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The effectiveness of nurse-led care in people with rheumatoid arthritis: A systematic review

Authors:

Mwidimi Ndosi,¹ Karen Vinall,¹ Claire Hale,^{1,2} Howard Bird,³ Jackie Hill,¹

1. Academic & Clinical Unit for Musculoskeletal Nursing, Leeds Institute of Molecular Medicine, University of Leeds, Leeds, UK.
2. School of Healthcare, University of Leeds, Leeds, UK
3. Section of Musculoskeletal Disease, Leeds Institute of Molecular Medicine, University of Leeds, Leeds, UK

Corresponding Author:

Mwidimi Ndosi

Academic & Clinical Unit for Musculoskeletal Nursing, Section of Musculoskeletal Disease, 2nd Floor, Chapel Allerton Hospital Chapeltown Road, Leeds, LS7 4SA, United Kingdom
Tel: +441133924859, Fax: +441133924755 E-mail: M.E.Ndos@Leeds.ac.uk

What is already known about this topic?

- In the UK and many Western countries, Nurse-led care model has been deployed in primary care and in the management of chronic diseases.
- In several chronic diseases such as diabetes, chronic heart diseases and chronic obstructive pulmonary disease, nurse-led care has been shown to achieve health outcomes that are as good as those of doctors, and patients are satisfied with their care.
- In the UK, nurse-led care is established in the rheumatology outpatient services and it provides follow-up care to people with rheumatoid arthritis including monitoring, patient education and psychosocial support.

What this paper adds

- Systematic review evidence of effectiveness of nurse-led care in rheumatoid arthritis using a range of patient outcomes

- Meta-analysis showing the pooled effects of nurse-led care on rheumatoid arthritis disease activity and other secondary outcome measures.
- The use of ratio of means as a measure of effect which is easier for clinicians to interpret than the standardised mean differences.

Keywords

Clinical nurse specialist; Effectiveness; Meta-analysis; Nurse-led care; Ratio of means; Rheumatoid arthritis; Systematic review

Abstract

Objectives

The objective of this systematic review was to determine the effectiveness of nurse-led care in Rheumatoid Arthritis.

Design

Systematic review of effectiveness.

Data sources

Electronic databases (AMED, CENTRAL, CINAHL, EMBASE, HMIC, HTA, MEDLINE, NHEED, Ovid Nursing and PsycINFO) were searched from 1988 – January 2010 with no language restrictions. Inclusion criteria were: Randomised controlled trials, nurse-led care being part of the intervention and including patients with RA.

Review methods

Data were extracted by one reviewer and checked by a second reviewer. Quality assessment was conducted independently by two reviewers using the Cochrane Collaboration's Risk of Bias Tool. For each outcome measure, the effect size was assessed using Risk Ratio or Ratio of Means (RoM) with corresponding 95% confidence intervals (CI) as appropriate. Where possible, data from similar outcomes were pooled in meta-analysis.

Results

Seven records representing 4 RCTs with an overall low risk of bias (good quality) were included in the review. They included 431 patients and the interventions (Nurse-led care Vs, Usual care) lasted for 1-

2 years. Most effect sizes of disease activity measures were inconclusive (DAS28 RoM = 0.96, 95%CI [0.90-1.02], P=0.16; Plasma viscosity RoM =1 95%CI [0.8-1.26], p=0.99) except the Ritchie Articular Index (RoM = 0.89, 95%CI [0.84-0.95], P<0.001) which favoured nurse-led care. Results from some secondary outcomes (functional status, stiffness and coping with arthritis) were also inconclusive. Other outcomes (satisfaction and pain) displayed mixed results when assessed using different tools making them also inconclusive. Significant effects of nurse-led care were seen in quality of life, (RAQoL RoM = 0.83, 95%CI [0.75-0.92], P<0.001), patient knowledge (PKQ RoM = 4.39, 95%CI [3.35-5.72], P<0.001) and fatigue (Median Difference = -330, P = 0.02).

Conclusions

The estimates of the primary outcome and most secondary outcomes showed no significant difference between nurse-led care and the usual care. While few outcomes favoured nurse-led care, there is insufficient evidence to conclude whether this is the case. More good quality RCTs of nurse-led care effectiveness in rheumatoid arthritis are required.

1. Introduction

Rheumatoid Arthritis (RA) is a systemic inflammatory disease characterised by the presence of a destructive polyarthritis with a predisposition for affecting the peripheral joints (Hakim et al., 2006). It most commonly presents in the sixth and seventh decades and it is three times more likely to occur in women than men (Silman and Oliver, 2009). The incidence and prevalence of RA vary considerably between geographic areas and over time. The incidence rates in Anglo-Saxon populations have been reported to range between 0.02 to 0.05% (20-50 cases per 100,000) adults in North America (Doran et al., 2002, Gabriel et al., 1999) and Northern Europe (Aho et al., 1998, Riise et al., 2000, Söderlin et al., 2002, Symmons et al., 1994). Southern European countries have reported a relatively lower incidences 0.01 to 0.02% (Drosos et al., 1997, Guillemin et al., 1994) and there are no incidence data from developing countries. The prevalence in Northern Europe and North America ranges between 0.5–1.1% (MacGregor and Silman, 2003, Riise et al., 2000, Silman and Hochberg, 2001), Southern Europe 0.3-0.7% (Andrianakos et al., 2003, Carmona et al., 2002, Cimmino et al., 1998, Saraux et al., 1999, Stojanović et al., 1998), developing countries between 0.1-0.5% (Akar et al., 2004, Darmawan et al., 1993, Pountain, 1991, Silman and Hochberg, 2001, Spindler et al., 2002) and in some rural Africa 0 to 0.3% (Silman and Hochberg, 2001, Silman et al., 1993). Treatment of RA is multi-

disciplinary involving medications, regular follow-up, physiotherapy, joint protection, self-management and psychosocial support.

Increased life expectancy and the rise in chronic diseases in the western world has led to greater demand for health care in both hospitals and the community (Tulchinsky and Varavikova, 2009). This demand has led to innovation in health care where nurses and other allied health professionals undertake extended roles which sometimes include work previously done by doctors, thus allowing a flexible approach to the delivery of care, where the patient is at the centre and the traditional professional boundaries are less important (Richardson et al., 1998). One example of such innovations is nurse-led care.

