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Title Page

Full Title: The prevalence, impact and management of musculoskeletal disorders in older people living in care homes: a systematic review.

Concise Title: Musculoskeletal disorders in care home residents.

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Abstract

Purpose: To systematically review the literature describing the prevalence, impact and current management of musculoskeletal pain in older people living in care homes.

Materials and Methods: Published (AMED, CINAHL, EMBASE, psycINFO, MEDLINE, Cochrane Library) and unpublished (OpenGrey, the WHO International Clinical Trials Registry Platform, Current Controlled Trials, UK National Research Register Archive) literature was searched on the 1st March 2015. All studies assessing the prevalence, impact and management of musculoskeletal disorders in older people living in care homes was included. Literature was appraised using the CASP cohort and qualitative critical appraisal tools. Data were analysed using descriptive statistical approaches, meta-analysis and meta-ethnography techniques.

Principle Results: Twenty-four papers reporting the results of 263,775 care home residents in 12 countries were identified. The evidence-base was moderate in quality. Prevalence of musculoskeletal pain for people in care homes was 30.2% (95% confidence intervals: 29.9% to 30.5%; n=105,463). Care home residents reported that musculoskeletal pain had a significant impact on their perceived independence and overall ability to participate in everyday activities of daily living. Three papers which presented data on interventions demonstrated that whilst multi-component assessment and management packages did not significantly change clinical outcomes, these empowered care home staff to feel more confident in managing these patients.

Major Conclusions: Musculoskeletal pain is a common problem in care homes worldwide and residents report significant impact on their lives. However there is uncertainty regarding how to assess and manage such pain.

Keywords: Pain; Elderly; Residential Home; Nursing Home; Treatment; Prevalence

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Introduction

There are numerous reasons why people require support and care within care homes. This may be due to physical as well as cognitive functional decline. Pain is a common problem for older people. Musculoskeletal disorders (i.e. disorders of the bone, joint, ligament and muscles) have been estimated to affect as many as 80% of people over the age of 65 years [1-3]. Osteoarthritis is the most commonly seen musculoskeletal disorder in older people, with an estimated 70% of all people over the age of 65 years affected with osteoarthritis [4]. As a result, musculoskeletal disorders in the older population are a major cause of disability and loss of independence. In addition, chronic pain has also been associated with increased anxiety, depression, decreased socialisation, cognitive impairment and falls [4].

Frequently older people present with numerous co-morbidities including cardiac failure, asthma, chronic obstructive pulmonary disease, diabetes and depression [5]. The consequence of these can be a reduction in a person's ability to engage in physical activity and exercise, which are the core treatments in the management of musculoskeletal disorders such as osteoarthritis [6]. Furthermore, people perceive co-morbidities such as cardiac failure, respiratory condition and cancer as more important to their overall health than osteoarthritis [7]. In addition, symptoms of musculoskeletal disorders such as pain, fatigue, joint stiffness and weakness may be considered by older people as an expected part of ageing [8,9]. Analgesic options, especially pharmacological therapies, are very limited in older people [10]. For all these reasons, musculoskeletal disorders may be regarded as low priority complaints, resulting in less attention to assessment and management by carers and clinicians [7]. Adding to these challenges, assessing pain and the symptoms of musculoskeletal disorders can be difficult in the older population, complicated by cognitive decline, co-morbidities and environmental barriers which people can have in accessing healthcare services [11,12].

Whilst cancer pain has been reported in the literature in care homes, the evidence-base on non-malignant pain has been less well investigated. Furthermore, there is uncertainty about the prevalence and management strategies for people with musculoskeletal disorders who live in care homes. This is partly attributed to the challenges in reporting pain and associated symptoms of musculoskeletal disorders by older people [13,14] as well as the detection and recording by carers [15]. Furthermore no previous studies have systematically reviewed the evidence surrounding the assessment and management of musculoskeletal disease in older people who live in care homes. In response to this, the aim of this paper was therefore to explore the prevalence, impact and management of musculoskeletal disorders in care homes. In particular, our objectives were to determine: what musculoskeletal disorders are experienced by people living in care homes; the prevalence of different musculoskeletal disorders in this population; the attitudes and experiences of residents in care homes to musculoskeletal disorders; how do care home workers assess and monitor musculoskeletal disorders in their residents; and what are the attitudes and experiences of care home workers to musculoskeletal disorders in their residents?

