

Review article

Non-pharmacological interventions for agitation in dementia: systematic review of randomised controlled trials

Gill Livingston, Lynsey Kelly, Elanor Lewis-Holmes, Gianluca Baio, Stephen Morris, Nishma Patel, Rumana Z. Omar, Cornelius Katona and Claudia Cooper

Background

Agitation in dementia is common, persistent and distressing and can lead to care breakdown. Medication is often ineffective and harmful.

Aims

To systematically review randomised controlled trial evidence regarding non-pharmacological interventions.

Method

We reviewed 33 studies fitting predetermined criteria, assessed their validity and calculated standardised effect sizes (SES).

Results

Person-centred care, communication skills training and adapted dementia care mapping decreased symptomatic and

severe agitation in care homes immediately (SES range 0.3–1.8) and for up to 6 months afterwards (SES range 0.2–2.2). Activities and music therapy by protocol (SES range 0.5–0.6) decreased overall agitation and sensory intervention decreased clinically significant agitation immediately. Aromatherapy and light therapy did not demonstrate efficacy.

Conclusions

There are evidence-based strategies for care homes. Future interventions should focus on consistent and long-term implementation through staff training. Further research is needed for people living in their own homes.

Declaration of interest

None.

The number of people with dementia is rising rapidly with increased longevity. Although dementia's core symptom is cognitive deterioration, agitation is common, persistent and distressing. Nearly half of all people with dementia have agitation symptoms every month, including 30% of those living at home.¹ Four-fifths of those with clinically significant symptoms remain agitated over 6 months,² and 20% of those initially symptom-free develop symptoms over 2 years.² Agitation in dementia is associated with poor quality of life,³ because it is unpleasant, impedes activities and relationships, causes helplessness and anger in family and paid caregivers,⁴ and predicts nursing home admission,⁵ where the agitated behaviour adversely influences the environment.⁴ Several reviews, including our previous systematic review,⁶ considered all neuropsychiatric symptoms' management together. We found direct behavioural management therapies (BMT) with the person with dementia and specific staff education had lasting effectiveness, but this may be limited to affective symptoms.⁷ A recent meta-analysis of family caregiver interventions for overall neuropsychiatric symptoms in dementia found an effect size of 0.23, but did not consider which symptoms improved.⁸

Neuropsychiatric symptoms in dementia are heterogeneous, therefore symptoms should be considered individually as successful strategies may differ. The one published, well-conducted systematic review of non-pharmacological management of agitation in dementia included only randomised controlled trials (RCTs) published before 2004 in English or Korean; it found just 14 papers and evidence of effectiveness only for sensory interventions.⁹ The review did not consider whether interventions were effective only during the intervention or whether the effect lasted longer; the settings in which the intervention had been shown to be effective (e.g. in the community or in care homes); or whether the intervention reduced levels of agitation symptoms and was preventive or treated clinically significant agitation.

Psychotropic medication was routinely used to treat agitation but is now discouraged since benzodiazepines and antipsychotics increase cognitive decline,¹⁰ and antipsychotics cause excess mortality and are of limited efficacy.¹¹ Similarly, citalopram has some efficacy but has cardiac side-effects and reduces cognition.¹² Cholinesterase inhibitors and memantine appear ineffective.^{13,14} Preliminary evidence suggests mirtazapine may reduce agitation.¹⁵ One RCT (not placebo-controlled) found analgesics improved agitation in people with dementia, with an effect size comparable to antipsychotics.¹⁶

Effective agitation management could in theory improve the quality of life of people with dementia and their caregivers, reduce distress, decrease inappropriate medication, enable positive relationships and activities, delay institutionalisation and be cost-effective. We aimed therefore to review systematically the evidence for non-pharmacological interventions for agitation in people with dementia, both immediately and longer-term; the costs of the successful interventions are reported in a separate paper.¹⁷

Method

We registered our protocol with the Prospero International Prospective Register of Systematic Reviews (http://www.crd.york.ac.uk/PROSPERO/display_record.asp?ID=CRD42011001370). We began electronic searches on 9 August 2011, repeating them on 12 June 2012. We searched PubMed, Web of Knowledge, British Nursing Index, the Health Technology Assessment (HTA) Programme Database, PsycINFO, NHS Evidence, System for Information on Grey Literature, The Stationery Office Official Publications website, the National Technical Information Service, INAHL and the Cochrane Library. Search terms were agreed in consultation with caregiver representatives, older adults and

professionals. We hand-searched included papers' reference lists and contacted all authors about other relevant studies. We translated eight non-English papers.

Inclusion and exclusion criteria

We included studies in any language that met the following criteria:

- (a) the participants all had dementia, or those with dementia were analysed separately;
- (b) the study evaluated non-pharmacological interventions for agitation, defined as inappropriate verbal, vocal or motor activity not judged by an outside observer to be an outcome of need,¹⁸ encompassing physical and verbal aggression and wandering;
- (c) agitation was measured quantitatively;
- (d) a comparator group was reported or agitation was compared before and after the intervention.

We excluded studies if every individual was given psychotropic drugs or some participants received medication as the sole intervention. In this paper we report the highest-quality studies – randomised controlled trials (RCTs) with more than 45 participants – since none of the trials with a smaller sample size provided a full and appropriate sample size calculation.

Data extraction

The first 20 search results were independently screened by G.L. and L.K. to assess exclusion procedure reliability. No paper was excluded incorrectly. All other papers were screened by L.K. and E.L.H. If exclusion was unclear, L.K., E.L.H. and G.L. discussed and reached consensus. Data extracted from the papers (by L.K. and E.L.H.) included methodological characteristics; description of the intervention; whether the intervention was applied to the person with dementia, family caregivers or staff; statistical methods; length of follow-up; diagnostic methods; and summary outcome data (immediate and longer-term). Paper quality, including bias, was scored independently by L.K. and E.L.H., discussing discrepancies with G.L. and/or G.B. They used Centre for Evidence-Based Medicine (CEBM) RCT evaluation criteria (<http://www.cebm.net/index.aspx?o=1025>); this approach gives points for randomisation and its adequacy, participant and rater masking, outcome measures validity and reliability, power calculations and achievement, follow-up adequacy, accounting for participants, and whether analyses were intention to treat and appropriate. Possible scores range from 0 to 14 (highest quality). Where a randomised design was used but the intervention was not compared with the control group, we considered this a within-subject design, for example the study by Raglio *et al.*¹⁹ We assigned CEBM evidence levels as follows:

- (a) level 1b: high-quality RCTs (these were at least single-blind, had follow-up rates of at least 80%, were sufficiently powered, used intention-to-treat analysis, had valid outcome measures and findings reported with relatively narrow confidence intervals);
- (b) level 2b: lower-quality RCTs.

Intervention categories

The authors L.K., E.L.H. and G.L. categorised the interventions independently and then by consensus. The interventions were activities; music therapy (protocol-driven); sensory interventions (all involved touch, and some included additional sensory stimulation such as light); light therapy; training paid caregivers

in person-centred care or communication skills (interventions focused on improving communication with the person with dementia and finding out what they wanted), with and without supervision; dementia care mapping; aromatherapy; training family caregivers in behavioural management therapies or cognitive-behavioural therapy (CBT); exercise; cognitive stimulation therapy; and simulated presence therapy.

