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BMJ Open Effects of non-pharmacological and non-surgical interventions on health outcomes in systemic sclerosis: protocol for a living systematic review

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ABSTRACT

Introduction Systemic sclerosis (SSc; scleroderma) is a rare, chronic, autoimmune disease with a high level of burden, a significant impact on the ability to carry out daily activities, and a considerable negative impact on health-related quality of life. Non-pharmacological interventions could be provided to potentially improve mental and physical health outcomes. However, the effectiveness of non-pharmacological interventions on health and well-being among individuals with SSc has not been well established. The proposed living systematic review aims to identify and evaluate randomised controlled trial (RCT) evidence on the effectiveness of non-pharmacological and non-surgical interventions on mental and physical health outcomes and on the delivery of such services in SSc.

Methods and analysis Eligible studies will be RCTs that examine non-pharmacological and non-surgical interventions aimed at improving health outcomes among individuals with SSc or the delivery of services intended to improve healthcare or support of people with SSc (eg, support groups). All RCTs included in a previous systematic review that sought studies published between 1990 and March 2014 will be evaluated for inclusion. Additional trials will be sought from January 2014 onwards using a similar, augmented search strategy developed by a health sciences librarian. We will search the MEDLINE, Embase, CINAHL, PsycINFO, Cochrane Library and Web of Science databases and will not restrict by language. Two independent reviewers will determine the eligibility of identified RCTs and will extract data using a prespecified standardised form in DistillerSR. Meta-analyses will be considered if ≥2 eligible RCTs report similar non-pharmacological interventions and comparable health outcomes. We will conduct a qualitative synthesis for interventions that cannot be synthesised via meta-analysis.

Ethics and dissemination We will post initial and ongoing results via a website, publish results periodically via peer-reviewed journal publication, and present results at patient-oriented events.

PROSPERO registration number CRD42020219914.

Strengths and limitations of this study

- Our living systematic review will be conducted using rigorous methods that comply with recommendations in the Cochrane Handbook for Systematic Reviews of Interventions and Cochrane guidance for living systematic reviews, will include a risk of bias assessment, and will be conducted with peer-reviewed searches developed by a research librarian.
- Our systematic review will only include randomised controlled trial (RCT) evidence in order to avoid sources of bias more common in non-randomised trials, particularly pre–post comparisons.
- Our systematic review team includes experts in a wide variety of disciplines and areas of knowledge relevant to non-pharmacological care and treatment in systemic sclerosis (SSc), as well as two patient collaborators with experience participating in research and providing first-hand insight into the needs of people with SSc.
- We will conduct a living systematic review; results will be continually updated as new evidence is published and will be distributed across well-established dissemination networks.
- Our search will seek eligible trials published from 2014 onwards to supplement RCTs identified by a previous systematic review, meaning it is possible, although unlikely, that studies published prior to 2014 may have been missed and will not be picked up by our searches.

INTRODUCTION

Systemic sclerosis (SSc; scleroderma) is a rare, chronic, autoimmune disease characterised by vasculopathy and excessive collagen production.¹ Onset typically occurs at around 50 years, and approximately 80% of people with SSc are women.^{1,2} SSc can affect multiple



organ systems, including the skin, lungs, gastrointestinal tract and heart. Common manifestations include Raynaud's phenomenon, skin thickening, dyspnoea and cough, gastro-oesophageal reflux and other gastrointestinal symptoms.^{1 2} Disease presentation is extremely heterogeneous, and the course of the disease is highly unpredictable.^{1 2} People with SSc commonly experience hand function and mobility limitations, pain, fatigue, sleep problems, pruritus, depression and body image distress from disfigurement (eg, skin tightening, pigment changes, hand contractures, telangiectasias).³⁻⁹ These symptoms often have a considerable negative impact on health-related quality of life.^{5 10 11} There is currently no cure for SSc. Non-pharmacological interventions (eg, psychological, educational and rehabilitation interventions) could potentially be used to improve quality of life.¹²

The effects of non-pharmacological and non-surgical interventions on health and well-being among individuals with SSc has not been well established. A previous systematic review¹³ of the effectiveness of non-pharmacological interventions in SSc identified 23 eligible studies published between 1990 and March 2014, of which 9 were randomised controlled trials (RCTs). Included RCTs evaluated a multifaceted oral health intervention, multidisciplinary team care, and a variety of rehabilitation strategies. They all included small numbers of participants (range 25–53 total participants; median 35), and risk of bias was high in most trials.

Two more recent systematic reviews have evaluated exercise therapies¹⁴ and dietary interventions.¹⁵ A 2019 review¹⁴ included nine studies on the safety and effectiveness of exercise therapies published between 1990 and 2019, of which four were RCTs. The four RCTs evaluated hand exercises, orofacial exercises and muscle strengthening exercises. The small numbers of participants included in trials (range 4–48 total participants) and generally high risk of bias across trials, however, made it difficult to draw conclusions. A 2019 review¹⁵ of dietary interventions for gastrointestinal symptoms in SSc included three studies, published between 2011 and 2017, but none were RCTs.

Since 2015, several larger, more robust RCTs on non-pharmacological interventions in SSc have been published, and others are in progress. Published RCTs include an evaluation of a personalised physical therapy programme (N=220),¹⁶ an internet-based self-management programme (N=247),¹⁷ a home-based exercise programme (N=44)¹⁸ and a comparison of two educational interventions in the rehabilitation of microstomia (N=63),¹⁹ for example. RCTs in progress with results expected in the next year include a web-based hand rehabilitation programme (N=466),²⁰ a support-group leader educational programme (N targeted=180),²¹ and a COVID-19 related mental health intervention (N targeted=162).²²

The proposed living systematic review aims to identify and evaluate RCT evidence on the effectiveness of

non-pharmacological and non-surgical interventions on health outcomes, including quality of life outcomes, and on the delivery of services in SSc. This will be accomplished via an initial systematic review followed by updates as new evidence is identified. The review will facilitate decisions on non-pharmacological healthcare options for people with SSc and will identify gaps in knowledge, which will facilitate planning of future research.

METHODS AND ANALYSIS

The living systematic review was registered in the PROSPERO prospective register of systematic reviews, and any future changes to the study protocol will be registered as amendments. The protocol was developed based on methodological guidance from the Cochrane Handbook for Systematic Reviews of Interventions and Cochrane guidance for living systematic reviews.^{23 24} The present protocol is reported according to Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols.²⁵ The systematic review will be reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement.²⁶ Initial searches were conducted on 30 November 2020, following registration and initial submission of this protocol for peer review. There is no planned end date.

