

# Osteoarthritis and Cartilage



## Osteoarthritis year in review 2022: rehabilitation

M.A. Holden †\*, P.J.A. Nicolson ‡, M.J. Thomas †§, N. Corp †, R.S. Hinman ||, K.L. Bennell ||

† School of Medicine, David Weatherall Building, Keele University, Staffordshire, UK

‡ Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences (NDORMS), University of Oxford, UK

§ Haywood Academic Rheumatology Centre, Midlands Partnership NHS Foundation Trust, Haywood Hospital, Staffordshire, UK

|| Centre for Health, Exercise & Sports Medicine, Department of Physiotherapy, University of Melbourne, Australia

### ARTICLE INFO

#### Article history:

Received 20 July 2022

Accepted 6 October 2022

#### Keywords:

Osteoarthritis

Rehabilitation

Review

Non-pharmacological

Weight loss

Exercise

Education

Adjuncts

Implementation

### SUMMARY

This year in review presents key highlights from research relating to osteoarthritis (OA) rehabilitation published from the 1<sup>st</sup> April 2021 to the 18<sup>th</sup> March 2022. To identify studies for inclusion in the review, an electronic database search was carried out in Medline, Embase and CINAHLplus. Following screening, included studies were grouped according to their predominant topic area, including core OA rehabilitation treatments (education, exercise, weight loss), adjunctive treatments, novel and emerging treatments or research methods, and translation of rehabilitation evidence into practice. Studies of perceived high clinical importance, quality, or controversy in the field were selected for inclusion in the review. Headline findings include: the positive role of technology to support remote delivery of core OA rehabilitation treatments, the importance of delivering educational interventions alongside exercise, the clinical and cost-effectiveness of a stepped approach to exercise, controversy around the potential mechanisms of action of exercise, mixed findings regarding the use of splinting for thumb base OA, increasing research on blood flow restriction training as a potential new intervention for OA, and evidence that the beneficial effects from core OA treatments seen in randomised controlled trials can be seen when implemented in clinical practice. A consistent finding across several recently published systematic reviews is that randomised controlled trials testing OA rehabilitation interventions are often small, with some risk of bias. Whilst future research is warranted, it needs to be large scale and robust, to enable definitive answers to important remaining questions in the field of OA rehabilitation.

© 2022 The Authors. Published by Elsevier Ltd on behalf of Osteoarthritis Research Society International.

This is an open access article under the CC BY license (<http://creativecommons.org/licenses/by/4.0/>).

### Introduction

Rehabilitation is a key component of health care for multiple acute and long-term health conditions. It incorporates a range of interventions that aim to address the impact of a health condition on a person's life by reducing their experience of disability. Through addressing their underlying problems (e.g., physical limitations and pain), rehabilitation enables greater participation in meaningful life roles, including work<sup>1</sup>. This can have far-reaching health, social and economic benefits<sup>2</sup>. Given the global ageing population<sup>3</sup> and the rising prevalence of noncommunicable diseases<sup>4</sup>, rehabilitation is an increasingly important health service. However, the need for rehabilitation currently exceeds its availability<sup>1</sup>. In 2017, in response to the urgent need to strengthen rehabilitation

worldwide, the World Health Organisation launched the Rehabilitation 2030 initiative which identified 10 key areas that need to be addressed to reduce the unmet needs for rehabilitation. Among these is the need to incorporate rehabilitation into universal health coverage, build comprehensive rehabilitation service delivery models to achieve equitable access to quality services, and expand the availability of quality evidence for rehabilitation<sup>5</sup>.

Osteoarthritis (OA) is a long-term health condition that has no cure, is becoming increasingly prevalent, and is highly burdensome for individuals, health care systems, and society more generally<sup>6</sup>. Rehabilitation is therefore an increasingly important management strategy for people with OA. However, its underpinning evidence-base can be limited, its delivery in clinical practice can be sub-optimal<sup>7</sup>, and its effect sizes for improving pain and physical function can be modest<sup>[e.g. 8]</sup>. To better understand the current state of evidence, this year in review will summarise key updates that have been published in the field of OA rehabilitation between the 1st April 2021 to the 18th March 2022. For the purposes of this review, the focus of rehabilitation has been confined to non-

\* Address correspondence and reprint requests to: M.A. Holden, School of Medicine, David Weatherall Building, Keele University, Staffordshire, ST5 5BG, UK.

E-mail address: [m.holden@keele.ac.uk](mailto:m.holden@keele.ac.uk) (M.A. Holden).

<https://doi.org/10.1016/j.joca.2022.10.004>

1063-4584/© 2022 The Authors. Published by Elsevier Ltd on behalf of Osteoarthritis Research Society International. This is an open access article under the CC BY license (<http://creativecommons.org/licenses/by/4.0/>).

pharmacological and non-surgical treatments (i.e., physical, behavioural and mind-body management approaches).

## Methods

An electronic database search was carried out in Medline, Embase and CINAHLplus between the 1st of April 2021 and the 18th of March 2022 (see Supplementary Material One for the Medline search strategy). Titles and abstracts of identified articles were screened by one reviewer (either MAH, PJAN, or MJT) against the inclusion and exclusion criteria (Table 1). Included articles were then grouped according to their predominant topic area, which were a-priori agreed as: core OA rehabilitation treatments (education, exercise, weight loss), adjunctive treatments (defined as treatments that could supplement core OA rehabilitation), novel and emerging treatments or research methods, and translation of rehabilitation evidence into practice. MAH screened all remaining articles, and with iterative input from the wider authorship team, those of perceived high clinical importance, quality or controversy in the field were selected for inclusion in the review.

As shown in Fig. 1, after duplicates were removed, 6,137 articles were identified from the search. Following screening, 445 articles were identified as having a focus on OA rehabilitation. The majority of these were related to core treatments ( $n = 187$ ) and treatment

adjuncts ( $n = 152$ ), with a smaller number being related to novel and emerging treatments or research methods ( $n = 54$ ), or translation of evidence into practice ( $n = 52$ ). Findings from studies that were selected to feature in the review were narratively synthesised.

## Core rehabilitation treatments

### Education

The recommendation of patient education as a first line treatment for people with knee OA is often extrapolated from evidence conducted with participants who have OA at other joints, other forms of arthritis, or chronic pain more generally<sup>9</sup>. Goff *et al.*<sup>9</sup> therefore undertook a systematic review and meta-analysis to determine whether patient education is effective for people with knee OA in comparison to non-pharmacological treatment controls. In total, 29 randomised controlled trials (RCTs) (4,107 participants) were included in the review. Meta-analyses revealed that when delivered as a standalone intervention, patient education was superior to usual care for pain (standardised mean difference (SMD):  $-0.35$ ; 95% confidence interval (CI):  $-0.56$  to  $-0.14$ ) and physical function (SMD:  $-0.31$ ; 95% CI  $-0.62$  to  $0.00$ ) in the short-term, but benefits were small and of questionable clinical relevance. Although this questions the value of delivering education in