Cullum et al (2005) viewed nurse-led care as a continuum, with nurses undertaking highly protocol driven focused tasks at one end and responding to far more diverse challenges in terms of clinical decision-making, such as first contact care and rehabilitation at the other. Using the definitions of Nurse Practitioner, Advanced Practice Nurse and Advanced Nursing Practitioner (International Council of Nurses, 2001, NMC, 2005); we defined nurse-led care as a model of care where nurses who practice at an extended role, assume their own patient case loads and perform nursing interventions which include monitoring of patients' condition, providing patient education, giving psychosocial support and referring appropriately. This model of care has been used successfully in other chronic diseases where patients require regular follow-ups and monitoring such as diabetes (Carey and Courtenay, 2007), coronary heart diseases (Page et al., 2005), heart failure (Phillips et al., 2005) and chronic obstructive pulmonary disease (Sridhar et al., 2008).

In the UK, nurse-led care in rheumatology started in Leeds in the late 1980s where patients who had completed their clinical trials and had been returned to the general rheumatology clinics, began seeking further consultations with the nurses (Bird et al., 1980, Hill, 1985). Nurse-led clinics ran alongside rheumatologists' clinic and they provided follow-up care for stable patients giving patient education, advice and support. This model of care was replicated throughout the UK where rheumatology centres employed clinical nurse specialists and their role included drug monitoring, education of staff, patient education and counselling (Phelan et al., 1992).

Despite this innovative development, the evidence of effectiveness of nurse-led care in RA is limited. A search of the Database of Abstracts of Reviews of Effects (DARE), Health Technology Assessment (HTA) Database, Cochrane Database of Systematic Reviews (CDSR), NHS Economic Evaluation

Database (NHSEED) and Medline produced no systematic review of nurse-led care effectiveness in RA. Yet there were several systematic reviews of effectiveness in primary care (Horrocks et al., 2002, Laurant et al., 2004) and other chronic diseases (Carey and Courtenay, 2007, Page et al., 2005, Phillips et al., 2005, Sridhar et al., 2008, Taylor et al., 2005).

The objective of this current systematic review was to determine the effectiveness of nurse-led care in patients with RA. Effectiveness is defined as the extent to which an intervention produces an outcome under ordinary day-to-day circumstances and one way of assessing effectiveness of an intervention is comparing the intervention in question to another well-established intervention (Higgins and Green, 2009). The effectiveness of any intervention is said to be determined by 4 factors: i) the populations receiving the intervention, ii) the characteristics of the interventions, iii) the comparator - what the intervention is compared with iv) what outcomes are measured (Guyatt et al., 2008). Therefore we used the “participant-intervention-comparator-outcomes” (PICO) model (Higgins and Green, 2009) to formulate our research question: Are clinical outcomes of nurse-led care for patients with RA similar to those produced by usual care?

2. Methods

We conducted a systematic review in three phases over three years. Phase one was an overview of reviews in order to identify systematic reviews of nurse-led care effectiveness. Phase two was a scoping review which was broad and looked for primary studies of effectiveness of nurse-led care. The search strategy for this phase was developed with a librarian and two reviewers independently screened the titles and abstracts to assess for relevance. Relevant articles were categorised by study design and type of disease. Phase three was a refinement of the methods utilised in phase two, but the population of interest was limited to patients with rheumatoid arthritis. This last phase is reported in this paper. The review utilized methods recommended by the Centre for Reviews and Dissemination (2009) and the Cochrane Collaboration (Higgins and Green, 2009).

Inclusion and exclusion criteria

Our research objective was to determine whether nurse-led care was effective (i.e. produced outcomes that were similar to those of usual care). Therefore, we decided a priori to look for randomised controlled trials (RCTs) because when evaluating the effectiveness of an intervention, results generated by RCTs are likely to be closer to the true effects than the findings generated by

other research methods (Higgins and Green, 2009). Articles were included if they 1) described RCTs 2) included patients with RA 3) compared nurse-led care with any other routine care for RA patients 4) contained patient outcome data and 5) were conducted between 1988 – December 2009 since nurse-led care in the UK developed in the late 1980s (Department of Health Nursing Division, 1989, NHS Management Executive, 1994, United Kingdom Central Council for Nursing Midwifery and Health Visiting, 1992). We excluded articles describing protocols, studies utilizing other methods than RCT and those with only economic data. Although economic evaluations are important in informing cost-effectiveness, this was outside our scope and we focused on effectiveness to ascertain whether nurse-led care achieves the intended clinical outcomes.

Types of participants (P)

We included trials which included adult participants with a diagnosis of RA. The diagnosis of RA was based on the American College of Rheumatology 1987 revised criteria for classification of RA (Arnett et al., 1988). Recently, new (American College of Rheumatology/European League Against Rheumatism) RA classification criteria have been published (Aletaha et al., 2010) to help early identification of patients who are at high risk for persistent or erosive disease.

Types of interventions (I)

The intervention of interest is care delivered by specialist nurses, nurse practitioners or other nurses practising at an extended role. Both supplementation and substitution nurse-led care studies were included. Supplementation studies compare usual care by a doctor to an innovative service provided by a nurse working alongside a doctor. In the substitution studies, a nurse is responsible for providing the same health care as a doctor, and the performance of these two practitioners is compared (in terms of patient's outcomes).

Comparator (C)

Before the advent of nurse-led clinics in rheumatology services in the UK, usual care was provided by the multidisciplinary team led by a rheumatologist or by the general practitioners who managed stable patients in the primary care. Since RCTs of effectiveness would follow pragmatic trial designs (Roland and Torgerson, 1998), the comparators are likely to be the routine, usual or standard care. Therefore we decided to look for studies that compared nurse-led care with any other model of care for RA patients and we labelled this comparator "usual care".

Types of outcome measures (O)

Since there is no single outcome to evaluate disease severity or intervention effectiveness in RA, both objective and patient-reported outcome measures (PROMS) are used in research (Boers et al., 1994, Felson et al., 2005). The primary outcome of interest for this systematic review was RA disease activity while secondary outcomes were: functional status (disability), quality of life, patient knowledge, patient satisfaction with care, coping with arthritis, pain, fatigue and stiffness. Apart from disease activity, coping with arthritis, fatigue and stiffness which are particularly of interest in RA, the other outcomes have been used for assessing nurse-led care effectiveness in other diseases (Moore et al., 2002, Sharples et al., 2002, Sullivan et al., 2006).

