Running title: Interventions for QoL of people with dementia

Non-pharmacological interventions to improve depression, anxiety, and quality of life (QoL) in people with dementia: an overview of systematic reviews

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Abstract

This overview aimed to systematically synthesise evidence from existing systematic reviews to signpost practitioners to the current evidence base on non-pharmacological interventions to improve depression, anxiety, and quality of life (QoL) in people with dementia, and discuss priorities for future research. The databases MEDLINE, PsycINFO, Scopus, and Cochrane Central Register of Controlled Trials were searched in August 2017 with an updated search in January 2019. Fourteen systematic reviews of randomised controlled trials of non-pharmacological interventions were identified. Dementia stage was rated moderate or severe in the majority of the reviews and type of dementia varied. Interventions reported to be effective were: cognitive stimulation (*QoL*: SMD=0.38), music-based therapeutic interventions (*depression*: SMD=-0.27, *anxiety*: SMD=-0.43, *QoL*: SMD=0.32), and psychological treatments (mainly cognitive behaviour therapy) (*depression*: SMD=-0.22, *anxiety*: MD=-4.57). Whilst healthcare professionals are recommended to continue using these approaches, future research needs to focus on the type and form of interventions that are most effective for different stages and types of dementia.

158 words

Keywords

Dementia, Alzheimer's disease, quality of life, well-being, depression, anxiety

Introduction

Dementia is one of the greatest health challenges we face today[1]. Despite decades of research, a cure or effective preventative treatment for dementia remains elusive[2]. Therefore, post diagnostic support, the provision of non-pharmacological interventions alongside biomedical care to improve experiences of people with dementia, is critically important in the dementia care pathway[3].

The symptoms of dementia can vary greatly depending on the diagnosis and the stage of the disease. These may include difficulties in memory, disturbances in language, psychological and psychiatric changes, and impairments in activities of daily living[4]. Traditional assessments in the literature tended to have a biomedical focus[5]. However, in recent years, dementia care research has moved beyond the biomedical model to recognise and value the subjective experiences of those with dementia[6]. As such there is now a great emphasis on improving the quality of life (QoL) of people living with this condition as an important indicator of the overall impact of interventions along with improving cognitive and functional abilities and reducing behavioural changes[7]. Since there is no clear evidence that any pharmacological intervention improves QoL in people with dementia[8], there is strong potential for the role of non-pharmacological interventions.

QoL is a complex construct to define and measure in people with dementia[9]. Over the last 10 years Lawton's model of QoL, which emphasises multiple overarching dimensions that contribute to QoL including psychological well-being (e.g., positive and negative affect), behavioural competence (e.g., cognitive and functional abilities), and objective environment (e.g., caretakers and living situation), has undoubtedly been the most pervasive influence on conceptualisations of QoL and the development of QoL instruments for this population[10]. In addition to the broad, multi-dimensional concept, further complexity is added by the recognition that the way in which this outcome is measured can have an impact on the ratings. Carer-rated QoL of people with dementia is often influenced by the

carer's own level of burden[11] and people with dementia tend to report their QoL better than when rated by other observers[12,13].

As highlighted earlier, one important component of QoL is psychological well-being, an internal state that is inferred by observable displays of affect and self-reported mood states[14]. Recent studies demonstrate that psychological well-being (mood) is more strongly associated with QoL than other dimensions such as cognition or functional limitation suggesting that psychological well-being is a key predictor of QoL in people with dementia among other dimensions[12,15]. Therefore, depression and anxiety were included as target outcomes in addition to QoL in the current study.

This study is an overview of systematic reviews evaluating the efficacy of non-pharmacological interventions on QoL including depression and anxiety in people with dementia. The aim of overviews is not to repeat the searches or assessment of risk of bias from the included reviews, but to address a growing need to filter the information overload by systematically bringing evidence together and to signpost busy clinicians and policy makers to relevant sources to support their decision making[16]. Overviews are known by a variety of names including umbrella review, meta-review, and systematic review of systematic reviews but the term 'overview' has gained widespread acceptance[17]. Thus the term 'overview' is used throughout this article.

Recently, there have been some overviews which provided a comprehensive summary of the efficacy of non-pharmacological interventions for people with dementia on different outcomes such as activities of daily living (ADL)[18] and behavioural and psychological symptoms (BPSD)[17]. The findings of these overviews[18,19] highlighted that despite substantial variation of the intervention, only very limited types of non-pharmacological interventions are beneficial in improving ADL (e.g., exercise programmes) and BPSD (e.g., analysis and modification of antecedents and consequences of behaviour) and that health professionals need to select the evidence-based treatments that best match targeted outcomes.

McDermott et al.[20] have also conducted an overview of systematic reviews on psychosocial interventions for people with dementia. This review evaluated the efficacy of interventions on multiple outcomes including QoL. Although this comprehensive review provided a valuable 'high level' understanding of the range of psychosocial interventions, there were some methodological limitations, which made it difficult to draw strong conclusions.

First, there was heterogeneity in study designs used in selected reviews. The authors included reviews of randomised controlled trials (RCTs) and non-RCTs and thus those reviews that did not report an overall effect size on targeted outcomes were included. Second, the authors did not exclude any reviews that overlapped. Therefore, some studies were included more than three times across similar systematic reviews. Third, the authors did not report characteristics of participants studied in each review (e.g., age, dementia diagnosis, dementia severity). In addition, the intervention categories used were broad. The authors grouped psychotherapy, music therapy, and reminiscence therapy into one umbrella category (i.e., psychological/social interventions). Thus, it is not clear which theoretical framework work, for whom and under which conditions. As such, currently there is no clear guidance to allow clinicians and policy makers to make well-informed decisions on non-pharmacological interventions for individuals with dementia which may improve their QoL.

The aims of the current overview are to systematically synthesise evidence from existing systematic reviews to signpost practitioners to the current evidence base on interventions to improve depression, anxiety, and QoL in people with dementia, and discuss priorities for future research. Unlike the previous overview which solely focused on psychosocial interventions[20], the current overview includes all non-pharmacological interventions available in the community including health service interventions such as case management[20]. To obtain an empirically derived index of efficacy for QoL, the current review only includes systematic reviews of RCTs that reported an overall effect size on QoL, depression and/or anxiety.

