Clinical and cost-effectiveness of the Managing Agitation and Raising Quality of Life (MARQUE) intervention for agitation in people with dementia in care homes: a single-blind, cluster-randomised controlled trial

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Summary

Background Many people with dementia living in care homes have distressing and costly agitation symptoms. Interventions should be efficacious, scalable, and feasible.

Methods We did a parallel-group, cluster-randomised controlled trial in 20 care homes across England. Care homes were eligible if they had 17 residents or more with dementia, agreed to mandatory training for all eligible staff and the implementation of plans, and more than 60% of eligible staff agreed to participate. Staff were eligible if they worked during the day providing face-to-face care for residents with dementia. Residents were eligible if they had a known dementia diagnosis or scored positive on screening with the Noticeable Problems Checklist. A statistician independent of the study randomised care homes (1:1) to the Managing Agitation and Raising Quality of Life (MARQUE) intervention or treatment as usual (TAU) using computer-generated randomisation in blocks of two, stratified by type of home (residential or nursing). Care home staff were not masked to the intervention but were asked not to inform assessors. Residents with dementia, family carers, outcome assessors, statisticians, and health economists were masked to allocation until the data were analysed. MARQUE is an evidence-based manualised intervention, delivered by supervised graduate psychologists to staff in six interactive sessions. The primary outcome was agitation score at 8 months, measured using the Cohen-Mansfield Agitation Inventory (CMAI). Analysis of the primary outcome was done in the modified intention-to-treat population, which included all randomly assigned residents for whom CMAI data was available at 8 months. Mortality was assessed in all randomly assigned residents. This study is registered with the ISRCTN registry, number ISRCTN96745365.

Findings Between June 14, 2016, and July 4, 2017, we randomised ten care homes (189 residents) to the MARQUE intervention and ten care homes (215 residents) to TAU. At 8 months, primary outcome data were available for 155 residents in the MARQUE group and 163 residents in the TAU group. At 8 months, no significant differences in mean CMAI scores were identified between the MARQUE and TAU groups (adjusted difference –0·40 [95% CI –3·89 to 3·09; p=0·8226]). In the intervention care homes, 84% of all eligible staff completed all sessions. The mean difference in cost between the MARQUE and TAU groups was £204 (–215 to 623; p=0·320) and mean difference in quality-adjusted life-years was 0·015 (95% CI –0·004 to 0·034; p=0·127). At 8 months, 27 (14%) of 189 residents in the MARQUE group and 41 (19%) of 215 residents in the TAU group had died. The prescription of antipsychotic drugs was not significantly different between the MARQUE group and the TAU group (odds ratio 0·66; 95% CI 0·26 to 1·69, p=0·3880).

Interpretation The MARQUE intervention was not efficacious for agitation although feasible and cost-effective in terms of quality of life. Addressing agitation in care homes might require resourcing for delivery by professional staff of a more intensive intervention, implementing social and activity times, and a longer time to implement change.

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Introduction

Agitation or purposeless activity, which includes restlessness, pacing, repetitive vocalisations, and verbally or physically aggressive behaviours,[1,2] is one of the most common neuropsychiatric symptoms in dementia.[3,4] Such behaviours are unpleasant for the person with dementia,[1] can cause family distress and subsequent inability to continue to care at home,[5] can precipitate care home admission and, in care homes, are strongly associated with quality of life.[6] Agitation accounts for about 12% of dementia health and social care costs, and increases costs for care home residents.[7]

Most care home residents have dementia and complex needs, and around 50% of individuals with moderate or

Research in context

Evidence before this study

Our 2014 systematic review of randomised controlled trials of non-pharmacological interventions for agitation in people with dementia found activities, structured music therapy, and sensory interventions provided immediate but not lasting benefit. However, benefits of staff training in communication skills lasted months. In our update in May 2018, we searched PsycINFO and Embase for randomised controlled trials published between June 12, 2012, and May 15, 2018, that reported on care home interventions targeting agitation for people with dementia of any severity and how to sustain an intervention, using the terms: (agitation OR restless* OR irrita* OR aggression OR "aberrant motor behav*" OR "psychomotor activity" OR "challenging behav*" OR pacing OR sundowning OR wander* OR "walking about" OR "safe walking") AND (dement* OR alzheimer OR "vascular dement*" OR "pick's disease" OR huntington OR creutzfeldt OR cjd OR binswanger OR lewy) AND ("randomised control* trial*" OR RCT"), with no language restrictions. Our search identified 49 trials, of which 16 measured agitation as an outcome. Three studies reported clinically significant reductions in agitation. Successful interventions were intensive and multicomponent. The first intervention comprised staff training, increased social interaction, antipsychotic review, physician review of medical history, all medications and physical examination, assessment of pain, a doctor and nurse-led reflective case conference developing individualised treatment plans using a problem-solving model and a 3 h educational lecture, and role play for 8–12 weeks. This intervention reduced agitation at the end of the intervention. The second intervention included training and support of care home staff by a physician and specialist nurse for two 4 h blocks on behavioural symptoms in dementia using standardised assessments, non-pharmacological and pharmacological interventions, case conferences using standardised case vignettes, and activities delivered twice per week by activity co-coordinators or occupational therapists, for residents not already attending. This intervention was effective at 10 months for agitation. The third intervention combined training for staff and managers in person-centred care and the promotion of tailored person-centred activities and social interactions by a psychologist or occupational therapist working in the home for a month. Further training was provided for two champions (one training day per month) with coaching, supervision, and regular review with the therapist during the 9 month period. The intervention also included, if appropriate, triggering doctor's review of antipsychotic medications, and for individuals who did not participate in activities, implementation of activities. This intervention was effective at 9 months. One intervention was costed, but no cost-effectiveness analyses were done and we identified no reports of intervention effects being sustained. A separate systematic review found that interventions were sustained by interactive training, individual staff support after group training, retention of training materials, incorporating interventions into routine care, and nearly all staff attending.

Added value of this study

Our Managing Agitation and Raising Quality of Life (MARQUE) intervention, which comprised six sessions of staff training, was less intensive than some multicomponent interventions that have had positive outcomes and was primarily delivered by non-clinical staff. The intervention did not reduce agitation or affect secondary outcomes. The cost-effectiveness analysis estimated effectiveness using improvements in quality-adjusted life-years (QALYs) and found that the costs for QALY improvements were less than the National Institute for Health and Care Excellence threshold and thus the intervention was deemed cost-effective.