Study eligibility

Eligible studies must be RCTs that examine non-pharmacological and non-surgical interventions aimed at improving health outcomes among individuals with SSc or the delivery of services intended to improve healthcare or support of people with SSc (eg, support groups). Non-randomised trials will be excluded, because of important limitations on the ability to draw conclusions about intervention effectiveness, particularly when done without a control group. This is because many patients seek psychological, educational or rehabilitation services when they are experiencing high levels of symptoms, and, on average, symptoms subside to some degree over the course of a trial, regardless of whether treatment is provided. For instance, in placebo groups in antidepressant trials and in usual care groups in depression psychotherapy trials, approximately 40% of patients with major depression remit.²⁷ Since the course of SSc is highly unpredictable, and since symptom severity fluctuates substantially, tests of interventions that use non-RCT designs, including pre–post designs, would be difficult to interpret and could generate potentially misleading results. RCTs address this problem by randomly allocating participants to trial arms.

Eligible trials must be conducted with participants with SSc, verified by clinical diagnosis or based on participant self-report. If an RCT includes some participants with SSc, but other participants who do not have SSc, it will be included only if results for those with SSc are reported separately or if at least 80% of participants have SSc.

Studies that report results from <10 participants per trial arm will be excluded.

Eligible interventions include, but are not limited to, physical or occupational therapy, rehabilitation, exercise, psychological, self-management, educational, diet or nutrition, nursing, podiatry, and oral or dental hygiene interventions. All pharmacological interventions, or interventions with a drug component, will be excluded. Interventions will be classified as having a drug component if any form of the active intervention ingredient was listed by the US Food and Drug Administration (FDA) in the Drugs@FDA database at the time of review. If not listed, investigators will consult other relevant sources to determine drug status. Use of probiotics will be included as a dietary or nutrition intervention if delivered as a food product similar to products that could be obtained outside of a medical intervention (eg, yoghurt). They will be excluded if they are products registered as a drug or delivered in pill format. Biologicals will be excluded, even if autologous (eg, skin grafting, stem cells), regardless of regulation status. Eligible intervention comparators will include: (1) any inactive control condition (eg, no treatment, waitlist control, usual care) or (2) another eligible intervention designed to improve health outcomes in SSc or to improve delivery of services. At least one measured outcome must pertain to physical or psychological health or to aspects of delivery of health or support services (eg, e-health, support groups).

Search strategy

We will include all eligible RCTs from a previous systematic review,¹³ which searched for trials published between 1990 and March 2014. Additional trials will be sought using a similar, augmented, search strategy from January 2014 to the present, developed and performed by a health sciences librarian and peer-reviewed²⁸ (see online supplemental file 1). Articles for review will be identified from the MEDLINE, Embase, CINAHL, PsycINFO, Cochrane Library and Web of Science databases. Searches will not be restricted by language or publication status. The previous review¹³ did not include trials on interventions to improve the delivery of health services or support services to individuals with SSc; however, since health services interventions have changed considerably in recent years, we will only consider delivery of services trials that have been published from January 2014 onwards.

In addition to database searches, we will manually review references from other relevant reviews, search clinical trial registries and query authors of included RCTs about unpublished trials. After the initial search, automated searches will be set for monthly updates to facilitate continual review and update.

Selection of eligible studies

The results of the initial search and subsequent searches will be into the systematic review software DistillerSR (Evidence Partners, Ottawa, Canada) where duplicate references will be identified and removed. A two-stage

process will be used to determine the eligibility of each publication, using a predefined inclusion and exclusion coding manual (see online supplemental file 2). Two independent investigators will review the titles and abstracts of the articles identified through the search strategy in random order. If either of the two reviewers deems an article to be potentially eligible for inclusion, a full-text review of the article will be completed independently by two reviewers. Any disagreements that may arise at the full-text level will be resolved by consensus, with a third reviewer consulted as necessary.

Data extraction

For each included RCT, one investigator will extract data using a prespecified standardised form in DistillerSR. A second reviewer will validate the extracted data using the DistillerSR Quality Control function. Reviewers will extract (1) publication characteristics (eg, first author last name, publication year, journal, funding source, author conflicts of interest); (2) population characteristics and demographics (eg, country, study eligibility criteria, recruitment method, number of participants, age, sex, type of SSc, disease duration, symptom thresholds); (3) intervention components (eg, descriptions of the intervention and comparator, number of participants randomised to intervention and control groups, number of participants analysed in both groups, intervention length, intervention setting (where delivered), number of sessions, length of sessions, qualifications of intervention providers, tailoring, modifications and fidelity adherence, as described by the Template for Intervention and Description and Replication Checklist²⁹ and (4) health or service provision outcomes. See online supplemental file 3 for variables to be extracted. Disagreements will be resolved by consensus, with a third investigator consulted as necessary.

Two reviewers will independently assess included studies for risk of bias using the revised cochrane risk of bias tool for randomised trials.³⁰ The tool includes five domains through which bias could be introduced; they are assessed and scored according to whether study characteristics reflect low, high or some concerns regarding risk of bias. Domains include (1) risk of bias due to the randomisation process; (2) deviations from the intended intervention; (3) missing outcome data; (4) outcome measurement and (5) selection of the reported result. Disagreements will be resolved by consensus, and a third investigator will be consulted as necessary.

Data analysis

Meta-analyses will be considered if ≥ 2 eligible RCTs report similar non-pharmacological interventions and comparable health outcomes and if the trials are of sufficiently high general quality to draw conclusions, based on judgements about risk of bias, sample size and risk of publication bias. RCTs that are not meta-analysed will be described qualitatively. When studies are synthesised meta-analytically, data will be pooled using the

DerSimonian Laird random effects model.³¹ For dichotomous outcomes, we will report relative risks between groups with 95% CIs. For continuous outcomes, Hedges' *g* will be used to calculate standardised mean differences for continuous outcomes.³² We will prioritise postintervention comparisons adjusted for baseline values, then unadjusted comparisons, followed by comparisons of change scores. If multiple measures are used to assess the same outcome in a study, effect sizes from all relevant measures will be synthesised within the study before being entered into the meta-analysis. If we are not able to use a study's data in a meta-analysis because, for instance, only *p* values are reported, we will begin by querying the authors for the relevant results. If the full results are not able to be obtained, we will present what was provided in publications in tables. The *I*² statistic will be used to assess the heterogeneity of included trials.³³ Publication bias will be examined using funnel plots if there are at least 10 studies included for a given intervention.

Patient and public involvement

The research team includes people with SSc who are actively involved as members of the Scleroderma Patient-centered Intervention Network Patient (SPIN) Advisory Board. They have provided input on the protocol and study design and will be involved in review, interpretation and dissemination of results.

ETHICS AND DISSEMINATION

Ethics approval was not required for this systematic review because we will be including only published aggregate data.

