

## Effectiveness of Nonpharmacological and Nonsurgical Interventions for Patients With Rheumatoid Arthritis: An Overview of Systematic Reviews

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Conclusions based on systematic reviews of randomized controlled trials are considered to provide the highest level of evidence about the effectiveness of an intervention. This overview summarizes the available evidence from systematic reviews on the effects of nonpharmacological and nonsurgical interventions for rheumatoid arthritis (RA). Systematic reviews of studies of patients with RA (aged >18 years) published between 2000 and 2007 were identified by comprehensive literature searches. Methodological quality was independently assessed by 2 authors, and the quality of evidence was summarized by explicit methods. Pain, function, and patient global assessment were considered primary outcomes of interest. Twenty-eight systematic reviews were included in this overview. High-quality evidence was found for beneficial effects of joint protection and patient education, moderate-quality evidence was found for beneficial effects of herbal therapy (gamma-linolenic acid) and low-level laser therapy, and low-quality evidence was found for the effectiveness of the other interventions. The quality of evidence for the effectiveness of most nonpharmacological and nonsurgical interventions in RA is moderate to low.

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Rheumatoid arthritis (RA) is a chronic, systemic inflammatory disease of unknown etiology. It is present in 0.5% to 1% of the general population, twice as often in women, and the age at disease onset is mainly between 45 and 65 years.<sup>1</sup> The clinical picture of RA is characterized by pain, fatigue, disability, and reduced quality of life. The course of the disease is often unpredictable, and the symptoms may vary from day to day.

The main goals of treatment for RA are to prevent or control joint damage, prevent loss of function, and decrease pain.<sup>2</sup> Despite substantial progress in the pharmacological and surgical interventions over the last decade, many patients with RA will still experience disability, pain, psychological distress, fatigue, and poor quality of life.<sup>3</sup>

Besides pharmacological and surgical interventions, conventional therapies such as physical therapy, occupational therapy, and comprehensive rehabilitation and self-management programs are commonly and frequently used interventions. Not surprisingly, given the chronic and persistent nature of the disease, patients with RA tend to be particularly high users of complementary and alternative medicine (CAM) therapies.<sup>3</sup> Complementary medicine is used together with conventional medicine, whereas alternative medicine is used in place of conventional medicine. Research indicates that people with RA use a broad range of CAM therapies, such as dietary supplements (herbs and vitamins), movement therapies (yoga and tai chi) and manual therapy, homeopathy, and acupuncture.

Decisions on the provision and reimbursement of health care are increasingly based on the available evidence. Thus, purchasing organizations and policymakers in health

care are in need of information on the effectiveness of interventions. Similarly, patients, health care professionals, and researchers are in need of this information to improve self-management strategies, to improve clinical practice, and to set priorities for research, respectively. Conclusions based on a systematic review of randomized controlled trials (RCTs) are considered to provide the highest level of evidence about the effectiveness of an intervention.

While systematic reviews summarize the effectiveness of a specific treatment for a specific condition, an overview of overviews (sometimes called an “umbrella review”) typically summarizes the evidence from several systematic reviews on different treatment options for the same condition. Because the number of systematic reviews is rapidly increasing, there might be a need to provide patients and health care providers with synthesized and easily accessible information on different treatment options for a particular condition.

The aim of this overview is to summarize the available evidence from systematic reviews on the effect of nonpharmacological and nonsurgical interventions for patients with RA.

### Methods

Systematic reviews were considered if they were published from January 2000 to January 2007 and had the primary aim of investigating the effects of nonpharmacological and nonsurgical interventions for people with RA (aged >18 years). More specifically, the following inclusion criteria were used:

- **Participants:** People with RA according to the American College of Rheumatology criteria<sup>4</sup> or other acceptable diagnostic criteria. Reviews including participants with

various rheumatic diagnoses were accepted only if results for RA could be extracted separately.

- **Interventions:** All types of nonpharmacological and nonsurgical interventions. Excluded were interventions such as gene therapy, all types of invasive interventions (eg, injections, arthroscopy), therapeutic apheresis, or interventions related to pharmacological or surgical interventions (ie, therapeutic exercises after total joint replacement).
- **Outcomes:** For the purpose of this overview, the primary outcome measures were function, pain, and patient global assessment. The concept of “function” is based on the *International Classification of Functioning, Disability and Health* (ICF),<sup>5</sup> where “function” is an umbrella term for body function, body structure, activities, and participation. As secondary outcome variables, we considered the rest of the outcomes in the preliminary core set recommended by the International League of Associations for Rheumatology (ILAR)/Outcome Measures for Arthritis Clinical Trials (OMERACT).<sup>6</sup>

### Search Strategy

The following databases were searched from January 2000 to January 2007: MEDLINE, CINAHL, AMED, EMBASE, PsycINFO, The Cochrane Library, and PEDro.

The search strategy was formulated in Ovid (MEDLINE, CINAHL, EMBASE, and AMED) in cooperation with a medical librarian to make it applicable to all the databases. A broad computerized search strategy was developed (Appendix 1).

Retrieved hits were assessed by one of the authors (AC), who screened the titles and abstracts to identify relevant studies. If there was doubt about a study’s relevance, one of the other authors (KBH) was consulted.

Relevant full-text articles were read by 2 authors (AC, KBH).

### Assessment of Methodological Quality

The methodological quality of included reviews was independently assessed by 2 reviewers (AC, KBH) using a modified version of a previously validated checklist consisting of 9 criteria<sup>7</sup> (Appendix 2). Disagreement was resolved by discussion. Based on a summary of the 9 criteria, an overall scientific quality was applied to each review, as follows: “minor limitations” (at least 7 of the criteria were met), “moderate limitations” (at least 4 of the criteria were met), and “major limitations” (fewer than 4 of the criteria were met). Reviews with major limitations were excluded.

### Data Extraction and Synthesis

Data were extracted by one of the authors (AC). If doubt occurred, one of the other authors (KBH) was consulted. The following criteria were applied when data on effects were extracted:

- Adequate quantitative pooling of data in reviews was regarded as more valid than a qualitative data synthesis approach.
- If no direct comparisons between treatments were undertaken or no quantitative pooling of data was done, the results are reported as “no quantitative pooling,” and the authors’ statements were reported.
- When we found that the results were reported inconsistently in different sections of a review, the effects were extracted from the main results section.
- If possible, the 3 primary outcomes were collected and presented in the result tables. The secondary outcomes were collected if the primary outcomes were not reported. A maximum of 3 outcomes are reported.

**Table 1.**  
Quality of Evidence

Level	Based on
High-quality evidence	One or more updated, high-quality systematic reviews that are based on at least 2 high-quality primary studies with consistent results
Moderate-quality evidence	One or more updated systematic reviews of high or moderate quality <ul style="list-style-type: none"> <li>• Based on at least 1 high-quality primary study</li> <li>• Based on at least 2 primary studies of moderate quality with consistent results</li> </ul>
Low-quality evidence	One or more systematic reviews of variable quality <ul style="list-style-type: none"> <li>• Based on primary studies of moderate quality</li> <li>• Based on inconsistent results in the reviews</li> <li>• Based on inconsistent results in primary studies</li> </ul>

Finally, principles from Grading of Recommendations Assessment, Development, and Evaluation (GRADE) were used to assess an overall quality of evidence for each intervention and outcome.<sup>8</sup> The quality of evidence indicates the extent to which a person can be confident that the estimate of effect is correct. Based on judgments considering quality of primary studies, design of primary studies, consistency (similarity of estimates of effect across studies), and directness (the extent to which people, interventions, and outcome measures were similar to those of interest), the evidence for each intervention was classified as “high,” “moderate,” “low,” or “no evidence from systematic reviews.” The definitions are listed in Table 1. In the summary of findings (Tab. 2), the following statements were used to indicate direction of effect: improves (function) or reduces (pain) (ie, beneficial effects), no difference, and unclear (inconsistent or unclear evidence of effect).