Implications of all the available evidence

Evidence suggests that intensive, multicomponent, psychosocial interventions delivered by specialists to reduce agitated behaviour in people with dementia in care homes can be successful, but no evidence exists for the efficacy of less intensive, specialist, and costly interventions such as MARQUE. Helping people with dementia and agitation in care homes requires well-resourced interventions.

severe dementia have clinically significant agitation.[8] Agitation is associated with dementia severity and might also be associated with physical conditions (such as untreated or undertreated delirium or pain or medication side-effects), or other unmet needs such as boredom and social isolation. Activities in care homes are not necessarily attended by individuals with agitation.[6,9,10] Intensive multicomponent interventions in which physical, social, or occupational activities are implemented, and staff are trained to ensure people with dementia and agitation participate, had some success in reducing agitation in care home residents with dementia immediately after the intervention,[10–13] with a similar magnitude of effect to antipsychotic medication, but without the associated side-effects.[14,15] However, such interventions might not be scalable or cost-effective, since they require specialist professional training of care home staff, ongoing supervision to deliver person-centred care and improve communication, physical problems to be addressed, and the implementation of social or other activities, such as positive sensory experiences. Interventions are often difficult to implement.[16] It is unclear whether interventions can lead to cultural change that becomes embedded in care home practices, so that effects persist or even increase after the intervention. We therefore developed and piloted a manual-based intervention (Managing Agitation and Raising Quality of Life in dementia; MARQUE) comprising six sessions, delivered by supervised non-clinical psychology graduates, on the basis of evidence about what works for people with dementia and agitation,

and what enables interventions to become integrated into care practice long term.[17,18] This trial aimed to assess whether the MARQUE intervention reduced agitation in residents with dementia after 8 months compared with treatment as usual (TAU).

Methods

Study design and participants

We did a parallel-group, superiority, single-blind, cluster-randomised controlled trial that involved 20 care homes in England. We restricted recruitment to areas that were within 2 h travel distance of our base in London (UK). Eligible care homes had no plans to close in the following year, were not currently participating in an intervention study, and agreed, if randomised to the intervention, to allow eligible staff to attend mandatory training sessions and follow-up supervision during shifts, to train two staff champions to facilitate implementation (to promote shared ownership and because of possible staff turnover), and to change management procedures to integrate new techniques into care. Eligible staff worked during the day, providing face-to-face care to residents with dementia. Care homes were excluded before randomisation if fewer than 60% of eligible staff consented or if fewer than 17 potential residents with dementia lived at the care home.

All residents with dementia were eligible for the study. Care home managers identified residents with a known diagnosis of dementia and we screened other residents for probable dementia using the Noticeable Problems Checklist,[19] which has been validated against clinical diagnosis.[19,20] Care home staff approached residents and relatives. Staff identified residents with capacity to consent to the study, and researchers assessed their capacity using the Mental Capacity Act 2005[21] criteria. If residents lacked capacity to consent, we consulted the family carer or, if none were available, a professional consultee who knew the resident well to give written informed consent. We asked the care home manager to nominate staff who knew a resident well to give proxy ratings and also interviewed a consenting primary family carer if they saw the resident at least monthly. Full inclusion and exclusion criteria for care homes, residents, paid carers, and family carers are shown in the appendix.

The study was approved by the National Research Ethics Service Committee London (reference 14/LO/0697). The trial is registered with the ISRCTN registry, number ISRCTN96745365. The study protocol is available online and is included in the appendix.

Randomisation and masking

A statistician independent of the study randomised care homes (1:1) to the MARQUE intervention or TAU using a computer-generated randomisation sequence; care homes were randomised in blocks of two, stratified by type of home (residential or nursing). The randomisation list was held by Clinical Trials Unit staff who communicated pairs of allocations to the trial manager (AL) as required. Care home staff were not masked to the intervention but were asked not to inform assessors. Residents with dementia, family carers, assessors who collected data, statisticians and health economists were masked to allocation until the data were analysed. Trained psychology graduates worked as MARQUE facilitators and assessors in two separate teams to maintain masking; one group was allocated to complete baseline and follow-up assessments for an individual home and the other group to facilitate and deliver the intervention if randomly assigned to the intervention. We provided clear, repeated instructions to researchers and care home staff not to discuss treatment allocation and to put away materials associated with the intervention.

Procedures

We developed MARQUE, a six-session manual-based intervention, followed by an implementation and supervision period (panel), based on our systematic review of strategies to reduce or prevent agitation for people with dementia in care homes,[11] qualitative interviews with care home staff about their understanding of agitation and what facilitated use of successful strategies,[23] cross-sectional and longitudinal data on determinants of agitation in care homes,[6,24] a systematic review of components and strategies for successful implementation of psychosocial interventions in care homes,[17] and coproduction with stakeholders. We ran three focus groups with family carers of people with dementia who had experienced agitation and or lived in a care home, two before developing the intervention and one after, about what should be in the intervention. Additionally, we showed the draft manual to seven staff working in differing roles in four care homes and asked them to comment on the design, layout, content, and structure of the manual. Managers were asked about the practicality of delivering the intervention. We also sought feedback from a range of professionals and other stakeholders from the MARQUE steering group and our community of interest group (a network of academic researchers, policy makers, community stakeholders, and patient and public involvement representatives). In addition to presenting the overview of the intervention to the community of interest group, we consulted six of the members individually (a geriatrician, a sociologist, a research nurse, an occupational therapist, an academic psychologist, and a clinical psychologist) to get feedback. The six members suggested changes in formatting and language and requested more focus on risk, pain, and illness. We then piloted the intervention in one care home, and made changes after feedback from both facilitators and care home staff before testing it in the main trial. The changes included modification of the interaction level in some parts of the manual, making between-session tasks more specific, checking with

See Online for appendix

For the **study protocol** see http://www.isrctn.com/ISRCTN96745365

Panel: Managing Agitation and Raising Quality of Life in dementia manualised sessions

Sessions 1–5 all included one or two key topics for discussion, a specific plan or activity to try out between sessions, a stress reduction exercise with an accompanying CD or mp3 file, and a record form for staff to complete for monitoring progress between sessions. During each session, the participants shared examples from their practice to ensure that the intervention was individually focused and relevant.

Session 1: Getting to know the person with dementia
This session included psychoeducation about dementia and staff experiences of managing agitation, including what works. It also introduced the key theme that getting to know and understand the person with dementia can help staff to manage and prevent agitation from occurring. The session included a game to find out what the person with dementia enjoyed doing and included a focus on managing the stress that caring can bring.