Methods

Inclusion and Exclusion Criteria

Types of studies. Systematic reviews that used systematic and explicit methods to identify, select and critically appraise relevant primary research utilising RCT were included in the current overview. Publication language was limited to English. The recent guidelines for conducting an overview of systematic reviews[16] states that research syntheses conducted within past 5-10 years will reflect primary research conducted over past 30 years and thus the search for systematic reviews rarely needs to be extended beyond this. Therefore, only systematic reviews published after 2000 were included in the current overview.

Population. Reviews were included if they included population of people with a diagnosis of dementia. No restrictions were made for types or stages of dementia.

Intervention and comparison. Any types of non-pharmacological interventions aimed at improving the targeted outcomes as either primary or secondary end points were eligible. No restrictions were made for comparator groups. Both non-active control conditions (e.g., treatment as usual, waiting) and active control conditions (i.e., another form of intervention) were eligible.

Outcome. Reviews that reported the efficacy of intervention on depression, anxiety, or QoL were included. The targeted outcomes whether assessed by self-report or observation by clinicians and carers were eligible. If the review included both RCTs and non-RCTs, the pooled effect size for RCTs had to be reported separately from those of non-RCTs to be eligible for the current overview.

Search Strategies

The following electronic databases were searched on 09 August 2017: MEDLINE, PsycINFO, Scopus, and Cochrane Central Register of Controlled Trials. We used terms for

dementia (dementia, Alzheimer*), randomised control trials (RCT, random*), and systematic reviews (systematic review, meta-analysis). The detailed search strategies are described in Supplementary Table S1. The search was repeated using the same databases and terms in January 2019 to identify updated systematic reviews after the initial search.

Selection of Reviews

One author (NK) conducted the searches and excluded articles that were clearly irrelevant to the present research question on the basis of title and abstract. Each potentially eligible review was assessed in full text by two independent authors (NK and TB or NK and EM). Overlapping reviews (i.e. reviews exploring the same participants, interventions, comparisons, and outcomes) were systematically assessed based on quality and recency by at least two authors. We selected the most up-to-date and comprehensive reviews and older review articles that included the same set of trials with the most recent reviews were excluded to avoid duplication.

Data Extraction and Synthesis

Information was extracted independently by two authors (NK and TB or NK and EM) using a purposely designed electronic data extraction sheet. Disagreements were resolved through discussion, and consensus was obtained. For each included review, information was recorded on (a) date of last search, (b) the number of RCTs included in the review, (c) participant characteristics (mean age, dementia diagnosis, dementia severity), (d) intervention and comparator characteristics, (e) pooled effect sizes (the mean difference (MD) or the standardised mean difference (SMD)) on depression, anxiety, or QoL, and (f) the Grading of Recommendations, Assessment, Development and Evaluations (GRADE) ratings (i.e., levels of quality of the body of evidence) where available[21]. The rating of high GRADE presents that the authors are very confident that the true effect lies close to that of the estimate of the effect. The rating of low presents that confidence in the effect estimate is limited and the true effect may be substantially different from the estimate of the effect.

Details of the included reviews were synthesised following the recent guidelines for conducting an overview of systematic reviews[16].

Assessment of Methodological Quality of Included Reviews

Two authors (NK and TB or NK and EM) independently assessed the methodological quality of the included reviews using the A MeaSurement Tool to Assess systematic Reviews (AMSTAR) 2[22]. The AMSTAR 2 assesses a number of weakness of the review. The following seven items are categorised as critical items opposed to non-critical items: item 2 (protocol registered before commencement of the review), item 4 (adequacy of the literature search), item 7 (justification for excluding individual studies), item 9 (risk of bias from individual studies being included in the review), item 11 (appropriateness of meta-analytical methods), item 13 (consideration of risk of bias when interpreting the results of the review), and item 15 (assessment of presence and likely impact of publication bias). Identification of weakness in these critical items require particular attention as they may have more significant impacts on the overall confidence of the results of the review when assessing the methodological quality of each study.

Results

Study Selection

Figure 1 presents a flow diagram illustrating the study selection process. Our search conducted in August 2017 yielded 2,527 citations, and the abstracts of 1,959 were examined after removing duplicate publications. The first author (NK) excluded 1,763 articles based on abstract as clearly irrelevant to the present research question. Two authors (NK and TB or NK and EM) reviewed the remaining 196 full articles independently. Applying the inclusion criteria resulted in the identification of 14 studies. The updated search conducted in January 2019 identified additional 620 citations, five of which met criteria for inclusion. Overlapping reviews were systematically reassessed based on quality and recency and replacing with studies identified in the original search resulted in updated 14 studies.

Characteristics of the Included Reviews

Characteristics of the studies included in the review are presented in Table 1. Of the 14 reviews, eight (57.1%) were Cochrane Reviews. Eleven types of interventions were identified: case management[23], cognitive training and rehabilitation[24], cognitive stimulation[25], exercise[26-28], light therapy[29], massage[30], music based therapeutic sessions[31], occupational therapy[32,33], person-centred care[34], psychological treatment[35], and reminiscence therapy[36].

Two systematic reviews reporting the efficacy of exercises programmes on depression which were published in the same year (i.e., no observed difference in recency) were included in the current overview. The main reason for this was that one review[26] recruited participants with dementia in general while the second review[27] targeted only older adults (over 65) diagnosed as having dementia using accepted criteria. Only seven RCTs overlapped between these two reviews (i.e., 35% of included RCTs in the first review and 41% in the second review) and both reviews demonstrated the same findings (i.e., no significant effect on depression). In addition to these two reviews, the third review on exercise programmes[28] was included in the final dataset as this study reported the efficacy of interventions on QoL. Two systematic reviews on occupational therapy[32,33] were also included as they reported different outcomes.

All reviews included people with any form of dementia, with seven reviews (50.0%) requiring participants to have a formal clinical diagnosis of dementia using standardised criteria in order to be eligible for inclusion. Ten reviews (71.4%) reported the severity of dementia of participants using the Mini Mental State Examination (MMSE)[37]. Dementia stage was rated moderate (MMSE between13-20) for half of those reviews that reported MMSE scores. Overall, dementia stage was rated moderate or severe in the majority of the reviews that reported MMSE scores. The average age of participants in all reviews was individuals in their 70s or 80s (average range 73.85 – 83.26).

Characteristics of Interventions

Table 2 summarises the intensity of interventions in included reviews. The main contents of interventions are described below under each category.

