process and results of RA patients' evaluation of this new patient education resource.

Methods

a) Questionnaire development

A questionnaire was designed to seek patients' evaluation of the leaflet. This questionnaire was initially a synthesis of two existing questionnaires (14;15) as neither was entirely suitable on their

own. Thirty four questions evaluated the content of the leaflet (questions 1- 15), its literacy (questions 16 - 19), the graphics (questions 20 - 24), the layout (questions 25 - 29) and the ability to stimulate learning (questions 30 - 34). The response options were 'yes', 'somewhat' and 'no'. The questionnaire was reviewed by all authors and amendments made to simplify the language. An AR-UK patient representative suggested further amendments as well as an additional question about whether the leaflet described who to turn to for further help and advice (question 7). The opportunity for free text comments was provided. Basic demographic questions were included at the end of the questionnaire. The questionnaire was produced in a scannable format using 'Snap' software; scanned results were entered into Microsoft Excel™.

b) Procedure

Ethical approval was obtained from the Black Country Research Ethics Committee. In February 2010, the leaflet and questionnaire, together with a covering letter, were distributed by NRAS to 500 of their volunteers and members with a stamped addressed envelope for replies to be returned anonymously to the researchers. A total of 364 participants returned the questionnaire, a 72.8% response rate.

Results

a) Demographics of responders

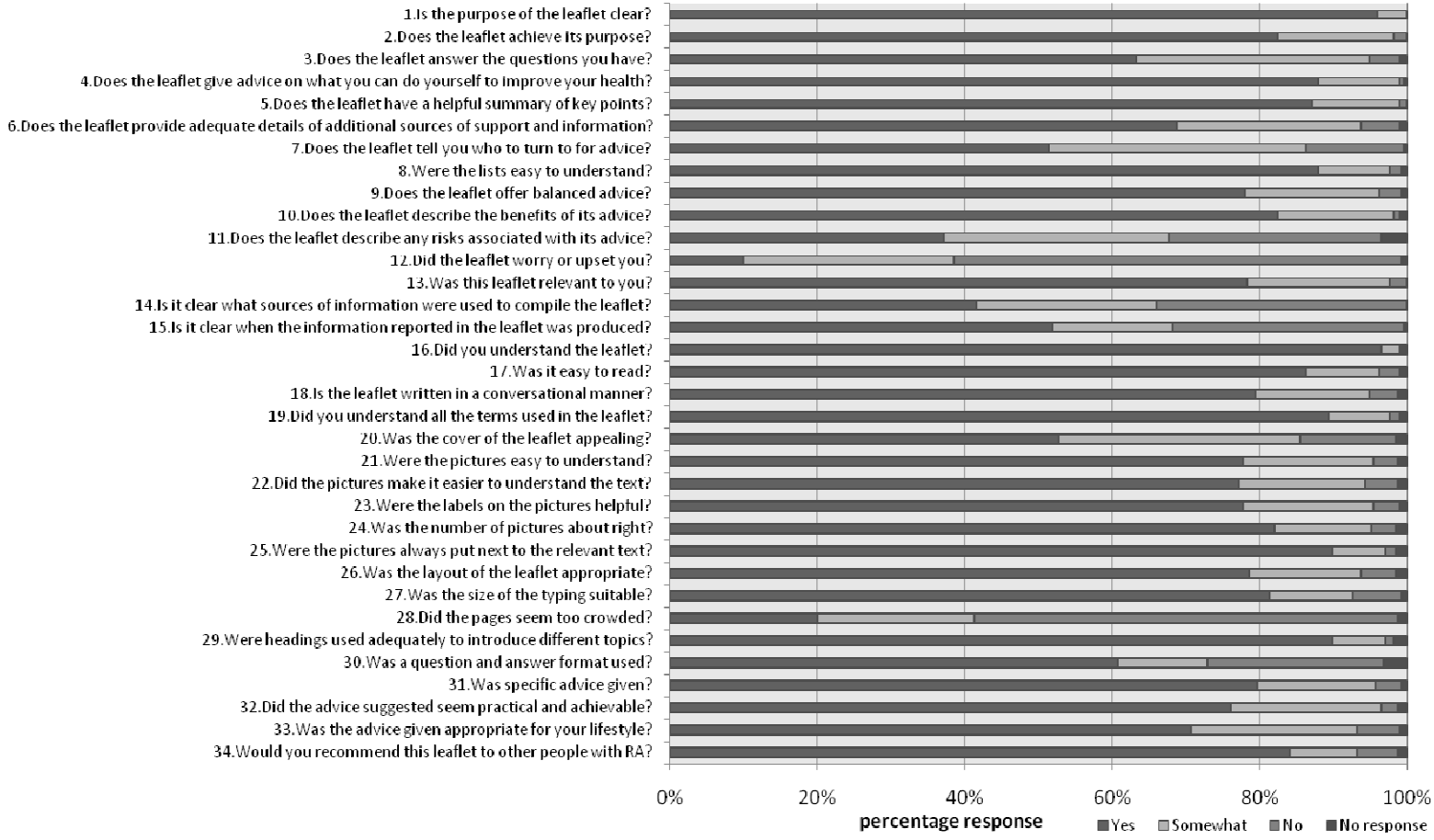
Most responders (299/364; 82%) were female. The median age category was 50 -59 years old, most were married (246/364; 68%) and most were of white ethnicity (337/364; 93%). The highest educational qualification obtained was GCSE/O-level by 49/364 (14%), A-

level/diploma/vocational qualification by 143/364 (39%), degree by 78/364 (21%), post-graduate qualification by 58/364 (16%); 36/364 (10%) had no qualifications or did not respond to the question.

b) Responses to the questionnaire

Frequencies of responses to the 34 questions are provided in Figure 1. Overall the responses to the content of the leaflet were positive with 96% of respondents agreeing the purpose of the leaflet was clear, 82% of respondents agreeing that the leaflet achieved its purpose and 78% of respondents agreeing the leaflet was relevant to them. Only 10% of respondents found the content worrying or upsetting. Whilst 82% of respondents felt the leaflet described the benefits of its advice, only 37% agreed that any risks associated with its advice were described. Only 41% and 52% of respondents respectively agreed it was clear what sources of information were used to compile the leaflet and when this information was produced. Literacy factors relating to the leaflet scored well; 96% of respondents agreed they understood the leaflet and 89% of respondents reported understanding all the terms used. The leaflets' graphics were considered helpful with 78% of respondents agreeing the pictures were easy to understand and 77% agreeing the pictures made it easier to understand the text. The cover graphics were less well received with 53% of respondents agreeing the leaflet cover was appealing. The layout of the leaflet was agreed to be appropriate by 78% of respondents and 81% agreed that the size of the typing was suitable. Questions to capture the leaflets ability to stimulate learning revealed that 76% of respondents agreed the leaflet's advice seemed practical and achievable and 71% agreed the advice was appropriate for their lifestyle. Overall, 84% of respondents would recommend this leaflet to other people with RA.

Figure 1: Responses to questionnaire to evaluate the patient information leaflet "Heart disease in rheumatoid arthritis"



The anonymous free text comments were analysed using a general thematic approach (16). Comments such as: “pictures are almost too graphic”, “ found leaflet quite frightening as I am a heavy smoker”, “I found it a little disturbing because I have never been told there was any link between RA and heart disease” and “some anti-inflammatory tablets …may also contribute to developing high blood pressure…worrying to read this” suggest reasons why a small percentage of respondents found the content worrying or upsetting. Many respondents felt that any risks associated with the leaflets advice were not described; the free text comments suggested that these risks, most commonly, were perceived to relate to exercise “if a person is very badly affected by RA or is having a long flare up, it is not always possible or advisable for them to exercise in the ways mentioned and this can add feelings of guilt” and “I certainly caused severe exacerbation when I tried cycling”. Comments about the cover graphics (of an older couple walking along a beach) explain why it was less appealing: “…bit dated”, “…brighter colours would be good”, “…rather ageist”, “I thought it looked like a brochure for holiday insurance!” and “I wouldn’t spot it in a rack of health info and think ‘that’s for me’”. Additionally, the free text comments captured the notion that many people felt more empowered as a result of reading the leaflet. Many felt confident to raise this topic with their rheumatologist or general practitioner (“I was not aware that the link between RA and heart disease was so strong…I now feel able to approach my consultant with this information”, particularly as “this leaflet provides an easier way to bring the subject up”) and others described valuing learning that there are things they can do themselves (“I found it very encouraging and left a feeling of ‘I can help myself’”).