	Inclusion criteria	Exclusion criteria
Population	<ul style="list-style-type: none"> <li>Joint pain in adults aged 45 years and over (mean age over 45 years)</li> <li>OA diagnosed by either: X-ray, clinical criteria, a health care professional, self-reported</li> </ul>	<ul style="list-style-type: none"> <li>Joint pain attributable to conditions other than OA</li> <li>Non-musculoskeletal conditions</li> <li>Rheumatoid arthritis/other defined inflammatory rheumatological problems</li> <li>People with 'patellofemoral pain syndrome' (overall a different problem to 'OA')</li> <li>Animal based studies</li> <li>Studies of children</li> </ul>
Intervention	<ul style="list-style-type: none"> <li>Any type of OA focused rehabilitation</li> </ul>	<ul style="list-style-type: none"> <li>Pharmacological interventions</li> <li>Surgical interventions</li> <li>Study not focused on a rehabilitation intervention (e.g., evaluating an outcome measure)</li> <li>Food supplements</li> </ul>
Comparator (if applicable)	<ul style="list-style-type: none"> <li>Other forms of OA rehabilitation</li> <li>Surgery</li> <li>Pharmacological intervention</li> <li>Sham treatment</li> <li>Different delivery modes of OA rehabilitation (e.g., exercise delivered remotely vs exercise delivered in person)</li> <li>Usual care</li> <li>Usual activities</li> <li>Waiting list/no treatment</li> </ul>	
Outcome measure	<ul style="list-style-type: none"> <li>Either a clinical outcome e.g., pain or function, or any feasibility or process outcome e.g., acceptability, adherence, satisfaction with care, quality of care.</li> </ul>	<ul style="list-style-type: none"> <li>No measure of self-reported pain or physical function or no feasibility or process outcome measures</li> </ul>
Study design	<ul style="list-style-type: none"> <li>Systematic review</li> <li>RCT or quasi-RCT</li> <li>Qualitative studies</li> <li>Observational studies (including pre-post test studies testing implementation of rehabilitation)</li> <li>Surveys</li> <li>Pilot/feasibility studies</li> <li>Available in full text</li> <li>Written in the English language</li> </ul>	<ul style="list-style-type: none"> <li>Study protocols</li> <li>Abstract/conference proceeding only</li> <li>Not written in English</li> </ul>

**Table 1**

Inclusion and exclusion criteria for the literature search

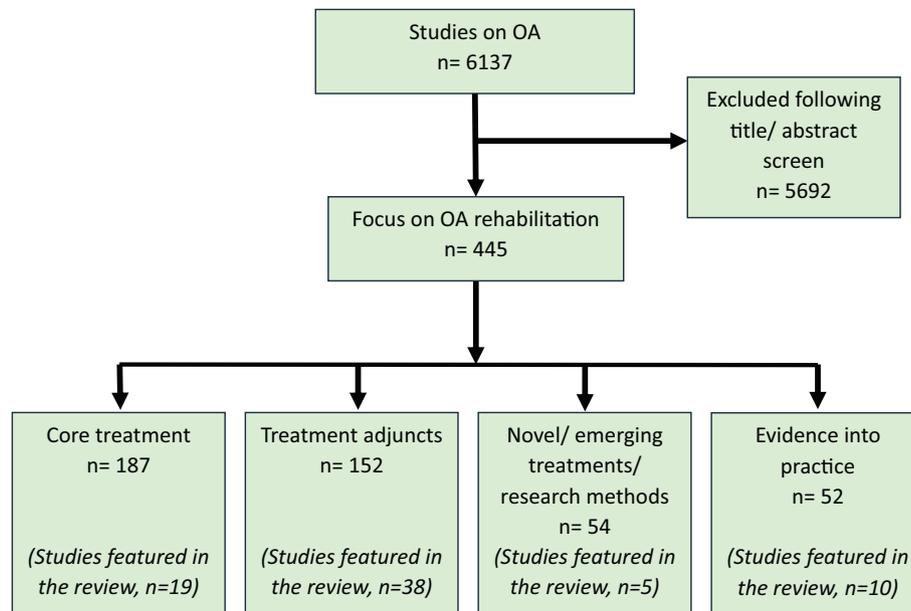


Fig. 1

Flow diagram of identified studies.

isolation for pain and physical function, education was also superior to usual care for pain coping in the short-term (SMD:  $-0.71$ ; 95% CI  $-1.32$  to  $-0.01$ ). This is an important outcome for people with a long-term condition such as OA and alongside knowledge, might be a more appropriate target outcome from standalone educational interventions. Meta-analyses also revealed that combining patient education with exercise produced short-term improvements in pain and physical function compared with patient education alone (pain: SMD:  $0.44$ , 95% CI  $0.19$  to  $0.69$ ; physical function: SMD:  $0.81$ ; 95% CI  $0.54$  to  $1.08$ )<sup>9</sup>. Although the mechanism of action for this enhanced effect is unknown, the authors hypothesise that this could be due to the delivery of education alongside exercise resulting in improved exercise adherence<sup>9</sup>. A recently published RCT by Rezende *et al.*<sup>10</sup> that included 191 participants also supports the beneficial effect of education when delivered alongside exercise (delivered as a 2-day exercise and education self-management program) compared to usual care for improving pain and physical function among people with knee OA.

Outcomes from education might be related to the intervention characteristics (e.g., education content, method of delivery, duration of instruction), or participant characteristics (treatment effect moderators). Tentatively supporting this hypothesis, a RCT by Lopez-Olivo *et al.*<sup>11</sup> found that among 219 participants with knee OA, an entertainment education video plus education booklets resulted in greater knowledge post intervention in comparison to when booklets were delivered alone (modified Patient Knowledge Questionnaire–Osteoarthritis<sup>12</sup> (range 0 (least knowledge) to 11 (greatest knowledge)): mean difference (MD):  $0.39$ ; 95% CI  $0.02$  to  $0.76$ ). However, this difference was small and not maintained at 6 months. Exploratory sub-group analysis revealed that the combination of the video plus booklets was more beneficial than booklets alone for Spanish-speaking patients, and for participants with lower education levels.

### Exercise

Over the past year, there have been important additions to the evidence base regarding exercise for knee OA. Allen *et al.*<sup>13</sup> conducted the first RCT to explore a stepped approach to exercise (beginning with a low resource intensive treatment and only “stepping up” to more intensive services as required) among 345 people with knee OA. The stepped exercise intervention began with access to an internet-based exercise program. After 3 months, participants not meeting the OMERACT-OARSI response criteria<sup>14</sup> progressed to biweekly telephone coaching. After a further 3 months, those still not meeting response criteria received a course of in-person physical therapy. Among the 230 participants who received the stepped exercise intervention, 150 progressed to step 2, and 81 progressed to step 3. At 9 months, there were modest improvements in knee OA symptoms (deemed on the lower end of clinically relevant improvement<sup>13</sup>) in those randomised to the stepped exercise intervention compared with the control group (who received postal educational materials every 2 weeks for 9 months) (Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC)<sup>15</sup> total score (range 0 (best symptoms) to 96 (worst symptoms): MD:  $-6.8$ ; 95% CI  $-10.5$  to  $-3.2$ )<sup>13</sup>. The stepped exercise intervention also improved quality of life and had a high probability of cost-effectiveness<sup>16</sup>. Bandak *et al.*<sup>17</sup> undertook a RCT to determine if the efficacy of an exercise and education program was equivalent to open-label placebo on pain and function in 206 individuals with knee OA. In the short-term, the exercise and education program provided improvements in knee pain equivalent to that of inert intra-articular saline (Knee Injury and Osteoarthritis Outcome Score (KOOS) pain subscale (range 0 (worst) to 100 (best)<sup>18</sup>: MD:  $2.7$ ; 95% CI  $-0.6$  to  $6.0$ ;  $P = 0.0008$  for test of equivalence). This finding raises important questions about the mechanisms of action of exercise on pain, which could be primarily driven

by other factors including the placebo response, contextual factors, and regression to the mean<sup>17</sup>.