Session 2: Pleasant events
This session focused on the importance of pleasant events for residents. It included a focus on how to plan for and include residents with severe dementia and how to build activities into day-to-day care. The session introduced the idea that even small interactions could be pleasant events.

Session 3: Improving communication
This session discussed communicating with people with dementia, with a particular focus on how to respond when residents are distressed. It also included discussion and exercises on effective communication within the team and with relatives.

Session 4: Understanding agitation
This session introduced the Describe, Investigate, Create, Evaluate approach,[22] focusing on describing and investigating episodes of agitation. The content is framed in terms of recognising and understanding the unmet needs of residents with agitation.

Session 5: Practical responses and making a plan
This session focused on creating strategies to manage agitation, including practical and environmental changes and when to ask for additional help. The session also introduced the importance of building these strategies into a plan that can be evaluated.

Session 6: What works? Using skills and strategies in the future
This session recapped on earlier sessions and focused on what staff had found useful and what worked. It included the development of a specific action plan, individual to each home, to enable staff to continue to use helpful strategies and approaches and to inform the supervision phase of the intervention.

Supervision process
Team members met with the care home manager to ensure they agreed with the plan and set up supervision and troubleshooting meetings.

participants that they had understood tasks, and simplifying some of the content. Additionally, the pleasant events section was restructured and greater emphasis was placed on how pleasant events did not need to be time and resource intensive stand-alone activities, but could be part of routine care. We also added more detail to the manual regarding what the supervision and troubleshooting period would involve and placed more emphasis on the supervision period during training sessions. We arranged to meet with managers and champions halfway through the intervention sessions to review and plan follow-up supervision and troubleshooting.

We delivered a multidisciplinary training programme for the MARQUE facilitators. Each facilitator was required to be signed off from a competency checklist as ready to deliver the intervention before initial delivery.

Two facilitators delivered the intervention to groups of up to 12 care home staff (care assistants, nurses, and activities coordinators). Managers were encouraged to attend training to promote the idea that they, as well as the care staff, were part of implementing the intervention, and to support with implementation of strategies. We delivered sessions several times in each home to ensure groups were kept to a size that enabled interaction and the attendance of all eligible staff. For staff who missed a session, we arranged a time to deliver an individual abbreviated version. We offered care homes reimbursement for staff cover to allow staff to attend sessions and worked closely with managers to facilitate attendance and engagement with the intervention.

A clinical psychologist (PR) supervised facilitators in two groups to maintain masking with additional individual support as needed. Facilitators were encouraged to be empathetic, adhere to the intervention, work with staff to reflect on and try different strategies, not be discouraged as change might be slow, and encourage staff to communicate and use the whole team rather than respond in isolation. The staff were encouraged to raise any challenging interactions and report any potentially abusive behaviour. We monitored intervention fidelity using checklists, which were tailored to the content of each session. The checklists were used to rate whether the most important components of every session were delivered, on a Likert scale from 1 (not at all) to 5 (very focused) for each item. The checklists also included four items to rate process factors (keeping to time, keeping the group focused on the manual, keeping the group engaged in the session, and managing group dynamics). All items were summed to give an overall score out of 40 for the individual facilitator. Facilitators recorded one training session per training group per home, which the trial manager selected randomly for review by researchers who had not delivered the intervention.

The manualised sessions are described in the panel. All materials were retained by attendees. MARQUE incorporated a variety of heuristics designed to become part of the team working, specifying ideas to try and how to implement them. The heuristics included a board game (Call to Mind) played with residents to find what they like to do, a CD or mp3 of stress reduction exercises for staff, pleasant events tick lists, and a decision making model to manage agitation adapted for UK practice (Describe, Investigate, Create, Evaluate).[21] Each session included interactive group tasks, talking points, summaries, and some discussion with staff about earlier sessions, finishing with a relaxation session. We asked staff to try out strategies and practice relaxation exercises between sessions. In the final session, staff developed specific, measurable, attainable, relevant, and time-based

(SMART) action plans of useful strategies for their care home and residents. Facilitators discussed and refined the plans for each care home with the home manager to ensure they were supportive and that plans were realistic and deliverable, and to discuss practicalities of how best to deliver long-term support. PR offered monthly clinical supervision to care home staff alternating with the facilitators who visited monthly to support staff to implement their action plans.

Residents, relatives, carers, and staff recruited to the study had data collected at baseline and at 8 month follow-up assessments. We also recorded sociodemographic characteristics of eligible non-consenting residents at baseline. Assessors completed interviews with residents and staff in a private room at the care home. Family carers chose the interview location, usually a private room at the care home. We recorded sociodemographic details of residents and staff at baseline (sex, staff role at care home, years working in current home) and care home characteristics, including size and whether the home was residential or nursing.

Outcomes

The primary endpoint was agitation score at 8 months, measured using the Cohen-Mansfield Agitation Inventory (CMAI).[2] The CMAI assesses the frequency of 29 agitated behaviours, each scored on a seven-point Likert scale from 1 (never) to 7 (several times an hour), and summed to give a total score, ranging from 29 to 203.

Resident data for the following secondary outcomes were obtained at baseline and 8 month follow-up through proxy interviews with staff: agitation symptoms (CMAI) and clinically significant agitation (defined as CMAI score >45);[6,25] reduction in neuropsychiatric symptoms (measured using the Neuropsychiatric Inventory[26]) with 12 symptoms scored in the previous 4 weeks, with the total score ranging from 0 to 144, whereby higher scores indicate worse symptoms; dementia-specific health-related quality of life (measured by the DEMQOL-Proxy),[27] with 31 items scored from 1 (a lot) to 4 (not at all) giving a total score ranging from 31 to 124 whereby a higher score indicates better quality of life; service use using the Client Services Receipt Inventory[28] modified for care homes to cost health and social care services and carer time; cost of manual training and intervention; and generic health-related quality of life using the proxy-rated European quality of life five dimensions questionnaire (EQ-5D-5L),[29] with five dimensions (mobility, self-care, usual activities, pain or discomfort, and anxiety or depression), scored from 1 (no problems) to 5 (extreme problems), summarised using a 5 digit number that can be converted into a preference weight.