Materials and Methods

Search Strategy

Our primary search strategy investigated the following databases: MEDLINE, EMBASE, CINAHL, AMED (via Ovid), BNI, PsycINFO, Cochrane Library, PubMed and the PEDro databases. These were reviewed from database inception to 1st March 2015. Our secondary strategy was of the unpublished and trial registry databases: OpenGrey, the WHO International Clinical Trials Registry Platform, Current Controlled Trials and the UK National Research Register Archive, to 1st March 2015. Finally, we screened the reference lists of all potentially eligible papers and review articles, and corresponding authors for each included paper were contacted to review the search results and to identify any omitted studies.

Eligibility Criteria

We included all papers which provided data on the epidemiology, attitudes and experiences of musculoskeletal disorders in care home residents (sheltered, residential, nursing). Musculoskeletal disorders were defined as a pathology of the bone, joint or muscle but excluding acute traumatic fractures fracture. Through this, people with long-term, chronic non-unions or insufficiency fractures through osteoporosis were eligible. We included all studies where the mean age of the (resident) cohort was 65 years or over and a minimum of 85% of the cohort were aged 65 years or above. Data from all stakeholders involved in the care of this population as well as residents themselves were included. Workers in residential homes may include: carers, managers, nurses, healthcare professionals (of all levels and professions within the community setting). We excluded those people living independently with or without formal support, those

living in hospital (acute or rehabilitation care centres) where the care home was not their permanent residence.

We included cohort study designs to assess the prevalence, incidence data, impact and studies assessing the management of musculoskeletal disorders for older people living in care homes. Qualitative investigations were included for studies assessing the attitudes and experiences of residents and care home workers towards musculoskeletal disorders.

We excluded single case-study papers. No restrictions were placed on language of paper or date of publication.

Identification of Studies

Two reviewers independently reviewed the titles and abstracts from potentially relevant papers identified through the search strategy (TS, SL). They reviewed the full-texts of all potentially eligible papers before making a final decision on eligibility. Any disagreements in paper eligibility were resolved through a third reviewer (RP).

Data Extraction

For each eligible paper, data were independently extracted by one reviewer (RP) and verified by a second (TS). Data extracted included: characteristics of participants including age, gender, reasons for care home residence, duration of living in care homes, duration of symptoms, medical co-morbidities, method of assessing presence of musculoskeletal disorder, type and frequency of musculoskeletal disorder presented, and attitudes and experiences of care home workers and/or care home residents towards musculoskeletal disorders for older people living in care homes.

Any disagreements in data extraction were resolved through discussion between the reviewers (RP, TS), and, if required, adjudicated by a third reviewer (SL).

Outcome Measures

Primary Outcome:

1. Prevalence or incidence of musculoskeletal disorders in older people living in care homes.

Secondary Outcome Measures:

1. Frequency of different musculoskeletal disorders in older people living in care homes.
2. Attitudes and experiences of care home residents towards their musculoskeletal disorders.
3. Identification of specific care pathways for musculoskeletal disorders, used by care workers when caring for people living in care homes.
4. Attitudes and experience of care home workers towards musculoskeletal disorders in their residents.

Quality Assessment

We critically appraised each included paper using the CASP 'Case Control' or the "Qualitative" appraisal tools [16,17]. These tools were considered appropriate since they have been widely adopted for the review of previous musculoskeletal clinical studies and meta-ethnographies [7,18]. Each included paper was reviewed by one reviewer (RP) and independently verified by a second (TS). Any disagreements in appraisal score were discussed and resolved by a third reviewer (SL).

Data Analysis

Quantitative Analysis: Data extraction tables were assessed for study heterogeneity. When there was strong clinical homogeneity for the population and assessment methods, meta-analysis was undertaken to determine the prevalence and 95% confidence intervals (CI) of musculoskeletal disorders of people in care homes. When considerable methodological heterogeneity was detected, a narrative review was conducted.

