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## The management of hand osteoarthritis: The rheumatologist's perspective

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### ABSTRACT

Hand osteoarthritis (OA) is treated by several medical professionals. In this review the rheumatologist's perspective will be conveyed. The rheumatologist tasks are to diagnose hand OA, exclude other causes of patient's complaints, and provide treatment. The rheumatologist therefore has a distinctive and important role in hand OA treatment. Although no disease modifying treatment exists, there are multiple options for managing hand OA in rheumatology practice, with the goal of achieving symptom relief and optimizing hand function. These treatments can be non-pharmacological or pharmacological. In this review we will provide a summary of evidence-based management options based on existing guidelines. Furthermore, we will describe common practice among rheumatologists for hand OA management. In order to do so, we performed a literature review of studies addressing treatment modality usage for hand OA. The review comprised 25 studies, which were heterogeneous in terms of treatment modality usage. In addition, a detailed description of care usage by patients in a Rheumatology outpatient clinic is given, based on data of our Hand Osteoarthritis in Secondary care primary hand OA cohort. The large majority of these patients used any form of hand OA treatment (83%). Non-pharmacological treatment was less frequently used (47%) than pharmacological treatment (77%).

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### Introduction

Osteoarthritis (OA) is a prevalent rheumatic musculoskeletal disorder affecting more than 300 million individuals worldwide.<sup>1</sup> One of the most common types of OA affects the hands.<sup>2,3</sup> Symptomatic hand OA is present in 3%- 16% of the general population.<sup>4</sup> It is associated with high clinical burden due to symptoms of hand pain, weakness, stiffness, limited hand mobility, functional limitations and a diminished quality of life,<sup>2,5</sup> which means adequate management is crucial. As no disease-modifying treatments are available yet, hand OA treatment remains symptomatic.<sup>6</sup> OA care to patients with OA in the hands is provided by general practitioners, orthopedic and plastic surgeons, occupational and physical therapists, amongst others. Their perspectives are given elsewhere

in this issue. This review will focus on the rheumatologist's perspective.

In many countries such as the Netherlands patients with complaints of the hands due to OA first visit their general practitioner, and are referred to health care professionals in secondary care if indicated. The role of the rheumatologist consists of diagnostics in case there is doubt about the diagnosis and subsequently of starting OA management. Sometimes the diagnosis is already clear and patients are referred solely for disease management. The diagnosis of hand OA can be made clinically when typical clinical hallmarks are present, and then no laboratory tests and radiography is needed.<sup>7</sup> However, making a confident diagnosis can be difficult when marked inflammatory symptoms and/or signs are present, especially if involving atypical sites such as the wrist or metacarpophalangeal joints.<sup>7</sup> The differential diagnosis of hand OA is wide. Depending on patient characteristics as age, sex, family history, occupational and recreational activities, symptoms and signs, including the presence of psoriasis, and results of laboratory tests and radiography, diseases must be considered such as psoriatic arthritis, rheumatoid arthritis, (polyarticular)

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**Table 1**

Overview of several recommendations and statements for pharmacological and non-pharmacological treatment modalities of hand OA by EULAR and ACR, and of polyarticular OA by OARSI.

	EULAR [10]	OARSI [11]	ACR [12]
<b>Non-pharmacological therapy</b>			
Exercise	Should be considered for every patient to improve function and muscle strength	Core treatment	Strongly recommended
Physical therapy	Should be offered to every patient	Core treatment	Likely benefit for most patients
Occupational therapy	Should be offered to every patient	N/A	Likely benefit for most patients
Education	Should be offered to every patient	Core treatment	Strongly recommended (“self-efficacy and self-management programs”)
Orthoses	Should be considered for patients with CMC1 OA, long term use is advocated	N/A	Strongly recommended for CMC1 OA, conditionally for other hand joints
Assistive devices	Should be offered to every patient	N/A	N/A
<b>Pharmacological therapy</b>			
Paracetamol (acetaminophen)	Can be regarded, preferably for a limited duration, in selected patients (for example if oral NSAIDs are contraindicated)	Recommended against	Conditionally recommended
NSAIDs, oral	Effective, but should be considered for a short time in lowest effective dose only due to adverse effects	Conditional recommended	Strongly recommended
NSAIDs, topical	First pharmacological choice. Preferred over systemic treatment due to safety profile	Conditional recommended	Conditionally recommended
Tramadol	Regarded as an alternative oral analgesic	N/A	Conditionally recommended
Non-tramadol opioids	N/A	Recommended against	Conditionally recommended against
Nutraceuticals	Chondroitin sulfate may be used for pain relief and improvement in functioning	Recommended against	Chondroitin conditionally recommended
Intra-articular glucocorticoid injections	Should generally not be used in patients with hand OA, but may be considered in patients with painful IP joints	Recommended against	Conditionally recommended

Abbreviations: OA = OsteoArthritis, EULAR = European Alliance of Associations for Rheumatology, OARSI = OsteoArthritis Research Society International, ACR = American College of Rheumatology NSAID = non-steroidal anti-inflammatory drug. N/A = Not available (not explicitly reported by the concerning guideline).

gout, haemochromatosis and calcium pyrophosphate dehydrate deposition disease. Sometimes, these diseases coexist with hand OA. These rheumatic musculoskeletal disorders ask for different treatments and are therefore important to distinguish. Distinguishing the type of hand OA the patient has is also relevant in order to help explaining complaints, prognosis and direct choices of therapy. Examples of hand OA types are nodal OA, thumb base OA and erosive hand OA. Erosive hand OA is a phenotype more often accompanied by inflammation and has a worse prognosis than other types.<sup>8,9</sup>

#### International management guidelines

Management of hand OA by the rheumatologist consists of patient education (sometimes supported by a nurse practitioner or an education program), selecting the appropriate treatment options and sometimes referring the patient for further treatment. This further treatment is often provided by hand therapists, for example occupational therapists who provide non-pharmacological modalities such as orthoses, assistive devices, joint protection education and by physical therapists, who provide for example exercise programs. The exact role of health care professionals differs per patient and country and depends on several circumstances. This role of other health care professionals than the rheumatologist is further described elsewhere in this special issue. There are several national and international guidelines available for hand OA management to guide in these choices. Well-known treatment recommendations for hand OA are those provided by the European Alliance of Associations for Rheumatology (EULAR) and the guideline of American College of Rheumatology (ACR),<sup>10-12</sup> which are sum-

marized in **Table 1**. Also the guideline for polyarticular OA from the OsteoArthritis Research Society International (OARSI) has relevance, since many patients with hand OA also have OA in other joint groups.<sup>5</sup> These three guidelines are all based on systematic literature reviews,<sup>10-13</sup> survey and interdisciplinary group discussion. Education and exercise form the core of these guidelines, which comprise non-pharmacological and pharmacological treatment modalities. The guidelines are largely in concordance with each other, but there are some minor differences. Several general principles for hand OA management are given by the guidelines, which are relevant for every patient. EULAR gives these as five “overarching principles,” describing that hand OA management should aim to control symptoms, all patients should offered information on the disease and treatment options which should be individualized in shared decision with the patient, including different disciplines. OARSI mentions “CORE” treatments for patients with polyarticular OA, which comprise arthritis education and structured land-based exercise programs. ACR reports for all patients some form of exercise and individualized treatment decisions taking into account values, preferences, comorbidities and medical status. All of these guidelines therefore recommend non-pharmacological treatment for patients with hand OA, which is in line with national guidelines.<sup>14</sup>

