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A Scoping Review of Systematic Reviews of Complementary Medicine for Musculoskeletal and Mental Health.

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Complete List of Authors:	Lorenc, Ava Feder, Gene; University of Bristol, Community based medicine MacPherson, Hugh; University of York, Health Sciences Little, Paul; University of Southampton, Primary Care and Population Science; Mercer, Stewart; University of Glasgow, Institute of Health and Wellbeing Sharp, Deborah; University of Bristol, Population Health Sciences
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A Scoping Review of Systematic Reviews of Complementary Medicine for Musculoskeletal and Mental Health.

Ava Lorenc*, Population Health Sciences, Bristol Medical School, Bristol, UK.

Gene Feder, Population Health Sciences, Bristol Medical School, Bristol, UK

Hugh MacPherson, Department of Health Sciences, University of York, York, UK

Paul Little, Primary Care and Population Sciences Unit, University of Southampton, Southampton, UK

Stewart W Mercer, General Practice and Primary Care, Institute of Health and Wellbeing, University of Glasgow, Scotland, UK

Deborah Sharp, Population Health Sciences, Bristol Medical School, Bristol, UK

*Corresponding author: Ava.lorenc@bristol.ac.uk; 0117 3313902

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ABSTRACT

Background: Musculoskeletal (MSK) and mental health (MH) conditions have a high disease burden, and their co-existence is common, yet evidence for interventions is weak. Complementary and alternative medicine (CAM) may have a role in managing MSK –MH comorbidity.

Objective: This literature review aimed to identify effective CAM for MSK –MH comorbidity, by collating the evidence on effectiveness, cost-effectiveness and safety from recent systematic reviews (SRs).

Design: Review of systematic reviews.

Methods: We searched literature databases, registries, reference lists, and contacted key authors and professional organisations, to identify SRs of RCTs for CAM and either MSK or MH. Inclusion criteria were: published after 2004, studying adults, in English and scoring > 50% on AMSTAR (quality appraisal checklist). SRs were analysed to identify key research priorities, based on high-quality evidence of effectiveness, total sample size, and any indication of cost-effectiveness and safety, in MSK-MH comorbidity.

Results: We included 84 MSK reviews and 27 MH reviews. The best MSK evidence (moderate/good quality for effectiveness in a moderate/large population, indications of cost-effectiveness/safety) was for low back pain (yoga, acupuncture, spinal manipulation/mobilisation, osteopathy, spa/balneotherapy and tai chi), myofascial trigger point pain (acupuncture), osteoarthritis (acupuncture, tai chi), neck pain (manipulation/manual therapy), fibromyalgia (acupuncture, manual therapy) and lateral epicondylitis (manual therapy). The best MH evidence was for depression (meditation/mindfulness, tai chi, relaxation and acupuncture), anxiety (meditation/mindfulness, moving meditation, yoga), sleep disorders (meditative/mind-body movement), and stress/distress (mindfulness). Very few SRs considered comorbid populations, however, acupuncture, yoga, tai chi and mindfulness/meditation have evidence for both MSK and MH conditions.

Conclusions: Promising CAMs for future research in this area are yoga, mindfulness, tai chi and acupuncture, for low back pain, osteoarthritis, fibromyalgia and depression, anxiety and sleep problems. Despite the large number of SRs and RCTs, high quality, sufficiently powered RCTs with long-term follow up and cost-effectiveness estimates are needed.

STRENGTHS AND LIMITATIONS OF THIS STUDY:

- A review with a comprehensive scope covering a wide range of topics
- This review used systematic searching and screening techniques
- Results are limited by our pragmatic choice to only include high-quality systematic reviews and definition of CAM as including a practitioner in its delivery.
- Date and language limitations may have excluded some topics.

INTRODUCTION

Musculoskeletal (MSK) and mental health (MH) disorders are two conditions resulting in some of the highest burden in terms of disability, accounting for 30.5% and 21.1% of Years Lived with Disability respectively.[1] Both affect one in four UK adults at some point in their life.[2-4] MSK disorders lead to very high healthcare expenditure and loss of work, [5] in the UK accounting for 7.5 million working days lost annually[6] and 60% of occupational sick leave.[2] In England, it has been estimated that MH costs £105 billion, and treatment costs are expected to rise substantially.[7]

Low back pain (LBP) is one of the most common health conditions,[8-10] with a mean global prevalence of 31% [10] and a UK prevalent population of 17.3 million,[11] costing the NHS over £500 million/year.[12] In the UK, 8.75 million people have sought treatment for osteoarthritis[13] which is estimated to have caused £14.8 billion indirect costs.[14]

The most common MH conditions are depression and anxiety.[3,4] In England, 19% of adults reported ever being diagnosed with depression and 6% of adults have been diagnosed with generalised anxiety disorder.[15] Insomnia is another common MH problem, affecting 6.4% of the UK general population.[16]

There is an increasing recognition of the importance of multimorbidity, that is, the co-existence of two or more physical and/or mental long-term conditions in an individual, which is now the norm in the UK.[17-19] In a study in Scotland, 8.3% of all patients (36% of those with multimorbidity), had both a physical and a mental health disorder[20] and around 50% of patients with depression have pain symptoms.[21] Long term MSK disorders are closely associated with multimorbidity.[22]

Complementary and alternative medicine (CAM) is “a diverse group of health-related therapies and disciplines which are not considered to be a part of mainstream medical care”, including osteopathy, chiropractic, acupuncture, herbal medicine and homeopathy.[23] Estimates of 12-month prevalence of use of any CAM are 0.3-86% in Europe[24] and 26% in England.[25] One of the key roles for CAM is ‘effectiveness gaps’ where effective conventional treatment options are limited,[26,27] which includes many areas of MSK and MH, particularly depression.[27] Both MH[28-30] and MSK[31,32] are common reasons for patients to use CAM.

It is likely that there is a potential role for CAM in the care of patients with multimorbid MH and MSK conditions in primary care. This scoping review aims to identify which CAM treatments might be effective and worth researching further, in a formal, systematic and transparent way (which is often lacking in research priority setting exercises). This is thought to be an essential step in the development of a strategy for the integration of CAM with conventional care.[27]

METHODS

Aims

This study aimed to review the current evidence for the use of practitioner-based CAM for musculoskeletal disorders (MSK) and mental health conditions (MH) in order to propose research priorities in terms of treatment choice and specific patient groups/conditions for a future trial of multimorbid MSK and MH in UK primary care. The specific aims were to:

- collate the evidence on effectiveness, cost-effectiveness and safety from recent systematic reviews (SRs) of trials of CAM for MSK and MH conditions
- identify areas where there is high quality evidence of effectiveness but sufficient uncertainty to justify a trial
- identify areas where there is also some evidence of cost-effectiveness and safety

Searches

As this was a scoping review, we used a wide range of methods to identify SRs (published, unpublished, in progress). Literature databases were searched (see below for details of searches): AMED, Medline, EMBASE, CINAHL, PsycINFO; Index to theses; Cochrane library; Epistemonikos; SIGLE. Three trial registries were searched (UKCRN; Health service research projects in progress; Prospero). Reference lists of 'overviews of SRs' and reports (from professional/patient organisations) were searched. We emailed key authors in the field. We also asked the project team, steering group and public and patient involvement (PPI) group, and used websites/social media (university websites, Research Gate and Twitter) to access the wider research community. We asked patient and professional organisations to ask their members for any information (by email, newsletters or social media), these included: disease specific organisations e.g. Arthritis Research UK, Back Care and MIND; CAM organisations e.g. Research Council for Complementary Medicine and Complementary and Natural Healthcare Council; primary care organisations e.g. UK Royal College of General Practitioners. We presented at one conference and distributed a flyer at another. We contacted the authors of eligible conference abstracts and protocols to ascertain if the SR was available e.g. submitted or in press.

For complementary medicine we used MeSH terms or subject headings, plus additional terms for CAM which were not indexed. To ensure relevance to a UK primary care model, we only included CAM which involve practitioner-led treatment. We therefore excluded herbal medicine, as the majority of studies do not involve a practitioner. For musculoskeletal conditions, we used 'musculoskeletal diseases/disorders' as index terms, adding in any which were missing. For mental health, we searched for minor mental health issues and symptoms rather than diagnosed mental disorders. Thus, words in titles/abstracts were searched for (rather than subject headings), as authors may not classify papers as 'mental health' unless diagnosed mental health conditions are part of the study. Reviews related to a secondary condition such as cancer or cardiovascular disease were included if relevant for a primary care population, i.e. are commonly treated in primary care e.g. including diabetes, obesity, respiratory conditions but excluding HIV, stroke, critical illness.

Database searches were conducted in June 2015 and updated in February 2016, in collaboration with a librarian. We used filters for SRs. We excluded reviews published pre-2005, in order to make the final number of papers manageable and with the understanding that these papers were more likely to be of poorer quality. We only included English language reviews. Databases were searched for two topics: complementary medicine + musculoskeletal disorders and complementary medicine + mental health. See Appendix 1 for details and Box 1 for an example search.

Box 1: Example search (OVID Medline)

1. "Alexander technique".tw.
2. "bowen technique".tw.
3. craniosacral.tw.
4. ("emotional freedom technique" or EFT).tw.
5. feldenkrais.tw.
6. Pilates.tw.
7. reiki.tw.
8. Shiatsu.tw.
9. trager.tw.
10. "complementary medicine".tw.
11. "integrative medicine".tw.
12. exp complementary therapies/
13. integrative medicine/
14. Manipulation, Spinal/
15. acupuncture/
16. Musculoskeletal manipulations/
17. Mindfulness/
- 18. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17**
19. exp Musculoskeletal System/
20. exp Musculoskeletal Diseases/
21. myalgia/
22. exp back pain/
23. neck pain/
24. chronic pain/
25. headache/ or exp headache disorders, primary/
- 26. 19 or 20 or 21 or 22 or 23 or 24 or 25**
27. ((systematic or structured or evidence or trials).ti. and ((review or overview or look or examination or update\$ or summary).ti. or review.pt.) or (meta analysis.pt. or meta-analysis/ or "0266-4623".is.) or (reviewed systematically or systematically reviewed).tw. or (1469-493X or 1366-5278 or 1530-440X).is.
28. ("review" or "review academic" or "review tutorial").pt.
29. (medline or medlars or embase or pubmed).tw,sh.
30. (scisearch or psychinfo or psycinfo).tw,sh.
31. (psychlit or psyclit).tw,sh.
32. cinahl.tw,sh.
33. ((hand adj2 search\$) or (manual\$ adj2 search\$)).tw,sh.
34. (electronic database\$ or bibliographic database\$ or computeri#ed database\$ or online database\$).tw,sh.
35. (pooling or pooled or mantel haenszel).tw,sh.
36. (retraction of publication or retracted publication).pt.
37. (peto or dersimonian or der simonian or fixed effect).tw,sh.
38. 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37
39. 28 and 38
40. meta-analysis.pt.
41. meta-analysis.sh.
42. (meta analys\$ or metaanalys\$).tw,sh.
43. (systematic\$ adj5 review\$).tw,sh.
44. (systematic\$ adj5 overview\$).tw,sh.
45. (quantitativ\$ adj5 review\$).tw,sh.
46. (quantitativ\$ adj5 overview\$).tw,sh.
47. (quantitativ\$ adj5 synthesis\$).tw,sh.
48. (methodologic\$ adj5 review\$).tw,sh.
49. (methodologic\$ adj5 overview\$).tw,sh.
50. (integrative research review\$ or research integration).tw.
51. 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48 or 49 or 50
- 52. 27 or 39 or 51**
- 53. 18 and 26 and 52**

We used the inclusion/exclusion criteria (see Appendix 1) to screen the results from each search. This was a multi-stage process involving the whole project team. AL screened the titles of all search

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3 results, and DS checked the results, with any disagreements discussed and inclusion criteria
4 amended accordingly. AL then screened the abstracts, which were also independently screened by
5 another of the authors. Results were compared, any disagreements discussed, and the criteria again
6 amended accordingly. Any remaining disagreements were discussed and resolved with a third
7 reviewer. AL then screened the full text of the agreed papers.
8

9 **Data extraction**

10 AL extracted the following data from each review: author, year, location, CAM/s, health condition/s,
11 for MSK reviews whether MH was included and for MH reviews whether findings applied to MSK
12 populations, methodological features (sources searched, inclusion/exclusion criteria,
13 quality assessment), results and conclusions (effectiveness, safety, cost-effectiveness).
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16 **Quality appraisal**

17 Although not essential,[33] quality assessment is recommended in scoping reviews.[34] We used a
18 limited quality appraisal to help inform prioritisation: AMSTAR, a validated checklist.[35] Due to
19 time constraints and the number of SRs to be appraised, a simple procedure was followed, using the
20 'search' function in the text of SRs to find particular terms. The emphasis was on obtaining relative
21 scores, allowing ranking of the included reviews, rather than an absolute score of quality. For each of
22 the 11 items on the AMSTAR checklist, a score of 0 was given if they did not meet the criteria, or if
23 information was unavailable, and a score of 1 if the criteria were met. The scores were summed to
24 give a score for each SR out of a total of 11.
25
26

27 Any reviews which scored 5 or less (half of the possible total) on AMSTAR were not considered in the
28 evidence synthesis.
29

30 **Analysis**

31 Reviews were placed into a matrix of health condition/symptom vs CAM. For each cell, data were
32 synthesised according to:
33

- 34 • effectiveness: where there was more than one SR on a similar topic, if possible, one SR was
35 prioritised, based on date, breadth, quality and level of analysis.
- 36 • quality of studies: conclusions from the prioritised review regarding the quality of its
37 included studies were reported
- 38 • cost effectiveness: any information on cost effectiveness was synthesised across all the
39 included reviews.
- 40 • safety: any information on safety was synthesised across all the included reviews.
- 41 • conclusion and research priorities: conclusions were drawn from across these four domains;
42 research priorities were extracted from each SR's conclusions and summarised regarding the
43 need for further research and any specific suggestions on methodology.
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46 Finally, a two stage process identified the priority areas (condition and CAM) for future research.
47 Stage one was based on consideration of the following criteria:
48

- 49 **1. Effectiveness** - areas were prioritised where there was enough high quality evidence to
50 establish proof of concept, but still key gaps (from the evidence synthesis). Data for these,
51 criteria came from the conclusions of the prioritised review(s) regarding effectiveness and
52 quality
- 53 **2. Cost** – areas where there was any indication that the intervention may have potential for
54 cost effectiveness were prioritised
- 55 **3. Safety** - areas where there was any indication that the intervention is safe were prioritised
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3 **4. Multimorbidity** - any indication that the intervention may be effective for multimorbid MH
4 and MSK patients were prioritised
5

6 Stage two: once a list of key priority areas had been compiled, information on total sample size for
7 the prioritised SRs (i.e. total number of participants in the trials included in the SR/s was added to
8 allow further discrimination, classified as: small (<500 participants); moderate (501 to 3000); or large
9 (>3000).
10

11 RESULTS

12 Search results

13
14 Figure 1 shows the PRISMA flowchart of the searches.[36] Searches resulted in 8393 references –
15 4304 for MH and 4089 for MSK, plus 3 for MH identified elsewhere (a journal email update). After
16 removing duplicates, Cochrane reviews which were withdrawn, Cochrane reviews which had been
17 updated, or those not in English, 5230 records remained, for title screening. This resulted in 486 MH
18 and 739 MSK records for the abstract screening phase. We then excluded 49 (13 MH and 36 MSK)
19 records i.e. editorials, commentaries, abstracts etc. After abstract screening, there remained 444
20 studies (180 MH and 264 MSK). At this stage, a further 12 records were added – 3 from grey
21 literature (Prospero/Sigle/HSRProj), 5 from conference abstracts, and 4 from the reference lists of
22 overviews of SRs and other key reports. This produced 456 records to be screened at the full text
23 stage, after which 206 records remained: 48 MH, 158 MSK.
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3 During screening at the title stage (AL and DS) there were 49 disagreements (out of 4411 records;
4 1%). During abstract screening (AL and each of the 6 authors) there were a total of 296 initial
5 disagreements (out of 1165 records; 25%). Most were resolved by discussion without requiring a
6 third reviewer.
7

8 Of the 158 MSK systematic reviews, 84 were included as high quality (scored 6 or more on AMSTAR).
9 They covered 17 different CAMs and 15 different disorders. The overall matrix is shown below in
10 Table 1. Low back pain was by far the most common topic, addressed by 40% of reviews.
11 Fibromyalgia was the next most common, followed by osteoarthritis then neck pain/disorders.
12 Acupuncture was the most common CAM studied (37%), followed by manual therapy (including
13 manipulation and mobilisation). The mean AMSTAR score for methodological quality of MSK reviews
14 was 6/11 (ranging from 0 to 11). Appendix 2 shows which items on the AMSTAR checklist were
15 reported by the reviews.
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Table 1: Matrix of MSK reviews (numbers = number of reviews)		LBP		Fibro-myalgia		Neck pain/disorders		Osteo arthritis		Rheumatoid arthritis		MSK pain/conditions		Myofascial pain		Shoulder pain/disorder		Other		Total
		Total number	High quality	Total number	High quality	Total number	High quality	Total number	High quality	Total number	High quality	Total number	High quality	Total number	High quality	Total number	High quality	Total number	High quality	
Acupuncture related	Acupressure	2	2			2	1					1	1					1	0	6
	Acupuncture	12	6	9	6	5	2	10	6	4	2	4	2	6	3	2	1	6	5	58
	Moxibustion	1	0	1	0			1	0	2	1							1	0	6
Manipulation	Chiropractic	2	1	3	1			1	0					1	0					7
	Manual therapy/spinal manipulation/mobilisation	12	9	8	4	14	9	2	1			1	0	1	0	5	3	3	2	46
	Osteopathy	3	2	2	1							1	1							6
Other	Integrative therapies/Multiple CAM	2	2	2	2															4
	Tai chi	1	1	1	0	1	0	7	5	3	1	1	1							14
	Qigong					1	0	1	0	1	0									3
	Pilates	10	5																	10
	CAM exercise			2	2															2
	Yoga	8	4	1	1	1	0	3	0	1	0	1	1							15
	Mindfulness/meditation	2	0	5	3					2	0	4	2							13
	Relaxation			3	1			1	0	1	0	1	0							6
	Hypnotherapy	1	0	1	1			1	0	1	0									4
	Spa therapy/balneotherapy	2	1	2	1					1	1									5
	TCM bodywork	2	1			1	0					1	0							4
Massage/therapeutic touch	4	2			4	2	1	0	1	0	1	0			1	0	1	1	13	
Homeopathy			2	0															2	
Total		64	36	42	23	29	14	28	12	17	5	16	8	8	3	8	4	12	8	

Of the 48 MH systematic reviews, 27 were high quality (scored 6 or more on AMSTAR). They covered 18 different CAMs and five different categories of MH symptom or disorder. The overall matrix is shown below in Table 2. Many of the reviews included more than one MH condition. 75% of reviews included depression. Meditation, yoga, acupuncture and meditative movement were the most common CAM. Appendix 2 shows which items on the AMSTAR checklist were reported by the reviews.