We planned to undertake subgroup analyses based on: participant age (less than 75 years versus equal to or over 75 years of age); cognitive impairment (a dementia diagnosis or not); country of origin (particularly when assessing care pathways). However, due to the limited size of evidence, this was not possible for these variables.

Qualitative Analysis: We synthesised qualitative study data using a meta-ethnography synthesis approach. Through this, after emersion in the included studies, all emerging themes were identified and placed in a grid to examine how the concepts juxtaposed or related to one another [19]. The relevant themes were then grouped into categories by two reviewers independently (RP, TS). We then created categories on the basis of primary data from the included studies rather than prior knowledge [19]. Constant comparative techniques were then used to compare how these emergent categories related to the primary data/original texts. The results of this were compared between each review and consensus was reached through discussion to identify all agreed primary and secondary-order themes. Analysis of these key categories was then undertaken through the reciprocal translation and development of lines of argument as advocated by Atkins *et al's* [19] interpretation of Noblit and Hare's [20] description.

Results

Search Results

A summary of the search results is presented in Figure 1. In total 651 citations were identified from the search strategy with 278 subsequently screened after duplication removal. Twenty-nine were considered potentially eligible. After reviewing the full-texts of these, 24 met the eligibility criteria and were included in the review.

Study Characteristics

A total of 263,775 individuals were represented in the included cohorts. This consisted of 5978 males and 19,228 females. Five studies did not present the gender-mix of their cohorts accounting for 238,569 people [1,10,121-23]. Accordingly, the gender from the majority of the review cohort was not identifiable, and resultantly it was not possible to stratify the results due to gender status. Mean ages of residents ranged from 51 years [24] to 86 years [25,26]. The type of care home was described in 14 studies. This was categorised as residential home in one study [21] and as a nursing home in 13 [1,10,22,25,26-34]. No studies itemised the reasons for admission to the care home. All papers explored musculoskeletal pain with no other symptoms recorded such as joint stiffness of weakness, fatigue, paraesthesia or fear-avoidance for example.

The majority of the studies were undertaken in the United States of America (USA) (n=10) [1,22,23,25,31,35-3739]. Two studies were undertaken in the Netherlands [21,32], Canada [40,41], and China [29,42]. There was a single study from each of the following countries: Turkey [27], Taiwan [28], Japan [24], Norway [26], Italy [30], the United Kingdom (UK) [10], Australia [33] and Singapore [34].

Methodological Quality

A summary of the results of the critical appraisal findings are presented in Supplementary Table 2.

Cohort study assessment: The findings of the CASP modified-cohort study appraisal tool indicated that the evidence was largely moderate in quality. Recurrent strengths across the evidence-base were that the studies clearly presented a research question (n=23), recruitment was clearly presented and appropriately recruited in all but three studies [24,29,35], the assessment of musculoskeletal pain was clearly presented and followed an accurate method in all but 10 studies [10,21,22,24,25,28,33,34,37,39]. Whilst studies also reported the results to the previous evidence, and provided results and reporting of findings to permit the generalisability of these to the general population in seven papers (Table 3). Only three studies provided sufficient follow-up periods to answer their research questions [31,32,40] and only five studies reported sufficient follow-up of their cohorts to account for attrition [29,31,32,40,42].

Qualitative study assessment: One study was assessed using the qualitative study tool [36]. This demonstrated high methodological quality with the only weakness identified being that ethical issues was not taken into account as to the role of the researcher in their respondent-research interactions. Strengths included that the study clearly presented the aim of the studies, adopting an appropriate study design, recruitment was appropriate and clearly presented and data collection was clearly reported in this paper. The relationship between the researcher and participant was adequately considered. Data analysis was clearly and rigorously conducted with the results clearly presented and of value to clinical practice.

Incidence

No studies were identified presenting data on the incidence of musculoskeletal disorders in people who live in care homes.

Prevalence

The prevalence of musculoskeletal pain in care homes was estimated as 30.2% (95% CI: 29.9% to 30.5%; n=105,463) from 20 studies [1,10,21-28,30,32,34,35,37-42]. No studies were identified assessing the incidence of musculoskeletal disorders in care home residents. Similarly, no studies reported that specific types of musculoskeletal disorders present in this population.