### Results

The literature search identified 1,189 references, which were first examined on the basis of titles and abstracts. Of these, 1,078 references were clearly not relevant, and 111 references were retrieved in full

text. Eighty-three reviews were excluded: 41 because of major limitations (Appendix 3), 6 because of duplicate publications, 16 because of mixed populations, 9 because of use of nonrelevant interventions, and 11 were not reviews or mixed review and single studies. Twenty-eight reviews were included in this overview (Fig. 1).

### Acupuncture

Two reviews<sup>9,10</sup> reported the effect of acupuncture (Tab. 3). The reviews described the intervention as “a kind of herbal acupuncture (bee venom acupuncture)”<sup>9(p79)</sup> and as “a technique based on Chinese medical practice whereby needles are inserted into specific exterior body locations to relieve pain and for other therapeutic purposes.”<sup>10</sup> Study populations were “adult patients with classic or definite rheumatoid arthritis.”

The methodological quality of the primary studies either was not assessed or was of low to moderate quality. One review<sup>9</sup> included 1 RCT and 2 uncontrolled studies and reported a significant decrease in pain, but did not report on function or patient global assessment. Casimiro et al<sup>10</sup> found conflicting results regarding pain, but no significant im-

**Table 2.**  
Summary of Findings

Intervention	Comparison	Results	Quality of Evidence
Acupuncture	Control/placebo	Unclear	Low
Balneotherapy	Different types of balneotherapy/other interventions/ placebo/no intervention	Unclear	Low
Diets	Control/usual diet	Reduces pain	Low
Electrical stimulation	Control	Unclear	Low
Herbal therapy	Placebo/alternative herbal intervention	Reduces pain and patient global assessment	Moderate
Occupational therapy			
Advice/instruction about assistive devices	Usual care/no control	Unclear	Low
Comprehensive occupational therapy	No intervention	Improves function, no difference in pain	Low
Joint protection	Alternative intervention/no intervention	Improves function, no difference in pain	High
Provision of splints	No intervention/control/different types of splints	Unclear	Low
Training of motor function	No intervention/alternative intervention	Unclear	Low
Hand/foot orthosis	Placebo/no intervention/other intervention	Unclear	Low
Patient educational intervention	No intervention/usual care/other educational intervention/waiting list controls	Improves function and patient global assessment	High
Exercise	No intervention/alternative intervention/different types of exercises	Reduces pain and improves function, no difference in patient global assessment	Low
Low-level laser therapy	Alternative intervention/placebo	Reduces pain and improves function	Moderate
Therapeutic ultrasound	Placebo/alternative intervention	Reduces pain and improves function	Low
Thermotherapy	Placebo/no intervention/alternative interventions	Unclear	Low
Transcutaneous electrical nerve stimulation	Placebo/alternative interventions	Unclear	Low

improvements in function or patient global assessment. Both reviews concluded that there is little evidence that acupuncture relieves RA symptoms, but underscored that this conclusion is limited by methodological flaws. We find this conclusion to be reasonable and conclude that the effect of acupuncture is unclear (Tab. 2). One of the reviews reported no harmful side effects, while the other concluded that a greater understanding of the risks and benefits of bee venom acupuncture is needed.

**Balneotherapy**

Two reviews<sup>11,12</sup> included balneotherapy, reporting on interventions as “bathing in water containing minerals (added or natural)”<sup>11</sup> or “any type of balneotherapy (mud packs, sulphur baths, Dead Sea baths).”<sup>12</sup> Patients were included if they had “clinically confirmed RA”<sup>11</sup> or “only RA.”<sup>12</sup> Again, the methodological quality of the primary studies was low to moderate. One review<sup>12</sup> provided quantitative pooling of results (Tab. 3). The pooled results (mudpacks versus control)

were based on 2 studies with small sample sizes and showed no statistically significant improvements in pain or patient global assessment. Results from single primary studies showed conflicting evidence related to pain and function (grip strength [force-generating capacity]). Both reviews concluded that firm conclusions on the effectiveness of balneotherapy for people with RA cannot be drawn, mainly because of the heterogeneity of the interventions and the poor methodological quality of the included studies. We

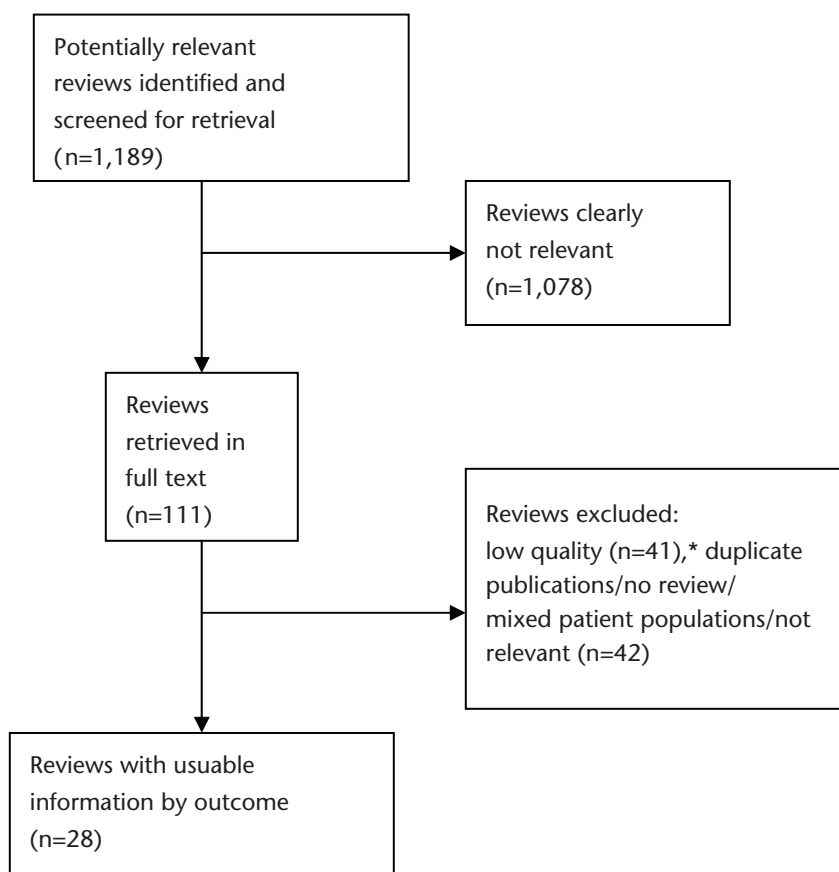
conclude, therefore, that the effect of balneotherapy is unclear (Tab. 2). Possible harmful aspects of balneotherapy, such as cardiac problems or risk of bacterial contamination, were not reported in any of the reviews.

### Diets

One review<sup>13</sup> reported on the effect of fasting followed by a vegetarian diet for at least 3 months (Tab. 4). Patients included were diagnosed with RA. The primary studies were of mixed quality, but the pooling of data from 2 RCTs showed significant improvement in pain. However, based on one review of moderate quality, we conclude that there is low-quality evidence that fasting followed by a vegetarian diet (3 months) reduces pain (Tab. 2). Diets might have a negative effect on nutritional status, but the review did not report on this issue.

### Electrical Stimulation (ES)

One review<sup>14</sup> based on 1 RCT of low quality reported the outcome of ES (Tab. 4). The review defined the intervention as “electrical stimulation applied to the motor point of a muscle and is used to recruit motor units that are not activated at a given moment by voluntary recruitment.” The patient population (age=30–75 years) had RA affecting the metacarpophalangeal joint. The authors concluded that the evidence for the use of ES to improve muscle strength and resistance to fatigue is limited. The study included 6 participants in the intervention group and 3 participants in the control group. The Ottawa Panel excluded the RCT because: “Evidence with acceptable research design, interventions, group comparisons, or outcomes could not be identified.”<sup>15(p1026)</sup> Thus, we conclude that the effect of ES is unclear (Tab. 2). The review did not comment on safety and possible harmful effects.



**Figure.**

Selection process of eligible reviews from all identified citations. \*Excluded reviews listed in Appendix 3.