Agitation level

We separated studies according to the inclusion criteria of participants in terms of level of symptoms of agitation: 1, no agitation symptom necessary for inclusion; 2, some agitation symptoms necessary for inclusion; 3, clinically significant agitation level; 4, level unspecified. We used the usual thresholds: a score above 39 on the Cohen-Mansfield Agitation Inventory (CMAI),²⁰ and a score above 4 on the Neuropsychiatric Inventory (NPI) agitation scale,¹ to denote significant agitation.

Statistical analysis

We decided *a priori* to meta-analyse when there were three or more RCTs investigating sufficiently homogeneous interventions using the same outcome measure, but no intervention met these criteria. To facilitate comparison across interventions and outcomes, where possible, we estimated interventions' standardised effect sizes (SES) with 95% confidence intervals.²¹ In some studies the outcome was measured and reported at several time-points during the intervention. We used data from the last time-point to estimate the SES, since individual patient data were not available to incorporate repeated measures in the calculation. We also recalculated results for studies not directly comparing intervention and control groups but reporting only within-group comparisons and with one-tailed significance tests, so some of our results differ from the original analysis.

Results

We found 1916 records, including 33 relevant RCTs with at least 45 participants (Fig. 1). Online Tables DS1 and DS2 list methodological characteristics, SES and quality ratings; Table DS1 contains the findings from interventions for which there appeared to be adequate evidence, and Table DS2 contains those for which there was not adequate evidence (either evidence that they were not effective or where there was simply insufficient evidence).

Efficacious interventions

Working with the person with dementia

Activities. Five of the included RCTs implemented group activities; those with standard activities reduced mean agitation levels, and decreased symptoms in care homes while they were in place.^{22,23} One high-quality RCT found no additional effect on agitation of individualising activities according to functional level and interest,²⁴ although two lower-quality RCTs did.^{25,26} All studies were in care homes except one, in which some participants attended a day centre and others lived in a care home.²⁷ None specified a significant degree of agitation for inclusion. Only one study measured agitation after the intervention finished, and did not show effects at 1-week and 4-week follow-up.²⁴

Although activities in care homes reduced levels of agitation significantly while in place, there is no evidence regarding longer-term effect, and it is unclear whether individualising

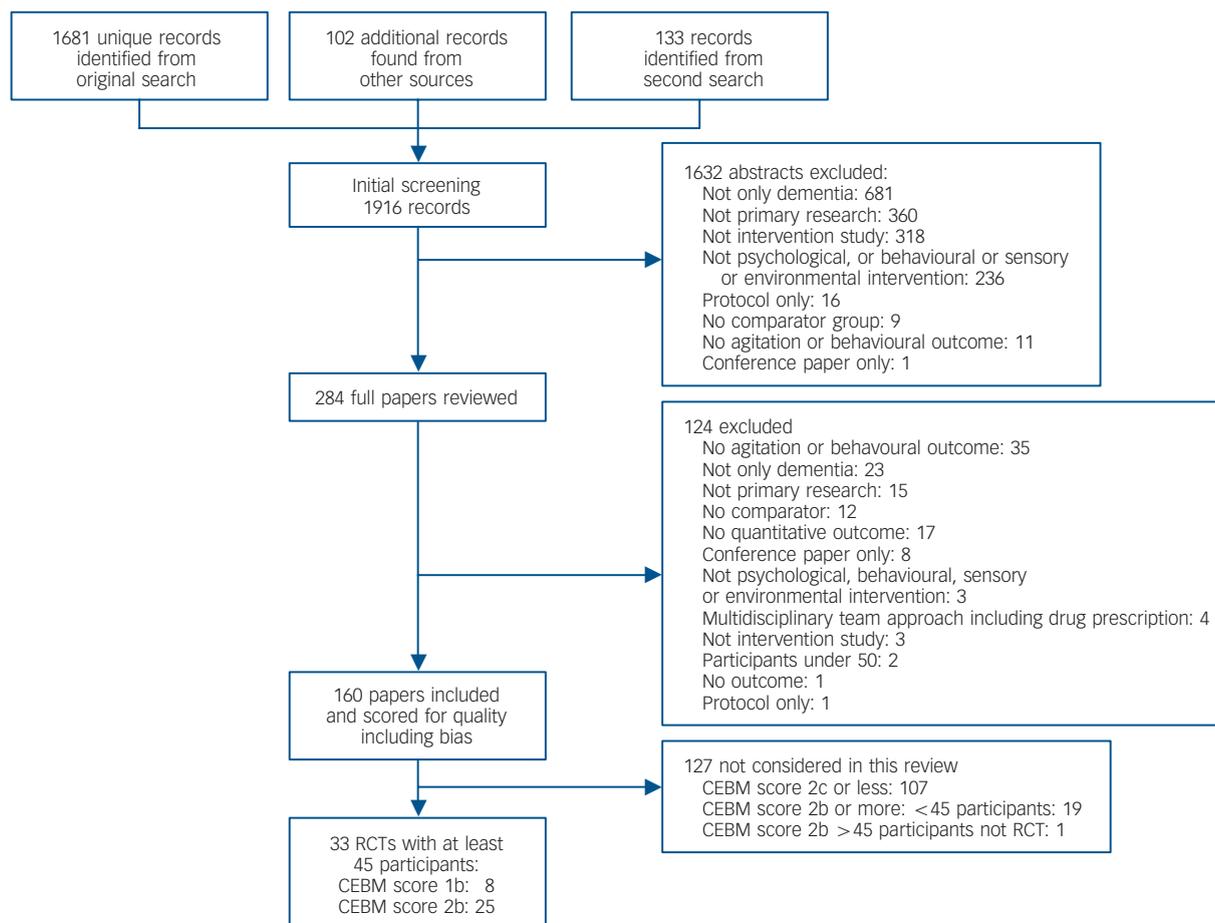


Fig. 1 Study search profile (CEBM, Centre for Evidence-Based Medicine; RCT, randomised controlled trial).

activities further reduces agitation. There is no evidence for activities in severe agitation or outside care homes.

Music therapy. Three RCTs, all in care homes, evaluated music therapy by trained therapists using a specific protocol – typically involving warming up with a well-known song, listening to and then joining in with the music.^{28–30} The largest study, which included participants irrespective of agitation level, found music therapy twice a week for 6 weeks was effective compared with the usual care group.²⁸ A second study found a significant effect in comparison with a reading group,³⁰ and the third found a borderline significant effect.²⁹ Reduction in symptoms of agitation was immediate (SES = 0.5–0.9). There is little evidence longer-term, and no evidence for people with severe agitation or outside care homes.

