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 **TITLE**:Factors associated with hand and upper arm functional disability in people with rheumatoid arthritis: A systematic review

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**DECLARATION:**

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**ABSTRACT**

**Aim**: This original systematic review aimed to summarize evidence within observational studies on the factors associated with hand functional disability in adults with Rheumatoid Arthritis (RA).

**Methods**: A rigorous extensive systematic literature search was conducted in six medical databases for peer-reviewed English-language observational studies exploring the factors associated with hand function for people with RA. Factors were critically classified under the domains of the International Classification of Functioning, Disability and Health (ICF) framework and health related factors. The methodological quality was determined using the quality of cross-sectional studies (AXIS) tool. Factors related to hand function that were investigated in two or more studies were explored using a best-evidence synthesis.

**Results**: Twenty articles met the inclusion criteria from 1,271 citations. All presented cross-sectional data (five high and 15 low quality articles), resulting in limited evidence in the best-evidence synthesis. For the factors classified under the ICF domains, the best-evidence synthesis indicated that a diverse range of positive and negative factors were associated with hand function. However, key factors were hand strength, disease activity, and pain intensity. It is evident that few sociodemographic factors have been explored for the association with hand function.

**Conclusion**: The level of evidence was limited, but identified that modifiable factors such as grip strength, disease activity and pain are the most influential factors on hand function in people with rheumatoid arthritis. The review findings indicate that important sociodemographic factors that impact on hand function in people with RA are not yet considered or reported in clinical research.

**SIGNIFICANCE AND INNOVATIONS**

* Studies focused predominantly on body structure and function factors, highlighting a lack of consideration and investigation into personal and environmental factors when considering the impact of RA on hand function
* Modifiable factors such as grip or pinch strength, disease activity and pain are the most influential factors on hand function in people with RA
* Well-designed longitudinal, preferably cohort, studies are now needed to better understand the influence of sociodemographic factors on hand functional disability in people with RA

**INTRODUCTION**

Rheumatoid arthritis (RA) is an inflammatory, systemic autoimmune and chronic disease affecting approximately 1% of individuals worldwide. The disease pathogenesis remains unknown (1). Hand involvement is typically present in 80- 90% of the people with RA (2) and results in stiffness, swelling, pain, range of motion (ROM) limitation, deformity and muscle weakness (3). These impairments have a formidable impact on hand function and daily life activities (4) causing hand functional disability for a substantial percentage (81%) of people with RA (5).

Current management of RA focuses on early diagnosis and early intensive intervention with disease-modifying anti-rheumatic drugs (DMARDS) together with biological medication. These new generation drugs have delivered substantial improvements in decreasing disease activity and minimising disability (6). However, with recent analysis of cohorts of people with RA on DMARDS and biological treatments, it is evident that hand impairments and activity limitations remain a significant problem (7). Moreover, hand problems exacerbate progressively even in patients in remission or with low disease activity (8), and hand function was reported to be substantially worse when compared to referents despite low disease activity (9). Despite new drug advances and targeted medical treatment hand function problems for people with RA still persist. Hand function is an important component of disability in people with RA (10). Fortuitously, hand function assessments can be sensitive tools for assessing change in hand functional status (11).

Since the focus of rehabilitation interventions is to maintain and improve hand function abilities for people with RA (12), it is important to identify the factors that influence the impact of RA disease on hand function in daily living activities. Consequently, more knowledge about the factors influencing hand functional outcome in people with RA is needed. Hand function interventions for people with RA can be improved by understanding and considering these factors in planning and delivering treatment intervention. No review has yet reported an overview of factors, which are associated with hand functional disability for people with RA. Therefore, this study aimed to provide a comprehensive synthesis of the evidence reported within observational studies for the factors associated with hand functional disability in patients with RA in a real-world setting rather than RCT**.**

**MATERIALS AND METHODS**

**Protocol registration**

The protocol for this systematic review was registered with the International Prospective Register of Systematic Reviews (PROSPERO) in May 2017 (protocol reference: CRD42017065856).