Table 2 : Matrix of MH reviews (numbers = number of reviews)		Depression		Anxiety		Stress		Insomnia / sleep		Distress (psychological)		Total ¹
		Total number	High quality	Total number	High quality	Total number	High quality	Total number	High quality	Total number	High quality	
Acupuncture	Acupuncture	9	3	2	1			2	1			6
	Auricular acupuncture							3	1			4
Multiple	CAM (multiple) (did not separate CAM in analysis)	1	0	1	0			2	1			4
Meditation/ mindfulness	Mindfulness	3	2	1	1	1	1			1	1	5
	Meditation			3	3	1	1	1	0			9
Exercise	Meditative Movement							3	3			6
	Qigong	4	1	2	1	1	1					5
	Tai chi	4	2	1	0			3	1			5
	Yoga	4	2	3	3	1	0	1	0			8
Other	Homeopathy							1	1			2
	Hypnosis	2	0					2	2			4
	Music therapy	3	2	1	1							2
	Relaxation	3	1	1	1			1	1			4
	Reflexology							1	0			1
	Reiki	1	1	1	1							2
	Spinal manipulation											0
	Massage/Therapeutic touch	2	1	2	2							4
Morita therapy			1	1								2
Total¹		36	15	19	15	4	3	20	11	1	1	
1. Note that reviews can occur in more than one row/column												

The following sections present a summary of the areas, as described above, where SRs found moderate/good quality evidence of effectiveness (from prioritised SRs), and where there is some indication of cost-effectiveness and safety (from any of the included SRs).

Evidence for MSK disorders

The MSK disorders with the most evidence were low back pain, myofascial trigger point pain, osteoarthritis, neck pain, fibromyalgia and lateral epicondylitis. All other combinations of condition/CAM/comparator were either poor quality, ineffective, or moderate quality but harmful.

Low back pain

There was good quality evidence in a medium size population for:

- yoga for low back pain compared to any control, for pain, global improvement and disability in the short-term.[37] There is some evidence of safety,[37-39] although none on cost-effectiveness. Evidence for long term effects or compared to other active interventions is of moderate quality.[37]
- osteopathy for low back pain compared to spinal manipulation/heat/physical therapy, although there is some evidence of harm.[40]

There was moderate quality evidence in a large population for:

- acupuncture for low back pain compared to usual care (for pain, function, wellbeing, disability, ROM, quality of life) and placebo (for pain and quality of life; negative evidence for disability),[41 ,42] as well as some evidence of safety[43 ,44] and cost-effectiveness.[41]
- spinal manipulation/mobilisation for low back pain compared to other active interventions, although results only apply for chronic low back pain,[41 ,45 ,46] and some evidence of safety.[40 ,41 ,45-47]

There was moderate quality evidence in a small population for:

- spa/balneotherapy for low back pain compared to medication/exercise (balneotherapy) or usual care (spa therapy), and some evidence it is safe.[48]
- tai chi for low back pain compared to usual care, but nothing on safety, costs or impact on MH outcomes.[44]

Myofascial trigger point pain

Acupuncture for myofascial trigger point pain compared to placebo and other active interventions had good quality evidence in a medium size population for pain in the short and medium term but not in the long term.[49] However, there is no evidence for safety, cost-effectiveness, or impact on MH outcomes.[49-51]

Osteoarthritis

There was good quality evidence:

- in a large population for acupuncture for knee or peripheral joint OA compared to placebo,[52 ,53] although there is some evidence of harm.[53 ,54]
- in a small population for tai chi for knee OA, compared to usual care or any control, for pain, physical function and stiffness, and physical quality of life, but only in the short term,[55] and some evidence of safety.[55-57]

Neck pain

For manual therapy plus exercise compared to exercise alone there was good quality evidence in a medium sized population,[58] and moderate quality evidence in a large population for manipulation compared to other mobilisation/medication (cervical manipulation) or any control (thoracic manipulation).[59] There was moderate quality evidence in a medium sized population for a range of other techniques.[58-60] There is some evidence of cost-effectiveness,[58 ,60] but also some evidence of potential harm.[59 ,61]

Acupuncture for neck pain compared to placebo or usual care had moderate quality evidence in a medium sized population for,[62] although no evidence of cost-effectiveness.[41]

Fibromyalgia

There was moderate quality evidence in a small population for acupuncture for fibromyalgia, compared to placebo for stiffness (acupuncture) and for pain and sleep disorders (electroacupuncture), and poor quality evidence in a small population compared to usual care for pain (electroacupuncture).[63] However there was some evidence that acupuncture is less effective than usual care for MH outcomes in fibromyalgia.[63] There is some evidence of safety[63-67] but none of cost effectiveness.

Only poor quality evidence existed in a small population for manual therapy (myofascial release) for fibromyalgia for both pain and MH (anxiety and depression) compared to placebo,[68] with some evidence of safety[69] but no evidence of cost-effectiveness.

Lateral epicondylitis

Moderate quality evidence was documented (but the sample size was not reported) for manual therapy (mobilisation with movement) for lateral epicondylitis, although no evidence of safety.[70]

Evidence for mental health

No reviews provided good quality evidence for CAM for any MH condition nor any evidence of cost-effectiveness, mainly because the latter was not reported.

Depression

There was moderate quality evidence in a medium size population for using MBSR for depression compared to usual care[71] and for meditation compared to other active interventions,[72] as well as some evidence of effectiveness in an MSK population.[71 ,72] Evidence for using mindfulness meditation (other than MBSR/meditation) for depression was poor quality in a medium sized population but there was some evidence of effectiveness in an MSK population.[72] MBSR/mindfulness/meditation all have some evidence of safety.[72]

For older adults, there was moderate quality evidence in a medium sized population for tai chi for depression, compared to usual care,[73] although it may be less effective in multimorbid populations (including some MSK conditions).[74]

There was moderate quality evidence (sample size not reported) for relaxation for depression compared to any control, but no evidence of safety or cost-effectiveness.[75].

Only poor quality evidence in a medium sized population was available for acupuncture for depression compared to medication,[76] with some evidence of safety.[76 ,77]

Anxiety

There was moderate quality evidence in a medium sized population for:

- meditation for anxiety, compared to usual care, placebo or other active interventions,[78] and moderate quality evidence in a medium sized population for MBSR compared to usual care,[71] and for moving meditation compared to static meditation,[78] as well as some evidence of safety[72 ,78 ,79] and effectiveness in an MSK population.[71 ,72]
- yoga for anxiety but only for women with breast cancer,[80] and nothing on safety.[81]

Sleep disorders

For older adults, there was moderate quality evidence in a medium sized population for meditative/mind-body movement for sleep disorders, compared to usual care and other active interventions,[82] as well as some evidence of safety,[82] and effectiveness in an MSK population.[83]

Stress and distress

There was moderate quality evidence in a medium sized population for:

- mindfulness for stress compared to usual care and placebo, and some evidence of effectiveness in an MSK population.[71]
- mindfulness for distress compared to usual care, and some evidence of effectiveness in an MSK population.[71]

There was only poor quality evidence for all other combinations of condition/CAM/comparator.

Evidence for effectiveness in multimorbidity

Very few of the SRs considered multimorbid populations. However, there are some CAM which appear to be effective for both MSK and MH conditions.

Acupuncture shows some effectiveness in both MSK and MH conditions. However, for MSKs, the effects are compared to usual care (low back pain, neck pain and fibromyalgia) and for MH they are only compared to other active interventions (medication; for depression).

Yoga appears to be effective for both low back pain and anxiety compared to other active interventions, although the anxiety finding was only from studies of women with breast cancer. Meditative movement, which includes yoga, is effective for sleep disorders, although only for older adults (there is some evidence in chronic pain and fibromyalgia populations as well).

Tai chi appears to be effective compared to usual care for low back pain, knee osteoarthritis and depression, in older people (although it appears less effective in multimorbid depressed patients). Meditative movement, which includes tai chi, is effective for sleep disorders, although only for older adults (there is some evidence in chronic pain and fibromyalgia populations as well).

There is evidence of effectiveness for mindfulness/meditation/MBSR in depression, anxiety and distress, which may apply equally to MSK populations.

DISCUSSION

This review has highlighted the large and increasing number of systematic reviews of CAM for musculoskeletal and mental health disorders, covering 29 different CAM approaches. The MSKs with the best evidence (moderate/good quality for effectiveness in a moderate/large population, some indication of cost-effectiveness and safety) were low back pain (yoga, acupuncture, spinal manipulation/mobilisation, osteopathy, spa/balneotherapy and tai chi), myofascial trigger point pain (acupuncture), osteoarthritis (acupuncture, tai chi), neck pain (manipulation/manual therapy), fibromyalgia (acupuncture, manual therapy) and lateral epicondylitis (manual therapy). The MH conditions with the best evidence were depression (MBSR/meditation/mindfulness, tai chi, relaxation and acupuncture), anxiety (meditation/MBSR, moving meditation, yoga), sleep disorders (meditative/mind-body movement), and stress/distress (mindfulness). Very few systematic reviews considered multimorbid populations, however, acupuncture, yoga, tai chi and mindfulness/meditation/MBSR appear to have evidence for both MSK and MH conditions.

The quality of the SRs in the areas of CAM and MSK/MH was very variable, and the quality of included trials also varied widely; it is notable that none of the MH SRs concluded that trial quality was 'good' overall. Very few of the MSK SRs mentioned cost-effectiveness, and none of the mental health SRs. Future systematic reviews in the areas of CAM and MSK/MH need to ensure they include *a priori* design/protocol registration, a list of excluded studies, and conflict of interest statements, use duplicate study selection and data extraction, assess publication bias, and search for grey literature.

The key strengths of this review were its comprehensive scope which included a wide range of CAM approaches and types of MSK and MH condition, and its systematic searching techniques, using MeSH terms where possible, and search techniques to capture grey and unpublished literature. The whole project team were involved in independently screening the literature search results. We did include a quality appraisal of the reviews, although time constraints meant this was an abbreviated assessment. One of the key limitations is the pragmatic decision to only include systematic reviews, which may have led to exclusion of some CAMs, and means results are subject to the limitations of systematic review and trial methodology, study designs sometimes challenging for use with CAM.[84-86] Another key limitation is our definition of CAM as including a practitioner in its delivery (which relied on review authors reporting these details), which excluded over the counter products or self-care practices, herbal medicine in particular. We are aware that by excluding reviews published pre-2005 we may have excluded some topics. We were unable to include non-English publications.

Although CAM is commonly used by patients in the UK,[25] it is not widely available via the NHS. Given the high burden of MSK and MH conditions to individuals and society in the UK, and the prevalence of multimorbidity, CAM may be worth considering for some patients, where there is evidence of effectiveness, cost-effectiveness and safety.

One of the main aims of this study was to inform the design of a future trial for the effectiveness and cost effectiveness of an integrative medicine (IM) intervention for patients with multimorbid musculoskeletal and mental health disorders. We have identified five areas which we feel have potential:

- Yoga for low back pain, anxiety and sleep (in a population other than cancer or older adults). Since we conducted our review, a new Cochrane review has been published which suggests there is some (very low quality) evidence for yoga improving depression in low back

pain),[87] and two other SRs which support the evidence for yoga for anxiety and depression.[88 ,89] Recent randomised trials suggest that yoga can reduce pain, anxiety and sleep in low back pain[90-92] and sleep may be a mediator for some of the effects of yoga on low back pain.[93]

- MBSR/mindfulness/meditation for mental health (depression, anxiety, stress, distress), and may be effective in an MSK population, but there is a need to evaluate effectiveness in specific MSK populations. Since we conducted our review, two new SRs have been published which provide evidence for mindfulness and mental health and for mindfulness in LBP, including some evidence for mindfulness helping with depression in LBP (and FMS).[94 ,95] The majority of current mindfulness literature focuses on MH rather than physical dysfunction; most of the studies of physical conditions are not RCTs[96] - one trial has shown that mindfulness can improve psychological distress, self-efficacy, and fatigue in chronic pain from inflammatory rheumatic joint diseases,[97] but another found no difference of MSBR compared to a multidisciplinary pain intervention.[98] There is some recent pilot/feasibility evidence for mindfulness-based approaches improving depression in back pain.[99 ,100] An observational study found improvements in depression, anxiety, pain in chronic pain patients who also had MH symptoms.[101]
- Acupuncture (compared to other active interventions) in for MSK (low back pain, neck pain or fibromyalgia) and depression. Since we conducted our review two new SRs have confirmed the effectiveness of acupuncture on OA of the knee[102 ,103] and three others have identified effectiveness of acupuncture for insomnia.[104-106]
- Tai chi for low back pain or osteoarthritis and depression, possibly in older people, although there is no SR evidence in a multimorbid population (and some evidence that tai chi may be less effective for depression in those with (not just MSK) multimorbidities). A recent trial shows that tai chi reduces depression in OA of knee compared to physiotherapy.[107]
- Meditative/mind-body movement (yoga or tai chi) for sleep disorders, with perhaps chronic pain or fibromyalgia.

Systematic reviews of CAMs consistently conclude that further high quality trials in this area are needed, with long term follow up and larger sample sizes, assessing cost-effectiveness and use of appropriate, sensitive, validated outcome measures. The need for high quality trials was particularly highlighted in SRs of fibromyalgia, arthritis (both osteoarthritis and rheumatoid), sleep disorders, manual therapies and tai chi.

This scoping review suggests that the most promising CAM for future research in the areas of MSK-MH comorbidity are yoga, mindfulness, tai chi and acupuncture. The comorbid populations that would most benefit are less clear, as few studies focus on comorbidity, but may include low back pain, osteoarthritis, fibromyalgia and depression, anxiety and sleep. It is clear that, despite the volume of SRs and RCTs identified, there is still a need for further research in many areas. There is a particular need for high quality, large RCTs with long-term follow up, which include cost-effectiveness.

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3 *Study*). The views expressed in the publication are those of the author(s) and not necessarily those of
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8 **Competing interests**

9

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14

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17

19 **Contributions**

20

21 AL conducted all literature searches, data extraction and quality appraisal, with the project
22 team (GF, HM, PL, SM and DS) all screening papers for inclusion. The team (GF, HM, PL, SM
23 and DS) all provided input into the inclusion/exclusion criteria. DS advised on the review
24 process. GF, HM, PL, SM and DS were all involved in the prioritisation of topics from the
25 review results. AL drafted the paper and all authors reviewed and edited it.
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28 **Data sharing**

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30 We are able to provide copies of searches and lists of excluded references on request.
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37 Therapy for Knee Osteoarthritis: A Randomized Trial. *Annals of Internal Medicine*
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Appendix 1: Inclusion and exclusion criteria for review

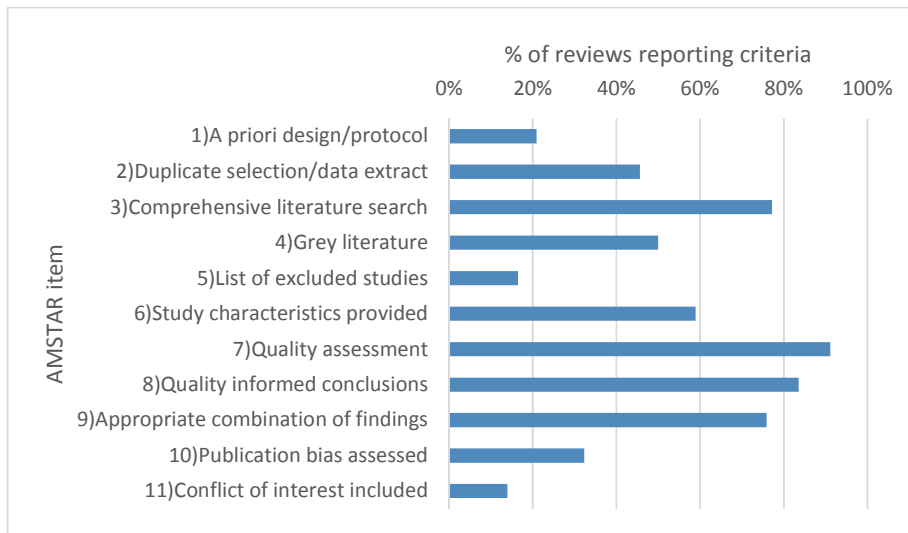
	Include	Exclude
Types of review	Systematic review and/or meta-analysis	Non-systematic searches; clinical summaries; mechanism reviews; conceptual reviews; historical reviews; herbal monographs; opinions/editorials; reviews of qualitative studies. Reviews including case studies.
Topic of review	Efficacy, effectiveness, cost-effectiveness, safety	Any other focus including prevalence, mechanisms
CAM	Any under the MeSH term CAM, except those in the adjacent column (acupuncture (body or ear), acupressure, electroacupuncture, laser acupuncture, Alexander technique, aromatherapy, art therapy, anthroposophy, autogenic training, balneotherapy/hydrotherapy, Bowen, chiropractic, craniosacral, emotional freedom technique, Feldenkrais, guided imagery, kinesiology, homeopathy, hypnosis, integrative medicine, massage, manual therapy or manipulation, meditation, mindfulness, moxibustion, music therapy, naturopathy, osteopathy, Pilates, qi gong, reflexology, relaxation therapy, reiki, shiatsu, spiritual therapies, spiritual healing, tai chi, therapeutic touch, traditional medicine (all types - including TCM approaches such as tuina and guasha), trager, yoga)	Those which are not considered CAM in a UK NHS setting: acoustic stimulation, bee venom acupuncture, biofeedback, breathing exercises, cell therapy, colour therapy, dance therapy, detoxification, deep transverse friction massage, diets, horticultural therapy, light therapy, leech therapy, lifestyle changes, laughter therapy, low level laser therapy (included laser acupuncture which is based on TCM acupuncture points), MBCT, mental healing, magnet therapy, NLP, neural therapy, prayer, play therapy, psychodrama, psychophysiology, prolotherapy, sensory art therapy, suggestion, transcranial magnetic stimulation, TENS rejuvenation, western medicine Herbal medicine/phytotherapy, as the majority of studies do not involve a practitioner Oral or topical CAM which are given to the patient without the input of a practitioner
Intervention details	Practitioner-based CAM only The CAM must be the main focus of the paper.	Over-the-counter, online, self-help only. CAM is only mentioned amongst a list of other active interventions
MSK: muscular diseases	Muscular diseases	Carpal tunnel; compartment syndromes; contracture; craniomandibular disorders; esinophilia-myalgia syndrome; muscle cramp; muscular abnormalities; muscle neoplasms; mitochondrial myopathies; myositis; paralysis;

		rhabdomyolysis; spinal stenosis
MSK: bone diseases	Osteoarthropathy	All other bone diseases
MSK: rheumatic diseases	Arthritis, Fibromyalgia	Juvenile arthritis; rheumatic fever; sternocostoclavicular; hyperostosis; infectious arthritis; Reiter's disease; rheumatic fever
MSK: other	Musculoskeletal pain	Abdominal pain; cranial pain; ear ache; eye pain; facial pain; headache/migraine; jaw disorders; labour pain; nipple pain; neuralgia; neuropathic pain; pelvic pain; phantom limb pain; sprains
MH	Anxiety; stress; bipolar; loneliness, low mood	Autism; Alzheimer's; ADHD; child/domestic abuse; delusions; dementia; delirium; eating disorders; learning/intellectual disorders; OCD; Parkinson's; personality disorders; psychotic conditions; psychological trauma; PTSD; quality of life; sexual/gender disorders; substance misuse/abuse; substance abuse; schizophrenia; serious mental health; suicide; sexual disorders;
	Somatoform disorders	Hypochondriasis
	Depression	Postpartum or premenstrual depression; postoperative depression; depressive psychosis; atypical depression
	Stress, stress management	Financial strain; oxidative stress; physiological stress; posttraumatic stress; stress incontinence
	Sleep problems, insomnia	Restless leg syndrome
Other multimorbidities/ populations: serious/long term conditions	Cancer; cardiovascular; diabetes; digestive issues; obesity; respiratory;	Asthma; brain injury; chronic fatigue syndrome; cystic fibrosis; epilepsy; hepatitis; HIV/AIDS; kidney disease; multiple sclerosis, stroke/post stroke; sleep apnoea
Other multimorbidities/ populations: acute conditions	None	Injuries, infections
Other multimorbidities/ populations: settings	Carers	Critical illness; intensive care; military; nursing home; palliative care; prisons; surgery
Other multimorbidities/ populations: women's health	-	Endometriosis; infertility; labour/postpartum/pregnancy; PCOS; menopause; menstrual pain; pelvic pain
Other	-	Memory impairment

multimorbidities/ populations: disabilities	-	Hearing loss/impairment
	-	Vision loss/impairment
Population	Adults only \geq 18yrs (include if children were included but reported and analysed separately)	Animal studies or laboratory studies
	Need to be generalisable to GP population	Healthy populations or specific occupations (e.g. nurses, teachers)
Language	English only	Any other language
Date of publication	2005 or later	Pre 2005
For trial registries	Only those which were completed and we had not picked up in other searches	Currently recruiting or not recruiting
Country	Reviews including studies from Western countries	Review of studies from only non-Western countries