Additional outcomes for residents were dementia severity, assessed using the Clinical Dementia Rating,[30] a widely used measure of global dementia severity, scored from 0 (none) to 3 (severe), and psychotropic medication prescribed in the previous month. Additional outcomes for staff were the Maslach Burnout Inventory,[31,32] which is a validated measure with three subscales (emotional exhaustion, depersonalisation, and personal accomplishment) with items scored as 0 (never) to 6 (every day) and summed to provide subscale scores; the sense of competence in dementia (SCID)[33] scale, which provides a self-report measure of subjective competence in care staff, with four subscales (professionalism, building relationships, care challenges, and sustaining personhood) whereby higher scores indicate greater competence; and the Staff Tactics Scale,[34] which uses a Likert scale to measure observed acts of possibly abusive and positive behaviours committed by staff or observed in other staff in the previous 3 months.[34] The Staff Tactics Scale is anonymous and scores range from 0 (never) to 4 (all the time) and a score of 2 or more was defined as caseness. We collected questionnaires from each care home and we informed the care home manager if we identified physical abuse.

We did not collect safety outcomes separately, but did record mortality and antipsychotic prescribing.

Statistical analysis

The sample size was calculated using inflation by the design effect of the numbers required for analysis in an individually randomised parallel group trial.[35] The calculation used the observed effect size (0·5) of a standardised intervention in reducing emergent or symptomatic agitation in care home participants.[11] To detect this clinically significant difference[36] with 90% power at the 5% significance level would require 54 residents per group for an individually randomised design based on the use of analysis of covariance to adjust for baseline (correlation 0·6).[37] We aimed to randomise 20 care homes, allowing for the possibility that two homes might drop out. With a sample size of 18 care homes and assuming an intra cluster correlation coefficient of 0·087,[38] an average of 12 residents would be needed per cluster. To allow for up to 30% loss to follow-up, we aimed to recruit 17 residents from each care home. Statistical analyses were done in accordance with a predefined statistical analysis plan using Stata (version 14). We summarised differences in characteristics between eligible consenting and non-consenting residents. We reported sociodemographic and baseline clinical characteristics for each randomised group and adherence to the intervention as number of sessions delivered in each home, number of staff attending, number of sessions each member of staff attended, and fidelity scores. We calculated the proportion of care homes in which more than 80% of staff attended all six sessions (group sessions or catch up sessions) and the intracluster correlation coefficient for the primary outcome. We imputed DEMQOL scores using mean imputation when more than 50% of data was present, but did not impute any other data.

We summarised CMAI scores at 8 months by treatment group and compared them using a two-level

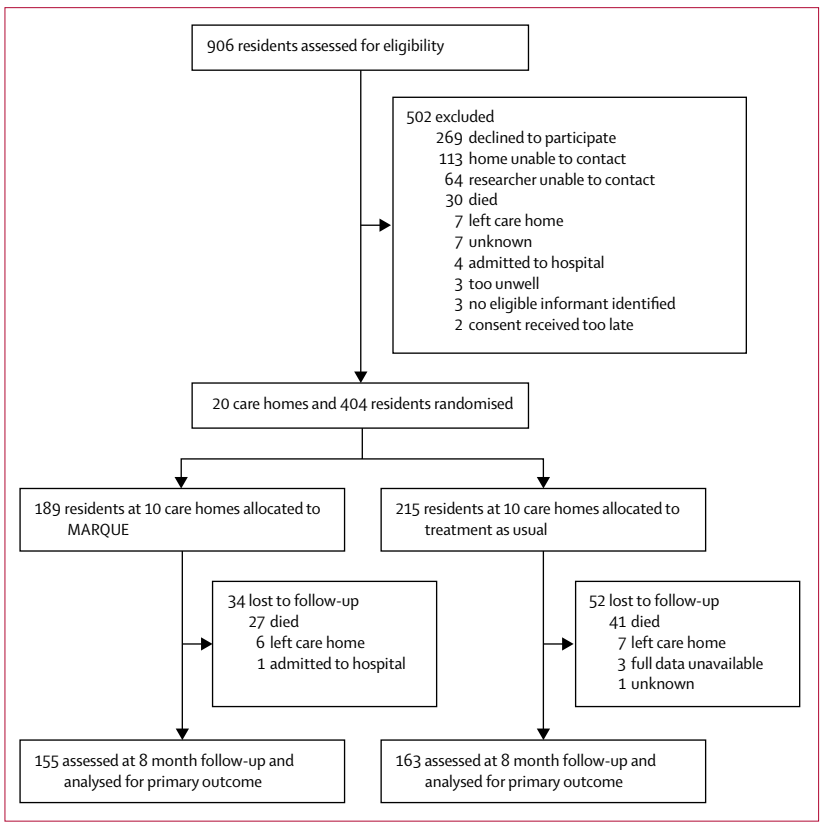

Figure 1: **Recruitment and follow-up of residents**

mixed effects linear regression model allowing for care home clustering. The model was adjusted for baseline CMAI score, type of care home (residential *vs* nursing), and baseline severity of dementia (Clinical Dementia Rating). Similar analyses were done for the following secondary outcomes and prespecified additional outcomes: total Neuropsychiatric Inventory score, DEMQOL-Proxy, SCIDS, Maslach Burnout Inventory, and Staff Tactics Scale. We used mixed effects logistic regression to assess clinically significant agitation (CMAI scores >45) and use of psychotropic drugs. Although Staff Tactics Scale data were anonymous, other care home level factors were included in models for this outcome; thus we could identify the care home at which staff worked. Reasons for missing outcome data were examined for each randomised group. We compared characteristics of residents with and without missing outcome data using mixed effects logistic regression models (and identified characteristics predicting missingness). Model residuals were checked using normal plots and plots of fitted values against residuals. The primary outcome was assessed in the modified intention-to-treat population, which included all randomly assigned residents for whom CMAI data was available at 8 months. Mortality was assessed in all randomly assigned residents.

We did the following sensitivity analyses to estimate the treatment effect for the primary and secondary outcomes: unadjusted treatment effect estimate (from mixed effects models allowing for clustering); additional adjustments for baseline factors that predicted missingness of outcomes; and adjustment for imbalances in baseline characteristics. After checking model residuals we found some non-normality for CMAI and the Neuropsychiatric Inventory, which have positively skewed distributions. We did sensitivity analyses for these outcomes refitting our model using quantile regression.

The cost of the MARQUE intervention included the cost of training the therapists, and the cost of delivery of the intervention (appendix). Hourly costs for therapists and care home staff were taken from the Personal Social Services Research Unit.[39]

Data regarding health-care service use was collected using the Client Services Receipt Inventory for the previous 4 months and medication prescriptions from medication charts. Unit costs from published sources[37,40,41] were attached to each resource item. The economic analysis was done from the health-care cost perspective. All costs are reported in pounds sterling at 2015–16 prices.