Case management. The review included any case management intervention delivered in the community (not in hospital or in residential care settings) that predominantly focused on the planning and co-ordination of care required to meet the identified needs of the person with dementia[23]. More specifically, RCTs included in the effect size calculation for the targeted outcomes of this overview (i.e., depression, anxiety, or QoL) utilised multiple case management tasks such as assessment, care planning, giving advice and information, arranging services, monitoring of care plan, and case closure.

Cognitive training and rehabilitation. Cognitive training was defined as an intervention which involved guided practice on a set of standardised tasks designed to reflect particular cognitive functions such as memory, attention, or problem-solving while cognitive rehabilitation aimed to tackle specific impairments directly in the real-life context (e.g., focusing on patient-derived personal goals and practicing the use of aids in the real-life setting)[24]. Only one RCT of cognitive rehabilitation was identified, and thus meta-analysis was not conducted for the latter category. RCTs of cognitive training included in the effect size calculation employed various training such as face-name learning and recall, verbal elaboration, and over repetition.

Cognitive stimulation. Cognitive stimulation was defined as a range of activities and discussions (usually in a group) aimed at general enhancement of cognitive and social functioning[25]. Reality orientation (e.g., discussion of current orientating information through newspapers, photographs, etc. with materials selected to stimulate five senses) was also considered as one form of cognitive stimulation intervention. RCTs included in the effect size calculation utilised various approaches including reality orientation, discussion of hobbies and activities, and the presentation of visual images of families, animals, and objects followed by group discussions.

Exercise programmes. The two reviews, one reporting the pooled effect size for depression[27] and the other reporting the pooled effect size for QoL[28], used the similar definition which explained physical exercise as a combination of techniques aimed at improving strength, flexibility, and balance. RCTs included in these two reviews utilised techniques such as exercises on a treadmill, walking, and exercises to improve muscle strength and balance. The third review which reported the pooled effect size for depression used a broader definition and included wider physical activities such as Tai chi[26]. Overall, RCTs included in the analysis across these three reviews utilised various interventions ranging from 30 min walking at self-selected pace to 120 min aerobic exercises.

Light therapy. The review which reported the pooled effect size for depression defined light therapy as any intervention involving the bright light[29]. RCTs included in the analysis utilised the different length of bright light exposure during the day (1 hour to 9 hours).

Massage and touch. The review defined massage and touch approached to be any of the following interventions: hand/foot massage, acupressure, slow-stroke back massage, reflexology or therapeutic touch[30]. RCTs included in the effect size calculation utilised either 10-30 min daily massage or reflexology.

Music based therapeutic interventions. Any music-based interventions, either active or receptive, delivered to individuals or groups were eligible for the review. However, the intervention had to be provided by a qualified music therapist or delivered based on a therapeutic relationship and involve a minimum of five sessions[31]. That is, RCTs had to clearly demonstrate the implementation of a therapeutic intervention (i.e., not just simply playing any kinds of music for a short period of time in the background).

Occupational therapy. The two reviews, one reporting the pooled effect size for depression[32] and the other reporting the pooled effect size for QoL[33], used the similar definition describing occupational therapy as systematic approaches designed to maintain

and enhance the ability to perform activities of daily living and allow people with dementia to participate in social activities. RCTs included in the effect size calculation involved performing functional task activities using practical aids and strategies, environmental modification, and caregiver education and supervision.

Person-centred care. The review defined person-centred care as a sociopsychological treatment approach that recognises the individuality of the patient in relation to the attitudes and care practices that surround them[34]. These approaches indirectly target people with dementia by training the health care provider (e.g., care staff) to conduct meaningful activities, make well-being of people with dementia a priority, and improve the quality of the relationship between staff and service users.

Psychological treatments. The review defined psychological treatments as an intervention that was based on a psychological theory and involved a structured interaction between a facilitator and a participant which incorporated psychological methods[35]. Interventions were grouped into the following categories where possible: Cognitive Behaviour Therapy (CBT), progressive muscle relaxation, psychodynamic therapies, interpersonal therapies, and counselling. RCTs included in the effect size calculation used either CBT (*n* = 3), psychodynamic therapies (*n* = 1), or counselling (*n* = 2). Only RCTs that utilised CBT reported the efficacy of interventions on anxiety.

Reminiscence therapy. The review defined reminiscence therapy as approaches that had a focus on the individual making sense of their own life story[36]. Life story work was also included as reminiscence therapy in this review.

Methodological Quality of Included Reviews

The AMSTAR 2 reflects the scientific rigour of the review itself with regard to design, method, execution and analysis rather than the quality of evidence for interventions. The AMSTAR 2 total score ranged from 7 to 30 (see Table 1). Reviews on case management[23], music-based therapeutic interventions[31], and reminiscence therapy[36] were of the highest

quality with no weakness identified in any of critical items of the scale. Reviews on psychological treatments[35] and cognitive stimulation[25] also demonstrated high methodological quality with weakness identified for only one or two critical items. Reviews on massage[30] and occupational therapy[32,33] showed weakness in more than half of the critical items.

Quality of Evidence in Included Reviews

We did not reassess the quality of evidence by evaluating the risk of bias of primary studies included in each review as this was beyond the scope of this overview. Overall, the quality of evidence was reported to be low to moderate across included reviews. This was mainly due to the limited number of studies included in the meta-analysis, the small sample size used in primary studies included, and insufficient detail regarding the methods used (e.g., random group allocation sequence). All reviews also highlighted that the interpretation of the results is limited by significant heterogeneity in types, frequency, and the duration of interventions.

Effects of Interventions

The overall effects of interventions are summarised in Table 3.

Depression. All eleven types of interventions identified reported the pooled effect size for depression. The most commonly used measures of depression across included systematic reviews were the Geriatric Depression Scale (GDS) and the Cornell Scale for Depression in Dementia (CSDD). The systematic review on cognitive training[24] and cognitive stimulation[25] only reported that depression was assessed using the self-reported measure in all original primary studies. The reviews on the remaining nine approaches did not clearly specify whether depression was self-reported or carer-/clinician-rated in each included study when computing the pooled effect size. Only music based therapeutic interventions[31] (SMD = -0.27, 95% CI -0.45 to -0.09) and psychological treatment, which was mainly CBT,[35] (SMD = -0.22, 95% CI -0.41 to -0.03) demonstrated a significant effect.