According to EULAR, OARSI and ACR, the non-pharmacological modalities of education and exercise should be recommended to all symptomatic patients with hand OA. In addition, ACR strongly recommends self-efficacy and self-management programs for hand OA. Regarding exercise, EULAR and ACR refrain from recommending specific types of exercise due to insufficient evidence. Orthoses for thumb base OA are recommended by EULAR and ACR. How-

ever, due to heterogeneity of studies on orthoses no straightforward advice was given on type of orthosis and instructions for use. EULAR advocates long-term use. ACR conditionally recommends orthoses for OA in other hand joints. Concerning assistive devices, EULAR recommends these to be offered to all patients with hand OA. Concerning hand OA surgery, EULAR recommends that this should be considered for patients with structural abnormalities when other treatment modalities have not been sufficiently effective in relieving pain. For heat therapy, cognitive behavioral therapy, acupuncture, kinesiotaping and paraffin, EULAR did not provide any recommendations. OARSI gave a conditional recommendation for cognitive behavioral therapy in case of widespread pain/depression and ACR conditionally recommended all of these modalities.

Topical non-steroidal anti-inflammatory drugs (NSAIDs) are considered the first choice by EULAR and ACR if analgesic hand OA treatment is needed due to their favorable toxicity profile. ACR only recommends these conditionally as also done by OARSI, due to among others a lack of direct evidence for efficacy. If systemic analgesics are deemed necessary, ACR strongly recommends oral NSAIDs, while EULAR notes effective pain and function improvement but makes a recommendation to only consider oral NSAIDs for a limited duration in the lowest effective dose. OARSI conditionally recommends NSAIDs, but warns for adverse event risks. EULAR mentions to consider paracetamol (acetaminophen) for a limited duration in selected patients (for example if oral NSAIDs are contraindicated) due to small effect size and hepatotoxicity. Paracetamol is not recommended by OARSI because evidence for adequate pain relief is lacking and because of risk of hepatotoxicity. It is conditionally recommended by ACR, but only for those with limited pharmacological options. This is among others due to small effect size. It is not clear why OARSI does not recommend paracetamol while the EULAR and ACR guidelines do, especially as the considerations the guidelines describe are similar (low effect size, risk of hepatotoxicity). Concerning tramadol, EULAR regards this as an alternative oral analgesic if for example NSAIDs are contraindicated, although currently no evidence is available for efficacy specifically in patients with hand OA. ACR conditionally recommends tramadol, while recommending against non-tramadol opioids. Concerning intra-articular glucocorticoid injections, EULAR recommends to generally not use these but states that these may be considered in patients with painful interphalangeal (IP) joints due to OA, while OARSI generally not recommends these, and ACR states that intra-articular glucocorticoid injections are “conditionally recommended” instead of “recommended” due to lack of evidence specifically for polyarticular OA. Chondroitin sulfate may be used according to EULAR for pain relief and improvement in function; ACR conditionally recommends it. Regarding symptomatic slow-acting drugs for OA, or Disease-Modifying OsteoArthritis Drugs, EULAR recommends against conventional or biological disease-modifying antirheumatic drugs. ACR strongly recommends against glucosamine, biologics, bisphosphonates, methotrexate, and hydroxychloroquine. Duloxetine was conditionally recommended by OARSI in case of comorbid widespread pain and/or depression, but was conditionally recommendation against by ACR (Table 1).

Altogether, the guidelines of OARSI, EULAR and ACR provide comprehensive information about hand OA treatment. For future guidelines on hand OA, it would be helpful addition to read the considerations of the voting panel for recommending a therapy or not. This is especially the case for therapies that differ between the guidelines in degree of recommendation (such as paracetamol and injections). Also, for the guideline of ACR it would be interesting to have level of evidence reported, as this would facilitate comparison with the other guidelines.

### Management of hand OA in clinical rheumatology practice

A recent study suggests that the guidelines that recommend non-pharmacological and pharmacological treatment are not that well implemented.<sup>15</sup> Dr Gravas and colleagues reported that only 21% of patients with thumb base OA referred for thumb base surgery used non-pharmacological treatment, while 63% of patients used any analgesics.<sup>15</sup> Systematic data on the actual usage of treatments for hand OA in rheumatology practice is lacking. Information on the implementation of the aforementioned treatment guidelines could help to improve the quality of the management of patients with hand OA.

We therefore investigated the treatment usage of patients with hand OA in rheumatology practice in two ways. First, we performed a systematic literature search for studies providing information on hand OA treatment modality usage. Second, we investigated treatment usage in our own hand OA cohort (Hand OsteoArthritis in Secondary care (HOSTAS) cohort).<sup>16</sup> We investigated whether treatment usage in clinical practice is concordant with the guidelines of EULAR, OARSI, and ACR.

### Literature review

We conducted a systematic search in PubMed/MEDLINE, Embase and Cochrane CENTRAL up to August 30, 2021. Additionally, reference lists of included studies and relevant reviews were screened. The search strategy and flow diagram of included studies can be found in **appendix 1**.<sup>17</sup> Eligible study types were all trials and observational studies that described treatment usage by patients with hand OA anywhere in the article, with at least ten patients included in the study. If the usage of a form of therapeutic care was an inclusion criterion, that specific type of care was excluded from this review. One reviewer (ST) determined eligibility for inclusion according to predefined inclusion criteria. In case of doubt, a second reviewer was consulted (LS).

The systematic literature search yielded 3728 unique results, of which 25 were eligible for inclusion in this review. Most of the studies we found were randomized trials ( $n = 19$ ), and the others ( $n = 6$ ) were cohort studies. The studies amounted to a total of 5508 participants. The studies were very heterogeneous. The study group size ranged widely (13–2113 patients). Four studies solely investigated carpometacarpal (CMC) 1 OA and two studies investigated IP OA. Furthermore, disease severity at inclusion differed: one study required any hand OA diagnosis for inclusion,<sup>18</sup> while another investigated patients referred for surgery due to hand OA pain.<sup>19</sup> Studies varied also in terms of hand OA characteristics, such as symptom severity (mean Visual Analog Scale pain range: 45.5<sup>18</sup>–76.5<sup>20</sup>), and radiographic severity (Kellgren-Lawrence (KL) score  $> 1$  present in 43%<sup>21</sup>–100%<sup>22</sup> of all patients, with KL grade  $> 1$  being an inclusion criterion in the latter). **Table 2** reports the study and patient characteristics, as well as the treatment modality usage for all studies included.