Given that depression is a common, recognised co-morbidity among people with OA<sup>19</sup>, it is also important to consider the effectiveness of exercise on mental health outcomes. A systematic review and network meta-analysis of 17 clinical trials by Hall *et al.*<sup>20</sup> explored the comparative effectiveness of exercise programs for psychological well-being in people with knee OA. Strengthening exercise was most beneficial for overall mental health compared to aerobic exercise, mixed exercise, mind-body exercise, stretching and controls (e.g., standard care, waiting list, education). Strengthening exercise and mixed exercise interventions were more beneficial for depressive symptoms compared to stretching exercise. A systematic review and meta-analysis by Hu *et al.*<sup>21</sup> (16 RCTs, 986 participants) also confirmed the beneficial effect of tai-chi in comparison to controls (either no exercise, education class, standard care or physical therapy) on psychological health (e.g., SF-36 Mental Component Summary<sup>22</sup>; SMD: 0.26; 95%CI: 0.06 to 0.45), in addition to pain and physical function among people with knee OA.

### Weight loss

Although weight loss is a recognised core treatment for people with OA who are overweight or obese, the optimal weight loss strategy remains uncertain, and the recommended amount of weight loss needed for symptom improvement is variable<sup>23</sup>. A recent network meta-analysis by Panunzi *et al.*<sup>23</sup> including 22 RCTs in knee OA (2,656 participants) found that the most effective rehabilitation interventions for significantly reducing pain were low calorie diet and exercise (effect size (ES):  $-34.4$ ; 95% credibility interval (CrI):  $-48.1$  to  $-19.5$ ), and intensive weight loss and exercise (ES:  $-27.1$ ; 95% CrI:  $-40.4$  to  $-13.6$ ). These were the second and third most effective interventions for reducing pain behind only bariatric surgery (ES:  $-62.7$ ; 95% CrI:  $-74.6$ ,  $-50.6$ ), respectively. The study found that the greater the weight loss, the larger the pain reduction; for every 1% weight loss, WOMAC pain scores decreased by approximately two points. Stiffness and physical function also improved with the reduction of body weight. However, when more than 1% of lean body mass was lost, improvement in physical function plateaued. The authors conclude that performing physical exercise is essential alongside rapid and massive weight loss to preserve lean body mass and to avoid sarcopenia<sup>23</sup>.

### The role of technology

Within the studies published on core OA rehabilitation treatments, many utilised technologies for intervention delivery<sup>[e.g. 24–32]</sup>. This is perhaps unsurprising given the need to adapt to new remote ways of working in response to the COVID-19 pandemic. A systematic review and meta-analysis by Chen *et al.*<sup>32</sup> synthesised findings from 12 RCTs that tested technology-supported exercise programs for people with knee OA in comparison to conventional care (e.g., face-to-face physical therapy), educational materials on OA management (e.g., presented in brochures and booklets) or no/minimal care control groups. Utilised technologies included telephone, web, mobile app, computer, and virtual reality. Interventions were delivered over a period ranging from 4 weeks to 6 months. Meta-analysis showed that in the short-term, compared to controls, these programs were associated with significant improvements in knee pain (SMD:  $-0.29$ ; 95% CI:  $-0.48$  to  $-0.10$ ) and quality of life (SMD:  $0.25$ ; 95% CI:  $0.04$  to  $0.46$ ) but not in physical function. Similar findings were also reported within a systematic review and meta-analysis by Xie *et al.*<sup>29</sup>. Along with other recently published RCTs<sup>24,25,28,31</sup>, this suggests that technology supported

programs are an important option for remote delivery of exercise for people with OA.

### Cost-effectiveness of core rehabilitation treatments

This past year has seen the cost-effectiveness of core rehabilitation treatments for OA re-evaluated. A systematic review by Mazzei *et al.*<sup>33</sup> examined the cost-effectiveness of education, exercise and dietary weight management for hip and knee OA, yielding 23 studies for synthesis (22 RCTs, 1 non-randomised clinical trial). Compared with education or physician-delivered care, these core treatments appear to be cost-effective (observed in 15 out of 16 studies). Despite differences in health care systems and intervention and comparator group across included studies, the authors concluded that implementing core treatments within health systems to augment physician-delivered primary care appears cost-effective. Secondary analysis of an RCT (156 participants) also concluded that an initial course of physical therapy (up to eight treatment sessions including education, exercise and joint mobilization over 4–6 weeks, with 1–3 sessions at 4-month and 9-month reassessment as required) was cost-effective compared with an intra-articular glucocorticoid injection for knee OA at 1 year<sup>34,35</sup>. Although delivery costs for physical therapy were initially higher, quality-adjusted life-years were superior.

### Adjunctive treatments

Whilst over the past 12 months there has been ongoing interest in adjunctive rehabilitation treatments for the management of OA, of particular note across the body of evidence is the predominant lack of sufficiently large-scale high-quality trial designs. This continues to highlight the lack of strong available evidence regarding many adjunctive treatments, which can explain conflicting recommendations about their use in international guidelines for OA<sup>[e.g. 19,36,37]</sup>.

### Biomechanical interventions

The correction of aberrant biomechanics presents an attractive target for rehabilitation interventions, designed to modify onset, progression, and symptomatic experience of OA. A systematic review of seven RCTs and 17 cohort studies (579 participants) examining the effectiveness of knee valgus braces for knee OA identified short-term improvements in pain and function for some participants<sup>38</sup>. However, long-term follow-up data were found to be lacking, and included study quality was deemed low. Similarly, a systematic review examining biomechanical devices (braces, taping and footwear) for symptomatic patellofemoral OA by Callaghan *et al.*<sup>39</sup> (11 RCTs, 658 participants) reported short-term reductions in pain (measured on a visual analogue scale (VAS)) when taping was used in multimodal physiotherapy interventions compared to controls (no tape/no treatment) (data from two RCTs, SMD:  $-0.41$ ; 95% CI:  $-0.71$  to  $-0.09$ ). Overall, the absence of long-term follow-up data was noted. The long-term effectiveness of knee valgus braces has been explored in a recently published RCT<sup>40</sup>. Among 120 patients with medial knee OA, a knee valgus brace combined with usual care demonstrated significant clinical benefits over 1 year compared to usual care alone (e.g., VAS pain (range 0 (least pain) to 100 (most pain): adjusted MD:  $-11.8$ ; 95% CI:  $-21.1$  to  $-2.5$ ), as well as potential cost-utility from a societal perspective. More broadly, foot-based modification with insoles for knee OA does not appear effective according to a systematic review and meta-analysis including 15 studies (1,086 participants) predominantly evaluating lateral wedges<sup>41</sup>. In addition, an RCT by Paterson *et al.*<sup>42</sup> did not show any superior benefit of flat flexible shoes compared to

supportive shoes in 164 participants with medial knee OA. In fact, knee pain on walking improved to a greater extent with stable supportive shoes than with flat flexible shoes (numeric rating scale (NRS) (range 0 (least pain) to 11 (most pain)): MD: 1.1; 95% CI: 0.5 to 1.8). Systematic reviews examining the efficacy of elastic tape (e.g., Kinesio-Tape/Rocktape) for knee OA also provided little in the way of robust evidence supporting their use compared with sham tape<sup>43,44</sup>.