Search methods

The following databases were searched: MEDLINE, EMBASE, Cumulative Index to Nursing and Allied Health Literature (CINAHL), Ovid Nursing, Allied and Complementary Medicine (AMED), Health Management Information Consortium (HMIC), PsycINFO, Health Technology Assessment (HTA), NHS Economic Evaluation Database (NHEED) and The Cochrane Central Register of Controlled Trials (CENTRAL) which covers conference proceedings. The search strategy was developed with the help of a medical librarian. The research question was broken down into concepts using the “I” and the “P” elements of the PICO model to help structure the search. Although nurse-led care is delivered by practitioners that use different titles such as nurse practitioner, clinical nurse specialist, advanced practitioner; nurse-led care interventions are indexed under the term “nurse practitioner”. The initial search was conducted using terms describing nurse-led care. The search strategy was later refined by adding the terms that represent the population of interest (patients with RA). The terms for the comparator or the outcomes were not added in the search to facilitate sensitivity of the search. The search was restricted from 1988 – January 2010 and no language restrictions were imposed. The search in MEDLINE used the search terms below.

- 1 (Nurs\$ adj led).mp. [mp=title, original title, abstract, name of substance word, subject heading word, unique identifier]
- 2 (Nurs\$ adj clinic).mp. [mp=title, original title, abstract, name of substance word, subject heading word, unique identifier]

- 3 (Nurs\$ adj directed).mp. [mp=title, original title, abstract, name of substance word, subject heading word, unique identifier]
- 4 (Nurs\$ adj managed).mp. [mp=title, original title, abstract, name of substance word, subject heading word, unique identifier]
- 5 Clinical nurse specialist.mp. or *clinical nurse specialist/ or *nurse practitioner/
- 6 Rheumatology nurs*.mp. [mp=title, original title, abstract, name of substance word, subject heading word, unique identifier]
- 7 arthritis.mp. or exp Arthritis, Rheumatoid/
- 8 RA.mp. [mp=title, original title, abstract, name of substance word, subject heading word, unique identifier]
- 9 1 or 2 or 3 or 4 or 5 or 6
- 10 7 or 8
- 11 9 and 10
- 12 limit 11 to yr="1988 - 2010"

Identification of studies

The results were managed using Endnote X software (Thomson ResearchSoft, 2006) and Microsoft Excel datasheet. Duplicate records of the same reports were removed. One reviewer (MN) read all the retrieved titles and abstracts assessing the relevance of retrieved studies. The articles were selected if they reported RCTs, involved patients with RA and if nurse-led care was part of the intervention. Data were extracted by one reviewer (MN) using Microsoft Excel datasheet and checked for relevance by a second reviewer (KV). Disagreements were resolved by a consensus.

Quality appraisal

Several tools for assessing the quality of RCTs exist (Moher et al., 1995), but most of them contain elements attributable to reporting and design that are not related to bias. The risk of bias tool was developed by the Cochrane Collaboration (Higgins and Green, 2009) to address some of the shortcomings of existing quality assessment tools. The tool asks questions about 6 domains: sequence generation, allocation concealment, blinding, incomplete outcome data, selective outcome reporting and 'other sources of bias', then judgements on the risk of bias (high, low, unclear) are made for each domain. Flaws in these domains have been shown to lead to exaggerated pooled

estimates of treatment effects (Moher et al., 1998, Schulz et al., 1995). Information addressed by these domains was obtained from the published reports and authors were contacted if additional information was required. Two reviewers (MN & KV) assessed the quality of the included studies independently by using the risk of bias tool.

Data synthesis and statistical analysis

Throughout this review, the intervention group was nurse-led care and the control group was usual care. The studies that measured the same outcomes using the same measures were combined in a meta-analysis to obtain a pooled effect size. Results from some of the outcomes could not be pooled because they were assessed using different measures (for example; Hill (1997) used the Leeds Satisfaction Questionnaire to measure satisfaction but Tijhuis et al (2003) used a different questionnaire). In some studies, different measures were used to assess different aspects of the same outcome and it would not be appropriate to combine the results of, for example, disease activity measured by plasma viscosity (Hill et al., 1994, Hill et al., 2003) with those measured by DAS28 (Hill et al., 2003, Ryan et al., 2006, Tijhuis et al., 2002). The outcomes that could not be combined were summarised in a tabular form with corresponding sizes of effect, 95% confidence intervals and P-values where applicable.

In each outcome, an appropriate measure of effect was used to assess the magnitude of the intervention effect. For dichotomous outcomes the risk ratio (RR) was used (Higgins and Green, 2009) and for continuous outcomes the ratio of means (RoM) was used (Friedrich et al., 2008). Ratio of means is the ratio of mean values between the experimental and the control groups.

$$\text{Ratio of Means (RoM)} = \frac{\text{Mean}_{exp}}{\text{Mean}_{cont}}$$

Where subscripts “exp” and “cont” stand for the experimental and the control groups respectively.

Each individual study RoM was converted to its natural logarithm (lnRoM) and its standard error (se[lnRoM]) calculated before being pooled. Values of lnRoM and se[lnRoM] for each study were entered into RevMan software (The Cochrane Collaboration, 2008) and analysed using the

generalised Inverse-Variance method. The pooled result (lnRoM) is then back transformed to obtain a pooled RoM and 95% confidence interval (similar to odds ratio and risk ratio meta-analysis used for dichotomous outcomes). As a measure of effect, the RoM compares favourably to Standardised Mean Differences (SMD) in terms of bias, coverage, and statistical power (Friedrich et al., 2008). However, RoM has an added advantage over SMD due to simplicity of its interpretation. Whereas the interpretation of meta-analysis results using SMD requires the knowledge of Cohen's effect sizes (Cohen, 1988) and pooled standard deviation, the interpretation of RoM is much easier. In most outcomes where lower scores are desirable, the effect size is interpreted as: RoM = 1 for no effects, RoM < 1 favours the experimental (nurse-led care) group while RoM > 1 favours the control (usual care) group. In some outcome measures where higher scores are desirable such as patient knowledge or satisfaction; RoM > 1 favours the experimental group and RoM < 1 favours the control group. Since the ratio is unit-less, RoM can be used to combine related outcomes which are measured using different scales such as pain or quality of life scales.

When results were pooled in the meta-analysis, inter-study heterogeneity was tested and reported as a Chi-square (X^2) statistic with corresponding degrees of freedom (df) and p-values. Heterogeneity is said to be present if X^2 statistic is bigger than its degrees of freedom or if its p-value is significant (Thompson, 1994). In the presence of few studies, X^2 statistic has low power of detecting heterogeneity therefore significance level of 0.10 is used to indicate heterogeneity rather than the usual 0.05 (Fleiss, 1986). Where significant heterogeneity was present, random-effects models were applied due to their advantage in accounting for study-to-study variations otherwise fixed-effects models were used (Fleiss, 1993).