Appendix 2

AMSTAR items reported in MSK reviews



AMSTAR items reported in MH reviews

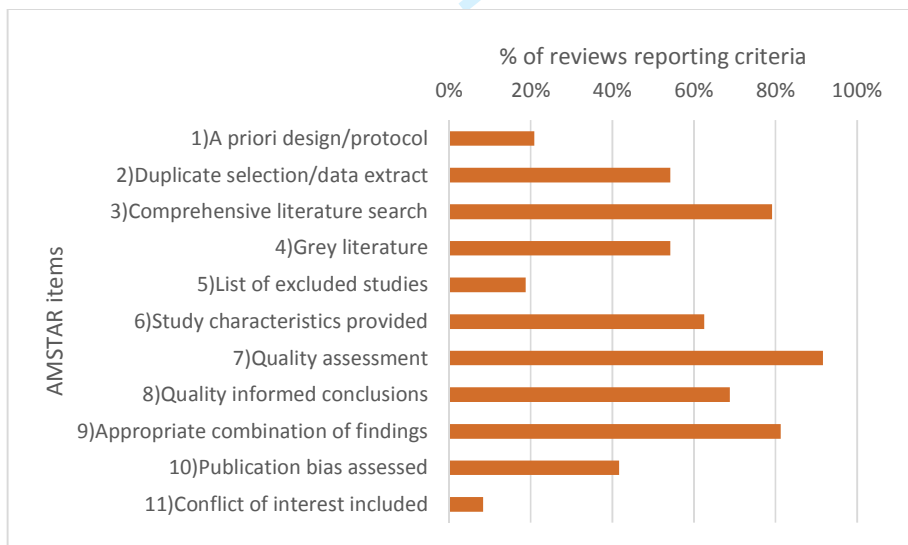
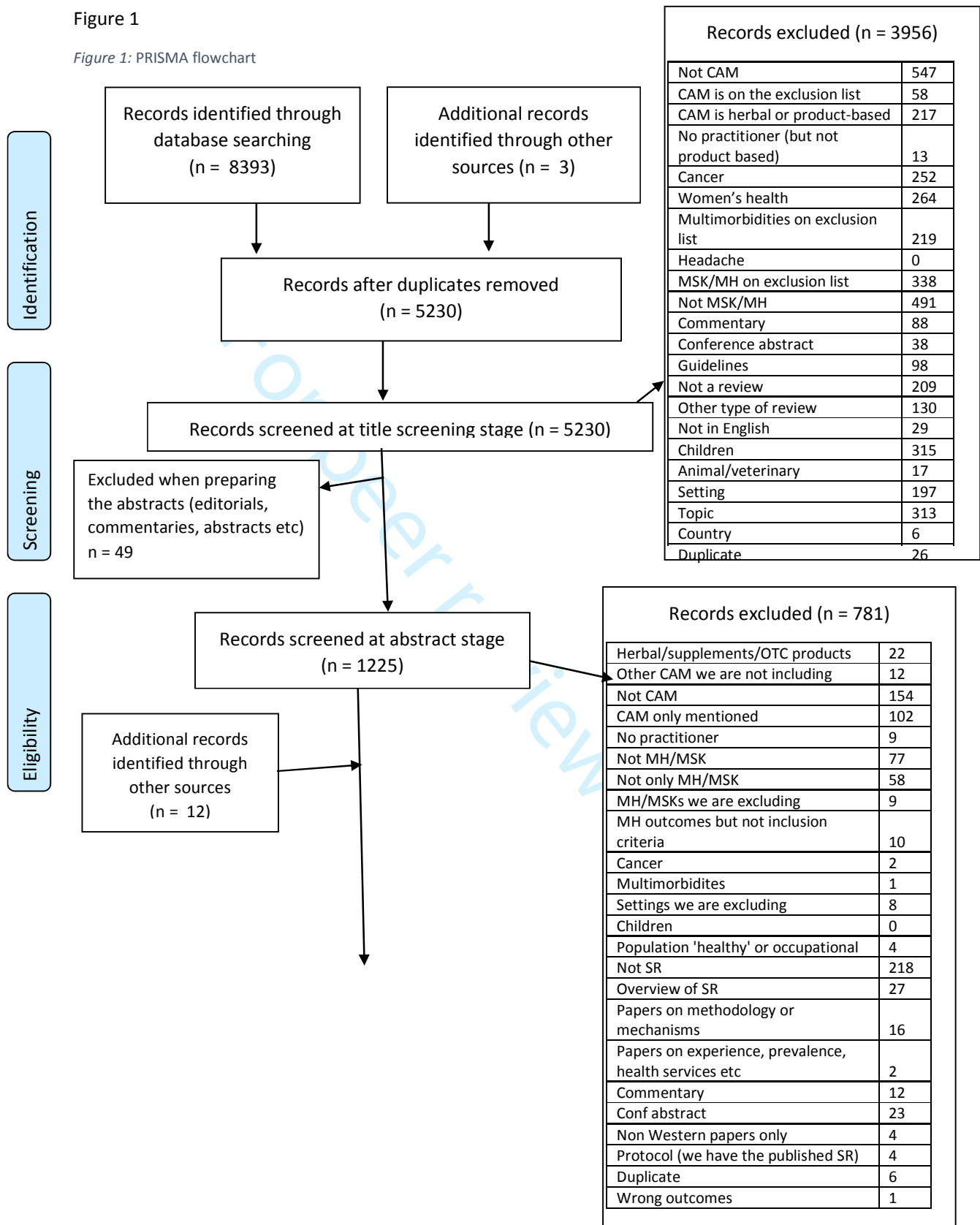
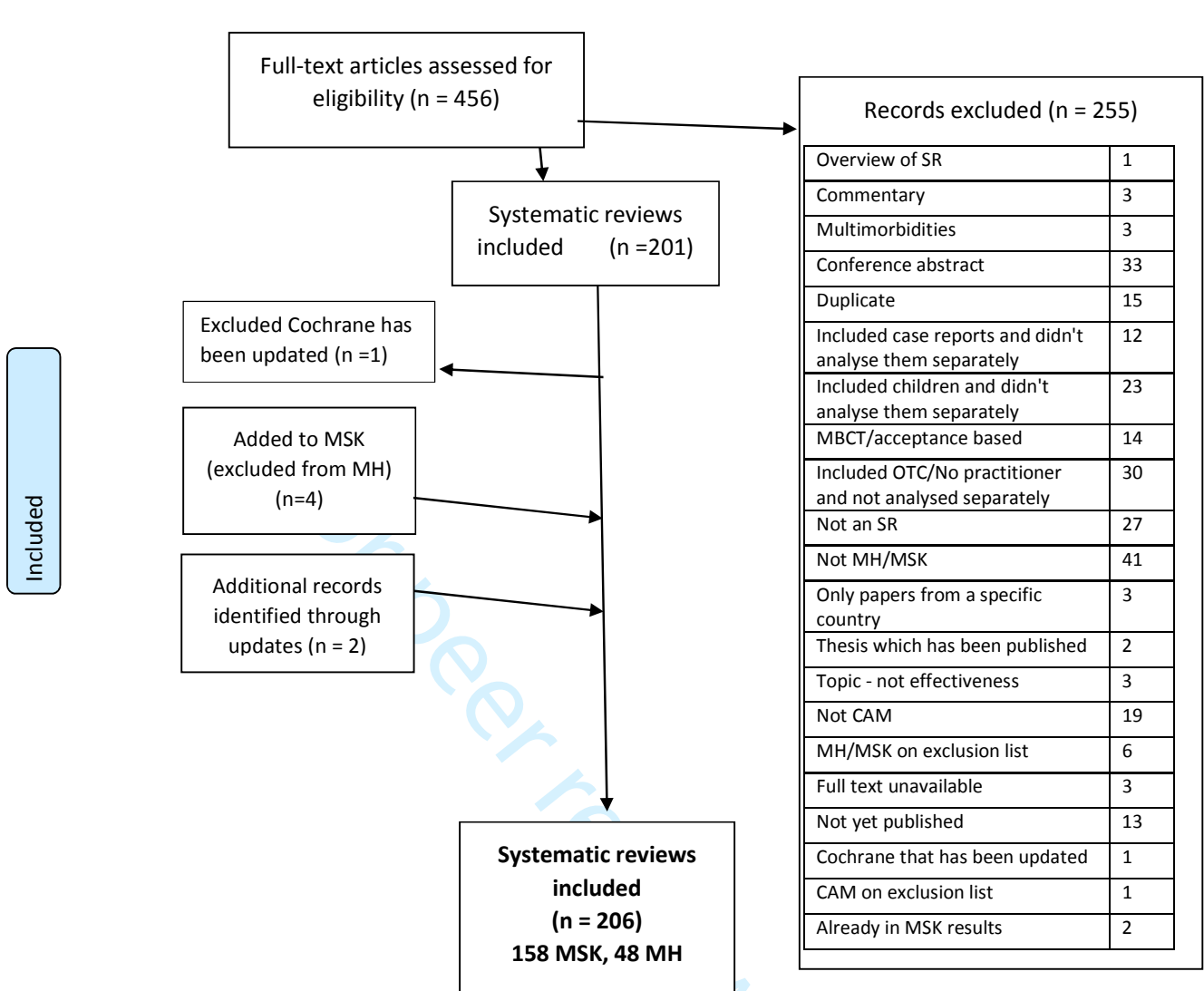


Figure 1

Figure 1: PRISMA flowchart





BMJ Open

A Scoping Review of Systematic Reviews of Complementary Medicine for Musculoskeletal and Mental Health Conditions.

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2017-020222.R1
Article Type:	Research
Date Submitted by the Author:	26-Feb-2018
Complete List of Authors:	Lorenc, Ava Feder, Gene; University of Bristol, Community based medicine MacPherson, Hugh; University of York, Health Sciences Little, Paul; University of Southampton, Primary Care and Population Science; Mercer, Stewart; University of Glasgow, Institute of Health and Wellbeing Sharp, Deborah; University of Bristol, Population Health Sciences
Primary Subject Heading:	Complementary medicine
Secondary Subject Heading:	Mental health, General practice / Family practice
Keywords:	COMPLEMENTARY MEDICINE, Musculoskeletal disorders < ORTHOPAEDIC & TRAUMA SURGERY, MENTAL HEALTH, PRIMARY CARE

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A Scoping Review of Systematic Reviews of Complementary Medicine for Musculoskeletal and Mental Health conditions.

Ava Lorenc*, Population Health Sciences, Bristol Medical School, Bristol, UK.

Gene Feder, Population Health Sciences, Bristol Medical School, Bristol, UK

Hugh MacPherson, Department of Health Sciences, University of York, York, UK

Paul Little, Primary Care and Population Sciences Unit, University of Southampton, Southampton, UK

Stewart W Mercer, General Practice and Primary Care, Institute of Health and Wellbeing, University of Glasgow, Scotland, UK

Deborah Sharp, Population Health Sciences, Bristol Medical School, Bristol, UK

*Corresponding author: Ava.lorenc@bristol.ac.uk; 0117 3313902

Word count: 4201

ABSTRACT

Background: Musculoskeletal (MSK) and mental health (MH) conditions cause high disease burden. Comorbidity is common, yet evidence for interventions is weak. Complementary and alternative medicine (CAM) may have a role in MSK –MH comorbidity.

Objective: To identify potentially effective CAM for MSK –MH comorbidity, by synthesising evidence on effectiveness, cost-effectiveness and safety from systematic reviews (SRs).

Design: Scoping review of systematic reviews.

Methods: We searched literature databases, registries, reference lists, and contacted key authors and professional organisations, to identify SRs of RCTs for CAM for MSK or MH. Inclusion criteria were: published after 2004, studying adults, in English and scoring > 50% on AMSTAR (quality appraisal checklist). SRs were analysed to identify research priorities, based on high-quality evidence of effectiveness, total sample size, and indication of cost-effectiveness and safety.

Results: We included 84 MSK SRs and 27 MH SRs. Only one focussed on MSK-MH comorbidity. Three reported that meditative approaches may improve MH in MSK populations. Acupuncture, yoga, tai chi and mindfulness/meditation had evidence for MSK and MH conditions. The best MSK evidence (moderate/good quality for effectiveness in a moderate/large population, indications of cost-effectiveness/safety) was for low back pain (yoga, acupuncture, spinal manipulation/mobilisation, osteopathy, spa/balneotherapy and tai chi), myofascial trigger point pain (acupuncture), osteoarthritis (acupuncture, tai chi), neck pain (manipulation/manual therapy), fibromyalgia (acupuncture, manual therapy) and lateral epicondylitis (manual therapy). The best MH evidence was for depression (meditation/mindfulness, tai chi, relaxation and acupuncture), anxiety (meditation/mindfulness, moving meditation, yoga), sleep disorders (meditative/mind-body movement), and stress/distress (mindfulness).

Conclusions: Only one SR studied MSK-MH comorbidity. Research priorities for CAM for both MSK and MH (low back pain, osteoarthritis, fibromyalgia, depression, anxiety and sleep problems) are yoga, mindfulness, tai chi and acupuncture. Despite the large number of SRs and the prevalence of comorbidity, more high quality, large RCTs in comorbid populations are needed.

STRENGTHS AND LIMITATIONS OF THIS STUDY:

- A comprehensive scoping review covering a wide range of individual MSK and MH conditions, in the notable dearth of SRs/RCTs in comorbid populations
- This review used systematic searching and screening techniques
- Results are limited by our pragmatic choice to only include high-quality systematic reviews and definition of CAM as including a practitioner in its delivery.
- Date and language limitations may have excluded some topics.

INTRODUCTION

Musculoskeletal (MSK) and mental health (MH) disorders are two conditions resulting in some of the highest burden in terms of disability, accounting for 30.5% and 21.1% of Years Lived with Disability respectively.[1] Both affect one in four UK adults at some point in their life.[2-4] MSK disorders lead to very high healthcare expenditure and loss of work,[5] in the UK accounting for 7.5 million working days lost annually[6] and 60% of occupational sick leave.[2] In England, it has been estimated that MH costs £105 billion, and treatment costs are expected to rise substantially.[7]

Low back pain (LBP) is one of the most common health conditions,[8-10] with a mean global general population prevalence (regardless of prevalence period) of 31% [10] and a UK prevalent population of 17.3 million, with 3.1 million adults suffering during an entire year[11], costing the NHS over £500 million/year.[12] In the UK, 8.75 million people sought primary care treatment for osteoarthritis (over a 7 year consultation period)[13] which is estimated to have resulted in £14.8 billion indirect costs.[14]

The most common MH conditions are depression and anxiety.[3 4] In England, 19% of the general adult population reported ever being diagnosed with depression and 6% ever being diagnosed with generalised anxiety disorder.[15] Insomnia is another common MH problem, affecting 6.4% of the UK general population.[16]

There is an increasing recognition of the importance of multimorbidity, that is, the co-existence of two or more physical and/or mental long-term conditions in an individual, which is becoming the norm in the UK.[17-19] In a cross-sectional study in Scotland, 8.3% of primary care patients (36% of those with multimorbidity), had both a physical and a mental health disorder[20] and around 50% of patients with depression had pain symptoms.[21] Long term MSK disorders are closely associated with multimorbidity.[22]

Complementary and alternative medicine (CAM) is “a diverse group of health-related therapies and disciplines which are not considered to be a part of mainstream medical care”, including osteopathy, chiropractic, acupuncture, herbal medicine and homeopathy.[23] Estimates of 12-month prevalence of use of any CAM are 0.3-86% in Europe[24] and 26% in England.[25]

Many MSK and MH conditions, and comorbid MSK and MH, have limited conventional treatment options - ‘effectiveness gaps’, which are potential key areas for CAM.[26 27] Both MH[28-30] and MSK[31 32] are common reasons for patients to use CAM. We used scoping methodology to identify priority areas where CAM may be useful.[33] The overall aim of scoping studies is ‘to map rapidly the key concepts underpinning a research area and the main sources and types of evidence available’ in a formal, systematic and transparent way (which is often lacking in research priority setting exercises).[34] Scoping study methodology was used to identify gaps in the research base and priorities for future research. Scoping work is an essential step in the development of a strategy for the integration of CAM with conventional care.[27] Preliminary searches showed that evidence for comorbid populations was very limited, so we chose to include independent evidence on MSK and MH conditions. This review was part of a wider scoping study, which obtained a breadth of perspectives - the results of this review were combined with findings from consultation with conventional and CAM practitioners, a public survey, and case studies of NHS provision of CAM, to inform the final choice of conditions and CAM approaches for an RCT.

