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REVIEW PAPER

The efficacy of balneotherapy, mud therapy and spa therapy in patients with osteoarthritis: an overview of reviews

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Abstract

Osteoarthritis is a degenerative disease considered a leading cause of functional disability. Its treatment is based on a combination of pharmacological and non-pharmacological interventions, but the role of these latter is still debated. This overview of systematic reviews aimed at evaluating the short-term efficacy of different thermal modalities in patients with osteoarthritis. We searched PubMed, Scopus, CINHAL, Web of Science, ProQuest and the Cochrane Database of Systematic Reviews from inception until October 2020, with no language restrictions. We selected the following outcomes a priori: pain, stiffness and quality of life. Seventeen systematic reviews containing 27 unique relevant studies were included. The quality of the reviews ranged from low to critically low. Substantial variations in terms of interventions studied, comparison groups, population, outcomes and follow-up between the included SRs were found. From a re-analysis of primary data, emerged that balneotherapy was effective in reducing pain and improving stiffness and quality of life, mud therapy significantly reduced pain and stiffness, and spa therapy showed pain relief. However, the evidence supporting the efficacy of different thermal modalities could be seriously flawed due to methodological quality and sample size, to the presence of important treatment variations, and to the high level of heterogeneity and the absence of a double-blind design. There is some encouraging evidence that deserves clinicians' consideration, suggesting that thermal modalities are effective on a short-term basis for treating patients with AO.

Keywords Osteoarthritis · Thermal care · Balneotherapy · Overview of reviews · Spa therapy · Mud pack therapy

Introduction

Osteoarthritis (OA) is the most common musculoskeletal joint disease that mainly affects the hips, knees, hands and spine. It leads to pain and impaired function, especially in the elderly (Harzy et al. 2009). Its prevalence is expected to increase in the coming decades due to an ageing and increasingly obese population (Ackerman et al. 2018). OA significantly impacts patients' quality of life by limiting their normal daily activities and by increasing the risk of further morbidity and of mortality (Corsi et al. 2018). Consequently, it is a heavy burden for people and, in time, will become a more significant healthcare problem (French et al. 2015).

Management of OA currently includes non-pharmacological and pharmacological treatments (French et al. 2015; Tenti et al. 2015). Among the non-pharmacological interventions, the most widely used include balneotherapy, mud therapy and spa therapy in addition to and alternating with other options (i.e. physiotherapy and exercise) (Forestier et al. 2017; Paoloni et al. 2017).

Specifically, balneotherapy is defined as the use of thermal mineral water in which the sum of the cations and anions is greater than 1 g/l, the temperature is not lower than 20 °C and

Daniela D'Angelo, Daniela Coclite and Antonello Napoletano co-shared role in the authorship, specifically DC and NA contributed equally to this work and are the co-first authors

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the body is completely immersed (Bender et al. 2005; Branco et al. 2016; Tenti et al. 2015). It is commonly used in many European and Middle Eastern countries with the aim to improve pain and stiffness, strengthen muscle, relieve muscle spasm and maintain or improve functional mobility (Antonelli and Donelli 2018).

Mud therapy utilises a natural product consisting of a mixture of a solid component with a liquid component (mineral or thermal water) and applied in the form of a wrap, either locally or to the whole body (Fraioli et al. 2018; Paoloni et al. 2017; Tenti et al. 2015). Its application causes vasodilation and increases blood flow, metabolism and connective tissue elasticity resulting in a relief of muscle spasms and pain (Sarsan et al. 2012).

While spa therapy employs several treatment modalities, the most common are the combination of balneotherapy and mud therapy as employed in health resorts (Verhagen et al. 2015).

In the past decades, several clinical studies and reviews have evaluated the efficacy of balneotherapy, mud therapy and spa therapy in the treatment of musculoskeletal disorders (Fraioli et al. 2018; Harzy et al. 2009; Kulisch et al. 2014), but due to poor methodological quality and inadequate statistical analysis, the evidence is still unclear (Verhagen et al. 2015). Furthermore, in most studies, balneotherapy, mud therapy and spa therapy have been combined with other treatments such as exercise programmes, massage and rehabilitation. These multicomponent interventions hindered the possibility of measuring the effectiveness of a single intervention (Falagas et al. 2009).

Despite the wide implementation of a broad spectrum of therapeutic thermal modalities for the management of OA, and several systematic reviews and meta-analyses to evaluate their effectiveness (Antonelli et al. 2018; Beasley et al. 2019; Forestier et al. 2017; Paoloni et al. 2017), to our knowledge, there has been no systematic effort to summarise and critically appraise this body of evidence.

Therefore, we adopted an overview of systematic reviews to combine evidence from a wide range of interventions and outcomes, focussing on evidence from systematic review articles evaluating different thermal modalities for the management of OA.

Specifically, our systematic review addressed the following question: In adults suffering from OA, do balneotherapy, mud therapy and spa therapy lead to a reduction of pain and stiffness and an improvement in quality of life?

Materials and methods

We applied the guidelines for conducting an overview of reviews from the Cochrane Handbook for Systematic Reviews of Interventions (Higgins et al. 2019), and adhered to the preferred reporting items for systematic review and meta-analyses (PRISMA) statement (preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation 2016). The study protocol was registered in the Prospective Register of Systematic Reviews (PROSPERO) and it is publicly available under registration number CRD42019133930.

Criteria for considering reviews for inclusion

Eligibility criteria for the overview were established using the Population, Intervention, Comparator, Outcome and Study design (PICOS) framework, to include the following:

Participants: adults (≥ 18 years) with osteoarthritis (OA).

Interventions and comparators: interventions included balneotherapy, mud therapy and spa therapy versus usual care, placebo or no interventions. Specifically, when we referred to balneotherapy (bathing in natural mineral or thermal/sulphur waters) and mud therapy (mud bath, mud pack/peloid), we considered them as a 'solitary' approach outside the spa context. This is because the spa context may have some psychological effects capable of influencing the subjective outcome measurement.

We did not include reviews/trials in which the above interventions were provided in combination with exercise/physiotherapy/training interventions. These co-interventions were only admitted in the trials if the exercises were provided in both branches of the studies (with the same duration /frequency/intensity). We also excluded any trials performed in a specific thermal location with unique environmental conditions (climate, altitude, barometric pressure) that could be confounding factors. Hydrotherapy trials, defined as the use of normal tap water for therapeutic purposes, were also excluded.

Outcome measures: the primary outcomes of interest were pain (VAS, WOMAC scale), stiffness (WOMAC scale) and quality of life (SF36-12, Nottingham Health Profile, Stanford Health Assessment Questionnaire, EQ-5D index). We included these outcomes because the European League Against Rheumatism (EULAR) recommendations (Fernandes et al. 2013; Kloppenburg et al. 2019) consider the control of such symptoms the primary goal of OA management.

Studies: any systematic reviews (SR) of randomised controlled trials (RCT) and non-randomised controlled studies (NRS) used for evaluating the effects of interventions.

SRs were those that were in accordance with the definition proposed by the Cochrane Collaboration's Handbook (Cumpston et al. 2019).

Information sources and search

We searched PubMed, Scopus, Web of Science, CINHAL, Cochrane Library, PEDro and ProQuest databases from

inception until 30 October 2020, with no language restrictions. The complete search strategy is summarised in Online Resource 1.