### Herbal Therapy

Effect of herbal therapy was reported in 3 reviews<sup>16–18</sup> (Tab. 4), defining the interventions as “Ayurvedic medicines as usually complex mixtures of multiple plants administered orally,”<sup>8(p705)</sup> “any whole plant extract except homeotherapy, aroma therapy or any preparation of synthetic origin or consisting only of plant derivatives,”<sup>16(p2)</sup> or “herbal preparations administered orally or topically for RA.”<sup>17(p652)</sup> Patient populations included were “RA patients”<sup>17,18</sup> or “all persons diagnosed with RA.”<sup>16</sup> All reviews found conflicting evidence for the effect of herbal therapy on pain and function. When reporting on the effect of gamma-linolenic acid (GLA) specifically, 2

reviews<sup>16,17</sup> found statistically significant improvement in pain and patient global assessment based on pooled results from 3 RCTs of moderate quality, but they emphasized that further studies are needed to examine the efficacy, safety, and potential drug interactions. We conclude, therefore, that there is moderate-quality evidence that herbal therapy (GLA) reduces pain and improves patient global assessment, while the evidence for other herbals is unclear (Tab. 2). Frequently reported adverse events from ayurvedic medicines included anorexia, nausea, diarrhea, constipation, and abdominal pain, but in general the reviews concluded that the adverse effects reported were few and minor. Thus, the reviews con-

**Table 3.**  
Description of Included Reviews: Acupuncture/Balneotherapy<sup>a</sup>

Reference	No. of Included Studies and Participants	Methodological Quality of Review and Primary Studies	Results
An overview of bee venom acupuncture in the treatment of arthritis (Lee et al) <sup>9</sup>	1 RCT 2 CTs (152 participants)	<u>Review</u> Moderate limitations <u>Primary studies</u> Mean quality score (1 RCT)=4 (Jadad scale: 0-5) 2 CTs: not assessed	<u>No quantitative pooling</u> “Due to paucity and methodological flaws in the existing clinical studies, it is premature to draw any firm conclusions at this time. However, the effectiveness of bee venom acupuncture for arthritis is likely to be a promising area of future research.”
Acupuncture and electroacupuncture for the treatment of rheumatoid arthritis (Casimiro et al) <sup>10</sup>	2 RCTs (84 participants)	<u>Review</u> Minor limitations <u>Primary studies</u> Mean quality score=3 (Jadad scale: 0-5)	<u>No quantitative pooling</u> “With a silver level of evidence, we conclude that there is little evidence that acupuncture relieves RA symptoms.”
Balneotherapy for rheumatoid arthritis and osteoarthritis (Verhagen et al) <sup>11</sup>	6 RCTs (355 participants)	<u>Review</u> Minor limitations <u>Primary studies</u> Mean quality score=4.8 (Delphi list: 0-9)	<u>No quantitative pooling</u> “One cannot ignore the positive findings reported in most trials. However, the scientific evidence is insufficient because of the poor methodological quality, the absence of an adequate statistical analysis, and the absence, for the patient, of most essential outcome measures. Therefore, the noted ‘positive findings’ should be viewed with caution. Because of the methodological flaws, an answer about the apparent effectiveness of balneotherapy cannot be provided at this moment. A large, methodological sound trial is needed.”
Efficacy of balneotherapy for rheumatoid arthritis: a meta-analysis (Brosseau et al) <sup>12</sup>	7 RCTs (374 participants)	<u>Review</u> Minor limitations <u>Primary studies</u> Mean quality score=2.4 (Jadad scale: 0-5)	<u>Pain</u> Swollen/tender joints (Ritchie Index Scale): WMD=−7.07, 95% CI=−11.98 to 2.19 (2 RCTs) <u>Patient global assessment</u> VAS: WMD=0.2, 95% CI=−1.08 to 1.8 (2 RCTs)

<sup>a</sup> RCT=randomized controlled trial, CT=clinical trial, RA=rheumatoid arthritis, WMD=weighted mean difference, CI=confidence interval, VAS=visual analog scale.

cluded that further research is needed, not only research on the efficacy of herbal interventions but also research on safety and potential drug interactions.

### Occupational Therapy Interventions

One review,<sup>19</sup> including 38 studies, explored several occupational therapy intervention categories for RA (Tab. 5). Occupational therapy interventions either were classified into 6 specific intervention categories

(training of motor function, training of skills, instruction on joint protection and energy conservation, counseling, advice and instruction in the use of assistive devices, or provision of splints and hand orthoses) or were regarded as “comprehensive occupational therapy” (when all 6 interventions were part of the evaluated occupational therapy treatment). The review found no studies concerning the interventions training of skills and counseling. Studies with patients who fulfilled a clinical diagno-

sis of RA were included. Each intervention category is presented separately below.

**Advice and instruction in the use of assistive devices.** Two studies (non-RCTs) evaluated advice and instruction in the use of assistive devices versus alternative treatment. Only one study reported function as an outcome variable and found no statistically significant improvement. The 2 studies reported conflicting results regarding pain. Based on the

Table 4.

Description of Included Reviews: Diets/Electrical Stimulation/Herbal Therapy<sup>a</sup>

Reference	No. of Included Studies and Participants	Methodological Quality of Review and Primary Studies	Results
Fasting followed by vegetarian diet in patients with rheumatoid arthritis: a systematic review (Muller et al) <sup>13</sup>	2 RCTs 2 CCTs (143 participants)	<u>Review</u> Moderate limitations <u>Primary studies</u> Not reported	<u>Pain</u> Effect size=0.58, $r=.28$ , $P<.01$ (2 RCTs)
Electrical stimulation for the treatment of rheumatoid arthritis (Brosseau et al) <sup>14</sup>	1 RCT (15 participants)	<u>Review</u> Minor limitations <u>Primary studies</u> Mean quality score=2 (Jadad scale: 0-5)	<u>No quantitative pooling</u> "ES was shown to have a clinically beneficial effect on grip strength and fatigue resistance for RA patients with muscle atrophy of the hand. However, these conclusions are limited by the low methodological quality of the trial included. More well-designed studies are therefore needed to provide further evidence of the benefits of ES in the management of RA."
Herbal therapy for treating rheumatoid arthritis (Little and Parsons) <sup>16</sup>	11 RCTs (398 participants)	<u>Review</u> Minor limitations <u>Primary studies</u> Mean quality score=3.4 (Jadad scale: 0-5)	<u>Pain</u> VAS: WMD=-32.83, 95% CI=-56.25 to -9.42 (3 RCTs) Pain scale (0-4): WMD=-25.88, 95% CI=-46.73 to -5.02 (3 RCTs) <u>Patient global assessment</u> Scale (0-4): WMD=-20.87, 95% CI=-39.43 to -2.31 (3 RCTs)
Herbal medicines for the treatment of rheumatoid arthritis: a systematic review (Soeken et al) <sup>17</sup>	14 RCTs (493 participants)	<u>Review</u> Moderate limitations <u>Primary studies</u> Mean quality score=3.9 (Jadad scale: 0-5)	<u>Pain</u> VAS: WMD=0.76, 95% CI=0.37 to 1.15 (3 RCTs)
Ayurvedic medicine for rheumatoid arthritis: a systematic review (Park and Ernst) <sup>18</sup>	7 RCTs (508 participants)	<u>Review</u> Minor limitations <u>Primary studies</u> Mean quality score=2.1 (Jadad scale: 0-5)	<u>No quantitative pooling</u> "There is a paucity of RCTs of Ayurvedic medicines for RA. The existing RCTs fail to show convincingly that such treatments are effective therapeutic options for RA."

<sup>a</sup> RCT=randomized controlled trial, CCT=controlled clinical trial, ES=electrical stimulation, RA=rheumatoid arthritis, VAS=visual analog scale, WMD=weighted mean difference, CI=confidence interval.

conflicting results and the low quality of the primary studies, we conclude that the effect of advice and instruction in the use of assistive devices is unclear (Tab. 2). No safety or side effects were assessed in the included studies.