All studies reported analgesic usage, while 15 of these also reported other modalities of which ten reported nutraceutical usage, four orthoses, two assistive devices, two injections, and three occupational and/or physiotherapy. Regarding non-pharmacological modalities, three studies described physiotherapy usage, ranging from 8%<sup>23</sup> to 30%<sup>24</sup> of all patients. One of these described occupational therapy usage as well (used by 3% of all patients<sup>23</sup>). Three studies described usage of assistive devices for hand OA (tools used for symptom relief such as a hand orthosis, an ergonomic computer mouse or customized cutlery): two described orthoses and one described unspecified assistive devices. These orthoses were used by 54%<sup>25</sup> and 61%<sup>26</sup> of the patients, while unspecified assistive devices were used by 47%<sup>24</sup> (**Table 2**).

**Table 2**  
Characteristics of the studies included in the literature search ( $n = 25$ )

Author, year of publication, reference	Study design, category of intervention <sup>‡</sup> , patient characteristics	Number of patients with hand OA	Relevant inclusion/exclusion criteria, primary care or secondary care <sup>†</sup>	$n$ (%) per type of care usage
Aitken et al. 2018 <sup>30</sup>	RCT crossover (p), mean age 62, 77% women	43	Age >50 y, ACR criteria, 2	20 (47%) paracetamol, 18 (42%) NSAID, 5 (12%) COX-2 inhibitors
Altman et al. 2009 <sup>42</sup>	RCT (p), mean age 64, 77% women	285	ACR criteria, pain in dominant hand for $\geq 12$ mo, use of NSAIDs for $\geq 1$ pain episode, $u$	52% NSAIDs
Amaral et al. 2018 <sup>20</sup>	RCT (np), mean age 60	39	ACR criteria, difficulties in daily life, $u$	40% HCQ, 40% diacerein, 16% glucosamine, 4% others
Boustedt et al. 2009 <sup>34</sup>	RCT (np), mean age 60, 100% women	35	Clinical or radiographic hand OA, CMC1 pain, <i>both</i>	7 (20%) nutraceuticals, 9 (26%) analgesics
Dauvissat et al. 2018 <sup>26</sup>	Prospective cohort (p), mean age 60, 76% women, disease duration 36 mo	122	Symptomatic TMC OA, not sufficiently relieved by conventional first-line treatment, 2	51% analgesics, 28% NSAIDs, 17% nutraceuticals, 61% orthoses, 21% steroid injections, 7% hyaluronic acid injections
Deveza et al. 2021 <sup>21</sup>	RCT (b), mean age 66 y, 76% women	204	Thumb base pain, VAS > 40, FIHOA > 6, <i>both</i>	88 (43%) paracetamol, 72 (35%) NSAIDs, 10 (5%) opioids
Dziedzic et al. 2007 <sup>23</sup>	Cross-sectional cohort (-), 56% women	-	Hand pain and problems (swelling, stiffness), 1	44% analgesics, 26% prescription medication, 8% physiotherapy, 3% occupational therapy, 3% hand surgery, 2% hand injections
Fioravanti et al. 2012 <sup>43</sup>	RCT (np), mean age 71, 87% women	60	ACR criteria, bilateral OA, 1	2.30 tablets per wk of symptomatic drugs
Gravas et al. 2019 <sup>19</sup>	RCT (np), mean age 63, 79% women, 65% comorbidities,	180	Surgical consultation for CMC1 OA, 2	114 (63%) analgesics, 36 (29%) previous hand surgery, 37 (21%) non-pharmacological treatment
Grifka et al. 2004 <sup>29</sup>	RCT (p), mean age 61, 62% women	594	ACR criteria > 3 mo, 2	508 (86%) NSAIDs
Haugen et al. 2015 <sup>44</sup>	Cohort study (-), mean age 62, 54% women, BMI 28	526	Age < 75 y. Symptomatic hand OA: >1 painful hand joint with radiographic OA. Radiographic hand OA: 1 joint with KL > 1, 1	19% NSAIDs in symptomatic hand OA, 12% in radiographic hand OA, 25% daily aspirin in symptomatic hand OA, 24% in radiographic Hand OA
Hennig et al. 2013 <sup>45</sup>	RCT (np), mean age 61, 100% women	80	ACR criteria, stable medication, activity limitations, 2	33 (42%) using any analgesics, 7 (9%) NSAIDs, 2 (3%) cortisone injections, 6 (8%) glucosamine, 5 (6%) other medication
Jamison et al. 2018 <sup>28</sup>	RCT (np), mean age 63, BMI 28	69	OA pain >3 mo, pain intensity >4 (score range: 0-10), unclear	6 (9%) opioids, 3 (4%) NSAIDs, 34 (49%) over the counter medication
Kjeken et al. 2019 <sup>18</sup>	RCT (np), mean age 61, 97% women, mean disease duration 11 y	70	ACR criteria, 2	34 (49%) analgesics, 30 (43%) NSAIDs, 0 (0%) cortisone injections, 5/70 (7%) glucosamine
Kwok et al. 2011 <sup>24</sup>	Cohort study (np), mean age 59, 7% erosive OA	1076	Primary hand OA diagnosed by rheumatologist, 2	107 (47%) assistive devices, 100 (45%) paracetamol, 69 (31%) NSAIDs, 65 (30%) physiotherapy
Nery et al. 2021 <sup>33</sup>	RCT (np), mean age 67, 98% women	60	Age >50 y, ACR criteria >1 y, 2	14 (23%) nutraceuticals, 9 (15%) DMARD, 3 (5%) analgesics
Rannou et al. 2009 <sup>35</sup>	RCT (np), mean age 64, 89% women	112	Disabling thumb base OA (VAS > 30 mm), 2	12 (11%) opioids, 34 (30%) NSAIDs, 44 (39%) nutraceuticals
Sillem et al. 2011 <sup>46</sup>	Randomized crossover trial (np), mean age 64, 91% women, OA duration 3 y (4.7)	56	Bilateral CMC1 OA referred for thumb orthosis/willing to complete 9 wk of follow-up, <i>both</i>	25 (45%) medication for symptoms
Spolidoro Paschoual Nde et al. 2015 <sup>47</sup>	RCT (p), mean age 61, 97% women	60	ACR criteria, PIP or DIP OA, 2	3 (5%) HCQ, 10 (17%) glucosamine sulfate, 3 (5%) glucosamine + chondroitin sulfate, mean 2.0 (SD 13.7) mg/patient/day of sodium diclofenac, 0.4 paracetamol tablets per day of 750 mg (SD 0.8)
Stukstette et al. 2013 <sup>31</sup>	RCT (np), mean age 59, 83% women, BMI 27	151	ACR criteria, experiencing important hand OA-related problems and limitations, 2	52 (35%) NSAIDs, 5 (3%) opioids, 10 (7%) DMARDs, 5 (4%) glucosamine
Tenti et al. 2020 <sup>39</sup>	Retrospective cohort (np), mean age 66, 85% women, BMI 25	212	ACR criteria, bilateral, KL > 1, $u$	72 (34%) symptomatic drugs, 24 (11%) physiotherapy, nutraceuticals 53 (25%)
Vegt et al. 2017 <sup>25</sup>	RCT (np), mean age 60, 70% women	59	Primary CMC1 OA without previous surgery, 2	33 (52%) analgesics, 16 (25%) previous treatment, 34 (54%) orthosis
Verbruggen et al. 2012 <sup>48</sup>	RCT (p), mean age 61, 85% women, BMI 26	100	ACR criteria, $\geq 1$ joint in "erosive" phase, $u$	17/60 (28%) analgesics