Anxiety. Only four types of interventions identified (reminiscence therapy, psychological treatment, massage, and music based therapeutic interventions) reported the pooled effect size for anxiety. Various measures of anxiety were used across included systematic reviews (see Table 1). The review on reminiscence therapy[36] reported that anxiety was assessed using the self-reported measure in all original primary studies. The review on psychological treatment[35] reported the pooled effect size for self-reported and carer-rated anxiety separately. The review on massage[30] and music based therapeutic sessions[31] did not clearly specify whether anxiety was self-reported or carer-/clinician-rated in each included studies. Music based therapeutic interventions[31] (SMD = -0.43, 95% CI -0.72 to -0.14) demonstrated a significant effect on anxiety. Psychological treatment[35] which was all CBT based demonstrated a significant effect on staff-reported anxiety (MD = -4.57, 95% CI -7.81 to -1.32) but did not show a significant effect on self-reported anxiety.

Quality of life. Eight types of interventions identified reported the pooled effect size for QoL. There was some variance in the measures used but well-established QoL measures specifically designed for people with dementia were employed across included systematic reviews (see Table 1). The systematic review on occupational therapy[33], psychological treatment[35], and reminiscence therapy[36] reported the pooled effect size for self-reported and carer-rated QoL separately. The review on cognitive stimulation[25] reported that QoL was assessed using the self-reported measure in all included studies. The review on exercise[28] combined data from self-reported and carer-rated QoL to compute the single pooled effect size. The review on case management[23], music based therapeutic sessions[31], and person-centred care[34] did not clearly specify whether QoL was self-reported or carer-/clinician-rated in each included study. Only cognitive stimulation[25] (SMD = 0.38, 95% CI 0.11 to 0.65) and music based therapeutic sessions[31] (SMD = 0.32, 95% CI 0.02 to 0.62) demonstrated a significant effect.

Discussion

This overview of systematic reviews identified 14 systematic reviews, which included 189 RCTs in total. Eleven types of non-pharmacological interventions were identified. Of those identified, three non-pharmacological approaches were found to be successful in improving depression, anxiety, or QoL immediately after the treatment period. Cognitive stimulation therapy demonstrated a significant small effect on QoL. Music based therapeutic interventions demonstrated a significant small effect on depression and QoL and a medium effect on anxiety. The overall effect size of psychological treatments (mainly CBT) for depression was small while demonstrating a large effect on staff-rated anxiety.

Case management, cognitive training, exercise, light therapy, massage, occupational therapy, person-centred care, and reminiscence therapy did not show a significant effect on depression, anxiety, or QoL. There are some possible reasons for these results. Some systematic reviews (particularly reviews on occupational therapy) demonstrated a low methodology quality rating on the AMSTAR2 while cognitive stimulation therapy, music-based therapy and psychological interventions - that were found to be effective on targeted outcomes, demonstrated a high quality rating. The quality of the reviews themselves may have underestimated the true effect of interventions.

The quality of evidence was also rated low to moderate in the original systematic reviews with the majority of reviews using the Cochrane Collaboration's risk assessment tool[38] which evaluates study quality in terms of design, conduct, analysis, and presentation. The low to moderate quality of evidence was mainly due to the limited number of studies included in the meta-analysis and the small sample size used in primary studies. There are no simple criteria in terms of how many studies are needed to calculate the meaningful pooled effect size. However, the combination of very few studies with very different characteristics makes any kind of synthesis untenable in most cases[39]. The number of RCTs included in the meta-analysis was less than five for all outcomes for case management, cognitive training, light therapy, and massage. Systematic reviews on exercise, occupational therapy, person-centred care, and reminiscence therapy included a slightly larger number of

studies for calculating the pooled effect size for depression and QoL, but these reviews still did not demonstrated any significant effects.

Potential Mechanism of Change in Interventions

Cognitive stimulation. Of the 15 RCTs included in the review on cognitive stimulation[25], data from four RCTs were available for calculating the pooled effect size for QoL which produced a significant effect. All four RCTs used small group session, typically with groups of five to seven participants. Although activities during sessions varied across RCTs, all studies involved group discussion of particular topics such as current orientating information through newspapers. The intensity of interventions across four RCTs varied from five days a week over four weeks to once a week over six months.

Recent studies showed that the cognitive domains which appear to be most influenced by cognitive stimulation therapy are language and memory while the intervention may not have an impact on other domains such as working memory or executive function[40,41]. Another important aspect of cognitive stimulation therapy is that it is a person-centred approach which encourage individuals to give their opinions and make a contribution, with questioning, thinking and interaction being positively reinforced within the group, something which might not always occur in care settings[42].

These effects on improved language and communication together with therapeutic elements of the intervention are considered to have generalised benefits, explaining improvements in QoL[40]. This coheres with the findings of the current overview that the small-group format is likely to be one of the critical components when delivering cognitive stimulation therapy. There is still little consensus on the duration and frequency of cognitive stimulation therapy and activities involved during sessions that are critical to bring about the desired change.

Music based therapeutic interventions. Of the 22 RCTs included in the review on music based therapeutic sessions[31], data from 11 RCTs, 13 RCTs, and 9 RCTs were

available for calculating the pooled effect size for depression, anxiety, and QoL respectively which all produced a significant effect. There was no clear consensus on the effective format of interventions as a mixture of group and individual sessions of either or both active or receptive approaches was used across RCTs. The intensity of interventions across these RCTs included in the analysis varied from six sessions over three weeks to 30 sessions over six months.

A recent literature review[43], which provided a conceptual framework for the neural mechanisms of music therapy in mental health treatment, suggested that there are several key elements of music therapy which lead to beneficial neurobiological changes and thus improvements in mental health difficulties. These elements include establishing participant comfort early in therapeutic process by using emotionally positive music, developing trust in participant-therapist relationship, accessing participant emotions through referential music therapy, increasing reminiscence through autobiographically relevant music, inducing music pleasure, changing behaviour patterns, and improving social functioning.

It is still not clear which of these elements are particularly important for people with dementia, however considering that only interventions provided by a qualified music therapist or delivered based on a therapeutic relationship were included in the identified systematic review[31], it is possible that the involvement of a qualified therapist and a therapeutic relationship are critical to induce clinically meaningful changes in depression, anxiety, and QoL.