**Comprehensive occupational therapy.** Four studies evaluated comprehensive occupational therapy versus no treatment or alternative treatment. *Comprehensive*

*occupational therapy* was defined as "when all 6 interventions (training of motor function, training of skills, instruction on joint protection and energy conservation, counseling, advice and instruction in the use of assistive devices, and provision of splints and hand orthoses) were part of the evaluated occupational therapy treatment." One RCT of high quality reported a statistically significant positive effect on functional ability, whereas 3 low-quality studies

reported no effect. No statistically significant results were found for pain. Based on conflicting results, we conclude that there is low-quality evidence that comprehensive occupational therapy improves function and makes no difference in pain (Tab. 2).

**Instruction on joint protection and energy conservation.** Eight studies evaluated instruction in joint protection versus no treatment or al-

**Table 5.**  
Description of Included Reviews: Occupational Therapy/Orthosis<sup>a</sup>

Reference	No. of Included Studies and Participants	Methodological Quality of Review and Primary Studies	Results
Occupational therapy for rheumatoid arthritis (Stultjens et al) <sup>19</sup>	16 RCTs 6 CCTs 16 ODs (1,789 participants)	<u>Review</u> Minor limitations <u>Primary studies</u> Mean quality score (RCT/CCT)= 9.3 (van Tulder scale, 1997) <sup>b</sup> Mean quality score (OD)=8.1 (adapted van Tulder scale)	<u>No quantitative pooling</u> “We found strong evidence for the efficacy of instruction of joint protection on functional ability. Studies that evaluated comprehensive OT showed limited evidence for the effectiveness on functional ability. Studies that evaluated splint interventions reported indicative findings for the effectiveness on pain.”
A critical review of foot orthoses in the rheumatoid arthritic foot (Clark et al) <sup>21</sup>	6 RCTs 5 CCTs (419 participants)	<u>Review</u> Moderate limitations <u>Primary studies</u> Criteria used to assess methodological quality reported	<u>No quantitative pooling</u> “From the review there is limited and conflicting evidence upon which to base clinical practice. The suggestion is that foot orthoses may reduce pain and improve ability, but these outcomes are not achieved by all studies.”
Splints and orthosis for treating rheumatoid arthritis (Egan et al) <sup>20</sup>	12 studies (RCT/CCT/OD)	<u>Review</u> Minor limitations <u>Primary studies</u> Mean quality score=2.3 (Jadad scale: 0-5)	<u>No quantitative pooling</u> “There is insufficient evidence to make firm conclusions about the effectiveness of working wrist splints in decreasing pain or increasing function for people with RA. . . . There is evidence that extra-depth shoes and molded insoles decrease pain during weight-bearing activities such as standing, walking, and stair climbing. Extra-depth shoes with semi-rigid insoles provide better pain relief than extra-depth shoes alone.”

<sup>a</sup> RCT=randomized controlled trial, CCT=controlled clinical trial, OD=other designs, OT=occupational therapy, RA=rheumatoid arthritis.

<sup>b</sup> Van Tulder MW, Assendelft WJ, Koes BW, Bouter LM. Method guidelines for systematic reviews in the Cochrane Collaboration Back Review Group for Spinal Disorders. *Spine*. 1997;22:2323-2330.

ternative treatment. Two RCTs of high quality found statistically significant improvements in functional ability, and the findings were supported by 2 studies of lower quality. Two RCTs of high quality found no statistically significant improvement in pain. There was insufficient information about the results from the low-quality studies. The authors concluded that there is strong evidence that instruction on joint protection leads to an improvement of functional ability. We support this conclusion and conclude that there is high-quality evidence for a positive effect on function, but no difference in pain (Tab. 2). Only one of the included studies reported decreases in grip strength and range of motion

(ROM) as possible effects, but the authors questioned whether this was due to improved joint protection behavior or a determinant of increased joint protection behavior.

**Provision of splints and hand orthoses.** Sixteen studies related to provision of splints (hand, finger, or wrist) versus other types of splints or no treatment. Three non-RCTs found a statistically significant decrease in pain while participants were wearing working splints, whereas the effects on pain after splinting were conflicting. Only 2 of the studies were RCTs of high quality and reported no difference in pain. Statistically significant improvements in grip strength while wearing

a splint were reported (2 non-RCTs), whereas 2 RCTs of high quality reported no statistically significant increase in grip strength after a period of time. The authors concluded that there are indicative findings that splints are effective in reducing pain. Furthermore, they stated that there are indicative findings for a gain in grip strength immediately after provision of the splints.

Egan et al<sup>20</sup> included 12 studies assessing the same interventions versus placebo or alternative interventions. Splints and orthoses were defined as “any medical device added to a person’s body to support, align, position, immobilize, prevent or correct deformity, assist weak

muscles, or improve function.” The primary studies were of low to moderate quality. The studies showed conflicting results regarding pain and function, and the authors concluded that there is insufficient evidence to make firm conclusions about the effectiveness of working splints or resting splints on pain and function. Based on the conflicting results in both of the reviews,<sup>19,20</sup> we conclude that the effect of splints (hand, finger, or wrist) is unclear (Tab. 2). Twelve of the included studies reported on safety or side effects,<sup>19</sup> and both reviews<sup>19,20</sup> concluded that there were some indicative findings that splinting has a negative effect on dexterity.

**Training of motor function.** Six studies evaluated training of motor function versus no treatment or alternative treatment. One RCT with high methodological quality reported no significant differences between groups on pain and functional ability after training of hand function. The other studies were of low quality, showed conflicting results, and did not report sufficient data to calculate effect sizes. The authors concluded that there is no evidence for the effectiveness of training of motor function on pain or function. Based on the conflicting results, we conclude that there is unclear evidence for the effect of motor function training on pain and function (Tab. 2). One study reported problems with the upper extremity after resistance exercises.

**Foot orthoses.** Effects of foot orthoses and special shoes versus placebo, no intervention, or other intervention were reported in 2 reviews,<sup>20,21</sup> with 4 and 11 studies included, respectively (Tab. 5). Foot orthoses are prescribed by clinicians as a form of intervention for the symptomatic foot in patients with RA to relieve forefoot, midfoot, and rear-foot pain and to normalize the

pain pattern.<sup>21</sup> All patients included had a confirmed diagnosis of RA. One review<sup>20</sup> reported that 2 low-quality studies found significant improvements in pain, but not in function, and 2 high-quality studies found no significant changes in either pain or function (up to 3 years of orthosis wear). Clark et al<sup>21</sup> reported conflicting results on both pain and function, but no exact results were presented. Thus, we conclude, based on the 2 reviews, that the effect of orthosis is unclear (Tab. 2). Safety or side effects were not reported in any of the reviews.

**Patient education.** Four reviews<sup>3,22-24</sup> reported on the effects of patient education for patients with RA (Tab. 6), describing the interventions as “any set of planned educational activities designed to improve patients health behavior or health status,” “a multidisciplinary intervention delivered by a team of health care professionals, providing a systematic approach to care, and including a patient education component,” and “psychosocial interventions.” Patients included had either “a clinical confirmation of RA” or “adult RA.”

Riemsma et al<sup>22</sup> included 31 RCTs. The interventions were patient education interventions versus control and were categorized into 3 groups: “information only,” “counseling,” and “behavioral treatment.” No significant effects of information only or counseling were reported. Significant effects on disability, patient global assessment, and depression were found for behavioral treatment interventions after treatment. The authors concluded that patient education had small short-term effects on disability, joint counts, patient global assessment, psychological status and depression, but there was no evidence of long-term benefits.

Niedermann et al<sup>23</sup> concluded that the results on physical health status are conflicting, and no long-term changes in disability and physical function were found in any study. Badamgarav et al<sup>24</sup> reported that pooled effect sizes were small and nonsignificant, but studies with interventions of greater than 5 weeks’ duration showed significant differences in functional status. Astin et al<sup>3</sup> concluded that there are small, but statistically significant, effect sizes for pain, functional disability, depression, coping, and self-efficacy after treatment.

All included reviews concluded that different types of patient education interventions have small short-term effects on different health outcomes, but there is no evidence for the long-term benefits. Based on the many studies with consistent results, we conclude that there is high-quality evidence that patient education improves function and patient global assessment (Tab. 2).