Impact

One qualitative investigation was identified [36]. Baird et al [36] investigated the consequences of musculoskeletal pain on respondents. Their themes were that of 'restrictive themes' where pain restricted function and independence where people felt that their musculoskeletal disorder limited their tasks and activities of daily living (ADLs), through a fear that such pursuits would exacerbate symptoms. The second theme was that of 'constriction' where people reported that they felt their musculoskeletal disorder put a constraint on their environment which limited their geographical location and reach into society, impacting on their social interaction.

Management

Three intervention studies were identified from the search results. Two presented the results of the same eight-week integrated pain management programme designed for older people living in nursing homes and their carers [29,42]. On meta-analysis (N=554), the findings indicated that there was no significant difference between the introduction of the integrated pain management

programme compared to conventional nursing home pain management systems in respect to pain, UCLA Loneliness Scale [43], life satisfaction index [44] and Geriatric Depression Scale [45,46] ($p \geq 0.10$; Table 2). There was however a statistical significant difference with greater subjective happiness scores in residents for the integrated pain management programme compared to the conventional programme (MD: 1.18; 95% CI: 0.21 to 2.15; Figure 2), although this did not reach a clinically significant difference level which was regarded as a minimum of a four point difference [47].

The third study (N=22) was a trial investigating cognitive behaviour therapy in 10 weekly group sessions incorporating education of pain, coping skills and consolidation of skills sections, compared to an attention support treatment which was aimed to provide participants with greater empathy and support in 10 weekly group discussion sessions [40]. The findings indicated that cognitive behaviour therapy was successful in reducing pain and pain-related disability, in both those with and without cognitive impairment. Both groups demonstrated improvement at four months post-intervention. There were lower pain scores at four months in the cognitive behaviour therapy intervention compared to the attention support group but this did not reach a statistically significant difference (mean score 13.3 (Standard Deviation (SD): 6.6) versus 21.4 (SD: 10.3) points).

One qualitative investigation was identified [24] reporting the perceptions of care staff to pain management rather than residents. The principle theme arising was that of limited knowledge. This was demonstrated both with the recognition that a training need was unmet, and the limited knowledge of, acceptability and ultimately use of pain guidelines in care homes [24]. These findings were supported from survey studies with data suggesting that care home workers felt poorly supported in the use of analgesics and physical activity [35]. Takai *et al* [24] reported limited use of pain guidelines which was reiterated in Allcock *et al's* [10] survey of care homes.

They reported that few nursing homes had a written policy for managing chronic musculoskeletal pain [10].

Discussion

The findings of this review suggested that the prevalence of musculoskeletal pain in care homes was approximately 30%. Care home residents reported that musculoskeletal pain has a detrimental effect on quality of life, restricting their mobility, social engagement and overall independence. Whilst musculoskeletal pain is therefore a considerable problem, there is a paucity of literature on the effectiveness of pain management strategies or intervention programmes.

The meta-ethnography identified that the awareness of residents about their pain and its causes was perceived as a major problem [29]. A lack of understanding can lead to depression, anxiety and a deterioration of quality of life magnified by the symptoms of pain and subsequent immobility, both physically and with reduced societal interaction whilst living in a care home [29]. Poor pain control was considered by Baird et al [35] as a possible consequence of either resident's perceptions that pain was 'normal' and a part of ageing, therefore not requiring medication, or secondly as a control mechanism where they could control one aspect of their care and exert independence by refusing or choosing not to take the medications administered by care home workers. Further exploration of these perceptions would be valuable to begin to understand the relationships between care home workers, residents and musculoskeletal pain management. Furthermore, this will address the lack of awareness of residents to their condition, to prioritise their educational needs, and thus to better manage their symptoms together with care home workers.

Won *et al* [37] reported that persistent pain was very high in those with musculoskeletal pain and those with a history of falls, fracture or surgery. This therefore suggests that these may be important variables to better identify those who are at greater risk of experiencing pain within a

care home. Given the acknowledged difficulties in assessing pain in certain care home residents, most notably those with cognitive impairment, gaining an indication of possible proxy measures of identification for people at greatest risk of pain may be valuable. If it is possible to identify these 'at risk' people, appropriate management strategies may be adopted to better manage these symptoms, thereby improving symptom management and quality of life for a targeted few rather than adopting a blanket approach to include those who do not require such attention.