Quality-adjusted life-years (QALYs) were calculated as the area under the curve adjusting for baseline differences over 8 months between the MARQUE and TAU groups. QALYs were calculated using the EQ-5D-5L. We used multivariate imputation by chained equation for missing data, generating 20 imputed data sets. For each dataset, we used non-parametric bootstrapping (with 1000 replications) to resample observations with replacements. The bootstrap results were combined to calculate the mean values for costs and utilities and the SEs for the imputed values were used to calculate 95% CIs. We calculated the incremental cost per QALY gained and the probability of cost-effectiveness of intervention versus TAU for a range of values of willingness to pay for each QALY gained.

We did a sensitivity analysis including the cost of the intervention for all residents living in care homes randomly assigned to the intervention since the intervention was delivered to staff and therefore affected the whole care home.

Role of the funding source

The funders and sponsors of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Results

Between June 14, 2016, and May 3, 2017, we approached 33 care homes, of which 28 homes were eligible, and 20 (71%) of 28 eligible homes were recruited. Of the 33 care homes approached, seven did not respond after

initial contact, four had too few residents with dementia, one was involved in another intervention study, and one could not participate because the care home management refused permission. By June 4, 2017, we had randomised 20 care homes. Of the 20 randomised homes, 15 were private and five were charity-run; eight were residential, and 12 were nursing or mixed nursing and residential homes. Care Quality Commission ratings for consented homes are shown in the appendix. 767 eligible residents were identified, of whom 410 (53%) consented to take part. Six participants withdrew between consent and randomisation; thus, 404 (53%) eligible residents were randomly allocated. Participating residents had similar characteristics (age, sex, dementia diagnosis) to non-participants; however, staff deemed 59 (15%) of 404 of participants to have capacity to consent compared with 30 (8%) of 363 non-participants. Ten care homes (189 residents) were assigned to the MARQUE intervention and ten care homes (215 residents) to the TAU group. A mean of 20·2 residents (SD 3·8) were recruited in each care home. No participating care homes withdrew from the study. Figures 1 and 2 show resident and staff flow through the study. The flow of family carers is shown in the appendix.

Most residents were female (mean age 86 years [SD 8]), and 90% spoke English as their first language (table 1). Mean CMAI score at baseline was 42 (SD 16) in the MARQUE group and 44 (15) in the TAU group; 59 (31%) of 189 residents in the MARQUE group and 81 (39%) of 210 patients in the TAU group had clinically significant agitation. Demographic characteristics of the 492 care home staff and baseline burnout, SCID, and Staff Tactics Scale scores are shown in table 2. Most staff were women (mean age 44 years [SD 12]) and 74 (31%) of 241 in the MARQUE group and 112 (45%) of 248 in the TAU group were white; 115 (48%) of 242 staff and 124 (50%) of 248 staff spoke English as their first language.

At baseline, we obtained consent from 129 family carers in the MARQUE group and 163 in the TAU group. 39 (30%) of 129 carers in the MARQUE group and 51 (31%) of 163 carers in the TAU group were men (mean age 60 years [SD 12] *vs* 62 years [9]). Family carers were most often the children of the residents with dementia. The median number of visits made per month was 9 (IQR 4–13) for the MARQUE group and 9 (IQR 4–14) for the TAU group.

Each facilitator delivered sessions in a median of six homes (range one to seven) and seven of eight facilitators were women. The facilitators delivered a mean of 3 sessions per week (range 2–4) with a mean of 27 staff (range 17–41) trained in each home. The mean eligible staff attendance at all six sessions across the intervention care homes, including catch-ups, was 84% (range 67–100). Of the ten care homes assigned to the MARQUE intervention, more than 80% of staff attended all six sessions in six homes, 70–80% of staff attended all six sessions in three homes, and 67% attended all six sessions in one home. One session per training group was recorded (n=32) and the mean fidelity score for all recorded sessions was 37·7 out of 40 (range 34·0–39·3). The median supervision time after completion of the six sessions was 640 min (IQR 581–885) per care home for 59% of staff that attended training; each member of staff received a median of 1 supervision session (0–2) after training, and newly employed staff received a median of 1 supervision session (1–2).

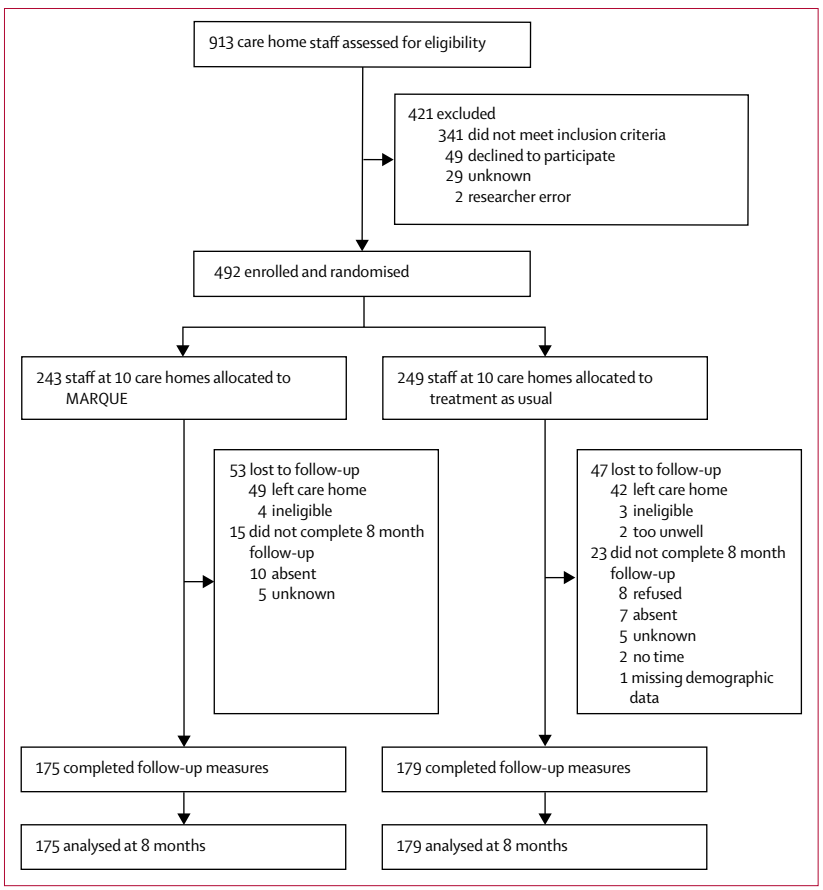

Figure 2: **Recruitment and follow-up of care home staff**

Primary outcome data were collected for 155 (82%) of 189 residents in the MARQUE group and 163 (76%) of 215 residents in the TAU group; thus, these residents were included in the modified intention-to-treat analysis set. The intracluster correlation coefficient was 0·03 (95% CI 0·00 to 0·20). CMAI scores were not significantly different between the two groups at 8 month follow-up (difference –0·40, 95% CI –3·89 to 3·09; p=0·8226). Differences in CMAI remained non-significant in sensitivity analyses controlling for predictors of missingness (resident age, resident sex, and family carer sex) and imbalances in baseline characteristics (resident sex, resident marital status, psychotropic medication) and also in unadjusted analyses and quantile regression (table 3).