METHODS

The scoping study followed Arksey and O'Malley's [33] framework plus the refinements suggested by Levac et al.[35], Daudt et al [36] and Colquhoun et al.[37] Scoping reviews are broader and more exploratory than systematic reviews. They: review a large number of papers to map the evidence – focussing on breadth rather than detail; have few preconceived ideas regarding focus (particularly types of MSK/MH in this context); do not necessarily assess individual study quality; and use a narrative approach to analysis, rather than synthesising or aggregating quantitative data.[33] The reader is advised to refer to original SRs for more detail.

Aims

This study aimed to identify which practitioner-based CAM have evidence for both musculoskeletal disorders (MSK) and mental health conditions (MH) in order to identify research priorities in terms of treatment choice and specific patient groups/conditions for a future pragmatic trial of comorbid MSK and MH in UK primary care. The specific aims were to:

- collate the evidence on effectiveness, cost-effectiveness and safety from recent systematic reviews (SRs) of trials of CAM for MSK and MH conditions
- identify areas where there is high quality evidence of effectiveness but sufficient uncertainty to justify a trial
- identify areas where there is also some evidence of cost-effectiveness and safety

Searches

As this was a scoping review, we used a wide range of methods to identify SRs (published, unpublished, in progress). Literature databases were searched (see below for details of searches): AMED, Medline, EMBASE, CINAHL, PsycINFO; Index to theses; Cochrane library; Epistemonikos; SIGLE. Three trial registries were searched (UKCRN; Health service research projects in progress; Prospero). Reference lists of 'overviews of SRs' and reports (from professional/patient organisations) were searched. We emailed key authors in the field. We also asked the project team, steering group and public and patient involvement (PPI) group, and used websites/social media (university websites, Research Gate and Twitter) to access the wider research community. We asked patient and professional organisations to ask their members for any information (by email, newsletters or social media), these included: disease specific organisations e.g. Arthritis Research UK, Back Care and MIND; CAM organisations e.g. Research Council for Complementary Medicine and Complementary and Natural Healthcare Council; primary care organisations e.g. UK Royal College of General Practitioners. We presented at one conference and distributed a flyer at another. We contacted the authors of eligible conference abstracts and protocols to ascertain if the SR was available e.g. submitted or in press.

For complementary medicine we used MeSH terms or subject headings, plus additional terms for CAM which were not indexed. To ensure relevance to UK primary care, we only included CAM which involve practitioner-led treatment. We therefore excluded herbal medicine, as the majority of studies do not involve a practitioner. We included manipulation, manual therapy and mobilisation as techniques commonly practised by some CAM practitioners (as well as conventional practitioners). For musculoskeletal conditions, we used 'musculoskeletal diseases/disorders' as index terms, adding in any which were missing. For mental health, we searched for common, minor mental health disorders and symptoms, excluding long term/severe mental illnesses. Thus, words in

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2
3 titles/abstracts were searched for (rather than subject headings), with reviews needing to include
4 patients with MH symptoms/diagnoses rather than just measuring MH outcomes. Reviews related to
5 a secondary condition such as cancer or cardiovascular disease were included if relevant for a
6 primary care population, i.e. commonly treated in primary care e.g. diabetes, obesity, respiratory
7 conditions but excluding HIV, stroke, critical illness.
8

9 Database searches were conducted in June 2015 and updated in February 2016, in collaboration
10 with a librarian. We used filters for SRs. We excluded reviews published pre-2005, in order to make
11 the final number of papers manageable with minimal impact on our results (given that the majority
12 of SRs were published in 2010 and after (122/158 SRs) . We only included English language reviews.
13 Databases were searched for two topics: complementary medicine + musculoskeletal disorders and
14 complementary medicine + mental health. See Appendix 1 for details and Box 1 for an example
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Box 1: Example search (OVID Medline)

1. "Alexander technique".tw.
2. "bowen technique".tw.
3. craniosacral.tw.
4. ("emotional freedom technique" or EFT).tw.
5. feldenkrais.tw.
6. Pilates.tw.
7. reiki.tw.
8. Shiatsu.tw.
9. trager.tw.
10. "complementary medicine".tw.
11. "integrative medicine".tw.
12. exp complementary therapies/
13. integrative medicine/
14. Manipulation, Spinal/
15. acupuncture/
16. Musculoskeletal manipulations/
17. Mindfulness/
18. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17
19. exp Musculoskeletal System/
20. exp Musculoskeletal Diseases/
21. myalgia/
22. exp back pain/
23. neck pain/
24. chronic pain/
25. headache/ or exp headache disorders, primary/
26. 19 or 20 or 21 or 22 or 23 or 24 or 25
27. ((systematic or structured or evidence or trials).ti. and ((review or overview or look or examination or update\$ or summary).ti. or review.pt.)) or (meta analysis.pt. or meta-analysis/ or "0266-4623".is.) or (reviewed systematically or systematically reviewed).tw. or (1469-493X or 1366-5278 or 1530-440X).is.
28. ("review" or "review academic" or "review tutorial").pt.
29. (medline or medlars or embase or pubmed).tw,sh.
30. (scisearch or psycinfo or psycinfo).tw,sh.
31. (psychlit or psyclit).tw,sh.
32. cinahl.tw,sh.
33. ((hand adj2 search\$) or (manual\$ adj2 search\$)).tw,sh.
34. (electronic database\$ or bibliographic database\$ or computeri#ed database\$ or online database\$).tw,sh.
35. (pooling or pooled or mantel haenszel).tw,sh.
36. (retraction of publication or retracted publication).pt.
37. (peto or dersimonian or der simonian or fixed effect).tw,sh.
38. 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37
39. 28 and 38
40. meta-analysis.pt.
41. meta-analysis.sh.
42. (meta analys\$ or metaanalys\$).tw,sh.
43. (systematic\$ adj5 review\$).tw,sh.
44. (systematic\$ adj5 overview\$).tw,sh.
45. (quantitativ\$ adj5 review\$).tw,sh.
46. (quantitativ\$ adj5 overview\$).tw,sh.
47. (quantitativ\$ adj5 synthesis\$).tw,sh.
48. (methodologic\$ adj5 review\$).tw,sh.
49. (methodologic\$ adj5 overview\$).tw,sh.
50. (integrative research review\$ or research integration).tw.
51. 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48 or 49 or 50
52. 27 or 39 or 51
53. 18 and 26 and 52

We used the inclusion/exclusion criteria (see Appendix 1) to screen the results from each search. This was a multi-stage process involving the whole project team. AL screened the titles of all search results, and DS checked the results, with any disagreements discussed and inclusion criteria

1
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3 amended accordingly. AL then screened the abstracts, which were also independently screened by
4 another author. Results were compared, any disagreements discussed, and the criteria again
5 amended accordingly. Any remaining disagreements were discussed and resolved with a third
6 author. AL then screened the full text of the agreed papers.
7

8 **Data extraction**

9 AL extracted the following data from each SR: author, year, location, CAM/s, health condition/s, for
10 MSK reviews whether MH was included and for MH reviews whether findings applied to MSK
11 populations, methodological features (sources searched, inclusion/exclusion criteria, quality
12 assessment), results and conclusions (effectiveness, safety, cost-effectiveness). Where possible
13 these data were copied and pasted directly to avoid any misinterpretation.
14
15

16 **Quality appraisal of SRs**

17 Although not essential,[33] quality assessment is recommended in scoping reviews.[38] We used a
18 limited quality appraisal to help inform prioritisation: AMSTAR, a validated checklist.[39] Due to
19 time constraints and the number of SRs to be appraised, a simple procedure was followed, using the
20 'search' function in the text of SRs to find particular terms. The emphasis was on obtaining relative
21 scores, allowing ranking of the included reviews, rather than an absolute score of quality. For each of
22 the 11 items on the AMSTAR checklist, a score of 0 was given if they did not meet the criteria, or if
23 information was unavailable, and a score of 1 if the criteria were met. The scores were summed to
24 give a score for each SR out of a total of 11.
25
26

27 Any reviews which scored 5 or less (half of the possible total) on AMSTAR were not considered in the
28 evidence synthesis.
29

30 **Analysis**

31 In line with Arksey & O'Malley's [33] framework for conducting scoping reviews, we used a
32 'descriptive-analytical' method, based in the narrative tradition, applying a common analytical
33 framework to the reviews. Analysis was performed by AL and all authors met regularly to discuss the
34 process and emerging results.
35
36

37 Reviews were placed into a matrix of health condition/symptom vs CAM.

38 Where there was more than one SR on a similar topic, one SR was prioritised, based on recency,
39 breadth, quality and level of analysis (e.g. meta-analysis).
40

41 There were three steps to the analysis: 1) Extraction and narrative synthesis of data from prioritised
42 SRs, 2) Ranking of areas (condition and CAM) using an Excel framework, 3) Analysis of sample size.
43

44 Step 1: For each cell in the matrix, data were synthesised for:
45

- 46 • effectiveness: the conclusions on effectiveness were extracted from the prioritised SR/s.
- 47 • quality of studies: in line with guidance on scoping reviews [33] we did not assess the
48 quality of the individual RCTs in each SR, but synthesised the conclusions from the prioritised
49 review (i.e. we had three categories of quality – poor, moderate or good. Moderate
50 included SRs reporting mixed results.
- 51 • cost effectiveness: any information on cost effectiveness was synthesised across all the
52 included reviews.
- 53 • safety: any information on safety was synthesised across all the included reviews.
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- conclusion and research priorities: conclusions were drawn from across these four domains; research priorities were extracted from each SR's conclusions and summarised regarding the need for further research and any specific suggestions on future methodology.

Step 2: We ranked the areas in the matrix (condition and CAM), based on consideration of the following criteria:

1. **Effectiveness** - areas were ranked highly where there was enough high quality evidence to establish proof of concept, but still key gaps (from the evidence synthesis). Data on effectiveness came from the conclusions of the prioritised SRs) regarding effectiveness and quality
2. **Cost** – areas where there was any indication that the intervention may have potential for cost effectiveness were ranked highly
3. **Safety** - areas where there was any indication that the intervention is safe were ranked highly
4. **Comorbidity** - any indication that the intervention may be effective for comorbid MH and MSK patients were ranked highly

Step 3: once a ranked list of areas had been compiled, information on total sample size for the prioritised SRs (i.e. total number of participants in the trials included in the SR/s) was added to allow further discrimination, classified as: small (<500 participants); medium (501 to 3000); or large (>3000).

Patient and Public Involvement

The scoping study as a whole included a patient and public involvement (PPI) group of seven people with experience of MSK/MH issues, who advised the research team on a variety of issues as the study took shape and progressed. They met 4 times over the study period and provided input into the literature review questions, search strategy and selection criteria. The PPI group also provided ideas on ways to disseminate the findings to the general public and to patient groups.

RESULTS

Search results

Error! Reference source not found. shows the PRISMA flowchart of the searches.[40] Searches resulted in 8393 references – 4304 for MH and 4089 for MSK, plus 3 for MH identified elsewhere (a journal email update). After removing duplicates, Cochrane reviews which were withdrawn, Cochrane reviews which had been updated, or those not in English, 5230 records remained for title screening. This resulted in 486 MH and 739 MSK records for the abstract screening phase. We then excluded 49 (13 MH and 36 MSK) records i.e. editorials, commentaries, abstracts etc. After abstract screening, there remained 444 studies (180 MH and 264 MSK). At this stage, a further 12 records were added – 3 from grey literature (Prospero/Sigle/HSRProj), 5 from conference abstracts, and 4 from the reference lists of overviews of SRs and other key reports. This produced 456 records to be screened at the full text stage, after which 206 records remained: 48 MH, 158 MSK.

During screening at the title stage (AL and DS) there were 49 disagreements (out of 4411 records; 1%). During abstract screening (AL and each of the 6 authors) there were a total of 296 initial

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3 disagreements (out of 1165 records; 25%). Most were resolved by discussion without requiring a
4 third reviewer.

5
6 Of the 158 MSK systematic reviews, 84 were included as high quality (scored 6 or more on AMSTAR):
7 Low back pain,[41-70] fibromyalgia,[71-82] neck pain,[41 83-91] osteoarthritis,[92-102] rheumatoid
8 arthritis,[98 103-106] general MSK pain/conditions,[107-111] shoulder pain/disorders,[112-116]
9 myofascial trigger point pain,[107 117 118] and other MSD conditions.[107 119-124]

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11 The 158 reviews covered 17 different CAMs and 15 different disorders. The overall matrix is shown
12 below in Table 1. Low back pain was by far the most common topic, addressed by 64/158 (40%) of
13 reviews. Fibromyalgia was the next most common, followed by osteoarthritis then neck
14 pain/disorders. Acupuncture was the most common CAM studied (58/158 SRs; 37%), followed by
15 manual therapy (including manipulation and mobilisation). The mean AMSTAR score for
16 methodological quality of MSK reviews was 6/11 (ranging from 0 to 11). Appendix 2 shows which
17 items on the AMSTAR checklist were reported by the reviews.
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Table 1: Matrix of MSK reviews (numbers = number of reviews)		LBP		Fibro-myalgia		Neck pain/disorders		Osteo arthritis		Rheumatoid arthritis		MSK pain/conditions		Myofascial pain		Shoulder pain/disorder		Other		Total ¹
		Total number	High quality	Total number	High quality	Total number	High quality	Total number	High quality	Total number	High quality	Total number	High quality	Total number	High quality	Total number	High quality	Total number	High quality	
Acupuncture related	Acupressure	2	2			2	1					1	1					1	0	6
	Acupuncture	12	6	9	6	5	2	10	6	4	2	4	2	6	3	2	1	6	5	58
	Moxibustion	1	0	1	0			1	0	2	1							1	0	6
Manipulation	Chiropractic	2	1	3	1			1	0					1	0					7
	Manual therapy/spinal manipulation/mobilisation	12	9	8	4	14	9	2	1			1	0	1	0	5	3	3	2	46
	Osteopathy	3	2	2	1							1	1							6
Other	Integrative therapies/Multiple CAM	2	2	2	2															4
	Tai chi	1	1	1	0	1	0	7	5	3	1	1	1							14
	Qigong					1	0	1	0	1	0									3
	Pilates	10	5																	10
	CAM exercise			2	2															2
	Yoga	8	4	1	1	1	0	3	0	1	0	1	1							15
	Mindfulness/meditation	2	0	5	3					2	0	4	2							13
	Relaxation			3	1			1	0	1	0	1	0							6
	Hypnotherapy	1	0	1	1			1	0	1	0									4
	Spa therapy/balneotherapy	2	1	2	1					1	1									5
	TCM bodywork	2	1			1	0					1	0							4
Massage/therapeutic touch	4	2			4	2	1	0	1	0	1	0			1	0	1	1	13	
Homeopathy			2	0															2	
Total¹		64	36	42	23	29	14	28	12	17	5	16	8	8	3	8	4	12	8	158

Of the 48 MH systematic reviews, 27 were high quality (scored 6 or more on AMSTAR): depression, [125-135] anxiety,[125 126 130 134 136-143] sleep,[144-151] stress,[125 126 141] and other.[125] The 49 reviews covered 18 different CAMs and five different categories of MH symptom or disorder. The overall matrix is shown below in Table 2. Many of the reviews included more than one MH condition. Of the 48 reviews 36 (75%) included depression. Meditation, yoga, acupuncture and meditative movement were the most common CAM. Appendix 2 shows which items on the AMSTAR checklist were reported by the reviews.

Table 2 : Matrix of MH reviews (numbers = number of reviews)		Depression		Anxiety		Stress		Insomnia / sleep		Distress (psychological)		Total ¹
		Total number	High quality	Total number	High quality	Total number	High quality	Total number	High quality	Total number	High quality	
Acupuncture	Acupuncture	9	3	2	1			2	1			6
	Auricular acupuncture							3	1			4
Multiple	CAM (multiple) (did not separate CAM in analysis)	1	0	1	0			2	1			4
Meditation/ mindfulness	Mindfulness	3	2	1	1	1	1			1	1	5
	Meditation			3	3	1	1	1	0			9
Exercise	Meditative Movement							3	3			6
	Qigong	4	1	2	1	1	1					5
	Tai chi	4	2	1	0			3	1			5
	Yoga	4	2	3	3	1	0	1	0			8
Other	Homeopathy							1	1			2
	Hypnosis	2	0					2	2			4
	Music therapy	3	2	1	1							2
	Relaxation	3	1	1	1			1	1			4
	Reflexology							1	0			1
	Reiki	1	1	1	1							2
	Spinal manipulation											0
	Massage/Therapeutic touch	2	1	2	2							4
Morita therapy			1	1								2
Total¹		36	15	19	15	4	3	20	11	1	1	48 (27)
1. Note that reviews can occur in more than one row/column												

The following sections present a summary of the areas where we found moderate/good quality evidence of effectiveness (from the prioritised SRs), and where there was some indication of cost-effectiveness and safety (from any of the included SRs).

Evidence for MSK disorders

The highest ranked MSK disorders were low back pain, myofascial trigger point pain, osteoarthritis (OA), neck pain, fibromyalgia and lateral epicondylitis. All other combinations of condition/CAM/comparator were either poor quality, ineffective, or moderate quality but harmful. It should be noted that the quality of evidence is based on the overall assessment of quality of the included RCTs by the SR authors, which is subject to some limitations.