The current evidence-base was unable to answer a number of study objectives. There was no evidence exploring the frequency of different musculoskeletal conditions in care home residents. There was no incident data, only prevalence data. There was insufficient data to undertake the planned subgroup analyses to explore the potential importance of age, cognitive impairment or country of origin on meta-analysis outcomes. There were limited data on the frequency of different anatomical sites of pain. For example Asghari *et al* [48] reported the most frequent region for musculoskeletal pain were the "hips and legs" in 43%. This corresponds with the profile of musculoskeletal joint pain within the general community [49]. However, there were no details on diagnosis such as proportions with osteoarthritis, back pain or inflammatory arthritis in care home resident datasets. A final limitation was that all the data on prevalence was gained from care home workers (who admit limited knowledge about the field) rather than by experienced musculoskeletal clinicians or researchers. Accordingly, the prevalence data should be viewed with some caution and there may be some underestimation of the actual prevalence. Future studies should include validation exercises where the assessment of musculoskeletal disorders can be verified to better understand the true prevalence in the care home population. Furthermore, there was variability in the data collection methods from the included studies. Therefore the closed-questions provided from certain types of chart reviews and questionnaires may have provided less opportunity to gain information on the unexpected attitudes, perceptions or lived experiences of older people with musculoskeletal pain.

Conclusions

This systematic literature review has highlighted a high burden of musculoskeletal pain in residents in care homes. This pain has significant impact on residents' quality of life. There is a paucity of literature on effective therapeutic strategies for patients and care home staff. Important information that may underpin such strategies, such as understanding diagnostic causes for the pain, has not been well documented. In a rapidly ageing society, there is an urgent need to address these issues.

Highlights

- There is a pooled prevalence of musculoskeletal pain of 30.2% in care home residents internationally.

- Research priorities are highlighted principally on the identification and assessment of musculoskeletal pain in residents.

- There is a paucity of evidence on the appropriate management of musculoskeletal disorders in care home residents.

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List of Figure and Table Legends

Figure 1: PRISMA flow-chart depicting the search strategy results

Figure 2: Forest-plot of subjective happiness score for integrated pain management programme versus conventional management at eight-weeks post-randomisation.

Table 1: Included Study Characteristics Table

Table 2: Meta-analysis results from Integrated Pain Management Programme versus conventional pain management approaches for people living in care homes at eight week post-randomisation outcomes.

Supplementary Table 1: Search strategy for EMBASE search (modified for other database searches)

Supplementary Table 2: Critical Appraisal – Modified Cohort CASP

Table 1: Included Study Characteristics Table

Study	Study country of origin	Sample Size	Gender (m/f)	Age in years (mean or range or both)	Type of care home	Method of data collection
Allcock et al [10]	UK	672	N/S	>65	Nursing home	Tick box survey to nursing staff in homes.
Altiparmak and Altiparmak [27]	Turkey	326	156/170	65-94	Nursing home	Face to face interviews
Asghari et al [47]	Iran	114	56/58	69 (SD: 8.5; 56-90)	Nursing home	Face to face interviews to capture data for questionnaires
Baird et al [35]	USA	60	0/60	69-95	Long term care	Interviews
Boerlage et al [21]	Netherlands	157	N/S	83-92	3 residential homes	Interviews using scales such as McGill Pain Questionnaire
Cook [40]	Canada	21	8/13	61-98	55 bed interim (awaiting housing) 311 bed personal care home 198 bed long term for war vets.	Questionnaires on pain, disability, depression, pain medication
D'Astolfo and Humphreys [41]	Canada	140	97/43	51-101	Long term care	Chart review of patient records
Decker et al [25]	USA	215	52/163	86.4	Rural nursing home	Interview
Lapane et al [22]	USA	2508	N/S	N/S	Nursing homes (one for profit chain)	Chart review of patient records
Leong and Nuo [34]	Singapore	315	129/176	N/S	3 nursing homes	Face to face interviews or with nurses for residents