CBT. Of the six RCTs included in the review on psychological treatment[35] which was mainly CBT based, data from six RCTs and two RCTs were available for calculating the pooled effect size for depression and anxiety respectively which both produced a significant effect. CBT is an active, directive, time-limited, structured approach based on the cognitive model: the way that individuals perceive a situation is more closely connected to their reaction than the situation itself[44,45]. CBT has established itself as an efficacious and

appropriate psychological treatment for use with individuals with anxiety disorders across the lifespan[46].

CBT approaches used in RCTs included in the analysis utilised techniques from conventional CBT such as challenging dysfunctional thoughts, developing positive coping skills to manage the effects of the disease, and participating in pleasant activities[35]. Some procedural modifications (e.g., repeated instructions, more in-session practice, and reminder cues) were made to conventional CBT in order to meet the needs of people with dementia. Some RCTs offered telephone contact between sessions in addition to regular therapy sessions and some employed a multimodal approach such as combining CBT with Tai Chi exercise and support groups. The intensity of interventions across these RCTs included in the analysis varied from six sessions over six weeks to weekly sessions over 20 weeks.

The findings of the current overview highlight that some modifications to conventional CBT are important when working with people with dementia. However, it is not clear whether simple procedural modifications (e.g., reminder cues) are enough to bring about the desired change or inclusion of additional components such as support groups are critical to meet the needs of people with dementia.

Research Implications

Three types of non-pharmacological interventions (cognitive stimulation therapy, music based therapeutic interventions, and psychological treatments (mainly CBT)) showed beneficial effects on depression, anxiety, and QoL. The theoretical framework of these interventions, with a focus on relationships and engaging the individual, also explain why these approaches may be successful in targeting psychological well-being or overall QoL. However, this overview highlights the need to develop further evidence to draw more clinically meaningful conclusions.

As noted earlier, large heterogeneity in the format of interventions identified poses difficulties in concluding how intense these effective interventions need to be in order to be

beneficial. Population ageing is having a profound impact on the emergence of the dementia epidemic and the prevalence of dementia is estimated to continue to expand rapidly in many countries[47]. Considering the impact of increased needs on the overall economic healthcare burden, it is critical to develop interventions that enable the efficient use of resources in society. Therefore, it is essential for future trials utilising approaches that seem most beneficial to evaluate the effect of moderator factors such as trials comparing the same approach with different frequency, duration, or types of activities involved on proposed outcomes.

The majority of included reviews targeted people with moderate-severe dementia in their 70s or 80s. It is not clear whether the findings from the current overview can be generalised to people with early onset dementia or more rare forms of dementia. Understanding the differential efficacy of non-pharmacological interventions for people at different stages of the illness is essential as standard psychological treatments such as CBT can bring challenges to people whom the loss of insight or memory loss is more apparent[48]. Currently, well-controlled RCTs of non-pharmacological interventions for people with more severe dementia are particularly scarce in the dementia literature. The review conducted by Boote et al.[49], which focused on the efficacy of psychosocial interventions for people with moderate to severe dementia identified only two RCTs. None of these RCTs included depression, anxiety, or QoL as outcomes.

Individuals with early onset dementia are also often neglected in studies exploring the benefits of non-pharmacological interventions[50]. Given their younger age, individuals with early onset dementia may require different types of support than those available for individuals with late onset dementia[51]. In addition, all identified reviews included people with any form of dementia. Cognitive impairments and functional abilities differ between typical Alzheimer's disease and other types of dementia such as frontotemporal dementia[52,53]. Future research needs to explore whether interventions that found to be most effective are

equally beneficial to those who do not fall into the typical population being studied (i.e., individuals with moderate Alzheimer's disease in their 70s or 80s).

Finally, depression and anxiety can be difficult to identify in people with dementia as some of presentations may overlap with symptoms of dementia. For example, common symptoms of dementia such as apathy can mimic depression[54]. Focusing on common symptoms of anxiety such as concentration difficulties are not likely to discriminate well between anxious and non-anxious individuals with dementia[55]. People with dementia may also present difficulties communicating or remembering their symptoms which can further complicate the identification of relevant symptoms.

Therefore, the literature suggests using an assessment tool which is designed specifically to assess depression and anxiety in dementia and derives information from multiple resources including both the person with dementia and an informant[54,56] (e.g., CSDD, Rating anxiety in Dementia scale). However, this was not always the case for primary studies included in the identified reviews. The literature also suggests that between 68% and 75% of individuals with dementia and generalised anxiety disorder meet the criteria for major depressive disorder suggesting that both mental health difficulties are highly co-morbid in people with dementia[55]. Despite this, only four of the 14 included reviews reported the efficacy of interventions on anxiety highlighting that anxiety is currently neglected in the dementia literature. Future trials should consider the use of depression and anxiety measures particularly designed for this population (i.e., which might be more sensitive to changes) and to target anxiety which the evidence is currently scarce as well as depression.

Great strides have been made in recent years to conceptualise, define, and systematically measure QoL in dementia resulting in a range of instruments with promising preliminary psychometric data[10]. Unlike depression and anxiety measures, the majority of primary studies included in the identified reviews used one of the well-established QoL measures specifically designed for people with dementia. Eight of the 14 included reviews reported the efficacy of interventions on QoL. Of those eight reviews, three reported the

efficacy on self-reported and carer-reported QoL separately and one review only reported the results for self-reported QoL. The remaining reviews did not specify whether the outcome was based on self-reports or proxy reports or they combined both types of measures to calculate a single pooled effect size.

Although the literature suggests that people with dementia tend to report their QoL better than those rated by other observers[12,13], three reviews which reported the efficacy on both self-reported and carer-reported QoL demonstrated consistent findings (i.e., occupational therapy, psychological treatment, and reminiscence therapy demonstrated no significant effect on both self-reported and carer-reported QoL). Future trials are recommended to include both self-reported and carer-reported QoL and subsequent systematic reviews should report the evidence on both self-reports and proxy reports to conclude whether sensitivity to changes can differ depending on how the outcome of interest is assessed.

Clinical Implications

This overview aimed to address a growing need to filter the information overload by systematically bringing evidence on the effectiveness of different types of non-pharmacological interventions in improving depression, anxiety and QoL together and to signpost busy clinicians and policy makers to relevant sources to support their decision making. The findings suggest that the most promising interventions for people with moderate dementia in their 70s and 80s appeared to be cognitive stimulation therapy, music based therapeutic interventions and psychological treatments (mainly CBT). Whilst services are recommended to continue using these approaches, further funding is critical to address research limitations, particularly identifying whether interventions that have proven to be effective need to be adapted for those who do not fall into the typical population being studied and investigating how intense these effective interventions need to be in order to be beneficial.

