

Démence: quelles interventions non pharmacologiques?

KCE reports 160B

Le Centre fédéral d'expertise des soins de santé

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Disclaimer :	<p>- Les experts externes ont été consultés sur une version (préliminaire) du rapport scientifique. Leurs remarques ont été discutées au cours des réunions. Ils ne sont pas co-auteurs du rapport scientifique et n'étaient pas nécessairement d'accord avec son contenu.</p> <p>- Une version (finale) a ensuite été soumise aux validateurs. La validation du rapport résulte d'un consensus ou d'un vote majoritaire entre les validateurs. Les validateurs ne sont pas co-auteurs du rapport scientifique et ils n'étaient pas nécessairement tous les trois d'accord avec son contenu.</p> <p>- Finalement, ce rapport a été approuvé à l'unanimité par le Conseil d'administration.</p>

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PRÉFACE

Le sujet de la démence n'est pas neuf pour le KCE. En 2009, notre 111^{ème} rapport relatif à la maladie d'Alzheimer avait mis en évidence les limites certaines et les dangers des médicaments. Il avait également identifié des traitements non pharmacologiques qui se révélaient prometteurs.

Ces traitements non pharmacologiques à domicile et en institution sont actuellement analysés plus en détail, à la lumière des publications scientifiques récentes. Bien sûr il s'agit d'un domaine d'intervention où les études sont plus complexes à réaliser et l'efficacité des interventions plus difficile à démontrer que dans le domaine des traitements médicamenteux.

Néanmoins, une conférence européenne réalisée dans le cadre de la présidence belge en 2010 affirmait récemment qu'il était grand temps d'envisager des solutions qui sortent des sentiers battus afin d'améliorer la qualité de vie des personnes démentes et de leur entourage.

Ce rapport, réalisé en collaboration avec Abacus International[®], passe au peigne fin les traitements actuellement proposés et détaille les études qui ont analysé leur efficacité. L'éventail des traitements proposés est très large, à l'opposé des budgets disponibles. Il est donc primordial d'investir dans les initiatives les plus prometteuses afin de faciliter la vie des personnes démentes et de leur entourage dans ces circonstances souvent difficiles.

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Résumé

OBJECTIF

Ce rapport a pour objectif d'analyser l'efficacité des traitements non pharmacologiques actuellement proposés dans le cadre de la démence au domicile et en institution.

METHODOLOGIE

La revue systématique de littérature s'est basée sur les interventions et résultats publiés dans le cadre du rapport KCE relatif au diagnostic et au traitement de la maladie d'Alzheimer^a. Pour les interventions non pharmacologiques, ce précédent rapport synthétisait les revues systématiques de littérature publiées jusqu'en 2008. Le présent rapport complète cette revue de littérature par les publications plus récentes (2008 à 2010) identifiées dans Cochrane, Medline, EMBASE et Psychinfo.

Des tableaux présentés en annexe résument l'évaluation de la qualité et le contenu des revues systématiques et essais randomisés contrôlés (RCTs). L'attribution du niveau de preuve s'est basé sur la classification GRADE. Dans un second temps, des experts externes consultés ont défini un niveau de recommandation basé sur cette même classification.

RESULTATS

Vingt-deux revues systématiques de littérature et 30 essais randomisés contrôlés ont été sélectionnés sur base de leur qualité méthodologique et analysés. Mises à part les études relatives au soignant informel, la majorité des études se déroulait en institution.

De manière générale, peu de données probantes sont disponibles au sujet des interventions non pharmacologiques pour la démence. Par ailleurs, il n'existe pas de données de qualité permettant d'affirmer qu'une intervention soit non efficace.

QUATRE INTERVENTIONS SUPPORTÉES PAR LA LITTÉRATURE

Des données de qualité modérée ont été identifiées pour quatre types d'intervention qui ont un effet positif.

1. Interventions de type psychosocial/psychoéducation : impact sur les soignants informels et sur l'institutionnalisation

Former de manière efficace des soignants informels ou leur apporter un support de type psychosocial sont des interventions qui recouvrent un vaste champ d'actions différentes. Toutefois leur objectif est commun : développer les capacités des aidants (contrôle du stress, stratégies pour faire face aux problèmes de comportement, diminution de la charge de travail, augmentation de la satisfaction).