Discussion

This study describes the development and evaluation of a new leaflet for people with RA which broadly has been well received by a large group of NRAS members. The excellent response rate to a non-requested survey suggests that NRAS members wanted to support it and saw it as a valuable resource. Specifically, the leaflet was perceived to be relevant, its advice was practical for their lifestyle and respondents would recommend the leaflet to others with RA. Moreover, qualitatively, the leaflet appears to have had an empowering effect on its readers.

This quality-based evaluation methodology is in contrast to other studies of patient information leaflets. Previous studies of patient information leaflets for people with RA have evaluated the effectiveness by patients completing subsequent knowledge questionnaires (5-7). However, with increasing emphasis on the patients' experience in the health service we believe that ensuring the quality of educational material is also important, paying attention to factors such as presentation, font size and suitability of graphics. Other specialties have assessed the quality of their leaflets, but health professionals, rather than patients, have assessed them (17-19) often focusing on content and readability alone (17;19). If the leaflet is designed for patients then it is logical that their opinion should be sought to ensure it addresses their questions and is presented in a user-friendly style (13).

The balance between content and readability is crucial. It has been suggested that inadequate attention has been paid towards the content of patient leaflets (13) and certainly inaccuracies or omissions have been identified in leaflets (17-19). Patients identified that our novel CVD-RA leaflet lacked detail about what sources of information were used to compile the leaflet, when this information was produced and what the risks associated with its advice are; similar findings were

observed in a review of 31 renal replacement therapy leaflets available nationwide (17). The challenge is to convey all the necessary information, whilst maintaining readability; the review of renal leaflets revealed that 28/31 leaflets had readability scores ranging from fairly to extremely difficult with only 3/31 leaflets having a similar readability score to our leaflet (described as 'standard' readability).

A small proportion of our respondents were upset by the leaflet. This may relate to the fact that it 'broke bad news' about co-morbid CVD associated with RA (11;12). The converse would be to adopt a more paternalistic view that patients couldn't cope with bad news (13); however, this denies patients the opportunity to make informed decisions about their lifestyle (12). Certainly the empowerment that respondents wrote about in the free text comments suggests that the information was appreciated and would be acted upon.

The strengths of the study relate to the fact that a novel and urgently required leaflet has been developed following appropriate consultation with relevant stakeholders, including patients. The anonymous evaluation of the leaflet by its target audience, and by a large number of people geographically dispersed across the UK increases the validity of the evaluation.

Limitations of this study include the acknowledgement that NRAS members may be more enthusiastic to seek and receive information than other people with RA. The questionnaire responses reflect those of a group of predominantly white females, who were well educated with the median having obtained A-levels/diploma or a vocational qualification. How this leaflet is received by a more diverse group of people is unknown. Also, the leaflet was only provided in

English, making it less helpful for people from ethnic minorities for whom English is not their first language. This is particularly important as people of South Asian origin living in the UK have been found to be at increased risk of CVD (20).

Future work will require further iterations of the leaflet, including correcting current omissions as well as improving the cover graphics to attract attention and highlight the leaflets importance. Producing versions in other languages will also be required ensuring cultural sensitivity and cultural competence (21). Despite suggestions in this study that patients would be empowered to help themselves and discuss CVD with their doctor, ultimately the test of the leaflet will be if patients alter their behaviour having received this leaflet and if this in turn translates into real benefit for their well-being and longevity.

In summary, people with RA require access to information and education about their chronic disease, its medications as well as relevant co-morbidities; currently no AR-UK leaflet is available discussing CVD in the context of having RA. Patient evaluation of our leaflet addressing this unmet need has been broadly positive and has identified areas where improvements could be made. We would encourage others to involve patients in the evaluation of patient education resources to ensure their information needs are met, their questions answered and it is presented in a user-friendly style.

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CHAPTER 8: TRANSLATING PATIENT EDUCATION THEORY INTO PRACTICE: DEVELOPING MATERIAL TO ADDRESS THE CARDIOVASCULAR EDUCATION NEEDS OF PEOPLE WITH RHEUMATOID ARTHRITIS

Abstract

Objective: This paper describes the rationale and design of a theory-informed patient education programme addressing cardiovascular disease for people with rheumatoid arthritis (RA) to illustrate how theory can explicitly be translated into practice.

Methods: A steering group of rheumatologists and psychologists was convened to design the programme. The Common Sense Model, the Theory of Planned Behaviour and the Stages of Change Model were used to underpin the topics and activities in the programme. User involvement was sought. The programme was formatted into a manual and the reading age of the materials was calculated.

Results: A small group 8 week programme was designed. The structure of the patient education programme, including topics, underlying psychological theory as well as behaviour change techniques, is described.

Conclusion: This patient education programme addresses a currently unmet educational need for patients with RA and uses theory to design, not just evaluate, the programme. This will allow both enhanced interpretation of the results when the programme is implemented and replication by other units if successful. The actual design and detail of education programmes merit wider dissemination to facilitate progress in the process of development and application.

Introduction

Patient education has been defined as "any set of planned educational activities designed to improve patients' health behaviours and/or health status" (1). In rheumatoid arthritis (RA), education interventions addressing articular symptoms are well established (2;3). However, it is the co-morbidities of RA that mostly account for increased mortality, poor quality of life and work disability (4). In particular, co-morbid cardiovascular disease (CVD) is evident early on (5) and accounts for ~50% of the mortality in RA (6). Therefore, there is a need to educate RA patients about CVD prevention, particularly aiming to change modifiable CVD risk factors, such as smoking, sedentarity (7), obesity (8) and a high-fat diet (9). No standard, widely available resources currently exist that are designed specifically for RA patients: new educational material is required to meet this currently unmet need (10).

Patient education may involve information only, counselling or behavioural therapies. Although many believe (11) and have shown (12) that improved knowledge is fundamental to behaviour change, such improvements alone do not necessarily translate into behaviour change (13). Behavioural-style education programmes have shown the best outcomes (3;14) in both secondary (15) and primary (16) CVD prevention by effecting improvements in lifestyle factors, cardiac risk factors and incidence of CVD events. However, results are variable; interventions grounded in the theories of human behaviour seem more effective (17;18). Health psychology models of human behaviour provide a theoretical framework on which behavioural interventions can be constructed or evaluated (19). The Common Sense Model of Illness Perceptions has been used to understand how patients may (or may not) develop coping strategies, such as making appropriate

behavioural changes, when faced with new symptoms or illness (20); the model postulates this depends on an individuals representation of that illness, influenced by both their lay beliefs (based on the identity, perceived cause, timeline, consequences and control/curability) as well as emotional response to that illness (20). Social Cognition Theory postulates that behaviour critically depends on a person's representations of their social world, as well as the expectations and consequences relating to behaviour; the concept of self efficacy lies at the centre of this theory and describes one's belief in one's ability to succeed in certain situations (21). Several social cognition models have been developed e.g, the Theory of Planned Behaviour considers that a person's attitude to a behaviour (based on beliefs of risk and evaluation of outcome), the socially determined norms and their perceived behavioural control predict behavioural intentions (22). The Stages of Change Model (or Transtheoretical Model) describes the 5 stages (pre-contemplation, contemplation, preparation, action and maintenance) a person may pass, and cycle through, in order to achieve behaviour change (23); identifying what stage a person is at can allow an intervention to be tailored appropriately (24).

Collectively, a set of factors can be identified from the literature as being associated with successful patient education interventions (Table 1).

The Medical Research Council Framework for developing and evaluating complex (non-pharmacological) interventions, advocates this theory-based approach (25); it recommends reviewing the evidence, then a modelling phase to identify components of the intervention, (suggesting qualitative research to define relevant components) and later a randomized controlled trial of the intervention (25). There are some descriptions of these recommended phases (26-28),

Table 1: Recommendations for designing a patient education initiative

- Conduct a problem analysis prior to developing an education programme (29).
- Research both the patient's health needs and beliefs (30) and the health professional's agenda (31).
- Use a theoretical model (29).
- Design an intervention to deliver clinical benefits, as well as educational benefits (30).
- Ensure the aims, content and endpoints of a patient education initiative are congruent (31).
- Organise group education and involve partners (32).
- Learn what are existing patient health beliefs and modify if necessary (32).
- Include opportunities whereby patients can learn and develop the skills necessary to overcome adverse habits, in order to encourage behaviour change (11); these may be self-management techniques, problem-solving or self-efficacy techniques (30;33).
- Encourage goal-setting and redefine unrealistic goals (32).
- Provide feedback (32).
- Evaluate the programme (29).

but these are in the minority. Systematic reviews of behaviour change interventions suggest that theoretical models are used more to evaluate, rather than develop, interventions (18;34) and greater attention to theoretical development is required (34). In addition, explicit description of behavioural interventions would allow replication of effective programmes by others (18).