### Physical Therapy Interventions

**Exercises.** Five reviews<sup>25-29</sup> reported the effects of therapeutic exercises (Tab. 7), including “tai chi instructions,” “any form of exercise for the hand,” “therapeutic exercises, with an emphasis on the intensity of exercise program,” and “aerobic activities.” Target populations were ambulatory adults with a diagnosis of RA or clinically confirmed RA. Generally, the methodological quality of the primary studies was low or not reported, and the interventions were heterogeneous. One of the included reviews<sup>28</sup> provided quantitative pooling of results based on 2 primary studies of very low quality. Most of the reviews stated that further studies were needed, but the results indicated that exercises may have some beneficial effects on pain and function. One review<sup>25</sup> rated the evidence on pain and overall function as “good,” but the con-

## Effectiveness of Nonpharmacological and Nonsurgical Interventions for RA

**Table 6.**

Description of Included Reviews: Patient Education Intervention<sup>a</sup>

Reference	No. of Included Studies and Participants	Methodological Quality of Review and Primary Studies	Results
Psychological interventions for rheumatoid arthritis: a meta-analysis of randomized controlled trials (Astin et al) <sup>3</sup>	25 RCTs (1,676 participants)	<u>Review</u> Minor limitations <u>Primary studies</u> Mean quality score=2.24 (Jadad scale: 0-5) Mean quality score=5.84 (van Tulder scale: 0-10)	<u>Pain</u> Pooled effect size (postintervention)=0.22, 95% CI=0.07 to 0.37 (13 RCTs) Pooled effect size (follow-up)=0.06, 95% CI=-0.17 to 0.29 (6 RCTs) <u>Function</u> Pooled effect size (postintervention)=0.27, 95% CI=0.12 to 0.42 (12 RCTs) Pooled effect size (follow-up)=0.12, 95% CI=-0.09 to -0.33 (7 RCTs) <u>Self-efficacy</u> Effect size (postintervention)=0.35, 95% CI=0.11 to 0.59 (5 RCTs) Effect size (follow-up)=0.20, 95% CI=-0.08 to -0.48
Effects of disease management programs on functional status of patients with rheumatoid arthritis (Badamgarav et al) <sup>24</sup>	8 RCTs 3 CCTs (701 participants)	<u>Review</u> Moderate limitations <u>Primary studies</u> Type of quality score not reported	<u>Function</u> Effect size=0.27, 95% CI=-0.01 to 0.54 (7 RCTs/1 CCT) Interventions lasting >5 wk: effect size=0.49, 95% CI=0.12 to 0.86 (2 RCTs/1 CCT) Interventions lasting ≤5 wk: effect size=0.13, 95% CI=-0.25 to 0.52 (4 RCTs)
Gap between short- and long-term effects of patient education in rheumatoid arthritis patients: a systematic review (Niedermann et al) <sup>23</sup>	11 RCTs (931 participants)	<u>Review</u> Moderate limitations <u>Primary studies</u> Mean quality score=5.6 (Cochrane/Amsterdam-Maastricht, range=0-11)	<u>No quantitative pooling</u> "Methodologically better-designed studies had more difficulties demonstrating positive outcome results. Short-term effects in program targets are generally observed, whereas long-term changes in health status are not convincingly demonstrated."
Systematic review of rheumatoid arthritis patient education (Riemsma et al) <sup>22</sup>	31 RCTs No. of included participants: not possible to assess (8,632 participants?)	<u>Review</u> Minor limitations <u>Primary studies</u> Mean quality score=2.6 (modified Jadad scale: 0-8)	<u>Pain</u> Posttreatment SMD=-0.08, 95% CI=-0.16 to 0.00 (37 CTs) <sup>b</sup> Follow-up SMD=-0.07, 95% CI=-0.19 to 0.05 (19 RCTs) <u>Function</u> Posttreatment SMD=-0.17, 95% CI=-0.25 to -0.09 (37 RCTs) <sup>b</sup> Follow-up SMD=-0.09, 95% CI=-0.20 to 0.02 (23 RCTs) <u>Patient global assessment</u> Posttreatment SMD=-0.28, 95% CI=-0.49 to -0.07 (6 RCTs) Follow-up SMD=-0.06, 95% CI=-0.22 to 0.10 (7 RCTs)

<sup>a</sup> RCT=randomized controlled trial, CCT=controlled clinical trial, CT=clinical trial, CI=confidence interval, SMD=standardized mean difference.

<sup>b</sup> Some studies contained more than 2 comparative interventions and were included as independent studies in the statistical pooling.

**Table 7.**

Description of Included Reviews: Physical Therapy Interventions (Exercises/Electrotherapy/Thermotherapy)<sup>a</sup>

Reference	No. of Included Studies and Participants	Methodological Quality of Review and Primary Studies	Results
Ottawa Panel Evidence-Based Clinical Practice Guidelines for Therapeutic Exercises in the Management of Rheumatoid Arthritis in Adults (Ottawa Panel) <sup>25</sup>	6 RCTs 10 CCTs (661 participants)	<u>Review</u> Minor limitations <u>Primary studies</u> Mean quality score=1.2 (Jadad scale: 0-5)	<u>No quantitative pooling</u> “Good evidence (level I, RCT) exists that therapeutic exercises, including functional strengthening and low- or high-intensity exercises, relieve pain and improve overall function.”
Tai chi for treating rheumatoid arthritis (Han et al) <sup>28</sup>	3 RCTs 1 CCT (206 participants)	<u>Review</u> Minor limitations <u>Primary studies</u> Mean quality score=0.25 (Jadad scale: 0-5)	<u>Function</u> ADL index: WMD=0.001, 95% CI=-2.94 to 2.97 (1 RCT/1 CCT) 50-ft walking test: WMD=0.35, 95% CI=-1.14 to 1.84 (1 RCT/1 CCT)
The effectiveness of hand exercises for persons with rheumatoid arthritis: a systematic review (Wessel) <sup>26</sup>	9 CCTs or case series (262 participants)	<u>Review</u> Moderate limitations <u>Primary studies</u> Mean quality score=28 (type of scale not reported: 0-48)	<u>No quantitative pooling</u> “There is not strong research evidence for or against the value of hand exercise in the treatment of persons with rheumatoid arthritis, although results of this review suggest that appropriate exercise might lead to long-term strength changes and very short-term changes in stiffness.”
Training effects on pain in rheumatoid arthritis (Enger et al) <sup>27</sup>	6 RCTs Unknown number of participants	<u>Review</u> Moderate limitations <u>Primary studies</u> Quality score not reported (Jamtvedt and Hilde, 2000) <sup>b</sup>	<u>No quantitative pooling</u> “The results indicate that exercise leads to unchanged or reduced self-reported pain and joint tenderness for patients with rheumatoid arthritis. Further studies are needed in order to demonstrate to what extent and how different kinds of exercise influence pain and joint tenderness in rheumatoid patients.”
A health professional’s guide to exercise prescription for people with arthritis: a review of aerobic fitness activities (Westby) <sup>29</sup>	11 RCTs 7 CCTs or pretest-posttest studies	<u>Review</u> Moderate limitations <u>Primary studies</u> Quality score not reported (Squires, 1989) <sup>c</sup>	<u>No quantitative pooling</u> “Although more comprehensive evaluation is necessary, present evidence suggests that aerobic fitness activities have minimal to moderate positive short-term effects on arthritis-related impairment, disease activity, or accelerating joint damage. The long-term effects of aerobic exercise are less well understood. Available data do not suggest that one mode of aerobic exercises is better than another when comparing the changes in aerobic capacity, disease activity, pain, physical activity, and depression.”
Low level laser therapy (classes I, II and III) in the treatment of rheumatoid arthritis (Brosseau et al) <sup>30</sup>	6 RCTs (222 participants)	<u>Review</u> Minor limitations <u>Primary studies</u> Mean quality score: 3.0 (Jadad scale: 0-5)	<u>Function</u> ROM: WMD=-18.03, 95% CI=-31.80 to -4.27 (2 RCTs) Flexibility-tip to palm distance: WMD=-1.28, 95% CI=-1.72 to -0.85 (2 RCTs) <u>Pain</u> VAS: WMD=-1.10, 95% CI=-1.82 to -0.39 (3 RCTs)

