Symptom complexes at the earliest phases of rheumatoid arthritis: a synthesis of the qualitative literature.

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Abstract

Objective: Understanding the features and patterns of symptoms that characterise the earliest stages of rheumatoid arthritis (RA) is of considerable importance if patients are to be identified and started on treatment early. However, little is known about the characteristics of symptoms at the onset of a disease that eventually progresses to RA.

Methods: A systematic review of qualitative peer-reviewed publications was conducted to identify the earliest symptoms associated with the onset of RA. 1736 abstracts were searched to identify relevant publications. Twenty-six publications were identified assessed for quality and subjected to analysis informed by thematic and grounded theory frameworks.

Results: Several interacting themes describing the early symptoms of RA were identified including swelling, pain and tenderness, stiffness, fatigue and weakness and the emotional impact of symptoms. For each symptom, different and evolving intensities were described, in some cases patterns of symptoms onset and symptom complexes at the onset of RA were highlighted. Importantly, this review has highlighted major deficiencies in the literature. None of the studies reviewed originally aimed to explore symptoms at RA onset (often discussions about symptom onset were secondary to the study's primary aim). Also, many of the articles identified sampled people diagnosed with RA many years previously, making their recollection of symptom at onset less reliable.

Conclusion: In order for clinicians to fully understand the earliest phases of disease the nature of symptoms at onset needs to be understood. The current work represents a useful starting point but this area needs further qualitative investigation. This should be followed by quantitative explorations of symptom clusters and their associated features.

Significance and Innovations

This systematic review of the qualitative literature identifies what is currently known about the symptoms, and patterns of symptoms, that characterise the earliest phases of RA, in particular swelling, pain and tenderness, stiffness, fatigue and weakness and the emotional impact of symptoms.

Importantly, this review also highlights the major deficiencies in the current literature and that additional qualitative research focused on exploring the nature of symptoms in the earliest phases of RA is needed.

Introduction

The rapid identification of patients with rheumatoid arthritis (RA) is vital. Irreversible joint damage can occur during the early stages of disease and the first three months following symptom onset represent a critical therapeutic window during which time drug treatment is particularly effective at controlling synovitis and limiting long term joint damage.(1-4) Recognising this, algorithms have been developed and validated to predict the development of RA in patients with newly presenting unclassified arthritis.(5;6) In addition, the 2010 ACR/EULAR classification criteria for RA have been developed to facilitate the early identification of patients with inflammatory arthritis requiring disease modifying therapy.(7) Typical features of established RA, including joint pain and swelling (with a characteristic joint distribution), and morning stiffness are key features of these predictive algorithms and classification criteria.

As attention is focussed on ever earlier phases of RA, it has become increasingly clear that for many patients there is a prodromal phase associated with joint pain, and sometimes the presence of autoantibodies, before the development of clinically overt synovitis.(8) The nature of symptoms during the earliest phase of disease can influence how quickly patients present to professionals and are started on disease modifying treatment.(9) However, the full symptomatology that characterises this phase, and the phase of early unclassified arthritis, has not been well studied. Cohort studies addressing these phases typically capture and report data on a limited number of symptoms known to be associated with established RA (for example joint pain, joint swelling and morning stiffness). In doing this, it is possible that key symptoms and symptom complexes, specific to these early phases and thus potentially relevant to the prediction of outcome, and treatment outcomes, are overlooked. The fact that the synovium is histologically normal in patients with joint pain and ACPA positivity,(10) suggests that pathological processes operating during this phase may be different to those operating in established RA; the symptoms associated with these phases may also be different.

The importance of understanding the initial symptoms and symptom complexes in patients with a new onset of a disease that will evolve into RA has been highlighted in several recent reports including the EULAR Study Group on Risk Factors for RA.(8;11) To address the symptomatology of the earliest phases of RA in a systematic way, the full range of symptoms experienced by patients with RA at the onset of their disease needs to be explored in a qualitative manner. Qualitative data can then be used to inform the development of questionnaire items for use in quantitative studies. The recent emergence of "fatigue" as a key disease outcome measure in established RA is testament to the importance of exploring the patient's perspective in the context of the symptomatology of RA, and to the fact that relying on expert health professional opinion in the absence of patient opinion can lead to important symptoms being overlooked.(12)

We have systematically reviewed published qualitative research exploring patients' experiences of the symptoms of RA at the onset of their disease. Our synthesis of these data highlights what is already known about this area and importantly identifies the deficiencies in the current literature, emphasising where further research is needed.