Sensory interventions

Five RCTs of sensory interventions, all in care homes, targeted perceived understimulation of people with dementia. Some focused on touch, such as massage; others were multisensory interventions of tactile, light and auditory stimulation, such as Snoezelen therapy.^{22,31–34} Studies comparing touch found a significant improvement in symptomatic and clinically significant agitation compared with usual care.^{22,34} We report three ‘therapeutic touch’ studies; defined as a healing-based touch intervention focusing on the whole person.^{31–33} Despite therapeutic touch being efficacious in before-and-after analyses, in between-group analyses therapeutic touch tended towards being less

efficacious than ordinary massage or usual treatment. Sensory interventions significantly improved symptomatic agitation and clinically significant agitation during the intervention, but therapeutic touch did not demonstrate added advantage, and there is insufficient evidence about long-term effects or in settings outside care homes.

Working through care-home staff

Person-centred care, communication skills training and dementia care mapping all seek to change the caregiver’s perspective, communication with and thoughts about people with dementia, encouraging the caregiver to see and treat them as individuals rather than being task-focused. Training paid caregivers in these techniques was investigated in five RCTs.^{35–39} All interventions included supervision during training and implementation.

Person-centred care. One high-quality study of person-centred care training found severe agitation significantly improved during the intervention and 8 weeks later.³⁵ Two studies of improving communication skills or person-centred care for participants with symptomatic agitation found significant improvements compared with the control group during the intervention,^{37,38} and up to 6 months afterwards.³⁷ A large study including participants without high agitation levels found agitation improved significantly during 8 weeks of person-centred care training and 20 weeks later.³⁶ One small study, where participants’ agitation levels were unspecified, showed immediate improvement in agitation during bathing compared with the control group.³⁹

Dementia care mapping. One large, high-quality care home study evaluated dementia care mapping. The researchers observed and assessed each resident's behaviour, factors improving well-being and potential triggers; explained the results to caregivers, and supported proposed change implementation. Severe agitation decreased during the intervention and 4 months afterwards.³⁵

Effect sizes. Training paid care-home staff in communication skills, person-centred care or dementia care mapping with supervision during implementation was significantly effective for symptomatic and severe agitation immediately (SES = 0.3–1.8) and for up to 6 months (SES = 0.2–2.2). There was no evidence in other settings.

Interventions without evidence of efficacy

Working with the person with dementia

Light therapy. Light therapy hypothetically reduces agitation through manipulating circadian rhythms, typically by 30–60 min daily bright light exposure. We included three RCTs, all in care homes.^{40–42} Among participants with some or significant agitation, light therapy either increased agitation or did not improve it. The SES was 0.2 (for improvement) to 4.0 (for worsening symptoms) compared with the control group. There is therefore no evidence that light therapy reduces symptomatic or severe agitation in care homes and it may worsen it.

Aromatherapy. The two RCTs of aromatherapy both took place in care homes.^{43,44} One large, high-quality blinded study found no immediate or long-term improvement relative to the control group for participants with severe agitation.⁴⁴ The other, non-blinded, study found significant improvement compared with the control group.⁴³ When assessors are masked to the intervention, aromatherapy has not been shown to reduce agitation in care homes.

Training family caregivers in BMT. Two high-quality studies found no immediate or longer-term effect (at 3 months, 6 months or 12 months) of either four or eleven sessions training family caregivers in BMT for severe or symptomatic agitation in people with dementia living at home.^{45,46} Two studies training family caregivers in CBT for people with severe agitation also found no improvement compared with controls.^{47,48} There is thus high-quality evidence that teaching family caregivers BMT or CBT is ineffective for severe agitation, but insufficient evidence to draw conclusions regarding symptomatic agitation.

Interventions with insufficient evidence

For the following interventions there was insufficient evidence to make a definitive recommendation.

Exercise

There is no evidence that exercise is effective. The one sufficiently sized exercise RCT was conducted in a care home and found no effect on agitation levels either immediately or 7 weeks later.

Training caregivers without supervision

Training in communication skills and person-centred care without supervision was ineffective.^{49,50}

Other interventions

One study found that simulated presence therapy – playing a recording mimicking a telephone conversation with a relative

when the participant was agitated – was not effective.⁵¹ One study testing a mixed psychosocial intervention, including massage and promoting residents' activities of daily living skills, did not find agitation improved significantly compared with the control group.⁵²

Standardised effect sizes

Figure 2 illustrates the effect of person-centred care, communication, dementia care mapping, music therapy and activities in reducing agitation. Long-term effects (in months) of changing the way caregivers interact with residents are at least as good as the short-term effects.^{35,38}

Discussion

This is the first up-to-date systematic review to focus on agitation. It uniquely analyses whether the intervention was potentially preventive, by reducing mean levels of agitation symptoms including those not clinically significant at baseline or managed clinically significant agitation; whether effects were observed only while the intervention was in place or lasted longer; and the settings in which the intervention had been shown to be effective: the community or in care homes.

Effective interventions

Effective interventions seem to work through care staff, particularly in the long term. There is convincing evidence that when implementation is supervised, interventions that aim to communicate with people with dementia, helping staff to understand and fulfil their wishes, reduce symptomatic and severe agitation during the intervention and for 3–6 months afterwards. This suggests that training paid caregivers in communication, person-centred care skills or dementia care mapping are clinically important interventions, as shown by a 30% decrease in agitation⁴³ or a standardised effect size of 0.2, which is clinically small, 0.5 medium and 0.8 large.⁵³

Sensory interventions significantly improved agitation of all severities while in place. Therapeutic touch had no added advantage. We also found replicated, good-quality evidence that activities and music therapy by protocol reduce overall and symptomatic agitation in care homes while in place. Although we were surprised that individualised activities were no more effective than prescribed activities, the low numbers in the activity intervention groups may suggest that it was only those who were particularly suited to the activity who participated. There is no evidence for severe agitation. Theory-based activities (neurodevelopmental and Montessori) were no more effective than other pleasant activities.

Other interventions

Light therapy does not appear to be effective and may be harmful. Non-blinded interventions with aromatherapy appeared effective, possibly owing to rater bias, but masked raters do not find it effective. Training family caregivers in BMT and CBT interventions for the person with dementia was not effective. Learning complex theories and skills and maintaining fidelity to an intervention may be almost impossible to combine with looking after a family member with dementia and agitation on a 24-hour basis.