To disseminate results, we will post initial and ongoing results via a website (<https://www.spinsclero.com/en/projects/non-pharm-interventions>) and publish results periodically via peer-reviewed journal publications. Updated results will be updated to the website as soon as new trials are identified. We will submit updated results from journal publication when the author team identifies that there are substantive changes in the evidence base. We will further disseminate results to the international scleroderma patient community through the SPIN social media accounts and by distribution of announcements to SPIN's patient organisation partners. Systematic review team members present regularly at national and international scleroderma patient congresses, and we plan to disseminate results at those congresses.

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Provenance and peer review Not commissioned; externally peer reviewed.

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Supplementary File 1. Search strategies**Ovid MEDLINE(R) ALL**

1 exp Nutrition Therapy/
2 exp Diet/
3 diet therapy.fs.
4 exp Dietary Supplements/
5 (nutrition or diet or dietary or nutritional or probiotic*).tw,kf.
6 1 or 2 or 3 or 4 or 5
7 (physical therap* or physiotherap* or physio therap*).ti,ab,kf.
8 Physical Therapists/ or Physical Therapy Modalities/
9 Physical Therapy Specialty/
10 occupational therap*.ti,ab,kf.
11 exp Physical Therapy Modalities/
12 Occupational Therapy/
13 exp balneology/ or Massage/ or Hyperthermia, Induced/ or baths/ or vocational
rehabilitation/ or recreation therapy/ or splints/ or orthotic devices/ or energy metabolism/
or podiatry/ or cryotherapy/
14 (hydrotherapy or balneology or balneotherapy or massage* or skin mobilization or
thermotherapy or induced hyperthermia or paraffin wax or wax bath* or recreation
therapy or splint* or orthotic* or joint protection or activity pacing or energy
conservation or podiatr* or foot care or cryotherap*).tw,kf.
15 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14
16 exp Adaptation, Psychological/
17 exp Psychotherapy/
18 exp Counseling/
19 "Self-Help Groups"/
20 "Social Support"/
21 Patient Education as Topic/ or "Early intervention (education)"/
22 ((non-surgical or psychological or behavio*r or behavio*ral or cognitive or psychosocial
or psycho-social or psychoeducation*) adj3 (intervention* or treatment* or therap* or
program* or modification)).tw,kf.
23 (Coping adj (skill* or behavio?r*)).tw,kf.
24 Mindfulness.tw,kf. or mindfulness/
25 Patient education.tw,kf.
26 (group therapy or support group* or self help group*).tw,kf.
27 ((peer or psychosocial or social or patient) adj support).tw,kf.
28 (Psychotherapy or psychotherapies or CBT).tw,kf.
29 counsel*ing.tw,kf.
30 self-management.tw,kf.
31 psychoeducation.tw,kf.
32 exp health education/ or self care/ or self management/ or Self-Help Devices/
33 (assistive technolog* or assistive device* or education* or health literacy or health
information or self care or Self-Help Device*).tw,kf.
34 or/16-33

- 35 telemedicine/ or telerehabilitation/ or remote consultation/ or cell phone/ or text
messaging/
36 ((mobile adj1 (health or rehabilitation)) or tele health or telehealth or telemedicine or e-
health or ehealth or m-health or mhealth or mobile based or (virtual adj1 (medicine or
rehabilitation)) or ((remote or distance) adj1 (medicine or rehabilitation or consultation))
or videoconferenc* or video conferenc* or tele conferenc* or teleconferenc* or tele
education or tele-education or telementoring or tele-mentoring or tele-care or telecare or
live video*).tw,kf.
37 (cell phone* or text messag*).tw,kf.
38 35 or 36 or 37
39 Dental Health Services/ or Oral Health/ or Oral Hygiene/ or dental care/ or dental care for
chronically ill/ or dental care for disabled/
40 ((Oral or dental or periodontal or Gingival) adj2 (rehabilitation or health or pathology or
hygiene or care or therap* or treatment* or activit* or exercise* or disease*).tw,kf.
41 39 or 40
42 exp Exercise/ or exp Exercise Therapy/ or physical endurance/ or sports/ or motor
activity/ or physical fitness/
43 (exercis* or stretching or resistance training or strength training or running or jogging or
swimming or walking or physical endurance or sports or sport or physical activity or
treadmill* or bicycling or cycling or physical conditioning or muscle strength*).tw,kf.
44 42 or 43
45 ((non pharmacological or nonpharmacological or multidisciplinary or multicomponent or
interdisciplinary or multimodal) adj (treatment or intervention or therap* or
management)).tw,kf.
46 *Rehabilitation/ or rehabilitation.fs. or rehabilitation.tw,kf.
47 45 or 46
48 Acupuncture Therapy/ or Cupping Therapy/ or Dry Needling/ or Bioresonance Therapy/
or Homeopathy/ or Medicine, Traditional/ or exp Mind-Body Therapies/ or exp
Musculoskeletal Manipulations/ or Naturopathy/ or Prolotherapy/ or Reflexotherapy/ or
exp Sensory Art Therapies/ or Spiritual Therapies/ or exp phototherapy/ or laser therapy/
49 (Acupuncture or Cupping or Dry Needling or Bioresonance or Homeopath* or
Traditional medicine or Mind-Body Therap* or Aromatherap* or Biofeedback or
Breathing or Hypnosis or Imagery or Laughter Therap* or Meditation or Mental Healing
or Psychodrama or Psychophysiology or Relaxation Therap* or Tai Ji or Tai chi or
Therapeutic Touch* or Yoga or Musculoskeletal Manipulation* or applied Kinesiology
or Chiropractic or Osteopathic or Soft Tissue therap* or Naturopath* or Prolotherap* or
Reflexotherap* or Sensory Art Therap* or Acoustic Stimulation or Art Therap* or Color
Therap* or Dance Therap* or Music Therap* or Play Therap* or Spiritual Therap* or
Relaxation Technique* or reflexolog* or phototherap* or light therap* or laser*).tw,kf.
50 ((Alternative or Complementary) adj2 (medicine or therap* or treatment*).tw,kf. 61064
51 48 or 49
52 6 or 15 or 34 or 38 or 41 or 44 or 47 or 51
53 exp Scleroderma, Systemic/ or (scleroderma* or systemic sclerosis or CREST
syndrome*).ti,ab,kf.
54 52 and 53
55 randomized controlled trial.pt.