Materials and methods

Inclusion criteria

Qualitative studies using an interpretative paradigm to understand the descriptions of symptoms experienced by adults (>18 years) at RA onset were included. The definition of symptoms used in this search was physical or psychological signals that indicated a change from normal functioning or health, or indicated the presence of illness. The search was restricted to English language peer reviewed publications.

Search strategy

The search was restricted to peer-reviewed published articles. Abstracts were excluded as quality indicators were frequently not included in abstracts and primary data (i.e. quotations from participants) were presented in only a very limited way, if at all. The following databases were searched to identify relevant papers: Ovid MEDLINE (Pubmed;1950 – June 2012), CINHAL (1937 June - 2012) and PsycINFO (1806 – June 2012). The search terms presented in Table 1 were used. When multiple publications of the same data reporting similar findings were identified, one exemplar publication was selected.

Analysis

Selected publications were critically assessed for methodological quality using established criteria.(13;14) As with other published syntheses we chose an inclusive strategy, evaluating all studies that contributed relevant data.(15;16) Detailed information about the aims, sample, methodologies and quality indicators of the included studies is shown in Table 2. Each article was initially independently coded by MS and RJS. Initial coding was applied to first order constructs, where the initial coding of participants' quotations were undertaken, and to second order constructs, where the key findings and interpretations of the papers' authors were coded. Coding of first and second order constructs were extracted and used to describe the relevant themes in each article. All initial codes were categorised and labelled under broad headings. To develop reliable and broader themes, the initial independently derived codes were triangulated between researchers (RS, MS and KR). Coding categories that lacked concordance were discussed and finally absorbed into the overall coding framework. Concepts that were common across studies were identified and summarised, and subsequently grouped according to overarching themes. These were rechecked by MS and RJS, who re-read all relevant articles, adjusted themes and also incorporated illustrative quotations.

Results

The search strategy identified 1736 peer reviewed publications (excluding duplicates). The abstracts of all articles were read to identify papers potentially meeting the inclusion criteria. Subsequently, 91 abstracts were identified as potentially relevant, and each article was read in full MS and RJS. Twenty-six publications were included in the final analysis (see Table 2). Most studies were from either Europe or North America. The majority of participants sampled across individual studies were female, with some studies exclusively focusing on the perspectives of females with RA. Importantly, no studies had, as their primary aim, the exploration of symptoms at the onset of RA. In addition to this, most studies explored issues surrounding the onset of symptoms many years after participants had been diagnosed with RA. The methodological quality of the majority of articles reviewed was high. Methods included in-depth methods and validity checks including blind coding and respondent validation. Only three studies reported no checks on the validity of the data collected (see Table 2, column 6).

Themes:

Five major themes were developed describing the physical and, to a lesser extent, the psychological symptoms experienced at the onset of RA: [1] Swelling. [2] Pain and tenderness. [3] Stiffness. [4] Fatigue and weakness. [5] The emotional impact of symptoms.

Concepts which cut across all these "symptom" themes were: [1] Descriptors of the intensity of each of these symptoms and their speed and pattern of onset. [2] Complexes of symptoms, either occurring together from onset or gradually accumulating over time. In addition, there were frequent descriptions of the development of symptoms following pregnancy, functional impairment associated with early symptoms and the impact of early symptoms on social relationships and work. These are not systematically reported here as we regarded them as reflecting the causes and consequences of symptoms rather than being symptoms themselves.