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Figure legend

Figure 1 PRISMA 2009 flow diagram. Note. ES = effect size, PwD = people with dementia

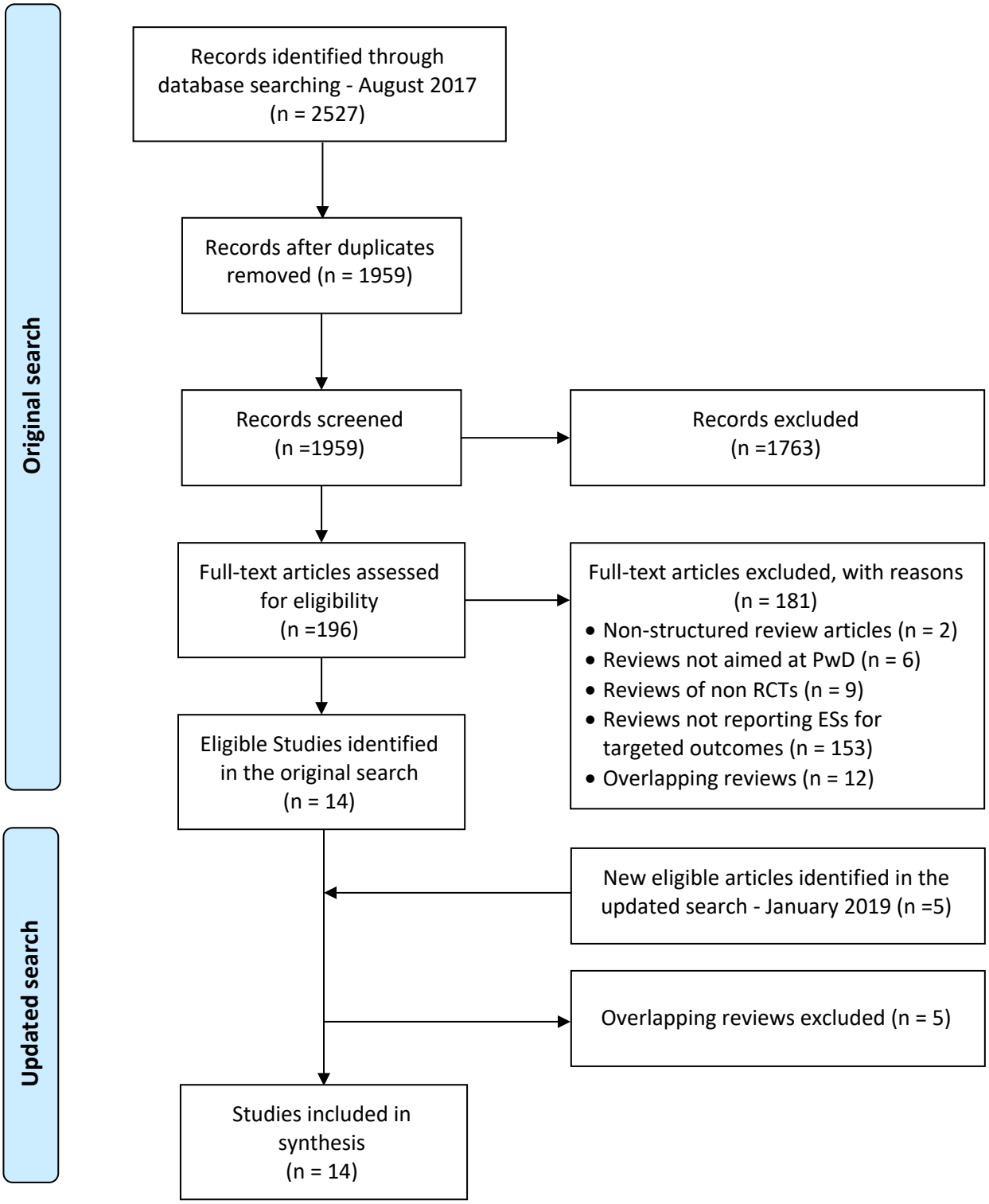

Figure 1 PRISMA 2009 flow diagram

Note. ES = effect size, PwD = people with dementia

Table 1 Characteristics of included reviews

Author (year)	Date of search	Intervention addressed in the review	No of RCTs included in the review	Population	Mean age	Mean MMSE	Dementia types	Psychological QoL outcomes for which effect sizes are reported	Quality of the review (AMSTAR2)
Reilly et al. 2015	Dec 2013	Case management	13	Individuals with dementia	77.03	17.64 (*n*=9)	Only AD (*n*=4) Mainly AD (*n*=1) AD + other dementias (*n*=3) Dementia types not specified (*n*=5)	QoL (DQOL, HUI3, PWI-ID) Depression (CSDD, GDS)	28/32
Bahar-Fuchs et al. 2013	Nov 2012	Cognitive training Cognitive rehabilitation	12	Individuals with dementia, possibly further diagnosed as having AD, VD, or mixed AD/VD using accepted criteria (e.g., DSM)	73.85	22.20 (*n*=9)	AD (*n*=8) AD + other dementias (*n*=2) Dementia types not specified (*n*=2)	Depression (CESD, GDS)	19/32
Woods et al. 2012	Dec 2011	Cognitive stimulation	15	Individuals with dementia	78.80	19.7 (*n*=11)	AD or mainly AD (*n*=7) AD + VD (*n*=1) Dementia types not specified (*n*=7)	QoL (LSI, QoL-AD) Depression (CSDD, GDS, MADRS, MOSES) Anxiety (RAID)	25/32
Barreto et al. 2015	Mar 2015	Exercise programmes[1)]	20	Individuals with dementia	–	–	–	Depression (CSDD, GDS, MADRS)	22/32
Forbes et al. 2015	Oct 2013	Exercise programmes[1)]	17	Older adults (over 65) diagnosed as having dementia using accepted criteria (e.g., DSM)	80.74	14.21 (*n*=14)	Mainly AD (*n*=10) AD + VD (*n*=1) Dementia types not specified (*n*=6)	Depression (CSDD, GDS, MADRS)	23/32
Ojagbemi and Akin-Ojagbemi 2019	Feb 2016	Exercise programmes	7	Individuals with dementia	80.00	19.23 (*n*=7)	Only AD (*n*=4) Dementia types not specified (*n*=3)	QoL (AQoL, DEMQOL, EuroQoL, PGCMS, QoL-AD, QUALID)	19/32
Forbes et al. 2014	Jan 2014	Light therapy	13	Individuals diagnosed as having dementia using accepted criteria (e.g., DSM)	83.26	8.31 (*n*=9)	Only AD (*n*=3) AD + VD (*n*= 3) AD + other dementias (*n*=3) Dementia types not specified (*n*=4)	Depression (CSDD, GDS, NPI-NH)	21/32
Wu et al. 2017	Jan 2016	Massage and touch	10	Older adults (over 60) diagnosed as having dementia using accepted criteria (e.g., DSM)	83.13	–	–	Sadness (AARS) Anxiety (AARS, BEHAVE-AD, Campbell, OERS)	20/32