So as to include other potentially eligible reviews, the lists of references from the retrieved reviews were also examined.

Study selection

Eligible studies were selected using a multi-stage approach (title-abstract, full-text reading) by two independent researchers (LI and DD), and any discrepancies were resolved by consensus. If there was any disagreement, this was discussed in detail with a third researcher (DC) until consensus was reached.

Assessment of methodological quality of reviews

Two review authors (LI and FG) independently assessed the included reviews using the AMSTAR2 methodological quality measure tool (Shea et al. 2017). It is an updated version of the original AMSTAR (Shea et al. 2007) tool, specifically developed to assess the methodological quality of systematic reviews that include both randomised and non-randomised studies of healthcare interventions. AMSTAR2 includes the following critical domains: protocol registered before start of review; adequacy of literature search; justification for excluded studies; risk of bias for included studies; appropriateness of meta-analytic methods; consideration of risk of bias when interpreting results; and assessing presence and likely impact of publication bias.

Data collection and analysis

Data were extracted from the full text by one of the authors (DD) and reviewed independently by another (LI).

Data were extracted at two levels, the first regarding the SRs and, the second, the studies included in each SR. The following data were extracted:

RS characteristics: authors, years of publication, research questions, databases searched, year searched, type of studies included, number of studies included, number of participants, interventions/comparator, outcome investigated, main findings.

Overlap among studies (only RCT) included in the SRs: As the degree to which the reviews shared the same RCTs could affect interpretation of results, the overlap between reviews and the number of RCTs that were unique to each review were assessed. An evidence map was prepared for the entire overview and used to calculate the 'corrected covered area' (CCA) (Pieper et al. 2014).

Data synthesis, analyses and classification of RCTs: A re-analysis of outcome data was planned for this overview, as a substantial difference in analysis results across the systematic reviews, and/or a lack of meta-analysis was expected (Higgins et al. 2019).

The following data were extracted from SRs: RCT sample size, intervention, property, duration and follow-up points. In cases where data on trial characteristics were not available in the included SRs, the missing data were extracted and/or the missing quality assessments were completed independently by two reviewers (LI and DC) using the primary research paper. Quality assessment was performed using the JADAD scale, which describes items pertaining to description of randomisation (2 points), appropriateness of blinding (2 points) and dropouts and withdrawals (1 point) (Jadad et al. 1996).

For quantitative analysis, outcome data were extracted from RCTs and meta-analysed using REVIEW MANAGER 5.3 (The Nordic Cochrane Centre, The Cochrane Collaboration, 2014). In order to conduct the statistical analysis for meta-analysis, sample sizes, means and standard deviations for the experimental and control groups were extracted. Continuous outcomes were expressed using mean differences with 95% CIs. All analyses used random-effects models and, to reduce heterogeneity, sample data were normalised using appropriate scale factors to obtain comparable means and standard deviations. Heterogeneity was assessed using the I^2 statistic, and whenever possible, publication bias was assessed using funnel plots. A post hoc sensitivity analysis was conducted excluding studies that may impact the results of meta-analysis.

The clinical efficacy outcome as assessed at the short-term follow-up point, which was used in each trial, was taken as the defining moment for identifying the effectiveness of the treatment. When we encountered incomplete data, the authors of the trial were contacted.

For NRSs, qualitative analysis via a narrative approach was used.

Results

Search results

The literature search retrieved 116 unique references, of which 92 were excluded after title and abstract screening. Of the 24 potentially relevant SRs, 7 were excluded after a full-text reading (Online Resource 2). Therefore, 17 SRs were included in this overview. The Study Flow Diagram according to the PRISMA statement is reported in Fig. 1.

Characteristics of the SRs and their trials

Included SRs were heterogeneous in terms of interventions studied, comparison groups, population, outcomes and

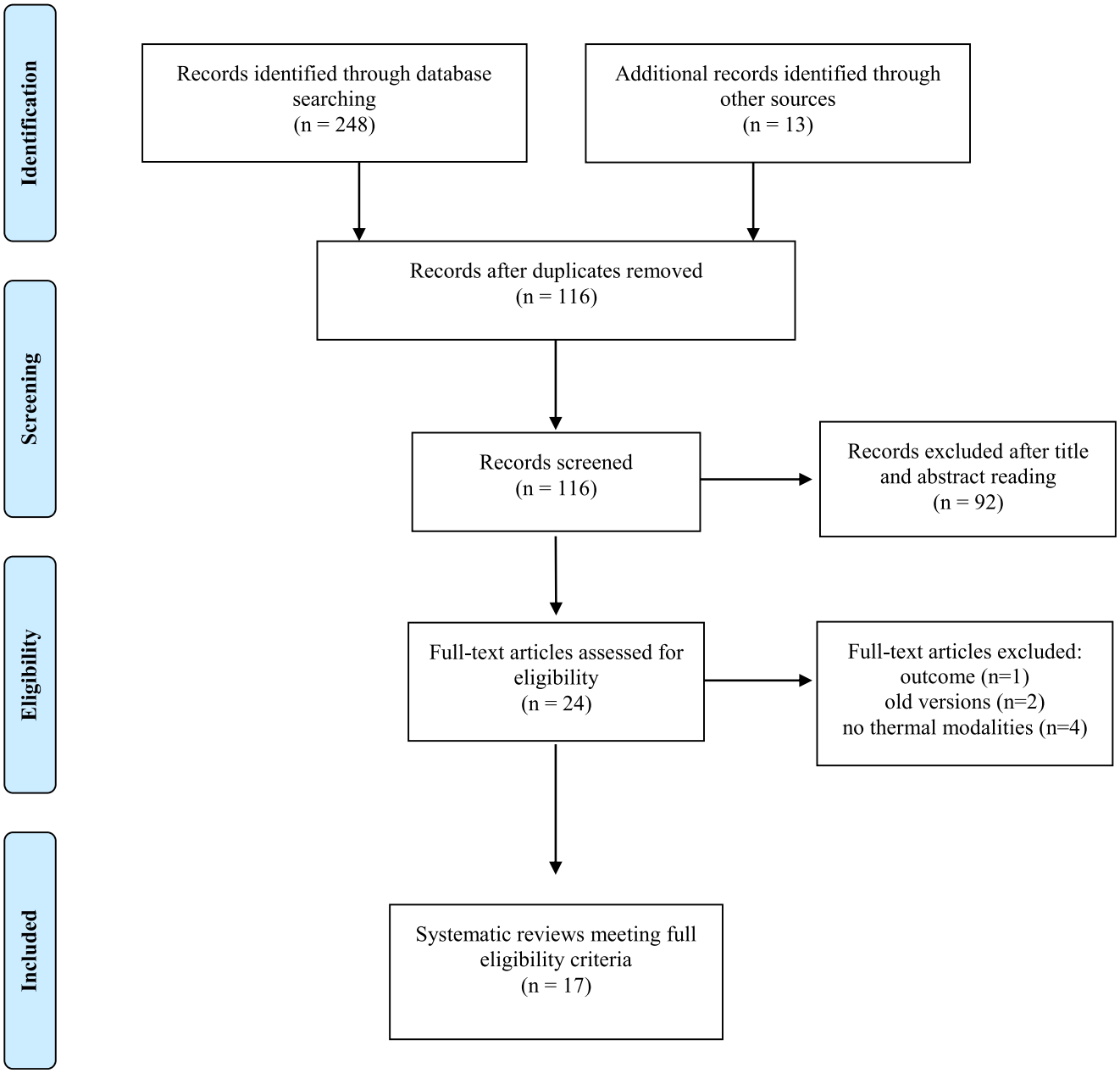


Fig. 1 Flow diagram of study selection process

follow-up. A detailed description of the included SRs is shown in Table 1.