**Eligibility criteria**

Studies were included if they fulfilled the following criteria: (1) Full length peer-reviewed studies published in English language; (2) Observational studies exploring and reporting factors associated with hand functional disability (3) Involvement of participants with the diagnosis of RA, either according to the American College of Rheumatology (ACR) criteria (13) or 2010 ACR/European League Against Rheumatism (EULAR) criteria (14) for RA; (4) Studies that have used hand functional disability outcome measures either self-reported or objective measures commonly used with persons with rheumatic diseases, have psychometric support and evaluate hand-related activity limitations and/or participation restrictions.

Articles that have only used self-reported hand function subscales from generic disability measures or hand functional disability outcome measures of impairment were excluded. This is because generic disability measures are not designed to provide detailed feedback on hand function and include insufficient coverage on hand use. Studies including participants diagnosed with seropositive criteria were excluded, since seropositive criteria are majorly based on the Rheumatoid Factor (RF) which can occur in other autoimmune conditions and chronic infection.

**Information Sources and Search Strategy**

A computerized literature search was performed in the following databases: MEDLINE, EMBASE, CINAHL, PsycINFO, AMED, and Web of Sciences. MeSH terms and free text search keywords have been utilized to develop the search for this review. The search strategy was formulated in MEDLINE (Table 1) and adapted for use in other databases after consultation with an experienced medical librarian. Published filters were used to identify studies published in English language and from January 1990 up to March 2017. Reference lists of all studies meeting the inclusion criteria have been checked. Using Google Scholar, forward citation searching was performed in the current review. Key studies that have been identified by the database searches and selected as meeting the inclusion criteria have been used to carry out citation searching. All citations were imported into a single EndNote® (version X7) library for data management.

**Study selection and data collection**

Following removal of duplicates (using EndNote® software); the study selection process was completed in two stages. The first stage included examining only the titles and abstracts of the search results to eliminate all clearly ineligible publications. Secondly, a full-text review of articles that appeared to meet the inclusion criteria or in cases when a decision cannot be made based on the title and abstract alone was conducted. The selection process was completed entirely by the first author. The research team were consulted where any ambiguity arose.

Pertinent data were extracted and documented by the first author, and cross-checked by the research team for completion and accuracy. A predesigned data extraction form was used to extract the following data: General information (author and year of publication), characteristics of participants (sample size, disease duration, age and gender), study characteristics, hand function outcome measures, factors, and association between factors and outcome. Factors tested for association with hand function have been categorised under the domains of the International Classification of Functioning, Disability and Health (ICF) framework and health related factors.

**Assessment of methodological quality**

Three reviewers independently assessed the methodological quality of the included articles. The first author (HA) assessed all studies included in the review, and each one of the other reviewers (JA and AMH) assessed half each of the included articles. The quality and risk of bias of the included studies were assessed using a critical appraisal checklist to assess the quality of cross-sectional studies (AXIS) (15). The AXIS comprises 20 items focus mainly on the presented methods and results. Seven questions of the AXIS are related to the quality of reporting, seven questions are related to the study design quality and six questions are related to the risk of biases. Each item was scored by means of the following scoring system: ‘yes’ (Y) is ‘1’; and ‘no’ (N) or ‘don’t know’ (DK) is scored as ‘0’. The overall score is a percentage score of all 20 items. Studies with an overall score of ≥60% were rated as high quality (16). Disagreements regarding quality assessments between the reviewers were resolved by discussion.

**Best-evidence synthesis**

Included studies exhibited marked heterogeneity in terms of patient characteristics, outcome measures, statistical analysis, and reporting of results. Consequently, meta-analysis was not possible and the best-evidence synthesis approach was used instead as recommended by Slavin (17). Only factors tested for association with hand functional disability, which have been measured and reported in the same manner and investigated in two or more studies, were included in the best-evidence synthesis. For studies that used two tools to evaluate hand function and reported an association between a factor and one tool but no association with another tool, the following conditions were applied: (1) If the study used a generic hand function tool and a hand specific tool, then only the results of the later were considered (2) If the study used two specific hand function tools, then the results of the tool, which has been used more frequently in the included studies, were considered. The Van Tulder ranking system for the level of evidence (18) was used as this is widely used and contemporaneous (16) (Table 2). Initially, the studies were categorised according to the type of study design. The favoured design was cohort study followed by case-control design and, at last, cross-sectional design. After that, the studies were ranked according to their methodological quality overall score. A result was consistent if the factor was significantly associated to hand function with the same direction of the association.