Les interventions à composantes multiples sont généralement efficaces tandis que les études avec une seule intervention présentent des résultats contradictoires. Les composantes sont par exemple des sessions de conseils (30 à 90 minutes), la participation à des groupes de support, des conseils par téléphone, l'évaluation de la situation individuelle du patient, une référence à un psychiatre, un réseau entre familles.

Ces interventions à composantes multiples réduisent le risque et augmentent le délai d'institutionnalisation. Par ailleurs, on note une amélioration de l'humeur du soignant (surtout lorsqu'il présente des troubles psychologiques), de son bien-être et de sa qualité de vie. Il est à noter que les interventions ponctuelles (par exemple quelques séances étalées sur quelques années) ne produisent pas d'effet sur le risque d'institutionnalisation ou les autres facteurs étudiés. Il n'existe cependant pas de données relatives à la fréquence optimale de ces interventions.

^a http://kce.fgov.be/index_fr.aspx?SGREF=3461&CREF=13576

Tous les experts consultés (de même que les validateurs) jugent que cette intervention bénéficie d'un niveau élevé de recommandation (IB : recommandation de niveau élevé qui peut être appliquée à la plupart des patients dans la plupart des circonstances). Les avis sont partagés pour les trois interventions suivantes.

2. Formation du personnel soignant en institution

La formation de ce personnel soignant consiste en un programme d'aide à la prise en charge adéquate des résidents souffrant de démence. Elle vise à produire un effet sur les résidents (entre autres sur les comportements agressifs) et à diminuer l'usage des contentions.

Les interventions qui ont un effet démontré sur l'usage des contentions se déroulent durant 8 semaines au moins et sont mises en place par des formateurs expérimentés. Par contre plus d'études sont nécessaires pour analyser l'impact de ces interventions sur le résident (comportement, communication, ADL).

La majorité des experts consultés a attribué un niveau de recommandation élevé (IB) pour cette intervention.

3. Programmes d'activité physique

La majorité des études concluent que des programmes d'activité physique (marche, exercices divers) ont un effet positif chez les patients atteints de démence. La forme physique est améliorée et d'autres effets positifs varient suivant les études (état cognitif, bien-être, humeur du patient).

Une revue systématique avec des résultats positifs s'est intéressée spécifiquement aux patients atteints de démence légère à modérée avec des exercices sous la supervision d'un thérapeute. Les autres publications définissent plus largement les groupes cibles et programmes analysés.

La majorité des experts consultés a attribué un niveau de recommandation élevé (IB) pour cette intervention.

4. Stimulation/entraînement cognitif du patient

Cette intervention comprend des activités qui stimulent la fonction cognitive du patient (par ex. associations de mots, catégorisation). Deux méta-analyses de bonne qualité concluent à un effet modéré de la stimulation/entraînement cognitif sur les paramètres suivants : fonction cognitive, activités quotidiennes (« Activities of Daily Living », ADL), humeur, comportement du patient et bien-être du soignant. La plupart des études n'analyse cependant que l'effet à court terme (quelques semaines ou mois).

D'autres études, de moindre qualité, concluent qu'il est nécessaire de disposer de plus de données pour tirer des conclusions relatives à cette intervention.

Les avis des experts étaient partagés quant au niveau de recommandation : la préférence pour un niveau élevé (IB) prédomine mais certains experts notaient des variations de résultats entre études de même qu'un risque de pression psychologique de la part de l'entourage sur le patient.

PEU OU PAS DE DONNÉES PROBANTES POUR LA MAJORITÉ DES INTERVENTIONS NON PHARMACOLOGIQUES

Résultats contradictoires pour la revalidation relative aux activités journalières

Il existe des données de qualité modérée relatives à la revalidation par des activités journalières (thérapie qui vise à maintenir les capacités du patient : se laver, manger etc). Toutefois, les résultats contradictoires de ces études ne permettent pas de formuler une recommandation.