(continued on next page)

Table 2 (continued)

Author, year of publication, reference	Study design, category of intervention <sup>†</sup> , patient characteristics	Number of patients with hand OA	Relevant inclusion/exclusion criteria, primary care or secondary care <sup>†</sup>	n (%) per type of care usage
Wajed et al. 2012 <sup>27</sup>	Cross-sectional cohort (-), mean age 61, 100% women	13	Hand pain due to primary OA of DIP and PIP, ACR criteria, 2	7 (46%) oral NSAIDs, 5 (39%) paracetamol, 1 (8%) topical NSAIDs, 1 (8%) opioids
Wenham et al. 2012 <sup>22</sup>	RCT (p), mean age 62, 82% women, median disease duration 60 mo (30-120)	70	ACR criteria, VAS pain > 40 mm, symptoms on most days, KL > 1, 2	38 (54%) NSAIDs, 22 (32%) opioids, 6 (5%) HCQ

Outcomes are summarized as mean (standard deviation (SD). In case of non-normally distributed or ordinal variables median (interquartile range (IQR)) was used.

\* Hand complaints population similar to osteoarthritis.

<sup>†</sup> Defined as appearing mostly first line (1), second line (2), both (b) or unknown/unclear (u).

<sup>‡</sup> Categories of treatment modalities subdivided into pharmacological (p), non-pharmacological (np), both (b) or none (-). Abbreviations: RCT = randomized controlled trial; ACR = American College of Rheumatology; OA = osteoarthritis; MRI = magnetic resonance imaging; SD = standard deviation; KL = Kellgren and Lawrence; BML = bone marrow lesion; VAS = Visual Analog Scale; HCQ = hydroxychloroquine; CMC = carpometacarpal; TMC = trapeziometacarpal; NRS = numerical rating scale; NSAID = non-steroidal anti-inflammatory drug; FIHOA = Functional Index of Hand Osteoarthritis; AUSCAN = Australian-Canadian Osteoarthritis hand Index; DMARD = disease-modifying anti rheumatic drug.

Regarding pharmacological modalities, various types of analgesics were described. Seventeen studies described oral NSAIDs, of which one described topical NSAIDs as well. These topical NSAIDs were used by 8% of the study population of female patients with painful hand OA.<sup>27</sup> The amount of patients using any NSAIDs ranged from 4%<sup>28</sup> to 86%.<sup>29</sup> Five studies described usage of paracetamol. Four of these described the proportion of patients having any usage, which ranged from 38.5% to 45%.<sup>21,24,27,30</sup> The fifth described the mean amount of paracetamol tablets per day (0.4 tablets of 750 mg). Six studies described opioid usage, ranging from 3%<sup>31</sup> to 32% of all patients.<sup>32</sup> Seven studies described analgesics without further specification. Usage of these ranged from 5%<sup>33</sup> to 63%<sup>19</sup> (Table 2). Ten studies described nutraceuticals. Out of these ten, five described nutraceuticals without further specification and six described glucosamine. Of these, one described the combination of glucosamine and chondroitin, and one described the combination of glucosamine and diacerein. General nutraceutical usage (described by five studies) ranged widely from 11%<sup>34</sup> to 39%<sup>35</sup> of the patients. Glucosamine usage was 4%<sup>31</sup> up to 16%<sup>20</sup> of the patients. Four studies described usage of intra-articular injections, which ranged from 0% in patients with hand OA according to ACR,<sup>18</sup> to 21% glucocorticoid injections and 7% hyaluronic acid injections in patients with insufficient response to analgesics and/or thumb orthosis<sup>26</sup>.

The studies showed a large difference in treatment modality usage. This might be explained in several ways. First, patients involved in the different studies varied in age, sex, and hand OA characteristics, which might have influenced optimal hand OA treatment. Second, there are differences in treatment reimbursement between the countries,<sup>36</sup> which might have caused a difference in financial barrier for patients seeking hand OA care. For example, in countries such as the United States exercise therapy is only reimbursed for the part of the population that has health insurance, while in countries such as the United Kingdom and the Netherlands it is mostly reimbursed.<sup>37,38</sup> However, in the Netherlands topical NSAIDs are not reimbursed, and in the United Kingdom only if on prescription. This financial barrier might be stronger for non-pharmacological modalities such as exercise therapy than for pharmacological, as non-pharmacological OA treatment is generally more expensive than analgesics. Another reason could be the recent updates of the guidelines; studies were already performed before that time. However, this cannot explain the under usage of non-pharmacological treatments.

#### Usage of treatments for hand OA – a retrospective cohort

at the rheumatology department of the Leiden University Medical Center (LUMC),<sup>16</sup> which serves both as a secondary and tertiary referral center for hand OA. Consecutive patients were included between June 2009 and October 2015. Hand OA was diagnosed according to the clinical judgment of the treating rheumatologist. Written informed consent was obtained from all participants. The study was approved by the LUMC Ethical Committee.

Patient and hand OA characteristics and treatment modality usage for joint complaints were collected using questionnaires. Physical examination was performed, and conventional dorsal-volar radiographs of hands were scored according to the KL system with good reliability.<sup>16</sup> Treatment modalities were categorized as non-pharmacological (assistive devices or exercise therapy) and pharmacological (analgesics, nutraceuticals and injections).

The number of missing values for all outcomes was collected in appendix 2 and did not exceed 7% for any value. Summed scores were regarded as missing in case of any missing items, or in case of more than one missing item (self-reported pain or function by the Australian Canadian Osteoarthritis Hand Index subscales).<sup>16</sup> SPSS software for Windows, version 25.0 (IBM, Armonk, NY) was used.

In the cohort, 538 patients were included. Mean age was 61 years, 86% were women, and 88% fulfilled ACR classification criteria (Table 4). Of all patients, 445 (83%) were using any treatment for joint complaints. Non-pharmacological treatment was used by 254 (47%) of the patients, of which the most frequent modality was assistive devices (188 patients, 35%). Pharmacological treatment was used by 412 (77%) of the patients, of which the most frequent modality was paracetamol (257 patients, 48%). Pharmacologic care without any non-pharmacologic treatment was used by 191 patients (36%), while 221 (41%) used a combination of non-pharmacological and pharmacological treatment modalities, as shown in Figure 1. Non-pharmacological without pharmacological care was present for 33 patients (6%). The usage of treatment modalities in the cohort is described in Table 5, and the overlap in treatment modalities per patient is shown in Figure 2.