Often neglected joint sites in the hand and the foot have received research attention in the past year. Focusing on the hand, Adams *et al.*<sup>45</sup> investigated the efficacy, clinical- and cost-effectiveness of splints among 349 people with symptomatic basal thumb joint OA. Supported self-management plus a thumb splint was compared to supported self-management plus a placebo splint, and supported self-management alone. There were no clinically relevant or statistically significant differences in pain and physical function outcomes between groups at 8 weeks. Adding splinting to supported self-management was also not cost-effective over 12 weeks compared with supported self-management alone<sup>45</sup>. Whilst this questions the value of adding splinting to a supported self-management program for thumb base OA, a second RCT by Deveza *et al.*<sup>46</sup> including 204 participants found that a conservative package of care that included a thumb-base splint (alongside education, exercise and diclofenac sodium, 1% gel) improved hand function significantly more than education alone at 6 weeks (Functional Index for Hand Osteoarthritis<sup>47</sup> (range 0–30): between group difference: –1.7; 95% CI, –2.9 to –0.5). However, there was no difference in pain improvement between groups. Due to the combination of interventions utilised within this treatment package, it is impossible to tease out the extent to which the thumb-base splint contributed to the improvement in physical function. Based on the findings Adams *et al.*<sup>45</sup>, it could be hypothesised that the other interventions (education, exercise and diclofenac sodium 1% gel) were the ‘active ingredients’ behind the improvements, but this is unknown. The type of thumb splint used could be an important factor in the relative effectiveness of interventions. A recently published systematic review and network meta-analysis by Marotta *et al.*<sup>48</sup> (11 RCTs, 619 participants) explored the comparative effectiveness of orthoses for thumb OA. The four different orthoses explored were found to be superior to placebo for pain reduction, with the top-ranked intervention being the short rigid thermo-plastic carpometacarpal splint.

With regards to the foot, Munteanu *et al.*<sup>49</sup> undertook a RCT comparing a carbon-fibre shoe-stiffening insert with a sham insert among 100 people with 1st metatarsophalangeal joint OA. At 12 weeks shoe-stiffening inserts were more effective at reducing pain than the sham insert (pain domain of the Foot Health Status Questionnaire<sup>50</sup> (range 0–100 (optimal foot health): adjusted MD: 6.66; 95% CI: 0.65 to 12.67). Due to the level of uncertainty (wide confidence interval), this may not represent a clinically meaningful change for some individuals, and the potential for biomechanical effects from the sham insole cannot be completely discounted.

### Acupuncture

At least 10 RCTs<sup>51–60</sup> and five systematic reviews<sup>61–65</sup> were published in the last year that explored the effectiveness of a range of acupuncture and acupressure modalities, with variable and contradictory findings. Araya-Quintanilla *et al.*<sup>61</sup> published an overview of 15 systematic reviews examining the effect of acupuncture compared to control interventions for pain and function among people with knee OA. In the short-term, there were statistically significant differences in pain intensity (VAS (range

0 (least pain) to 100 (most pain) MD: –0.32; 95% CI: –0.57 to –0.08) and knee function (MD: –8.74; 95% CI: –13.36 to –4.12) in favour of acupuncture vs control interventions. However, these differences were not clinically significant. For acupuncture vs sham acupuncture, no differences were observed for pain intensity or knee function. Evidence was of low to very low quality<sup>61</sup>. A network meta-analysis by Liu *et al.*<sup>63</sup> summarised the efficacy of different acupuncture-related therapies for improving pain and function among people with knee OA (40 RCTs, 3,215 participants). Probability ranking results found fire needle to be superior to warm needle and electro-acupuncture, whereas warm needle and electro-acupuncture were better than conventional acupuncture, western medicine, sham moxibustion and sham acupuncture in overall curative effect. There were limitations in the findings due to poor reporting of interventions, small sample sizes and publication bias of included RCTs.

### Electrotherapy

Over the past year, at least six studies<sup>66–71</sup> have explored the effectiveness of electrotherapy modalities in OA populations. Maheu *et al.*<sup>70</sup> found a new wearable transcutaneous electrical nerve stimulation (W-TENS) device demonstrated non-inferiority to weak opioids at 3-months and was better tolerated among 110 participants with moderate to severe nociceptive knee OA pain. However, questioning the mechanism of action of TENS, Reichenbach *et al.*<sup>71</sup> found that TENS did not improve knee OA pain when compared to placebo TENS ( $n = 220$  participants). In a systematic review and meta-analysis by Dantas *et al.*<sup>66</sup> (4 RCTs, 234 participants), treatment with therapeutic ultrasound was found to have short-term small, statistically significant benefits for pain (SMD: –0.33; 95% CI: –0.60 to –0.07) and self-reported physical function (SMD: –0.33; 95% CI: (–0.65 to –0.01) compared to sham controls. Notably the overall quality of the evidence was very low. The effects of interferential current and photobiomodulation on pain and function were examined in an RCT of 168 patients with knee OA<sup>67</sup>. Combined interferential current plus photobiomodulation significantly reduced pain and improved function compared to interferential current alone or placebo groups, post-treatment, three and 6 months after the end of the treatment. Observed effect sizes were moderate to large, representing a clinically relevant improvement.

### Laser

Over the past year, several studies have focused on the role of laser in the management of OA, despite its use not being recommended in any clinical management guidelines. A systematic review and meta-analysis by Ahmad *et al.*<sup>72</sup> (including 10 RCTs and 495 participants) explored the effects of low-level and high-intensity laser therapy adjunctive to rehabilitation exercise on pain, stiffness and function among people with knee OA. When combined with exercise, both high- and low-level laser therapy were found to be effective in reducing symptoms compared to exercise alone or placebo laser. Supporting this finding, a RCT by Robbins *et al.*<sup>73</sup> found that in the short-term, low-level laser therapy combined with stretching resulted in significantly greater improvements in pain compared to a control (education booklet) among 215 people with knee OA. Laser therapy alone, and when combined with stretching, led to significantly greater improvement in disability compared to control.

### Balneotherapy/mud therapy

An overview of reviews by D'Angelo *et al.*<sup>74</sup> examined the efficacy of balneotherapy, mud therapy and spa therapy in patients with OA. Seventeen systematic reviews including 27 RCTs of low to critically low quality were included. Compared to controls (no intervention or usual care), balneotherapy was found to be effective in reducing pain (MD:  $-19.73$ ; 95% CI:  $-35.72$  to  $-3.74$ ), and improving stiffness (MD:  $-20.39$ ; 95% CI:  $-38.21$  to  $-2.57$ ) and quality of life (MD:  $-20.48$ ; 95% CI:  $-32.44$  to  $-8.52$ ). Mud therapy reduced pain (MD:  $-8.79$ ; 95% CI:  $-17.33$  to  $-0.25$ ) and stiffness (MD:  $-14.10$ ; 95% CI:  $-17.87$  to  $-10.33$ ), and spa therapy reduced pain only (MD:  $-11.72$ ; 95% CI:  $-22.18$  to  $-1.26$ ) compared to controls. Mennuni *et al.*<sup>75</sup> reported a meta-analysis of 21 RCTs (1816 participants) exploring the effectiveness of mud-bath therapy on pain and function among people with knee OA. They found significant improvements in pain and function scores at short-term follow-up after mud-bath therapy compared to no intervention controls.

### Manual therapy

In a recently published systematic review, Tsokanos *et al.*<sup>76</sup> narratively summarised the existing RCT evidence for the efficacy of manual therapy compared to controls (no intervention) for pain and function among people with knee OA. In total 6 RCTs and 730 participants were included in the review, which concluded that manual therapy can induce a short-term reduction in pain, increased knee range of movement and improved physical function. However long-term findings from existing RCTs are conflicting. In a further systematic review and meta-analysis, Li *et al.*<sup>77</sup> investigated the effectiveness of two specific types of manual therapy among people with knee OA: Maitland and Mulligan mobilization methods (8 RCTs, 471 participants). Mulligan mobilization was found to be more effective at improving pain and function scores compared to Maitland mobilization (pain: SMD: 0.60, 95% CI: 0.17 to 1.03; WOMAC physical function score: SMD: 7.41; 95% CI: 2.36 to 12.47). There was no difference in the effect of the two kinds of mobilization on improving range of motion.