Theme 1: Swelling

Swelling was described as the joint becoming "puffed out".(17;18) The feet and hands were most often affected.(18;19) Swelling was often described as severe; one woman found the swelling in her feet was so bad at the onset of RA that she had begun to wear her husband's slippers.(20) The impact of swelling in the small joints was often described in the context of its effect on day to day activities such as walking, gripping, writing and cooking.(18)

"*I couldn't even make the chapatti. The swelling had gone really worse and I thought I have to go to the GP."*(21)

"My feet began to swell and my hands began to swell. I couldn't hold a pen, I had difficulty getting between machines and difficulty getting hold of small things."(18)

"Aware of swelling to fingers of the right hand . . . . . waited two weeks to see if condition improved."(22)

"I noticed that my feet and ankles started to swell and I thought, I am doing too much walking."(21)

"Then one day, all of a sudden my joints all swelled up. All over. And they were so tender and horrible. My legs swelled up and my hands were so sore I couldn't touch anything. When my feet swelled up, I finally went to the doctor."(17)

Bury highlighted that that symptoms (such as swelling and pain) often "creep up", with a transition from trivial symptoms to severe symptoms associated with significant functional impairment.(17;23;24)

"To begin with I thought I had sprained my wrist, 'cos my wrist went as you normally do if you sprain it, it hurt and it became swollen a little bit, so I stuck a wrist strap on it and carried on. It did not get any better for a week and a half, but then the swelling started from the wrist into the back of the hand. . ... and that all swollen up until it got quite large. Now, at that stage, I thought well I had better go up and see the doctor."(25)

In some cases, it was reported that other symptoms (such as pain) were present before swelling occurred.(25-28) For example, the quotation below suggests that the individual was experiencing problems before their swelling appeared.

"I think I probably would have tolerated it for a while. . . I was trying to figure out what was going on because I had been seeing my physiotherapist on a regular basis and, I finally noticed myself one night that my legs seemed swollen, which kind of said to me, you know: 'Is there a blood pressure thing going on here, or what's going on here'?" (26)

However, this was not always the case, in some instances it was suggested that swelling occurred first, and that joint pain occurred later (19;21).

"My fingers all of a sudden started to swell. Then gradually these became very painful. I thought it was because of the heat. It was summer time, and you know how your feet swell sometimes and that was my thought."(21)

Theme 2: Pain and tenderness

Where the onset of RA symptoms was slow, descriptors such as "diffuse", "gradual" or "episodic" were used to describe symptoms.(24;29) In these circumstances, pain was often described as "mild", "vague", and "non-disabling" making it very difficult for people to understand its cause (with some attributing their symptoms to exertion or minor trauma).(30;31) The vagueness of symptoms was emphasised, with symptoms being described as "everyday aches and pains" (25;30;32) or "twinges".(17;33) These early symptoms were described as a nuisance (23) but usually became more severe and were then associated with functional impairment.(17;21;23;27;33)

"It was harrowing. When I got up in the morning my feet were so painful I couldn't stand on them. I would slide out of bed and with my elbow and rump get into the bathroom. I learned to turn the faucets with my elbows."(34)

Whilst pain sometimes came on insidiously, a rapid onset was also often reported.(17;18;25-27;33) Rapid onset symptoms were described as "new resistant", "severe", "abnormal" and "debilitating".(26;35) A rapid onset of pain was often associated with the onset of additional symptoms and led to rapid help seeking.(29) The suddenness and extreme nature of RA onset in some patients was described as a "light switch" or being "cut off".(36)

"My illness started like someone turned a light switch on one day. All I can remember, it was like a light switch went off."(36)

"In my case, I guess if it was a real gradual thing it wouldn't be so bad, but like it was it was pretty hard to take just to be cut off all at once like I was. The last day that I worked out there I never felt better in my life. And the next day I never felt worse in my life... It just, it was pretty hard to take."(36)

In such situations, severe pain was described with descriptors such as “unbearable” or “overpowering”.(21;36) One person likened the pain to “bone cancer”,(25) and another believed the origin of the pain was a broken or chipped bone.(23)

“Well at first I thought I'd broken, chipped the bone in the finger, with it being a knuckle. I thought, I bet I've banged it, really, because I do bang my hands a lot sometimes and I thought I'd chipped it and I thought, ‘oh it'll go off’ ” (23)

“It was crazy, I used to cry with the pain that’s how bad it was.”(21)

“I just found that I was in the most intense pain I've ever been in.” (19)