Those with any modality usage (445 patients, 83%) were of comparable age to those without treatment modality usage (93 patients, 17%), had more comorbidities, longer median symptom duration, worse self-reported pain and function (Table 6) and a higher body mass index. This might be explained by a too high body mass index causing for example comorbidities and disease burden, which can lead to more hand OA symptoms and therefore to more therapeutic care usage for these symptoms. Among those with erosive hand OA (154 patients), the proportion with therapeutic care usage (130/154, 84%) was comparable with the proportion

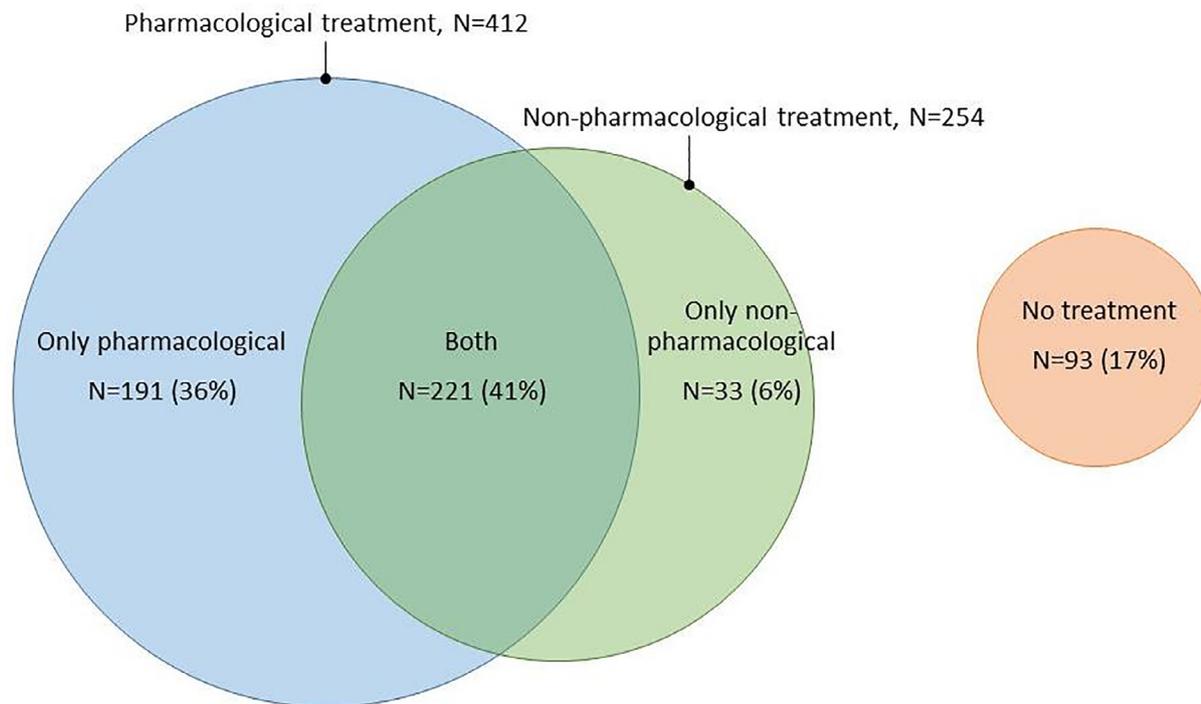


Fig. 1. Venn-diagram of the amount of patients using non-pharmacologic and pharmacologic treatment usage in the HOSTAS cohort (n = 538, 100%).

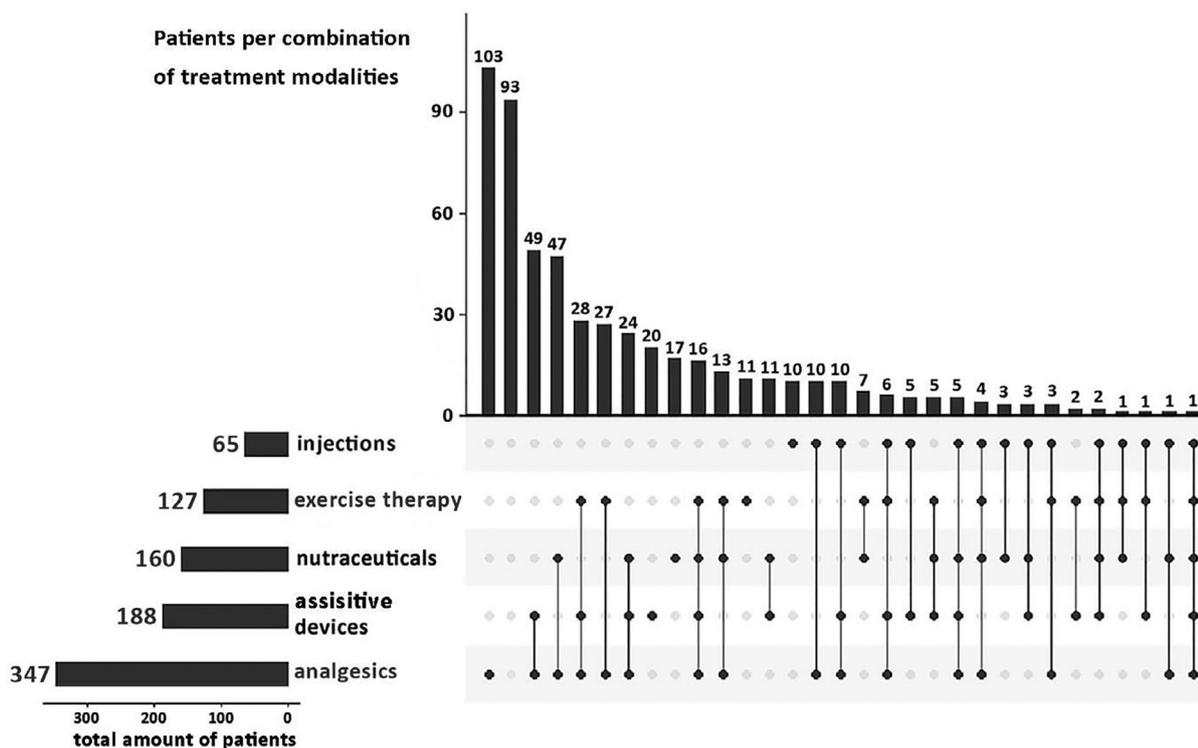


Fig. 2. The combinations of treatment modalities for patients in the HOSTAS cohort (n = 538). Connected dots signify combinations of multiple categories of usage.

**Table 3**Care usage characteristics of patients with hand osteoarthritis by category of referral ( $n = 538$ )

	Any treatment usage ( $n = 445, 83\%$ )	No treatment usage ( $n = 93, 17\%$ )	Total cohort ( $n = 538, 100\%$ )
No referral letter	10 (2%)	1 (1%)	11 (2%)
<b>Diagnostic or therapeutic referral</b>			
Predominantly diagnostic	143 (32%)	30 (32%)	173 (32%)
Predominantly therapeutic	82 (18%)	15 (16%)	97 (18%)
Both diagnostic and therapeutic	192 (43%)	43 (46%)	235 (44%)
Unclear	18 (4%)	4 (4%)	22 (4%)
<b>Referring medical professional</b>			
General practitioner	375 (84%)	83 (89%)	458 (85%)
Other medical professional	53 (12%)	7 (8%)	60 (11%)
Unclear	7 (2%)	2 (2%)	9 (2%)

Numbers represent amount of patients (% of total cohort). Patients were referred to the Rheumatology outpatient clinic of the Leiden University Medical Center and included in the Hand Osteoarthritis Secondary Care (HOSTAS) cohort.