### Novel/emerging treatments

Blood flow restriction training appears to be of growing interest in the field of OA rehabilitation, with at least four systematic reviews published in the last year<sup>78–81</sup>, and one new empirical study<sup>82</sup>. Blood flow restriction training involves a cuff being applied to the proximal region of the limb to restrict blood flow at the same time as completing resistance training<sup>81</sup>. Although the precise mechanism of action of blood flow restriction training is unknown, it is believed to promote biochemical and physiological changes that induce muscle hypertrophy. This can increase muscle strength and mass, which in turn can improve function in people with OA<sup>81</sup>. Whether it is an effective treatment for people with knee OA remains unclear. A systematic review by Grantham *et al.*<sup>78</sup> included 5 RCTs ( $n = 199$  participants) exploring blood flow restriction training compared to resistance training alone for people with knee OA. Included trials were small and of low-to-moderate quality. Although there were fewer exercise-induced pain adverse events from blood flow restriction training compared to resistance training, there was no evidence for improvement in: pain, physical function, or muscle strength in blood flow restriction training. Due to the sparsity of the current literature, new high quality RCTs would need to more robustly explore the clinical- and cost-effectiveness of blood flow restriction training for people with knee OA.

In addition, the extent to which blood flow restriction is currently used in clinical practice is unknown.

### Translation of rehabilitation evidence into practice

As the impact of the COVID-19 pandemic continues to be felt across all healthcare systems, delay and disruption to OA healthcare provision continues to be examined and discussed<sup>83,84</sup>. The flexible adoption of telemedicine and telerehabilitation that the pandemic accelerated may ultimately lead to improvements in multimodal OA care<sup>85</sup>. In response to COVID-19, Physiotherapy Exercise and Physical Activity for Knee Osteoarthritis (PEAK) e-learning modules were made freely available to support OA care provision through telehealth, with 6,720 people from 97 countries registering for access<sup>86</sup>. Module completers demonstrated increased confidence with videoconferencing and increased likelihood of using core OA treatments compared to pre-course. However, there were high levels of attrition, highlighting the challenge of maintaining engagement in self-directed web-based learning.

Over the past year, implementation of The Good Life with osteoarthritis from Denmark (GLA:D<sup>®</sup>) program, which provides education and exercises over an 8-week period for people with knee or hip OA, has also been evaluated. It demonstrated positive patient-reported outcomes when implemented across different contexts, populations and health care systems in Denmark, Canada and Australia<sup>87</sup>. Whilst these international comparisons are encouraging, as the authors attest, these findings are limited by the absence of a control group within a robust RCT design. In Australia, targeted training for physiotherapists in GLA:D program delivery supported implementation<sup>88</sup>. This included increasing physiotherapists' confidence in treatment delivery, as well as increasing the number of physiotherapists discussing treatment goals (baseline vs post-course ES = 0.14), prescribing neuromuscular exercise (ES = 0.26), using supervised exercise (ES = 0.19), and discussing the importance of weight management (ES = 0.10) all or most of the time<sup>88</sup>. Observational cohort data also supports the viability of the GLA:D program among individuals with comorbid conditions<sup>89</sup> and indicates that engagement with the program can lead patients to reduce analgesic use<sup>90</sup>. Together with emerging evidence of cost-effectiveness in Denmark<sup>91</sup> and the development of a national quality and outcomes registry in Canada<sup>92</sup>, broad application of the GLA:D<sup>®</sup> program in real-world settings looks set to grow.

Although evidence supporting the implementation of rehabilitation for people with OA in real world settings is expanding, this predominantly focuses on education and exercise. Evaluation of implementation of weight loss interventions for people with OA, and of adjunctive treatments are therefore important areas for future research.

### Conclusion

There has been considerable research activity in the field of OA rehabilitation in the past 12 months, predominantly focused on core recommended rehabilitation treatments and adjunctive treatments. Due to the large volume of studies published, it was not possible to summarise all the studies identified as being important, and/or of high quality. However, from the research included, it is clear that there have been advances in the field, including development and testing of novel approaches to the delivery of core treatments (e.g., stepped exercise provision, technology-delivered interventions), and the generation of novel, more robust evidence to support and refute delivery of some adjunctive treatments (e.g., splinting for thumb base OA). Existing evidence has also been synthesised, with several network meta-analyses allowing the relative effects of various rehabilitation interventions to be

compared for the first time. It has also been demonstrated that the positive outcomes from education and exercise generally seen in RCTs can be replicated when implemented in clinical practice. However, evidence published over the past year has also raised some questions, including the mechanisms of action of exercise for OA, the optimal delivery of some adjunctive treatments, and whether blood flow restriction training is an effective new treatment for people with knee OA. Future research therefore continues to be needed in the field of OA rehabilitation. Given the consistent finding across many recently published systematic reviews, that existing studies are small and of limited quality, new research needs to be large-scale and robust, to enable definitive answers to these important questions.

### Contributions

All authors were involved with the study design, manuscript editing, and reviewed the final manuscript. MAH, PJAN, MJT and NC were involved with study searching. MAH, PJAN and MJT contributed to manuscript drafting.

### Conflict of interest

MAH receives grants from the National Institute for Health and Care Research and the Chartered Society of Physiotherapy, Physiotherapy Research Foundation. PJAN receives grants from vs Arthritis. MJT receives grants from the National Institute for Health and Care Research. KLB receives grants from National Health and Medical Research Council, Medical Research Futures Fund and Medibank for rehabilitation research in OA and Wolters Kluwer for UpToDate Knee OA clinical guidelines. RSH receives grants from National Health and Medical Research Council, Australian Research Council, Medical Research Futures Fund and Medibank for rehabilitation research in OA.

### Funding sources

PJAN is supported by a Versus Arthritis Foundation Fellowship (#22428). KLB is supported by a National Health and Medical Research Council (NHMRC) Investigator Grant (#1174431). RSH is supported by a NHMRC Fellowship (#1154217).

### Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.joca.2022.10.004>.