Strengths and weaknesses of the study

This is an exhaustive systematic review; two raters independently evaluated studies to ensure reliability in study inclusion and quality ratings. We searched all health and social sciences

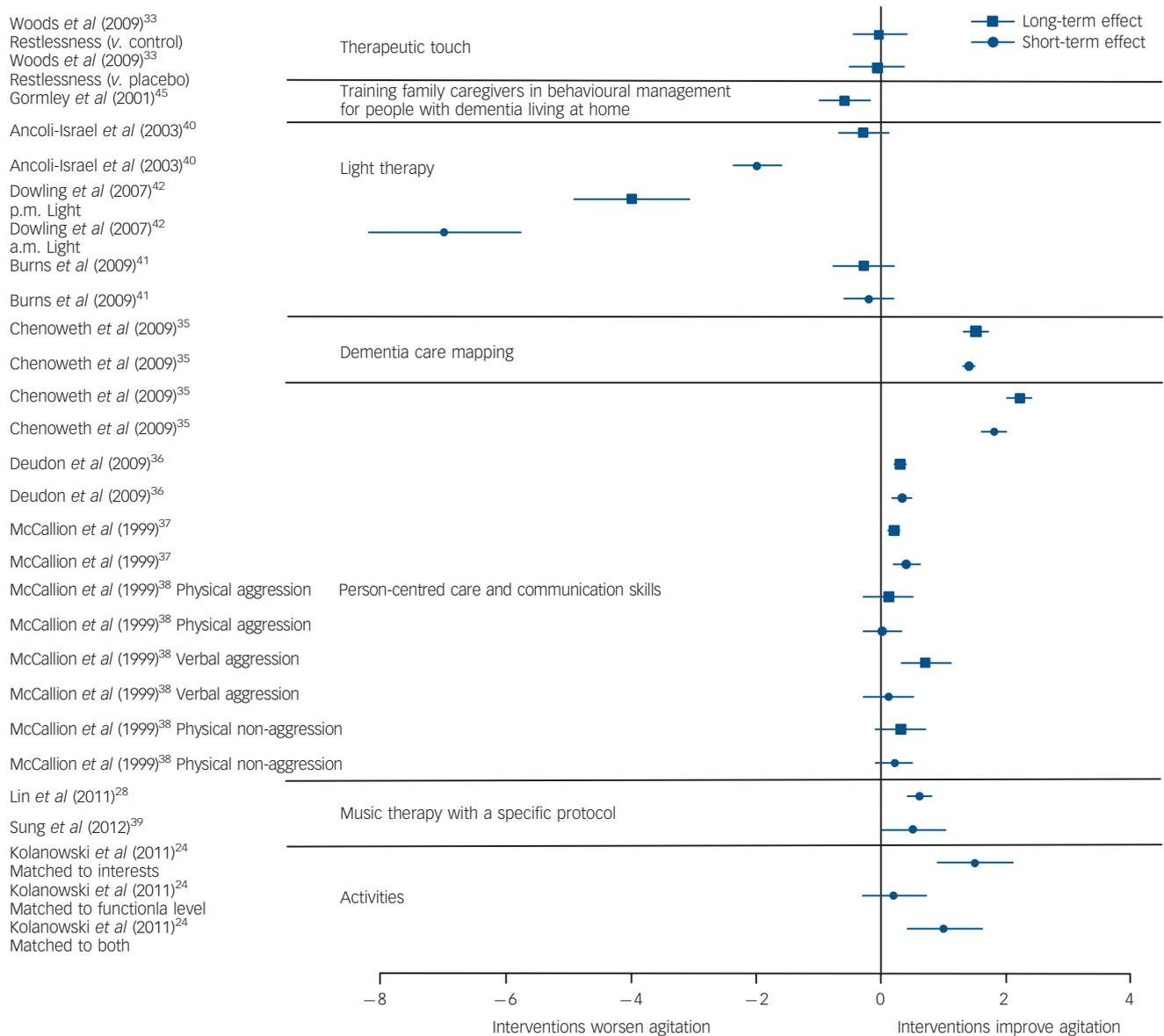


Fig. 2 Standardised effect size and 95% confidence intervals where calculable of randomised controlled trials compared with controls for each reported outcome immediately and in the longer term.

databases, translated non-English publications, reduced publication bias by searching the grey literature and asking experts about other studies, then repeated our searches. Some interventions were multicomponent and we made judgements about which category they belonged in and described them in the text. Most interventions had been tried only in care homes and we do not know their effect or practicality in people's own homes where most people with dementia live. Although we excluded interventions in which all participants received medication, we cannot assess if medication use was uneven in different arms. Most studies included participants with any dementia and we cannot comment on the effect of interventions on different dementia subtypes.

Studies were heterogeneous in both intervention and measuring effects. This meant we were unable to meta-analyse and our conclusions are mostly based on a qualitative synthesis. Many studies were underpowered, possibly because residents were unwilling or unable to participate, or of low quality and therefore excluded. There were only eight level 1 studies and this is not evidence of lack of efficacy; there were several interventions with

insufficient evidence to draw conclusions. Several interventions were implemented differently to usual practice and this may have altered the effect, for example in dementia care mapping.³⁵ Finally, although most studies used the CMAI many did not, and the definition of agitation varied between studies.

Other research

Early studies did not have the opportunity to use valid instruments for agitation; these now exist but may vary in their sensitivity to detect change. Differences in effect sizes between study results may therefore sometimes be due to instrument difference. Thus although our study's strength is the literature integration, it underlines how much more work is needed. There are some RCTs currently in progress which should add to the evidence base. A recent study, considering overall neuropsychiatric symptoms (in contrast to our review specifically about agitation) found working with family caregivers to be effective, and it would be useful to

examine which symptoms contributed to this effect and if it were mood rather than agitation.⁸

Study implications

Although agitation in dementia has been regarded as due to brain changes, our findings suggest agitation also arises from lack of understanding or unmet needs in someone whose dementia makes them unable to explain or understand this. This is in line with the need-driven, dementia-compromised behaviour theory of Algate *et al*,⁵⁴ and the hypothesis of Kitwood & Bredin that behaviours arise from need and occur when care is task-driven not person-centred (relevant to all neuropsychiatric symptoms).⁵⁵ Our findings suggest clinicians should stop considering agitation as an entity but instead often as a symptom of lack of understanding or unmet need that the person with dementia is unable to explain or understand. This may be physical discomfort or need for stimulation, emotional comfort or communication.

Future research

More evidence is required about implementing group activities in care homes over longer periods to prevent agitation. We recommend the development and evaluation of a manual-based training for staff in care homes employing interventions with evidence for efficacy, to allow translation to different settings. We suggest these interventions should focus on changing culture to implement programmes permanently. In general it seems that there is no evidence about settings outside care homes. The lack of effective interventions, despite 70–80% of people with dementia living at home and the potential of interventions to delay care home admission, suggests further research should start from qualitative interviews considering how agitation is experienced by people with dementia living at home, and how their families manage. This, together with synthesised evidence from other settings, could help in the development of a pilot intervention. Our review may suggest that it should have elements of sensory stimulation (including music), activities and teaching the family caregiver communication skills, to change themselves rather than the person with dementia.

Gill Livingston, MD, **Lynsey Kelly**, BSc, **Elanor Lewis-Holmes**, BSc, Unit of Mental Health Sciences, **Gianluca Baio**, PhD, Departments of Statistical Science and PRIMENT Clinical Trials Unit, **Stephen Morris**, PhD, **Nishma Patel**, MSc, Department of Applied Health Research, **Rumana Z. Omar**, PhD, Departments of Statistical Science and PRIMENT Clinical Trials Unit, **Cornelius Katona**, MD, **Claudia Cooper**, PhD, Unit of Mental Health Sciences, University College London, UK

Correspondence: Professor Gill Livingston, Charles Bell House, 67–73 Riding House Street, London W1W 7EH, UK. Email: g.livingston@ucl.ac.uk

First received 30 Oct 2013, final revision 29 Apr 2014, accepted 12 Jul 2014

Funding

This article presents independent research commissioned by the UK National Institute for Health Research (NIHR) Health Technology Assessment Programme: HTA 10/43/01. The views and opinions expressed therein are those of the authors and do not necessarily reflect those of the HTA Programme, NIHR, the National Health Service or the Department of Health. The study was sponsored by University College London. Neither funders nor sponsors had a role in the study design and the collection, analysis, and interpretation of data and the writing of the article and the decision to submit it for publication. The researchers were independent from funders and sponsors.