In some cases symptoms were transient (palindromic) in nature,(18;33) with some patients describing intermittent episodes of intense pain.(31) Migratory pain was also described.(19)

“The next morning I had an awful pain in my shoulder. However, eventually it went away and during the next twelve months I had a travelling rheumatism, all round the joints.”(19)

Pain was described in a number of locations, most frequently in the feet (including the balls of the feet and toes)(22;28;28;34;35;37) and hands.(22;34;35) Symptoms in the large joints (shoulder, knee, elbows and hip pain) were described less frequently.(22;28)

It was noted that eight studies described the onset of RA symptoms or severe aggravation of early RA in the postnatal period.(17;21;22;28;30;33;35;38)

Theme 3: Joint stiffness

General stiffness was less commonly described across the literature, and where it was described descriptions were brief.(24) Also, there were no descriptions of the meaning of stiffness, nor were attempts found to deconstruct the concept of stiffness at RA onset. On occasions, stiffness was briefly mentioned in combination with other symptoms such as “fatigue, morning stiffness and swollen knee”.(33) At onset, stiffness was a symptom which could be bothersome at night because it prevented sleep.(21)

“I stayed with a family, and in London they did so many things with us. But I noticed only afterwards how much stiffness and rigidity there was.”(39)

Aches and pains in the morning were described by a person in Griffiths and Carr’s paper, however, the word “stiffness” was not specifically used.(19)

"In my own mind I knew I had something like that, because my joints were aching and creaking, and I was full of aches and pains in the morning when I got up." (19)

However, in three papers stiffness was a specific problem for patients.(20;26) In these cases stiffness was notable because it was localised to a specific area of the body for example the shoulder or neck.(20;31) In another instance, palindromic episodes of stiffness and swelling were described.(28)

"I didn't really notice that I had symptoms. I had a stiff shoulder. . . I had a heavy coat. . . I had trouble getting it on and off . . . my daughter had helped me taking it off already but I needed to get it back on."(26)

"I went to the doctor because I had a stiff neck, and she said: "oh I think it's to do with your neck.", so she gave me pain killers. And 6 weeks later I went back again no difference, still in terrible, terrible pain."(20)

Theme 4: Fatigue and weakness

A general sense of weakness was described by some people at the onset of RA.(28) Some described generalised "flu like" symptoms but were not explicit about the specific symptoms that comprised this experience.(40)

In addition, descriptions of weakness in the affected limb and fatigue were identified.(17;19;21;33;39;41) Stamm described the experience of a person who was suddenly unable to lift his tray in the canteen, and he was unable to drive home that day.(39) Others described only noticing the increasing weakness after being unable to undertake routine daily activities, one person dropping a number of bowls while preparing dinner, and another described being unable to lift a baby.(21) In other instances when weakness was mentioned, it was suggested to be a mild problem.(25)

"As months went by I noticed that I couldn't lift my baby very well. It was difficult to dress and feed her."(21)

"First noticed there was a problem, there was a weakness in the hands. Just slight weakness."(25)

Hewlett described fatigue as a very important symptom at the onset of RA.(41) For one person weariness was one of the most significant problems faced at the onset of symptoms.

But what I do remember about the beginning of the rheumatoid arthritis was the massive weariness being almost, almost the biggest symptom."(41)

In addition sleep disturbance was a common feature and may have aggravated the symptoms of fatigue. People described symptoms interfering with and preventing sleep (21;19).

"When I noticed it was preventing me doing things and it interfered in my sleep, it woke me during the night, then I thought, gosh, this is not right, something needs to be done about this."(21)

"I must have woken in the middle of the night with a vicious pain in my right elbow, which travelled down my fingertips and I just couldn't sleep: I just walked the floor."(19)

"It used to take me a good couple of hours before I could do anything really. It was keeping me awake at night."(21)

Theme 5: Emotional impact

The emotional impact of symptoms at the onset of RA was noted in several studies.(19;29;32;33;42) For some, the symptoms were associated with feelings of depression and suicidal thoughts, while others described anger or feelings of fearfulness.