### References

1. Rehabilitation in Health Systems. Geneva: World Health Organization; 2017. Licence: CC BY-NC-SA 3.0 IGO.
2. World Report on Disability. Geneva: World Health Organization and The World Bank; 2011.
3. Wong MCS, Huang J, Wang J, Chan PSF, Lok V, Chen X, et al. Global, regional and time-trend prevalence of central obesity: a systematic review and meta-analysis of 13.2 million subjects. *Eur J Epidemiol* 2020;35(7):673–83.
4. World Health Organization (WHO). Global Status Report on Non-communicable Diseases 2010. Geneva, Switzerland.
5. Gimigliano F, Negrini S. The world health organization "rehabilitation 2030: a call for action". *Eur J Phys Rehabil Med* 2017;53:155–68.
6. Hunter DJ, Bierma-Zeinstra S. Osteoarthritis. *Lancet* 2019;393:1745–59.
7. Hagen KB, Smedslund G, Østerås N, Jamtvedt G. Quality of community-based osteoarthritis care: a systematic review and meta-analysis. *Arthritis Care Res* 2016;68:1443–52.
8. Fransen M, McConnell S, Harmer AR, Van der Esch M, Simic M, Bennell KL. Exercise for osteoarthritis of the knee. *Cochrane Database Syst Rev* 2015;1:CD004376.
9. Goff AJ, De Oliveira Silva D, Merolli M, Bell EC, Crossley KM, Barton CJ. Patient education improves pain and function in people with knee osteoarthritis with better effects when combined with exercise therapy: a systematic review. *J Physiother* 2021;67:177–89.
10. Rezende MU, Brito NLR, Farias FES, Silva CAC, Cernigoy CHA, Rodrigues da Silva JM, et al. Improved function and strength in patients with knee osteoarthritis as a result of adding a two-day educational program to usual care. *Prospective randomized trial. Osteoarthritis Cartilage Open* 2021;3, 100137.
11. Ma Lopez-Olivo, des Bordes JK, Lin H, Volk RJ, Rizvi T, Suarez-Almazor MEA. Randomized controlled trial comparing two self-administered educational strategies for patients with knee osteoarthritis. *ACR Open Rheumatol* 2021;3:185–95.
12. Hill J, Bird H. Patient knowledge and misconceptions of osteoarthritis assessed by a validated self-completed knowledge questionnaire (PKQ- OA). *Rheumatology* 2007;46:796–800.
13. Allen KD, Woolson S, Hoenig HM, Bongiorni D, Byrd J, Caves K, et al. Stepped exercise program for patients with knee osteoarthritis a randomized controlled trial. *Ann Intern Med* 2021;174:298–307.
14. Pham T, van der Heijde D, Altman RD, Anderson JJ, Bellamy N, Hochberg M, et al. OMERACT-OARSI initiative: osteoarthritis Research Society International set of responder criteria for osteoarthritis clinical trials revisited. *Osteoarthritis Cartilage* 2004;12:389–99.
15. Bellamy N, Buchanan WW, Goldsmith CH, Campbell J, Stitt LW. Validation study of WOMAC: a health status instrument for measuring clinically important patient relevant outcomes to antirheumatic drug therapy in patients with osteoarthritis of the hip or knee. *J Rheumatol* 1988;15:1833–40.
16. Kaufman BG, Allen KD, Coffman CJ, Woolson S, Caves K, Hall K, et al. Cost and quality of life outcomes of the STepped exercise program for patients with knee OsteoArthritis trial. *Value Health* 2022;25:614–21.
17. Bandak E, Christensen R, Overgaard A, Erik Kristensen LE, Ellegaard K, Guldberg-Møller J, et al. Exercise and education versus saline injections for knee osteoarthritis: a randomised controlled equivalence trial. *Ann Rheumatic Diseases* 2022;81:537–43.
18. Roos EM, Roos HP, Lohmander LS, Ekdahl C, Beynon BD. Knee Injury and osteoarthritis outcome score (KOOS)—development of a self-administered outcome measure. *J Orthop Sports Phys Ther* 1998;28:88–96.
19. Bannuru RR, Osani MC, Vaysbrot EE, Arden NK, Bennell K, Bierma-Zeinstra SMA, et al. OARSI guidelines for the non-surgical management of knee, hip, and polyarticular osteoarthritis. *Osteoarthritis Cartilage* 2019;27:1578–89.
20. Hall M, Dobson F, Van Ginckel A, Nelligan RK, Collins NJ, Smith MD, et al. Comparative effectiveness of exercise programs for psychological well-being in knee osteoarthritis: a systematic review and network meta-analysis. *Semin Arthritis Rheum* 2021;51:1023–32.
21. Hu L, Wang Y, Liu X, Ji X, Ma Y, Man S, et al. Tai Chi exercise can ameliorate physical and mental health of patients with knee osteoarthritis: systematic review and meta-analysis. *Clin Rehabil* 2021;35:64–79.
22. McHorney CA, Ware JE, Raczek AE. The MOS 36-Item Short-Form Health Survey (SF-36): II. Psychometric and clinical tests of validity in measuring physical and mental health constructs. *Med Care* 1993;31(3):247–63.
23. Panunzi S, Maltese S, De Gaetano A, Capristo E, Bornstein SR, Mingrone G. Comparative efficacy of different weight loss