Mindful of these recommendations, background research was performed to: define the nature and magnitude of co-morbid CVD in RA (5); highlight current recommendations for CVD risk management as an integral component of the long term care of RA (10); reveal that no widely available RA-specific CVD patient education resources are currently available (10); identify the suppositions, agenda, health needs and beliefs of healthcare professionals and RA patients (35;36). This supported developing a small group educational intervention and suggested three models were particularly pertinent: the Common Sense Model, the Theory of Planned Behaviour,

and the Stages of Change Model. Interventions addressing cardiovascular risk factors using these models have effected significant change (24;37;38).

This paper aims to illustrate how this background theory can be translated into practice by describing the rationale and design of a theory-informed patient education programme.

Methods

A steering group was convened to design the education programme consisting of 2 rheumatologists with special interests in patient education (HJ) and CVD in RA (GDK), 1 rheumatology chartered health psychologist (EDH), and 2 academic psychologists specialising in cardiovascular psychophysiology (DC) and coping with the threat of ill health (PB). There was consensus that the above three models were appropriate and would help participants identify the most suitable CVD risk factor for them to modify first. Techniques relating to these models were inserted into an outline for the educational programme. Other topics were identified, including accurate estimation of 10-year CVD risk, promoting personal responsibility for one's health (39), challenging perceptions of the type of person likely to get heart trouble (coronary candidacy (40)) and screening for depression (36). Different cognitive behavioural therapy techniques were discussed; graded goal setting was agreed to be particularly important in supporting and achieving behaviour change (24;32;41). EDHs' clinical experience offered valuable insight into which techniques have proved helpful in RA. The structure of weekly meetings was chosen as this format has proved successful for the Arthritis Self Management Programme (42), a multifaceted education programme based on the principles of self-efficacy, pioneered by Lorig in

the 1970s in the USA and now successfully delivered in Australia and Europe (43). After several cycles of discussion/evolution of the programme, led by HJ, the educational content and activities were formatted into a patient manual, with a chapter per weekly meeting; identical interactive written and web versions were produced. User involvement was provided through the membership of the National Rheumatoid Arthritis Society; most feedback was specific suggestions to simplify the language in the manual and appropriate amendments were made. One respondent said he did not like group work, contrary to previous research (36;44) but this is perhaps inevitable; most respondents commented favourably on the benefits of group work. The reading age of the manual was calculated using the Flesch-Kincaid readability test (45). This score, which measures comprehension difficulty, is calculated using a readability calculator available at: http://www.editcentral.com/gwt/com.editcentral.EC/EC.html. The Flesch reading ease score was 73.4% overall (i.e. it is easily readable by someone with a reading age of a 13 year old).

The steering committee agreed that external input on the course would be very helpful. A person with RA was recruited (modelling by other patients may be very powerful and is the principle behind the use of lay leaders on the Arthritis Self Management Programme (42)), as well as a dietician, exercise physiologist and smoking cessation advisor to provide tailored expert advice and resources as appropriate. All steering group members agreed on the final version of the programme.

Results

The educational intervention has been developed as a small group (eight participants) eight week programme, involving weekly 2 1/2 hour meetings in weeks 1-4 and week 8 with the opportunity to practice behaviour changes in weeks 5, 6 and 7. The course is led by a health professional and works through the corresponding 8 chapters of the manual; the interactive nature gives lots of opportunities for group discussion and peer support. Table 2 summarises the content and activities of the course in chronological order, and relates this to the underpinning psychological theory. The full manual, subject to copyright law, is available by contacting the first author.

The Common Sense Model of Illness Perceptions particularly underpins the first weeks' meeting. Some patients with RA have previously described incorrect aetiological models of disease (36), which Leventhal posits will (incorrectly) inform their representations of CVD . Therefore, currently-held lay beliefs are explored and challenged in small group discussions; accurate knowledge about the symptoms of CVD, its cause, chronic nature and consequences is imparted, which provides the rationale, and explains the importance of making lifestyle changes, or adopting 'active coping' techniques. A patient, who has recently made remarkable improvements in these health behaviours, then describes their personal story. This programme will support participants similarly develop and maintain their coping efforts so their experiences feedback constructively into their controllability representations of CVD.

The Theory of Planned Behaviour and the Stages of Change models are translated into practice in week 2. Participants are asked to rate the importance, their intention, confidence, perceived ease/difficulty and readiness to: stop smoking, increase exercise, eat heart-healthy low-fat diet and achieve a normal weight. This makes manifest patients' readiness to change behaviour,

Table 2: CVD patient education programme for people with RA

Week	Topic	Theoretical model/concept	Activity and behavioural techniques employed
1	Introduction		
	Current beliefs about CVD	Common Sense Model	Group discussion
	CVD and RA; CVD risk factors	Common Sense Model	Information giving, group discussion
	Reaction to learning about CVD	Common Sense Model	Encouraging coping rather than avoidance techniques
	Lifestyle modifications	Common Sense Model	Concept of personal responsibility for health Self management Patient example
2	Risk factors for CVD	Common Sense Model	Calculating personal risk for CVD, including a BMI calculation
	Consideration of which CVD lifestyle risk factor is most appropriate for them to modify	Theory of Planned Behaviour	Importance, intention, perceived behavioural control over CVD lifestyle factors (46),
		Stages of Change	Readiness to change lifestyle risk factors for CVD Motivational interviewing (39)
3	Identification of CVD risk factor to be modified	Stages of Change	Target goal identified in writing for each participant
	Graded goal setting	Stages of Change	Identification of first goal, using modelling by other participants, examples from relevant health professionals, setting SMARTS goals (47) and identification of relevant organisations
4	Review	Stages of Change	Comparison of performance against initial goal set
	Graded goal setting	Stages of Change	Further SMARTS goals (47) including rewards and contingency plan to cope with setbacks
5-7	Graded goal setting and weekly review	Stages of Change	Skills mastery (42) Regular practice Practicing positive health behaviours Self monitoring Self management (19)
8	Review of progress	Theory of Planned Behaviour	Comparing intention and perceived behavioural control for lifestyle modifications against Week 2 scores (46)
	The future	Stages of Change	Identification of which cognitive behavioural techniques they have found most helpful personally

BMI = Body mass index; SMARTS = Specific, Measurable, Action-orientated, Realistic, Time-orientated with contingency plans in case of Sabotage.

permitting them to identify which CVD risk factor would be the most suitable to modify first. Activities such as identifying the advantages and disadvantages of making, or not making, this change as well as considering what friends or family would want them to do, spring from both these theories and may be powerful triggers for behaviour change.

The Stages of Change Model is further translated into practice in weeks 3 to 7. In week 3, participants commit to the behaviour they wish to modify and identify their target goal. Graded goal setting is introduced (41), subdividing stages of the model, eg, setting several stages of preparation and action goals gradually increasing in intensity or duration. Experience from other participants and advice from a visiting dietician, exercise physiologist and smoking cessation advisor may help identify useful resources. Participants commit to their first graded goal and ensure it is 'SMARTS'; Specific, Measurable, Action-orientated, Realistic, Time-orientated with contingency plans in case of Sabotage (47). In week 4 the participants review their performance against their first graded goal set. The group provide praise, constructive feedback and contingency planning as appropriate. Each participant now commits to a series of graded (SMARTS) goals for the forthcoming weeks when the group does not meet. In this way, weeks 5, 6 and 7 give participants the opportunity to practice their new behaviour, self monitor, master skills necessary for long term behaviour change and gain confidence in their ability to implement lifestyle changes.

The Theory of Planned Behaviour underpins the activities in week 8. Each participant reviews their progress over the course and re-evaluates their intention, confidence and perceived ease/difficulty in making lifestyle changes. Testing out the experience of making behaviour

change, seeing the response of family/friends, gaining confidence in their mastery of a behaviour and reflecting back on their progress should, according to the Theory of Planned Behaviour affect their attitude towards behaviour change and predict improved behavioural intentions for the future.

Discussion

This article describes the translation of health behaviour theory into practice, through a process underpinned by relevant stakeholder involvement, background research and theoretical models (as recommended by the Medical Research Council framework (25)), in order to develop novel educational material. This process and product meets all the recommendations described in Table 1; evaluating the programme is described below.

The specific use of the Common Sense, Theory of Planned Behaviour and Stages of Change Models in this programme allows each participant to personally determine which CVD risk factor they should aim to modify first, based on which risk factor they believe they are most likely to succeed at modifying; advice from health professionals to modify a risk factor that the patient has no intention or readiness to change undermines self-efficacy skills and may be futile (48). Whilst intention does not always translate into action, the flexible nature of this programme and the different cognitive behavioural techniques it uses should optimise the process that individuals go through in their decision making. In this way, the content of the programme is congruent with the aims and endpoints of the programme.