"I used to get real, real depressed. Very depressed. And there were times I would just lay in bed you know thinking, you know, well what is wrong with me."(29)

"I felt suicidal before I came in here; I didn't know what to do with it. I think it was more I didn't know what it was."(19)

Yoshida suggested that when the onset of symptoms was rapid that feelings of fear were greater.(32) In the early stages of RA where the onset of symptoms was slow, uncertainty about the significance of symptoms was described. Bury described how an insidious onset and fluctuating symptoms created ambivalence and indecision.(28) Others suggested that the ambiguity and vagueness of symptoms was related to uncertainty and in some cases emotional upset.(31;32)

"I went through the whole summer not well, sick and I'd keep going back to the doctor and she couldn't figure out what was wrong with me and I was getting upset with it."(32)

For those experiencing high levels of uncertainty or uncertainty over a long period of time the eventual diagnosis of RA provided some relief,(32) validating the symptoms experienced, and confirming that they had physical origins.

"I was relieved to know that it was not in my mind [laugh], that I was not going crazy."(32)

Discussion

Understanding the features and patterns of symptoms that characterise the earliest stages of RA is of considerable importance. Primary care physicians, for whom patients with articular / peri-articular pain make up a considerable proportion of their workload, need to be able to identify symptoms and patterns of symptoms which most accurately predict the development of RA and which should guide decisions about further investigation and referral to Rheumatologists. Even within secondary care, the ability to predict the development of RA in patients at risk is an important aim and an understanding of the role of patients' symptoms in this process needs detailed consideration.

In this review we have identified five major symptoms describing patients' experiences at the onset of their RA. For each of these symptoms, different and frequently evolving intensities were described, different patterns of symptoms were described (rapid onset and gradual onset, gradually progressive and palindromic) and different complexes of symptoms, at onset and during evolution were noted. However, perhaps most importantly this review has highlighted major deficiencies in the current literature in relation to this area. We were able to identify only a small number of relevant qualitative papers. Importantly, none of the studies set out specifically to examine the full depth and breadth of initial symptoms, their nature, evolution over time and the coexistence of symptoms in symptom complexes. Furthermore, characteristics of patients included in the studies were often poorly described, men were significantly underrepresented and few participants were from non-Caucasian populations. These issues are important as socio-demographic differences in the experience of illness have been reported, for example, people from different ethnic backgrounds have been shown to experience illness in different ways.(43) Interestingly people with RA from a South Asian background delay in seeking help for longer than white British patients.(21) Whether this is because of a different initial symptom experience or because their response to those symptoms differs has not been fully elucidated. One of the most important deficiencies in the current literature is that patients were frequently interviewed many years after the onset of their RA when their recollections of initial symptoms may have been poor or coloured by more recent symptom experiences. Ideally, explorations of early RA symptoms should be carried out in patients shortly after a diagnosis of RA. In addition, exploring symptom experience in symptomatic individuals at risk of RA, may help to avoid the drawbacks of retrospective data and help to fully characterise the range of initial symptoms at different phases of disease.

We note that symptoms occasionally reported by patients with established RA (e.g. numbness,(44) tingling,(45) jaw pain (46) and symptoms of restless legs and leg cramps (47;48)) were not found in the literature included in this review which focussed on disease onset and the presence of these should be explored in further qualitative work. A systematic review of the symptoms of established RA has yet to be undertaken, however, it is important to consider the symptoms identified in the present review in relation to

the symptoms that are recognised to be associated with established RA. Particular symptoms of established RA have been identified as being indicators of disease activity and for distinguishing RA from other inflammatory arthritides. Thus joint swelling, tenderness and pain are key features of disease activity measures and of measures to assess change in disease activity.(49-51) Furthermore, the patient perspective has highlighted fatigue as an important disease activity indicator.(41;52) However, whilst disease activity measures capture information on clinically important symptoms they do not, and are not intended to, capture the breath of symptoms which an individual with established RA may experience. Work to define a flare of established RA has identified a broader range of symptoms which characterise periods of worsening disease activity including sleep disturbance, systemic disturbance, stiffness, emotional distress and reduction in functional and participation.(53-55) Furthermore, classification criteria for RA have incorporated a range symptom related characteristics including morning stiffness and joint swelling (1987 ACR criteria) as well as joint tenderness (2010 ACR/EULAR criteria).(7;56) Classification criteria aim to distinguish patients with one condition from those with another and so will include only the most discriminatory symptom variables rather than the totality. However, these comparisons do illustrate that many of the symptoms identified in early disease are also key features of established RA.