**RESULTS**

**Study selection**

The search of the selected databases resulted in the retrieval of 1,254 citations (MEDLINE 395; EMBASE 566; CINAL 122; AMED 54; PsychINFO 18; Web of Sciences 99), and another source search yielded 17 citations. After the removal of duplicate citations, 764 articles remained. Screening of citation titles and abstracts excluded 703 citations from the review. Out of the remaining 61 citations, 41 were excluded with reasons as presented in Figure 1. Finally, 20 articles met all inclusion criteria and were included in the present review. Hand searching of these articles resulted in the retrieval of one additional article, which was published in the Turkish language; thus, it was excluded. Forward citation tracking did not yield any further articles for inclusion in the review.

**Study characteristics**

The articles in the review were based on 19 independent studies of people with RA. Fifteen (75%) of the 20 articles were cross-sectional (2, 3, 19-31), two were case-control (32, 33), and three studies were cohort (11, 34, 35). Case-control and cohort studies included in this review presented cross-sectional data on the association between factors and hand function, therefore all studies were considered to be cross-sectional, resulting in at best limited evidence in the best-evidence synthesis. A full overview of study characteristics of the included studies is presented in a supplementary file 1.

**Methodological quality**

There was initial disagreement between the leading author (HA) and the second author (AMH) and third author (JA) on 19% and 27% respectively of the methodological quality items scored. Almost all disagreements were due to reading errors or a difference in interpretation of the methodological quality criteria. After four consensus meetings, no disagreement persisted and a third reviewer was not required to achieve consensus. Overall quality, assessed by the reviewers as the total percentage of quality appraisal items endorsed for each study, was high (≥ 60%) for five studies (25%) (2, 3, 21, 22, 29). The mean quality score over the 20 included articles was 49.5% with a range of 25% to 75%. The risk of bias items (6, 7, 13, and 14) were inadequately met by the included studies even for the studies with high overall quality scores. Unlike risk of bias, 80% (n=16) of the included studies have a high score for reporting quality. The mean quality score for reporting was 75% with a range of 29% to 100%. The overall scores of methodological quality, and quality scores for reporting, design and risk of bias domains of the included studies are presented in a supplementary file 2.

**Factors related to hand function**

A summary of all factors considered for best evidence analysis is presented in Tables 3 and 4. Regarding body structure and function factors, limited hand function was found to be associated with: weak hand strength measures (power, lateral pinch, tip pinch and tripod pinch strength), increase of dominant hand fingers flexion deficit, high disease activity (composite measure, tender joints count, C-reactive Protein and Patient’s global assessment of disease activity), presence of deformities in dominant hand, increase of ulnar deviation angle of dominant and non-dominant hand, low mental health status, high pain intensity (bodily pain and pain during activity), and more hand structural damage. Also, limited evidence was found to support non-dominant hand fingers flexion deficit is not associated with hand function. Conflicting evidence was found for the association between the factors swollen joint count, Erythrocyte Sedimentation Rate (ESR), presence of deformities in both hands, vitality, sum of painful Sequential Occupational Dexterity Assessment (SODA) tasks, hand pain intensity at rest, stiffness (intensity and duration) and hand function.

For functional status factors, limited evidence was found that reduced hand function is associated with low functional status level (physical functioning, social functioning and emotional function). In considering personal factors, there was conflicting evidence for the association between age and hand function. Seven studies reported that the difference between men and women with regard to hand function was not statistically significant; consequently, limited evidence is documented in the best-evidence synthesis. Regarding environmental factors, limited evidence was found that work activity is not associated with hand function. Finally, for health related factors there is conflicting evidence for the association between the factors of disease duration, general health status and hand function. Also, limited evidence was found that the level of RF is not associated with hand function.