The review question investigated the effect of different thermal modalities on knee joints in 10 SRs, on hand joints in 3 SRs and on any part of the body in 4 SRs. The intervention studied was balneotherapy in 7 SRs (Antonelli et al. 2018; Brosseau et al. 2002; Falagas et al. 2009; Harzy et al. 2009; Katz et al. 2012; Matsumoto et al. 2017; Verhagen et al. 2007) and mud therapy in 5 SRs (Crespin 2017; Espejo-Antunez et al. 2013b; Hou et al. 2020; Liu et al. 2013; Xiang et al. 2016), while 4 SRs researched both modalities (balneo-mud therapy) and their combination within a resort (spa therapy), and one SR (Fraioli et al. 2018) analysed 4 different thermal modalities separately.

The publication dates of SRs ranged from 2002 to 2020. Thirteen SRs (76%) included RCTs only. The number of included studies (RCT/NRS) per SR ranged from 19 (Forestier et al. 2016) to 1 (Katz et al. 2012), and the number of participants from 1612 (Forestier et al. 2016) to 44 (Katz et al. 2012). Only two NRSs were considered eligible.

A detailed look at thermal modalities for all the RTCs included in the meta-analysis is shown in Online Resource 3.

Table 1 Characteristics of the included reviews

Authors, years	Research questions	Databases searched	Year searched	Primary study design	Quality assessment
Reviews without meta-analysis					
Beasley 2018[1]	To determine effective conservative therapeutic interventions for OA of the finger joints	PubMed, CINAHL, Web of Science, PEDro, and OT seeker	Database inception to January 2017	RCT	SEQUES
Brosseau et al. 2002	To evaluate and compare the efficacy of various forms of balneotherapy for treating patients with OA of the knee	MEDLINE, Embase, HealthStar, Sports Discus, CINAHL, Cochrane Central Register of Controlled Trials, PEDro	Up to 2002	RCT	JADAD
Espejo-Antunez et al. 2013a, b[2]	Systematically review scientific studies that analyse the therapeutic effects of mud pack application in patients diagnosed with OA	PubMed, PEDro, Scopus, Cochrane Library, EMBASE, CINAHL and Science Direct	From 2000 to the present	RCT, NRS	The Cochrane handbook for systematic reviews of interventions 4.2.5 (update May 2005)
Falagas et al. 2009[3]	To review the existing evidence regarding randomised controlled trials (RCTs), examining the clinical effects of balneotherapy	PubMed, Scopus and Cochrane Library	1950–2006	RCT	Oxford Quality Scale (OQS)
Forestier et al. 2016[4]	To systematically review the highest evidence provided by published trials to estimate the clinical effect of crenobalneotherapy for OA of the knee	MEDLINE via PubMed, PEDro, Cochrane Central Register of Controlled Trials	Up to September 2015	RCT, NRS	A checklist to evaluate a report on a non-pharmacological trial (CLEAR NTP)
Fortunati 2015	To summarise the information currently available on the clinical effects and mechanisms of action of Spa therapy in OA of the hand	Cochrane Library, PubMed, EMBASE, WOS, Scopus, PEDro, Web of Knowledge databases, ClinicalTrials.gov	1952 to June 2015	RCT	Not reported
Fraioli 2018[5]	To investigate the efficacy of Spa therapy in the treatment of OA of the knee	MEDLINE via PubMed	Articles published between 2002 and 2017	RCT, NRS	Not reported
Harzy et al. 2009	To evaluate short- and long-term therapeutic effectiveness of natural thermal mineral waters in patients with OA of the knee	PubMed, Cochrane Central Register of Controlled Trials, and AMED (British Library)	Not reported	RCT	JADAD
Katz et al. 2012[6]	To critically present the level of evidence for the claims of therapeutic effects of Dead Sea treatments in rheumatic diseases and psoriasis	MEDLINE	Not reported	RCT, NRS	Not reported
Tenti 2014[7]	To summarise the information currently available on the clinical effects, and briefly discuss the possible mechanisms of action, of Spa therapy in OA of the knee	PubMed, Scopus, Cochrane Library and EMBASE	October 2003 and September 2013	RCT	Not reported
Verhagen et al. 2007[8]	To perform a systematic review on the effects of balneotherapy in patients with OA	EMBASE, PubMed, Cochrane: 'Rehabilitation and Related Therapies' 'Central Register of Controlled Trial', PEDro	Up to October 2006	RCT	The Delphi list
Review with meta-analysis					
Antonelli et al. 2018[9]	To explore the possible effects of different BT treatments (thermal mineral baths and/or mud/peloid packs, or hay baths) and Spa therapy on QoL in patients with OA of the knee	MEDLINE via PubMed, Scopus, Web of Science, Cochrane Library, and PEDro (Physiotherapy Evidence Database)	All databases were screened up to December 2017	RCT	Criteria of the Cochrane risk of bias tool for trials

Table 1 (continued)

Crespin 2017	To examine the effects of mud pack therapy versus to improve functionality and decrease pain in older adults suffering with OA of the knee	CINAHL, PubMed, and Science Direct	January 2010 to September 2016	RCT	PEDro scale
Hou et al. 2020	To systematically evaluate the short-term efficacy of mud therapy in the treatment of knee osteoarthritis	PubMed, Embase, and the Cochrane Library databases	Up to July 20, 2019	RCT	Cochrane risk of bias tool
Liu et al. 2013[10]	A meta-analysis was performed to determine the effect of mud therapy on pain relief in OA of the knee	MEDLINE	From the earliest records up to and including 9 March 2013	RCT	Scale for randomised clinical trials (Cochrane Collaboration)
Matsumoto et al. 2017[11]	This meta-analysis was performed to determine the effect of balneotherapy on relieving pain and stiffness, and improving function in patients with OA of the knee	MEDLINE, Embase, the Cochrane Library, and the Japan Medical Abstracts Society Database	From 2004 to Dec 31, 2016	RCT	Cochrane risk of bias tool
Xiang et al. 2016[12]	To assess the efficacy of mud pack therapy in treating OA of the knee	MEDLINE, EMBASE, Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews	MEDLINE (1945–2014), Embase (1980–2014), Cochrane Central Register Controlled Trials (1970–2014)	RCT	JADAD