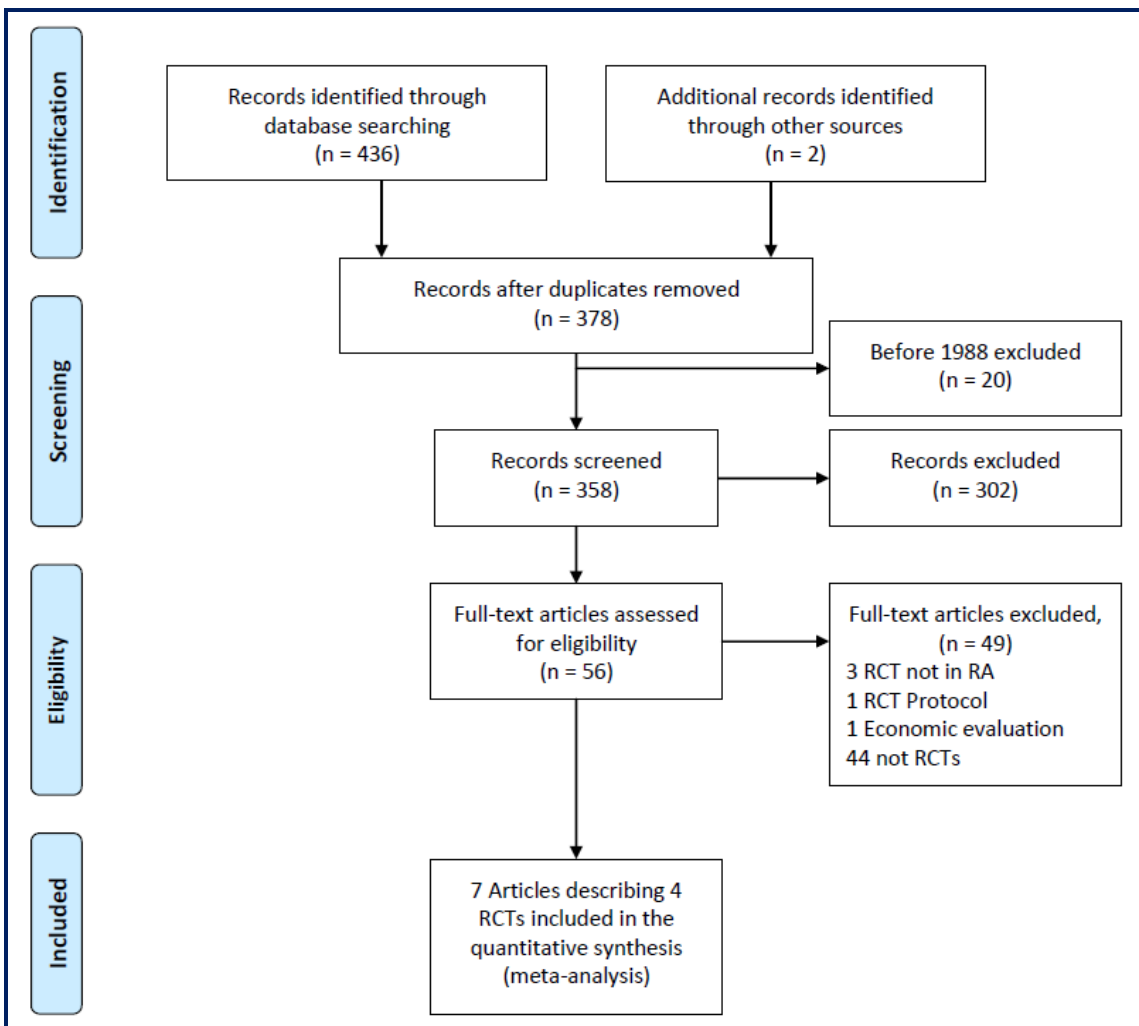
Where the continuous outcomes in the published reports are reported as medians with corresponding P-values, the difference in medians was used as an effect size index as suggested by Green & Salkind (2003). Where only the P-values were reported, authors were contacted to supply other values and if they were unavailable the results are presented by a narrative.

3. Findings

The search results

The complete search output is summarised in figure 1. The search strategy identified 438 publications out of which 60 duplicates were removed and 20 articles published before 1988. A further 302 articles were removed based on titles and abstracts. Full reports were obtained for 56 articles but only 9 described RCTs of nurse-led care in RA, one of which was an economic evaluation and the other a protocol. The remaining 7 articles were retained for the full review.

Figure 1: Study selection flow diagram



Characteristics of included studies

The 7 included articles (Hill, 1997, Hill et al., 1994, Hill et al., 2003, Ryan et al., 2006, Tjihuis et al., 2003, Tjihuis et al., 2003, Tjihuis et al., 2002) represented only 4 RCTs. All studies were conducted in the UK and the Netherlands and the pooled sample size was 431 patients (nurse-led care = 181, usual care = 250). They had a mean age of 57 years, mean disease duration of 8.3 years and a male:female ratio of 1: 3 consistent with the RA population (Symmons et al., 2002). The characteristics of the included studies are summarised in table 1.