	Treatment as usual (n=215)	MARQUE (n=189)
Sex		
Men	74 (34%)	41 (22%)
Women	141 (66%)	148 (77%)
Age (years)*	86 (7)	86 (8)
Ethnicity		
White	169/207 (82%)	167/186 (90%)
Asian	6/207 (3%)	3/186 (2%)
Black	25/207 (12%)	16/186 (9%)
Other	7/207 (3%)	0/186
First language English	184/205 (90%)	162/178 (90%)
Marital status		
Married or partner	42/195 (22%)	30/177 (17%)
Not currently married	153/195 (78%)	147/177 (83%)
Education		
None	66/152 (43%)	40/122 (33%)
O levels, GCSEs, NVQ (levels 1–3), or A levels†	49/152 (32%)	37/122 (30%)
Degree or postgraduate	24/152 (16%)	31/122 (25%)
Other	13/152 (9%)	14/122 (11%)
Diagnosis of dementia pre-study	182/215 (85%)	148/189 (78%)
Dementia severity (Clinical Dementia Rating)		
Mild dementia	28/207 (14%)	36/170 (21%)
Moderate dementia	82/207 (40%)	69/170 (41%)
Severe dementia	97/207 (47%)	65/170 (38%)
CMAI score		
Mean CMAI score‡	44 (15)	42 (16)
Median CMAI score‡	41 (31–52)	37 (29–50)
Clinically significant agitation (CMAI >45)	81/210 (39%)	59 (31%)
Aggressive behaviour	17 (8)	17 (8)
Physically non-aggressive behaviour§	11 (6)	10 (6)
Verbally agitated¶	8 (5)	7 (5)
NPI		
Mean NPI‖	16 (16)	14 (14)
Mean NPI agitation‡**	2 (3)	2 (3)
NPI agitation	105/212 (49%)	93/188 (49%)
Psychotropic drugs		
Any psychotropic drug	107/214 (50%)	75/187 (40%)
Antipsychotics	27/214 (13%)	23/187 (12%)
Antidepressants	77/214 (36%)	52/187 (28%)
Anxiolytic or hypnotic	33/214 (15%)	23/187 (12%)

Data are n (%), n/N (%), mean (SD), or median (IQR). GCSE=General Certificate of Secondary Education. NVQ=National Vocational Qualification. CMAI=Cohen-Mansfield Agitation Inventory. NPI=neuropsychiatric inventory. *n=403. †UK qualifications are broken down into academic advanced levels (A levels or equivalent, post compulsory education), higher secondary education (O levels, GCSEs, or equivalent), secondary education, and vocational qualifications (NVQ or equivalent). ‡n=399. §n=401. ¶n=400. ‖n=398. **Calculated as frequency × severity.

Table 1: **Baseline characteristics of care home residents**

No significant differences in secondary outcomes were identified between the two groups in the main or sensitivity analyses (table 3). Although the prescription of antipsychotic drugs (odds ratio 0·66; 95% CI 0·26 to 1·69, p=0·3880) and reporting of any abusive behaviours (0·67; 0·43 to 1·05, p=0·0790) were lower in the MARQUE group than the TAU group, the differences were not statistically significant. More staff completed the Staff Tactics Scale than were interviewed at follow-up (n=356). 8 month interview follow-up data were available for 354 (72%) of 492 staff (175 in the MARQUE group and 179 in the TAU group). No statistically significant differences in Maslach Burnout Inventory or SCID overall scores were identified between the two groups (table 4).

The total cost of training and delivery of the intervention was £41 510 (appendix). Assuming this would be the cost required to train and deliver the intervention to the 189 residents randomly assigned to receive the MARQUE intervention, the total cost per resident was £220.

Health and social cost resource use and utility values for residents in each group are shown in the appendix. The mean total cost per resident in the intervention group, including the cost of the MARQUE intervention, was £1379 (95% CI 1041 to 1718) compared with £1175 (917 to 1433) in the TAU group. The mean difference in cost between the MARQUE and the TAU groups was £204 (–215 to 623; p=0·320).

Non-parametric bootstrapping after multiple imputation showed that residents in the MARQUE group gained 0·346 QALYs (95% CI 0·330 to 0·362) and residents in the TAU group gained 0·332 QALYS (0·322 to 0·342) with a mean difference of 0·015 QALYs (–0·004 to 0·034), which was not statistically significant (p=0·127).

Combining the difference in costs and difference in QALYs, the mean incremental cost per QALY gained of the MARQUE intervention compared with TAU was £14 064. Residents receiving the MARQUE intervention accrued a higher cost and gained more QALYs than residents in the TAU group, but the differences between groups were not significant. The MARQUE intervention has a 62% probability of being cost-effective at a willingness to pay of £20 000 and 77% probability of being cost-effective at a willingness to pay of £30 000 (appendix).

Including all residents living in care homes that were allocated to the intervention (n=282), the cost of MARQUE intervention per resident would become £147 (£41 510/282). The mean total cost per resident in the MARQUE group would decrease to £1307 (95% CI 968 to 1646), which remains higher than that in the TAU group (£1175). The mean difference in cost between groups was £132 (–287 to 551), which was not statistically significant (p=0·518). Combining difference in costs and QALYs results in an incremental cost-effectiveness ratio of £9078. Using this approach, the MARQUE intervention has a 73% probability of being cost-effective at a willingness to pay of £20 000 and an 83% probability of being

cost-effective at a willingness to pay of £30 000. These results are conservative and should be interpreted with caution because resource use and utility values were not available for the additional residents considered to benefit from the intervention and, therefore, mean resource use costs and utility values of those allocated to receive the MARQUE intervention were used.