Authors, years	No. of included studies	No. of participants	Interventions/comparator	Outcomes	Main findings (narrative)
Reviews without meta-analysis					
Beasley 2018[1]	3/18	224	Thermal modalities (balneo and mud therapy)/other usual intervention	Pain, tenderness, hand grip strength, hand function	There is some evidence of high quality to support the thermal modalities of paraffin wax, and balneotherapy at 38 °C combined and/or not combined with mud packs and magnetotherapy to decrease pain and tenderness, and improve grip strength, pinch strength and hand function
Brosseau et al. 2002	3	172	Balneotherapy/placebo, untreated or active interventions	Pain, function, timed stair climbing, range of motion (ROM)	Balneotherapy may have the potential to become an efficacious non-pharmacological treatment option for OA of the knee. The results of this review suggest that balneotherapy can be effective on a short-term basis for measures of pain severity and function as well as for improved ROM and timed stair climbing
Espejo-Antunez et al. 2013a, b[2]	7 (RCT), 1 (NR-S)/18	637 (RCT), 61 (NRS)	Mud therapy/usual care	Pain, functionality, quality of life	Mud pack therapy is an effective alternative treatment, in the management of knee OA. Studies with better methodological quality on mud pack therapy dealing with knee OA are needed
Falagas et al. 2009[3]	5/29	248	Thermal modalities/therapeutic modalities, not comprising balneotherapy	Substantial improvement of symptoms	There is a possibility that balneotherapy is associated with clinical improvement, mainly in rheumatic disease such as osteoarthritis, fibromyalgia, ankylosing spondylitis, rheumatoid arthritis and in chronic low back pain
Forestier et al. 2016[4]	18 (RCT), 1(NR-S)/30	1289 (RCT), 61 (NRS)	Spa therapy/any other intervention or no treatment	Pain, function, global assessment of patient (stiffness, quality of life)	This systematic review of Spa therapy for OA of the knee shows that the treatment delivered in spa centres across Europe and the Middle East can improve symptoms
Fortunati 2015	3 RCT	168	Spa therapy with another intervention or with routine medical care	Pain, stiffness, disability, tender/swollen joints, withdrawals	

Table 1 (continued)

					Spa therapy seems to have a role in the treatment of OA of the hand, despite the fact that therapeutic options for this condition are still limited
Fraioli 2018[5]	6 (RCT, 2 (NR-S)/12	669 (RCT), 142 (NRS)	Thermal modalities/usual care	Severity of symptoms, reduction in analgesic and NSAID consumption, quality of life	Spa therapy allows the reduction of conventional treatment dosage, possibly resulting in lower costs and fewer drug-related adverse events, and further improving patients' quality of life
Harzy et al. 2009	7	395	Natural thermal mineral waters	Pain, Western Ontario and McMaster Universities OA index (WOMAC), function (Lequesne/LAFI), analgesic intake	In conclusion, there is some encouraging evidence suggesting that thermal mineral waters are safe and effective for treating patients with knee OA. It may be may considered as one treatment option in a multidisciplinary approach in the treatment of this disease
Katz et al. 2012[6]	1 (RC-T)/23	44	Dead Sea water balneotherapy, Dead Sea springs' water balneotherapy-sulphur balneotherapy, and Dead Sea mud	Pain, quality of life, function	Regarding OA of the knee, there is evidence that Dead Sea water balneotherapy, Dead Sea sulphur balneotherapy, and Dead Sea mud are beneficial
Tenti 2014[7]	12/14	1063	Spa therapy comprises a broad spectrum of therapeutic modalities including hydrotherapy, balneotherapy, mud pack therapy, physiotherapy and exercise	Pain, function, severity	Spa therapy seems to have a role in the treatment of OA of the knee. It cannot substitute conventional therapy, but it can complement it
Verhagen et al. 2007[8]	7/3	175	Balneotherapy/another intervention or no intervention	Pain, function, global assessment of patient, quality of life	Our conclusion is that there appears to be silver level evidence in favour of balneotherapy when compared to no treatment and that it is not possible to draw a firm conclusion on the effectiveness of several forms of balneotherapy in patients with OA
Review with meta-analysis					
Antonelli et al. 2018[9]	12/17	1290	Studies in which intervention comprised thermal mineral water immersion, hay baths or mud-peloid pack applications/all types of intervention	QoL	Even though limitations of included studies must be taken into account, evidence shows that BT and Spa therapy can significantly improve QoL of patients with OA of the knee. More trials with a higher number of patients and different types of balneological interventions are needed to better determine their effects on QoL
Crespin 2017	4	256	Mud pack therapy/hot pack treatment	Pain, function	This meta-analysis determined the use of mud pack therapy to be statistically significant in reducing pain and improving functionality for people suffering with OA of the knee
Hou et al. 2020	11	1106	Mud therapy/control group was not limited	Function, Pain, stiffness	Based on existing evidence, the short-term efficacy of mud therapy was significant in relieving pain and improving joint functions for patients with KOA
Liu et al. 2013[10]	6/7	379	Mud therapy/usual care, placebo, or no intervention	Pain	In conclusion, mud therapy appears to be a favourable option for pain relief in patients with OA of the knee
Matsumoto et al. 2017[11]	7/8	509	Balneotherapy	Pain relief, stiffness, and physical function	This meta-analysis appears to confirm that existing clinical trials on balneotherapy found it to be associated with a reduction in pain and stiffness, and an improvement in function in patients with OA of the knee

Table 1 (continued)

Xiang et al. 2016[12]	9/10	952	Mud therapy/other intervention, placebo	Relief of pain and improvement of function	There was no significant difference in the improvement of joint function over the 4-month follow-up period between the knee OA patients' treated with mud pack therapy and control subjects

[1] Beasley included 18 studies, but only 3 RCTs were included in this review

[2] Espenjo-Antunez included 18 studies, but only 8 studies met our inclusion criteria

[3] Falagas included 29 trials, 6 RCTs specifically focused on AO. Of these, 5 met our inclusion criteria

[4] Forestier included 30 studies, 19 of them met our inclusion criteria

[5] Fraioli included 12 studies. Of these, 8 met our inclusion criteria

[6] Katz included 23 studies. Of these, only 4 were on OA patients and 1 met our inclusion criteria

[7] Tenti included 14 studies. Only two did not meet our inclusion criteria

[8] Verhagen included 7 RCTs, of which 3 met our inclusion criteria

[9] Antonelli included 17 RCTs. Of these, 13 included our inclusion criteria

[10] Liu included 7 RCTs. Only one did not meet our inclusion criteria

[11] Matsumoto included 8 RCT. Only one did not meet our inclusion criteria

[12] Xiang included 10 studies, of which only one did not meet our inclusion criteria

Overlap of RCTs between SRs

After accounting for overlapping RCTs contained within multiple SRs, a total of 25 unique RCTs (about 1780 participants) remained (Online Resource 4). Only 4 (16%) RCTs did not overlap among SRs, giving an overlap percentage of 84%. A total of 25 primary studies were cited 108 times across the 17 SRs included in this overview, resulting in a CCA of 30% and indicating a very high overlap (Table 2).

Methodological quality of included reviews and RCTs

The quality assessment of the seventeen SRs is presented in Table 3.

All included reviews had multiple flaws according to the AMSTAR-2 assessment tool.