(Continued)

**Table 7.**  
Continued

Reference	No. of Included Studies and Participants	Methodological Quality of Review and Primary Studies	Results
Ottawa Panel Evidence-Based Clinical Practice Guidelines for Electrotherapy and Thermotherapy Interventions in the Management of Rheumatoid Arthritis in Adults (Ottawa Panel) <sup>15</sup>	<u>Low-level laser therapy</u> 5 RCTs (204 participants) <u>Therapeutic ultrasound</u> 1 RCT (50 participants) <u>TENS</u> 3 RCTs (94 participants) <u>Electrical stimulation</u> No reviews found	<u>Review</u> Minor limitations <u>Primary studies</u> Low-level laser therapy: mean quality score=4.0 (Jadad scale: 0-5) Therapeutic ultrasound: mean quality score=3.0 (Jadad scale: 0-5) TENS: mean quality score=2.3 (Jadad scale: 0-5)	<b>Low-level laser therapy</b> <u>Function</u> ROM: WMD=-1.26, 95% CI=-1.72 to -0.85 (2 RCTs) <u>Pain</u> VAS: WMD=-1.05, 95% CI=-1.58 to -0.53 (4 RCTs) <b>Therapeutic ultrasound</b> <u>No quantitative pooling</u> “The Ottawa Panel found good evidence (level I, RCT) of the effects of therapeutic ultrasound for RA of the hand.” <b>TENS</b> <u>No quantitative pooling</u> “The Ottawa Panel found good evidence (level I, RCT) on the effects of TENS for management of RA in the hand and wrist.” <b>Electrical stimulation</b> Evidence with acceptable research design, interventions, group comparisons, or outcomes could not be identified.
Therapeutic ultrasound for the treatment of rheumatoid arthritis (Casimiro et al) <sup>31</sup>	2 RCTs (80 participants)	<u>Review</u> Minor limitations <u>Primary studies</u> Mean quality score=2 (Jadad scale: 0-5)	<u>No quantitative pooling</u> “Ultrasound in combination with exercises, faradic current, and wax bath treatment modalities is not supported and cannot be recommended. Ultrasound alone can, however, be used on the hand to increase grip strength, and to a lesser extent and based on borderline results, increase wrist flexion, decrease morning stiffness, reduce the number of swollen joints, and reduce the number of painful joints. It is important to note that these conclusions are limited by methodological considerations.”
Transcutaneous electrical nerve stimulation (TENS) for the treatment of rheumatoid arthritis in the hand (Brosseau et al) <sup>34</sup>	3 RCTs (78 participants)	<u>Review</u> Minor limitations <u>Primary studies</u> Mean quality score: 2.3 (Jadad scale: 0-5)	<u>No quantitative pooling</u> “There are conflicting effects on pain outcomes in patients with RA. AL-TENS is beneficial for reducing pain intensity and improving muscle power scores over placebo, while, conversely, C-TENS resulted in no clinical benefit on pain intensity compared with placebo. However, C-TENS resulted in a clinical benefit on patient assessment of change in disease over AL-TENS. More well-designed studies with a standardized protocol and adequate number of subjects are needed to fully conclude the effect on C-TENS and AL-TENS in the treatment of RA of the hand.”
Efficacy of paraffin wax baths for rheumatoid arthritic hands (Ayling and Marks) <sup>32</sup>	4 RCTs (303 participants)	<u>Review</u> Moderate limitations <u>Primary studies</u> Mean quality score=10 (Beckerman et al, 1992: 0-25) <sup>d</sup>	<u>No quantitative pooling</u> “A critical review of the literature concerning the clinical efficacy of paraffin wax as a treatment for hands afflicted with RA has not revealed any study without serious bias. Thus, no definitive evidence exists either in support of this treatment approach. In addition, studies suggesting that the techniques of wax baths may be temporarily useful, or not useful at all, did not necessarily employ optimal application methods. Related data do suggest, though, that physiotherapists should avoid using this modality when their patients’ joint disease is active.”

(Continued)

**Table 7.**  
Continued

Reference	No. of Included Studies and Participants	Methodological Quality of Review and Primary Studies	Results
Ottawa Panel Evidence-Based Clinical Practice Guidelines for Electrotherapy and Thermotherapy Interventions in the Management of Rheumatoid Arthritis in Adults (Ottawa Panel <sup>15</sup> )	2 RCTs (76 participants)	<u>Review</u> Minor limitations <u>Primary studies</u> Mean quality score=1 (Jadad scale: 0-5)	<u>No quantitative pooling</u> “The Ottawa Panel found good evidence (level I, RCT) that thermotherapy, especially wax combined with exercise, benefits ROM, pain, and stiffness in the management of RA.”
Thermotherapy for treating rheumatoid arthritis (Robinson et al) <sup>33</sup>	7 RCTs (328 participants)	<u>Review</u> Minor limitations <u>Primary studies</u> Mean quality score=1.6 (Jadad scale: 0-5)	<u>No quantitative pooling</u> “The results of this systematic review on thermotherapy in the treatment of RA found that there was no significant effect of hot or ice pack applications or faradic baths on objective measures of disease activity, including joint swelling, pain, medication intake, ROM, grip strength, or hand function, when compared to a control or alternate treatment.”

<sup>a</sup> RCT=randomized controlled trial, SMD=standardized mean difference, CI=confidence interval, CT=clinical trial, ADL=activities of daily living, WMD=weighted mean difference, ROM=range of motion, VAS=visual analog scale, TENS=transcutaneous electrical nerve stimulation, RA=rheumatoid arthritis, AL-TENS=acupuncture-like transcutaneous electrical nerve stimulation, C-TENS=conventional transcutaneous electrical nerve stimulation.

<sup>b</sup> Jamtvedt G, Hilde G. Evidence-based physiotherapy: critical appraisal of a randomized controlled trial [in Norwegian]. *Norwegian Physiotherapy Journal*. 2000;67:7-12.

<sup>c</sup> Squires BP. Biomedical review articles: what editors want from authors and peer reviewers. *Can Med Assoc J*. 1989;141:195-197.

<sup>d</sup> Beckerman H, de Bie RA, Bouter LM, et al. The efficacy of laser therapy for musculoskeletal and skin disorders: a criteria-based meta-analysis of randomized clinical trials. *Phys Ther*. 1992;72:483-491.

clusion is based on studies with conflicting results and no quantitative pooling. Patient global assessment was not statistically significant in the studies that reported this outcome. Based on the conflicting results, we conclude that there is low-quality evidence that exercises reduce pain and improve function and that there is no difference in patient global assessment (Tab. 2).

Tai chi instructions caused some joint and muscle pain complaints that diminished during the course of the study, but it did not cause withdrawals. One review<sup>29</sup> found that aerobic fitness activities do not exacerbate disease activity or accelerate joint damage, whereas another review<sup>25</sup> concluded that, although no harmful side effects were reported in

the original studies, the effects of high-intensity exercise on pain raise concern.

#### Low-level laser therapy (LLLT).

Two reviews were identified,<sup>15,30</sup> defining *low-level laser therapy* as “a light source that generates extremely pure light, of a single wavelength.” All patients included had clinically confirmed RA. The methodological quality of the primary studies varied from low to good, and both reviews provided quantitative pooling of results (Tab. 7). Three RCTs of moderate quality showed statistically significant improvements in pain, and 2 RCTs of moderate quality found significant improvements in function (ie, ROM, flexibility). Patient global assessment was not reported. The reviews agreed on the conclusion

that LLLT could be considered for relief of pain and rated the evidence to be of “silver” quality<sup>30</sup> and “good” quality,<sup>15</sup> respectively. We conclude, therefore, that there is moderate-quality evidence that LLLT reduces pain and improves function (Tab. 2). None of the reviews reported on possible side effects and safety.