						Outcome measures: Pain assessment in advanced dementia, GDS, adjusted activity scale
McClean and Higginbotham [33]	Australia	917	261/656	81	Nursing home: Charity and private for profit	Cross sectional survey, audit medical records, and interviews
Prete and Phan [39]	USA	50	50/0	75-103	Veterans affairs	Arthritis questionnaire ADL Scale, MSK examination, MMSE, GDS
Sawyer et al [38]	USA	27715	6901/20814	82.8	For profit Non profit Government	Data analysis from admission notes and pain score
Smalbrugge et al [32]	Holland	350	109/241	55-99	Nursing home	Data collection from previous study, outcome measure assessments
Takai et al [24]	Japan	439	26/413	50.9	3 month stay intermediate facility	Questionnaire
Torvik et al [26]	Norway	106	31/75	86	Nursing home	Cross sectional interview
Tsai et al [28]	Taiwan	150	62/88	N/S	Nursing home	Self report Semi structured interviews Interview form/questionnaire
Tse et al [42]	China	33 staff 90 residents	0/33: staff 56/34: residents	60-89	Nursing home	Questionnaires
Weiner et al [23]	USA	158 residents 31 staff	N/S	35-99	Veterans affairs med centre Community based people	Chart review of patient records
Won et al [37]	USA	21380	4763/16616	65-85>	Long term care facility	Database info Assessment instruments
Won et al [31]	USA	10372	N/S	83	Nursing home	Database info Assessment instruments
Won et al [1]	USA	49971	N/S	65-85>	Nursing home	Database info Assessment instruments

Zanocchi et al [30]	Italy	105	31/74	82.9	Nursing home	Questionnaire

ADLs – Activities of Daily Living; GDS – Geriatric Depression Scale; MMSE – mini mental state examination; MSK – musculoskeletal; N/S – Not Stated; SD – Standard Deviation; Vets – Veterans; UK – United Kingdom; USA – United States of America

Table 2: Meta-analysis results from Integrated Pain Management Programme versus conventional pain management approaches for people living in care homes at eight week post-randomisation outcomes.

Outcome	N	Mean Difference (95% CI)	P-Value	I-consistency value (%)
Pain Score	554	-1.48 (-3.25, 0.29)	0.10	92
Subjective Happiness Scale	554	1.18 (0.21, 2.15)	0.02	12
UCLA Loneliness Scale	554	-4.84 (-2.92, 1.08)	0.25	90
Life Satisfaction Index	554	1.56 (-0.69, 3.81)	0.17	80
Geriatric Depression Scale	554	-0.84 (-2.61, 0.93)	0.35	77

CI – confidence interval; N – number of participants; P-value – probability value; UCLA – University of California Los Angeles