The quality of the reviews ranged from low (Hou et al. 2020; Matsumoto et al. 2017; Verhagen et al. 2007) to critically low (Antonelli et al. 2018; Beasley et al. 2019; Brosseau et al. 2002; Crespin 2017; Espejo-Antunez et al. 2013b; Falagas et al. 2009; Forestier et al. 2016; Fortunati et al. 2016; Fraioli et al. 2018; Harzy et al. 2009; Katz et al. 2012; Liu et al. 2013; Xiang et al. 2016). Other than the SR by Matsumoto et al. (Matsumoto et al. 2017), all other SRs failed to satisfy critical item 2 (protocol registered), and only the SR by Verhaegen et al. (Verhagen et al. 2007) met critical item 7 (list of excluded studies). Thus, all SRs judged critically low failed to satisfy these two specific critical items. The quality of the included RCTs ranged from 2 to 5 (Online Resource 5). A study was considered to be of high/moderate quality if the score was 3 to 5, and of low quality if the score was 1 to 2. The most common reason for point deduction was the absence of double blinding (63%), probably due to the nature of the intervention. Four RCTs (Kovacs et al. 2012; Kovacs and Bender 2002; Tefner et al. 2013; Yurtkuran et al. 2006) were assigned a JADAD score of 5 (highest score), five RCTs (Forestier et al. 2010; Giannitti et al. 2017; Pascarelli et al. 2016; Szucs et al. 1989; Wigler et al. 1995) received a score of 4, eleven RCTs (Balint et al. 2007; Branco et al. 2016; Fioravanti et al. 2015; Fioravanti et al. 2012; Fioravanti et al. 2010; Gungen et al. 2012; Horvath et al. 2012; Karagulle et al. 2007; Mahboob et al. 2009; Odabasi et al. 2008; Sherman et al. 2009) a score of 3 and five RCTs (Espejo-Antunez et al. 2013a; Evcik et al. 2007; Mika et al. 2006; Sarsan et al. 2012; Tishler et al. 2004) scored 2.

Data synthesis and meta-analysis

Balneotherapy

Four eligible RCTs (Horvath et al. 2012; Kovacs et al. 2012; Kovacs and Bender 2002; Tishler et al. 2004) were not

Table 2 Number of included RCTs that overlapped among reviews

Numbers of included RCTs that overlapped among reviews																	
	Antonelli 2018 n= 17	Beasley 2018 n=3	Brosseau 2002 n=2	Crespin 2017 n=3	Espejo A 2012 n=6	Falagas 2009 n=5	Forestier 2016 n=18	Fortunati 2015 n=3	Fraioli 2018 n=6	Harzy 2009 n=7	Hou 2020 n=10	Kats 2012 n=1	Liu 2013 n=6	Matsumoto 2017 n=7	Tenti 2014 n=12	Verhagen 2007 n=3	Xiang 2016 n=9
Antonelli, 2018		1	-	3	4	1	10	1	2	2	8	1	4	5	8	-	7
Beasley 2018	1		-	-	-	-	-	2	-	-	1	-	-	-	-	-	-
Brosseau, 2002	-	-		-	-	2	2	1	-	1	-	-	-	-	-	1	-
Crespin, 2017	3	-	-		-	-	3	-	-	-	3	-	2	-	2	-	3
Espejo A.2012	4	-	-	-		-	4	-	3	1	4	-	3	2	4	-	5
Falagas 2009	1	-	2	-	-		4	1	1	4	-	-	-	2	2	2	-
Forestier 2016	10	-	2	3	4	4		1	6	7	8	1	5	6	12	3	8
Fortunati 2015	1	2	1	-	-	1	1		1	1	1	-	-	-	-	1	-
Fraioli 2018	2	-	-	-	3	1	6	1		3	2	-	1	2	5	2	3
Harzy 2009	2	-	1	-	1	4	7	1	3		1	-	1	4	5	3	1
Hou, 2020	8	1	-	3	4	-	8	1	2	1			5	2	5	-	8
Kats, 2012	1	.	-	-	-	-	1	-	-	-			-	1	1	-	-
Liu 2013	4	.	-	2	3	-	5	-	1	1	5	-		1	3	-	6
Matsumoto 2017	5	.	-	-	2	2	6	-	2	4	2	1	1		6	1	2
Tenti 2014	8	.	-	2	4	2	12	-	5	5	5	1	3	6		1	6
Verhagen, 2008	-	.	1	-	-	2	3	1	2	3	-	-	-	1	1		-
Xiang 2016	7	-	-	3	5	-	8	-	3	1	8	-	6	2	6	-	

Table 3 Quality assessment of included SR according AMSTAR 2

Author, year	Items							
	PICO elements	Protocol and deviation	Study selection	Search strategy	Appropriate study selection	Appropriate data extraction	List of exclusion	Included studies details
Antonelli et al. 2018	Y	N	Y	Y	Y	Y	N	Y
Beasley 2018	N	N	N	Y	Y	Y	N	Y
Brosseau et al. 2002	Y	PY	Y	Y	Y	Y	N	Y
Crespin 2017	Y	N	N	PY	Y	N	N	Y
Espejo-Antunez 2012	Y	N	N	Y	N	N	N	Y
Falagas et al. 2009	Y	N	Y	Y	Y	Y	N	Y
Forestier et al. 2016	Y	N	Y	Y	Y	Y	N	PY
Fortunati 2015	Y	N	Y	PY	N	Y	N	Y
Fraioli et al. 2018	N	N	N	N	Y	N	N	Y
Harzy et al. 2009	Y	N	Y	PY	N	N	N	Y
Hou et al. 2020	Y	N	Y	PY	Y	Y	N	Y
Katz et al. 2012	N	N	N	N	N	N	N	Y
Liu et al. 2013	Y	N	Y	N	N	Y	N	Y
Matsumoto et al. 2017	Y	Y	Y	Y	N	Y	N	Y
Tenti 2014	Y	N	Y	Y	N	N	N	Y
Verhagen et al. 2007	Y	N	Y	Y	NA	Y	Y	Y
Xiang et al. 2016	Y	N	Y	PY	Y	Y	N	PY

Author, year	Items								Overall rating
	Risk of bias	Funding	Appropriate meta-analysis	Impact of bias (results)	Impact of bias (discussion)	Heterogeneity	Risk of bias investigation	Conflict	
Antonelli et al. 2018	Y	N	Y	N	N	Y	N	Y	Critically low
Beasley 2018	Y	Y	NA	NA	N	NA	NA	Y	Critically low
Brosseau et al. 2002	Y	N	NA	NA	N	Y	NA	N	Critically low
Crespin 2017	Y	N	Y	Y	Y	Y	N	N	Critically low
Espejo-Antunez 2012	PY	N	NA	NA	Y	N	NA	N	Critically Low
Falagas et al. 2009	Y	N	NA	NA	Y	Y	NA	Y	Critically low
Forestier et al. 2016	Y	N	NA	NA	Y	Y	Y	Y	Critically low
Fortunati 2015	N	N	NA	NA	N	N	N	Y	Critically low
Fraioli et al. 2018	N	N	NA	NA	N	N	NA	Y	Critically low
Harzy et al. 2009	PY	N	NA	NA	N	Y	NA	N	Critically low
Hou et al. 2020	PY	N	Y	N	Y	Y	Y	N	Low
Katz et al. 2012	N	N	NA	NA	N	NA	NA	N	Critically low
Liu et al. 2013	Y	N	Y	N	N	N	Y	Y	Critically low
Matsumoto et al. 2017	Y	N	Y	Y	Y	Y	Y	N	Low
Tenti 2014	N	N	NA	NA	N	NA	NA	Y	Critically low
Verhagen et al. 2007	Y	N	NA	NA	Y	NA	NA	Y	Low
Xiang et al. 2016	Y	N	Y	Y	Y	Y	Y	Y	Critically low

Y, yes; *N*, no; *PY*, partial yes; *NA*, not applicable

AMSTAR2 items 2, 4, 9, 11, 13 and 15 are considered critical items that are believed to critically affect the validity of a review and its conclusion

Studies were judged: High: in presence of no or one non-critical item; moderate: with more than one non-critical items; low: in presence of one critical item with or without non-critical items; critically low: more than one critical item with or without non-critical items

included in the analysis due to a lack of data, seven RCTs were included in the analysis (Fig. 2).