Low back pain

There was good quality evidence in a medium size population for:

- yoga for low back pain – four high-quality reviews.[52 61-63] The prioritised review found evidence for yoga compared to any control, for pain, global improvement and disability in the short-term.[63] There is some evidence of safety (no serious adverse events associated with the yoga),[52 61 63] although none on cost-effectiveness. Evidence for long term effects or compared to other active interventions is of moderate quality.[63]
- osteopathy for low back pain – two high-quality reviews [65 66]. The prioritised review found evidence for osteopathy compared to spinal manipulation/heat/physical therapy, although there is some evidence of harm (2 studies reported minor adverse events).[66]

There was moderate quality evidence in a large population for:

- acupuncture for low back pain – six high-quality reviews.[42 50 51 54 55 152] The prioritised reviews found evidence for acupuncture compared to usual care (for pain, function, wellbeing, disability, ROM, quality of life) and placebo (for pain and quality of life; negative evidence for disability).[51 152] There was some evidence of safety (5% minor adverse events and no serious adverse events)[54 55] and cost-effectiveness (in the short term relative to usual care and to usual care in subjects with back pain).[152]
- spinal manipulation/mobilisation for low back pain – nine high-quality reviews.[42-44 46-49 152 153] The prioritised reviews found evidence compared to other active interventions, although results only apply for chronic low back pain.[44 45 152] There was some evidence of safety (one review identified serious adverse events,[153] but this appeared unrelated to treatment. Minor adverse events included muscle soreness, stiffness, and/or transient increase in pain).[43-45 66 152]

There was moderate quality evidence in a small population for:

- spa/balneotherapy for low back pain – one high-quality review[53] which found evidence compared to medication/exercise (balneotherapy) or usual care (spa therapy), and some evidence it is safe (no adverse events from one study).[53]
- tai chi for low back pain – one high-quality review [55], which found evidence compared to usual care, but nothing on safety, costs or impact on MH outcomes.[55]

Myofascial trigger point pain

Acupuncture for myofascial trigger point pain – three high-quality reviews [107 117 118]. The prioritised review found good quality evidence in a medium size population compared to placebo and other active interventions for pain in the short and medium term but not in the long term.[118] However, there was no evidence for safety, cost-effectiveness, or impact on MH outcomes.[107 117 118]

Osteoarthritis

There was good quality evidence for:

- Acupuncture for OA - six high-quality reviews.[92-97] The prioritised reviews found evidence in a large population for acupuncture for knee or peripheral joint OA compared to placebo for pain.[93 95] There is some evidence of harm (up to 45% frequency of minor adverse events).[92 93]
- Tai chi for OA – five high-quality reviews.[98-102] The prioritised review found evidence in a small population for tai chi for knee OA, compared to usual care or any control, for pain, physical function and stiffness, and physical quality of life, but only in the short term.[100] Some evidence of safety (SRs concluded tai chi is safe).[99-101]

Neck pain

Seven high-quality reviews on manual therapy/manipulation.[83-89 152] For manual therapy plus exercise compared to exercise alone there was good quality evidence in a medium sized population for pain and QoL,[88] and moderate quality evidence in a large population for manipulation compared to medication (but not mobilisation) (cervical manipulation) for pain and function, or any control (thoracic manipulation) for pain.[83] There was moderate quality evidence in a medium sized population for a range of other techniques.[83 88 89] There is some evidence of cost-effectiveness (reduced cost of therapy),[88 89] but also some evidence of potential harm (minor adverse events and rare but devastating adverse effects from manipulation).[83 84]

Two high-quality reviews considered acupuncture for neck pain[152 154]. The prioritised review found moderate quality evidence in a medium sized population compared to placebo or usual care for pain.[90] No evidence of cost-effectiveness.[152]

Fibromyalgia

Five high-quality reviews reported findings for acupuncture.[71-73 75 155] The prioritised review found moderate quality evidence in a small population compared to placebo for stiffness (acupuncture) and for pain and sleep disorders (electroacupuncture), and poor quality evidence in a small population compared to usual care for pain (electroacupuncture).[73] However, there was some evidence that acupuncture is less effective than usual care for MH outcomes in fibromyalgia.[73] There is some evidence of safety (no serious adverse events)[71-73 75 156] but none of cost effectiveness.

Four high-quality reviews provided data on manual therapy.[72 76-78] The prioritised review found poor quality evidence existed in a small population for manual therapy (myofascial release) for both pain and MH (anxiety and depression) compared to placebo.[78] Some evidence of safety (no adverse events)[77] but no evidence of cost-effectiveness.

Lateral epicondylitis

One high-quality review [157] found moderate quality evidence (but the sample size was not reported) for manual therapy (mobilisation with movement) for pain free grip strength and pressure pain threshold in lateral epicondylitis, although no evidence of safety.[157]

Evidence for mental health

No reviews provided good quality evidence for CAM for any MH condition nor any evidence of cost-effectiveness, mainly because the latter was not reported.

Depression

There were two high-quality reviews on mindfulness/meditation for depression.[126 158] Both were prioritised and found moderate quality evidence in a medium size population for MBSR (mindfulness based stress reduction) for depression compared to usual care[125] and for meditation compared to other active interventions,[126] as well as some evidence of effectiveness for both in MSK populations.[125 126] Evidence for mindfulness meditation (other than MBSR/meditation) for depression was poor quality in a medium sized population but there was some evidence of

effectiveness in MSK populations.[126]. Meditation for depression appears safe, as although few meditation trials reported harms, one SR found that 9 trials found no adverse events. [126]

Two high-quality reviews reported on tai chi for depression.[133 135] Both were prioritised and found for older adults, there was moderate quality evidence in a medium sized population for depression, compared to usual care,[135] although it may be less effective in comorbid populations (including some MSK conditions).[133]

There was one high-quality review on relaxation for depression.[130] There was moderate quality evidence (sample size not reported) compared to any control, but no evidence of safety or cost-effectiveness.[130]

Three high-quality reviews provided data on acupuncture for depression.[127-129] The prioritised review found poor quality evidence in a medium sized population compared to medication,[127] with some evidence of safety (no serious adverse events, fewer side effects than antidepressants).[127 128]

Anxiety

There was moderate quality evidence in a medium sized population for:

- meditation for anxiety – three high-quality reviews.[126 138 139] The prioritised review found evidence compared to usual care, placebo or other active interventions.[139] Moving meditation was more effective than static meditation.[139]
- MBSR for anxiety – one high-quality review,[158] which found evidence compared to usual care[125]
- yoga for anxiety – three high-quality reviews.[130 137 159] The prioritised review found evidence for yoga but only for women with breast cancer,[137] and nothing on safety.[136]

Three SRs mentioned that MBSR/meditation appeared safe for anxiety.[126 138 139] Two SRs found that MBSR/meditation was also effective for anxiety (as an outcome) in an MSK population.[125 126]

Sleep disorders

Three high-quality reviews considered meditative/mind-body movement for sleep.[145 146 160] The prioritised review found for older adults, there was moderate quality evidence in a medium sized population, compared to usual care and other active interventions.[144] There was some evidence of safety (no adverse events),[144] and effect on sleep quality in an MSK population.[146]

Stress and distress

There was moderate quality evidence in a medium sized population for:

- mindfulness for stress – one high-quality review,[158] compared to usual care and placebo, and some evidence of effectiveness on stress as an outcome in an MSK population.[125]
- mindfulness for distress– one high-quality review ,[158] compared to usual care, and some evidence of effectiveness on distress as an outcome in an MSK population.[125]

There was only poor quality evidence for all other combinations of condition/CAM/comparator.

Evidence for effectiveness in comorbidity /MH outcomes in MSK

Only one SR provided data on comorbid MSK and MH conditions (depression and a variety of comorbid MSK conditions)[133]. Three SRs provided data on MH outcomes in MSK populations (but did not specify a MH score/diagnosis as inclusion criteria). Tai chi for depression and comorbid

conditions (including MSKs) may be less effective than non-comorbid;[133] MBSR/meditation was effective for MH outcomes in an MSK population;[125 126] meditative/mind-body movement was effective for sleep outcomes in an MSK population;[146] and mindfulness was effective for stress/distress outcomes in an MSK population.[125]

CAM with evidence for both MSK and MH conditions

From the above synthesis, CAM with evidence for both MSK and MH conditions are:

- Acupuncture, however, for MSKs (low back pain, neck pain and fibromyalgia), the effects are compared to usual care and for MH (depression) they are only compared to other active interventions (medication).
- Yoga appears to be effective for both low back pain and anxiety compared to other active interventions, although the anxiety finding was only from studies of women with breast cancer. Meditative movement, which includes yoga, is effective for sleep disorders, although only for older adults (there is also some evidence in chronic pain and fibromyalgia populations).
- Tai chi appears to be effective compared to usual care for low back pain, knee osteoarthritis and depression, in older people (although it appears less effective in comorbid depressed patients). Meditative movement, which includes tai chi, is effective for sleep disorders, although only for older adults (there is some evidence in chronic pain and fibromyalgia populations as well).
- There is evidence of effectiveness for mindfulness/meditation/MBSR in depression, anxiety and distress, which may apply equally to MSK populations.

Update

Since completing this review, we searched for recent SRs and RCTs on the highest ranking topics. These new studies either provide additional evidence for MH outcomes in an MSK population, or evidence supporting our original conclusions.

- Yoga. A new Cochrane review has been published which suggests there is some (very low quality) MH evidence for yoga improving depression (as an outcome not a diagnosis) in low back pain),[161] and two other SRs which support the evidence for yoga for anxiety and depression.[162 163] Recent RCTs suggest that yoga can reduce pain, anxiety and sleep in low back pain[164-166] and sleep may be a mediator for some of the effects of yoga on low back pain.[167]
- MBSR/mindfulness/meditation. Two new SRs provide evidence for mindfulness and MH and for mindfulness in LBP, including some evidence for mindfulness helping with depression (as an outcome not a diagnosis) in LBP (and FMS).[168 169] One trial has shown that mindfulness can improve psychological distress, self-efficacy, and fatigue in chronic pain from inflammatory rheumatic joint diseases,[170] but another found no difference of MSBR compared to a multidisciplinary pain intervention.[171] There is some recent pilot/feasibility evidence for mindfulness-based approaches improving depression in back pain.[172 173]
- Acupuncture (compared to other active interventions). Two new SRs confirm the effectiveness of acupuncture on OA of the knee[174 175] and three others have identified effectiveness of acupuncture for insomnia.[176-178]
- Tai chi. A recent trial shows that tai chi reduces depression in OA of knee compared to physiotherapy.[179]

DISCUSSION

This scoping review has highlighted the large and increasing number of systematic reviews of CAM for MSK and MH disorders, covering 29 different CAM approaches, but identified no high-quality SR evidence for CAM for MSK-MH comorbid populations. Three reviews showed that MBSR/meditation/meditative movement may improve MH outcomes in MSK populations. Acupuncture, yoga, tai chi and mindfulness/meditation have evidence for both MSK and MH conditions. The MSKs with the best evidence (moderate/good quality for effectiveness in a moderate/large population, some indication of cost-effectiveness and safety) were low back pain (yoga, acupuncture, spinal manipulation/mobilisation, osteopathy, spa/balneotherapy and tai chi), myofascial trigger point pain (acupuncture), osteoarthritis (acupuncture, tai chi), neck pain (manipulation/manual therapy), fibromyalgia (acupuncture, manual therapy) and lateral epicondylitis (manual therapy). The MH conditions with the best evidence were depression (MBSR/meditation/mindfulness, tai chi, relaxation and acupuncture), anxiety (meditation/MBSR, moving meditation, yoga), sleep disorders (meditative/mind-body movement), and stress/distress (mindfulness).

The quality of the SRs was very variable. We used a quality tool, AMSTAR, which itself has some limitations, as it includes both methodological and reporting items which are not all necessarily equal in importance, and some of which can be difficult to interpret. Future reviews may consider prioritising certain items on AMSTAR, using the new version of AMSTAR,[180] or using an alternative checklist such as Cochrane or GRADE.

The quality of included trials also varied greatly; it is notable that none of the MH SRs concluded that trial quality was 'good' overall. In addition, assessment of individual RCT study quality is likely to have varied between SR authors, a common issue with CAM studies which rarely fit conventional quality criteria (particularly blinding). Very few of the MSK SRs and none of the mental health SRs mentioned cost-effectiveness. Safety was rarely adequately reported in SRs or the studies they included. Future systematic reviews in the areas of CAM and MSK/MH need to ensure they include *a priori* design/protocol registration, a list of excluded studies, and conflict of interest statements, and use duplicate study selection and data extraction, assess publication bias, and search for grey literature.

Both a strength and limitation of this scoping review was its comprehensive scope which included a wide range of CAM approaches and types of MSK and MH condition, but limited the depth of analysis and discussion.

Other key strengths were the systematic searching techniques, prioritising high-quality SRs using MeSH terms where possible, and search techniques to capture grey and unpublished literature. The whole project team were involved in independently screening the literature search results, although a limitation was that only one author conducted data extraction. We included a quality appraisal of the reviews, although time constraints meant this was an abbreviated assessment. One of the key limitations was the pragmatic decision to only include systematic reviews, which may have led to the exclusion of some CAMs, and means results are subject to the limitations of systematic review and trial methodology, study designs which are sometimes challenging for CAM.[181-183] Another key limitation is our definition of CAM as including a practitioner in its delivery (which relied on review authors reporting these details), which excluded over the counter products or self-care practices,

herbal medicine in particular, but was necessary to limit the scope of the review to CAM which may be appropriate for an integrative care model using referral from a GP. We are aware that by excluding reviews published pre-2005 we may have excluded some topics. We were unable to include non-English publications.

Although CAM is commonly used by patients in the UK,[25] it is not widely available via the NHS. Given the high burden of MSK and MH conditions to individuals and society in the UK, and the prevalence of comorbidity, CAM may be worth considering for some patients, where there is evidence of effectiveness, cost-effectiveness and safety.

One of the main aims of this study was to inform the design of a future trial to assess the effectiveness and cost effectiveness of an integrative medicine (IM) approach for patients with comorbid musculoskeletal and mental health disorders. We have identified four CAM which we feel have potential as they have good evidence in both MSK and MH conditions/symptoms from our scoping review, which was confirmed by update searches – yoga, MBSR/mindfulness/meditation, acupuncture, and tai chi. These results will be combined with the views of conventional and CAM practitioners, the public and NHS providers, to inform the final focus for an RCT.

Systematic reviews of CAMs consistently conclude that further high quality trials are needed, with longer follow up and larger sample sizes, assessing cost-effectiveness and use of appropriate, sensitive, validated outcome measures.

This scoping review suggests that the most promising CAM for future research in the areas of MSK-MH comorbidity are yoga, mindfulness, tai chi and acupuncture. The comorbid populations that would most benefit are less clear, as so few reviews focus on comorbidity, but may include low back pain, osteoarthritis, fibromyalgia and depression, anxiety and sleep.

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Competing interests

No competing interests to declare

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Contributions

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3 AL conducted all literature searches, data extraction and quality appraisal, with the project team
4 (GF, HM, PL, SM and DS) all screening papers for inclusion. The team (GF, HM, PL, SM and DS) all
5 provided input into the inclusion/exclusion criteria. DS advised on the review process. GF, HM, PL,
6 SM and DS were all involved in the prioritisation of topics from the review results. AL drafted the
7 paper and all authors reviewed and edited it.
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9 **Data sharing**

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11 We are able to provide copies of searches and lists of excluded references on request.
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Appendix 1: Inclusion and exclusion criteria for review

Appendix 2: AMSTAR items reported in SRs

Figure 1: PRISMA flowchart

For peer review only

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For peer review only

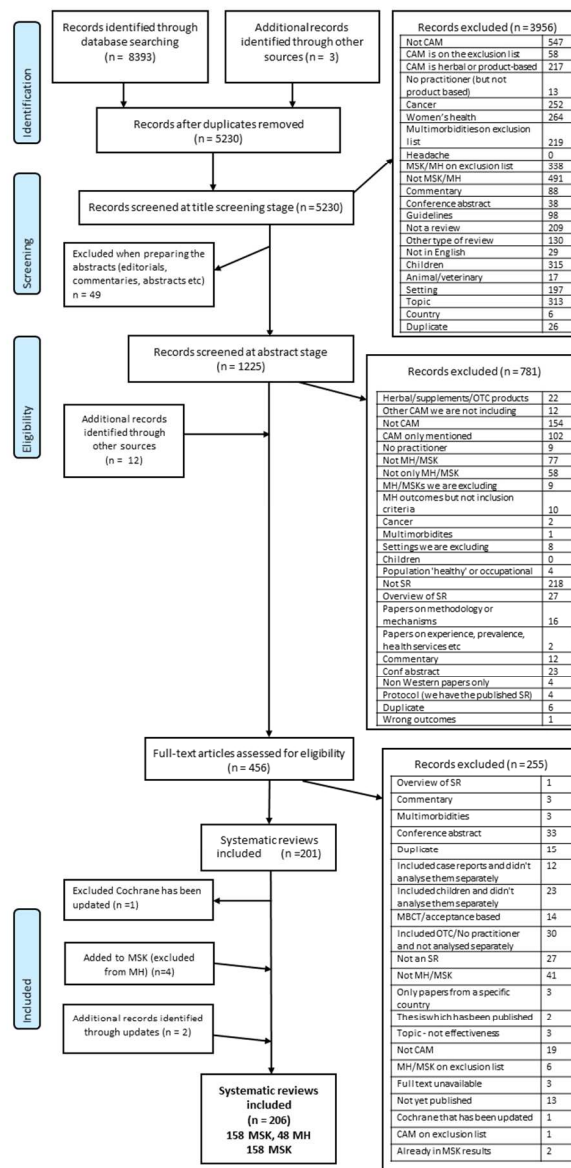


Figure 1: PRISMA flowchart

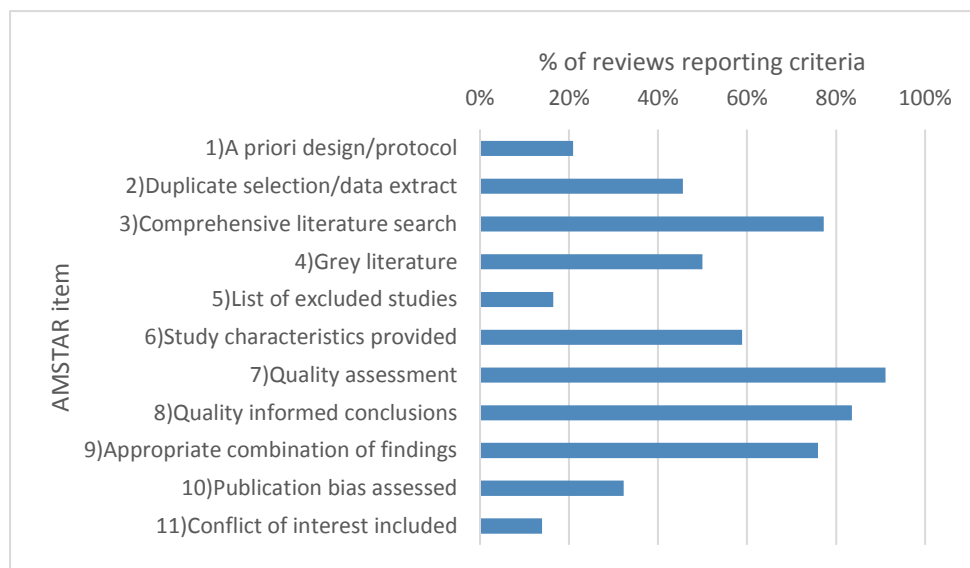
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	Include	Exclude
Types of review	Systematic review and/or meta-analysis	Non-systematic searches; clinical summaries; mechanism reviews; conceptual reviews; historical reviews; herbal monographs; opinions/editorials; reviews of qualitative studies. Reviews including case studies. Reviews only available as an abstract
Topic of review	Efficacy, effectiveness, cost-effectiveness, safety	Any other focus including prevalence, mechanisms
CAM	Any under the MeSH term CAM, except those in the adjacent column (acupuncture (body or ear), acupressure, electroacupuncture, laser acupuncture, Alexander technique, aromatherapy, art therapy, anthroposophy, autogenic training, balneotherapy/hydrotherapy, Bowen, chiropractic, craniosacral, emotional freedom technique, Feldenkrais, guided imagery, kinesiology, homeopathy, hypnosis, integrative medicine, massage, manual therapy or manipulation, meditation, mindfulness, moxibustion, music therapy, naturopathy, osteopathy, Pilates, qi gong, reflexology, relaxation therapy, reiki, shiatsu, spiritual therapies, spiritual healing, tai chi, therapeutic touch, traditional medicine (all types - including TCM approaches such as tuina and guasha), trager, yoga)	Those which are not considered CAM in a UK NHS setting: acoustic stimulation, bee venom acupuncture, biofeedback, breathing exercises, cell therapy, colour therapy, dance therapy, detoxification, deep transverse friction massage, diets, horticultural therapy, light therapy, leech therapy, lifestyle changes, laughter therapy, low level laser therapy (included laser acupuncture which is based on TCM acupuncture points), MBCT, mental healing, magnet therapy, NLP, neural therapy, prayer, play therapy, psychodrama, psychophysiology, prolotherapy, sensory art therapy, suggestion, transcranial magnetic stimulation, TENS rejuvenation, western medicine Herbal medicine/phytotherapy, as the majority of studies do not involve a practitioner Oral or topical CAM which are given to the patient without the input of a practitioner
Intervention details	Practitioner-based CAM only	Over-the-counter, online, self-help only.
	The CAM must be the main focus of the paper.	CAM is only mentioned amongst a list of other active interventions
MSK: muscular diseases	Muscular diseases	Carpal tunnel; compartment syndromes; contracture; craniomandibular disorders; eosinophilia-myalgia syndrome; muscle cramp; muscular abnormalities; muscle neoplasms; mitochondrial myopathies; myositis; paralysis; rhabdomyolysis; spinal stenosis