- 56 controlled clinical trial.pt.
- 57 randomi?ed.ab.
- 58 placebo.ab.
- 59 drug therapy.fs.
- 60 randomly.ab.
- 61 trial.ab.
- 62 groups.ab.
- 63 or/55-62
- 64 exp animals/ not humans.sh.
- 65 63 not 64
- 66 54 and 65

EMBASE

- 1 exp *diet therapy/
- 2 exp *diet/
- 3 *dietary supplement/
- 4 (nutrition or diet or dietary or nutritional or probiotic*).tw,kw.
- 5 1 or 2 or 3 or 4
- 6 exp *physiotherapy/
- 7 *physiotherapist/
- 8 *occupational therapy/
- 9 occupational therap*.tw,kw.
- 10 (physical therap* or physiotherap* or physio therap*).tw,kw.
- 11 exp *balneotherapy/
- 12 exp *massage/
- 13 exp *bath/
- 14 *vocational rehabilitation/
- 15 *recreational therapy/
- 16 exp *splint/
- 17 exp *orthosis/
- 18 *energy conservation/
- 19 *podiatry/
- 20 *cryotherapy/
- 21 exp *thermotherapy/
- 22 *induced hypothermia/
- 23 *foot care/
- 24 or/6-23
- 25 *coping behavior/ or *meaning-making/ or *stress management/
- 26 exp *psychotherapy/
- 27 exp *counseling/

- 28 exp *self help/
29 *social support/
30 *patient education/
((non-surgical or psychological or behavior* or behavior* or cognitive or psychosocial or
31 psycho-social or psychoeducation*) adj3 (intervention* or treatment* or therap* or
program* or modification)).tw,kw.
32 (Coping adj (skill* or behavior?r*)).tw,kw.
33 exp *mindfulness/
34 (Patient education or mindfulness).tw,kw.
35 (group therapy or support group* or self help group*).tw,kw.
36 ((peer or psychosocial or social or patient) adj support).tw,kw.
37 (Psychotherapy or psychotherapies or CBT).tw,kw.
38 counsel*ing.tw,kw.
39 self-management.tw,kw.
40 psychoeducation.tw,kw.
41 exp *health education/
42 *self care/
43 *self help device/
44 (assistive technolog* or assistive device* or education* or health literacy or health
information or self care or Self-Help Device*).tw,kw.
45 or/25-44
46 exp *telemedicine/
47 exp *mobile phone/
48 *text messaging/
((mobile adj1 (health or rehabilitation)) or tele health or telehealth or telemedicine or e-
health or ehealth or m-health or mhealth or mobile based or (virtual adj1 (medicine or
49 rehabilitation)) or ((remote or distance) adj1 (medicine or rehabilitation or consultation)) or
videoconferenc* or video conferenc* or tele conferenc* or teleconferenc* or tele education
or tele-education or telementoring or tele-mentoring or tele-care or telecare or live
video*).tw,kw.
50 (cell phone* or text messag*).tw,kw.
51 or/46-50
52 *dental procedure/
53 *mouth hygiene/
54 ((Oral or dental or periodontal or Gingival) adj2 (rehabilitation or health or pathology or
hygiene or care or therap* or treatment* or activit* or exercise* or disease*)).tw,kw.
55 or/52-54
56 exp *exercise/
57 exp *kinesiotherapy/
58 exp *sport/

59 exp *motor activity/
60 *fitness/
(exercis* or stretching or resistance training or strength training or running or jogging or
61 swimming or walking or physical endurance or sports or sport or physical activity or
treadmill* or bicycling or cycling or physical conditioning or muscle strength*).tw,kw.
62 or/56-61
((non pharmacological or nonpharmacological or multidisciplinary or multicomponent or
63 interdisciplinary or multimodal) adj (treatment or intervention or therap* or
management)).tw,kw.
64 *Rehabilitation/
65 rehabilitation.fs.
66 rehabilitation.tw,kw.
((non pharmacological or nonpharmacological or multidisciplinary or multicomponent or
67 interdisciplinary or multimodal) adj (treatment or intervention or therap* or
management)).tw,kw.
68 or/63-67
69 exp *acupuncture/
70 *alternative medicine/ or *bioresonance therapy/ or *cupping therapy/ or dry needling/ or
*homeopathy/ or *naturopathy/ or *prolotherapy/
71 exp *musculoskeletal manipulation/
72 *art therapy/
73 *spiritual healing/
74 exp *phototherapy/
(Acupuncture or Cupping or Dry Needling or Bioresonance or Homeopath* or Traditional
medicine or Mind-Body Therap* or Aromatherap* or Biofeedback or Breathing or
Hypnosis or Imagery or Laughter Therap* or Meditation or Mental Healing or
Psychodrama or Psychophysiology or Relaxation Therap* or Tai Ji or Tai chi or
75 Therapeutic Touch* or Yoga or Musculoskeletal Manipulation* or applied Kinesiology or
Chiropractic or Osteopathic or Soft Tissue therap* or Naturopath* or Prolotherap* or
Reflexotherap* or Sensory Art Therap* or Acoustic Stimulation or Art Therap* or Color
Therap* or Dance Therap* or Music Therap* or Play Therap* or Spiritual Therap* or
Relaxation Technique* or reflexolog* or phototherap* or light therap* or laser*).tw,kw.
76 ((Alternative or Complementary) adj2 (medicine or therap* or treatment*)).tw,kw.
77 or/69-76
78 5 or 24 or 45 or 51 or 62 or 68 or 77
79 exp *scleroderma/
80 (scleroderma* or systemic sclerosis or CREST syndrome*).tw,kw.
81 79 or 80
82 78 and 81
83 "randomized controlled trial (topic)"/
84 Randomized Controlled Trial/

85 Randomization/
86 Double Blind Procedure/
87 single blind procedure/
88 placebo/
89 (random* or sham or placebo*).ti,ab,hw.
90 ((singl* or doubl*) adj (blind* or dumm* or mask*)).ti,ab,hw.
91 ((trip1* or trebl*) adj (blind* or dumm* or mask*)).ti,ab,hw.
92 or/83-91
93 82 and 92
 (201403* or 201404* or 201405* or 201406* or 201407* or 201408* or 201409* or
94 201410* or 201411* or 201412* or 2015* or 2016* or 2017* or 2018* or 2019* or
 2020*).dc.
95 93 and 94

PsycInfo

1 Nutrition/
2 exp dietary supplements/
3 Diets/
4 (nutrition or diet or dietary or nutritional or probiotic*).tw,id.
5 1 or 2 or 3 or 4
6 physical therapy/
7 (physical therap* or physiotherap* or physio therap*).tw,id.
8 occupational therapy/
9 occupational therap*.tw,id.
10 Massage/
11 vocational rehabilitation/ or disability management/ or rehabilitation counseling/
12 recreation therapy/ or creative arts therapy/ or exp adventure therapy/ or art therapy/ or
 dance therapy/ or horticulture therapy/ or movement therapy/ or music therapy/
 (hydrotherapy or balneology or balneotherapy or massage* or skin mobilization or
13 thermotherapy or induced hyperthermia or paraffin wax or wax bath* or recreation therapy
 or splint* or orthotic* or joint protection or activity pacing or energy conservation or
 podiatr* or foot care or cryotherap*).tw,id.
14 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13
15 coping behavior/ or emotional adjustment/
16 exp psychotherapy/
17 exp counseling/
18 exp Support Groups/ or exp Self-Help Techniques/
19 exp Social Support/
20 client education/