Once results from formal qualitative studies of the emergence of symptoms in people at risk of RA, and those with a new-onset of disease are available, these can be used to inform the development of a 'symptom questionnaire' to assess the frequency of symptoms and their evolution in individuals at risk of RA. Through this approach, refinement of algorithms for use in secondary care to predict RA development in patients with unclassified arthritis (57) and patients with inflammatory joint symptoms and RA related autoantibodies (58) may be achieved. Importantly, tools also need to be developed for use in primary care to direct management pathways including determining which patients with joint related symptoms should be investigated (e.g. with autoantibody testing or imaging) and who should be referred to a rheumatologist.(59) The patient's history is readily available and cheap. Maximising value from this history and assessing the predictive utility of its components in the earliest phases of RA can only be achieved once these components are fully understood.

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Table 1. Search terms used for systematic synthesis

Symptom(s), OR Onset, OR Early OR Fatigue OR Pain OR Stiffness OR Swelling	AND	Arthrit* OR Rheumat* OR Synovitis	AND	Qualitative

Table 2: Summary of papers identified through the systematic search which met the criteria for this systematic synthesis and from which data were extracted

Reference	Country	Aim of the paper	Sample characteristics: (1) number (2) gender (3) Disease duration (4) Definition & diagnosis of RA	Qualitative method and analysis used	Quality check
Backman et al; 2007 Ref no. 35	Canada	To explore the impact of chronic inflammatory arthritis on parenting and to develop a conceptual framework for subsequent study of mothering.	1. Six participants with RA (six participants with other inflammatory arthropathies were also sampled) 2. Six women 3. Not specified for the six patients with RA (overall range for the 12 patients was 3 to 40 years) 4. Rheumatologist's diagnosis (use of classification criteria not reported)	In-depth semi-structured interviews, analysed using grounded theory.	Transcripts were independently reviewed by two researchers. Member checking was undertaken with one participant checking results.
Bernatsky et al; 2010 Ref no. 40	Canada	To identify barriers to optimal care for individuals with RA.	1. Eighteen participants with RA (fifty four healthcare professionals were also sampled) 2. Thirteen women 3. Not reported 4. Rheumatologist's diagnosis (use of classification criteria not reported)	Structured focus groups analysed using content analysis (analysis reported to also draw on grounded theory principals).	Transcripts were independently coded, also the results were view by stakeholders to confirm validity.
Brown & Williams; 1995 Ref no. 31	UK	To explore women's experiences of RA.	1. Seven participants 2. Seven women 3. Not reported 4. Sample consisted of in-patients admitted due to the symptoms of RA (use of	Conversational interviews guided by an interview schedule. Data were interpreted using narrative analysis.	None reported.

			classification criteria not reported)		
Bury; 1982 & 1988 Ref no. 23 & 28	UK	To explore the problems of recognition and challenges in life situation and relations occasioned by the development of RA.	1. Thirty participants 2. Twenty-five women 3. Participants were new referrals to secondary care (exact disease duration not reported) 4. A "definite diagnosis [of RA] was ... confirmed" in twenty nine patients (use of classification criteria not reported)	Semi-structured interviews with follow-up interviews. Analysis informed by narrative approaches.	Themes uncovered were validated against theoretical models.
Dilby 1996 Ref no. 36	USA	To explore the nature of suffering in people with RA.	1. Fourteen participants 2. Nine women 3. Range 6 months to 35 years from time of diagnosis 4. Physician's diagnosis (use of classification criteria not reported)	The interview process was described as an "intense interview strategy" with follow up interviews. The analysis was informed by grounded theory.	Two researchers examined the data to establish reliability and consistency in coding. Findings were validated and confirmed with the informants through the second telephone interview.
Fair; 2003 Ref no. 42	USA	To investigate explanations of RA from women's perception of the illness experience and providers'	1. Seventeen participants 2. Seventeen women 3. Not reported 4. Physician's diagnosis (use of classification criteria not reported)	Semi-structured interviews supported by field notes. Thematic analysis and framework approaches drawn upon.	Member checking: participants were sent copies of the explanations of RA. Dependability