Table 1 Characteristics of included reviews *(continues)*

van der Steen et al. 2018	Jun 2017	Music based therapeutic interventions	22	Individuals diagnosed as having dementia using accepted criteria (e.g., DSM)	82.54	11.56 (*n*=8)	Only AD (*n*=7) AD + other dementias (*n*=6) Dementia types not specified (*n*=9)	QoL (ADRQOL, CBS-QoL, DCMW, DQOL, DEMQOL, QoL-AD, Facial expressions) Depression (BEHAVE-AD, CSDD, GDS NPI) Anxiety (BEHAVE-AD, HAM-A, NPI, RAID, STAI-A)	30/32
Kim et al. 2012	Mar 2011	Occupational therapy	9	Individuals with dementia	79.36	–	AD (n=3) AD + VD (n=2) Dementia types not specified (*n*=4)	Depression (CSDD, HADS)	13/32
Ojagbemi and Owolabi 2017	Dec 2015	Occupational therapy	8	Individuals with dementia	78.96	13.54 (*n*=7)	AD (*n*=1) AD + VD (*n*=1) Dementia types not specified (*n*=6)	QoL (ADRQL, QoL-AD, DQOL)	7/32
Kim and Park 2017	Sep 2015	Person-centred care	15	Individuals with dementia	82.52	10.83 (*n*=6)	NA	QoL (DEMQOL, QoL-AD, QUALID) Depression (CSDD, GDS)	17/32
Orgeta et al. 2014	Jan 2013	Psychological treatments (therapeutic counselling, CBT, and psychodynamic therapy)	6	Older adults (no age criteria specified) diagnosed as having dementia using accepted criteria (e.g., DSM)	78.88	20.64 (*n*=5)	AD (*n*=2) Mostly AD + other dementias (*n*=2) Dementia types not specified (*n*=2)	QoL (QoL-AD) Depression (CSDD, GDS, MADRS, HADS) Anxiety (GAI, HADS, NPI, RAID)	24/32
Woods et al. 2018	Apr 2017	Reminiscence therapy	22	Individuals diagnosed as having dementia using accepted criteria (e.g., DSM)	81.35	–	Only AD = 5 Only VD = 3 Dementia types not specified = 14	QoL (QoL-AD, SR-QoL) Depression (CSDD, GDS, HADS, MADRS, MOSES) Anxiety (HADS, RAID)	28/32

Note. 1) Seven RCTs overlapped between two reviews. AD = Alzheimer's disease, AMSTAR = A MeaSurement Tool to Assess systematic Reviews, CBT = Cognitive Behaviour Therapy, DSM = The Diagnostic and Statistical Manual of Mental Disorders, QoL= Quality of life, RCTs = Randomised control trials, VD = Vascular dementia. n = number of RCTs

Anxiety measures: AARS = Apparent Affect Rating Scale, BEHAVE-AD = Behavioral Pathology in Alzheimer's Disease Rating Scale, Campbell = Campbell scale, GAI = Geriatric Anxiety Inventory, HADS = Hospital Anxiety and Depression Scale, HAM-A = Hamilton Anxiety Scale, NPI = Neuropsychiatric Inventory, OERS = Observed Emotion Rating Scale, RAID = Rating Anxiety in Dementia Scale, STAI-A = State-Trait Anxiety Inventory for Adults.

Depression measures: BDI = Beck Depression Inventory, BEHAVE-AD = Behavioral Pathology in Alzheimer's Disease Rating Scale, CESD = Centre for Epidemiological Studies Depression Scale, CSDD = Cornell Scale for Depression in Dementia, GDS = Geriatric Depression Scale, Geriatric Depression Scale or the, HADS = Hospital Anxiety and Depression Scale, MADRS = Montgomery Asberg Depression Rating Scale, MOSES = Multidimensional Observation Scale for Elderly Subjects, NPI = Neuropsychiatric Inventory, NPI-NH = NPI - Nursing Home version.

Sadness measure: AARS = Apparent Affect Rating Scale.

QoL measures: AQoL=Assessment of Quality of Life, ADRQL = Alzheimer’s Disease-Related Quality of Life, Cornell-Brown Scale for Quality of Life in Dementia (CBS-QoL), Dementia Care Mapping Wellbeing score (DCMW), DEMQOL = Dementia quality of life assessment, DQOL = Dementia quality of life instrument, EuroQoL = The European Health Related Quality of Life Scale, Facial expressions = Counts of positive and negative facial expressions as assessed from the first two minutes of filmed interviews, HUI3 = Health Utilities Index Mark 3, LSI = Life Satisfaction Index, PGCMS = Philadelphia Geriatric Center Morale Scale, PWI-ID = Personal Well-Being Index-Intellectual Disability, QoL-AD = Quality of Life in Alzheimer's Disease, QUALID = Quality of life in late-stage dementia, SR-QoL = Self-Report Quality of Life.