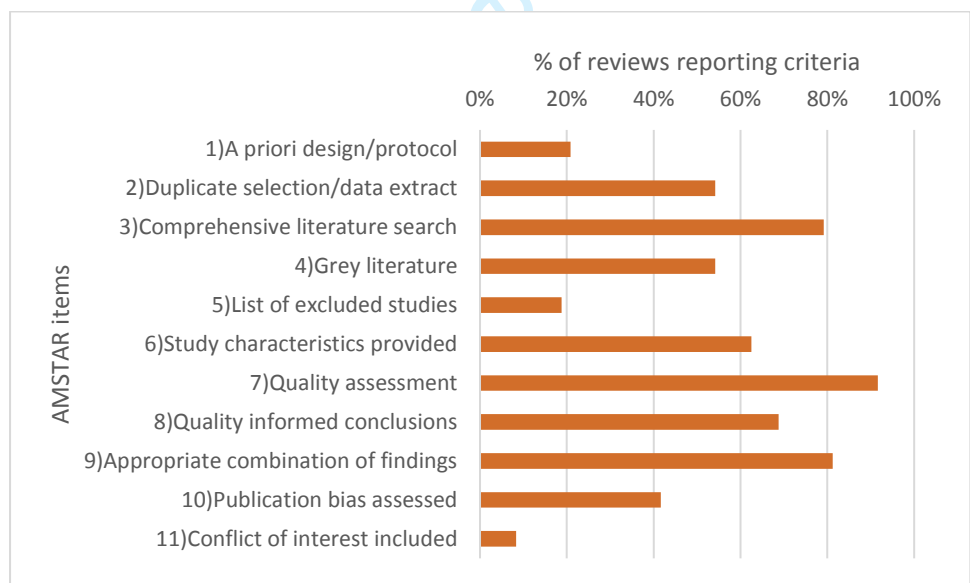
MSK: bone diseases	Osteoarthropathy	All other bone diseases
MSK: rheumatic diseases	Arthritis, Fibromyalgia	Juvenile arthritis; rheumatic fever; sternocostoclavicular; hyperostosis; infectious arthritis; Reiter's disease; rheumatic fever
MSK: other	Musculoskeletal pain	Abdominal pain; cranial pain; ear ache; eye pain; facial pain; headache/migraine; jaw disorders; labour pain; nipple pain; neuralgia; neuropathic pain; pelvic pain; phantom limb pain; sprains
MH (as diagnoses or symptoms not just outcomes)	Anxiety; stress; bipolar; loneliness, low mood	Autism; Alzheimer's; ADHD; child/domestic abuse; delusions; dementia; delirium; eating disorders; learning/intellectual disorders; OCD; Parkinson's; personality disorders; psychotic conditions; psychological trauma; PTSD; quality of life; sexual/gender disorders; substance misuse/abuse; substance abuse; schizophrenia; serious mental health; suicide; sexual disorders;
	Somatoform disorders	Hypochondriasis
	Depression	Postpartum or premenstrual depression; postoperative depression; depressive psychosis; atypical depression
	Stress, stress management	Financial strain; oxidative stress; physiological stress; posttraumatic stress; stress incontinence
	Sleep problems, insomnia	Restless leg syndrome
Other multimorbidities/ populations: serious/long term conditions	Cardiovascular; diabetes; digestive issues; obesity; respiratory;	Asthma; brain injury; cancer chronic fatigue syndrome; cystic fibrosis; epilepsy; hepatitis; HIV/AIDS; kidney disease; multiple sclerosis, stroke/post stroke; sleep apnoea
Other multimorbidities/ populations: acute conditions	None	Injuries, infections
Other multimorbidities/ populations: settings	Carers	Critical illness; intensive care; military; nursing home; palliative care; prisons; surgery
Other multimorbidities/ populations: women's health	-	Endometriosis; infertility; labour/postpartum/pregnancy; PCOS; menopause; menstrual pain; pelvic pain
Other multimorbidities/ populations: disabilities	-	Memory impairment
	-	Hearing loss/impairment
	-	Vision loss/impairment

Population	Adults only \geq 18yrs (include if children were included but reported and analysed separately)	Animal studies or laboratory studies
	Need to be generalisable to GP population	Healthy populations or specific occupations (e.g. nurses, teachers)
Language	English only	Any other language
Date of publication	2005 or later	Pre 2005
For trial registries	Only those which were completed and we had not picked up in other searches	Currently recruiting or not recruiting
Country	Reviews including studies from Western countries	Review of studies from only non-Western countries

AMSTAR items reported in MSK reviews



AMSTAR items reported in MH reviews



BMJ Open

A Scoping Review of Systematic Reviews of Complementary Medicine for Musculoskeletal and Mental Health Conditions.

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Secondary Subject Heading:	Mental health, General practice / Family practice
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A Scoping Review of Systematic Reviews of Complementary Medicine for Musculoskeletal and Mental Health conditions.

Ava Lorenc*, Population Health Sciences, Bristol Medical School, Bristol, UK.

Gene Feder, Population Health Sciences, Bristol Medical School, Bristol, UK

Hugh MacPherson, Department of Health Sciences, University of York, York, UK

Paul Little, Primary Care and Population Sciences Unit, University of Southampton, Southampton, UK

Stewart W Mercer, General Practice and Primary Care, Institute of Health and Wellbeing, University of Glasgow, Scotland, UK

Deborah Sharp, Population Health Sciences, Bristol Medical School, Bristol, UK

*Corresponding author: Ava.lorenc@bristol.ac.uk; 0117 3313902

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ABSTRACT

Objective: To identify potentially effective complementary and alternative medicine (CAM) for musculoskeletal (MSK)- mental health (MH) comorbidity, by synthesising evidence on effectiveness, cost-effectiveness and safety from systematic reviews (SRs).

Design: Scoping review of systematic reviews.

Methods: We searched literature databases, registries, reference lists, and contacted key authors and professional organisations, to identify SRs of randomised controlled trials for CAM for MSK or MH. Inclusion criteria were: published after 2004, studying adults, in English and scoring > 50% on AMSTAR (quality appraisal checklist). SRs were synthesised to identify research priorities, based on moderate/good quality evidence, sample size, and indication of cost-effectiveness and safety.

Results: We included 84 MSK SRs and 27 MH SRs. Only one focussed on MSK-MH comorbidity. Meditative approaches and yoga may improve MH outcomes in MSK populations. Yoga and tai chi had moderate/good evidence for MSK and MH conditions. SRs reported moderate/good quality evidence (any comparator) in a moderate/large population for: low back pain (LBP; yoga, acupuncture, spinal manipulation/mobilisation, osteopathy), osteoarthritis (acupuncture, tai chi), neck pain (acupuncture, manipulation/manual therapy), myofascial trigger point pain (acupuncture), depression (MBSR, meditation, tai chi, relaxation), anxiety (meditation/MBSR, moving meditation, yoga), sleep disorders (meditative/mind-body movement), and stress/distress (mindfulness). The majority of these CAM had some evidence of safety - only three had evidence of harm. There was some evidence of cost effectiveness for spinal manipulation/mobilisation and acupuncture for LBP, and manual therapy/manipulation for neck pain, but few SRs reviewed cost effectiveness and many found no data.

Conclusions: Only one SR studied MSK-MH comorbidity. Research priorities for CAM for both MSK and MH (low back pain, osteoarthritis, depression, anxiety and sleep problems) are yoga, mindfulness, and tai chi. Despite the large number of SRs and the prevalence of comorbidity, more high quality, large randomised controlled trials in comorbid populations are needed.

STRENGTHS AND LIMITATIONS OF THIS STUDY:

1. A comprehensive scoping review covering a wide range of individual MSK and MH conditions, in the notable dearth of SRs/randomised controlled trials in comorbid populations
2. This review used systematic searching and screening techniques
3. Results are limited by our pragmatic choice to only include high-quality (high scoring on AMSTAR) systematic reviews and definition of CAM as including a practitioner in its delivery.
4. Date and language limitations may have excluded some topics.

INTRODUCTION

Musculoskeletal (MSK) and mental health (MH) disorders are two conditions resulting in some of the highest burden in terms of disability, accounting for 30.5% and 21.1% of Years Lived with Disability respectively.[1] Both affect one in four UK adults at some point in their life.[2-4] MSK disorders lead to very high healthcare expenditure and loss of work,[5] in the UK accounting for 7.5 million working days lost annually[6] and 60% of occupational sick leave.[2] In England, it has been estimated that MH costs £105 billion, and treatment costs are expected to rise substantially.[7]

Low back pain is one of the most common health conditions,[8-10] with a mean global general population prevalence (regardless of prevalence period) of 31% [10] and a UK prevalent population of 17.3 million, with 3.1 million adults suffering during an entire year[11], costing the NHS over £500 million/year.[12] In the UK, 8.75 million people sought primary care treatment for osteoarthritis (over a 7 year consultation period)[13] which is estimated to have resulted in £14.8 billion indirect costs.[14]

The most common MH conditions are depression and anxiety.[3 4] In England, 19% of the general adult population reported ever being diagnosed with depression and 6% ever being diagnosed with generalised anxiety disorder.[15] Insomnia is another common MH problem, affecting 6.4% of the UK general population.[16]

There is an increasing recognition of the importance of multimorbidity, that is, the co-existence of two or more physical and/or mental long-term conditions in an individual, which is becoming the norm in the UK.[17-19] In a cross-sectional study in Scotland, 8.3% of primary care patients (36% of those with multimorbidity), had both a physical and a mental health disorder[20] and around 50% of patients with depression had pain symptoms.[21] Long term MSK disorders are closely associated with multimorbidity.[22]

Complementary and alternative medicine (CAM) is “a diverse group of health-related therapies and disciplines which are not considered to be a part of mainstream medical care”, including osteopathy, chiropractic, acupuncture, herbal medicine and homeopathy.[23] Estimates of 12-month prevalence of use of any CAM are 0.3-86% in Europe[24] and 26% in England.[25]

Many MSK and MH conditions, and comorbid MSK and MH, have limited conventional treatment options - ‘effectiveness gaps’, which are potential key areas for CAM.[26 27] Both MH[28-30] and MSK[31 32] are common reasons for patients to use CAM. We used scoping methodology to identify priority areas where CAM may be useful.[33] The overall aim of scoping studies is ‘to map rapidly the key concepts underpinning a research area and the main sources and types of evidence available’ in a formal, systematic and transparent way (which is often lacking in research priority setting exercises).[34] Scoping study methodology was used to identify gaps in the research base and priorities for future research. Scoping work is an essential step in the development of a strategy for the integration of CAM with conventional care.[27] Preliminary searches showed that evidence for comorbid populations was very limited, so we chose to include independent evidence on MSK and MH conditions. This review was part of a wider scoping study, which obtained a breadth of perspectives - the results of this review were combined with findings from consultation with conventional and CAM practitioners, a public survey, and case studies of NHS provision of CAM, to inform the final choice of conditions and CAM approaches for an RCT.

METHODS

The scoping study followed Arksey and O'Malley's [33] framework plus the refinements suggested by Levac et al.[35], Daudt et al [36] and Colquhoun et al.[37] Scoping reviews are broader and more exploratory than systematic reviews. They review a large number of papers to map the evidence – focussing on breadth rather than detail; have few preconceived ideas regarding focus (particularly types of MSK/MH in this context); do not necessarily assess individual study quality; and use a narrative approach to analysis, rather than synthesising or aggregating quantitative data.[33] The reader is advised to refer to original SRs for more detail.

Aims

This study aimed to identify which practitioner-based CAM have evidence for both musculoskeletal disorders (MSK) and mental health conditions (MH) in order to identify research priorities in terms of treatment choice and specific patient groups/conditions for a future pragmatic trial of comorbid MSK and MH in UK primary care. The specific aims were to:

- collate the evidence on effectiveness, cost-effectiveness and safety from recent systematic reviews (SRs) of trials of CAM for MSK and MH conditions
- identify areas where there is high quality evidence of effectiveness but sufficient uncertainty to justify a trial
- identify areas where there is also some evidence of cost-effectiveness and safety

Searches

As this was a scoping review, we used a wide range of methods to identify SRs (published, unpublished, in progress). Literature databases were searched (see below for details of searches): AMED, Medline, EMBASE, CINAHL, PsycINFO; Index to theses; Cochrane library; Epistemonikos; SIGLE. Three trial registries were searched (UKCRN; Health service research projects in progress; Prospero). Reference lists of 'overviews of SRs' and reports (from professional/patient organisations) were searched. We emailed key authors in the field. We also asked the project team, steering group and public and patient involvement (PPI) group, and used websites/social media (university websites, Research Gate and Twitter) to access the wider research community. We asked patient and professional organisations to ask their members for any information (by email, newsletters or social media), these included: disease specific organisations e.g. Arthritis Research UK, Back Care and MIND; CAM organisations e.g. Research Council for Complementary Medicine and Complementary and Natural Healthcare Council; primary care organisations e.g. UK Royal College of General Practitioners. We presented at one conference and distributed a flyer at another. We contacted the authors of eligible conference abstracts and protocols to ascertain if the SR was available e.g. submitted or in press.

For complementary medicine we used MeSH terms or subject headings, plus additional terms for CAM which were not indexed. To ensure relevance to UK primary care, we only included CAM which involve practitioner-led treatment. We therefore excluded herbal medicine, as the majority of studies do not involve a practitioner. We included manipulation, manual therapy and mobilisation as techniques commonly practised by some CAM practitioners (as well as conventional practitioners). For musculoskeletal conditions, we used 'musculoskeletal diseases/disorders' as index terms, adding in any which were missing. For mental health, we searched for common, minor mental health disorders and symptoms, excluding long term/severe mental illnesses. Thus, words in

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2
3 titles/abstracts were searched for (rather than subject headings), with reviews needing to include
4 patients with MH symptoms/diagnoses rather than just measuring MH outcomes. See Appendix 1
5 for a full list of included and excluded non MSK or MH conditions.

6
7 Database searches were conducted in June 2015 and updated in February 2016, in collaboration
8 with a librarian. We used filters for SRs. We excluded reviews published pre-2005, in order to make
9 the final number of papers manageable with minimal impact on our results (given that the majority
10 of SRs were published in 2010 and after (122/158 SRs). We only included English language reviews.
11 Databases were searched for two topics: complementary medicine + musculoskeletal disorders and
12 complementary medicine + mental health. See Appendix 1 for details and Appendix 2 for an example
13 search.
14

15 We used the inclusion/exclusion criteria (see Appendix 1) to screen the results from each search.
16 This was a multi-stage process involving the whole project team. AL screened the titles of all search
17 results, and DS checked the results, with any disagreements discussed and inclusion criteria
18 amended accordingly. AL then screened the abstracts, which were also independently screened by
19 another author. Results were compared, any disagreements discussed, and the criteria again
20 amended accordingly. Any remaining disagreements were discussed and resolved with a third
21 author. AL then screened the full text of the agreed papers.
22
23

24 **Data extraction**

25 AL extracted the following data from each SR: author, year, location, CAM/s, health condition/s, for
26 MSK reviews whether MH was included and for MH reviews whether findings applied to MSK
27 populations, methodological features (sources searched, inclusion/exclusion criteria, quality
28 assessment), results and conclusions (effectiveness, safety, cost-effectiveness). Where possible
29 these data were copied and pasted directly to avoid any misinterpretation.
30
31

32 **Quality appraisal of SRs**

33 Although not essential,[33] quality assessment is recommended in scoping reviews.[38] We used a
34 limited quality appraisal of SRs to help inform prioritisation: AMSTAR, a validated checklist.[39] Due
35 to time constraints and the number of SRs to be appraised, a simple procedure was followed, using
36 the 'search' function in the text of SRs to find particular terms. The emphasis was on obtaining
37 relative scores, allowing ranking of the included reviews, rather than an absolute score of quality.
38 For each of the 11 items on the AMSTAR checklist, a score of 0 was given if they did not meet the
39 criteria, or if information was unavailable, and a score of 1 if the criteria were met. The scores were
40 summed to give a score for each SR out of a total of 11.
41
42

43 Any reviews which scored 5 or less (half of the possible total) on AMSTAR were not considered in the
44 evidence synthesis.
45

46 **Evidence synthesis**

47 In line with Arksey & O'Malley's [33] framework for conducting scoping reviews, we used a
48 'descriptive-analytical' method, based in the narrative tradition, applying a common analytical
49 framework to the reviews. Evidence synthesis was performed by AL and all authors met regularly to
50 discuss the process and emerging results.
51

52 Reviews were placed into a matrix of health condition/symptom vs CAM, for example low back pain
53 and acupuncture (see Tables 1 and 2).
54
55
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Where there was more than one SR in an area, one (occasionally more than one – where they studied different interventions e.g. types of manipulation) was prioritised, based on recency, breadth, quality (AMSTAR score) and level of analysis (e.g. meta-analysis).

There were three steps to the evidence synthesis: step 1) extraction and narrative synthesis of data from prioritised SRs, step 2) ranking of areas (condition vs CAM) using an Excel framework (see below for ranking criteria), step 3) computation of sample size.

Step 1 Data extraction: For each area (condition vs CAM) in the matrix, data were synthesised for:

- effectiveness: the conclusions on effectiveness were extracted from the prioritised SR/s, including information on comparator and outcomes.
- quality of studies: in line with guidance on scoping reviews [33] we did not assess the quality of the individual RCTs in each SR, but synthesised the SR authors' conclusions about quality, from the prioritised review/s. We had three categories of quality – poor, moderate or good. Moderate included SRs reporting mixed results.
- safety: any information on safety was synthesised across all the included SRs
- cost effectiveness: any information on cost effectiveness was synthesised across all the included SRs.