**Table 4**Characteristics of the HOSTAS study population ( $n = 538$ )

<b>General patient characteristics</b>	
Age, y	61 (8.6)
Sex, women, $n$ (%)	463 (86%)
BMI, kg/m <sup>2</sup>	27.1 (4.8)
Education, high, $n$ (%)	179 (34%)
Paid work, $n$ (%)	232 (43%)
<b>Hand OA characteristics</b>	
Fulfilling ACR hand OA criteria, $n$ (%)	485 (90%)
Erosive hand OA, $n$ (%) <sup>‡</sup>	154 (29%)
Symptom duration, y <sup>†</sup>	5.2 (1.9- 5.3) <sup>†</sup>
Self-reported hand pain (0-20)	9.3 (4.3)
Self-reported hand function (0-36)	15.6 (8.5)
Tender joint count (0-30) <sup>†,§</sup>	3 (1-7)
KL summated score (0-120) <sup>†,§</sup>	17 (8-29)
<b>General burden</b>	
Any comorbidity present, $n$ (%)	352 (65%)
Amount of comorbidities <sup>†</sup>	1 (0-2)
Fulfilling ACR hip osteoarthritis criteria, $n$ (%)	37 (7%)
Fulfilling ACR knee osteoarthritis criteria, $n$ (%)	181 (34%)

Numbers represent mean (standard deviation) unless otherwise specified.

<sup>†</sup> median (IQR).

<sup>‡</sup> Defined as a hand joint in Verbruggen-Veys (VV) anatomical phases E ("erosive") or R ("remodelling").<sup>16</sup>

<sup>§</sup> Physically assessed for the DIP, PIP, IP, MCP and first CMC hand joints.<sup>16</sup>

<sup>#</sup> Scored on conventional dorsal-volar radiographs according to the Kellgren-Lawrence (KL) system system with good reliability.<sup>16,49</sup> Abbreviations: SD = standard deviation; BMI = Body Mass Index; ACR = American College of Rheumatology; OA = osteoarthritis; AUSCAN = Australian Canadian Osteoarthritis Hand Index; KL = Kellgren Lawrence.

having therapeutic care usage in the total HOSTAS cohort (445/538, 83%).

Most patients (89%) were referred by their general practitioner; 7 (8%) were referred by other health care professionals.<sup>16</sup> Patients were often referred for either diagnostic reasons (32%) or for a combination of diagnostic and therapeutic reasons (44%, **Table 3**). Most referrals (55%) were solely for complaints of the hands. However, referrals for complaints in the hands in combination with complaints in other joints were also common (37%).

#### Comparison with the rheumatology management guidelines and implications for clinical practice

We found several differences between the aforementioned hand OA management guidelines and treatment in daily clinical practice based on our systematic literature review and retrospective cohort.

First, non-pharmacological modalities seem underused. The combination of non-pharmacological and pharmacological modalities recommended by EULAR, OARSI as well as ACR was only partially seen. The literature review data indicated generally less non-pharmacological than pharmacological usage. Out of the six articles reporting both non-pharmacological and pharmacological treatment modalities, three reported less patients receiving non-pharmacological than pharmacological treatment modality us-

**Table 5**Usage of treatment modalities for joint complaints for patients with hand osteoarthritis in the HOSTAS cohort ( $n = 538$ )

	Any non-pharmacological care usage	254 (47%)
Usage of occupational therapy or physiotherapy	127 (23%)	
Usage of any assistive device	188 (35%)	
Usage of assistive devices that are likely hand-specific	118 (22%)	
Any care usage*	445 (83%)	
Any systemic pharmacological treatment usage	412 (77%)	
Usage of analgesics	347 (64%)	
Paracetamol	257 (48%)	
Anti-inflammatory medication	168 (31%)	
Tramadol	21 (4%)	
Any usage of nutraceuticals	160 (30%)	
Glucosamine	132 (25%)	
Chondroitin sulfate	64 (12%)	
Other nutraceutical	34 (6%)	
Usage of injections in hand	65 (12%)	
In thumb base	35 (7%)	
In fingers	32 (6%)	

Numbers represent amount of patients (% of total cohort).

\* defined as analgesics, nutraceuticals, assistive devices, injections, or exercise therapy (occupational therapy or physiotherapy).

age<sup>19,23,39</sup> (**Table 2**). One out of these six studies reported more patients having non-pharmacological treatment modality usage than pharmacological usage.<sup>26</sup> The remaining two articles reported similar usage of non-pharmacological and pharmacological modalities.<sup>24,25</sup> In the HOSTAS cohort 50% of all patients using any treatment modality. Pharmacological treatment without non-pharmacological treatment was prevalent (43%), while non-pharmacological without pharmacological was rarely seen (7%, **Fig. 2**).

Second, our literature review revealed patients using treatment modalities that were not recommended by the guidelines, such as non-tramadol opioids and diacerein. Thirdly, prescription of topical NSAIDs seems to be underused as well, as usage of these was low in the sole article that described this (8% of all patients,<sup>27</sup>), even though these are deemed first choice by EULAR and OARSI if pharmacological treatment is necessary. Whether the low number of studies reporting on topical NSAID usage might have to do with lack of awareness for this treatment, or with under-reporting, since topical NSAIDs are often not prescribed, but used as over-the-counter medication is not clear. Better reporting could improve our knowledge of the usage of this treatment.

Consequently, our study implies for practice that the implementation of hand OA management guidelines such as from EULAR, OARSI, and ACR could be improved. There could be several reasons for this under usage. In the general practice of a rheumatologist, patients' expectancies and wishes are often focused on pharmacological treatment. Maybe also rheumatologists perceive pharmacological treatment as easier, less expensive and less time consum-

**Table 6**

Patient characteristics of the HOSTAS cohort by treatment usage (n = 538)

	Any treatment usage (n = 445, 83%)	No treatment usage (n = 93, 17%)	Mean difference (95% confidence Interval)
Age, y	61.0 (8.4)	60.9 (9.4)	0.2 (-1.8 to 2.1)
BMI, kg/m <sup>2</sup>	27.5 (4.9)	25.5 (4.1)	1.9 (-0.9 to 3.0)
Any comorbidities	248 (56%)	39 (42%)	14% (2%-25%)
Symptom duration, y†	5.7 (2.3-13.0)	3.1 (1.0-8.6)	3.1 (1.0-5.3)
Erosive hand OA, n (%)	130 (29%)	24 (26%)	4% (-6% to 14%)
ACR hip and/or knee OA, n (%)	51 (14%)	5 (5%)	8% (0%-18%)
Self-reported hand pain (0-20)	9.7 (4.3)	7.0 (4.2)	2.7 (1.7-3.8)
Self-reported hand function (0-36)	16.6 (8.4)	11.8 (7.6)	5.7 (3.8-7.7)
KL summated score (0-120)†	18 (9-31)	15 (6-27)	3 (-6 to 1)

Numbers represent mean<sup>1</sup> unless otherwise specified.