**DISCUSSION**

This is the first systematic review that provides an overview of factors associated with hand functional disability in people with RA. From reviewing the literature, there is a lack of consistency with the variation in measures used in reporting hand impairments, leading to a limited ability to make comparison between studies. For instance, measuring and reporting ROM was inconsistent between the included studies, and the majority of studies did not provide a clear description of what is being measured (i.e. active or passive ROM). In addition, there were deficiencies associated with hand impairment outcome measurements, such as subjectively reporting hand deformities with lack of detail about assessment or grading methods. Based on these observations, it is evident that protocols for assessments of hand impairments in the RA population need to be agreed and implemented. Consistency in reporting hand function is also now required.

Although quality of reporting was satisfactory for the majority of the studies identified in this review, almost all studies failed to account for and minimise systematic errors. Therefore, conclusions from this review could be at risk of bias due to weaknesses in those studies included. Improving selection and reporting of study participants, especially response rates and information about non-respondents would address these biases and should be incorporated into future research.

This review showed that studies that consider hand disability in people with RA reported predominantly on body structure and function factors. There was a lack of consideration of, and investigation into, personal and environmental factors when considering the impact of RA on hand function. Many factors of body structure and function were significantly associated with hand functional disability. Importantly, grip strength is routinely recorded in rheumatology clinical trials. This is appropriate and relevant as grip strength is a valid indicator of disability (36), has been shown to predict later hand function (37) and contributes to hand function improvements (38) in people with RA. In this review, more than half of the included studies assessed the association between power grip strength and hand function, and all reported statistically significant relationships, regardless of the measurement or reporting method. This confirms what has been suggested that power grip strength is a valid and reliable indicator of hand function in RA population and clinicians can have confidence in this finding for using it in clinical practice.

Disease activity variables have been found to be associated with hand function except for ESR and swollen joint count, for which there was conflicting evidence. An explanation of this observation may be due to the fact that different hand function assessment tools covers different spectrum of functioning (39), and people with RA show unique and different clinical presentations; thus, no single disease activity variable can accurately detect every patient’s disease activity at any given point in time (40). This review results suggests that disease activity is a modifiable parameter that significantly contributes to hand function.

Pain in RA is the main treatment target for patients and clinician (41). Results from RA cohorts conducted during an era when biological treatments were available demonstrated that pain still remains a problem and influences performing valued life activities (7, 42). In the present review, limited evidence was found that higher intensity of bodily pain and hand pain during activity were associated with an increase of hand functional disability, and conflicting evidence was found for the association with hand pain at rest. This indicates that hand pain during activity may substantially contribute to hand functional disability. In line with these results, a recent longitudinal report on a Swedish RA cohort indicated that general pain was higher than hand pain during activity, which in turn was higher than hand pain at rest (7).

Reviewed studies indicate an association between structural damage and hand function, and that an increase of radiographic joint damage is correlated with an increase of hand functional limitations. However, in line with recent evidence that radiographic joint damage is less influential in the context of modern treatment (43) the relative importance of structural damage may be of less importance in future research.

The fact that conflicting evidence was found for the association between hand function and hand stiffness duration and intensity is remarkable, since stiffness is a symptom widely experienced by patients with RA. Besides methodological explanations (i.e. only cross-sectional studies with relatively small sample size), evidence from a systematic review of stiffness measures demonstrated that there is limited evidence to support the validity of the currently available stiffness measures (44). Furthermore, qualitative evidence suggested that RA patients experience stiffness differently, and reported stiffness in terms of impact rather than by duration or severity (45).

In examining functional status, there was limited evidence that reduced hand function is associated with poor physical function, social function and emotional role. The association found between hand function and functional status measures may indicate that hand disability influences both the activity and participation level of functioning. This is because physical function measures such as Health Assessment Questionnaire (HAQ), are measuring activity limitations, whereas social functioning and emotional role scales are measuring participation restrictions (46).

Few personal factors have been explored for the association with hand function. Out of 12 personal factors identified as meaningful for general functioning in RA (47), only coping could be categorized as a personal factor and was included in one study as a factor for hand function (34); thus, it was not included in the best evidence synthesis. Important personal factors in relation to specific hand functional outcome are not identified. Identifying the role of these factors as determinants and modifiers of hand function can facilitate the process when evaluating and planning interventions for people with RA.