Step 2 Ranking: Using the information extracted in step 1 we ranked the areas in the matrix (condition vs CAM), based on consideration of the following criteria:

1. **Effectiveness** - Areas were ranked highly where there was enough moderate/good quality evidence to establish proof of concept, but still key gaps. Data on effectiveness came from the conclusions of the prioritised SRs regarding effectiveness and quality.
2. **Safety** - areas where there was evidence of harm were ranked lower
3. **Cost** – areas where there was any indication that the intervention may have potential for cost effectiveness were ranked highly
4. **Comorbidity** - any interventions that showed an indication (of any quality) for comorbid MH and MSK patients were ranked highly

Step 3 Sample size: once a ranked list of areas had been compiled, information on total sample size for the prioritised SR/s (i.e. total number of participants in the trials included in the SR/s) was added to allow further discrimination, classified as: small (<500 participants); medium (501 to 3000); or large (>3000).

Patient and Public Involvement

The wider scoping study included a patient and public involvement (PPI) group of seven people with experience of MSK/MH issues, who advised the research team on a variety of issues as the study took shape and progressed. They met 4 times over the study period and provided input into the literature review questions, search strategy and selection criteria. The PPI group also provided ideas on ways to disseminate the findings to the general public and to patient groups.

RESULTS

Search results

Error! Reference source not found. shows the PRISMA flowchart of the searches.[40] Searches resulted in 8393 references – 4304 for MH and 4089 for MSK, plus 3 for MH identified elsewhere (email update sent by journal publisher). After removing duplicates, Cochrane reviews which were withdrawn, Cochrane reviews which had been updated, or those not in English, 5230 records remained for title screening. This resulted in 486 MH and 739 MSK records for the abstract screening phase. We then excluded 49 (13 MH and 36 MSK) records i.e. editorials, commentaries, abstracts etc. After abstract screening, there remained 444 studies (180 MH and 264 MSK). At this stage, a further 12 records were added – 3 from grey literature (Prospero/Sigle/HSRProj), 5 from conference abstracts, and 4 from the reference lists of overviews of SRs and other key reports. This produced 456 records to be screened at the full text stage, after which 206 records remained: 48 MH, 158 MSK.

During screening at the title stage (AL and DS) there were 49 disagreements (out of 4411 records; 1%). During abstract screening (AL and each of the 6 authors) there were a total of 296 initial disagreements (out of 1165 records; 25%). Most were resolved by discussion without requiring a third reviewer.

Of the 158 MSK systematic reviews, 84 were included as high quality (scored 6 or more on AMSTAR): Low back pain,[41-70] fibromyalgia,[71-82] neck pain,[41 83-91] osteoarthritis,[92-102] rheumatoid arthritis,[98 103-106] general MSK pain/conditions,[107-111] shoulder pain/disorders,[112-116] myofascial trigger point pain,[107 117 118] and other MSD conditions.[107 119-124]

The 158 reviews covered 17 different CAMs and 15 different disorders. The overall matrix is shown below in Table 1. Low back pain was by far the most common topic, addressed by 64/158 (40%) of reviews. Fibromyalgia was the next most common, followed by osteoarthritis then neck pain/disorders. Acupuncture was the most common CAM studied (58/158 SRs; 37%), followed by manual therapy (including manipulation and mobilisation). The mean AMSTAR score for methodological quality of MSK reviews was 6/11 (ranging from 0 to 11). Appendix 3 shows which items on the AMSTAR checklist were reported by the reviews.

Table 1: Matrix of MSK reviews (numbers = number of reviews)		Low back pain		Fibro-myalgia		Neck pain/disorders		Osteo arthritis		Rheumatoid arthritis		MSK pain/conditions		Myofascial pain		Shoulder pain/disorder		Other		Total ¹
		Total number	High quality	Total number	High quality	Total number	High quality	Total number	High quality	Total number	High quality	Total number	High quality	Total number	High quality	Total number	High quality	Total number	High quality	
Acupuncture related	Acupressure	2	2			2	1					1	1					1	0	6
	Acupuncture	12	6	9	6	5	2	10	6	4	2	4	2	6	3	2	1	6	5	58
	Moxibustion	1	0	1	0			1	0	2	1							1	0	6
Manipulation	Chiropractic	2	1	3	1			1	0					1	0					7
	Manual therapy/spinal manipulation/ mobilisation	12	9	8	4	14	9	2	1			1	0	1	0	5	3	3	2	46
	Osteopathy	3	2	2	1							1	1							6
Other	Integrative therapies/Multiple CAM	2	2	2	2															4
	Tai chi	1	1	1	0	1	0	7	5	3	1	1	1							14
	Qigong					1	0	1	0	1	0									3
	Pilates	10	5																	10
	CAM exercise			2	2															2
	Yoga	8	4	1	1	1	0	3	0	1	0	1	1							15
	Mindfulness/meditation	2	0	5	3					2	0	4	2							13
	Relaxation			3	1			1	0	1	0	1	0							6
	Hypnotherapy	1	0	1	1			1	0	1	0									4
	Spa therapy/balneotherapy	2	1	2	1					1	1									5
	TCM bodywork	2	1			1	0					1	0							4
Massage/therapeutic touch	4	2			4	2	1	0	1	0	1	0			1	0	1	1	13	
Homeopathy			2	0															2	
Total¹		64	36	42	23	29	14	28	12	17	5	16	8	8	3	8	4	12	8	158 (84)

1. Note that reviews can occur in more than one row/column

Of the 48 MH systematic reviews, 27 were high quality (scored 6 or more on AMSTAR): depression, [125-135] anxiety,[125 126 130 134 136-143] sleep,[144-151] stress,[125 126 141] and other.[125] The 48 reviews covered 18 different CAMs and five different categories of MH symptom or disorder. The overall matrix is shown below in Table 2. Many of the reviews included more than one MH condition. Of the 48 reviews, 36 (75%) included depression. Meditation, yoga, acupuncture and meditative movement were the most common CAM. Appendix 3 shows which items on the AMSTAR checklist were reported by the reviews.

Table 2 : Matrix of MH reviews (numbers = number of reviews)		Depression		Anxiety		Stress		Insomnia / sleep		Distress (psychological)		Total ¹
		Total number	High quality	Total number	High quality	Total number	High quality	Total number	High quality	Total number	High quality	
Acupuncture	Acupuncture	9	3	2	1			2	1			6
	Auricular acupuncture							3	1			4
Multiple	CAM (multiple) (did not separate CAM in analysis)	1	0	1	0			2	1			4
Meditation/ mindfulness	Mindfulness	3	2	1	1	1	1			1	1	5
	Meditation			3	3	1	1	1	0			9
Exercise	Meditative Movement							3	3			6
	Qigong	4	1	2	1	1	1					5
	Tai chi	4	2	1	0			3	1			5
	Yoga	4	2	3	3	1	0	1	0			8
Other	Homeopathy							1	1			2
	Hypnosis	2	0					2	2			4
	Music therapy	3	2	1	1							2
	Relaxation	3	1	1	1			1	1			4
	Reflexology							1	0			1
	Reiki	1	1	1	1							2
	Spinal manipulation											0
	Massage/therapeutic touch	2	1	2	2							4
Morita therapy			1	1								2
Total¹		36	15	19	15	4	3	20	11	1	1	48 (27)
1. Note that reviews can occur in more than one row/column												

The following sections present a summary of the areas where we found moderate/good quality evidence of effectiveness (from the prioritised SRs). For those conditions with evidence for more than one intervention we have presented the results in tables.

Evidence for MSK disorders

The areas where there was moderate/good quality evidence were low back pain, myofascial trigger point pain, osteoarthritis (OA), neck pain, fibromyalgia and lateral epicondylitis. It should be noted that the SR quality of evidence is based on the overall assessment of quality of the included RCTs by the SR authors, which is subject to some limitations.

Low back pain

Moderate/good quality evidence for low back pain (see table 3) was found as follows:

- yoga: four high-quality reviews,[52 61-63] one prioritised[63]
- osteopathy: two high-quality reviews,[65 66] one prioritised[66]
- acupuncture: six high-quality reviews, [41 42 50 51 54 55] two prioritised - as highest quality [41] and most recent[51]
- spinal manipulation/mobilisation: nine high-quality reviews,[41-49] three prioritised (due to differences in types of back pain and interventions included)[41 44 45]
- spa/balneotherapy: one high-quality review[53]
- tai chi: one high-quality review[55]

Comparator	Quality	Population size	CAM	Safety	Cost-effectiveness
Active intervention	Good	Medium	Osteopathy[66]	Some evidence of harm[66] ¹	NR
	Moderate	Large	Spinal manipulation/mobilisation (chronic only)[41 44 45]	Some evidence of safety [45] ²	Mixed results – some evidence of CE [48] ⁴
		Medium	Yoga[63]	Some evidence of safety [52 61 63] ³	No data
		Small	Balneotherapy [53]	Some evidence of safety[53]	NR
Usual care	Moderate	Large	Acupuncture [41 51] (for pain, function, wellbeing, disability, ROM, quality of life)	Some evidence of safety[54 55] ⁶	Some evidence of CE [41] ⁷
		Small	Spa therapy[53]	Some evidence of safety[53] ⁵	NR
			Tai chi [55]	NR	NR
Placebo	Moderate	Large	Acupuncture (for pain and quality of life; negative evidence for disability). [41 51]	Some evidence of safety[54 55] ⁶	Some evidence of CE [41] ⁷

NR = not reported (by SRs)

CE = cost effectiveness

1. Two studies reported minor adverse events
2. One review identified serious adverse events, but this appeared unrelated to treatment. Minor adverse events included muscle soreness, stiffness, and/or transient increase in pain
3. No serious adverse events associated with the yoga
4. Mixed results regarding cost-effectiveness[41], with limited evidence that manual therapy is more cost-effective than usual care [48]
5. No adverse events from one study
6. 5% minor adverse events and no serious adverse events
7. Short-term only

Osteoarthritis

Moderate/good quality evidence for osteoarthritis (see table 4) was found as follows:

- acupuncture: six high-quality reviews.[92-97], two prioritised – [93] as a Cochrane review and [95] as most recent
- tai chi: five high-quality reviews.[98-102], one prioritised[100]

Comparator	Quality	Population size	CAM	Safety	Cost-effectiveness
Placebo	Good	Large	Acupuncture [93 95] ¹	some evidence of harm[92 93] ²	NR
Usual care	Moderate	Small	Tai chi [100] ³	Some evidence of safety[99-101] ⁴	NR

NR = not reported (by SRs)

1. Compared to pulsed electromagnetic fields, muscle-strengthening or aerobic exercise, weight loss
2. Up to 45% frequency of minor adverse events
3. Only in the short-term
4. SRs concluded tai chi is safe

Neck pain

Moderate/good quality evidence for neck pain (see table 5) was found as follows:

- manual therapy/manipulation: eight high-quality reviews[41 83-89], three were prioritised due to differing inclusion criteria.[83 88 89]
- Acupuncture: two high-quality reviews, [41 90] one prioritised[90]

Comparator	Quality	Population size	CAM	Safety	Cost-effectiveness
Active intervention	Good	Medium	Manual therapy[88] ¹	some evidence of	some evidence of CE[88 89] ⁴

				potential harm[83 84] ³	
	Moderate	Large	Manipulation[83] ^{2,5}	some evidence of potential harm[83 84] ³	some evidence of CE[88 89] ⁴
	Moderate	Small	Manual therapy[89] ⁶	some evidence of potential harm[83 84] ³	some evidence of CE[88 89] ⁴
Placebo	Moderate	Medium	Acupuncture [90]	some evidence of safety [90]	No data [41]
Usual care	Moderate	Medium	Acupuncture [90]	some evidence of safety [90]	No data [41]
<p>CE = cost effectiveness</p> <ol style="list-style-type: none"> 1. Manual therapy plus exercise compared to exercise alone 2. Compared to medication 3. Reduced cost of therapy 4. Minor adverse events and rare but devastating adverse effects from manipulation 5. Also showed effectiveness for pain compared to any control 6. Mobilisation, manipulation and soft tissue techniques <p>There was moderate quality evidence in a medium sized population for a range of other techniques.[83 88 89]</p>					

Fibromyalgia

Acupuncture for fibromyalgia - five high-quality reviews,[71-74 82] one prioritised [73]. The prioritised review found moderate quality evidence in a small population compared to placebo for stiffness (acupuncture) and for pain and sleep disorders (electroacupuncture). However, there was some evidence that acupuncture is less effective than usual care for MH outcomes in fibromyalgia.[73] There is some evidence of safety (no serious adverse events) [71-74 82] but none of cost effectiveness.

Myofascial trigger point pain

Acupuncture for myofascial trigger point pain – three high-quality reviews [107 117 118]. The prioritised review found good quality evidence in a medium size population compared to placebo and other active interventions for pain in the short and medium term but not in the long term.[118] However, safety, cost-effectiveness, or impact on MH outcomes were not reported.[107 117 118]

Lateral epicondylitis

One high-quality review [121] found moderate quality evidence for manual therapy (mobilisation with movement)) but the comparator and sample size were not reported so we are unable to include it in our synthesis.

Evidence for mental health

No reviews provided good quality evidence for CAM for any MH condition nor any evidence of cost-effectiveness, mainly because the latter was not reported.

Depression

Moderate quality evidence for depression (see table 6) was found as follows:

- mindfulness/meditation: two high quality reviews [125 126] both prioritised as included different types of meditation/mindfulness/MBSR or populations
- tai chi: two high quality reviews [133 135] both prioritised as [135] only reviewed studies of older people ([133] found only poor quality evidence)
- relaxation: one high quality review[130] but comparator and sample size were not reported so it is not included here

Comparator	Quality	Population size	CAM	Safety	Cost-effectiveness
Active intervention	Moderate	Medium	Meditation[126] ¹	Some evidence of safety[126]	No data [125]
Usual care	Moderate	Medium	MBSR (mindfulness based stress reduction) [125] ¹	Some evidence of safety[126]	No data [125]
			Tai chi[135] ^{3,4}	No data[135]	No data[135]
NR = not reported (by SRs) <ol style="list-style-type: none"> 1. Also some evidence of effectiveness for both in MSK populations.[125 126] 2. Nine trials found no adverse events 3. Older adults only 4. May be less effective in comorbid populations (including some MSK conditions).[133] 					

Anxiety

Moderate quality evidence for anxiety (see table 7) was found as follows:

- Meditation, including moving meditation (yoga, tai chi and qi gong): three high-quality reviews,[126 138 139] one prioritised[139]
- MBSR: one high-quality review[125]
- Yoga: three high-quality reviews,[130 136 137] one prioritised[137]

Comparator	Quality	Population size	CAM	Safety	Cost-effectiveness
Active intervention	Moderate	Medium	Meditation[139] ^{1,2}	Some evidence of safety [126 138]	NR

				139]	
	Moderate	Medium	Yoga[137] ³	No data[136]	NR
Placebo	Moderate	Medium	Meditation[139] 1,2	Some evidence of safety [126 138 139]	NR
Usual care	Moderate	Medium	Meditation[139] 1,2	Some evidence of safety [126 138 139]	NR
	Moderate	Medium	MBSR[125] ²	Some evidence of safety [126 138 139]	NR
<p>NR = not reported (by SRs)</p> <ol style="list-style-type: none"> 1. Moving meditation (tai chi, qi gong or yoga) was more effective than static meditation 2. MBSR/meditation was also effective for anxiety (as an outcome) in an MSK population.[125 126]. 3. For women with breast cancer only 					

Sleep disorders

Three high-quality reviews considered meditative/mind-body movement for sleep.[144-146] The prioritised review found for older adults, there was moderate quality evidence in a medium sized population, compared to usual care and other active interventions.[144] There was some evidence of safety (no adverse events),[144] and effect on sleep quality in an MSK population.[146] No cost-effectiveness data reported.

Stress and distress

There was one high-quality review of mindfulness for stress and distress. [125] For stress, they found moderate quality evidence in a medium sized population compared to usual care and placebo, and some evidence of effectiveness on stress as an outcome in an MSK population.[125] No data on cost-effectiveness; no data on safety. For distress they found moderate quality evidence in a medium sized population compared to usual care, and some evidence of effectiveness on distress as an outcome in an MSK population.[125] No data on cost-effectiveness; safety not reported.

There was only poor quality evidence for all other combinations of MH condition/CAM/comparator.

Evidence for effectiveness in comorbidity /MH outcomes in MSK

Only one SR provided data on comorbid MSK and MH conditions (depression and a variety of comorbid MSK conditions)[133]. Three SRs provided data on MH outcomes in MSK populations (but did not specify a MH score/diagnosis as inclusion criteria). Tai chi for depression and comorbid conditions (including MSKs) may be less effective than for depression alone;[133] MBSR/meditation was effective for MH outcomes (depression, anxiety, stress/distress) in an MSK population;[125 126] meditative/mind-body movement was effective for sleep outcomes in an MSK population.[146]

CAM with evidence for both MSK and MH conditions

From the above synthesis, CAM with moderate/good quality evidence for both MSK and MH conditions (from separate SRs) are yoga and tai chi. Yoga appears to be effective for both low back pain and anxiety compared to other active interventions, although the anxiety finding was only from studies of women with breast cancer. Meditative movement, which includes yoga, is effective for sleep disorders, although only for older adults (there is also some evidence in chronic pain and fibromyalgia populations). Tai chi appears to be effective compared to usual care for low back pain, knee osteoarthritis and depression, in older people (although it appears less effective in comorbid depressed patients). Meditative movement, which includes tai chi, is effective for sleep disorders, although only for older adults (there is some evidence in chronic pain and fibromyalgia populations as well).

Update

Since completing this review, in July 2017 we searched for recent SRs on the highest ranking topics (results are not included in tables 3 to 7 above). These either provide additional evidence for MH outcomes in an MSK population, or evidence supporting our original conclusions.

- Yoga: a new Cochrane review for low back pain has been published which suggests there is moderate quality evidence for yoga compared to other active interventions for pain, and for function at 6 months only, although they also found moderate quality evidence of harm for yoga (primarily exacerbation of back pain).[152] They also found very low quality MH evidence for yoga improving depression (as an outcome not a diagnosis) in low back pain (comparator not stated),[152]
- MBSR/mindfulness/meditation: a new SR provides evidence for mindfulness and MH, including high quality evidence (sample size not reported) for mindfulness helping with depression (compared to all controls – usual care, and active interventions (education, stress management); as an outcome not a diagnosis) in low back pain (and fibromyalgia).[153] Another SR of mindfulness for low back pain was recently published but cannot be included as there were no conclusions regarding study quality.[154]
- Acupuncture (compared to other active interventions). Two new SRs confirm the effectiveness of acupuncture for OA knee, with moderate quality evidence in a large sample compared to active interventions and placebo [155 156].