- treatments on knee osteoarthritis: a network meta-analysis. *Obes Rev* 2021;22, e13230.
24. Gohir SA, Eek F, Kelly A, Abhishek A, Valdes AM. Effectiveness of internet-based exercises aimed at treating knee osteoarthritis: the iBEAT-OA randomized clinical trial. *JAMA Netw Open* 2021;4, e210012.
  25. Hsu YI, Chen YC, Lee CL, Chang NJ. Effects of diet control and telemedicine-based resistance exercise intervention on patients with obesity and knee osteoarthritis: a randomized control trial. *Int J Environ Res Publ Health* 2021;18:7744.
  26. Jones SE, Campbell PK, Kimp AJ, Bennell K, Foster NE, Russell T, et al. Evaluation of a novel e-learning program for physiotherapists to manage knee osteoarthritis via telehealth: qualitative study nested in the PEAK (physiotherapy exercise and physical activity for knee osteoarthritis) randomized controlled trial. *J Med Internet Res* 2021;23, e25872.
  27. Pelle T, van der Palen J, de Graaf F, van den Hoogen FHJ, Bevers K, van den Ende CHM. Use and usability of the Dr. Bart app and its relation with health care utilisation and clinical outcomes in people with knee and/or hip osteoarthritis. *BMC Health Serv Res* 2021;21:444.
  28. Rafiq MT, Abdul Hamid MS, Hafiz E. The effect of rehabilitation protocol using mobile health in overweight and obese patients with knee osteoarthritis: a clinical trial. *Adv Rheumatol* 2021;61:63.
  29. Xie SH, Wang Q, Wang LQ, Wang L, Song KP, He CQ. Effect of internet-based rehabilitation programs on improvement of pain and physical function in patients with knee osteoarthritis: systematic review and meta-analysis of randomized controlled trials. *J Med Internet Res* 2021;23, e21542.
  30. Latif-Zade T, Tucci B, Verbovetskaya D, Bialkin E, Ng B, Heddon S, et al. Systematic review shows tele-rehabilitation might achieve comparable results to office-based rehabilitation for decreasing pain in patients with knee osteoarthritis. *Medicina (Kaunas)* 2021;57:764.
  31. Nelligan RK, Hinman RS, Kasza J, Crofts SJC, Bennell KL. Effects of a self-directed web-based strengthening exercise and physical activity program supported by automated text messages for people with knee osteoarthritis: a randomized clinical trial. *JAMA Intern Med* 2021;181:776–85.
  32. Chen T, Or CK, Chen J. Effects of technology-supported exercise programs on the knee pain, physical function, and quality of life of individuals with knee osteoarthritis and/or chronic knee pain: a systematic review and meta-analysis of randomized controlled trials. *J Am Med Inf Assoc* 2021;28:414–23.
  33. Mazzei DR, Ademola A, Abbott JH, Sajobi T, Hildebrand K, Marshall DA. Are education, exercise and diet interventions a cost-effective treatment to manage hip and knee osteoarthritis? A systematic review. *Osteoarthritis Cartilage* 2021;29: 456–70.
  34. Rhon DI, Kim M, Asche CV, Allison SC, Allen CS, Deyle GD. Cost-effectiveness of physical therapy vs intra-articular glucocorticoid injection for knee osteoarthritis: a secondary analysis from a randomized clinical trial. *JAMA Netw Open* 2022;5, e2142709.
  35. Deyle GD, Allen CS, Allison SC, Gill NW, Hando BR, Petersen EJ, et al. Physical therapy versus glucocorticoid injection for osteoarthritis of the knee. *N Engl J Med* 2020;382:1420–9.
  36. NICE: National Institute for Health and Care Excellence. Osteoarthritis. Care and Management in Adults 2014. Retrieved from London, <http://www.nice.org.uk/nicemedia/live/14383/66527/66527.pdf>.
  37. Kolasinski SL, Neogi T, Hochberg MC, Oatis C, Guyatt G, Block J, et al. 2019 American college of rheumatology/arthritis foundation guideline for the management of osteoarthritis of the hand, hip, and knee. *Arthritis Rheumatol* 2020;72:220–33.
  38. Alfatafta H, Onchonga D, Alfatafta M, Zhang I, Boncz I, Lohner S, et al. Effect of using knee valgus brace on pain and activity level over different time intervals among patients with medial knee OA. A systematic review. *BMC Musculoskeletal Disorders* 2021;22:687.
  39. Callaghan MJ, Palmer E, O'Neil T. Management of patellofemoral joint osteoarthritis using biomechanical device therapy: a systematic review with meta-analysis. *Syst Rev* 2021;10:173.
  40. Gueugnon M, Fournel I, Soilly A-L, Diaz A, Baulot E, Bussi ere C, et al. Effectiveness, safety, and cost-utility of a knee brace in medial knee osteoarthritis: the ERGONOMIE randomized controlled trial. *Osteoarthritis Cartilage* 2021;29:491–501.
  41. Yu L, Wang Y, Yang J, Wang J, Zhang Y. Effects of orthopedic insoles on patients with knee osteoarthritis: a meta-analysis and systematic review. *J Rehabil Med* 2021;53, jrm00191.
  42. Paterson KL, Bennell KL, Campbell PK, Metcalf BR, Wrigley TV, Kasza J, et al. The effect of flat flexible versus stable supportive shoes on knee osteoarthritis symptoms: a randomised trial. *Ann Intern Med* 2021;174:462–71.
  43. Heddon S, Sauliner N, Mercado J, Shalmiyev M, Berteau J-P. Systematic review shows no strong evidence regarding the use of elastic tape for pain improvement in patients with primary knee osteoarthritis. *Medicine (Baltim)* 2021;100, e25382.
  44. McManus KL, Kimmel LA, Holland AE. Rocktape provides no benefit over sham taping in people with knee osteoarthritis who are completing an exercise program: a randomised trial. *Physiotherapy* 2021;113:29–36.
  45. Adams J, Barratt P, Rombach I, Arden N, Barbosa Bouças S, Bradley S, et al. The clinical and cost effectiveness of splints for thumb base osteoarthritis: a randomized controlled clinical trial. *Rheumatology* 2021;60:2862–77.
  46. Deveza L, Robbins SR, Duong V, Bennell KL, Vicenzino B, Hodges PW, et al. Efficacy of a combination of conservative therapies vs an education comparator on clinical outcomes in thumb base osteoarthritis: a randomized clinical trial. *JAMA Intern Med* 2021;181:429–38.
  47. Visser AW, Bøyesen P, Haugen IK, Schoones JW, van der Heijde DM. Instruments measuring pain, physical function, or patient's global assessment in hand osteoarthritis: a systematic literature search. *J Rheumatol* 2015;42(11):2118–34.
  48. Marotta N, Demeco A, Marinaro C, Moggio L, Pino I, Barletta M, et al. Comparative effectiveness of orthoses for thumb osteoarthritis: a systematic review and network meta-analysis. *Arch Phys Med Rehabil* 2021;102:502–9.
  49. Munteanu SE, Landorf KB, McClelland JA, Roddy E, Cicuttini FM, Sheill A, et al. Shoe-stiffening inserts for first metatarsophalangeal joint osteoarthritis: a randomised trial. *Osteoarthritis Cartilage* 2021;29:480–90.
  50. Bennett PJ, Patterson C, Wearing S, Baglioni T. Development and validation of a questionnaire designed to measure foot-health status. *J Am Podiatr Med Assoc* 1998;88(9):419–28.
  51. Alinaghizadeh M, Hawkins J, Abbassian A, Seif Barghi T, Ayati MH, Alizadeh Vaghasloo M. Effect of Persian acupressure (ghamz) on patients with knee osteoarthritis: a single-blinded parallel clinical trial. *Pain Manag Nurs* 2021;22:820–7.
  52. Atalay SG, Durmus A, Gezginaslan Ö. The effect of acupuncture and physiotherapy on patients with knee osteoarthritis: a randomized controlled study. *Pain Physician* 2021;24: E269–78.
  53. Ho KK, Kwok AW, Chau WW, Xia SM, Wang YL, Cheng JC. A randomized controlled trial on the effect of focal thermal therapy at acupressure points treating osteoarthritis of the knee. *J Orthop Surg Res* 2021;16:282.