- 21 mindfulness/ or mindfulness-based interventions/
((non-surgical or psychological or behavio*r or behavio*ral or cognitive or psychosocial or
22 psycho-social or psychoeducation*) adj3 (intervention* or treatment* or therap* or
program* or modification)).tw,id.
23 (Coping adj (skill* or behavio?r*)).tw,id.
24 Mindfulness.tw,id.
25 Patient education.tw,id.
26 (group therapy or support group* or self help group*).tw,id.
27 ((peer or psychosocial or social or patient) adj support).tw,id.
28 (Psychotherapy or psychotherapies or CBT).tw,id.
29 counsel*ing.tw,id.
30 self-management.tw,id.
31 psychoeducation.tw,id.
32 health education/
33 (assistive technolog* or assistive device* or education* or health literacy or health
information or self care or Self-Help Device*).tw,id.
34 assistive technology/ or medical therapeutic devices/
35 or/15-34
36 exp telemedicine/
37 exp mobile phones/ or text messaging/
((mobile adj1 (health or rehabilitation)) or tele health or telehealth or telemedicine or e-
health or ehealth or m-health or mhealth or mobile based or (virtual adj1 (medicine or
38 rehabilitation)) or ((remote or distance) adj1 (medicine or rehabilitation or consultation)) or
videoconferenc* or video conferenc* or tele conferenc* or teleconferenc* or tele education
or tele-education or telementoring or tele-mentoring or tele-care or telecare or live
video*).tw,id.
39 (cell phone* or text messag*).tw,id.
40 36 or 37 or 38 or 39
41 exp Oral Health/
42 exp Dental Treatment/
43 exp Dental Health/
44 ((Oral or dental or periodontal or Gingival) adj2 (rehabilitation or health or pathology or
hygiene or care or therap* or treatment* or activit* or exercise* or disease*)).tw,id.
45 41 or 42 or 43 or 44
46 exp exercise/
47 exp Physical Endurance/
48 exp Sports/
49 exp Physical Fitness/

- (exercis* or stretching or resistance training or strength training or running or jogging or
 50 swimming or walking or physical endurance or sports or sport or physical activity or
 treadmill* or bicycling or cycling or physical conditioning or muscle strength*).tw,id.
 51 46 or 47 or 48 or 49 or 50
 52 rehabilitation/ or cognitive rehabilitation/ or psychosocial rehabilitation/
 (((non pharmacological or nonpharmacological or multidisciplinary or multicomponent or
 53 interdisciplinary or multimodal) adj (treatment or intervention or therap* or management))
 or rehabilitation).tw,id.
 54 52 or 53
 55 alternative medicine/ or acupuncture/ or faith healing/
 56 exp Phototherapy/
 57 exp Laser Irradiation/
 58 mind body therapy/
 59 exp Yoga/
 (Acupuncture or Cupping or Dry Needling or Bioresonance or Homeopath* or Traditional
 medicine or Mind-Body Therap* or Aromatherap* or Biofeedback or Breathing or
 Hypnosis or Imagery or Laughter Therap* or Meditation or Mental Healing or
 Psychodrama or Psychophysiology or Relaxation Therap* or Tai Ji or Tai chi or
 60 Therapeutic Touch* or Yoga or Musculoskeletal Manipulation* or applied Kinesiology or
 Chiropractic or Osteopathic or Soft Tissue therap* or Naturopath* or Prolotherap* or
 Reflexotherap* or Sensory Art Therap* or Acoustic Stimulation or Art Therap* or Color
 Therap* or Dance Therap* or Music Therap* or Play Therap* or Spiritual Therap* or
 Relaxation Technique* or reflexolog* or phototherap* or light therap* or laser*).tw,id.
 61 ((Alternative or Complementary) adj2 (medicine or therap* or treatment*)).tw,id.
 62 or/55-61
 63 (scleroderma* or systemic sclerosis or CREST syndrome*).tw,id.
 64 skin disorders/
 65 "Sclerosis (Nervous System)"/
 66 63 or 64 or 65
 67 14 or 35 or 40 or 45 or 51 or 54 or 62
 68 66 and 67
 (201403* or 201404* or 201405* or 201406* or 201407* or 201408* or 201409* or
 69 201410* or 201411* or 201412* or 2015* or 2016* or 2017* or 2018* or 2019* or
 2020*).up.
 70 68 and 69

CINAHL

Search ID#	Search Terms
S89	S87 AND S88

S88	EM 20140301-2020*
S87	S74 AND S86
S86	S75 OR S76 OR S77 OR S78 OR S79 OR S80 OR S81 OR S82 OR S83 OR S84 OR S85
S85	TX allocat* random*
S84	(MH "Quantitative Studies")
S83	(MH "Placebos")
S82	TX placebo*
S81	TX random* allocat*
S80	(MH "Random Assignment")
S79	TX randomi* control* trial*
S78	S4 TX ((singl* n1 blind*) or (singl* n1 mask*)) or TX ((doubl* n1 blind*) or (doubl* n1 mask*)) or TX ((tripl* n1 blind*) or (tripl* n1 mask*)) or TX ((trebl* n1 blind*) or (trebl* n1 mask*))
S77	TX clinic* n1 trial*
S76	PT Clinical trial
S75	(MH "Clinical Trials+")
S74	S72 AND S73
S73	S6 OR S18 OR S36 OR S42 OR S47 OR S54 OR S58 OR S69
S72	S70 OR S71
S71	TI ((scleroderma* or systemic sclerosis or CREST syndrome*)) OR AB ((scleroderma* or systemic sclerosis or CREST syndrome*))
S70	(MH "Scleroderma, Systemic+")
S69	S59 OR S60 OR S61 OR S62 OR S63 OR S64 OR S65 OR S66 OR S67 OR S68
S68	TI (((Alternative or Complementary) N2 (medicine or therap* or treatment*))) OR AB (((Alternative or Complementary) N2 (medicine or therap* or treatment*)))
S67	TI ((Acupuncture or Cupping or Dry Needling or Bioresonance or Homeopath* or Traditional medicine or Mind-Body Therap* or Aromatherap* or Biofeedback or Breathing or Hypnosis or Imagery or Laughter Therap* or Meditation or Mental Healing or Psychodrama or Psychophysiology or Relaxation Therap* or Tai Ji or Tai chi or Therapeutic Touch* or Yoga or Musculoskeletal