Pain: Seven RCTs (499 participants) included in six reviews assessed the effect of balneotherapy on pain (Fig. 2 panel a). Their quality ranged from 2 to 5 (mean 3.7). The results of our meta-analysis indicate that, on average, balneotherapy reduced the pain score by 19.73 when compared with controls (MD = − 19.73; 95% CI − 35.72 to − 3.74; $p < 0.02$). There was a higher degree of statistical heterogeneity across studies ($I^2 = 99\%$; $p < 0.00001$). Funnel plot examination showed asymmetry, suggestive of publication bias in the context of four smaller studies in favour of controls.

Stiffness: Five RCTs (382 participants) included in six reviews addressed the effect of balneotherapy on stiffness (Fig. 2, panel b). Their quality ranged from 3 to 5 (mean 3.4). The results indicate that balneotherapy improved the clinical effective rate of relieving stiffness by 20.39 when compared with controls (MD = − 20.39; 95% CI − 38.21 to − 2.57; $p < 0.02$). There was a higher degree of late statistical heterogeneity across studies ($I^2 = 98\%$; $p = 0.00001$). Funnel plot examination showed the presence of symmetry between studies. Sensitivity analysis (Online source….) performed excluding the study by Branco et al. (Branco et al. 2016) did not find any significant differences (MD = − 20.39; CI − 38.21–2.57).

Quality of life: Three RCTs (281 participants) included in two SRs evaluated the effect of balneotherapy on quality of life (Fig. 2, panel c). Their quality ranged from 2 to 5 (mean 3.3). The results showed that balneotherapy improved quality of life by − 20.48 when compared with controls (MD = − 20.48; 95% CI − 32.44 to − 8.52; $p = 0.00008$). There was a higher degree of statistical heterogeneity across these studies ($I^2 = 90\%$; $p = 0.00001$).

Sensitivity analysis (Online source 6) performed excluding the study by Branco et al. (Branco et al. 2016) reproduced relatively similar point estimates with lower heterogeneity confirming the significant differences for pain (MD = − 20.39; 95% CI − 38.21 to 2.57) and stiffness (MD = − 7.7; 95% CI − 12.70 to − 1.35). Nevertheless, the sensitivity analysis showed a no longer significant effect of balneotherapy on quality of life (MD = − 1.55; 95% CI − 12.48 to 9.35).

Mud therapy

Eleven RCTs were included in the analysis (Fig. 3).

Pain: Eleven RCTs (693 participants), included in nine SRs, evaluated the effect of mud therapy on pain (Fig. 3, panel a). Their quality ranged from 2 to 5 (mean 3.1). The analysis showed slightly significant differences between the experimental group that received mud therapy and controls (MD = − 8.79; CI − 17.33 to − 0.25; $p = 0.04$), with high heterogeneity level ($I^2 = 87\%$). Funnel plot examination showed no publication bias.

Stiffness: Seven RCTs (380 participants), included in ten SRs, assessed mud therapy on stiffness (Fig. 3, panel b). Their quality ranged from 2 to 5 (mean 3.2). Results showed that mud therapy significantly reduced stiffness (MD = − 14.10; CI − 17.87 to 10.33; $p < 0.00001$) with moderate heterogeneity ($I^2 = 42\%$). There was no evidence of publication bias.

Quality of life: Four RCTs (238 participants), included in eight SRs, assessed mud therapy on quality of life (Fig. 3, panel c), but no statistically significant difference in quality of life was observed between groups (MD = − 0.71; CI − 15.07 to 13.64; $p = 0.92$). Their quality ranged from 2 to 5 (mean 3).

SPA therapy

One eligible RTC (Wigler et al. 1995) was excluded because of missing data.

Quality of life: Three RCTs (481 participants), included in six SRs, assessed the effect of spa therapy on pain relief (Fig. 4). Results showed that patients receiving spa therapy experienced less pain compared with a control group (MD = − 11.72; CI − 22.18 to − 1.26; $p = 0.03$), with substantial heterogeneity ($I^2 = 83\%$).

Narrative synthesis of NRS

Balneotherapy

Pain and quality of life: In the study by Gaal et al. (Gaal et al. 2008), included in one SR (Fraioli et al. 2018), the effects of balneotherapy on chronic musculoskeletal pain, functional capacity and quality of life in elderly patients with OA or chronic degenerative low back pain were analysed. The study population consisted of 81 patients (41 with OA) who underwent 15 balneotherapy sessions lasting 30 min and administered daily. A significant decrease in mean disease severity, rated by the patients on a visual analogue scale (VAS), and quality of life was observed during the period between the two initial visits ($p < 0.001$). Specifically, the VAS score was 68.53 mm (SD 10.6 mm) at visit 1, 15.63 mm (SD 7.98 mm) at visit 2 and 12.58 mm (SD 7.12 mm) at visit 3, while quality of life score was 216.93 (SD 61.17) at visit 1, 558.78 (SD 150.25) at visit 2 ($p < 0.001$) and 708.66 (SD 42.29) at visit 3.

Mud therapy

Pain: An NRS by Fraioli et al. (Fraioli et al. 2011), included in 4 SRs, established a comparison between an experimental group that received three full cycles of mud bath therapy (12 treatments) over 1 year, and a control group that continued with daily pharmacological treatment. The study population consisted of 61 patients with knee OA. After treatment, the mean value reported in the experimental group was