**Therapeutic ultrasound.** Two reviews<sup>15,31</sup> reported the effect of therapeutic ultrasound (pulsed or continuous), including 1 and 2 primary studies, respectively (Tab. 7). Patients included had clinically confirmed RA. Results from the 2 primary studies could not be combined in a meta-analysis. One RCT of moderate quality showed statistically significant improvements in pain (tender or painful joints) and function

(grip strength, ROM). Patient global assessment was not reported. Based on one primary study of moderate quality, therefore, we conclude that there is low-quality evidence that therapeutic ultrasound reduces pain and improves function (Tab. 2). Neither of the reviews reported side effects.

**Thermotherapy.** Three reviews<sup>15,32,33</sup> reported the effects of thermotherapy (Tab. 7), including the interventions “melted paraffin wax applications” and “superficial moist heat and cryotherapy.” All patients included had clinically confirmed RA. The methodological quality of the primary studies was low, and none of the included reviews provided quantitative pooling of the results. One primary study of low quality reported statistically significant improvements in pain and function (grip strength). The study was included in all 3 reviews, and the results were obtained in the group that received a combination of paraffin wax and exercise therapy. When paraffin wax alone was compared with a control, there were no significant differences in any of the outcomes. All 3 reviews agreed that thermotherapy is more effective as an adjunct therapy than it is alone. Patient global assessment was not reported as an outcome in any of the included studies. On these grounds, we find it reasonable to conclude that the effect of thermotherapy alone is unclear (Tab. 2). No side effects were reported.

**Transcutaneous electrical nerve stimulation (TENS).** Two reviews,<sup>15,34</sup> including the same primary studies, assessed the outcomes of TENS (low frequency, high frequency) (Tab. 7). All patients included had clinically confirmed RA. Based on a large variation in patients and methodological issues in the included studies, the results were not combined in a meta-analysis. Results

regarding pain were conflicting. Two studies, one of low quality and one of moderate quality, found statistically significant improvement in pain (visual analog scale score, joint tenderness), whereas one study of moderate quality found no significant improvement in pain (visual analog scale score). Because of the inconsistent results, we conclude that the effect of TENS is unclear (Tab. 7). No side effects were reported.

## Discussion

Based on the evidence from 28 systematic reviews, our overview indicates that the quality of evidence for the effectiveness of most of the interventions was low, except for patient educational programs, joint protection, LLLT, and GLA (herbal therapy).

Although our intention with the present overview was to provide useful information to patients, clinicians, researchers, and policymakers, it surely has several limitations. First, the results from this overview cannot be interpreted as treatment recommendations. Recommendations for practice are normally parts of clinical guidelines, and guideline recommendations should be based on both research evidence and clinical experience. Recommendations should be developed through a process involving both methodologists and clinicians and taking other factors, such as resources and culture, into account. This overview summarizes the empirical evidence, and the bottom line is what is known from systematic reviews. Thus, this overview could be the core element of a clinical guideline, but not a guideline in itself.

Second, based on our results, it is not possible to make conclusions regarding the effects of modalities on patients with various classes of disease because none of the included reviews were distinct on these topics.

An overview summarizes results of existing reviews. It does not re-review the literature or add more outcomes or studies. The results of an overview are dependent on the number of high-quality, updated systematic reviews and the quality of the primary studies included. Systematic reviews usually give us the answers in general terms, due to the primary studies’ heterogeneity in diagnosis, interventions, and outcomes, and seldom help the clinician who wants to know what type of intervention is most effective in treating a specific patient in a clinical practice. Given these limitations, an overview might be more valuable for policymakers than for clinicians.

Third, possible harmful effects or side effects of the interventions were seldom reported, and no conclusions were drawn in any of the included reviews. This is in accordance with Ethgen et al,<sup>35</sup> who found that harm was less often described in reports of nonpharmacological treatment trials than in reports of pharmacological treatment trials. This might partly be explained by a presupposed lower degree of harmful effects; however, most therapy might imply the risk of adverse effects. Unexpected side effects can only be detected if data on all events are systematically collected.

Our overview shows that the evidence for effects of the most common nonpharmacological and nonsurgical interventions for patients with RA is of low quality. Low-quality evidence is not the same as the intervention does not have effect, rather that there is insufficient evidence to draw firm conclusions with regard to the effectiveness of many of the interventions usually offered to patients with RA. The overall methodological quality of the primary studies was frequently relatively weak. However, there are probably better conducted newly

published RCTs not captured in the included reviews, which might enhance the quality of evidence for the effects of the interventions. This is possibly the case especially for exercise therapy.

Exercise therapy is considered to be a cornerstone in the treatment of RA in all stages of the disease.<sup>36</sup> The American College of Rheumatology<sup>2</sup> underscores the necessity of an interdisciplinary approach to the comprehensive management of RA. They recommend patient education, instruction in joint protection, conservation of energy, and a home program of ROM and strengthening exercises as important in achieving the treatment goals. Furthermore, the American College of Rheumatology reports that regular participation in dynamic and aerobic conditioning exercise programs improves joint mobility, muscle strength, aerobic fitness, and function as well as psychological well-being without increasing fatigue or joint symptoms. Apart from the recommendations of patient education and joint protection, their strong recommendations of exercise therapy are not supported by the present overview, which found low-quality evidence for exercise therapy.

Our results are supported by Smidt et al,<sup>37</sup> who conducted a best-evidence summary of systematic reviews on the effectiveness of exercise therapy. They concluded that there was insufficient evidence to support or refute the effectiveness of exercise therapy for patients with RA. The Ottawa Panel,<sup>25</sup> however, recommend the use of exercise therapy for RA in their guidelines, but they emphasize that their guidelines are limited by generally poorly reported descriptions of therapeutic exercise programs and the outcomes in the included studies.

The latest Cochrane review on exercise therapy for RA<sup>38</sup> was conducted in 1998. It concluded that dynamic exercise therapy had positive effects, but that research on long-term effects was needed. Lately, many high-quality studies have been carried out and concluded that exercise is both effective and safe in patients with RA.<sup>39-43</sup> Thus, it is likely that an updated, high-quality review on exercise therapy for patients with RA will make it possible to draw firmer conclusions on the effect of exercise therapy for this group of patients.

As pointed out earlier, better conducted primary studies are necessary to draw firm conclusions on the effectiveness of nonpharmacological and nonsurgical interventions for patients with RA. Foley et al<sup>44</sup> assessed the quality between pharmacological and nonpharmacological studies. They found that the greatest difference was for subject masking, in which virtually all drug trials succeeded, whereas only a small percentage (35%) of non-drug trials succeeded. It is obvious that masking the patients is difficult in most of the interventions in our study, but masking of the assessors is possible in most cases and should be carried out. Blinding is particularly important when the outcome measures involve patient-reported symptoms such as pain.<sup>45</sup> Outcome measures also should be standardized, using valid and reliable tools, and follow-up should be of sufficient length to assess long-term effects.

The summarized evidence may be used by patients, health care practitioners, policymakers, and researchers. The policymakers need research-based evidence to guide their budget decisions on which interventions to reimburse and what kind of research to fund. For the researchers, our overview might identify areas where research is missing and improvements are needed. Clinicians and pa-

tients are usually interested in what type of intervention is the most effective in a specific context. An overview of systematic reviews will most often not add new evidence for a single intervention, but rather synthesize available evidence on different interventions for the same condition and thus provide clinicians and patients with an overview of the evidence for the most commonly used interventions. Because the overview gives the answers in general terms, it might be more valuable for policymakers and researchers than for clinicians and patients.

The increasing need for valid, relevant health care information emphasizes the need for rigorous clinical research to guide health care decisions. In the present overview, we found that the quality of evidence for most nonpharmacological and nonsurgical interventions for patients with RA is low. This does not mean that most of the interventions are ineffective, but rather that the quality of research evidence is low. As long as the primary studies have serious limitations, our confidence in the estimate of effect is low. Better conducted primary studies are warranted to provide stakeholders with high-quality information needed in their health care decisions.