The reading age of the manual accompanying the programme is appropriate. Many RA patients have limited health literacy (49); however, 89% of an English sample of RA patients had a reading age of 13 years or above (50), suggesting that our intervention manual, despite focusing on complex health issues, should be accessible to the majority of patients.

Other studies of complex patient behavioural modification interventions often simply report the results of their programme, furnishing only limited details of its precise nature. This makes interpretation or replication harder. This intervention is currently being compared, in a randomized controlled trial, to a control group receiving a small factual leaflet about CVD and is due to report in late 2011. Outcome measures address educational (knowledge), behavioural and clinical endpoints. This detailed description of the programme will allow replication by other researchers if the trial shows the intervention to be effective. Should, however, the trial fail to show improvements then a detailed analysis will be possible, knowing the components of the intervention. This information can inform future patient education initiatives and minimise the cost (both time and money) and ethical implications in repeating research studies.

In summary, this paper describes the development of a theoretical and research based patient education programme. The requirement for patient education programmes is increasing due to recognition of their impact in managing chronic disease (51) and the increasing complexities and co-morbidities of chronic disease (4). Understanding the effective components of patient education will allow theory to successfully be translated into practice for the ultimate benefit of

patients. We would advocate further groups describe the education programmes they develop as individual research papers.

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CHAPTER 9: A RANDOMISED CONTROLLED TRIAL OF A COGNITIVE BEHAVIOURAL PATIENT EDUCATION INTERVENTION VERSUS A TRADITIONAL INFORMATION LEAFLET TO ADDRESS THE CARDIOVASCULAR ASPECTS OF RHEUMATOID DISEASE.

Abstract

Objectives: Cardiovascular disease (CVD) is responsible for 50% of the excess mortality for patients with rheumatoid arthritis (RA). This study aimed to evaluate a novel 8 week cognitive behavioural patient education intervention designed to effect behavioural change with regard to modifiable CVD risk factors in people with RA.

Methods: This was a non-blinded randomised controlled trial with a delayed intervention arm. Participants were randomised 1:1 to receive the education intervention or a control information leaflet. The primary outcome measure was knowledge of CVD in RA; secondary measures were psychological measures relating to effecting behaviour change, actual behaviour changes and clinical risk factors. Data were collected at baseline, 2 and 6 months.

Results: 110 participants consented (52 in intervention group; 58 in control group). At 6 months, those in the intervention group had significantly; higher knowledge scores ($p<.001$); improved behavioural intentions to increase exercise ($p<.001$), eat a low fat diet ($p=.01$) and lose weight ($p=.06$); lower mean diastolic blood pressure (DBP) of 3.7mmHg, whereas the control groups' mean DBP increased by 0.8mmHg.

Conclusion: Patient education has a significant role to play in CVD risk factor modification for patients with RA; the detailed development of the programme likely contributed to its successful results.

Introduction

Rheumatoid arthritis (RA) is the commonest inflammatory arthritis and is a chronic, disabling condition (1). As with all chronic diseases, patients require access to information about the condition, its medications and associated co-morbidities; this is re-inforced by RA-specific European and national guidelines (2-4). Such information may be presented in a variety of ways, including written (leaflets, mind maps, internet resources) or interactive (individual or group; information giving, counselling or behavioural) formats. However, systematic reviews of the patient education literature in RA have shown that successful interventions, that is, having significant effects on health outcomes, are behavioural (rather than information or counselling alone) (5) or psycho-educational (rather than education alone) programmes (6). Moreover, incorporating a psychological theoretical underpinning to an education programme is thought to be instrumental to its success (7). Educationalists should be mindful of these conclusions when developing future resources for people with RA.

A currently unmet educational need for patients with RA is information regarding associated cardiovascular disease (CVD) (8); this is particularly relevant as CVD is responsible for 50% of the excess mortality in RA, due to both clustering of traditional CVD risk factors and the role that systemic and local inflammation plays in driving the development and instability of the

atherosclerotic plaque (9). Existing generic resources addressing modifiable CVD factors are likely to be inadequate for people with RA as their advice about exercise and weight control is not set in the context of the physical and psychosocial constraints associated with having RA (8). Novel education resources are therefore required both to inform people with RA about the CVD risk and to effect behaviour change with regard to modifiable traditional CVD risk factors such as smoking cessation, increasing physical activity, adoption of a healthy low fat diet and weight control in order to achieve subsequent benefits on CVD risk factors such as lipid profiles, blood pressure and insulin resistance (8;10); concurrently, rheumatologists must aim to achieve control of the systemic inflammation (11).

We have designed a novel education resource to address the CVD co-morbidity in RA, informed by the Medical Research Councils' (MRC) recommendations for designing and evaluating complex interventions (12). During the theoretical phase we reviewed the literature; this revealed considerable theoretical common ground between successful RA education programmes and primary and secondary CVD prevention programmes which could be integrated to provide a framework from which to develop our intervention (13). Using a behavioural approach, underpinned by social cognition models (14) and stages of change theory (15) we developed a small group programme lasting two months, which should theoretically confer the greatest benefit (13). The modelling phase involved qualitative research with relevant stakeholders, both health professionals and patients (16;17), to provide further guidance on how such a novel intervention should be developed and implemented in practice. Theory was translated into practice in the exploratory trial phase and an eight week small group cognitive behavioural education programme was developed with accompanying patient manual; specific details about

the process of programme development and the details of the final programme, including specific weekly topics, underlying theoretical models and the activities and behavioural techniques employed are described elsewhere (18).

The next stage of the MRCs framework requires the novel intervention to be tested in a definitive randomised controlled trial (RCT). This paper describes this trial whereby the cognitive behaviour patient education programme about CVD designed for people with RA (18) is compared to a control group who receive a small factual information leaflet about CVD, akin to the information- giving component of the first week of the programme (19).

Methods

Ethical approval was obtained from the Black Country Research Ethics Committee.

a) Participants

Participants were recruited from a secondary care setting from a single rheumatology centre. The inclusion criteria were aged over 18, a diagnosis of RA, the ability to speak, read and write in English, agreeing to participate in an eight week small group education programme and to attend a research clinic to collect outcome data at baseline and two and six months later.

b) Trial design

The trial was a non-blinded randomised controlled trial with a waiting list delayed intervention arm. Participants were randomised 1:1 to the intervention immediately or the control group. After completing the six months follow up, those in the control group could subsequently attend the intervention programme should they wish, although this was not included as part of the trial.

c) Procedure

Consecutive patients attending outpatient clinics were approached by the chief investigator (HJ) and the study explained. Those interested in the study were given a patient information leaflet and contacted 48 hours later to identify if they would like to participate. Patients were randomised to the intervention or control group; a computer programme generated a randomization list which was applied to our list of recruits by an independent member of the research team. All participants provided informed consent and signed a consent form. Baseline data were collected; age, gender, ethnicity, employment and number of years in full time education. Medical records were used to confirm duration of RA, past medical history of a CVD event or diabetes, and whether patients currently received treatment for hypertension or dyslipidaemia. Biologic, disease modifying, steroid and non-steroidal treatments for their RA were documented and disease activity was scored in 28 joints (DAS 28). Control participants were given a copy of the control information leaflet to read at home. Intervention participants subsequently attended the small group cognitive behavioural education programme held in the hospital research unit. Follow up data were collected on all participants at two and six months.

d) Outcome measures

At baseline, two and six months follow-up, outcome data were collected. The primary outcome measure was knowledge of heart disease in rheumatoid arthritis using the Heart Disease Fact Questionnaire-Rheumatoid Arthritis (HDFQ-RA), a validated self-completion questionnaire, where scores range from 0 (no knowledge) to 13 (maximum knowledge) (20). Secondary outcomes measures were:

i) Psychological measures relating to effecting specific behaviour changes, namely smoking cessation, increasing exercise, eating a healthy low fat diet and losing weight. Specifically, these were:

    a. Attitudes to each individual behaviour change, measured by the mean response to six items rated on bipolar scales (-3 to +3) (21).

    b. Perceived behavioural control over each individual behaviour change, measured by the mean response to four items, measured on unipolar scales +1 to +7 (21).

    c. Behavioural intention towards each individual behaviour change, measured by the mean response to two items rated on bipolar scales (-3 to +3) (21).

ii) Behavioural outcomes

    a. Smoking status; categorised as current or ex/never smoked

    b. Participation in physical activity; the International Physical Activity Questionnaire (IPAQ) was used (22), a validated self-complete questionnaire from which total weekly physical activity can be expressed as weighted metabolic equivalent of task (MET) minutes per week

c. Dietary modifications; the short semi-quantitative food group questionnaire was used (23), from which questions pertaining to fruit and vegetable consumption, type of milk used, use of salt and removing fat from meat were used.