Données de qualité (très) faible pour la majorité des autres interventions

Pour 16 autres interventions, les données disponibles sont de (très) faible qualité : des RCTs de meilleure qualité sont nécessaires afin de formuler des recommandations en leur faveur ou de les déconseiller :

- Effet positif dans les études : interventions d'« orientation dans la réalité » ;
- Peu ou pas d'effet : acupuncture, luminothérapie, communication/interaction ;
- Effets contradictoires entre études: thérapie de réminiscence, thérapie de validation, “snoezelen”, aromathérapie, thérapie basée sur une présence simulée, musicothérapie, thérapie basée sur l'activité, unités de soins spécialisées, adaptation environnementale, « respite care »;
- Un seul RCT respectivement pour le massage et la nutrition.

Aucun RCT pour six interventions

Enfin, cette revue de littérature n'a identifié aucun RCT pour les interventions suivantes : thérapie comportementale individuelle avec le patient, méthode Montessori, “self-maintenance therapy”, instruction individualisée (“individualised special instruction”), “support intégré basé sur l'expérience” (“geïntegreerde belevingsgerichte ondersteuning”), thérapie axée sur le milieu.

DISCUSSION

Cette étude a identifié une trentaine d'interventions non pharmacologiques visant à aider les patients souffrant de démence ainsi que leurs soignants. Les données relatives à ces interventions sont tout au plus de qualité modérée : elles sont le plus souvent de qualité faible, voire insuffisante. Elles ont cependant permis aux experts de formuler des recommandations pour quatre types d'intervention.

Durant l'élaboration du présent document, Olazaran et al. ont publié une revue systématique de littérature de bonne qualité sur le même sujet, chez les patients souffrant de maladie d'Alzheimer^b. Leurs conclusions sont similaires en ce qui concerne les principales interventions, en particulier l'efficacité des interventions à multiples composantes pour retarder l'institutionnalisation. Comme dans la présente étude, ces auteurs concluent également à de nombreuses limitations des études, de même qu'à l'existence de résultats souvent contradictoires pour une même intervention.

Limitations des études analysées

La majorité des RCTs analysés ou rapportés dans le cadre des revues systématiques présentent plusieurs limitations méthodologiques et des imprécisions relatives à la description de l'intervention. Par ailleurs, les études qui rapportent des résultats au terme de l'intervention sont souvent en contradiction avec d'autres études dont la durée de suivi dépasse la fin de l'intervention.

En outre, le cadre des études ne permet pas toujours de transposer leurs résultats à la situation belge. Une illustration est le peu d'effet noté pour les unités de soins spécialisés. La littérature internationale tient peu compte de la taille de ces unités alors qu'en Belgique il s'agit d'une caractéristique importante des unités de vie adaptées.

Hétérogénéité des résultats : hypothèses complémentaires

Des facteurs autres que méthodologiques peuvent expliquer le peu de résultats positifs et les résultats contradictoires des études :

- La difficulté de conduire des RCTs de qualité dans le domaine de traitements non pharmacologiques (le critère « en aveugle » par exemple est plus difficile à respecter) ;
- L'hétérogénéité des interventions regroupées sous la même bannière. Une illustration est la « stimulation/entraînement cognitif » qui couvre un vaste champ d'interventions, de fréquence et de durée variables ;
- L'hétérogénéité des paramètres considérés (et de leur méthode de mesure) pour apprécier les résultats, tant au niveau du patient (état cognitif, comportement, humeur) qu'au niveau du soignant (stress, charge de travail, qualité de vie) ;
- Une trop faible différence entre groupe contrôle et intervention : un « groupe contrôle » qui ne bénéficierait d'aucune intervention est impossible pour beaucoup d'interventions (telles que la communication avec la personne, le soutien psychosocial des aidants proches) ;
- Limites du design des études qui analysent ce type d'interventions : les interventions étaient appliquées à un groupe de personnes, indépendamment de leur sensibilité personnelle. Or certaines interventions spécifiques (telle la musicothérapie) pourraient avoir un effet plus marqué en fonction des caractéristiques individuelles (si on apprécie ou non la musique par exemple).