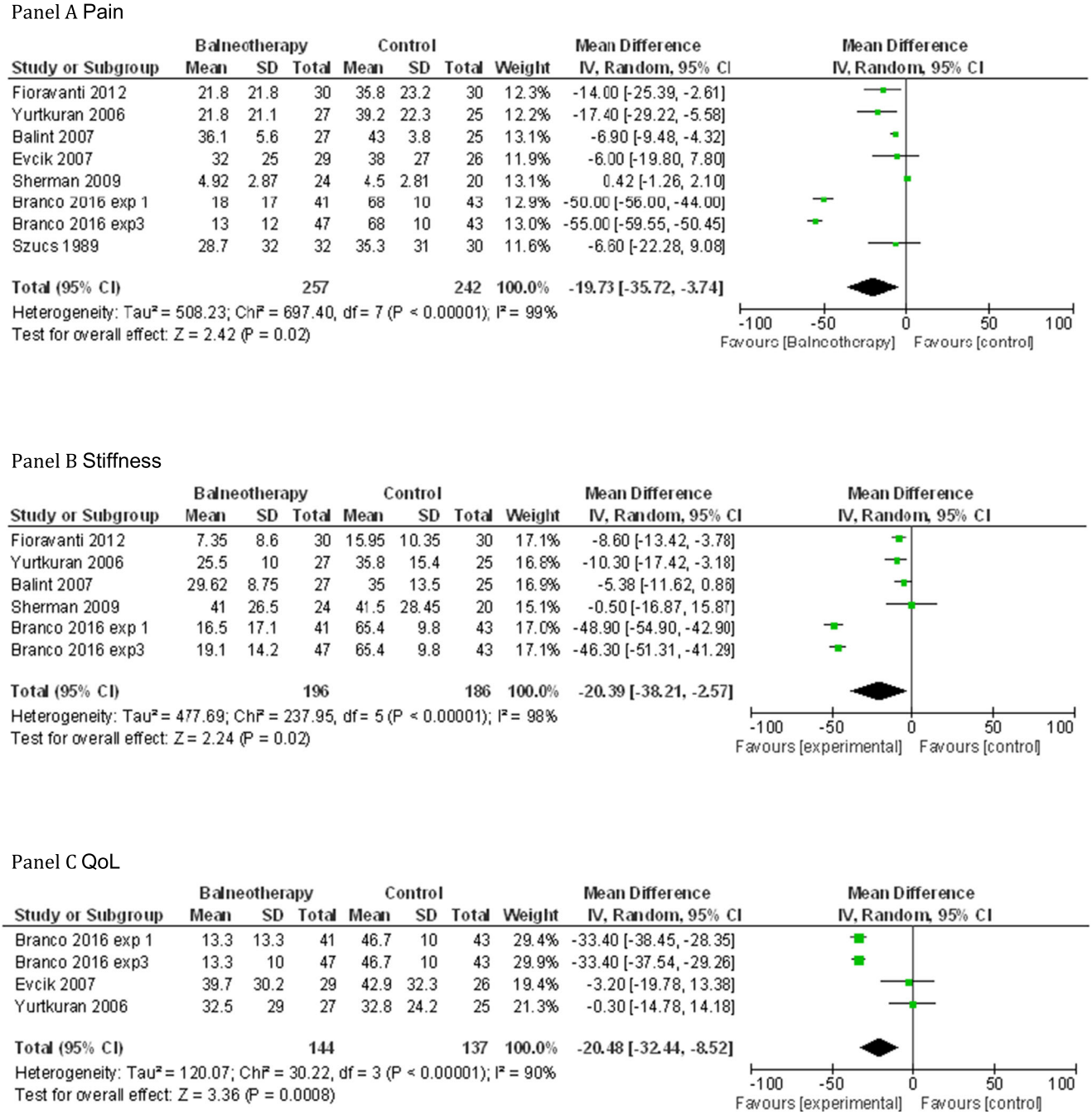


Fig. 2 The effect of balneotherapy on pain (panel **a**), stiffness (panel **b**) and QoL (panel **c**)

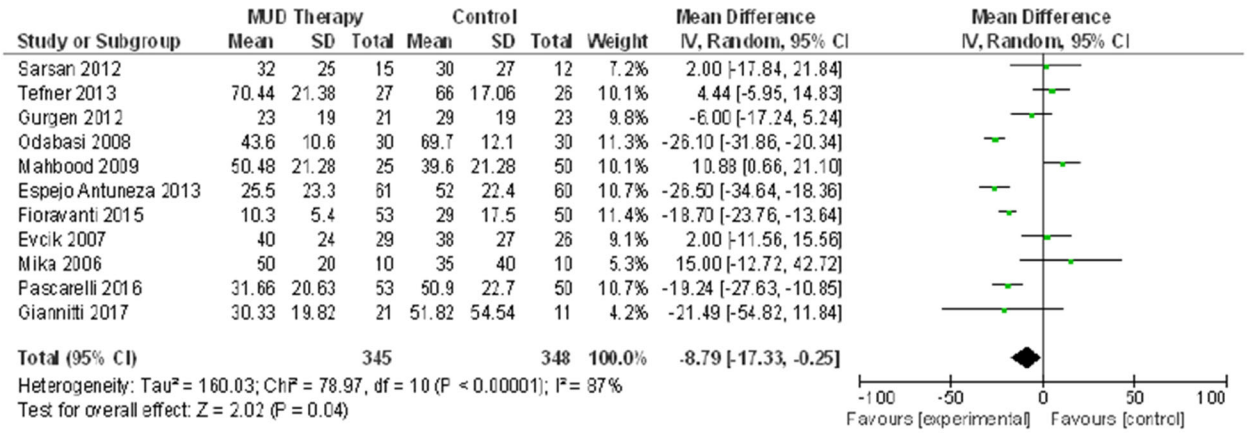
significantly lower than that reported in the control group (3.53 vs. 5.73), $p = 0.000$ (Student's t test).

Discussion

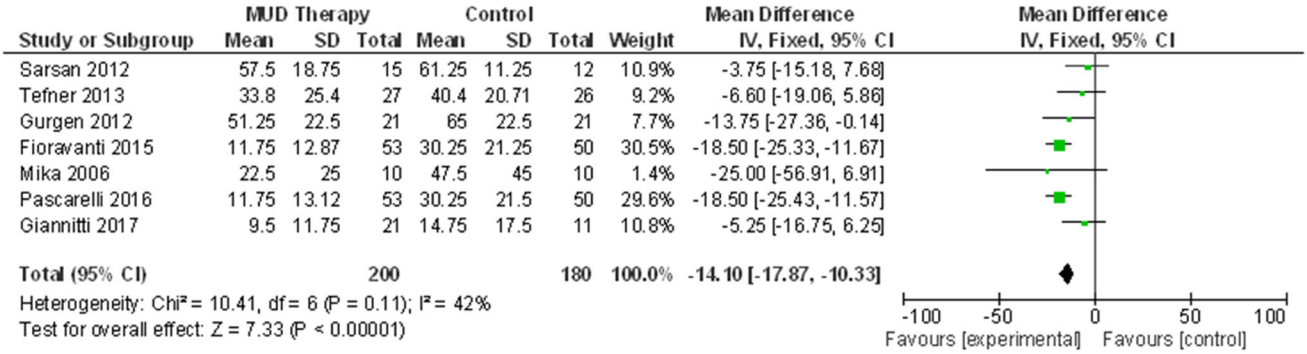
This overview represents a systematic, comprehensive and thorough review of the evidence supporting the efficacy of balneotherapy, mud therapy and spa therapy in patients with OA.

The SRs often categorised the interventions into the broad definition of 'thermal modalities' using the terms 'mud therapy', 'balneotherapy' and 'spa therapy' interchangeably and in connection with each other (Beasley et al. 2019; Falagas et al. 2009; Forestier et al. 2016; Fortunati et al. 2016; Fraioli et al. 2018; Harzy et al. 2009; Katz et al. 2012; Tenti et al. 2015). In fact, considerable heterogeneity was found in how the SRs classified the thermal modalities. The term 'balneotherapy', for instance, was used in both the broad (mineral/thermal water or mud bath/pack) and the strict sense (only mineral/

Panel A: Pain



Panel B: Stiffness



Panel C: QoL

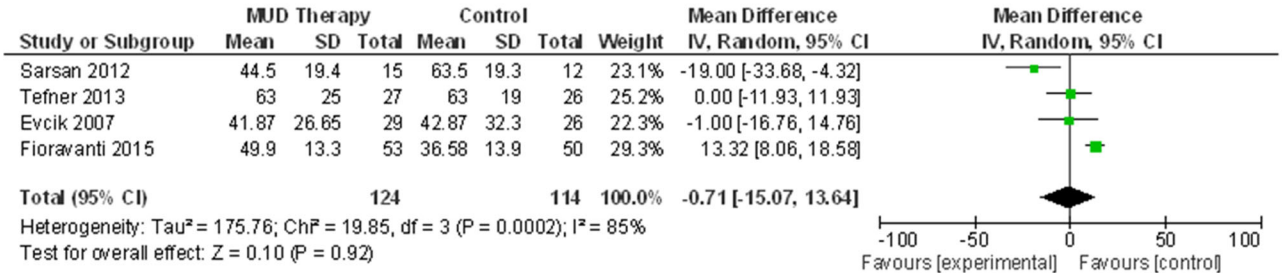


Fig. 3 The effect of mud therapy on pain (panel **a**), stiffness (panel **b**) and QoL (panel **c**)

thermal water), the term 'spa therapy' was employed to define a combination of interventions (mud pack, along with mineral bath and manual therapy), as well as a single treatment inside or outside a resort.