iii) Clinical outcomes

a. Body mass index

b. Blood pressure

c. Lipid profile, including total cholesterol to high density lipoprotein (TC:HDL) ratio (lipid levels are inversely associated with inflammation; this ratio has been shown to be a more robust measure in patients with RA (24;25)) and low density lipoprotein (LDL) levels.

e) Sample size

The sample size was based on the primary endpoint, i.e. evaluating for changes in knowledge of heart disease in RA, using the Heart Disease Fact Questionnaire-Rheumatoid Arthritis (20). This was set at 50 per group to provide 80% power at the 5% significance level. Therefore, 55 patients were recruited per group (110 in total) to allow for 10% attrition.

f) Statistical analysis

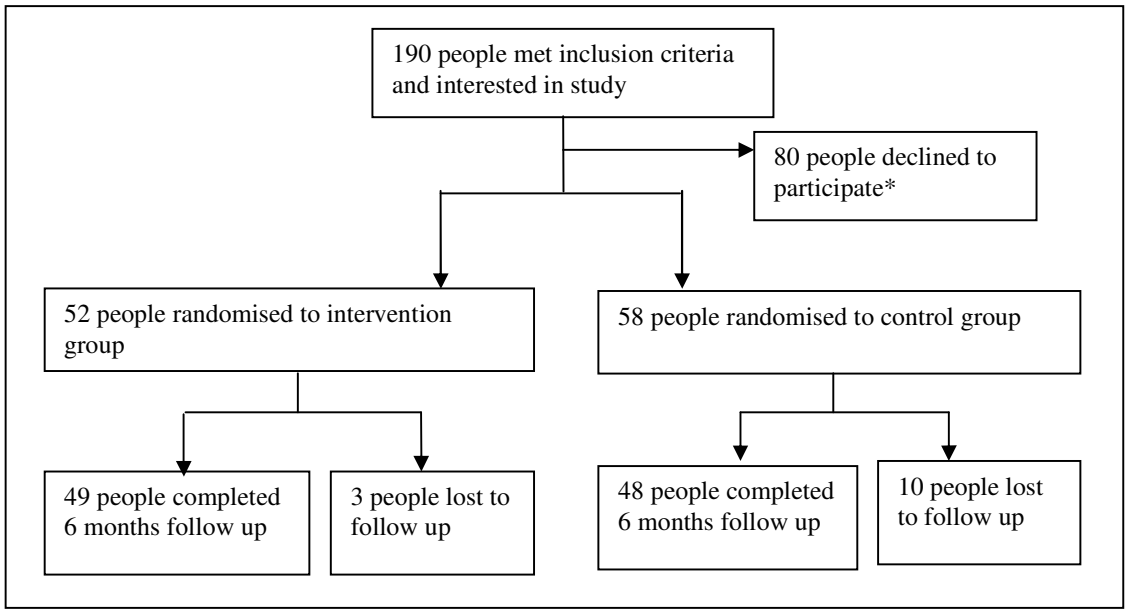
All data were collected and entered into SPSS software version 17 (SPSS, Chicago IL). The database was audited and cleaned for out of range values. Baseline characteristics for the

intervention and control group were compared using analysis of variance (ANOVA) for continuous data and chi-square for categorical data. An intention-to-treat analysis was performed. Continuous outcome data were compared between the intervention and control groups using analysis of covariance (ANCOVA), whereby the differences in outcome variables could be compared at two and six months follow up, with baseline values serving in each case as the covariate. The F statistic, degrees of freedom (df), probability and partial eta squared (η^2), an estimate of effect size, are reported. Probability values less than 0.05 are considered statistically significant. Categorical outcomes between groups were compared at the different time points using chi-square.

Results

One hundred and ten patients with RA consented to participate in the study, with 52 patients randomised to the intervention arm and 58 to the control arm. Figure 1 shows the flow of recruits through the study. Comparison of the baseline characteristics of the intervention and control groups is shown in Table 1. The only significant difference between the groups was that the participants in the intervention were more likely to be on biologic therapy.

Figure 1: Study design, number of participants and their progress through the study



*Reasons included did not have the time, could not fit it in, other commitments, could not get time off work, do not want to make any more visits to hospital and not interested.

Table 1: Comparison of baseline characteristics between the intervention and control groups

Characteristic	Intervention group n = 52	Control group n = 58	Test statistic	p value
Continuous data:				
	Mean (SD)	Mean (SD)	F statistic (df)	
Age	62.19 (10.59)	60.81 (10.67)	(1,108) = .46	.50
Years in full time education	11.27 (2.06)	11.18 (2.23)	(1,96) = .04	.85
Duration of RA	11.6 (11.35)	14.09 (13.91)	(1,106) = 1.03	.31
BMI	29.34 (6.87)	29.09 (5.17)	(1,107) = .05	.83
Waist circumference	98.19 (17.51)	97.42 (12.11)	(1,107) = .07	.79
SBP	143.50 (15.58)	141.48 (19.14)	(1,106) = .36	.55
DBP	83.60 (11.28)	82.14 (10.83)	(1,106) = .47	.50
Total cholesterol	5.00 (0.94)	5.24 (0.95)	(1,108) = 1.86	.18
HDL cholesterol	1.56 (0.41)	1.56 (0.34)	(1,108) = .01	.93
LDL cholesterol	2.79 (0.78)	3.05 (0.86)	(1,104) = 2.71	.10
Triglycerides	1.49 (0.83)	1.45 (0.63)	(1,108) = .06	.81
TC:HDL ratio	3.37 (0.96)	3.51 (0.89)	(1,108) = .64	.43
Glucose	4.83 (0.85)	4.85 (0.86)	(1,108) = .02	.89
DAS 28 score	3.27 (1.55)	2.93 (1.23)	(1,106) = 1.65	.20
Categorical data:				
	Number (%)	Number (%)	χ^2 (df)	p value
Number of females	37(71.15)	43(74.14)	(1)= 0.12	.73
Number of caucasians	50 (96.15)	57 (98.28)	(1)=0.47	.50
Employment • Retired • Full time work • Part time work • Unemployed • Homemaker	 38 (73.08) 6 (11.54) 5 (9.62) 1 (1.92) 2 (3.85)	 39 (69.64) 7 (12.5) 8 (14.29) 0 2 (3.57)	(4)=1.64	.80
PMHx CVD event	6 (11.54)	10 (17.24)	(1)=0.72	.40
PMHx treated hypertension	24 (46.15)	24 (41.38)	(1)=0.25	.61
PMHx treated dyslipidaemia	19 (36.54)	24 (41.38)	(1)=0.27	.60
PMHx DM	4 (7.69)	2 (3.45)	(1)=0.96	.33
Current biologic Rx	24 (46.15)	13 (22.41)	(1)=6.92	.01
Current DMARD RX	41 (78.85)	51 (87.93)	(1)=1.65	.20
Current steroid Rx	13 (25)	13 (22.41)	(1)=0.10	.75
Current NSAID Rx	12 (23.08)	17 (29.82)	(1)=0.63	.43
Smoking status • Current • Never or ex	 8 (15.38) 44 (84.82)	 11 (18.97) 47 (81.03)	(1)=0.25	.62

Abbreviations: (df) = degrees of freedom, RA = rheumatoid arthritis, BMI=body mass index, SBP=systolic blood pressure, DBP=diastolic blood pressure, TC:HDL=total cholesterol to high density lipoprotein ratio, DAS 28=disease activity score in 28 joints, PMHx=past medical history, CVD=cardiovascular disease, DM=diabetes mellitus, DMARD=disease modifying anti-rheumatic drug, NSAID=non-steroidal anti-inflammatory, Rx=treatment

a) Primary outcome measure; effect of intervention on knowledge

The intervention group had a statistically significant higher knowledge score measured using the HDFQ-RA immediately after the intervention and this difference was maintained at the final follow-up at six months. This is shown in Table 2.

Table 2: Comparison of the intervention and control groups' knowledge at two and six months, adjusting for knowledge at baseline.