† median (IQR). Abbreviations: SD = standard deviation; BMI = body mass index; OA = osteoarthritis; ACR = American College of Rheumatology.

ing. It remains a challenge to change this focus, especially if more effective pharmacological therapy may become available. An implementation strategy could be the stimulation of non-pharmacologic treatment modalities. Non-pharmacological therapy has low risk of adverse effects and can achieve symptom relief that cannot be achieved by pharmacological therapy. For example, orthoses and strengthening stabilizing muscles of the hand by exercise therapy can reduce instability of the CMC1 joint due to hand OA.<sup>40</sup> Stimulating non-pharmacological modalities such as those provided by hand therapists might therefore lead to successful symptom alleviation which can improve the daily life of patients with hand OA. In a large Swedish study, the necessity of analgesic usage for symptomatic knee or hip OA decreased from 80% to 74% of patients after implementation of a national treatment plan stimulating non-pharmacological treatment.<sup>41</sup> The results indicate that further study on the determinants of hand OA care usage would be useful, as knowing the facilitators and barriers of prescribing different treatment modalities could help to implement the recommended combination of non-pharmacologic and pharmacologic treatments.

In conclusion, the rheumatologist has a distinctive and important role in hand OA treatment, providing several evidence-based treatment options described by rheumatology guidelines as discussed in this review. Usage of treatment options in clinical rheumatology practice for hand OA is generally prevalent, but differences in usage are large. The balance between non-pharmacological and pharmacological hand OA care prescription could be optimized for example by more frequent referral to a physical or occupational therapist. As the health care and insurance system differs per country, we refrain from providing detailed recommendations on this topic. However, we recommend that the aforementioned guidelines of EULAR, OARSI and ACR should be taken into account for referral, as well as a multidisciplinary treatment approach. Also, topical NSAIDs could be prescribed more frequently instead of other pharmacological options. These improvements would likely lead to more successful hand OA symptom relief. Future research should indicate further determinants of hand OA treatment modality usage, as well as strategies to optimise concordance of hand OA management with treatment guidelines.

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## Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.jht.2022.08.001.

## References

- James SL, Abate D, Abate KH, et al. Global, regional, and national incidence, prevalence, and years lived with disability for 354 diseases and injuries for 195 countries and territories, 1990–2017: a systematic analysis for the Global Burden of Disease Study 2017. *Lancet*. 2018;392(10159):1789–1858.
- Branco JC, Rodrigues AM, Gouveia N, et al. Prevalence of rheumatic and musculoskeletal diseases and their impact on health-related quality of life, physical function and mental health in Portugal: results from EpiReumaPt– a national health survey. *RMD Open*. 2016;2(1):e000166.
- Haugen IK, Englund M, Aliabadi P, et al. Prevalence, incidence and progression of hand osteoarthritis in the general population: the Framingham Osteoarthritis Study. *Ann. Rheum. Dis.* 2011;70(9):1581–1586.
- Marshall M, Watt FE, Vincent TL, Dziedzic K. Hand osteoarthritis: clinical phenotypes, molecular mechanisms and disease management. *Nat Rev Rheumatol*. 2018;14(11):641–656.
- Loef M, Damman W, de Mutsert R, Rosendaal FR, Kloppenburg M. Health-related quality of life in patients with hand osteoarthritis from the general population and the outpatient clinic. *J. Rheumatol.* 2019;47(9):1409–1415.
- Kloppenburg M. Hand osteoarthritis—nonpharmacological and pharmacological treatments. *Nat Rev Rheumatol*. 2014;10(4):242–251.
- Zhang W, Doherty M, Leeb BF, et al. EULAR evidence-based recommendations for the diagnosis of hand osteoarthritis: report of a task force of ESCISIT. *Ann. Rheum. Dis.* 2008;68(1):8–17.
- Favero M, Belluzzi E, Ortolan A, et al. Erosive hand osteoarthritis: latest findings and outlook. *Nat. Rev. Rheum.* 2022;18:171–183.
- Ramonda R, Favero M, Vio S, et al. A recently developed MRI scoring system for hand osteoarthritis: its application in a clinical setting. *Clin Rheumatol*. 2016;35:2079–2086.
- Kloppenburg M, Kroon FPB, Blanco FJ, et al. 2018 update of the EULAR recommendations for the management of hand osteoarthritis. *Ann. Rheum. Dis.* 2018;78(1):16–24.
- Bannuru RR, Osani MC, Vaysbrot EE, et al. OARSI guidelines for the non-surgical management of knee, hip, and polyarticular osteoarthritis. *Osteoarthr. Cartil.* 2019;27(11):1578–1589.
- Kolasinski SL, Neogi T, Hochberg MC, et al. 2019 American College of Rheumatology/Arthritis Foundation guideline for the management of osteoarthritis of the hand, hip, and knee. *Arthritis Rheumatol*. 2020;72(2):220–233.
- Kroon FPB, Carmona L, Schoones JW, Kloppenburg M. Efficacy and safety of non-pharmacological, pharmacological and surgical treatment for hand osteoarthritis: a systematic literature review informing the 2018 update of the EULAR recommendations for the management of hand osteoarthritis. *RMD Open*. 2018;4(2):e000734.
- Ariani A, Manara M, Fioravanti A, et al. The Italian Society for Rheumatology clinical practice guidelines for the diagnosis and management of knee, hip and hand osteoarthritis. *Reumatismo*. 2019;71(S1):5–21.
- Gravás EMH, Tveter AT, Nossum R, et al. Non-pharmacological treatment gap preceding surgical consultation in thumb carpometacarpal osteoarthritis - a cross-sectional study. *BMC. Musculoskelet. Disord.* 2019;20(1).
- Damman W, Liu R, Kroon FPB, et al. Do comorbidities play a role in hand osteoarthritis disease burden? Data from the hand osteoarthritis in secondary care cohort. *J. Rheumatol.* 2017;44(11):1659–1666.
- Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *Bmj*. 2021;372:n71.
- Kjekem I, Darre S, Smedslund G, Hagen KB, Nossum R. Effect of assistive technology in hand osteoarthritis: a randomized controlled trial. *Ann. Rheum. Dis.* 2011;70(8):1447–1452.
- Gravás EMH, Österås N, Nossum R, et al. Does occupational therapy delay or reduce the proportion of patients that receives thumb car-