	Manipulation* or applied Kinesiology or Chiropractic or Osteopathic or Soft Tissue therap* or Naturopath* or Prolotherap* or Reflexotherap* or Sensory Art Therap* or Acoustic Stimulation or Art Therap* or Color Therap* or Dance Therap* or Music Therap* or Play Therap* or Spiritual Therap* or Relaxation Technique* or reflexolog* or phototherap* or light therap* or laser*)) OR AB ((Acupuncture or Cupping or Dry Needling or Bioresonance or Homeopath* or Traditional medicine or Mind-Body Therap* or Aromatherap* or Biofeedback or Breathing or Hypnosis or Imagery or Laughter Therap* or Meditation or Mental Healing or Psychodrama or Psychophysiology or Relaxation Therap* or Tai Ji or Tai chi or Therapeutic Touch* or Yoga or Musculoskeletal Manipulation* or applied Kinesiology or Chiropractic or Osteopathic or Soft Tissue therap* or Naturopath* or Prolotherap* or Reflexotherap* or Sensory Art Therap* or Acoustic Stimulation or Art Therap* or Color Therap* or Dance Therap* or Music Therap* or Play Therap* or Spiritual Therap* or Relaxation Technique* or reflexolog* or phototherap* or light therap* or laser*))
S66	(MH "Laser Therapy+")
S65	(MH "Phototherapy+")
S64	(MH "Prolotherapy")
S63	(MH "Manual Therapy")
S62	(MH "Mind Body Techniques+")
S61	(MH "Dry Needling")
S60	(MH "Cupping Therapy")
S59	(MH "Acupuncture") OR (MH "Homeopathy") OR (MH "Medicine, Traditional") OR (MH "Naturopathy") OR (MH "Alternative Therapies")
S58	S55 OR S56 OR S57
S57	TI rehabilitation OR AB rehabilitation
S56	MW "RH"
S55	TI (((non pharmacological or nonpharmacological or multidisciplinary or multicomponent or interdisciplinary or multimodal) N1 (treatment or intervention or therap* or management))) OR AB (((non pharmacological or nonpharmacological or multidisciplinary or multicomponent or interdisciplinary or multimodal) N1 (treatment or intervention or therap* or management)))
S54	S48 OR S49 OR S50 OR S51 OR S52 OR S53

S53	TI ((exercis* or stretching or resistance training or strength training or running or jogging or swimming or walking or physical endurance or sports or sport or physical activity or treadmill* or bicycling or cycling or physical conditioning or muscle strength*)) OR AB ((exercis* or stretching or resistance training or strength training or running or jogging or swimming or walking or physical endurance or sports or sport or physical activity or treadmill* or bicycling or cycling or physical conditioning or muscle strength*))
S52	(MH "Physical Fitness+")
S51	(MH "Motor Activity+")
S50	(MH "Sports+")
S49	(MH "Physical Endurance+")
S48	(MH "Exercise+") OR (MH "Therapeutic Exercise+")
S47	S43 OR S44 OR S45 OR S46
S46	TI (((Oral or dental or periodontal or Gingival) N2 (rehabilitation or health or pathology or hygiene or care or therap* or treatment* or activit* or exercise* or disease*))) OR AB (((Oral or dental or periodontal or Gingival) N2 (rehabilitation or health or pathology or hygiene or care or therap* or treatment* or activit* or exercise* or disease*)))
S45	(MH "Oral Hygiene")
S44	(MH "Oral Health")
S43	(MH "Dental Health Services+")
S42	S37 OR S38 OR S39 OR S40 OR S41
S41	TI ((cell phone* or text messag*)) OR AB ((cell phone* or text messag*))
S40	TI (((mobile N1 (health or rehabilitation)) or tele health or telehealth or telemedicine or e-health or ehealth or m-health or mhealth or mobile based or (virtual N1 (medicine or rehabilitation)) or ((remote or distance) N1 (medicine or rehabilitation or consultation)) or videoconferenc* or video conferenc* or tele conferenc* or teleconferenc* or tele education or tele-education or telementoring or tele-mentoring or tele-care or telecare or live video*)) OR AB (((mobile N1 (health or rehabilitation)) or tele health or telehealth or telemedicine or e-health or ehealth or m-health or mhealth or mobile based or (virtual N1 (medicine or rehabilitation)) or ((remote or distance) N1 (medicine or rehabilitation or consultation)) or videoconferenc* or video conferenc* or tele conferenc* or

	teleconferenc* or tele education or tele-education or telementoring or tele-mentoring or tele-care or telecare or live video*))
S39	(MH "Cellular Phone+")
S38	(MH "Remote Consultation")
S37	(MH "Telehealth+")
S36	S19 OR S20 OR S21 OR S22 OR S23 OR S24 OR S25 OR S26 OR S27 OR S28 OR S29 OR S30 OR S31 OR S32 OR S33 OR S34 OR S35
S35	(MH "Assistive Technology Devices+")
S34	(MH "Self Care") OR (MH "Self-Management")
S33	(MH "Health Education")
S32	TI ((assistive technolog* or assistive device* or education* or health literacy or health information or self care or Self-Help Device*)) OR AB ((assistive technolog* or assistive device* or education* or health literacy or health information or self care or Self-Help Device*))
S31	TI ((Psychotherapy or psychotherapies or CBT or counsel*ing or self-management or psychoeducation)) OR AB ((Psychotherapy or psychotherapies or CBT or counsel*ing or self-management or psychoeducation))
S30	TI (((peer or psychosocial or social or patient) N1 support)) OR AB (((peer or psychosocial or social or patient) N1 support))
S29	TI ((group therapy or support group* or self help group*)) OR AB ((group therapy or support group* or self help group*))
S28	TI (Patient education or mindfulness) OR AB (Patient education or Mindfulness)
S27	(MH "Mindfulness")
S26	TI ((Coping N1 (skill* or behavio?r*))) OR AB ((Coping N1 (skill* or behavio?r*)))
S25	TI ((Coping N (skill* or behavio?r*))) OR AB ((Coping N (skill* or behavio?r*)))
S24	TI (((non-surgical or psychological or behavio*r or behavio*ral or cognitive or psychosocial or psycho-social or psychoeducation*) N3 (intervention* or treatment* or therap* or program* or modification))) OR AB (((non-surgical or psychological or behavio*r or behavio*ral or cognitive or psychosocial or psycho-social or