HDFQ-RA score	Intervention group n=52 Mean score (SD)	Control group n=58 Mean score (SD)	F statistic (df)	p value	partial η^2
• 0 • 2 • 6	9.41 (2.50) 10.93 (2.18) 10.16 (2.41)	9.24 (2.71) 9.34 (2.84) 9.08 (2.75)	(1,79)=13.73	<.001	.148

HDFQ-RA=Heart Disease Fact Questionnaire-Rheumatoid Arthritis

b) Secondary outcome measures;

i) Effect of intervention on psychological measures

Attitudes, perceived behavioural control and behavioural intentions towards effecting specific behaviour changes are compared between the intervention and control groups in Tables 3, 4 and 5 respectively. The intervention group showed significant improvements in all psychological measures with regard to increasing exercise and in two out of the three measures with regard to adopting a healthy low fat diet when compared to the control group. However, there was no difference between groups with regard to stopping smoking; indeed, smoking was the only behaviour where both groups showed negative intentions towards changing throughout the study.

Table 3: Comparison of the intervention and control groups' attitudes at two and six months, adjusting for attitudes at baseline.

Attitude to:	Intervention group n=52 Mean score (SD)	Control group n=58 Mean score (SD)	F statistic (df)	p value	partial η^2
Stopping smoking			(1,9) = 1.40	.27	.134
• 0	0.48 (2.24)	1.11 (1.75)			
• 2	0.32 (2.23)	0.91 (1.64)			
• 6	0.03 (1.63)	1.58 (1.57)			
Increasing exercise			(1,67) = 7.44	.01	.100
• 0	1.46 (1.37)	1.17 (1.28)			
• 2	1.71 (1.35)	0.94 (1.38)			
• 6	1.71 (1.20)	1.07 (1.08)			
Healthy low fat eating			(1,77) = 7.57	.01	.089
• 0	1.36 (1.22)	1.5 (1.02)			
• 2	1.66 (1.33)	1.45 (1.19)			
• 6	1.78 (1.15)	1.35 (1.33)			
Losing weight			(1,75) = 2.48	.12	.032
• 0	2.06 (1.13)	2.09 (1.03)			
• 2	2.27 (0.88)	2.06 (1.06)			
• 6	2.21 (1.06)	2.08 (1.13)			

Table 4: Comparison of the intervention and control groups' perceived behavioural control at two and six months, adjusting for perceived behavioural control at baseline.

Perceived behavioural control over:	Intervention group n=52 Mean score (SD)	Control group n=58 Mean score (SD)	F statistic (df)	p value	partial η^2
Stopping smoking			(1,10) = .01	.92	.001
• 0	2.46 (1.95)	2.96 (1.00)			
• 2	3.13 (2.13)	3.36 (1.52)			
• 6	2.88 (2.00)	3.32 (1.83)			
Increasing exercise			(1,75) = 4.30	.04	.054
• 0	4.32 (1.69)	4.03 (1.55)			
• 2	4.79 (1.71)	4.06 (1.80)			
• 6	4.73 (1.79)	3.99 (1.71)			
Healthy low fat eating			(1,83) = 1.86	.18	.022
• 0	5.14 (1.53)	5.41 (1.33)			
• 2	5.52 (1.51)	5.42 (1.28)			
• 6	5.54 (1.71)	5.61 (1.20)			
Losing weight			(1,78) = 4.60	.04	.056
• 0	5.21 (1.47)	5.41 (1.41)			
• 2	5.51 (1.34)	5.15 (1.39)			
• 6	5.49 (1.35)	5.21 (1.47)			

Table 5: Comparison of the intervention and control groups' behavioural intentions at two and six months, adjusting for behavioural intentions at baseline.

Behavioural intentions to:	Intervention group n=52 Mean score (SD)	Control group n=58 Mean score (SD)	F statistic (df)	p value	partial η^2
Stopping smoking			(1,10) = .51	.49	.048
• 0	-1.00 (2.63)	-0.57 (2.16)			
• 2	-0.75 (2.42)	-0.43 (2.55)			
• 6	-0.17 (2.34)	-0.36 (2.48)			
Increasing exercise			(1,72)=14.11	<.001	.164
• 0	0.42 (1.95)	0.40 (1.70)			
• 2	1.28 (1.61)	0.32 (1.66)			
• 6	1.01 (1.64)	0.32 (1.76)			
Healthy low fat eating			(1,82) = 7.27	.01	.082
• 0	1.16 (1.88)	1.64 (1.35)			
• 2	1.70 (1.62)	1.54 (1.43)			
• 6	1.71 (1.61)	1.63 (1.27)			
Losing weight			(1,79) = 3.73	.06	.045
• 0	1.84 (1.35)	1.99 (1.15)			
• 2	2.26 (0.87)	1.86 (1.12)			
• 6	2.14 (1.05)	1.91 (1.11)			

ii) Effect of intervention on behavioural outcomes

There was no difference between groups on smoking status at the different time points. Analysis of dietary questionnaires showed no difference between the intervention and control groups on quantity of fruit and vegetables consumed, type of milk used, use of salt or removing fat from meat, at 0, 2 and 6 months. There was no significant difference between the groups at the three different time points on physical activity undertaken.

iii) Effect of intervention on clinical outcomes

A significant effect on diastolic blood pressure (DBP) was observed; over the 6 month follow up period the intervention groups mean DBP fell by 3.7mmHg, whereas the control groups' mean DBP increased by 0.8mmHg. The group effect on LDL was close to the conventional criterion

for statistical significance. The control groups' mean LDL levels increased during the trial by 0.25 mmol/l whereas the intervention groups mean LDL only increased by .09mmol/l. Table 6 shows the results of all clinical outcomes measured and compares them between the two groups.

Table 6: Comparison of the intervention and control groups' clinical outcomes at two and six months, adjusting for clinical variables at baseline.

	Intervention group n=52 Mean score (SD)	Control group n=58 Mean score (SD)	F statistic (df)	p value	partial η^2
BMI			(1,93) = .17	.68	.002
• 0	29.08 (6.55)	29.04 (5.32)			
• 2	29.09 (6.64)	29.05 (5.52)			
• 6	28.99 (6.51)	29.09 (5.65)			
SBP			(1,91) = .36	.55	.004
• 0	143.48 (15.73)	142.26 (19.71)			
• 2	139.50 (15.78)	135.35 (15.55)			
• 6	139.96 (16.01)	139.83 (20.97)			
DBP			(1,91) = 5.97	.02	.062
• 0	83.04 (10.75)	81.93 (11.18)			
• 2	78.81 (9.56)	81.63 (10.27)			
• 6	79.31 (9.50)	82.72 (10.66)			
TC:HDL ratio			(1,92) = 2.33	.13	.025
• 0	3.38 (0.99)	3.47 (0.87)			
• 2	3.47 (1.02)	3.66 (0.97)			
• 6	3.57 (0.98)	3.84 (1.04)			
LDL			(1,84) = 3.38	.07	.039
• 0	2.75 (0.79)	2.98 (0.84)			
• 2	2.72 (0.85)	3.02 (0.80)			
• 6	2.84 (0.87)	3.23 (0.85)			

Abbreviations: BMI=Body mass index;SBP=systolic blood pressure; DBP=diastolic blood pressure;TC:HDL=total cholesterol to high density lipoprotein ratio; LDL=low density lipoprotein

Discussion

Patient education is widely accepted as an integral part of patient care; benefits such as effecting positive patient behaviours and improving compliance with medication are essential to compliment the clinical decisions made by healthcare professionals (26). However, changing people's behaviour is a particularly challenging task, especially in a primary prevention setting (27). The positive outcomes that emerge from this study, therefore, give strong encouragement to the present approach to patient education. Not only have we shown significant improvements in knowledge, our primary outcome measure, but this has also translated into changing participants' psychological views, particularly their intentions, to make behaviour change. In turn, we have reported improvements in clinical risk factors, namely DBP. This concurs with Ajzens Theory of Planned Behaviour (28), which posits that attitudes and perceived behavioural control, alongside subjective norms, to a specific behaviour drive behavioural intentions which in turn translate into actual behaviour change. This theory is underpinned by the prerequisite of adequate knowledge and information provision and, in turn, the consequence of this theory is that behaviour change should translate into tangible benefits, namely changes in clinical CVD risk factors in this case. The improvement in DBP we observed is particularly relevant as the impact of hypertension on cardiovascular outcome in patients with RA is similar to those who do not have RA, that is, the risk of CVD increases in parallel with systolic or diastolic blood pressure, approximately doubling for every 20/10mmHg incremental increase in blood pressure that occurs within the range of 115–185/75-115mmHg (29). Pertinently, the prevalence of hypertension in secondary care cohorts of RA patients may be as high as 70% (30). Furthermore, the improvements we achieved in DBP were similar to or better than improvements in DBP observed longitudinally in patients commencing treatment with anti-tumour necrosis factor α (anti-TNFα) medication, where reductions in DBP of 5mmHg (31) and up to 2.8mmHg were observed (32).