The findings of a qualitative study recruiting RA patients with hand deformity proposed that environmental factors play a significant role in hand related activity limitations and participation restriction (48). However, in this review the impact of only a few environmental factors have been explored in relation to hand function. One factor; namely work activity, was included in the best evidence synthesis, since it was assessed in three independent studies (19, 20, 32). However, the relative importance and influence of environmental factors might vary according to the settings and culture. For instance, low-income countries tend to have limited or fewer resources in term of health care system, compared with high-income countries. Moreover, social support and beliefs about health disability may differ across countries. Considering these issues, important environmental factors in relation to hand functional outcomes in specific cultures and settings should be identified.

For health related factors, conflicting evidence was found regarding the relationship between hand function and disease duration and general health status. Long disease duration was expected to be significantly associated with poor hand function, since hand impairments are prevalent and deteriorate over time in patients with long disease duration (3, 8). Alongside, the limitations mentioned earlier concerning the methodologies of the included studies, a possible explanation for this finding might be related to the fact that patients with long disease duration may have adapted to their situation and they do not expect any effective treatment to be available (3). Cross-sectional studies have concluded that disease activity is the major explanatory factor for activity limitations in RA patients with disease duration less than 10 years (36). Accordingly, disease duration may be an irrelevant factor to consider when evaluating hand function, particularly with disease duration less than 10 years.

This review is not without limitations. Only the first author screened the titles and abstracts. However, citations were only considered irrelevant if the title or abstract did not include any information on hand function outcomes. Moreover, the review team were consulted where any ambiguity arose during the selection process. Therefore, the possibility of removing relevant studies was low. This review was limited by the wide variation in the included studies’ sample sizes (range: n=25 to 200). Accordingly, sample size may affect the results of associations reported in the included studies; small associations are significant in studies with a large sample size and not in studies with a small sample size. The included review studies did not all present the size of the association within their statistical analysis and reporting, so it is difficult to preclude that the results are biased by this. The studies included have used self-reported and performance based measures of hand function or both. This probably influenced the results of this review, since, performance based measures cover a narrow spectrum of hand functioning (39), and may not accurately reflect hand abilities (49). Furthermore, performance based and self-reported measures of hand function are not strongly associated (50). Future research may benefit from stratifying outcomes rather than combining them. The quality assessment tool (AXIS) used in this review was developed based on literature and methodological standards; however, further studies are required to explore its repeatability. Attention should be given to the disagreement (27% and 19%) between the reviewers on the methodological quality of the study. Reducing the scoring options into “yes”, “no, instead of including “don't know” may increase the simplicity of use of the AXIS and may minimise the disagreements between reviewers. The grey literature or unpublished studies were not searched as there are few studies focusing on hand function in RA patients (19); therefore, the number of extra studies identified by grey literature would also be small. Studies written in English were selected and included in the review. The percentage of all articles written in other languages was small (8%); consequently, it is unlikely that this percentage would introduce language bias into the review. Finally, out of the 20 articles included in the review, one reviewer (JA) involved in this review authored two articles. However, to ensure that the quality assessment process was unbiased, quality assessment of these two articles were completed by the first and second author.

This systematic review has summarised current evidence for the factors associated with hand function in RA patients. It has also underlined areas where methodology is lacking and potential directions for future research. There are numerous factors where current evidence is limited or conflicting. These factors can be classified as modifiable (e.g. disease activity, hand strength, psychosocial factors) and non-modifiable factors (e.g. age, sex, structural damage). Focusing on non-modifiable factors offers little added value to improve hand function in people with RA. Therefore, modifiable factors should be of key concern as some of these factors can be modified with specific strategies and interventions. Before new strategies and interventions are established to improve hand function in people with RA, well-designed longitudinal studies need to be performed to get more understanding in the causality between factors and hand function. Important sociodemographic factors in relation to hand function in RA patients need more considerations by future research.