54. Hou X, Yan Y, Peng L, Niu D, Wei J, Wang J. Clinical effect of warm needle penetration in treating knee osteoarthritis. *Am J Tourism Res* 2021;13:6766–71.
55. Lam WC, Au KY, Qin Z, Wu FM, Chong CO, Jiang F, et al. Superficial needling acupuncture vs sham acupuncture for knee osteoarthritis: a randomized controlled trial. *Am J Med* 2021;134:1286–94.
56. Li H, Zheng Y, Wang Y, Meng L, Guo Y, Bian C, et al. Therapeutic effect of Qinglong tail-wagging acupuncture method in knee osteoarthritis and its influence on inflammatory factors. *Am J Tourism Res* 2021;13:3206–13.
57. Rani M, Sharma L, Advani U. Acupressure combined with pharmacological treatment in patients with osteoarthritis of the knee: a randomized trial. *Advances in Integrative Medicine* 2022;9:30–6.
58. Tu JF, Yang JW, Shi GX, Yu ZS, Li JL, Lin LL, et al. Efficacy of intensive acupuncture versus sham acupuncture in knee osteoarthritis: a randomized controlled trial. *Arthritis Rheumatol* 2021;73:448–58.
59. Vervullens S, Meert L, Baert I, Delrue N, Heusdens CHW, Halleman A, et al. The effect of one dry needling session on pain, central pain processing, muscle co-contraction and gait characteristics in patients with knee osteoarthritis: a randomized controlled trial. *Scandinavian Journal of Pain* 2021;22:396–409.
60. Yu WZ, Huang CM, Ng HP, Lee YC. Distal acupoints outperform proximal acupoints in treating knee osteoarthritis: a randomized controlled trial. *Evid base Compl Alternative Med* 2021:4827123.
61. Araya-Quintanilla F, Cuyúl-Vásquez I, Gutiérrez-Espinoza H. Does acupuncture provide pain relief in patients with osteoarthritis knee? An overview of systematic reviews. *J Bodyw Mov Ther* 2022;29:117–26.
62. Chen J, Liu A, Zhou Q, Yu W, Guo T, Jia Y, et al. Acupuncture for the treatment of knee osteoarthritis: an overview of systematic reviews. *Int J Gen Med* 2021;14:8481–94.
63. Liu W, Fan Y, Wu Y, Hou X, Xue B, Li P, et al. Efficacy of acupuncture-related therapy in the treatment of knee osteoarthritis: a network meta-analysis of randomized controlled trials. *J Pain Res* 2021;14:2209–28.
64. Qu B, Wu X, Liu H, Cai W, Wang G, Song H, et al. Meta-analysis and systematic review of acupotomy combined with puncture and moxibustion in the treatment of knee osteoarthritis. *Ann Palliat Med* 2021;10:6637–49.
65. Ughreja RA, Prem V. Effectiveness of dry needling techniques in patients with knee osteoarthritis: a systematic review and meta-analysis. *J Bodyw Mov Ther* 2021;27:328–38.
66. Dantas LO, Osani MC, Bannuru RR. Therapeutic ultrasound for knee osteoarthritis: a systematic review and meta-analysis with grade quality assessment. *Braz J Phys Ther* 2021;25:688–97.
67. Alqualo-Costa R, Rampazo ÉP, Thome GR, Perracini MR, Liebano RE. Interferential current and photobiomodulation in knee osteoarthritis: a randomized, placebo-controlled, double-blind clinical trial. *Clin Rehabil* 2021;35:1413–27.
68. Chaturvedi R, Joshi S. Effect of transcranial direct current stimulation (tDCS) and transcutaneous electrical nerve stimulation (TENS) in knee osteoarthritis. *Physiother Quart* 2021;29:68–75.
69. Lawson D, Degani AM, Lee K, Beer EI, Gohlke KE, Hamidi KN, et al. Use of transcutaneous electrical nerve stimulation along with functional tasks for immediate pain relief in individuals with knee osteoarthritis. *Eur J Pain* 2022;26:754–65.
70. Maheu E, Soriot-Thomas S, Noel E, Ganry H, Lespessailles E, Cortet B. Wearable transcutaneous electrical nerve stimulation (actiTENS®) is effective and safe for the treatment of knee osteoarthritis pain: a randomized controlled trial versus weak opioids. *Ther Adv Musculoskelet Dis* 2022;14:1759720x211066233.
71. Reichenbach S, Jüni P, Hincapié CA, Schneider C, Meli DN, Schürch R, et al. Effect of transcutaneous electrical nerve stimulation (TENS) on knee pain and physical function in patients with symptomatic knee osteoarthritis: the ETRELKA randomized clinical trial. *Osteoarthritis Cartilage* 2022;30:426–35.
72. Ahmad MA, Hamid MS, Yusof A. Effects of low-level and high-intensity laser therapy as adjunctive to rehabilitation exercise on pain, stiffness and function in knee osteoarthritis: a systematic review and meta-analysis. *Physiotherapy* 2022;114:85–95.
73. Robbins SR, Alfredo PP, Junior WS, Marques AP. Low-level laser therapy and static stretching exercises for patients with knee osteoarthritis: a randomised controlled trial. *Clin Rehabil* 2022;36:204–13.
74. D'Angelo D, Coclite D, Napoletano A, Fauci AJ, Latina R, Gianola S, et al. The efficacy of balneotherapy, mud therapy and spa therapy in patients with osteoarthritis: an overview of reviews. *Int J Biometeorol* 2021;65:1255–71.
75. Mennuni G, Fontana M, Perricone C, Nocchi S, Rosso R, Ceccarelli F, et al. A meta-analysis of the effectiveness of mud-bath therapy on knee osteoarthritis. *Clin Ter* 2021;172:372–87.
76. Tsokanos A, Livieratou E, Billis E, Tsekoura M, Tatsios P, Tsepis E, et al. The efficacy of manual therapy in patients with knee osteoarthritis: a systematic review. *Medicina (Kaunas)* 2021;vol. 57.
77. Li LL, Hu XJ, Di YH, Jiao W. Effectiveness of Maitland and Mulligan mobilization methods for adults with knee osteoarthritis: a systematic review and meta-analysis. *World J Clin Cases* 2022;10:954–65.
78. Grantham B, Korakakis V, O'Sullivan K. Does blood flow restriction training enhance clinical outcomes in knee osteoarthritis: a systematic review and meta-analysis. *Phys Ther Sport* 2021;49:37–49.
79. Pitsillides A, Stasinopoulos D, Mamais I. Blood flow restriction training in patients with knee osteoarthritis: systematic review of randomized controlled trials. *J Bodyw Mov Ther* 2021;27:477–86.
80. Wang HN, Chen Y, Cheng L, Cai YH, Li W, Ni GX. Efficacy and safety of blood flow restriction training in patients with knee osteoarthritis: a systematic review and meta-analysis. *Arthritis Care Res* 2022;74:89–98.
81. dos Santos LP, do Espirito Santo RC, Ramis TR, Portes JKS, da Silva Chakr RM, Xavier RM. The effects of resistance training with blood flow restriction on muscle strength, muscle hypertrophy and functionality in patients with osteoarthritis and rheumatoid arthritis: a systematic review with meta-analysis. *PLoS One* 2021;16, e0259574.
82. Shakeel R, Khan AA, Ayyub A, Masood Z. Impact of strengthening exercises with and without blood flow restriction on quadriceps of knee osteoarthritis patients. *JPMA (J Pak Med Assoc)* 2021;71:2173–6.
83. Battista S, Dell'Isola A, Manoni M, Englund M, Palese A, Testa M. Experience of the COVID-19 pandemic as lived by patients with hip and knee osteoarthritis: an Italian qualitative study. *BMJ Open* 2021;11, e053194.
84. Garrido-Cumbrera M, Marzo-Ortega H, Christen L, Plazuelo-Ramos P, Webb D, Jacklin C, et al. Assessment of impact of the COVID-19 pandemic from the perspective of patients with rheumatic and musculoskeletal diseases in Europe: results

- from the REUMAVID study (phase 1). *RMD Open* 2021;7, e001546.
85. Alhassan E, Siaton BC, Hochberg MC. Did COVID-19 impact osteoarthritis – clinical perspective? *Curr Opin Rheumatol* 2022;34:62–72.
  86. Jorge AES, Bennell KL, Kimp AJ, Campbell PK, Hinman RS. An e-learning program for physiotherapists to manage knee osteoarthritis via telehealth during the COVID-19 pandemic: real-world evaluation study using registration and survey data. *JMIR Med Educ* 2021;7, e30378.
  87. Roos EM, Grønne DT, Skou ST, Zywił M, McGlasson R, Barton CJ. Immediate outcomes following the GLA:D® program in Denmark, Canada and Australia. A longitudinal analysis including 28,370 patients with symptomatic knee or hip osteoarthritis. *Osteoarthritis Cartilage* 2021;24:502–6.
  88. Barton CJ, Kemp JL, Roos EM, Shou ST, Dundules K, Pazzinatto MF, et al. Program evaluation of GLA:D® Australia: physiotherapist training outcomes and effectiveness of implementation for people with knee osteoarthritis. *Osteoarthritis Cartilage Open* 2021;3(3), 100175.
  89. Pihl K, Roos E, Taylor RS, Grønne DT, Skou ST. Associations between comorbidities and immediate and one-year outcomes following supervised exercise therapy and patient education – a cohort study of 24,513 individuals with knee or hip osteoarthritis. *Osteoarthritis Cartilage* 2021;29:39–49.
  90. Thorlund JB, Roos EM, Goro P, Ljungcrantz EG, Grønne DT, Skou ST. Patients use fewer analgesics following supervised exercise therapy and patient education: an observational study of 16 499 patients with knee or hip osteoarthritis. *Br J Sports Med* 2021;55:670–5.
  91. Grønne DT, Roos EM, Ibsen R, Kjellberg J, Skou ST. Cost-effectiveness of an 8-week supervised education and exercise therapy programme for knee and hip osteoarthritis: a pre-post analysis of 16 255 patients participating in Good Life with osteoArthritis in Denmark (GLA:D). *BMJ Open* 2021;11, e049541.
  92. Zywił M, Ellis K, Veillett CJH, Skou S, McGlasson R. Implementation of the Good Life with osteoArthritis in Denmark (GLA:D) program across Canada for the management of hip and knee osteoarthritis. *Healthc Q* 2021;24:54–9.