- po-metacarpal joint surgery? A multicenter randomized controlled trial. *RMD Open*. 2019;5(2):e001046.
20. Amaral DS, Duarte A, Barros SS, et al. Assistive devices: an effective strategy in non-pharmacological treatment for hand osteoarthritis—randomized clinical trial. *Rheumatol. Int.*. 2017;38(3):343–351.
  21. Deveza LA, Robbins SR, Duong V, et al. Efficacy of a combination of conservative therapies vs an education comparator on clinical outcomes in thumb base osteoarthritis. *JAMA Intern. Med.*. 2021;181(4):429.
  22. Tenti S, Ferretti F, Gusinu R, et al. Impact of thumb osteoarthritis on pain, function, and quality of life: a comparative study between erosive and non-erosive hand osteoarthritis. *Clin. Rheumatol.*. 2020;39(7):2195–2206.
  23. Dziedzic K, Thomas E, Hill S, Wilkie R, Peat G, Croft P. The impact of musculoskeletal hand problems in older adults: findings from the North Staffordshire Osteoarthritis Project (NorStOP). *Rheumatology (Oxford)*. 2007;46(6):963–967.
  24. Kwok WY, Kloppenburg M, Beaart-van de Voorde LJ, Huizinga TJW, Vliet Vlieland TP. Role of rheumatology clinical nurse specialists in optimizing management of hand osteoarthritis during daily practice in secondary care: an observational study. *J. Multidiscip. Healthc.*. 2011;4:403–411.
  25. Vegt AE, Grond R, Gröschke JS, et al. The effect of two different orthoses on pain, hand function, patient satisfaction and preference in patients with thumb carpometacarpal osteoarthritis. *Bone Joint J.* 2017;99(2):237–244 –B.
  26. Dauvissat J, Rizzo C, Lellouche H, et al. Safety and predictive factors of short-term efficacy of a single injection of mannitol-modified cross-linked hyaluronic acid in patients with trapeziometacarpal osteoarthritis. Results of a Multicenter Prospective Open-Label Pilot Study (INSTINCT Trial). *Clinical Medicine Insights: Arthritis Musculoskelet. Disord.* 2018;11:117954411878290.
  27. Wajed J, Ejindu V, Heron C, Hermansson M, Kiely P, Sofat N. Quantitative sensory testing in painful hand osteoarthritis demonstrates features of peripheral sensitization. *Int J Rheumatol.* 2012;2012:1–8.
  28. Jamison RN, Mei A, Edwards RR, Ross EL. Efficacy of vibrating gloves for chronic hand pain due to osteoarthritis. *Pain Med.* 2017;19(5):1044–1057.
  29. Grifka JK, Zacher J, Brown JP, et al. Efficacy and tolerability of lumiracoxib versus placebo in patients with osteoarthritis of the hand. *Clin Exp Rheumatol.* 2004;22(5):589–596.
  30. Aitken D, Laslett LL, Pan F, et al. A randomized double-blind placebo-controlled crossover trial of HUMira (adalimumab) for erosive hand Osteoarthritis – the HUMOR trial. *Osteoarthr. Cartil.*. 2018;26(7):880–887.
  31. Stukstette MJ, Dekker J, den Broeder AA, Westenberg JM, Bijlsma JWJ, van den Ende CHM. No evidence for the effectiveness of a multidisciplinary group based treatment program in patients with osteoarthritis of hands on the short term; results of a randomized controlled trial. *Osteoarthr. Cartil.* 2013;21(7):901–910.
  32. Wenham CY, Hensor E, Grainger AJ, et al. A randomized, double-blind, placebo-controlled trial of low-dose oral prednisolone for treating painful hand osteoarthritis. *Rheumatology (Oxford)*. 2012;51(12):2286–2294.
  33. Nery M, Natour JA, Jennings F, Fernandes A, Souza MC, Jones AA. Effects of a progressive resistance exercise program in patients with hand osteoarthritis: a randomized, controlled trial with a blinded assessor. *Clin Rehabil.* 2021;35(12):1757–1767.
  34. Boustedt C, Nordenskiöld U, Lundgren Nilsson Å. Effects of a hand-joint protection programme with an addition of splinting and exercise. *Clin. Rheumatol.* 2009;28(7):793–799.
  35. Rannou F, Dimet J, Boutron I, et al. Splint for base-of-thumb osteoarthritis: a randomized trial. *Ann. Intern. Med.*. 2009;150(10):661.
  36. OECD data - Health spending total/government/compulsory/voluntary/out of pocket 2021. Available at: <https://data.oecd.org/healthres/health-spending.html>.
  37. NHS. The National Health Service - Accessing physiotherapy. Available at: <https://www.nhs.uk/conditions/physiotherapy/accessing/>.
  38. Is fysiotherapie opgenomen in het basispakket? Available at: <https://www.rijksoverheid.nl/onderwerpen/zorgverzekering/vraag-en-antwoord/is-fysiotherapie-opgenomen-in-het-basispakket>. Accessed: October 5<sup>th</sup>, 2021
  39. Tenti S, Manica P, Cheleschi SA, Fioravanti A. Sulfurous-arsenical-ferruginous balneotherapy for osteoarthritis of the hand: results from a retrospective observational study. *Int J Biometeorol.* 2020;64(9):1561–1569.
  40. Bunning RD, Materson RS. A rational program of exercise for patients with osteoarthritis. *Semin. Arthritis Rheum.*. 1991;21(3):33–43.
  41. Abbott A, Limbäck-Svensson G, Zhou C, Gustafsson K, Rolfson O. Dispensed prescriptions of analgesics prior to entering an osteoarthritis care program. A national registry linkage study. *Osteoarthr. Cartil.*. 2020;28:S59–S60.
  42. Altman RD, Dreiser RI, Fisher CL, Chase WF, Dreher D, Zacher J. Diclofenac sodium gel in patients with primary hand osteoarthritis: a randomized, double-blind, placebo-controlled trial. *J. Rheumatol.*. 2009;36(9):1991–1999.
  43. Fioravanti A, Tenti S, Giannitti C, Fortunati N, Galeazzi M. Short- and long-term effects of mud-bath treatment on hand osteoarthritis: a randomized clinical trial. *Int J Biometeorol.* 2013;58(1):79–86.
  44. Haugen IK, Ramachandran VS, Misra D, et al. Hand osteoarthritis in relation to mortality and incidence of cardiovascular disease: data from the Framingham Heart Study. *Ann. Rheum. Dis.*. 2013;74(1):74–81.
  45. Hennig T, Hæhre L, Hornburg V, Mowinckel P, Norli ES, Kjeker I. Effect of home-based hand exercises in women with hand osteoarthritis: a randomized controlled trial. *Ann. Rheum. Dis.*. 2014;74(8):1501–1508.
  46. Sillem H, Backman C, Miller WC, Li LC. Comparison of two carpometacarpal stabilizing splints for individuals with thumb osteoarthritis. *J Hand Ther.* 2011;24(3):216–226.
  47. Spolidoro Paschoal NO, Natour J, Machado FS, de Oliveira HA, Furtado RN. Effectiveness of triamcinolone hexacetonide intraarticular injection in interphalangeal joints: a 12-week randomized controlled trial in patients with hand osteoarthritis. *J. Rheumatol.*. 2015;42(10):1869–1877.
  48. Verbruggen G, Wittoek R, Cruyssen B, Elewaut D. Tumor necrosis factor blockade for the treatment of erosive osteoarthritis of the interphalangeal finger joints: a double blind, randomized trial on structure modification. *Ann. Rheum. Dis.*. 2011;71(6):891–898.
  49. Kellgren J, Lawrence JS. Radiological assessment of osteo-arthrosis. *Ann. Rheum. Dis.*. 1957;16(4):494–502.