		understanding of disease.			or reliability of the study maintained by audit trail reviewed by four independent researchers.
Griffith & Carr; 2001 Ref no. 19	UK	To explore the experiences of coping with RA.	1. Not reported 2. Not reported 3. Not reported 4. Not reported	In-depth interviews. Method of analysis not reported.	None reported.
Hewlett et al; 2005 Ref no. 41	UK	To explore the concept of fatigue as experienced by RA patients.	1. Fifteen participants 2. Twelve women 3. Range 1.5 and 30 years (mean 12.6 years) from time of diagnosis 4. 1987 ACR classification criteria for RA fulfilled	Face to face semi-structured interviews. Analysed to establish themes grounded in data.	Interviews were transcribed individually by two researchers independently. Five random transcripts were analysed independently by two external researchers. Codes were also reviewed by a steering committee.
Hwang et al; 2003 Ref no. 38	South Korea	To explore and describe the illness experience of women with RA.	1. Five participants 2. Five women 3. Range 4 to 12 years (mean 7 years) 4. Participants were diagnosed with RA in secondary care (use	Informal unstructured interviews were undertaken. Phenomological analysis of data.	Member checking: participants checked the transcripts to ensure that an

			of classification criteria not reported)		accurate representation of their experience was gathered.
Kumar et al; 2010 Ref no. 21	UK	To assess the reasons underlying delay in consultation in RA patients from a South Asian background.	1. Ten participants 2. Nine women 3. Participants were newly presenting to secondary care with RA 4. 1987 ACR classification criteria for RA fulfilled	Face to face in-depth semi-structured interviews analysed using grounded theory analysis .	Member checking: by providing participants with a verbal summary of the areas covered and themes identified in the interview.
Lempp et al; 2006 Ref no. 20	UK	To explore direct personal experiences of living with RA and the impact of the illness upon patients' lives..	1. Twenty six patients 2. Twenty-two women 3. Range 1 to 29 years (Mean 10 years) 4. Participants were secondary care patients with RA (use of classification criteria not reported)	Face to face in-depth semi-structured interviews. Analysed using content analysis.	Plausibility of accounts judged by authors, cross-referencing of themes with an independent researcher.
Neill; 2002 Ref no. 24	Australia	To explore patterns in the life stories of women living with RA.	1. Three participants 2. Three women 3. Range 19 to 38 years symptom duration 4. Not reported	Four face to face unstructured interviews with each participant, supported by photos, field notes and telephone calls. The analysis drew on pattern and theoretical analysis techniques.	Repeated interviewing to explore concepts in depth and validate initial interpretations.

Nyman & Lützen; 1999 Ref no. 30	Sweden	To identify the caring needs of women with RA undergoing acupuncture treatment.	1. Six participants 2. Six women 3. Range 4 to 26 years (median 11 years) from time of diagnosis 4. Rheumatologist diagnosis (use of classification criteria not reported)	Twenty semi-structured interviews over a period of 11 week, conducted during acupuncture sessions. Data were analysed using content analysis.	Author suggested that data were validated but the method of validation was not explained.
Oliver et al; 2008 Ref no. 22	UK	To explore the experiences of those with RA in order to understand the impact on the individual and on healthcare resources.	1. Twenty-two participants 2. Sixteen women 3. Three years or less from time of diagnosis 4. Participants were asked to confirm with a healthcare professional that they had sero-positive RA (use of classification criteria not reported)	Telephone semi-structured interviews, analysed using thematic analysis.	Process maps were transcribed into individual participant maps and returned to the participant for verification and alteration. Themes reviewed by research team.
Sakalys; 1997 Ref no. 29	USA	To explore pre-diagnostic illness behaviour in RA.	1. Fifty participants 2. Fifty women 3. Two years or less from time of diagnosis 4. 1987 ACR classification criteria for RA fulfilled	Structured interviews. Data were analysed using content analysis.	Inter-coder agreement was checked periodically.
Sheppard et al; 2008 Ref no. 25	UK	To explore people's beliefs, feeling and actions at the onset of RA to gain insights into	1. Twenty-four participants 2. Ten women 3. Fourteen months or less from the time of diagnosis 4. 1987 ACR classification criteria for RA fulfilled	In-depth semi-structured interviews. Analysis followed a grounded theory approach.	Blind and independent coding. Self-selecting participants were sent a