	psychoeducation*) N3 (intervention* or treatment* or therap* or program* or modification)))
S23	(MH "Patient Education+")
S22	(MH "Support Groups+")
S21	(MH "Counseling+")
S20	(MH "Psychotherapy+")
S19	(MH "Adaptation, Psychological+")
S18	S7 OR S8 OR S9 OR S10 OR S11 OR S12 OR S13 OR S14 OR S15 OR S16 OR S17
S17	TI (hydrotherapy or balneology or balneotherapy or massage* or skin mobilization or thermotherapy or induced hyperthermia or paraffin wax or wax bath* or recreation therapy or splint* or orthotic* or joint protection or activity pacing or energy conservation or podiatr* or foot care or cryotherap*) OR AB (hydrotherapy or balneology or balneotherapy or massage* or skin mobilization or thermotherapy or induced hyperthermia or paraffin wax or wax bath* or recreation therapy or splint* or orthotic* or joint protection or activity pacing or energy conservation or podiatr* or foot care or cryotherap*))
S16	(MH "Podiatry")
S15	(MH "Energy Conservation, Metabolic")
S14	(MH "Orthoses+")
S13	(MH "Splints")
S12	(MH "Recreational Therapy")
S11	(MH "Rehabilitation, Vocational") OR (MH "Dance Therapy") OR (MH "Home Rehabilitation") OR (MH "Music Therapy") OR (MH "Rehabilitation, Athletic") OR (MH "Rehabilitation, Cognitive") OR (MH "Rehabilitation, Psychosocial") OR (MM "Rehabilitation") OR (MH "Art Therapy") OR (MH "Manual Therapy+")
S10	TI ((physical therap* or physiotherap* or physio therap* or occupational therap*)) OR AB ((physical therap* or physiotherap* or physio therap* or occupational therap*))
S9	(MH "Occupational Therapy+")
S8	(MH "Physical Therapists")
S7	(MH "Physical Therapy+")
S6	S1 OR S2 OR S3 OR S4 OR S5

S5	TI ((nutrition or diet or dietary or nutritional or probiotic*)) OR AB ((nutrition or diet or dietary or nutritional or probiotic*))
S4	(MW "DH")
S3	(MH "Dietary Supplements+")
S2	(MH "Diet+")
S1	(MH "Diet Therapy+")

Cochrane Trials

- #1 ((nutrition or diet or dietary or nutritional or probiotic* or (physical NEXT therap*) or physiotherap* or (physio NEXT therap*) or hydrotherapy or balneology or balneotherapy or massage* or “skin mobilization” or thermotherapy or “induced hyperthermia” or “paraffin wax” or “wax bath*” or “recreation therapy” or splint* or orthotic* or “joint protection” or “activity pacing” or “energy conservation” or podiatr* or “foot care” or cryotherap* or Acupuncture or Cupping or “Dry Needling” or Bioresonance or Homeopath* or “Traditional medicine” or Aromatherap* or Biofeedback or Breathing or Hypnosis or Imagery or “Laughter Therap*” or Meditation or “Mental Healing” or Psychodrama or Psychophysiology or (Relaxation NEXT Therap*) or “Tai Ji” or “Tai chi” or (Therapeutic NEXT Touch*) or Yoga or (Musculoskeletal NEXT Manipulation*) or “applied Kinesiology” or Chiropractic or Osteopathic or (“Soft Tissue” NEXT therap*) or Naturopath* or Prolotherap* or Reflexotherap* or “Acoustic Stimulation” or (Art NEXT Therap*) or (Color NEXT Therap*) or (Dance NEXT Therap*) or (Music NEXT Therap*) or (Play NEXT Therap*) or (Spiritual NEXT Therap*) or (Relaxation NEXT Technique*) or reflexolog* or phototherap* or (light NEXT therap*) or laser* or Mindfulness or “Patient education” or “group therapy” or “support group*” or “self help”)):ti,ab,kw
- #2 ((non-surgical or psychological or behavior* or behaviour* or cognitive or psychosocial or psycho-social or psychoeducation*) NEXT/3 (intervention* or treatment* or therap* or program* or modification)):ti,ab,kw
- #3 (Coping NEXT/1 (skill* or behavior* or behaviour*)):ti,ab,kw
- #4 (peer or psychosocial or social or patient) NEXT/1 (support):ti,ab,kw
- #5 (Psychotherapy or psychotherapies or CBT or counseling or counselling or “self-management” or psychoeducation or (assistive NEXT technolog*) or (assistive NEXT device*) or education* or “health literacy” or “health information” or “self care” or exercis* or stretching or “resistance training” or “strength training” or running or jogging or swimming or walking or “physical endurance” or sports or sport or “physical activity” or treadmill* or bicycling or cycling or “physical conditioning” or “muscle strength*” or rehabilitation):ti,ab,kw
- #6 ((mobile NEXT/1 (health or rehabilitation)) or tele health or telehealth or telemedicine or e-health or ehealth or m-health or mhealth or mobile based or (virtual NEXT/1 (medicine or rehabilitation)) or ((remote or distance) NEXT/1 (medicine or rehabilitation or consultation)) or videoconferenc* or video conferenc* or tele conferenc* or teleconferenc* or tele education or tele-education or telementoring or tele-mentoring or tele-care or telecare or live video* or cell phone* or text messag*):ti,ab,kw

- #7 ((Oral or dental or periodontal or Gingival) NEXT/2 (rehabilitation or health or pathology or hygiene or care or therap* or treatment* or activit* or exercise* or disease*)):ti,ab,kw
- #8 ((non pharmacological or nonpharmacological or multidisciplinary or multicomponent or interdisciplinary or multimodal) NEXT/1 (treatment or intervention or therap* or management)):ti,ab,kw
- #9 ((Alternative or Complementary) NEXT/2 (medicine or therap* or treatment*))
- #10 {OR #1-#9}
- #11 (scleroderma* or “systemic sclerosis” or CREST syndrome*)
- #12 #10 AND #11

Web of Science

((nutrition or diet or dietary or nutritional or probiotic* or (physical NEAR/1 therap*) or physiotherap* or (physio NEAR/1 therap*) or hydrotherapy or balneology or balneotherapy or massage* or “skin mobilization” or thermotherapy or “induced hyperthermia” or “paraffin wax” or “wax bath*” or “recreation therapy” or splint* or orthotic* or “joint protection” or “activity pacing” or “energy conservation” or podiatr* or “foot care” or cryotherap* or Acupuncture or Cupping or “Dry Needling” or Bioresonance or Homeopath* or “Traditional medicine” or Aromatherap* or Biofeedback or Breathing or Hypnosis or Imagery or “Laughter Therap*” or Meditation or “Mental Healing” or Psychodrama or Psychophysiology or (Relaxation NEAR/1 Therap*) or “Tai Ji” or “Tai chi” or (Therapeutic NEAR/1 Touch*) or Yoga or (Musculoskeletal NEAR/1 Manipulation*) or “applied Kinesiology” or Chiropractic or Osteopathic or (“Soft Tissue” NEAR/1 therap*) or Naturopath* or Prolotherap* or Reflexotherap* or “Acoustic Stimulation” or (Art NEAR/1 Therap*) or (Color NEAR/1 Therap*) or (Dance NEAR/1 Therap*) or (Music NEAR/1 Therap*) or (Play NEAR/1 Therap*) or (Spiritual NEAR/1 Therap*) or (Relaxation NEAR/1 Technique*) or reflexolog* or phototherap* or (light NEAR/1 therap*) or laser* or Mindfulness or “Patient education” or “group therapy” or (support NEAR/1 group*) or “self help”))