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| **Table 1: Search strategy in MEDLINE through Ebscohost** |
| # | Search terms |
| S1 | ((TI hand or TI hands) N3 (TI activit\* OR TI abilit\* or TI function\* OR TI perform\* OR TI skill\* OR TI impair\* OR TI disabilit\*)) OR ((AB hand OR AB hands) N3 (AB activit\* OR AB abilit\* OR AB function\* OR AB perform\* OR AB skill\* or AB impair\* OR AB disabilit\*)) |
| S2 | ((MH "Hand+") OR (MH "Hand Deformities") OR (MH "Hand Strength")) AND ((TI ADL OR TI “daily activit\*” OR TI “activity limitation\*” OR TI “activities of daily living”) OR (AB ADL OR AB “daily activit” OR AB “activity limitation\*” OR AB “activities of daily living”)) |
| S3 | S1 OR S2 |
| S4 | (MH "Arthritis, Rheumatoid") OR (TI RA) or (AB RA) OR (TI "Rheumatoid Arthritis") OR (AB "Rheumatoid Arthritis") |
| S5 | (MH "Arthritis, Juvenile") OR (TI "Juvenile Arthritis") OR (AB "Juvenile Arthritis") |
| S6 |  S4 NOT S5 |
| S7 |  S3 AND S6 |
| S8 | limit S7 (English language , yr="1990 -Current") |

Identification

Records after duplicates removed
(n =764)

Screening

Records screened (Titles and abstracts)
(n =764)

Additional records identified through other sources
(n = 17)

Full-text articles excluded, with reasons: n=41

* Conference abstracts (n =11)
* Thesis (n=1)
* Letters to the editors (n=1)
* Use of self-reported hand function subscale from a generic disability measure (n=4)
* Use of generic disability measure (n=8)
* Analysis is not reported (n=5)
* Use of hand impairment measure (n=1)
* patients are not diagnosed according to the ACR criteria or 2010 ACR/EULAR criteria (n=10)

Eligibility

Included

Records identified through database searching
(n =1254)

Records excluded
(n =703)

Full-text articles assessed for eligibility
(n=61)

Articles included in the review (n =20)

**Figure 1. PRISMA ﬂow chart of search results**

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|  **Table 2. Best-evidence synthesis** (18) |
|  **Level of evidence**  | **Description**  |
|  Strong | Generally consistent findings were presented in multiple high-quality cohort studies |
| Moderate | One high-quality cohort study and at least two high-quality case–control studies, or when at least three high-quality case–control studies show generally consistent findings |
| Limited | Generally consistent findings were found in a single cohort study, or in maximum two case–control studies, or in multiple cross-sectional studies |
| Conflicting | Less than 75% of the studies reported consistent findings |
| No evidence | No study could be found |

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| **Table 3.**  **Overview of findings regarding associations of body structure and function factors with hand function** |
| **Body Structure and function factors**  | **Association Found** | **No association found** | **Level of evidence** |
| **Strength**  |  |  |  |
|  Power grip (mean value of both hands)  | One HQ (22) and three LQ (23, 33, 35)  |  | Limited evidenceLimited evidenceLimited evidence |
|  Power grip (dominant hand)  | Two HQ (21, 29)and one LQ (27) |  |
|  Power grip (Non-dominant hand)  | Two HQ (21, 29) |  |
|  Lateral pinch (mean value of both hands) | One HQ (22) and one LQ (23)  |  | Limited evidence |
|  Tip pinch (mean value of both hands) | One HQ (22) and one LQ (23) |  | Limited evidence |
|  Tripod pinch (mean value of both hands) | One HQ (22) and one LQ (23) |  | Limited evidence |
| **Range of motion**  |  |  |  |
|  Dominant hand fingers flexion deficit  | One HQ (21) and one LQ (30) |  | Limited evidence |
|  Non-dominant hand fingers flexion deficit  |  | One HQ (21) and one LQ (30) | Limited evidence |
| **Disease activity**  |  |  |  |
|  Composite measure  | Two HQ (2, 21) and five LQ (19, 23, 24, 26, 34) | One LQ (11) | Limited evidence |
|  Swollen joint count | One HQ (2) and one LQ (24) | One LQ (31) | Conflicting evidence |
|  Tender joint count | One HQ (2) and two LQ (24, 31) |  | Limited evidence |
|  ESR  | Two LQ (19, 24) | One HQ (2) and two LQ (25, 35) | Conflicting evidence |
|  CRP | One HQ (2) and two LQ (24, 25) |  | Limited evidence |
|  PGA  | One HQ (2) and one LQ (24) |  | Limited evidence |
| CRP: C-reactive Protein; ESR: Erythrocyte Sedimentation Rate; HQ: High quality; LQ: low quality; PGA: Patient s’ global assessment of disease activity; SF-36: Short Form Health Survey Questionnaire |