One implication was that the SRs that focussed on different interventions often included the same primary studies and, consequently, we encountered serious difficulties in producing the primary studies' classification. For example, the study by Fioravanti et al. (Fioravanti et al. 2010) on spa therapy had been included in SRs addressing balneotherapy (Matsumoto et al. 2017), mud therapy (Espejo-Antunez et al. 2013b; Fraioli et al. 2018; Xiang et al. 2016) and spa therapy (Forestier et al. 2016; Tenti et al. 2015), respectively. This fact resulted in a very high

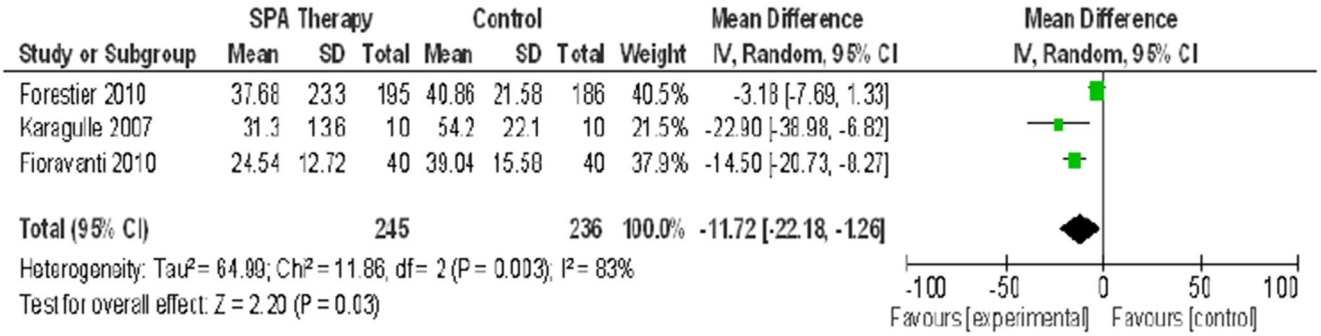


Fig. 4 The effect of SPA therapy on pain

level of overlap of primary studies among the 16 SRs and a possible misclassification.

Therefore, to improve our ability to address the research questions, we collected data directly from the primary studies originally reported by one or more of the 17 included SRs. In an attempt to reduce heterogeneity, the different thermal modalities were combined as specified in the 'methods' section of our review.

From a careful re-analysis of RCT data on balneotherapy, a significant reduction of pain and stiffness, and an improvement in quality of life emerged. Although the quality of the RCTs was rated as moderate, the high level of heterogeneity across the studies suggests that the pooled results of balneotherapy on the different outcomes should be interpreted with caution. As noted in other SRs (Matsumoto et al. 2017; Verhagen et al. 2007), we may reasonably believe that the high heterogeneity is a result of the small sample size in the considered RCTs, which were probably underpowered. Another reason for this finding may be that the specific scale indexes and specific measurement standards used in the various scales were inherently different. Furthermore, we should be aware that it is nearly impossible to maintain the exact content/ingredients of the mineral water across trials, as this depends on the country, area and specific location. Of note, sensitivity analysis yielded similar results with lower heterogeneity level for pain and stiffness, while showing no longer significant improvement in quality of life.

Data from RCTs on mud therapy showed a significant reduction in pain and stiffness with high/moderate heterogeneity, while the analysis of quality of life failed to show any significant beneficial effect. Worthy of note is that among the 5 RCTs on stiffness, only one RCT applied the double-blind design and all RCTs used a small number of subjects (ranging between 10 and 53 per branch). These factors may have contributed to an overestimate of the efficacy of therapies. It should be noted that each assessor used the same scale (WOMAC) to evaluate stiffness, thus reinforcing the importance of observing common and accepted outcome measures in order to limit heterogeneity in assessment contexts.

The summary measures on spa therapy showed significant pain relief, but high heterogeneity might impair the reliability of the results. The distinction between the effects of thermal applications per se and the benefits that could be derived from a stay in a spa environment is still debated (Bender et al. 2005; Falagas et al. 2009; Fioravanti et al. 2010).

Overall, the high level of heterogeneity in our results is consistent with the conclusions of other SRs (Antonelli et al. 2018; Matsumoto et al. 2017; Xiang et al. 2016). It highlights the need to consider different thermal modalities as separate entities (Bender et al. 2005) and to urge authors to keep them separate when planning interventions in order to make studies more comparable. Although we acknowledge that boundaries between these modalities may be blurred, it is crucial that organisations use some commonly accepted terminology and descriptions of content (Gutenbrunner et al. 2010).

Furthermore, as the quality of SRs ranged from low to very low, authors should improve SR quality by increasing the use of a priori protocols, and by providing a list of excluded studies with reasons for exclusion. They should also practise transparency in reporting the sources of funding of primary studies included in the review.

The included SRs had several methodological limitations that may have affected confidence in the reported results (Iannone et al. 2020). Heterogeneity of types and characteristics of interventions, even within the same thermal modality (balneotherapy, mud therapy or spa therapy), was the most significant problem that emerged from the present study. To mitigate this problem, we reanalysed data derived from primary studies that had previously been reported in the 17 SRs but that may not have reflected the entirety of the published literature. Furthermore, in some primary studies, the description of the interventions was too vague to provide sufficient understanding for appropriate classification. Even in cases in which the intervention was described in detail, both the duration (intensity and length) and modality used for its delivery varied considerably.

Finally, in an attempt to reduce variability, we decided to analyse only the short-term effect of different thermal modalities, even though the long-term effect is an important factor in determining continuing effectiveness and cost benefits.

Conclusion

Our overview of reviews provided an updated analysis of SRs focussing on different thermal modalities. Overall, there is some encouraging evidence that deserves clinicians' consideration, suggesting that thermal modalities are effective on a short-term basis for treating patients with AO.

However, the evidence supporting the efficacy of different thermal modalities is limited due to methodological quality and sample size, and to the presence of important treatment variations. The results of our meta-analysis, in particular, should be interpreted with caution, due mainly to the high level of heterogeneity and the absence of a double-blind design. That said, the difficulty in carrying out blind studies is widely known owing to the nature of such interventions.

Further high-quality RCTs are needed to help draw firm conclusions. Research should examine the effects of different thermal modalities while maintaining a clear distinction between them. When possible, the beneficial effect of spa therapy should be observed as a confounder or an effect modifier, and this should be considered in the study design.

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Declarations

Conflict of interest The authors declare no conflict of interest.

Ethics and consents Not applied to this study.

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