((non-surgical or psychological or behavior* or behaviour* or cognitive or psychosocial or psycho-social or psychoeducation*) NEAR/3 (intervention* or treatment* or therap* or program* or modification))

(Coping NEAR/1 (skill* or behavior* or behaviour*))

((peer or psychosocial or social or patient) NEXT/1 support)

(Psychotherapy or psychotherapies or CBT or counsel*ing or “self-management” or psychoeducation or (assistive NEAR/1 technolog*) or (assistive NEAR/1 device*) or education* or “health literacy” or “health information” or “self care” or exercis* or stretching or “resistance training” or “strength training” or running or jogging or swimming or walking or “physical endurance” or sports or sport or “physical activity” or treadmill* or bicycling or cycling or “physical conditioning” or “muscle strength*” or rehabilitation)

((mobile NEAR/1 (health or rehabilitation)) or tele health or telehealth or telemedicine or e-health or ehealth or m-health or mhealth or mobile based or (virtual NEAR/1 (medicine or

rehabilitation)) or ((remote or distance) NEAR/1 (medicine or rehabilitation or consultation)) or videoconferenc* or video conferenc* or tele conferenc* or teleconferenc* or tele education or tele-education or telementoring or tele-mentoring or tele-care or telecare or live video* or cell phone* or text messag*)

((Oral or dental or periodontal or Gingival) NEAR/2 (rehabilitation or health or pathology or hygiene or care or therap* or treatment* or activit* or exercise* or disease*))

((non pharmacological or nonpharmacological or multidisciplinary or multicomponent or interdisciplinary or multimodal) NEAR/1 (treatment or intervention or therap* or management))

((Alternative or Complementary) NEAR/2 (medicine or therap* or treatment*))

(scleroderma* or “systemic sclerosis” or CREST syndrome*)

Supplementary File 2. Inclusion and exclusion coding manual

Title/Abstract Coding Manual

No: no original human data. If it is clear from the title or abstract that the article is not an original report, but rather a letter, editorial, systematic review, meta-analysis, case series, or case report, it is excluded. Conference or symposium abstracts are eligible.

No: not about scleroderma/scleroderma patients. If the title or abstract do not describe the inclusion of participants with “scleroderma”, “systemic sclerosis” (SSc) or “CREST syndrome”, the study will be excluded. If the study reports data on people with SSc, along with people with other conditions, the study will be included if the SSc data are reported separately or if at least 80% of the included participants have SSc.

No: not a randomized controlled trial (RCT) with eligible comparators. If it clear from the title or abstract that the study is not an RCT that compares an intervention to an (1) inactive control condition (e.g., no treatment, waitlist control, usual care) or (2) another intervention, it will be excluded. If the trial includes fewer than 10 participants per trial arm, it is excluded.

No: not about a non-pharmacological intervention. If it is clear from the title or abstract that the intervention is not non-pharmacological or non-surgical, then it is excluded. Eligible interventions include, but are not limited to, physical or occupational therapy, rehabilitation, exercise, psychological, self-management, educational, diet or nutrition, nursing, podiatry, and oral or dental hygiene. All pharmacological interventions, or interventions with a drug component, will be excluded. Interventions will be classified as having a drug component if any form of the active intervention ingredient was listed by the US Food and Drug Administration (FDA) in the Drugs@FDA database at the time of review. Use of probiotics will be included as a

dietary or nutrition intervention if delivered as a food product similar to products that could be obtained outside of a medical intervention (e.g., yoghurt). They will be excluded if they are products registered as a drug or delivered in pill format. Biologics will be excluded, even if autologous (i.e. skin grafting, stem cells), regardless of regulation status.

No: does not target health outcomes or delivery of services. If it is clear from the title or abstract that the intervention does not target physical or psychological health or the delivery of health and support services, it will be excluded.

Yes: Study eligible for inclusion in full-text review.

Full Text Coding Manual

No: no original human data. If the article is not an original report, but rather a letter, editorial, systematic review, meta-analysis, case series, or case report, it is excluded. Conference or symposium abstracts are eligible.

No: not about scleroderma/scleroderma patients. If the study does not describe the inclusion of participants with “scleroderma”, “systemic sclerosis” (SSc) or “CREST syndrome”, the study will be excluded. If the study reports data on people with SSc, along with people with other conditions, the study will be included if the SSc data are reported separately or if at least 80% of the included participants have SSc.

No: not a randomized controlled trial (RCT) with eligible comparators. If the study is not an RCT that compares an intervention to an (1) inactive control condition (e.g., no treatment, waitlist control, usual care) or (2) another intervention, it will be excluded. If the trial includes fewer than 10 participants per trial arm, it is excluded.

No: not about a non-pharmacological intervention. If the intervention is not non-pharmacological or non-surgical, then it is excluded. Eligible interventions include, but are not limited to, physical or occupational therapy, rehabilitation, exercise, psychological, self-management, educational, diet or nutrition, nursing, podiatry, and oral or dental hygiene. All pharmacological interventions, or interventions with a drug component, will be excluded. Interventions will be classified as having a drug component if any form of the active intervention ingredient was listed by the US Food and Drug Administration (FDA) in the Drugs@FDA database at the time of review. Use of probiotics will be included as a dietary or nutrition intervention if delivered as a food product similar to products that could be obtained outside of a medical intervention (e.g., yoghurt). They will be excluded if they are products registered as a

drug or delivered in pill format. Biologics will be excluded, even if autologous (i.e. skin grafting, stem cells), regardless of regulation status.

No: does not target health outcomes or delivery of services. If the intervention does not target physical or psychological health or the delivery of health and support services, it will be excluded.

Yes: Study eligible for inclusion.

Supplementary File 3. Variables Included in Data Extraction Form**Study characteristics**

First author
Year
Journal
Funding source
Conflicts of interest
Country
Study eligibility criteria
Recruitment setting and method
Number of participants randomised
Percent female
Mean (standard deviation [SD]) age
Type of SSc
Mean (SD) years with SSc
Notes

Intervention and control group details

Group name
Number of participants randomised to group
Number of participants analysed in group
Description of intervention and comparator
Qualifications of intervention providers
Intervention setting
Intervention length
Number of sessions
Length of sessions
Tailoring
Modifications
Fidelity adherence
Notes

Outcomes

Outcome type
Outcome measure name
Timepoints collected
Measure of aggregation (e.g., mean, median) at post-test assessments
Measure of dispersion (e.g., SD) at post-test assessments
Number of participants analysed
Other relevant results at post-test assessments
Notes