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|  **Table 3.** (Cont’d) |
| **Body Structure and function factors**  | **Association Found** | **No association found** | **Level of evidence** |
| **Deformity**  |  |  |  |
|  Presence of deformities in dominant hand  | Two LQ (20, 32) |  | Limited evidence |
|  Presence of deformities in both hands  | One LQ (19) | One HQ (21) | Conflicting evidence |
|  Ulnar deviation of dominant hand  | One HQ (29) and two LQ (27, 34) |  | Limited evidence |
|  Ulnar deviation of non-dominant hand  | One HQ (29) and one LQ (34) |  | Limited evidence |
| **Mental health**  | One HQ (2) and two LQ (20, 24) |  | Limited evidence |
| **Vitality**  | One HQ (2) and one LQ (24) | One LQ (20) | Conflicting evidence |
| **Structural damage (radiographic)**  | One HQ (22) and three LQ (23, 25, 27) |   | Limited evidence |
| **Pain** |  |  |  |
|  Bodily pain (VAS) | Two LQ (23, 35) |  | Limited evidence |
|  Bodily pain (SF-36)  | One HQ (2) and LQ (24) |  | Limited evidence |
|  Hand pain during activity (SODA tasks) | Two LQ (30, 35) | One LQ (20) | Conflicting evidence |
|  Hand pain during activity (VAS) | Two HQ (2, 21) |  | Limited evidence |
|  Hand pain at rest (VAS) | One HQ (2) and one LQ (25) | One HQ (21) and LQ (30) | Conflicting evidence |
| **Stiffness**  |  |  |  |
|  Duration | One HQ (21) | One LQ (25) | Conflicting evidence |
|  Intensity  | One HQ (21) | One LQ (20) | Conflicting evidence |
| HQ: High quality; LQ: low quality; SODA: Sequential Occupational Dexterity Assessment; VAS: Visual Analog Scale  |

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| **Table 4.**  **Overview of findings regarding associations of functional status, personal, environmental, and health related factors with hand function** |
| **Factors**  | **Association Found**  | **No association found**  | **Level of evidence**  |
| **Functional status**  |  |  |  |
|  Physical functioning (HAQ)  | Two HQ (2, 21) and five LQ (11, 23, 24, 27, 30) | One LQ (19) | Limited evidence |
|  Physical functioning (SF-36) | One HQ (2) and one LQ (24) |  | Limited evidence |
|  Social functioning  | One HQ (2) and one LQ (24) |  | Limited evidence |
|  Emotional role  | One HQ (2) and one LQ (24) |  | Limited evidence |
| **Personal factors** |  |  |  |
|  Age | Three LQ (19, 28, 31) | Four LQ (20, 26, 30, 34, 35) **†** | Conflicting evidence |
|  Gender |  | One HQ (21) and six LQ (19, 20, 26, 30, 31, 34, 35)† | Limited evidence |
| **Environmental factors** |  |  |  |
|  Work activity |  | Three LQ (19, 20, 32) | Limited evidence |
| **Health related factors**  |  |  |  |
|  Health condition |  |  |  |
|  Disease duration | Seven LQ (19, 23, 25, 28, 30, 31, 34, 35) † | Two HQ (3, 21) and two LQ (20, 26) | Conflicting evidence |
|  Rheumatoid factor (RF) |  | Three LQ (19, 23, 32) | Limited evidence |
|  General state of health | One HQ (2) and one LQ (24) | One LQ (20) | Conflicting evidence |
| †:  Study (34) and (35) were considered as one body of evidence, since both studies reported the findings from the same sample of RA patients with regard to the association between hand function and disease duration, age and gender; HAQ: Health Assessment Questionnaire; HQ: High quality; LQ: low quality; SF-36: Short Form Health Survey Questionnaire |