At 8 months, the number of deaths was not significantly different between the two groups (27 [18%] of 189 residents had died in the MARQUE group *vs* 41 [19%] of 215 residents in the TAU group; figure 1) and antipsychotic drug prescription rate was similar between the MARQUE and TAU groups (table 3).

Discussion

We designed, developed, and tested the MARQUE intervention using evidence from systematic reviews on what works, and how to sustain interventions, and incorporated qualitative data, based on interviews with care home staff about their experience of agitation and ideas about what was possible in a care home.[11,17,23] We trained and supervised facilitators; the low intra cluster correlation, high attendance rates, and high fidelity scores indicate satisfactory delivery. The follow-up rate was high for resident measures and the majority of loss to follow-up was due to mortality. Despite successful delivery, the MARQUE intervention was not associated with a significant improvement in agitation, quality of life, a reduction in possibly abusive behaviours, or with staff reduction in burnout or improvement in sense of competence. This is the first trial to attempt the delivery of a pragmatic, scalable, and costed intervention. The intervention was designed to be scalable and affordable across UK care homes.

This trial has several limitations. The use of broad eligibility criteria for homes was designed to enhance external validity. However, consent was obtained for only around 60% of the residents assessed for eligibility, and for 177 residents with dementia who had a family carer, the family member could not be contacted and so these residents were not assessed, which highlights the possibility of recruitment bias. The facilitators noted that many residents who were discussed in training, and described as being the most agitated and whom they were told benefited greatly, were not included in the study. This suggests that the residents included might have been a more healthy population than residents who were not included. Correspondingly, more residents who had capacity to consent were included in the study than residents without capacity, suggesting our intervention population might have been biased in favour of residents with less severe cognitive impairment than residents who refused to participate and therefore the included residents probably had fewer symptoms of agitation than residents in care homes overall.[6]

The residents randomly assigned to the MARQUE group had less severe dementia than the population in a similar trial,[12] in which 90% had moderate or severe dementia. Similarly, although all staff attended training, the staff recruited to the study reported high levels of self-assessed competence at baseline and had higher personal accomplishment and lower depersonalisation scores on the burnout scale than did care home staff in general.[42]

We planned to analyse cost-effectiveness, which is important in the UK because it informs the National Institute for Health and Care Excellence (NICE) guidelines. The fact that the cost of MARQUE was not found to be significantly less than TAU might be explained by the fact that cost data has higher variance than effect data and the study was powered for the primary outcome. Clinical evaluation literature suggest that the aim of economic evaluation should be the estimation of a parameter (ie, incremental cost-effectiveness) with appropriate representation of uncertainty, rather than hypothesis testing and we reported the estimated uncertainty in cost-effectiveness results rather than tests of hypotheses.

	Treatment as usual (n=249)	MARQUE (n=243)
Sex		
Men	38/248 (15%)	32 (13%)
Women	210/248 (85%)	211 (87%)
Age (years)*	44 (13)	43 (12)
Ethnicity		
White	112/248 (45%)	74/241 (31%)
Asian	37/248 (15%)	39/241 (16%)
Black	85/248 (34%)	104/241 (43%)
Other	14/248 (6%)	24/241 (10%)
First language English	124/248 (50%)	115/242 (48%)
Time working in a care home (years)†	6 (2–13)	7 (2–12)
Time working in this care home (years)‡	2 (1–7)	2 (1–6)
Working as a qualified nurse in care home	27/249 (11%)	31/242 (13%)
Maslach Burnout Inventory		
Emotional exhaustion score§	19 (12)	16 (12)
Personal accomplishment score¶	41 (7)	41 (7)
Depersonalisation score‖	3 (4)	3 (4)
Sense of Competence in Dementia		
Total**	58 (6)	57 (6)
Professionalism††	18 (2)	18 (2)
Building relationships‡‡	13 (2)	13 (2)
Care challenges§§	13 (2)	13 (2)
Sustaining personhood‡	14 (2)	14 (2)
Staff Tactics Scale		
Any abusive behaviour (at least sometimes)	116/242 (48%)	124/234 (53%)
Any positive behaviour (never or almost never)	72/238 (30%)	84/232 (36%)

Data are n (%), n/N (%), mean (SD), or median (IQR). Denominators for the care staff vary because not all staff completed all assessments. *n=478. †n=484. ‡n=481. §n=462. ¶n=453. ‖n=471. **n=461. ††n=482. ‡‡n=480. §§n=476.

Table 2: **Baseline characteristics of care home staff**

	Treatment as usual (n=163)	MARQUE (n=155)	Mean difference (95% CI)*	p value
CMAI				
CMAI score†	44 (17)	42 (16)	−0·40 (−3·89 to 3·09); N=296	0·8226
Clinically significant agitation (CMAI >45)	55 (34%)	49 (32%)	1·14‡ (0·61 to 2·12); N=296	0·6828
NPI				
NPI score	16 (14), n=166	14 (16)	−0·84 (−5·51 to 3·84); N=299	0·7260
NPI agitation§	2 (3)	2 (3)	0·22 (−0·54 to 0·98); N=299	0·5647
NPI agitation	87/167 (52%)	81 (52%)	1·04‡ (0·61 to 1·80); N=318	0·8788
DEMQOL				
Staff proxy	104 (12), n=165	104 (12), n=154	0·09 (−3·87 to 4·05); N=298	0·9657
Family carer proxy	99 (13), n=117	100 (15), n=100	−0·03 (−2·87 to 2·82); N=205	0·9859
Psychotropic drugs				
Any psychotropic drugs	78/165 (47%)	66/152 (43%)	1·20‡¶ (0·61 to 2·39); N=316	0·5970
Antipsychotics	21/165 (13%)	15/152 (10%)	0·66‡¶ (0·26 to 1·69); N=316	0·3880
Antidepressants	57/165 (35%)	50/152 (33%)	1·49‡¶ (0·65 to 3·40); N=316	0·3475
Anxiolytics or hypnotics	21/165 (13%)	16/152 (11%)	0·92‡¶ (0·34 to 2·48); N=316	0·8707

Data are mean (SD), n (%), or n/N (%). The number of observations differ due to missing data. Treatment effect estimates were derived from hierarchical mixed models. The number of patients included in the hierarchical mixed models do not sum to the total number of patients due to missing covariate and outcome data. Patient denominators for secondary outcomes in the treatment as usual group exceed 163 because these analyses included residents for whom primary outcome data was not available, but data on medication was available at 8 months. CMAI=Cohen-Mansfield Agitation Inventory. N=number of patients included in the hierarchical mixed models. NPI=Neuropsychiatric Inventory. *Adjusted for baseline score (or caseness as appropriate), type of care home (residential only *vs* others), and dementia severity (Clinical Dementia Rating). †Sensitivity analyses for primary outcome: mean difference −2·08 (95% CI −7·14 to 2·97) for unadjusted analysis; −1·65 (−5·24 to 1·95) adjusted for predictors of missingness (age, sex, family carer sex); and −1·13 (−4·89 to 2·63) adjusted for baseline imbalances (sex, marital status, any psychotropic drugs). ‡Odds ratio. §Calculated as frequency × severity. ¶Adjusted for outcome caseness at baseline.