Acknowledgements

We wish to thank Shirley Nurock, dementia family carer, for her thoughts and contributions.

References

- Ryu SH, Katona C, Rive B, Livingston G. Persistence of and changes in neuropsychiatric symptoms in Alzheimer disease over 6 months – the LASER-AD study. *Am J Geriatr Psychiatry* 2005; **13**: 976–83.
- Savva GM, Zaccai J, Matthews FE, Davidson JE, McKeith I, Brayne C, et al. Prevalence, correlates and course of behavioural and psychological symptoms of dementia in the population. *Br J Psychiatry* 2009; **194**: 212–9.
- Wetzels RB, Zuidema SU, de Jonghe JFM, Verhey FRJ, Koopmans RTCM. Determinants of quality of life in nursing home residents with dementia. *Dementia and Geriatric Cognitive Disorders* 2010; **29**: 189–97.
- Draper B, Snowden J, Meares S, Turner J, Gonski P, McMinn B, et al. Case-controlled study of nursing home residents referred for treatment of vocally disruptive behavior. *Int Psychogeriatr* 2000; **12**: 333–44.
- Morris LW, Morris RG, Britton PG. The relationship between marital intimacy, perceived strain and depression in spouse caregivers of dementia sufferers. *Br J Med Psychol* 1988; **61**: 231–6.
- Livingston G, Johnston K, Katona C, Paton J, Lyketsos CG. Systematic review of psychological approaches to the management of neuropsychiatric symptoms of dementia. *Am J Psychiatry* 2005; **162**: 1996–2021.
- National Institute for Clinical Excellence, Social Care Institute for Excellence. *Dementia: Supporting People with Dementia and Their Carers in Health and Social Care*. NICE/SCIE, 2006.
- Brodsky H, Arasaratnam C. Meta-analysis of nonpharmacological interventions for neuropsychiatric symptoms of dementia. *Am J Psychiatry* 2012; **169**: 946–53.
- Kong EH, Evans LK, Guevara JP. Nonpharmacological intervention for agitation in dementia: a systematic review and meta-analysis. *Aging Ment Health* 2009; **13**: 512–20.
- Bierman EJ, Comijs HC, Gundy CM, Sonnenberg C, Jonker C, Beekman AT. The effect of chronic benzodiazepine use on cognitive functioning in older persons: good, bad or indifferent? *Int J Geriatr Psychiatry* 2007; **22**: 1194–200.
- Maher AR, Maglione M, Bagley S, Suttrop M, Hu JH, Ewing B, et al. Efficacy and comparative effectiveness of atypical antipsychotic medications for off-label uses in adults: a systematic review and meta-analysis. *JAMA* 2011; **306**: 1359–69.
- Porsteinsson AP, Drye LT, Pollock BG, Devanand DP, Frangakis C, Ismail Z, et al. Effect of citalopram on agitation in Alzheimer disease: the CiTAD randomized clinical trial. *JAMA* 2014; **311**: 682–91.
- Howard RJ, Juszcak E, Ballard CG, Bentham P, Brown RG, Bullock R, et al. Donepezil for the treatment of agitation in Alzheimer's disease. *N Engl J Med* 2007; **357**: 1382–92.
- Fox C, Crugel M, Maidment I, Auestad BH, Coulton S, Treloar A, et al. Efficacy of memantine for agitation in Alzheimer's dementia: a randomised double-blind placebo controlled trial. *PLoS One* 2012; **7**: e35185.
- Banerjee S, Hellier J, Dewey M, Romeo R, Ballard C, Baldwin R, et al. Sertraline or mirtazapine for depression in dementia (HTA-SADD): a randomised, multicentre, double-blind, placebo-controlled trial. *Lancet* 2011; **378**: 403–11.
- Husebo BS, Ballard C, Sandvik R, Nilsen OB, Aarsland D. Efficacy of treating pain to reduce behavioural disturbances in residents of nursing homes with dementia: cluster randomised clinical trial. *BMJ* 2011; **343**: d4065.
- Livingston G, Kelly L, Lewis-Holmes E, Baio G, Morris S, Patel N, et al. A systematic review of the clinical effectiveness and cost-effectiveness of sensory, psychological and behavioural interventions for managing agitation in older adults with dementia. *Health Technol Assess* 2014; **18**: 1–226, v–vi.
- Cohen-Mansfield J, Billig N. Agitated behaviors in the elderly. I. A conceptual review. *J Am Geriatr Soc* 1986; **34**: 711–21.
- Raglio A, Bellelli G, Traficante D, Gianotti M, Ubezio MC, Villani D, et al. Efficacy of music therapy in the treatment of behavioral and psychiatric symptoms of dementia. *Alzheimer Dis Assoc Disord* 2008; **22**: 158–62.
- Cohen-Mansfield J, Marx MS, Dakheel-Ali M, Regier NG, Thein K, Freedman L. Can agitated behavior of nursing home residents with dementia be prevented with the use of standardized stimuli? *J Am Geriatr Soc* 2010; **58**: 1459–64.
- Hedges L. Distribution theory for Glass's estimator of effect size and related estimators. *J Educ Behav Stat* 1981; **6**: 107–28.
- Lin LC, Yang MH, Kao CC, Wu SC, Tang SH, Lin JG. Using acupuncture and Montessori-based activities to decrease agitation for residents with dementia: a cross-over trial. *J Am Geriatr Soc* 2009; **57**: 1022–9.
- Buettner LL, Ferrario J. Therapeutic recreation-nursing team: a therapeutic intervention for nursing home residents with dementia. *Ann Therap Rec* 1997; **7**: 21.