b J. Olazaran et al. Nonpharmacological therapies in Alzheimer's disease: a systematic review of efficacy. *Dement Geriatr Cogn Disord* 2010;30:161–178. Available (June 2011) : <http://www.mariawolff.es/pdf/Non-pharmacological%20Therapies%20in%20AD,%20a%20Systematic%20Review%20of%20Efficacy.pdf>

Nécessité d'adapter l'intervention

Les interventions qui ont des résultats positifs sur le patient et son entourage présentent des caractéristiques communes :

- Elles sont adaptées au patient et à son entourage: Imposer un répit à l'entourage peut par exemple être source de stress et de travail supplémentaire pour les aidants s'ils ne sont pas demandeurs ou ne s'inscrivent pas dans ce projet.
- Elles sont adaptées au milieu de vie: les interventions publiées dans la littérature étaient le plus souvent testées en institution. On présume que la mise en place d'une intervention similaire à domicile nécessitera une adaptation au milieu de vie individuel du patient.

Par ailleurs, l'intervention sera probablement différente suivant le contexte culturel et les soins de santé. Les études sélectionnées se sont déroulées dans des contextes de soins différents du système belge. Certaines caractéristiques liées à l'organisation des soins de santé peuvent exercer une influence positive ou négative sur les résultats escomptés.

Des interventions qui répondent à un besoin de notre société

Le présent rapport répond au message lancé lors de la conférence européenne relative à l'amélioration de la qualité de vie des personnes souffrant de démence^c. Les conclusions soulignaient en effet l'importance d'interventions dans le domaine social. En particulier les experts présents ont souligné l'importance du support de l'entourage, de la collaboration entre soignants, de la continuité de la prise en charge et d'une intervention qui soit centrée sur le patient.

CONCLUSION

Cette recherche permettra d'orienter les patients souffrant de démence vers une prise en charge basée sur des interventions efficaces non pharmacologiques. A domicile, un support de type psychosocial du soignant informel a notamment un impact sur l'institutionnalisation. En institution, la formation des soignants diminue l'usage des contentions. Les programmes d'activité physique et une stimulation de type cognitif sont en outre potentiellement bénéfiques pour le patient tant à domicile qu'en institution.

Les données actuellement disponibles relatives aux autres interventions sont de qualité trop faible pour formuler des recommandations, ce qui n'est pas synonyme de leur inefficacité.

Enfin, aucune conclusion ne peut être formulée pour les aspects coût-efficacité qui n'ont pas été analysés dans le cadre de cette étude.

^c Onkelinx L. Concluding remarks on the conference 'Improving the quality of life of people with dementia: a challenge for European society'. Conference organised in the framework of the Belgian EU Presidency, 25-26 November 2010, Brussels.

RECOMMANDATIONS^d

Parmi tous les traitements non pharmacologiques existant dans le cadre de la prise en charge de la personne souffrant de démence, il existe des données scientifiques suffisantes pour recommander les catégories de traitements suivantes :

- Support et formation des aidants informels comprenant des interventions multiples à domicile : un effet positif est notamment noté sur l'institutionnalisation,
- Formation du personnel soignant en institution,
- Programmes d'activité physique à domicile ou en institution,
- Thérapie de stimulation/entraînement cognitif.

Bien que les modalités d'administration de ces traitements ne puissent être décrites de façon précise sur base d'études publiées, il est démontré que ces interventions sont plus efficaces si elles :

- sont adaptées au patient et à son entourage pour répondre au mieux à leurs besoins,
- bénéficient d'un suivi par un personnel spécifiquement formé,
- sont poursuivies dans la durée avec des contacts réguliers afin de produire des effets significatifs.

Pour les autres interventions non pharmacologiques, les données actuelles ne permettent pas de formuler de recommandations.

d Le KCE reste seul responsable des recommandations faites aux autorités publiques

Scientific summary

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I INTRODUCTION

I.1 BACKGROUND OF THE STUDY

In 2008, the Belgian Government asked the Federal Health Care Knowledge Centre (KCE) to conduct a study on existing diagnostic and therapeutic modalities for Alzheimer dementia. In answer to this question, the KCE conducted a short review summarizing the existing systematic reviews and HTA reports published between 2003 and 2008.