Figure 1: PRISMA flow-chart depicting the search strategy results

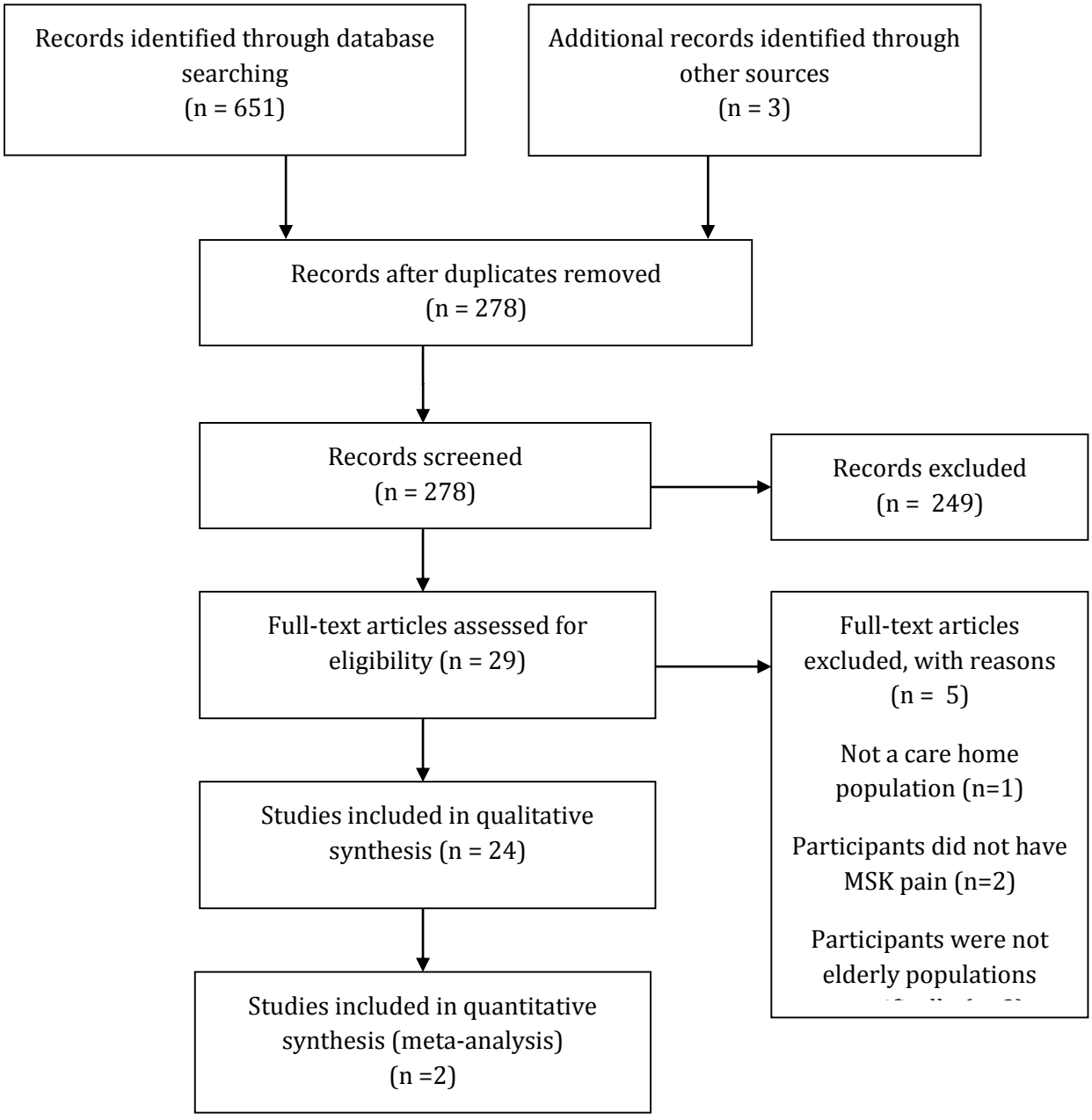
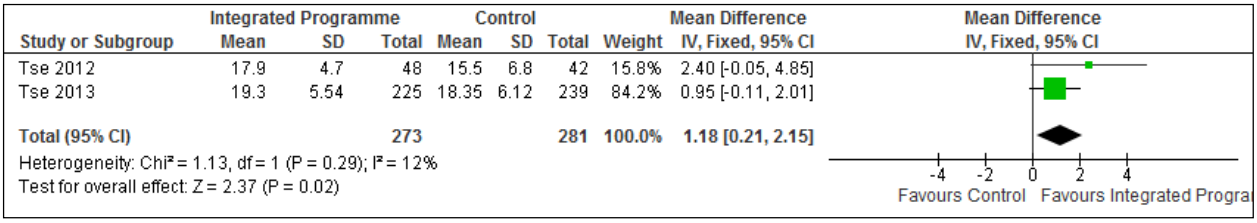


Figure 2: Forest-plot of subjective happiness score for integrated pain management programme versus conventional management at eight-weeks post-randomisation.



Supplementary Table 1: Search strategy for EMBASE search (modified for other database searches)