These results are comparable with other 'Healthy Heart' programmes aiming to modify multiple CVD risk factors; some delivered improvements in behaviours, such as nutrition and exercise (33), whereas others have, similar to our study, achieved some clinical benefits (34;35). It is particularly relevant to note that our study participants were an unstratified group of all ages and with a varying number of CVD risk factors, other than RA, from zero to several. Our results cannot, therefore, be directly compared to other primary prevention trials where the inclusion criteria required participants to have a specified cluster of CVD risk factors, such as diabetes, hypertension and dyslipidaemia (36). Further, this is the first programme to aim to modify CVD risk factors in an RA population where there are specific additional challenges participants may face in trying to modify adverse CVD behaviours; exercise despite joint pain, weight loss despite corticosteroid medication, blood pressure control despite the need for non-steroidal anti-inflammatory medication (13).

It is helpful to consider why this trial has delivered successful results, to inform future patient education initiatives. Reasons may relate to both the trial design and methodology, such as ensuring it was adequately powered and a sensible choice of outcome variables was used appropriate to the duration of the follow- up period. Over a six month period and with this sample size it would be unrealistic to aim to show differences in subsequent CVD events, particularly with a predominantly primary prevention intervention; much longer follow up would be required, such as the 8-year follow up period used by Rachmani et al where a significant reduction in CVD events was demonstrated (36). Further, the detailed and careful development of the actual cognitive behavioural patient education programme likely contributed to its successful results. Interventions developed specifically for purpose and their target audience are more likely to be

successful (8) and the MRCs framework reinforces the importance of thorough theoretical, modelling and exploratory phases to develop a complex intervention, prior to moving onto a RCT (12); completing these stages (13;16-18) ensured the intervention developed was truly focused on the specific needs of people with RA with regard to modifying their CVD risk.

Interestingly, there was a discrepancy between intentions to modify the different CVD risk behaviours, in particular smoking cessation appeared to be resistant to this intervention as measured by both psychological measures and actual changes in smoking habits. This may relate to the fact that there were only 19 smokers recruited to this study so the numbers were small, but may also reflect the public health challenge in getting people to quit this addictive behaviour; recent public health/government strategies have encouraged many to give up (37) so those remaining may represent a particularly resistant group. In contrast, the intervention group showed improved psychological parameters across all measures with regard to increasing exercise. People with RA have previously described both physical and psychological factors as barriers to exercise (38) as well as concerns that exercise could further damage their joints (17), whereas tailored advice from health professionals has consistently been identified as an exercise enabler (39). This study, where people in the intervention group received specific exercise advice from health professionals set in the context of having RA, provided as part of an interactive discussion, appears to be more effective in encouraging people with RA to increase their physical activity levels than the didactic written information provided to the control group.

This study is not without its limitations. First, despite randomisation, there were significantly more patients in the intervention group than the control group taking biologic medication and

biologic medications may have effects on the lipid profile and blood pressure. The anti-TNFα medication infliximab has been shown to increase TC and HDL but with no overall change in the atherogenic index (TC:HDL ratio), and tociluzimab, an interleukin-6 receptor antagonist, has also been shown to significantly increase components of the lipid profile, namely TC, HDL, triglycerides and LDL, although the impact on the atherogenic index is currently unclear (40). However, a comparison of TC:HDL ratio results of those not on biologic medications versus all subjects concluded that biologic therapy was not masking any change. Recent evidence also suggests that biologic treatment may decrease blood pressure (31;32); these results were observed comparing blood pressure readings pre and post commencement of biologic therapy. However, in this study, participants were on stable long-term treatment with biologic medication and so this is unlikely to provide an explanation for the decreases in DBP observed. Second, the study would have undoubtedly benefitted from a longer term follow-up, both to investigate whether currently observed benefits of the intervention are maintained longer term, as well as to test whether there are subsequent effects of the intervention on other clinical outcomes. We have previously discussed, in the context of the timing of a patient education programme, the concept of a 'golden moment', that is, a specific point in time when a patient will objectively self-assess their health and commit to a behaviour change (16). This golden moment will not necessarily happen during an education programme, especially a research education programme where consecutive patients are invited to attend, although the course may act as a trigger later on. Anecdotally, participants have reported modifying their behaviours but the golden moment which prompted them to act came after the six months follow-up had been completed. Longer term follow-up, over a period of years, would then be suitable to include CVD events as an outcome measure, although the study was not powered originally to detect a difference here. Lastly,

another limitation is that health economics data were not collected; this information would be useful for the future in deciding whether to implement this existing CVD education programme or whether changes are needed to improve its cost-effectiveness.

Future research should also include further analysis to identify predictors of successful outcomes from the cognitive behavioural patient education programme. Hypothesised possibilities could include baseline CVD risk factor profile; baseline knowledge of CVD; levels of anxiety and depression; health locus of control; self-efficacy measures, and number of sessions attended. If future education programmes were made available the imperative of cost-effectiveness would require physicians to pre-select participants most likely to benefit from the intervention. The identification of predictors of success would be a valuable tool here.

In conclusion, this cognitive behavioural education programme has effected significant changes in knowledge, and intentions to modify adverse CVD behaviours, as well as clinical improvements in diastolic blood pressure. These successful outcomes are thought to relate to the careful design of the education programme, informed by extensive theoretical and qualitative research with stakeholders. We would advocate the integration of patient education about CVD risk in RA into the standard care of patients with RA, as well as further research into developing and delivering effective patient education programmes.

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CHAPTER 10: DISCUSSION

Guidelines for the management of rheumatoid arthritis (RA) clearly state the importance of patient education to encourage patients to be active partners in the management of their disease, capable of self- management and implementing appropriate behaviour change as necessary (1;2). In addition, guidelines also emphasise the importance of addressing the cardiovascular co-morbidity for patients with RA, recommending that individuals should be screened and relevant risk factors medically managed (1-3). However, until now, these two principles have not been integrated to develop suitable and tailored patient education resources about cardiovascular disease (CVD) in RA. We identified this gap in our existing provision of care for patients with RA and this thesis has described our efforts to highlight this unmet need, as well as to develop and evaluate an education programme to fulfil this need.

Summary

We explicitly used the Medical Research Council (MRC) framework for developing complex interventions and the Chapters of this thesis chronologically relate to their recommended phases. Relevant stakeholder qualitative research identified important themes and health psychology behaviour change models which were employed to inform the design of the complex intervention (Chapters 4 and 5). Patients seemed unaware of their risk of CVD co-morbidity and few displayed extensive and accurate knowledge of CVD. Information about CVD was therefore required to accurately inform patients' illness cognitions (Common-Sense Model) and to provide the rationale for adopting approach-coping strategies, such as adopting appropriate lifestyle

behaviours. However, health professionals presumed that patients would not consider CVD a priority and perceived that they would be poorly motivated to adopt suitable lifestyle behaviours; in contrast, patient interviews revealed that patients were interested in learning about preventative strategies. Moreover, patients could identify factors that had specifically motivated them previously to change behaviour, for example, stopping smoking, and gave examples of changes in their attitude, social norms and perceived behavioural control, that is, self-efficacy, which had driven such behaviour change (Theory of Planned Behaviour). Additionally, patients identified inaccurate perception of risk, depression or fatalism as barriers to implementing behaviour change. Both health professionals and patients agreed that a personal 'golden moment' of realisation was needed to drive behaviour change, analogous to the preparation and action stages of the Transtheoretical Model. Accordingly, as well as providing accurate information, the education intervention needed to provide the opportunity to explore the breadth of social cognitive factors relating to behaviour change, enhance patients' self-efficacy, and signpost patients to resources supporting their commitment to change. Health professionals were unsure when CVD should be discussed with patients; patients revealed that they felt information about CVD would be both overwhelming but also seem irrelevant at diagnosis but, given time to adapt to their diagnosis, they would be able to cope with information about CVD. Practical issues relating to the development of an education programme included a majority request for a small group format and for secondary care health professionals to communicate with primary care so that patients are provided with a consistent message.

The next phase of the MRC framework required all components of the forthcoming trial to be defined. This included defining outcome measures, as well as determining the nature of the

control arm of the trial. Our primary outcome measure was knowledge of CVD in RA. However, no questionnaire existed to measure this. Therefore the Heart Disease Fact Questionnaire (HDFQ), designed to measure CVD knowledge in people with diabetes mellitus, was modified and a RA-specific version was developed (HDFQ-RA) (Chapter 6). Aware that repeat administration of a questionnaire may result in a respondent only learning the answers to the questionnaire, two parallel versions of the HDFQ-RA were developed. Parallel form reliability, internal consistency and test-retest stability of the questionnaires were established, as was face, content and discriminant validity. Thus, it was assured that the HDFQ-RA had robust psychometric properties and was a suitable measure to use to assess our novel education intervention.