Table 1: Characteristics of the included studies

Study ID (Country)	Patients (N)	Interventions	Comparator	Outcomes	Outcome measures	Follow-up period
Hill et al 1994 Hill 1997 (UK)	Patients with RA (70)	Follow-up by rheumatology Nurse Practitioner	Follow-up by a Rheumatologist	<ul style="list-style-type: none"> Inflammatory markers Disease activity Pain Morning stiffness Physical function & Psychological status Patient knowledge Patient satisfaction 	<ul style="list-style-type: none"> Plasma viscosity Ritchie's articular index Pain 1-5 point VAS Minutes Arthritis impact measurement scale (AIMS) Patient knowledge questionnaire (PKQ) Leeds satisfaction questionnaire (LSQ) 	48 weeks
Tjihuis et al 2002 Tjihuis et al 2003 Tjihuis et al 2003 (Netherlands)	Patients with RA (210)	Follow-up by a Rheumatology Clinical Nurse Specialist	Follow-up by an in-patient & outpatient rheumatology teams	<ul style="list-style-type: none"> Functional status Quality of life Disease activity Patient satisfaction 	<ul style="list-style-type: none"> Health assessment questionnaire – Disability Index (HAQ-DI) & Macmaster Toronto Arthritis (MACTAR) RAND 36 & RAQoL Disease Activity Score (DAS28) Satisfaction questionnaire 	104 weeks
Hill et al 2003 (UK)	Patients with RA (80)	Follow-up by a Rheumatology Clinical Nurse Specialist	Follow-up by Junior Hospital Doctors	<ul style="list-style-type: none"> Disease activity Inflammatory markers Morning stiffness (duration) Pain Physical function & psychological status Patient knowledge Satisfaction Fatigue (Duration) 	<ul style="list-style-type: none"> Disease Activity Score 28 (DAS28) Plasma viscosity (PV) Minutes Pain VAS Arthritis Impact Measurement Scale (AIMS) Patient knowledge questionnaire (PKQ) Leeds Satisfaction Questionnaire (LSQ) Minutes 	48 weeks
Ryan et al 2006 (UK)	Patients with RA (71)	Drug monitoring by a Clinical Nurse Specialist	Drug monitoring by a Rheumatology clinic Staff nurse + Standard rheumatologist care	<ul style="list-style-type: none"> Physical function & Psychological status Helplessness (coping with arthritis) Disease activity 	<ul style="list-style-type: none"> Arthritis Impact Measurement Scale (AIMS) Rheumatology Attitude Index (RAI) Disease activity Score 28 (DAS28) 	52 Weeks

The first study (Hill, 1997, Hill et al., 1994) was a 48-week parallel RCT where the outcomes of nurse-led clinic were compared to those of a rheumatologist clinic. Participants were 70 adults with RA with both mild and moderate/severe disease activity (35 nurse-led clinic/35 usual care, mean age = 52 years, male:female ratio = 18:52). Patients on the intervention arm consulted a nurse practitioner who managed their disease including making referrals to other health professionals as appropriate. Patients in the control arm saw the rheumatologist who also continued with normal practice. The outcomes were disease activity, pain and morning stiffness assessed at baseline, weeks 4, 12, 24, 36 and 48. Other outcomes were function, patient satisfaction and patient knowledge assessed at baseline, week 24 and 48.

The second study (Hill et al., 2003) was a 48-week parallel RCT where the outcomes of nurse-led care were compared to those of 4 junior hospital doctors. Participants were 80 adults with RA with both mild and moderate/severe disease activity (39 nurse-led care/41 usual care, mean age = 57 years, male:female ratio = 17:63). The intervention was consultation by the nurse practitioner and the control was consultation by 4 junior hospital doctors. The primary outcome was disease activity assessed at weeks 0, 24 and 48. Secondary outcomes included plasma viscosity, duration of morning stiffness, fatigue, pain, function, patient knowledge and satisfaction assessed at baseline, weeks 24 and 48.

The third study (Tijhuis et al., 2003, Tijhuis et al., 2003, Tijhuis et al., 2002) was a multicentre RCT where outcomes of nurse-led care were compared with those of an in-patient team and a day-patient team. Participants were 210 RA patients who had difficulty in performing activities of daily living in the previous 6 weeks. For this meta-analysis the outcomes of the nurse-led care were compared with those of combined in-patient and day-patient teams (70 nurse-led care/140 usual care, mean age = 57 years, male:female ratio = 52:158). Interventions were consultation by the clinical nurse specialists who provided patient information about RA, prescribed in consultation with a rheumatologist and referral to other health practitioners as required. The inpatient & outpatient teams comprised a rheumatologist, nurses, occupational therapist, physiotherapist and a social worker. Outcomes were functional status, Quality of life and disease activity all assessed at baseline, weeks 12, 52 and 104.

The fourth study (Ryan et al., 2006) compared drug monitoring by a clinical nurse specialist to outpatient clinic nurse monitoring (reporting to a rheumatologist). Participants were 71 adults with

RA who were starting new disease modifying anti-rheumatic drugs at a district hospital (36 nurse-led care/35 usual care, mean age = 58 years, male:female ratio = 31:40). The intervention included assessment for side effects, problems relating to coping with symptoms using Pendelton's model and referral to other health professionals as required. Patients in the control group were monitored by an outpatient clinic staff nurse. The outcomes were function, coping and disease activity assessed at baseline and at 3, 7 and 12 months.

Despite having different types of comparators, these studies had a number of features in common: all assessed the effectiveness of nurse-led care for patients with RA, practitioners giving the intervention were all clinical nurse specialists or nurse practitioners, all patients had RA with varying disease duration and were either attending a follow-up clinic or drug monitoring clinic.

Outcome measures

Prior to 1995, RA disease activity was measured by plasma viscosity which measures the viscosity of blood which is affected by the acute phase proteins (Normal range = 1.50 - 1.72 cP) and Ritchie Articular Index. However, this has been superseded by the Disease Activity Score (DAS28) (Prevoo et al., 1995). This composite score combines single measures into an overall continuous measure of RA disease activity. The DAS28 includes a 28-tender joint count, a 28 swollen joint count, erythrocyte sedimentation rate or C-reactive protein and a general health assessment on a visual analogue scale making it a more valid measure of disease activity than individual measures (Prevoo et al., 1995). DAS28 scores can range from 0 - 9.4 with higher scores corresponding to a high disease activity.

In the included studies, functional status was measured by 3 outcome measures: the disability index of Stanford Health Assessment Questionnaire (HAQ-DI) (Fries et al., 1982), the McMaster Toronto Arthritis patient preference questionnaire (MACTAR) (Tugwell et al., 1987) and the physical and psychological function scales of the Arthritis Impact Measurement Scale (AIMS) (Hill et al., 1990, Meenan et al., 1980). In the HAQ-DI, the domain of disability is assessed by eight categories of dressing, arising, eating, walking, hygiene, reach, grip and common activities. HAQ-DI scores range from zero (no disability) to three (completely disabled). In the MACTAR, patients identify 5 specific activities in which they would most like to have improvement. The scale is scored by assessing changes in the ability to perform these activities from baseline to follow-up. A summary score is created by weighting each change score according to its priority ranking, with the highest ranked

activity's change score multiplied by 5, and the lowest ranked multiplied by 1. Higher positive scores reflect improvement; negative scores reflect worsening. AIMS is a multidimensional questionnaire consisting of 9 scales which can be combined to form 3 major health components: physical function, psychological function and pain (Hill et al., 1990, Meenan et al., 1980). AIMS scores range from 0 to 10 (higher scores = poor health status).