DISCUSSION

This scoping review has highlighted the large and increasing number of systematic reviews of CAM for MSK and MH disorders, covering 29 different CAM approaches, but identified no high-quality evidence for CAM for MSK-MH comorbid populations. Three reviews showed that MBSR/meditation/meditative movement may improve MH outcomes in MSK populations. Acupuncture, yoga, tai chi and mindfulness/meditation have evidence for both MSK and MH conditions.

We have identified moderate/good quality evidence (as reported by SR authors) for effectiveness (any comparator) in a moderate/large population for : low back pain (yoga, acupuncture, spinal manipulation/mobilisation, osteopathy), osteoarthritis (acupuncture, tai chi), neck pain

1
2
3 (acupuncture, manipulation/manual therapy), myofascial trigger point pain (acupuncture),
4 depression (MBSR, meditation, tai chi, relaxation), anxiety (meditation/MBSR, moving meditation,
5 yoga), sleep disorders (meditative/mind-body movement), and stress/distress (mindfulness). The
6 majority of these CAM had some evidence of safety - only three had evidence of harm – osteopathy
7 for low back pain, acupuncture for osteoarthritis and manipulation/manual therapy for neck pain.
8 There was some evidence of cost effectiveness for spinal manipulation/mobilisation and
9 acupuncture for low back pain, and manual therapy/manipulation for neck pain, but few SRs
10 reviewed cost effectiveness and many found no data.
11

12 Regarding comorbidity, from our original searches the only evidence for MH outcomes in an MSK
13 population (not necessarily with MH conditions) was for MBSR/meditation/meditative
14 movement/mindfulness. Tai chi and yoga were effective for MSK and MH conditions in separate SRs
15 (not comorbid populations). Our 2017 update found new (but poor quality) evidence for yoga in
16 MSK-MH comorbidity and more evidence for mindfulness in MSK MH comorbidity.
17
18

19 Some of these studies showed effectiveness compared to an active comparator (spinal
20 manipulation/mobilisation and yoga for low back pain; meditation for depression and anxiety),
21 providing some evidence that these interventions have effects over and above non-specific
22 attention.
23

24 The quality of the SRs was very variable. We used a quality tool, AMSTAR, which itself has some
25 limitations, as it includes both methodological and reporting items which are not all necessarily
26 equal in importance, and some of which can be difficult to interpret. Future reviews may consider
27 prioritising certain items on AMSTAR, using the new version of AMSTAR,^[157] or using an alternative
28 critical appraisal tool such as the Oxford Centre for Evidence based medicine checklist
29 (<https://www.cebm.net/2014/06/critical-appraisal/>). An assessment of risk-of-bias, using for
30 example ROBIS, may be useful in addition to these quality assessments.
31

32 The quality of included trials also varied greatly; it is notable that none of the MH SRs concluded that
33 trial quality was ‘good’ overall. In addition, assessment of individual RCT study quality is likely to
34 have varied between SR authors, a common issue with CAM studies which rarely fit conventional
35 quality criteria (particularly blinding). Very few of the MSK SRs and none of the mental health SRs
36 mentioned cost-effectiveness. Safety was rarely adequately reported in SRs or the studies they
37 included. Future systematic reviews in the areas of CAM and MSK/MH need to ensure they include *a*
38 *priori* design/protocol registration, a list of excluded studies, and conflict of interest statements, and
39 use duplicate study selection and data extraction, assess publication bias, and search for grey
40 literature.
41
42

43 Both a strength and limitation of this scoping review was its comprehensive scope which included a
44 wide range of CAM approaches and types of MSK and MH condition, but limited the depth of
45 analysis and discussion.
46

47 Other key strengths were the systematic searching techniques, prioritising high-quality SRs using
48 MeSH terms where possible, and search techniques to capture grey and unpublished literature. The
49 whole project team were involved in independently screening the literature search results, although
50 a limitation was that only one author conducted data extraction. We included a quality appraisal of
51 the reviews, although time constraints meant this was an abbreviated assessment. One of the key
52 limitations was the pragmatic decision to only include systematic reviews, which may have led to the
53 exclusion of some CAMs, and means results are subject to the limitations of systematic review and
54 trial methodology, study designs which are sometimes challenging for CAM.^[158-160] Another key
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59

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2
3 limitation is our definition of CAM as including a practitioner in its delivery (which relied on review
4 authors reporting these details), which excluded over the counter products or self-care practices,
5 herbal medicine in particular, but was necessary to limit the scope of the review to CAM which may
6 be appropriate for an integrated care model using referral from a GP. We are aware that by
7 excluding reviews published pre-2005 we may have excluded some topics. We were unable to
8 include non-English publications.
9

10 Although CAM is commonly used by patients in the UK,[25] it is not widely available via the NHS.
11 Given the high burden of MSK and MH conditions to individuals and society in the UK, and the
12 prevalence of comorbidity, CAM may be worth considering for some patients, where there is
13 evidence of effectiveness, cost-effectiveness and safety.
14

15 One of the main aims of this study was to inform the design of a future trial to assess the
16 effectiveness and cost effectiveness of an integrated medicine (IM) approach for patients with
17 comorbid musculoskeletal and mental health disorders. We will combine the results of this review
18 with the views of conventional and CAM practitioners, the public and NHS providers, to inform the
19 final focus for an RCT. Our proposed trial would be pragmatic and focus on overall effectiveness, so
20 interventions with evidence compared to any comparator are potential candidates.
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23 Systematic reviews of CAMs consistently conclude that further high quality trials are needed, with
24 longer follow up and larger sample sizes, assessing cost-effectiveness and use of appropriate,
25 sensitive, validated outcome measures.
26

27 Based on our criteria of study quality, safety, cost-effectiveness, and evidence for MSK MH
28 comorbidity, this scoping review suggests that the most promising CAM for future research in the
29 area of MH-MSK comorbidity are: mindfulness (evidence for MH in MSK populations and evidence of
30 safety), yoga (evidence for MSK and MH conditions), and tai chi (evidence for MSK and MH
31 conditions, evidence of safety). The comorbid populations that would benefit most are less clear, as
32 so few reviews focus on comorbidity, but may include low back pain, osteoarthritis, and depression,
33 anxiety and sleep.
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39
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42 *Multimorbid Patients With Mental Health And Musculoskeletal Problems In Primary Care In The UK: A Scoping*
43 *Study*). The views expressed in the publication are those of the author(s) and not necessarily those of
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49 Competing interests

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51 No competing interests to declare
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5

6 **Contributions**

7
8 AL conducted all literature searches, data extraction and quality appraisal, with the project team
9 (GF, HM, PL, SM and DS) all screening papers for inclusion. The team (GF, HM, PL, SM and DS) all
10 provided input into the inclusion/exclusion criteria. DS advised on the review process. GF, HM, PL,
11 SM and DS were all involved in the prioritisation of topics from the review results. AL drafted the
12 paper and all authors reviewed and edited it.
13

14 **Data sharing**

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16 We are able to provide copies of searches and lists of excluded references on request.
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Appendix 1: Inclusion and exclusion criteria for review

Appendix 2: Example search

Appendix 3: AMSTAR items reported in SRs

Figure 1: PRISMA flowchart

For peer review only

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For peer review only

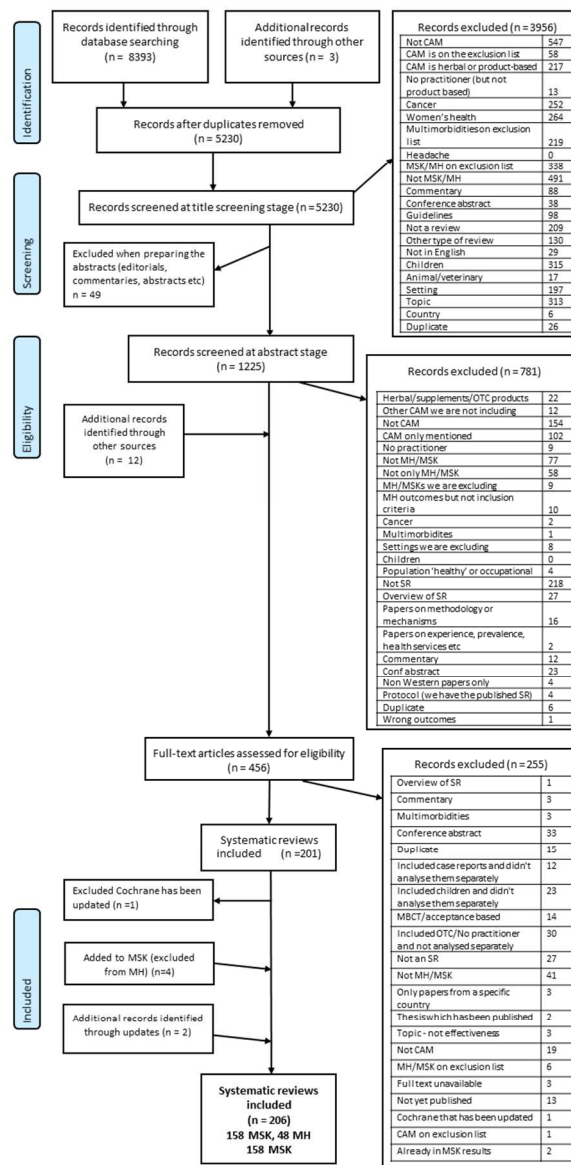


Figure 1: PRISMA flowchart

62x121mm (300 x 300 DPI)

Appendix 1: Inclusion and exclusion criteria

	Include	Exclude
Types of review	Systematic review and/or meta-analysis	Non-systematic searches; clinical summaries; mechanism reviews; conceptual reviews; historical reviews; herbal monographs; opinions/editorials; reviews of qualitative studies. Reviews including case studies. Reviews only available as an abstract
Topic of review	Efficacy, effectiveness, cost-effectiveness, safety	Any other focus including prevalence, mechanisms
CAM	Any under the MeSH term CAM, except those in the adjacent column (acupuncture (body or ear), acupressure, electroacupuncture, laser acupuncture, Alexander technique, aromatherapy, art therapy, anthroposophy, autogenic training, balneotherapy/hydrotherapy, Bowen, chiropractic, craniosacral, emotional freedom technique, Feldenkrais, guided imagery, kinesiology, homeopathy, hypnosis, integrative medicine, massage, manual therapy or manipulation, meditation, mindfulness, moxibustion, music therapy, naturopathy, osteopathy, Pilates, qi gong, reflexology, relaxation therapy, reiki, shiatsu, spiritual therapies, spiritual healing, tai chi, therapeutic touch, traditional medicine (all types - including TCM approaches such as tuina and guasha), trager, yoga)	Those which are not considered CAM in a UK NHS setting: acoustic stimulation, bee venom acupuncture, biofeedback, breathing exercises, cell therapy, colour therapy, dance therapy, detoxification, deep transverse friction massage, diets, horticultural therapy, light therapy, leech therapy, lifestyle changes, laughter therapy, low level laser therapy (included laser acupuncture which is based on TCM acupuncture points), MBCT, mental healing, magnet therapy, NLP, neural therapy, prayer, play therapy, psychodrama, psychophysiology, prolotherapy, sensory art therapy, suggestion, transcranial magnetic stimulation, TENS rejuvenation, western medicine Herbal medicine/phytotherapy, as the majority of studies do not involve a practitioner Oral or topical CAM which are given to the patient without the input of a practitioner
Intervention details	Practitioner-based CAM only The CAM must be the main focus of the paper.	Over-the-counter, online, self-help only. CAM is only mentioned amongst a list of other active interventions
MSK: muscular diseases	Muscular diseases	Carpal tunnel; compartment syndromes; contracture; craniomandibular disorders; eosinophilia-myalgia syndrome; muscle cramp; muscular abnormalities; muscle neoplasms;

		mitochondrial myopathies; myositis; paralysis; rhabdomyolysis; spinal stenosis
MSK: bone diseases	Osteoarthropathy	All other bone diseases
MSK: rheumatic diseases	Arthritis, Fibromyalgia	Juvenile arthritis; rheumatic fever; sternocostoclavicular; hyperostosis; infectious arthritis; Reiter's disease; rheumatic fever
MSK: other	Musculoskeletal pain	Abdominal pain; cranial pain; ear ache; eye pain; facial pain; headache/migraine; jaw disorders; labour pain; nipple pain; neuralgia; neuropathic pain; pelvic pain; phantom limb pain; sprains
MH (as diagnoses or symptoms not just outcomes)	Anxiety; stress; bipolar; loneliness, low mood	Autism; Alzheimer's; ADHD; child/domestic abuse; delusions; dementia; delirium; eating disorders; learning/intellectual disorders; OCD; Parkinson's; personality disorders; psychotic conditions; psychological trauma; PTSD; quality of life; sexual/gender disorders; substance misuse/abuse; substance abuse; schizophrenia; serious mental health; suicide; sexual disorders;
	Somatoform disorders	Hypochondriasis
	Depression	Postpartum or premenstrual depression; postoperative depression; depressive psychosis; atypical depression
	Stress, stress management	Financial strain; oxidative stress; physiological stress; posttraumatic stress; stress incontinence
	Sleep problems, insomnia	Restless leg syndrome
Other multimorbidities/populations: serious/long term conditions	Cardiovascular; diabetes; digestive issues; obesity; respiratory;	Asthma; brain injury; cancer chronic fatigue syndrome; cystic fibrosis; epilepsy; hepatitis; HIV/AIDS; kidney disease; multiple sclerosis, stroke/post stroke; sleep apnoea
Other multimorbidities/populations: acute conditions	None	Injuries, infections
Other multimorbidities/populations: settings	Carers	Critical illness; intensive care; military; nursing home; palliative care; prisons; surgery
Other multimorbidities/populations: women's health	-	Endometriosis; infertility; labour/postpartum/pregnancy; PCOS; menopause; menstrual pain; pelvic pain
	-	Memory impairment

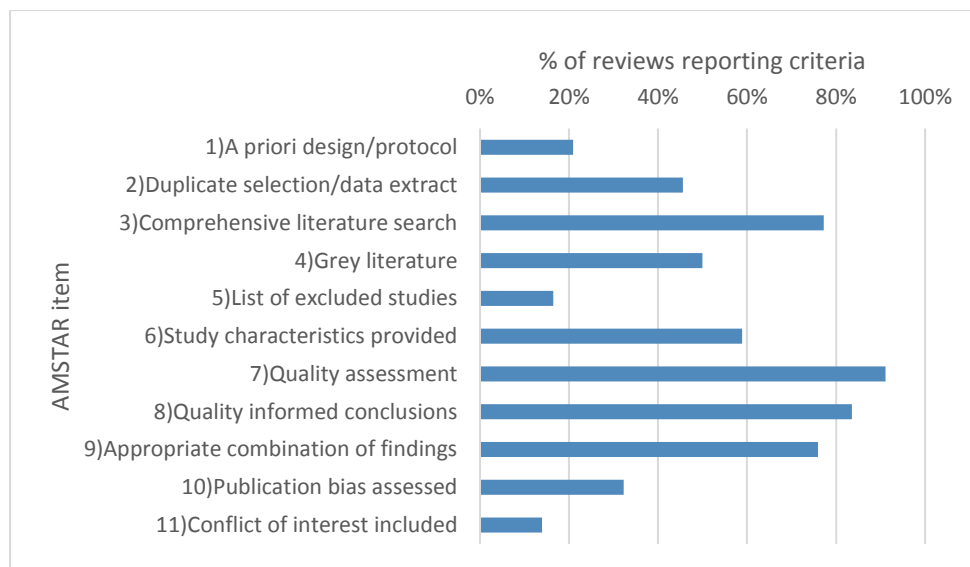
Other multimorbidities/ populations: disabilities	-	Hearing loss/impairment
	-	Vision loss/impairment
Population	Adults only \geq 18yrs (include if children were included but reported and analysed separately)	Animal studies or laboratory studies
	Need to be generalisable to GP population	Healthy populations or specific occupations (e.g. nurses, teachers)
Language	English only	Any other language
Date of publication	2005 or later	Pre 2005
For trial registries	Only those which were completed and we had not picked up in other searches	Currently recruiting or not recruiting
Country	Reviews including studies from Western countries	Review of studies from only non-Western countries

Appendix 2 Example search (OVID Medline)

1. "Alexander technique".tw.
2. "bowen technique".tw.
3. craniosacral.tw.
4. ("emotional freedom technique" or EFT).tw.
5. feldenkrais.tw.
6. Pilates.tw.
7. reiki.tw.
8. Shiatsu.tw.
9. trager.tw.
10. "complementary medicine".tw.
11. "integrative medicine".tw.
12. exp complementary therapies/
13. integrative medicine/
14. Manipulation, Spinal/
15. acupuncture/
16. Musculoskeletal manipulations/
17. Mindfulness/
18. **1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17**
19. exp Musculoskeletal System/
20. exp Musculoskeletal Diseases/
21. myalgia/
22. exp back pain/
23. neck pain/
24. chronic pain/
25. headache/ or exp headache disorders, primary/
26. **19 or 20 or 21 or 22 or 23 or 24 or 25**
27. ((systematic or structured or evidence or trials).ti. and ((review or overview or look or examination or update\$ or summary).ti. or review.pt.) or (meta analysis.pt. or meta-analysis/ or "0266-4623".is.) or (reviewed systematically or systematically reviewed).tw. or (1469-493X or 1366-5278 or 1530-440X).is.
28. ("review" or "review academic" or "review tutorial").pt.
29. (medline or medlars or embase or pubmed).tw,sh.
30. (scisearch or psychinfo or psycinfo).tw,sh.
31. (psychlit or psychlit).tw,sh.
32. cinahl.tw,sh.
33. ((hand adj2 search\$) or (manual\$ adj2 search\$)).tw,sh.
34. (electronic database\$ or bibliographic database\$ or computeri#ed database\$ or online database\$).tw,sh.
35. (pooling or pooled or mantel haenszel).tw,sh.
36. (retraction of publication or retracted publication).pt.
37. (peto or dersimonian or der simonian or fixed effect).tw,sh.
38. **29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37**
39. **28 and 38**
40. meta-analysis.pt.
41. meta-analysis.sh.
42. (meta analys\$ or metaanalys\$).tw,sh.
43. (systematic\$ adj5 review\$).tw,sh.
44. (systematic\$ adj5 overview\$).tw,sh.
45. (quantitativ\$ adj5 review\$).tw,sh.
46. (quantitativ\$ adj5 overview\$).tw,sh.
47. (quantitativ\$ adj5 synthesis\$).tw,sh.
48. (methodologic\$ adj5 review\$).tw,sh.
49. (methodologic\$ adj5 overview\$).tw,sh.
50. (integrative research review\$ or research integration).tw.
51. **40 or 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48 or 49 or 50**
52. **27 or 39 or 51**
53. **18 and 26 and 52**

Appendix 3: AMSTAR items reported

AMSTAR items reported in MSK reviews



AMSTAR items reported in MH reviews