- 24 Kolanowski A, Litaker M, Buettner L, Moeller J, Costa PT. A randomized clinical trial of theory-based activities for the behavioral symptoms of dementia in nursing home residents. *J Am Geriatr Soc* 2011; **59**: 1032–41.
- 25 Kovach C, Cashin S, Taneli Y, Dohearty P, Schlidt A, Silva-Smith A. Effects of the BACE intervention on agitation of demented residents in long-term care. *Gerontologist* 2003; **43**: 233.
- 26 Cohen-Mansfield J, Jensen B. Do interventions bringing current self-care practices into greater correspondence with those performed pre-morbidly benefit the person with dementia? A pilot study. *Am J Alzheimer Dis Other Demen* 2006; **21**: 312–7.
- 27 Cohen-Mansfield J, Parpura-Gill A, Golander H. Utilization of self-identity roles for designing interventions for persons with dementia. *J Gerontol Ser B: Psychol Sci Soc Sci* 2006; **61B**: 202–12.
- 28 Lin Y, Chu H, Yang CY, Chen CH, Chen SG, Chang HJ, et al. Effectiveness of group music intervention against agitated behavior in elderly persons with dementia. *Int J Geriatr Psychiatry* 2011; **26**: 670–8.
- 29 Sung HC, Lee WL, Li TL, Watson R. A group music intervention using percussion instruments with familiar music to reduce anxiety and agitation of institutionalized older adults with dementia. *Int J Geriatr Psychiatry* 2012; **27**: 621–7.
- 30 Cooke ML, Moyle W, Shum DH, Harrison SD, Murfield JE. A randomized controlled trial exploring the effect of music on agitated behaviours and anxiety in older people with dementia. *Aging Ment Health* 2010; **14**: 905–16.
- 31 Hawranik P, Johnston P, Deartrich J. Therapeutic touch and agitation in individuals with Alzheimer's disease. *West J Nurs Res* 2008; **30**: 417–34.
- 32 Woods DL, Craven RF, Whitney J. The effect of therapeutic touch on behavioral symptoms of persons with dementia. *Altern Ther Health Med* 2005; **11**: 66–74.
- 33 Woods DL, Beck C, Sinha K. The effect of therapeutic touch on behavioral symptoms and cortisol in persons with dementia. *Forsch Komplementmed* 2009; **16**: 181–9.
- 34 Van Weert JCM, van Dulmen AM, Spreeuwenberg PMM, Ribbe MW, Bensing JM. Behavioral and mood effects of Snoezelen integrated into 24-hour dementia care. *J Am Geriatr Soc* 2005; **53**: 24–33.
- 35 Chenoweth L, King MT, Jeon YH, Brodaty H, Stein-Parbury J, Norman R, et al. Caring for Aged Dementia Care Resident Study (CADRES) of person-centred care, dementia-care mapping, and usual care in dementia: a cluster-randomised trial. *Lancet Neurol* 2009; **8**: 317–25.
- 36 Deudon A, Maubourguet N, Gervais X, Leone E, Brocker P, Carcaillon L, et al. Non-pharmacological management of behavioural symptoms in nursing homes. *Int J Geriatr Psychiatry* 2009; **24**: 1386–95.
- 37 McCallion P, Toseland RW, Freeman K. An evaluation of a Family Visit Education Program. *J Am Geriatr Soc* 1999; **47**: 203–14.
- 38 McCallion P, Toseland RW, Lacey D, Banks S. Educating nursing assistants to communicate more effectively with nursing home residents with dementia. *Gerontologist* 1999; **39**: 546–58.
- 39 Sloane PD, Hoeffler B, Mitchell CM, McKenzie DA, Barrick AL, Rader J, et al. Effect of person-centered showering and the towel bath on bathing-associated aggression, agitation, and discomfort in nursing home residents with dementia: a randomized, controlled trial. *J Am Geriatr Soc* 2004; **52**: 1795–804.
- 40 Ancoli-Israel S, Martin JL, Gehrman P, Shochat T, Corey-Bloom J, Marler M, et al. Effect of light on agitation in institutionalized patients with severe Alzheimer disease. *Am J Geriatr Psychiatry* 2003; **11**: 194–203.
- 41 Burns A, Allen H, Tomenson B, Duignan D, Byrne J. Bright light therapy for agitation in dementia: a randomized controlled trial. *Int Psychogeriatr* 2009; **21**: 711–21.
- 42 Dowling GA, Graf CL, Hubbard EM, Luxenberg JS. Light treatment for neuropsychiatric behaviors in Alzheimer's Disease. *West J Nurs Res* 2007; **29**: 961–75.
- 43 Ballard CG, O'Brien JT, Reichelt K, Perry EK. Aromatherapy as a safe and effective treatment for the management of agitation in severe dementia: the results of a double-blind, placebo-controlled trial with Melissa. *J Clin Psychiatry* 2002; **63**: 553–8.
- 44 Burns A, Perry E, Holmes C, Francis P, Morris J, Howes MJ, et al. A double-blind placebo-controlled trial of Melissa officinalis oil and donepezil for the treatment of agitation in Alzheimer's disease. *Dementia Geriatr Cogn Disord* 2011; **31**: 158–64.
- 45 Gormley N, Lyons D, Howard R. Behavioural management of aggression in dementia: a randomized controlled trial. *Age Ageing* 2001; **30**: 141–5.
- 46 Teri L, Logsdon RG, Peskind E, Raskind M, Weiner MF, Tractenberg RE, et al. Treatment of agitation in AD – a randomized, placebo-controlled clinical trial. *Neurology* 2000; **55**: 1271–8.
- 47 Wright LK, Litaker M, Lارا MT, DeAndrade S. Continuum of care for Alzheimer's disease: a nurse education and counseling program. *Issues Ment Health Nurs* 2001; **22**: 231–52.
- 48 Huang HL, Shyu YIL, Chen MC, Chen ST, Lin LC. A pilot study on a home-based caregiver training program for improving caregiver self-efficacy and decreasing the behavioral problems of elders with dementia in Taiwan. *Int J Geriatr Psychiatry* 2003; **18**: 337–45.
- 49 Magai C, Cohen CI, Gomberg D. Impact of training dementia caregivers in sensitivity to nonverbal emotion signals. *Int Psychogeriatr* 2002; **14**: 25–38.
- 50 Finnema E, Drees RM, Ettema T, Ooms M, Ader H, Ribbe M, et al. The effect of integrated emotion-oriented care versus usual care on elderly persons with dementia in the nursing home and on nursing assistants: a randomized clinical trial. *Int J Geriatr Psychiatry* 2005; **20**: 330–3.
- 51 Camberg L, Woods P, Ooi WL, Hurley A, Volicer L, Ashley J, et al. Evaluation of Simulated Presence: a personalized approach to enhance well-being in persons with Alzheimer's disease. *J Am Geriatr Soc* 1999; **47**: 446–52.
- 52 Beck CK, Vogelwohl TS, Rasin JH, Uriri JT, O'Sullivan P, Walls R, et al. Effects of behavioral interventions on disruptive behavior and affect in demented nursing home residents. *Nurs Res* 2002; **51**: 219–28.
- 53 Long PW. *When is a Difference Between Two Groups Significant?* Internet Mental Health, 2011 (http://www.mentalhealth.com/dis-rs/rs-effect_size.html).
- 54 Algase DL, Beck C, Kolanowski A, Whall A, Berent S, Richards K, et al. Need-driven dementia-compromised behavior: an alternative view of disruptive behavior. *Am J Alzheimer Dis Other Demen* 1996; **11**: 10–9.
- 55 Kitwood T, Bredin K. Towards a theory of dementia care: personhood and well-being. *Ageing Soc* 1992; **12**: 269–87.
- 56 Remington R. Calming music and hand massage with agitated elderly. *Nurs Res* 2002; **51**: 317–23.
- 57 Weiner MF, Tractenberg RE, Sano M, Logsdon R, Teri L, Galasko D, et al. No long-term effect of behavioral treatment on psychotropic drug use for agitation in Alzheimer's disease patients. *J Geriatr Psychiatry Neurol* 2002; **15**: 95–8.
- 58 Eggermont LH, Blankevoort CG, Scherder EJ. Walking and night-time restlessness in mild-to-moderate dementia: a randomized controlled trial. *Age Ageing* 2010; **39**: 746–9.
- 59 Hong GR. [Effects of multisensory stimulation using familiarity: persons with dementia in long-term care facility in Korea]. *J Korean Acad Nurs* 2011; **41**: 528–38.