Quality of life was measured by the Rheumatoid Arthritis Quality of Life questionnaire (RAQoL) (De Jong et al., 1997) and RAND 36-item health survey (distributed by RAND) (Hays et al., 2006). RAQoL scores range from 0 – 30 with a high score representing a poor quality of life. The RAND-36 can be summarised into physical and mental summary scales. The scores range from 0 to 100, with higher scores indicating better health.

Patient satisfaction with care was measured by the Leeds Satisfaction Questionnaire (LSQ) (Hill et al., 1992) which comprises 6 subscales: provision of information, empathy, technical quality, attitude to the patient, access and continuity and overall satisfaction. Overall satisfaction with care is calculated by summing the scores of the subscales which range from 6 – 30, higher scores reflecting greater patient satisfaction. The study by Tjihuis et al (2003) developed a satisfaction questionnaire which comprised 11 domains (score range 0-100) and a visual analogue scale (range 0-100) on overall satisfaction; higher score reflecting greater patient satisfaction.

Knowledge was measured using the Patient Knowledge Questionnaire (PKQ) (Hill et al., 1991) which assesses patient knowledge in 4 areas; disease process, drug therapy, exercise and joint protection techniques. PKQ scores range from 0 – 30 with higher scores reflecting greater knowledge.

Coping with RA was assessed by the Rheumatology Attitudes Index (RAI) (Callahan et al., 1988) which is a 15-item questionnaire designed to assess patients' perceptions of helplessness in coping with arthritis. RAI scores range from 15-60 where lower scores are associated with better coping. Pain intensity was measured by a 10cm Visual Analogue Scale (VAS) and the pain domain of the AIMS. Pain VAS consists of 10cm horizontal line, usually anchored with verbal descriptors of no pain (0) and pain as bad as it could be (10). Length of fatigue and stiffness were measured in minutes.

Risk of bias of included studies

Although all articles reported about randomisation, allocation concealment and the use of a blind independent assessor, some reports lacked information about how random numbers were

generated. This information was not a requirement when some of these reports were published and the authors of the reports were contacted to provide the missing information. In this type of research, it would be difficult to blind patients or practitioners but if a blind independent assessor was used to perform the assessments the study was awarded a “Yes” for blinding. Selective reporting can be assessed by comparing a published protocol to the published reports. Unfortunately when these studies were conducted, publishing the protocol was not a requirement therefore we assessed this item by checking whether all outcomes mentioned in the reports were adequately reported in the results section. In two studies (Hill, 1997, Tijhuis et al., 2003) patient satisfaction was reported separately therefore these reports were combined with other reports of the same studies (Hill et al., 1994, Tijhuis et al., 2003) and awarded a full mark for having reported all outcomes. On average, the risk of bias for all included studies was low (Figure 2).

Figure 2 : Risk of bias summary figure

	Adequate sequence generation?	Allocation concealment?	Blinding?	Incomplete outcome data addressed?	Free of selective reporting?	Free of other bias?
Hill 1994 (1997)	?	?	+	+	+	+
Hill 2003	?	?	+	+	+	+
Ryan 2006	+	+	+	+	+	+
Tijhuis 2002 (2003)	+	+	+	+	+	+

Key: + present, - absent, ? unclear

Key findings

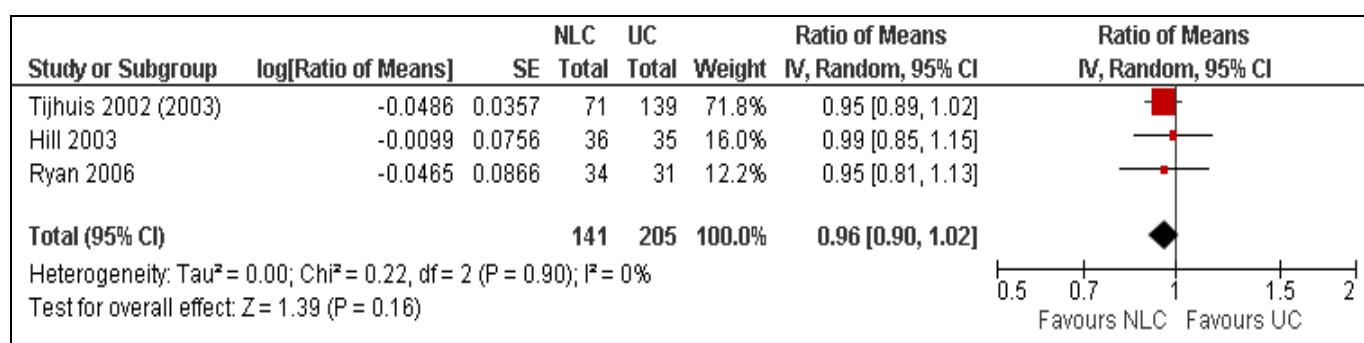
Key findings of nurse-led care effects in all outcomes are summarised in table 2. Measures of effects and effect sizes are given with corresponding 95% confidence intervals (CI), P-Values and heterogeneity statistics for the pooled results.