The control arm of our intervention would need to receive some basic information about CVD in RA. Standard information leaflets for people with RA are produced by Arthritis Research-UK, but there is no existing leaflet addressing CVD in RA. Therefore, an information leaflet was developed for the control group (Chapter 7); it was akin to the information-giving component at the beginning of the novel education intervention, but without the subsequent discussion or open questions to explore the complex web of social cognitive factors that underlie patients' behaviours. Evaluation by members of the National Rheumatoid Arthritis Society (NRAS) revealed that the leaflet was well received, perceived to be relevant and provided practical lifestyle advice; a majority of respondents indicated that they would recommend it to a patient with RA.

The last component of the intervention to be defined was the nature of the education programme itself. The theoretical models identified by the qualitative research were translated into practice and a small group, eight-week programme was developed (Chapter 8). The exact topics covered each week were defined, as was the underlying health psychological model and activities and behavioural techniques employed. The content was formatted into an interactive manual, with a chapter per weekly meeting, for each participant to keep; identical written and web versions were available.

The MRC then recommend a definitive randomised controlled trial of the intervention developed. Participants were randomised to the intervention immediately or the control group and were followed-up for six months (Chapter 9). Those in our intervention group showed significant improvements in knowledge, which translated into changing participants' psychological views, particularly behavioural intentions, and in turn we observed improvements in clinical risk, namely reduced diastolic blood pressure; this is particularly relevant as the prevalence of hypertension in RA may be as high as 70% and the risk of CVD events increases in parallel with increases in blood pressure (4). The positive outcomes from this trial suggest that patient education has a significant and important role to play in CVD risk factor modification for people with RA.

Strengths of this study

There are many strengths of this thesis as a whole; the strengths of individual Chapters have been previously described. Fundamentally, this thesis directly addresses an important and highly

prevalent co-morbidity for patients with RA where, previously, education and information resources were lacking. This thesis has not just hypothesised about what education resources would be ideal, neither has it developed education resources spontaneously. Instead it has followed a recommended structured framework to fully research the health beliefs and needs of the target population and, combined with what has been learnt from previous published education studies, produced and robustly evaluated a novel education intervention. The positive outcomes from the randomised controlled trial are a strong endorsement of this approach. Further, the materials produced can be used in routine patient care, so there is an immediate and direct clinical application from the research in this thesis.

Implications of this study

The implications of this study are twofold; firstly, that patient education has a significant role to play in CVD risk factor modification for patients with RA; secondly, that a rigorous and theoretically-driven process of development of patient education materials is the approach most likely to yield dividends.

Regarding the first implication, current guidelines for patients with RA recommend, in relation to their CVD risk, lifestyle advice to encourage smoking cessation, dietary modification, weight control, and exercise (1;2); this study adds to the evidence base for the benefits of this recommendation. How to provide this advice effectively to patients with RA, however, is not discussed by these guidelines and remains a challenge. A previous education intervention to address CVD risk factors in patients with RA used a one-to-one approach with a specialist nurse

who provided generic smoking and dietary booklets and invited patients to a weekly swimming group specifically for patients with arthritis; only modest benefits were observed (5). The benefits observed in our study may relate to one or, more likely, the interaction of several of the following strategies that were used; group education; eight-week course duration; advice provided within the context of having RA, rather than generic advice; cognitive behavioural approach; explicit use of techniques aimed to modify behaviour; role modelling using a 'successful' patient; supporting written and internet resources. Further research into the dynamics of these individual components may allow future guidelines to make more explicit recommendations about providing CVD lifestyle advice for people with RA.

With regard to the second implication, the process employed in developing these educational resources is transferable both to other RA co-morbidities and other chronic diseases where there is a lack of effective educational material. Indeed, others have also called for a theoretical approach to be used in the design of patient education materials in order to improve the efficacy of education programmes (6). Currently, such practice is only reportedly used in a minority of published interventions. Other examples include a patient education programme to encourage increased physical activity in those at risk of type 2 diabetes, whose design was underpinned by a causal modelling approach (7), a stroke secondary prevention programme (8) or a physician and patient education intervention aiming to improve the management of osteoporosis (9), informed by qualitative research (10), and described in detail (11). The diabetes education and self-management for ongoing and newly diagnosed (DESMOND) trial is a large UK multicentre cluster randomised controlled trial of a structured group education programme; its design and development, including explicit use of specific theoretical psychological models, has been

described in depth (12). At 12 months, the intervention participants showed significantly greater improvements in weight loss and smoking cessation as well as in illness beliefs (13). Inevitably, some would argue that adopting this advocated rigorous approach to the development of patient education resources is both time-intensive and expensive. However, a cost-effectiveness analysis of the DESMOND programme suggested it is likely to be cost-effective compared with usual care, even under the more modest assumptions that include the effects of the intervention being lost after one year (14).

Limitations of this study

Inevitably, there are limitations associated with the present research. Many of the limitations have already been identified in the individual Chapters. Overall, this was a single centre study in a predominantly Caucasian population. All the patients involved in the qualitative research phase were Caucasian; consequently the education intervention was developed to suit Western lifestyles and all educational resources were provided in English in a written format. While it is possible to conceptually generalise from qualitative research and comparisons can be made between similar people in similar circumstances (15), the findings of this study cannot be assumed to apply to those from a minority ethnic background. Further, the educational resources may need to be adapted to be culturally relevant to minority ethnic groups and their approaches to diet and exercise (16); the Chronic Disease Self-management Programme, run in the UK as the Expert Patient Programme, was adapted by a local community group before it was delivered to a Bangladeshi population (17). Additionally, educational resources would need to be provided in other languages or as an audio compact disc as a significant proportion of people from minority

ethnic groups cannot read the script of their spoken language (18). There may be a particular need for this as CVD risk is further increased in people of South Asian origin (19).

Future research

This thesis lends itself to a wealth of future studies. Initially, the programme could be applied on a larger scale to determine whether current results can be replicated. In the present study, a single person led all the educational meetings, which controlled for operator-dependent effects. However, to translate this from a research study into an accurate evaluation of the programme in a 'real-world' setting, a multi-centre study is needed which will require several course leaders/facilitators. Employing allied health professionals to deliver this course is a sensible option; using lay people to deliver the course could also be considered. Training the facilitators would be a priority, to ensure adequate knowledge and understanding across both the disciplines of rheumatology and cardiovascular medicine; provision of a script for the facilitators would help to optimise consistency. Indeed, the multicentre DESMOND education course provides two days of education for their healthcare professional educators (12). The programme could be delivered in a more ethnically diverse geographical area, but where participants can still speak and read English, or the course could be culturally and linguistically adapted to be delivered to minority ethnic groups of people. Future replications of the course could involve health economists at the outset so appropriate data are collected to allow a subsequent cost-effectiveness analysis.

If necessary, another future option would be to modify and shorten the course to improve its cost-effectiveness. Existing data could be analysed to identify if attending a critical number of

sessions is predictive of a successful outcome. If so, could the programme be truncated to this critical number of sessions? Could CVD education be a module of a general RA patient education programme? If the programme were to become shorter, some content would need to be sacrificed; qualitative research with 'successful' participants could help identify which aspects of the programme were pertinent and helpful and should be retained. Moreover, the identification of these particularly influential factors would be helpful in general for other patient education initiatives.

More broadly, future research will also need to include other formats for delivering CVD education to patients with RA, as, inevitably, some patients do not like attending group meetings (20) or cannot attend them due to other commitments. In principle, all interactions with healthcare professionals provide the opportunity for education (21) but this often needs to be supplemented with specific additional resources. Individual appointments could be available to discuss CVD risk management. For those that prefer a written format (22), the existing education course manual (Chapter 8) could be adapted to be used as a hand-out, rather than alongside group discussions; the manual can then still pose questions to the reader to prompt deeper thinking about their personal lifestyle behaviours which would offer a more cognitive-behavioural approach than the information leaflet in Chapter 7 currently does. For less able readers, Arthritis Research-UK currently provides information as 'mind maps' whereby information is presented more diagrammatically (23); this could be complemented by additional audio-visual resources to provide a more complete educational resource.

Conclusion

This thesis chronologically describes the identification of a highly prevalent co-morbidity for patients with RA, identifies the lack of existing patient education resources necessary to address it, and describes an attempt to systematically design, develop and evaluate a complex educational programme to meet this need. The positive outcomes that emerged from the intervention endorse the approach taken, and also highlight the beneficial role that patient education can play in the long term care of patients with RA. Future research could evaluate this novel education intervention in a larger scale and more ethnically diverse setting, with the ultimate goal of integrating the programme into a routine care package for patients with RA.

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