1. extremities/
2. joints /
3. pain/
4. OR/1,2
5. AND/3,4
6. musculoskeletal diseases/
7. musculoskeletal disorder.ti,ab.
8. (degenerative adj1 joint adj1 disease). ti,ab.
9. arthralgia.ti,ab.
10. arthritis,rheumatoid /
11. osteoarthrit$. ti,ab.
12. spondylitis. ti,ab.
13. (osteitis OR osteochondritis). ti,ab.
14. (arthropathy OR neurogenic OR bursitis). ti,ab.
15. myalgia. ti,ab.
16. back pain/
17. lordosis. ti,ab.
18. lumbargo. ti,ab..
19. sciatrica. ti,ab.
20. spondylosis. ti,ab.
21. cervicogenic. ti,ab.
22. neck pain.ti,ab.
23. headache.ti,ab.
24. tension headach.ti,ab.
25. dyskinesis. ti,ab.
26. tendinitis. ti,ab.
27. (joint adj1 pain). ti,ab.
28. (radicular adj1 pain). ti,ab.
29. allodynia. ti,ab.
30. hyperalgesia. ti,ab.
31. dislocation ti,ab.
32. subluxation. ti,ab.
33. misalignment. ti,ab.
34. OR/6-33
35. AND/5,34
36. Residential Facilities.ti,ab.
37. Homes for the Aged.ti,ab.
38. Assisted Living Facilities/ (772)
39. assisted living.ti,ab. (1104)
40. Residential homes.ti,ab.
41. Nursing Homes/
42. Long-Term Care.ti,ab.
43. Health Services for the Aged. ti,ab.
44. (home? adj1 (nursing or care or residential or environment?)). ti,ab.
45. ((longterm or long term) adj3 (care or facility or facilities)).ti,ab.
46. (healthcare adj2 (facility or facilities)).ti,ab.
47. OR/36-46
48. AND/35,47

Supplementary Table 2: Critical Appraisal – Modified Cohort CASP

Criterion	Allcock et al [10]	Altiparmak and Altiparmak [27]	Asghari et al [46]	Baird et al, [35]	Boerlage [21]	Cook [40]	D'Astolfo and Humphreys [41]	Decker et al [25]	Lapane et al [22]	Leong and Nuo [34]	McClean and Higginbotham [33]	Prete and Phan [39]	Sawyer et al [38]	Smalbrugge et al [32]	Takai et al [24]	Tsai et al [28]	Tse et al, [42]	Tse and Ho [29]	Torvik et al [26]	Weiner et al [23]	Won et al, [37]	Won et al [31]	Won et al [1]	Zanocchi et al [30]
1	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
2	✓	✓	✓	X	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	X	✓	X	✓	✓	✓	✓	✓	✓	✓
3	X	✓	X	✓	✓	✓	✓	X	✓	✓	X	✓	X	✓	X	✓	✓	✓	✓	✓	✓	✓	✓	✓
4	X	✓	X	✓	X	✓	✓	X	X	X	X	X	X	✓	X	X	✓	✓	✓	✓	✓	✓	✓	✓
5	X	✓	X	X	X	✓	✓	✓	✓	✓	X	✓	✓	✓	X	✓	X	✓	✓	✓	✓	✓	✓	X
6	N/C	N/C	✓	N/C	N/C	✓	N/C	N/C	N/C	N/C	N/C	N/C	N/C	✓	N/C	N/C	✓	✓	N/C	N/C	N/C	✓	N/C	N/C
7	N/C	N/C	✓	N/C	N/C	✓	N/C	N/C	N/C	N/C	N/C	N/C	N/C	✓	N/C	N/C	X	X	N/C	N/C	N/C	✓	N/C	N/C
8	X	✓	X	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
9	X	X	✓	X	X	✓	✓	✓	✓	✓	✓	X	✓	✓	X	✓	X	✓	✓	✓	✓	✓	✓	✓
10	✓	✓	✓	✓	✓	✓	✓	✓	✓	X	X	✓	X	X	X	✓	✓	✓	X	✓	✓	✓	✓	X
Quality Judgement	L	M	M	M	M	H	H	M	M	M	L	M	M	H	L	M	M	H	M	H	H	H	H	M

✓ - yes; x – no; N/C – Not Clear; Quality Judgement = 0-4 (L-Low); 5-7 (M-Moderate); 8-10 (H-High).

Criteria

1. Did the study address a clearly focused issue?
2. Was the cohort recruited in an acceptable way?
3. Was the exposure accurately measured to minimize bias?
4. Was the outcome accurately measure to minimize bias?

5. Have the authors identified all important confounding factors?
6. Was the follow up of the subjects complete enough?
7. Was the follow up of subjects long enough?
8. Where confidence intervals presented?
9. Were the results generalisable to the general population?
10. Do the results of this study fit with other available evidence?