Outcome (Outcome measure)	Trial	Patients (n)	Measure of effects	Intervention effect size (CI)	P-Value of effect	Heterogeneity			
						X ²	df	P-value	I ²
Disease activity (DAS28)	Hill 2003, Tijhuis 2003, Ryan 2006	361	RoM	0.96 (0.90 – 1.02)	0.160	0.22	2	0.900	0%
Disease activity (DAS28)	Hill 2003	80	RR (Improve)	1.78 (0.74 – 4.29)	0.200	N/A	N/A	N/A	N/A
Disease activity (DAS28)	Hill 2003	80	RR (Worse)	0.83 (0.31 – 2.23)	0.720	N/A	N/A	N/A	N/A
Disease activity (Plasma viscosity)	Hill 1994, Hill 2003	150	RoM	1.00 (0.80 – 1.26)	0.990	0.000	1	0.980	0%
Disease activity (Articular index)	Hill 1994, Hill 2003	150	RoM	0.89 (0.84 – 0.95)	<0.001	14.94	1	<0.001	93%
Functional status (HAQ-DI)	Tijhuis 2002 (2003)	210	RoM	0.78 (0.70 - 0.87)	0.001	N/A	N/A	N/A	N/A
Functional status (MACTAR)	Tijhuis 2002 (2003)	210	RoM	1.00 (0.90 – 1.10)	0.970	N/A	N/A	N/A	N/A
Physical function (AIMS)	Hill 2003, Ryan 2006	151	RoM	0.82 (0.63 – 1.07)	0.140	0.42	1	0.520	0%
Psychological function (AIMS)	Hill 2003, Ryan 2006	151	RoM	1.00 (0.78 – 1.29)	0.970	0.12	1	0.730	0%
Quality of life (RAQoL)	Tijhuis 2002 (2003)	210	RoM	0.83 (0.75 – 0.92)	<0.001	N/A	N/A	N/A	N/A
Quality of life – Physical (RAND)*	Tijhuis 2002 (2003)	210	RoM*	1.21 (1.05 – 1.37)	0.007	N/A	N/A	N/A	N/A
Quality of life – Mental (RAND)*	Tijhuis 2002 (2003)	210	RoM*	1.24 (1.12 – 1.37)	<0.001	N/A	N/A	N/A	N/A
Patient satisfaction (LSQ)*	Hill 1994 (1997), Hill 2003	150	RoM*	1.19 (1.14 – 1.23)	<0.001	1.36	1	0.240	26%
Patient satisfaction (Questionnaire)	Tijhuis 2002 (2003)	210	RoM	0.94 (0.90 - 0.98)	0.003	N/A	N/A	N/A	N/A
Patient knowledge (PKQ)*	Hill 1994, Hill 2003	151	RoM*	4.39 (3.36 – 5.72)	<0.001	0.49	1	0.480	0%
Pain (VAS)	Hill 1994	70	RoM	0.81 (0.74 – 0.89)	<0.001	N/A	N/A	N/A	N/A
Pain (AIMS)	Hill 2003, Ryan 2006	150	RoM	0.94 (0.80 – 1.07)	0.210	0.06	1	0.800	0%
Helplessness (RAI)	Ryan 2006	71	RoM	0.99 (0.93 – 1.05)	0.720	N/A	N/A	N/A	N/A
Morning stiffness (Minutes)	Hill 1994, Hill 2003	151	RoM	0.88 (0.29 – 2.66)	0.830	9.01	1	0.003	89%
Fatigue (Minutes)	Hill 2003	80	Mdn Diff	-330	0.020	N/A	N/A	N/A	N/A

3.1.1. Primary outcome

Three studies reported disease activity using DAS28 (Hill et al., 2003, Ryan et al., 2006, Tjshuis et al., 2003) and 2 used plasma viscosity and Ritchie articular index (Hill et al., 1994, Hill et al., 2003). The pooled effect size for DAS28 were inconclusive (RoM = 0.96, 95%CI = 0.90 – 1.02, P = 0.16) (Figure 3). One study (Hill et al., 2003) reported the number of patients whose DAS28 improved and those that got worse. Using this information, the risk ratio of DAS28 improvement was inconclusive (RR = 1.78, 95%CI = 0.74 – 4.29, P = 0.20) as well as that of DAS28 deterioration (RR = 0.83, 95%CI = 0.31 – 2.23, P = 0.72). The pooled effect size for plasma viscosity was also inconclusive mirroring the results of DAS28 (RoM = 1, 95%CI = 0.80 – 1.26, P = 0.99). The pooled effect size for the articular index favoured nurse-led care (ROM = 0.89, 95%CI = 0.84 – 0.95, P < 0.001).

Figure 3 Pooled Disease Activity Score



RoM: 1 = No effect, RoM <1 favours NLC, RoM > 1 Favours UC.

3.1.2. Secondary outcomes

Functional status was assessed in 3 studies. In 1 study (Tijshuis et al., 2003), HAQ-DI and MACTAR were used while the other 2 studies (Hill et al., 2003, Ryan et al., 2006) used physical function and psychological function components of AIMS. The results of HAQ-DI favoured nurse-led care (RoM = 0.78, 95%CI = 0.70 - 0.87, P = 0.001) while MACTAR scores showed no significant difference between the two groups (RoM = 1.00, 95%CI = 0.90 - 1.10, P = 0.97). The pooled effect size for the physical function domain of AIMS was inconclusive (RoM = 0.82, 95%CI = 0.63 – 1.07, P = 0.14). Similarly, the pooled effect size for the psychological function domain was inconclusive (RoM = 1, 95%CI = 0.78 – 1.29, P = 0.97).

Quality of life was assessed in 1 study (Tijhuis et al., 2003, Tijhuis et al., 2002) using 2 outcome measures the RAND 36-item Health survey and RAQoL questionnaire. Both the physical and the mental domains of the RAND 36-item Health survey favoured nurse-led care (RoM = 1.21, 95%CI = 1.05-1.37, P = 0.007 and 1.24, 95%CI = 1.12-1.37, P < 0.001 respectively). Similarly, RAQoL results favoured nurse-led care (RoM = 0.83, 95%CI = 0.75-0.92, P < 0.001).

Patient knowledge was assessed in 2 studies (Hill et al., 1994, Hill et al., 2003) using the Patient Knowledge Questionnaire and the pooled effect size favoured nurse-led care (RoM = 4.39, 95%CI 3.35 - 5.72, P < 0.001). Patient satisfaction was assessed in 3 studies, 2 used the Leeds Satisfaction Questionnaire (LSQ) (Hill, 1997, Hill et al., 2003) and 1 study (Tijhuis et al., 2003) used a different satisfaction questionnaire. In the first 2 studies, the pooled effect size for LSQ favoured nurse-led care (RoM = 1.19, 95%CI 1.14 – 1.23, P < 0.001) while satisfaction in the other study (Tijhuis et al., 2003) favoured the usual care (RoM = 0.94, 95%CI 0.90 – 0.98, P < 0.001). Patients' ability to control their arthritis was assessed in one study (Ryan et al., 2006) using Rheumatology Attitude Index (RAI) and this showed no significant difference between the two groups (RoM = 0.99, 95%CI = 0.93 – 1.05, P = 0.72).