Table DS1 Interventions with evidence of usefulness											
Study	Type of intervention	Degree of agitation of participants	Quality grade	Quality score	Total participants, <i>n</i>	Therapeutic regimen	Separate control group	Immediate outcome ^a	SES (95% CI)	Long-term outcome ^a	SES (95% CI)
Buettner & Ferrario (1997) ²³	Activities	None	2b	7	66	30 weeks of neuro-developmental sequenced activities (e.g. cooking group), frequency unclear	Usual care including activities	Significantly improved at 2 time-points but not third	NC	None	NC
Cohen-Mansfield <i>et al</i> (2006) ²⁷	Activities	None	2b	6	105	5 sessions of activity matched to self-identity roles	Standard activities	Significant improvement	NC	None	NC
Kolanowski <i>et al</i> (2011) ²⁴	Individualised activities	Some	1b	13.5	128	15 sessions activities adjusted to functional level (FL), personality (PSI) or both (FL+PSI)	Standard activities	NS	FL 0.2 (–0.3 to 0.7); PSI 1.5 (0.9 to 2.0); FL+PSI 1.0 (0.4 to 1.5)	No difference (1 week)	NC
Kovach <i>et al</i> (2003) ²⁵	Activities	Some	2b	7.5	78	Varied activities matched to arousal level (e.g. music, exercise, storytelling)	Usual care	Significant improvement in visual analogue scale of agitation	NC	None	NC
Lin <i>et al</i> (2009) ²²	Activities	Some	2b	6	133	28 sessions of Montessori activities	Presence (having researcher present)	Significant improvement	NC	None	NC
Cooke <i>et al</i> (2010) ³⁰	Music therapy using a specific protocol	Some	1b	11.5	47	Music therapy 3 times a week for 8 weeks	Reading group	Significant improvement	–0.9 (–1.2 to –0.6)	NC as crossover	NC
Lin <i>et al</i> (2011) ²⁸	Music therapy using a specific protocol	None	2b	9.5	104	Music therapy twice a week for 6 weeks	Usual care	Significant improvement	–0.6 (–0.9 to –0.4)	Significant improvement (1 month) ^b	–0.6 (–0.9 to –0.3)
Sung <i>et al</i> (2012) ²⁹	Music therapy using a specific protocol	Some	2b	10.5	55	Music therapy twice a week for 6 weeks	Usual care	NS	–0.5 (–1.0 to 0.0)	None	NC
Hawranik (2008) ³¹	Sensory interventions	Some	2b	7	51	5 sessions of therapeutic touch on consecutive days	Placebo therapeutic touch; usual care	NS (total agitation)	NC	NS	NC
Lin <i>et al</i> (2009) ²²	Sensory interventions	Some	2b	6	133	28 sessions of acupressure over 4 weeks	Presence (researcher present)	Significant improvement	NC	None	NC
Remington (2002) ⁵⁶	Sensory interventions	Some	2b	11	68	Hand massage, hand massage and calming music; given once	Usual care	Significant improvement	Hand massage –0.6 (–1.1 to –0.1); plus music –1.3 (–1.9 to –0.8)	None	NC
Van Weerte (2005) ^{34,c}	Sensory interventions	None	2b	10	125	Snoezelen over 18 months	Usual care	Significant improvement in aggression; PN and VA NS	PN –0.1 (–0.3 to 0.2); PA –1.4 (–1.7 to –1.0); VA –3.9 (–4.4 to –3.4)	None	NC
Woods <i>et al</i> (2005) ³²	Sensory interventions	Some	2b	11	60	Therapeutic touch twice a day for 3 days	Placebo massage: usual care	NS	NC	None	NC
Woods <i>et al</i> (2009) ³³	Sensory interventions	Some	2b	10	64	Therapeutic touch twice a day for 3 days	Placebo therapeutic touch or usual care	NS	NC	NS 5 days later (v. placebo or usual care)	NC

(continued)

Table DS1 Interventions with evidence of usefulness (*continued*)

Study	Type of intervention	Degree of agitation of participants	Quality grade	Quality score	Total participants, <i>n</i>	Therapeutic regimen	Separate control group	Immediate outcome ^a	SES (95% CI)	Long-term outcome ^a	SES (95% CI)
Chenoweth <i>et al</i> (2009) ³⁵	Person-centred care and communication skills	Significant	1b	11.5	180	Training plus 2 site visits and telephone-based supervision	Usual care	Significant improvement in restraint use; PRN and care recipient quality of life NS	-1.8 (-1.9 to -1.6)	Significant improvement (8 weeks) ^b	-2.2 (-2.4 to -2.0)
Deudon <i>et al</i> (2009) ³⁶	Person-centred care and communication skills	Not specific	2b	7.5	306	Training including issuing Staff Instruction Cards on BPSD, ongoing support	Usual care	Significant improvement	-0.32 (-0.48 to -0.16)	Significant improvement (20 weeks) ^b	-0.3 (-0.5 to -0.2)
McCallion <i>et al</i> (1999) ³⁸	Person-centred care and communication skills	Some	1b	10	66	Nursing assistants delivered 7 communication-focused sessions to family caregiver, with supervision	Usual care	Verbal agitation, physical non-aggression and irritability improved; aggression did not	PN -0.2 (-0.6 to 0.1); VA -0.1 (-0.4 to 0.3); PA 0.0 (-0.3 to 0.4)	Only verbal aggression and irritability remained significant (3 months) ^b	PN -0.6 (-1.0 to -0.3); VA -0.7 (-1.0 to -0.3); PA 0.1 (-0.3 to 0.4)
McCallion <i>et al</i> (1999) ³⁷	Person-centred care and communication skills	Some	2b	6	105	Communication skills training with ongoing support	Partial crossover – usual care	Significant improvement in all agitation	-0.4 (-0.7 to -0.2)	Significant improvement; physical restraints improved, PRN worsened (6 months) ^b	-0.2 (-0.5 to 0.1)
Sloane <i>et al</i> (2004) ³⁹	Person-centred care and communication skills	None	2b	6	73	Trained in person-centred bathing/towel bath with support implementing	Crossover – usual care	Significant improvement for both showering and towel bath conditions	NC	None	NC
Chenoweth <i>et al</i> (2009) ³⁵	Dementia care mapping	Significant	1b	11.5	191	12 h dementia care mapping plus support implementing	Usual care	Significant improvement. PRN, quality of life and restraint NS	-1.4 (-1.5 to -1.3)	Significant improvement. PRN and restraint NS (4 months) ^b	-1.5 (-1.6 to -1.3)

BPSD, Behavioural and Psychological Symptoms of Dementia; FL, (matched to) functional level; NC, not calculable; NS, not significant; PSI, (matched to) interest only; PA, physical aggression; PN, physical non-aggression; PRN, prescription of drugs as required; SES, standardised effect size; VA, verbal aggression/agitation.

a. In comparison with the control condition.

b. Original paper used a random effects model, a marginal model based on generalised estimating equations or repeated-measures analysis of variance/covariance.

c. Majority but not all participants were randomised. We were unable to access original data.