Table 3: **Resident outcomes at 8 months**

	Treatment as usual (n=179)	MARQUE (n=175)	Mean difference (95% CI)*	p value
Maslach Burnout Inventory				
Emotional exhaustion	18 (13), n=175	18 (13), n=169	0·50 (−1·89 to 2·89); N=326	0·6816
Personal accomplishment	42 (7), n=173	41 (7), n=167	−0·55 (−2·23 to 1·13); N=314	0·5243
Depersonalisation	2 (3), n=175	3 (4), n=170	0·61 (−0·06 to 1·29); N=332	0·0746
Sense of Competence in Dementia				
Overall	60 (6), n=170	59 (7), n=168	−0·65 (−2·10 to 0·80); N=320	0·3806
Professionalism	18 (2), n=173	18 (2), n=173	−0·21 (−0·60 to 0·19); N=340	0·2999
Building relationships	14 (2), n=174	13 (2), n=173	−0·14 (−0·66 to 0·38); N=340	0·5944
Care challenges	14 (2), n=172	13 (2), n=172	−0·16 (−0·64 to 0·32); N=335	0·5089
Sustaining personhood	14 (2), n=172	14 (2), n=173	−0·21 (−0·56 to 0·15); N=336	0·2623
Staff Tactics Scale				
Any abusive behaviour (at least sometimes)	82/178 (46%)	69/178 (39%)	0·67† (0·43 to 1·05); N=356	0·0790
Any positive behaviour (never or almost never)	33/178 (19%)	43/173 (25%)	0·78† (0·43 to 1·43); N=356	0·4249

Data are mean (SD) or n (%). The number of observations differ due to missing data. The number of care home staff included in the hierarchical mixed models do not sum to the total number of care home staff due to missing covariate and outcome data. N=number of care home staff included in the hierarchical mixed models. *Adjusted for baseline score and type of care home (residential only *vs* nursing or mixed nursing or residential). †Odds ratio, adjusted for percentage at baseline aggregated by care home and type of care home (residential only *vs* others).

Table 4: **Care home staff outcomes at 8 months**

Although the study was not powered to investigate changes in possible abuse scores and prescription of antipsychotic drugs, abuse scores decreased by around a third in the intervention group (reduction in abuse scores 2% in the TAU group *vs* 14% in the MARQUE group) and antipsychotic prescribing remained stable, which suggests that care practices and management strategies were changing. Considering the long-term nature of the study, it is possible that more differences between groups would have emerged as the intervention became part of culture over time.

Within MARQUE, we attempted to integrate strategies promoting change into routine care practices and for the successful strategies to be embedded—eg, by

encouraging reflective practice, co-creation of SMART action plans, training champions, and offering follow-up supervision and support.

Three studies[10,12,13] have reported clinically significant reductions in agitation in care homes. These interventions were intensive and multicomponent, combining the following elements: staff training; increased social interaction; antipsychotic review; physician review of medical history and medications; assessment of pain; a doctor and nurse-led reflective case conference developing individualised treatment plans; a 3 h educational lecture; staff role play; 45 min sessions of activity therapy for residents delivered twice a week; and training of care home staff by a doctor and nurse in two 4 h blocks. Few data are available on the cost of these time and resource intensive interventions and no data are available on their cost-effectiveness or whether it might be possible to deliver such interventions nationwide to the population at risk in care homes. Questions will always remain about whether less expensive and less intensive alternatives are as effective, or almost as effective, as time and resource-intensive interventions, so this study is a valuable contribution to knowledge. The MARQUE intervention represents a less intensive training intervention that was interactive, in which staff were asked to put ideas into practice and report on their effects, with ongoing support for staff to implement changes. The intervention was not delivered by experienced clinicians because they are scarce and costly.

Our economic analyses showed the intervention is cost-effective since the mean incremental cost per QALY gained of £14064 is less than the NICE threshold of £20000, but with a relatively low probability (62%) of being cost-effective at a willingness to pay of £20000 per QALY. The results are driven by assumptions about the cost of the intervention, and the sensitivity analysis suggests implementation on the basis of quality of life should be interpreted with caution.

The paucity of evidence for the effectiveness of the intervention for agitation, coupled with the economic analysis, indicates that the implementation of MARQUE should not be recommended on the basis of differences in costs, QALYs, or cost-effectiveness.

This study does not support the MARQUE intervention being implemented in care homes and suggests higher intensity interventions are required for people with agitation in care homes. These interventions would be delivered by professional staff with whole-home management and cultural change, implementing social and activity times with residents who are agitated, with a longer time period in which to implement change. The possible decrease in abuse and antipsychotic prescribing in addition to the cost-effectiveness data indicates that lower intensity, less costly interventions have the potential to improve some aspects of life for care home residents and care practices.

Contributors

GL, JB, CC, RH, and PR obtained funding, and were involved in initial design of the research. AS, MM, AL, FLF, and KL contributed to data acquisition. AS searched for and analysed new papers for the review. LM, FLF, and AL cleaned data. GL wrote the initial draft of the manuscript. PR and GL led the manual development and GL, PR, SR, and CC devised and delivered the training for psychology graduates. SB contributed to data interpretation. JB and LM did the statistical analysis and MP and RH did the health economic analysis. All authors critically revised the manuscript and approved the final Article for publication.

Declaration of interests

GL has received consultancy fees from Otsuka Pharmaceutical. SB reports grants and personal fees from Abbvie; personal fees and non-financial support from Lilly; and personal fees from Eleusis, Daval International, Boehringer Ingelheim, Axovant, Lundbeck, and Nutricia, outside the submitted work; and has been employed by the Department of Health for England. All other authors declare no competing interests.

Data sharing

The analyses codes and all original data except for those concerning abuse are available at Mendeley DOI:10.17632/dfgb64759j.1.

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