		the factors that influenced their decision to consult.			summary of the interview.
Schneider et al; 2008 Ref no. 27	South Africa	To explore a range of experiences including onset of disease, treatment, environmental barriers and facilitators, employment, and social inclusion.	1. Sixty participants 2. Sixty women 3. Range 1 to 26 years (or more) since time of diagnosis 4.1987 ACR classification criteria for RA fulfilled	Semi-structured in-depth interviews. Analyzed using a basic thematic analysis approach.	Data were transcribed and translated by the research assistant who did the interviews.
Shaul: 1995 Ref no. 17	USA	To explore how women manage RA and the demands of their everyday lives.	1. Thirty participants 2. Thirty women 3. Eighteen years or less from time of diagnosis. 4. "Definite, classical or probable RA" as assessed by a Rheumatologist	Semi-structured interviews, analysed using constant comparative methods.	Interview guide assessed for face validity by two women with RA. Independent coding of a sample of transcripts.
Shaul; 1997 Ref no. 33	USA	To explore the transition of women experiencing RA.	1. Thirty participants 2. Thirty women 3. Eighteen years or less from time of diagnosis. 4. "Definite, classical or probable RA" as assessed by a Rheumatologist	Semi-structured interviews, analysed using constant comparative methods.	Interview guide assess for face validity by two women with RA. Independent coding of a sample of transcripts.

Stamm et al; 2008 Ref no. 39	Austria	To explore the life story of people diagnosed with RA.	1. Ten participants 2. Eight women 3. Not reported 4. Attendees at a rheumatology out-patient clinic (use of classification criteria not reported)	Repeated narrative interviews, analysed using a narrative biographic method. qualitative approach.	Self-reflection and debriefing were undertaken and findings were discussed with co-authors.
Townsend et al; 2010 Ref no. 26	Canada	To identify ethical challenges in the early RA experience.	1. Eight participants 2. Not reported 3. Twelve months or less from time of diagnosis 4. Physician's diagnosis (use of classification criteria not reported)	In-depth interviews, including follow up interviews. Constant comparisons and thematic analysis.	Blind and independent coding of transcripts.
Weiner; 1975 Ref no. 34	USA	To explore the management of pain in RA.	1. Twenty-one participants 2. Not reported 3. Not reported 4. Not reported	Interviews and observational data were collected. Analysis informed by grounded theory.	None reported
Williams; 1984 Ref no. 18	UK	To explore the way in which beliefs about the aetiology of arthritis can be understood in terms of narrative reconstruction.	1. Thirty participants 2. Nineteen women 3. Five years or more 4. Not reported	In depth semi-structured interviews. Analysis informed by narrative approaches.	Themes uncovered were validated against theoretical models.
Williams & Graham; 2012	UK	To explore patients' experiences of foot problems	1. Twenty-two participants 2. Sixteen women 3. Mean 15 years for females and 13 years for males.	Focus groups facilitated by a researcher. Analysis of data	The focus transcripts were read and verified by one

Ref no. 37		associated with RA.	4. Rheumatoid Arthritis according to 1987 ACR classification criteria	was informed by thematic analysis.	participant from each focus group.
Yoshida; 1996 Ref no. 32	Canada	To explore various forms of uncertainly among people with RA.	1. Forty-six participants 2. Thirty-two females 3. Range 18 months to 53 years (mean 13.5 years) 4. Participants were members of the consultation and therapy service of the arthritis society (use of classification criteria not reported)	In-depth semi-structured interviews. Data was analysed using a constant comparative approach and grounded theory methods.	The coding scheme was developed by and refined by two researchers.