Table 2 The intensity of interventions in included reviews

Author (year)	Intervention	Duration of intervention	Length of each session	Total number of sessions (Frequency of sessions if not reported)
Reilly et al. 2015	Case management	4 months to 2 years	Contact was needs led	Contact was needs led
Bahar-Fuchs et al. 2013	Cognitive training Cognitive rehabilitation	4 weeks to 24 weeks	45 min to 60 min	5-72 sessions
Woods et al. 2012	Cognitive stimulation	4 weeks to 24 months	30 min to 90 min	(once a week to five days a week)
Barreto et al. 2015	Exercise programmes	6 weeks to 52 weeks	15 min to 60 min	(once a week to daily)
Forbes et al. 2015	Exercise programmes	2 weeks to 18 months	20 min to 75 min	(twice a week to daily)
Ojagbemi and Akin-Ojagbemi 2019	Exercise programmes	12 weeks to 48 weeks	80 min to 180 min	(once a week to daily)
Forbes et al. 2014	Light therapy	10 days to 2 months (one study provided the intervention over the mean of 15 months)	30 min to 120 min (one study provided the intervention for 9 hrs per day)	(5 times a week to twice a day)
Wu et al. 2017	Massage and touch	3 days to 3 months	10 min to 40 min	(5 times a week to twice a day)
van der Steen et al. 2018	Music based therapeutic interventions	2 weeks to 6 months	11 min to 120 min	6-156 sessions
Kim et al. 2012	Occupational therapy	4 weeks to 6 months	15 min to 90 min	(once a month to once a week)
Ojagbemi and Owolabi 2017	Occupational therapy	4 weeks to 48 weeks	one 30 min session to 130 min per week	–
Kim and Park 2017	Person-centred care	10 days to 2 years	–	–
Orgeta et al. 2014	Psychological treatments	6 weeks to 12 months	30 min to 90 min	–
Woods et al. 2018	Reminiscence therapy	4 weeks to 24 months	30 min to 120 min	(once a week to 5 times a week)

Table 3 Effects of interventions as reported in the included systematic reviews

Author (year)	Intervention and comparison intervention	Number of RCTs analysed	Measure of psychological QoL [1)]	Effect measure (expressed as SMD or MD)	Statistically significant	GRADE
Reilly et al. 2015	Case management Usual care, other non-case management or waiting-list controls	3 2 2 3 2	QoL at 12 mths Depression at 3-4 mths Depression at 6 mths Depression at 10-12 mths Depression at 18 mths	SMD 0.05 (95% CI -0.13 to 0.22) SMD 0.12 (95% CI -0.19 to 0.43) SMD 0.08 (95% CI -0.21 to 0.37) SMD -0.07 (95% CI -0.32 to 0.17) SMD -0.02 (95% CI -0.33 to 0.29)	No No No No No	High – – – –
Bahar-Fuchs et al. 2013	Cognitive training [2)] Usual care, no treatment, waiting-list, or active controls	4	Depression	SMD 0.03 (95% CI -0.34 to 0.41)	No	Moderate
Woods et al. 2012	Cognitive stimulation Usual care, no treatment, or placebo controls	4 5 4	QoL self-reported Depression self-reported Depression/anxiety combined staff-reported	SMD 0.38 (95% CI 0.11 to 0.65) SMD 0.22 (95% CI -0.09 to 0.53) SMD 0.05 (95% CI -0.21 to 0.31)	Yes No No	– – –
Barreto et al. 2015	Exercise programmes Usual care or an active-control group without exercise	7	Depression	SMD -0.31 (95% CI -0.57 to -0.04)	No	–
Forbes et al. 2015	Exercise programmes Usual care or social contact/activities	5	Depression	SMD 0.14 (95% CI -0.07 to 0.36)	No	Moderate
Ojagbemi and Akin-Ojagbemi 2019	Exercise programmes Any other type of therapy or no therapy	6	QoL	SMD 0.33 (95% CI -0.21 to 0.87)	No	–
Forbes et al. 2014	Light therapy Usual care, possibly with dim red light or dim, low-frequency blinking light	3	Depression	SMD 0.09 (95% CI -0.54 to 0.73)	No	–
Wu et al. 2017	Massage and touch Daily routine care or being accompanied	2 4	Sadness Anxiety	SMD -0.81 (95% CI -2.34 to 0.72) SMD -0.63 (95% CI -1.63 to 0.36)	No No	Low Low
van der Steen et al. 2018	Music based therapeutic interventions Any other type of therapy or no therapy	9 11 13	QoL Depression Anxiety	SMD 0.32 (95% CI 0.02 to 0.62) SMD -0.27 (95% CI --0.45 to -0.09) SMD -0.43 (95% CI -0.72 to -0.14)	Yes Yes Yes	Low Moderate Low
Kim et al. 2012	Occupational therapy Any controls	3	Depression	SMD 0.15 (95% CI -0.17 to 0.47)	No	–
Ojagbemi and Owolabi 2017	Occupational therapy Any controls	2 7	QoL self-reported QoL carer-reported	SMD 0.64 (95% CI -0.51 to 1.79) SMD 0.07 (95% CI -0.35 to 0.48)	No No	– –
Kim and Park 2017	Person-centred care Usual care	7 3	QoL Depression	SMD 0.20 (95% CI 0.09 to 0.31) SMD -0.24 (95% CI -0.39 to -0.09)	No No	– –

Table 3 Effects of interventions as reported in the included systematic reviews *(continues)*

Orgeta et al. 2014	Psychological treatments Usual care (no treatment) comparison or a comparison group engaging in non-specific psychosocial activity	3 2 6 2 2	QoL self-reported (QOL-AD) QoL care-reported (QOL-AD) Depression Anxiety self-reported Anxiety staff-reported (RAID)	MD 0.37 (95% CI -1.01 to 1.75) MD 0.66 (95% CI -0.77 to 2.09) SMD -0.22 (95% CI -0.41 to -0.03) SMD 0.05 (95% CI -0.44 to 0.54) MD -4.57 (95% CI -7.81 to -1.32)	No No Yes No Yes	– – Moderate Low Low
Woods et al. 2018	Reminiscence therapy Usual care (no treatment) comparison or social support	8 5 10 2	QoL self-reported QoL care-reported (QOL-AD) Depression Anxiety	SMD 0.11 (95% CI -0.12 to 0.33) MD 0.35 (95% CI -1.23 to 1.94) SMD -0.03 (95% CI -0.15 to 0.10) SMD -0.03 (95% CI -0.22 to 0.16)	No No No No	Moderate – High –

Note: 1) Multiple measures were used across included RCTs unless stated in brackets, 2) The overall effect size was not reported for cognitive rehabilitation. LSI = Life Satisfaction Index, MD = Mean difference, mths = Months, PwD = people with dementia, QoL= Quality of life, QOL-AD = The Quality of Life in Alzheimer's Disease, RAID = The Rating Anxiety in Dementia scale, RCTs = Randomised control trials, SMD = Standardised mean difference.