Table DS2 Interventions without evidence of usefulness

Study	Type of intervention	Degree of agitation for participation in the study	Quality grade	Quality score	Total patients, <i>n</i>	Therapeutic regimen	Separate control group	Immediate outcome	SES (95% CI)	Long-term outcome	SES (95% CI)
Ancoli-Israel <i>et al</i> (2003) ⁴⁰	Light therapy	Significant	2b	6	92	2 h daily light therapy for 10 days (a.m. or p.m.)	Placebo red light during a.m.	Verbal agitation worsened	-2.0 (-2.4 to -1.6)	None ^a	-0.3 (-0.6 to 0.1)
Burns <i>et al</i> (2009) ⁴¹	Light therapy	Some	1b	12.5	48	2 h daily light therapy for 2 weeks	Standard light	NS	-0.2 (-0.6 to 0.2)	NS (4 weeks) ^a	-0.3 (-0.7 to 0.2)
Dowling <i>et al</i> (2007) ⁴²	Light therapy	Some	2b	6	70	Activities in brightly lit area (outside/lightbox) 1 h/day for 10 weeks	Similar activities in a non-brightly lit area	Significantly worsened	p.m. light 4.0 (3.1 to 4.9); a.m. light 7.0 (5.8 to 8.3) (NPI)	None	NC
Ballard <i>et al</i> (2002) ⁴³	Aromatherapy	Significant	2b	6	72	56 sessions of Melissa oil massage	Odourless sunflower oil	Significant improvement	NC	None	None
Burns <i>et al</i> (2011) ⁴⁴	Aromatherapy	Significant	1b	12.5	94	168 sessions aromatherapy massage (plus placebo/donepezil)	Placebo aromatherapy massage (plus placebo/donepezil)	NS	NC	None	None
Gormley <i>et al</i> (2001) ⁴⁵	Training family caregivers in BMT	Some	1b	11.5	65	4 sessions training BMT	Given non-behavioural advice and signposting	NR	None	NS agitation and caregiver burden (2 weeks) ^a	-0.6 (-1.0 to -0.2) (RAGE)
Teri <i>et al</i> (2000), Weiner <i>et al</i> (2002) ^{46,57} (short- and long-term effects)	Training family caregivers in BMT	Significant	1b	11	77	11 sessions training BMT	Placebo medication (we did not consider psychotropic medication group)	NS (agitation, caregiver burden)	NC	NS (3, 6 and 12 months)	NC
Huang <i>et al</i> (2003) ⁴⁸	Training family caregivers in CBT	Significant	2b	8	59	2 home and 13 telephone consultations	Written educational materials and social telephone calls	Unclear as baseline/change scores not analysed; significantly different at T_2	-0.3 (-0.6 to -0.0)	Unclear (3 months)	-0.2 (-0.5 to 1.1)
Wright <i>et al</i> (2001) ⁴⁷	Training family caregivers in CBT	Significant	2b	7	93	3 home and 2 telephone consultations training CBT	Usual care	NS	NC	NS agitation, caregiver wellbeing (9 months)	NC
Eggermont <i>et al</i> (2010) ⁵⁸	Exercise	None	2b	6.5	112	30 sessions of walking	Social visit, outside	NS (restlessness)	NC	NS (7 weeks)	NC
Finnema <i>et al</i> (2005) ⁵⁰	Training programmes for paid caregivers without supervision	None	2b	8	146	Whole staff ethos training, selected staff intensive training, groups and supervision on emotion-oriented care	Usual care	NS	NC	None	None
Magai <i>et al</i> (2002) ⁴⁹	Training programmes for paid caregivers without supervision	None	2b	6.5	91	Non-verbal communication skills training, no supervision	Educational training (placebo), usual care (control)	NS	NC	NS (9, 12, 15 weeks)	NC

(continued)

Table DS2 Interventions without evidence of usefulness (*continued*)

Study	Type of intervention	Degree of agitation for participation in the study	Quality grade	Quality score	Total patients, <i>n</i>	Therapeutic regimen	Separate control group	Immediate outcome	SES (95% CI)	Long-term outcome	SES (95% CI)
Beck <i>et al</i> (2002) ⁵²	Other: mix of ADL, communication skills and psychosocial activities	Some	2b	7	96	60 sessions promoting functional independence, psychosocial Intervention or both	Social contact (placebo), usual care (control)	NS	NC	NS (1, 2 months)	NC
Hong (2011) ⁵⁹	As above	None	2b	7	55	Culturally familiar environment from youth with sensory activities	Same familiar environment but no activities	NS	-0.3 (-0.7 to 0.1)	None	2 NC
Camberg <i>et al</i> (1999) ⁵¹	Simulated presence	Not specified	2b	8	54	Simulated presence tape at least twice a day while care recipient agitated	Crossover – neutral tape (placebo), usual care	NS (total agitation)	NC	None	NC

ADL, activities of daily living; BMT, behavioural management therapy; CBT, cognitive-behavioural therapy; CMAI, Cohen-Mansfield Agitation Inventory; NC, not calculable; NPI, Neuropsychiatric Inventory; NR, not reported; NS, not significant ($P > 0.05$); PRN, prescription of drugs as required; RAGE, Rating Scale for Aggressive Behaviour in the Elderly; SES, standardised effect size.
a. Original paper used either a random effects model, a marginal model based on generalised estimating equations or repeated-measures analysis of variance/covariance.

BJPpsych

The British Journal of Psychiatry

Non-pharmacological interventions for agitation in dementia: systematic review of randomised controlled trials

Gill Livingston, Lynsey Kelly, Eleanor Lewis-Holmes, Gianluca Baio, Stephen Morris, Nishma Patel, Rumana Z. Omar, Cornelius Katona and Claudia Cooper
BJP 2014, 205:436-442.

Access the most recent version at DOI: [10.1192/bjp.bp.113.141119](https://doi.org/10.1192/bjp.bp.113.141119)

Supplementary Material

Supplementary material can be found at:
<http://bjp.rcpsych.org/content/suppl/2015/03/02/205.6.436.DC1.html>

References

This article cites 56 articles, 10 of which you can access for free at:
<http://bjp.rcpsych.org/content/205/6/436#BIBL>

Reprints/ permissions

To obtain reprints or permission to reproduce material from this paper, please write to permissions@rcpsych.ac.uk

You can respond to this article at

[/letters/submit/bjprcpsych;205/6/436](http://letters/submit/bjprcpsych;205/6/436)

Downloaded from

<http://bjp.rcpsych.org/> on July 7, 2015
Published by The Royal College of Psychiatrists