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- 43 Hakkinen A, Hannonen P, Nyman K, et al. Effects of concurrent strength and endurance training in women with early or longstanding rheumatoid arthritis: comparison with healthy subjects. *Arthritis Rheum.* 2003;49:789-797.
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## Appendix 1.

### Search Strategy

(A) Study type: systematic reviews

1. controlled.ab. [ab.=all searchable words from the abstract]
2. design.ab.
3. evidence.ab.
4. extraction.ab.
5. randomized controlled trials/[MESH]
6. meta-analysis.pt. [pt.=publication type]
7. review.pt.
8. sources.ab.
9. studies.ab.
10. OR/1-9
11. letter.pt.
12. comment.pt.
13. editorial.pt.
14. OR/11-13
15. 10 NOT 14

(B) Participants: rheumatoid arthritis

Arthritis, rheumatoid/OR (arthritis adj2 rheumat\$).tw. [Textword]

(C) Interventions: nonpharmacological and nonsurgical

exp "Therapeutics"/(exploded MESH term) OR therap\$.tw. OR dh.fs. [Diet Therapy as floating subheading to a MESH term]

exp "behavior and behavior mechanisms"/OR exp "psychological phenomena and processes"/OR exp "mental disorders"/OR exp "behavioral disciplines and activities"/

The following MESH terms and floating subheading were excluded from the search result with NOT:

exp "Specialties, Surgical"/OR su.fs [Surgery as floating subheading to a MESH term]

exp "inorganic chemicals"/OR exp "organic chemicals"/OR exp "heterocyclic compounds"/OR exp "polycyclic compounds"/OR exp "macromolecular substances"/OR exp "hormones, hormone substitutes, and hormone antagonists"/OR exp "enzymes and coenzymes"/OR exp "carbohydrates"/OR exp "lipids"/OR exp "amino acids, peptides, and proteins"/OR exp "nucleic acids, nucleotides, and nucleosides"/OR exp "complex mixtures"/OR exp "biological factors"/OR exp "biomedical and dental materials"/OR exp "pharmaceutical preparations"/OR exp "chemical actions and uses"/

(D) Language restrictions: English or Scandinavian language

(E) Publication year from 2000 to January 2007

### Appendix 2.

#### Quality Assessment Checklist for Systematic Reviews

The following 9 criteria was rated as “met,” “unclear/partly met,” or “not met” according to a criteria list modified from a previously validated checklist<sup>7</sup>:

1. Is the search strategy described in enough detail for the search to be reproducible?
2. Was the search for evidence reasonably comprehensive?
3. Were the criteria used for deciding which studies to include in the review reported?
4. Was bias in the selection of articles avoided?
5. Were the criteria used for assessing the validity of the studies that were reviewed reported?
6. Was the validity of all of the studies referred to in the text assessed using appropriate criteria in analyzing the studies that are cited?
7. Were the methods used to combine the findings of the relevant studies (to reach a conclusion) reported?
8. Were the findings of the relevant studies combined (or not combined) and analyzed appropriately relative to the primary question the review addresses and the available data?
9. Were the conclusions made by the author(s) supported by the data and/or the analysis reported in the review?

### Appendix 3.

#### Excluded Reviews (n=41)

- Bartels EM, Lund H, Nneskiold-Samsøe B. Pool exercise therapy of rheumatoid arthritis [in Danish]. *Ugeskrift for Laeger*. 2001;163:5507-5513. [Review] [49 references]
- Berman BM, Swyers JP, Ezzo J. The evidence for acupuncture as a treatment for rheumatologic conditions. *Rheum Dis Clin North Am*. 2000;26:103-115. [Review] [54 references]
- Cleland LG, James MJ, Proudman SM. The role of fish oils in the treatment of rheumatoid arthritis. *Drugs*. 2003;63:845-853. [Review] [47 references]
- Clyman B. Sports, exercise, and arthritis. *Bull Rheum Dis*. 2001;50:1-3. [Review] [22 references]
- de Jong Z, Vlieland TP. Safety of exercise in patients with rheumatoid arthritis. *Curr Opin Rheumatol*. 2005;17:177-182. [Review] [43 references]
- Ernst E. Chinese herbal medicines for consumers in the West. *Focus on Alternative & Complementary Therapies*. 2005;10:94-97.
- Ernst E. Complementary medicine. *Curr Opin Rheumatol*. 2003;15:151-155. [Review] [19 references]
- Ernst E. Musculoskeletal conditions and complementary/alternative medicine. *Best Pract Res Clin Rheumatol*. 2004;18:539-556. [Review] [100 references]
- Fransen M. When is physiotherapy appropriate? *Best Pract Res Clin Rheumatol*. 2004;18:477-489. [Review] [54 references]
- Grant KL, Schneider CD. Alternative therapies: turmeric. *Am J Health Syst Pharm*. 2000;57:1121-1122.
- Hakkinen A. Effectiveness and safety of strength training in rheumatoid arthritis. *Curr Opin Rheumatol*. 2004;16:132-137. [Review] [46 references]
- Hammond A. What is the role of the occupational therapist? *Best Pract Res Clin Rheumatol*. 2004;18:491-505. [Review] [68 references]
- Hardware B, Lacey A. Acupuncture and other alternative therapies in rheumatoid arthritis. *Professional Nurse*. 2002;17:437-439.
- Jonas WB, Linde K, Ramirez G. Homeopathy and rheumatic disease. *Rheum Dis Clin North Am*. 2000;26:117-123.
- Kettunen JA, Kujala UM. Exercise therapy for people with rheumatoid arthritis and osteoarthritis. *Scand J Med Sci Sports*. 2004;14:138-142. [Review] [31 references]
- Li LC, Iversen MD. Outcomes of patients with rheumatoid arthritis receiving rehabilitation. *Curr Opin Rheumatol*. 2005;17:172-176. [Review] [28 references]
- Lodha R, Bagga A. Traditional Indian systems of medicine. *Ann Acad Med Singapore*. 2000;29:37-41. [Review] [52 references]

(Continued)

## Appendix 3.

Continued

- Madsen OR. Significance of physical activity for bone mass and fracture risk in patients with rheumatoid arthritis [Danish]. *Ugeskrift for Laeger*. 2002;164:4528-4531. [Review] [40 references]
- Mulligan K, Newman S. Psychoeducational interventions in rheumatic diseases: a review of papers published from September 2001 to August 2002. *Curr Opin Rheumatol*. 2003;15:156-159.
- Munneke M, De Jong Z. The role of exercise programs in the rehabilitation of patients with rheumatoid arthritis. *International Sport Med Journal*. 2000;1:1-12.
- Nasermoaddeli A, Kagamimori S. Balneotherapy in medicine: a review. *Environmental Health & Preventive Medicine*. 2005;10:171-179.
- O'Grady M, Fletcher J, Ortiz S. Therapeutic and physical fitness exercise prescription for older adults with joint disease: an evidence-based approach. *Rheum Dis Clin North Am*. 2000;26:617-646. [Review] [137 references]
- Paternostro-Sluga T, Stieger M. Hand splints in rehabilitation. *Crit Rev Phys Rehabil Med*. 2004;16:233-256.
- Pedersen BK, Saltin B. Evidence for prescribing exercise as therapy in chronic disease. *Scand J Med Sci Sports*. 2006;16(suppl 1):3-63. [Review] [735 references]
- Ruxton C. Health benefits of omega-3 fatty acids. *Nurs Stand*. 2004;18:38-42. [Review] [44 references]
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- Stamp LK, James MJ, Cleland LG. Diet and rheumatoid arthritis: a review of the literature. *Semin Arthritis Rheum*. 2005;35:77-94.
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- Taibi DM, Bourguignon C. The role of complementary and alternative therapies in managing rheumatoid arthritis. *Fam Community Health*. 2003;26:41-52.
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- Tidow-Kebritchi S. Effects of diets containing fish oil and vitamin E on rheumatoid arthritis. *Nutr Rev*. 2001;59:335-338.
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- Vliet Vlieland TP. Rehabilitation of people with rheumatoid arthritis. *Best Pract Res Clin Rheumatol*. 2003;17:847-861. [Review] [96 references]
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