Pain was assessed in 3 studies; in 1 (Hill et al., 1994) using pain Visual Analogue Scale (VAS) and in the other two using the pain domain of AIMS (Hill et al., 2003, Ryan et al., 2006). In the first study, patients under nurse-led care improved significantly while those under usual care deteriorated (RoM = 0.81, 95%CI = 0.74-0.89, P < 0.001). In the other 2 studies, the pooled effect size for AIMS-Pain were inconclusive (RoM = 0.94, 95%CI = 0.85 - 1.04, P = 0.21). The duration of morning stiffness (minutes) was assessed in 2 studies (Hill et al., 1994, Hill et al., 2003) and the pooled effect size was inconclusive (RoM = 0.88, 95%CI = 0.29 - 2.66, P = 0.83). The duration of fatigue (minutes) was reported in one study (Hill 2003) and the patients under nurse-led care had a significant improvement in fatigue (-120 minutes) while the duration of fatigue for those under usual care had increased by 210 minutes (Median difference = 330, P = 0.02).

4. Discussion

Methods

This review included both nurse-led care substitution and supplementation studies. Supplementation studies have a risk of confounding the aspect of care provided by either the nurse or the doctor. This

could be important if details of the interventions were not specified in the reports or if outcome assessors were not blinded. The interventions in this review were mainly follow-up care and monitoring provided by clinical nurse-specialists (or nurse practitioners) and were delivered in a similar fashion allowing comparison of some outcomes. Blinded assessors were used to assess the objective outcomes in addition to the use of various patient-reported outcomes measures (PROMS). Accordingly, the effects seen in the supplementation studies were similar to those observed in the substitution studies.

The ratio of means method (RoM) was used successfully to measure effect sizes for individual studies and to determine the pooled effects in meta-analysis, thus providing a measure which is easier for clinicians to interpret. The reader can easily tell the direction of the effect by looking at the reported RoM value (RoM < 1 favours nurse-led care; RoM > 1 favours the usual care). One limitation of the RoM method is that it requires that both values of the intervention and the control group to be either negative or positive (because the logarithm of a negative number is undefined). This limitation may be important where change score in one group is negative while in the other is positive, which is not uncommon in physiological values or PROMS. To avoid this, final scores can be used given that the baseline scores were comparable; otherwise adjustment to baseline characteristics would be necessary.

Primary outcome

The effect sizes for DAS28 and Plasma viscosity showed no significant difference between the two groups but those of Ritchie Articular Index favoured nurse-led care. While these results are inconclusive [i.e. showing no evidence of difference (Altman and Bland, 1995)], none of the disease activity measures favoured usual care; therefore there is also no evidence of nurse-led care inferiority. Similar results have been reported in systematic reviews of effectiveness of nurse-led care in other chronic diseases (Carey and Courtenay, 2007, Page et al., 2005, Phillips et al., 2005).

Secondary outcomes

The effect sizes for most secondary outcomes were inconclusive (functional status, satisfaction, morning stiffness and coping with arthritis). We do not know why functional status had mixed results when measured by different tools in the same population (i.e. when measured by HAQ-DI, the results favoured nurse-led care but when measured by MACTAR the results were inconclusive) (Tijhuis et al.,

2003, Tjshuis et al., 2002). When effect size for AIMS is taken into account (Hill et al., 2003, Ryan et al., 2006), the overall result for functional status is inconclusive. A potential explanation for this is that nurse-led care is as effective as the usual care in improving patients' functional status or that the functional status was an indirect consequence of disease activity (the results of which were also inconclusive). The inconclusive results for morning stiffness could also be related to those of disease activity.

Two other outcomes (satisfaction and pain) displayed contradictory results when assessed using different tools. When measured by the LSQ, (Hill, 1997, Hill et al., 2003) the pooled satisfaction effect size favoured nurse-led care but when measured using another questionnaire (Tjshuis et al., 2003) it favoured the usual care. The measurement properties of the two PROMS used in these studies were different therefore pooling of results was impossible. However, evidence from other systematic reviews has associated patient satisfaction with nurse-led care (Horrocks et al., 2002, Laurant et al., 2004, Taylor et al., 2005). Nurse-led care has been shown to have longer consultations and more effective patient education both of which are directly associated with greater satisfaction (Brown and Grimes, 1995, Stewart, 1995). Similar to satisfaction, the results from different measures of pain yielded mixed results; Pain-VAS showed significant effects of nurse-led care while pooled effects of AIMS-pain were inconclusive. Again the data from these studies did not give enough evidence to make strong conclusions.

Nurse-led care displayed significant effects on patients' quality of life (Tjshuis et al., 2003, Tjshuis et al., 2002), patient knowledge (Hill et al., 1994, Hill et al., 2003) and fatigue (Hill et al., 2003). RA has a significant effect on patients' quality of life especially social functioning and energy levels, limiting their involvement in valued activities (Dominick et al., 2004). Since the quality of life and fatigue result from individual studies, there is not enough evidence to make overall conclusions. Patient education is an integral part of RA disease management and nurse-led care plays an important role in delivering this to patients (Goh et al., 2006). It is therefore no surprise that nurse-led care was associated with increased patient knowledge. Patient education increases self-efficacy which in turn enables patients to take control of their arthritis (Arvidsson et al., 2006). It is surprising that these positive results of patient knowledge were not supported by those of coping with arthritis.

Strengths and limitations of the review

The strengths of this review are: 1) inclusion of only RCTs most of which were shown to be of low risk of bias and measured a range of patient outcomes 2) the meta-analysis quantified the sizes of intervention effects using RoM as an effect measure by which a clinician can easily interpret and know the direction of the effect by simply looking at the RoM value 3) most of the studies were well-reported and authors were contacted for additional information 4) in most pooled results, the statistical heterogeneity was non-significant. This review is subject to a few limitations. Firstly, two reviewers were not used in all stages of the review process. Secondly, the review found a small number of RCTs, some of which were not powered to detect changes in the range of outcomes we have evaluated, we therefore cannot rule out the possibility of type II error. However the consistency of study effects reported in the included studies as well as those reported in other chronic diseases suggest that these results are likely to be valid. Lastly, publication bias was not tested. Publication bias occurs when trials showing no effects are selectively not published and this can be tested by plotting sample sizes for each study against the effect sizes. This test is not capable of detecting publication bias with less than 10 trials (Sutton et al., 2000) therefore we were unable to assess for publication bias in this review.

5. Conclusion

The objective of this systematic review was to determine whether nurse-led care was effective (produced effects that were similar to those of usual care). Most estimates of the primary outcome and secondary outcomes showed no significant difference between nurse-led care and usual care. While few estimates of secondary outcomes favoured nurse-led care, there is insufficient evidence to conclude whether this is the case. The main limiting factor is the absence of enough studies in this area. More good quality RCTs are required in order to provide evidence of nurse-led care effectiveness (or lack of it) in people with rheumatoid arthritis.

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