This first KCE report¹ focussed on diagnostic and pharmacological interventions. It concluded to a limited effectiveness of pharmacological interventions. However in the same time this report identified several non-pharmaceutical interventions targeting either the carer or the patient¹. These interventions were unimodal, multimodal (e.g. combination of reality orientation, validation therapy and self-maintenance therapy) or involved general procedures (e.g. milieu interventions).

This rapid assessment identified several potentially effective non-pharmacological interventions: cognitive training/stimulation, ADL rehabilitative care, music therapy, massage/touch, physical activity, education/training of professionals, education of informal caregivers, psychosocial support of informal caregivers. For none of them high quality evidence was found but the conclusion was that these therapies seemed promising and warranted further attention.

This report is a systematic review of non-pharmacological interventions to complete, update and analyse in detail the interventions described in the former rapid assessment published in 2009.

I.2 DEMENTIA

I.2.1 A disease with consequences

Age related cognitive changes encompass a wide spectrum of severity ranging from benign memory loss or age related cognitive decline, through mild cognitive impairment, to dementia². Dementia is progressive in nature: multiple higher cortical functions (including memory, thinking, orientation and language) are disturbed, leading to deterioration in daily living activities, emotional control, social behaviour and motivation. This decline eventually leads to complete psychological and physical dependency. People with dementia become increasingly reliant on family, friends and neighbours, and health and social care services.

Care for people with dementia is often provided by both health and social care organisations. Informal carers (family and friends) also provide a substantial amount of care, in Belgium up to 88% before institutionalisation³. In the UK, recent NICE guidance also emphasised the need to unite the clinical and social perspective⁴.

The total cost of illness of dementia in Belgium have been estimated around € 2394.2 million in 2008⁵. Costs of residential care have till this moment not been proven to outweigh costs in home care, because studies do not stress the economic loss suffered by caring relatives.

I.2.2 Diagnostic process

The clinical diagnosis of dementia commonly relies on clinical international classifications:

International classifications of dementias

Type of dementia	Diagnostic criteria
Alzheimer's disease	Preferred criteria: NINCDS/ADRDA. Alternatives include ICD-10 and DSM-IV
Vascular dementia	Preferred criteria: NINDS-AIREN. Alternatives include ICD-10 and DSM-IV
Dementia with Lewy bodies	International Consensus criteria for dementia with Lewy bodies
Frontotemporal dementia	Lund-Manchester criteria, NINDS criteria for frontotemporal dementia
DSM-IV, Diagnostic and Statistical Manual of Mental Disorders, fourth edition; ICD-10, International Classification of Diseases, 10th revision; NINCDS/ADRDA, National Institute of Neurological and Communicative Diseases and Stroke/Alzheimer's Disease and Related Disorders Association; NINDS-AIREN, Neuroepidemiology Branch of the National Institute of Neurological Disorders and Stroke-Association Internationale pour la Recherche et l'Enseignement en Neurosciences.	

The former KCE report¹ analysed the tests used for the diagnostic of dementia and the criteria proposed to confirm the diagnosis. Guidelines emphasize the need for including medical imaging and blood sampling to exclude reversible conditions and to estimate prognosis^{6,7}.

The National Institute on Aging and the Alzheimer's Association recently revised the clinical criteria for all-cause dementia and Alzheimer disease⁸.

1.2.3 Prevalence of dementia

Studies of dementia prevalence in Europe present varying prevalences by age, sex and country⁹⁻¹². The EURODEM Collaboration reports 2009 figures between 5.7% and 21.9%⁹.

Point prevalence estimates are available from The Netherlands by age and gender (for 1000 persons, 2007)¹³:

	Men	Women
65-69 y	3.05	4.10
70-74 y	7.36	9.91
75-79 y	16.26	21.89
80-84 y	32.47	43.55
> 85 y	54.57	72.54

In Belgium the last available data (study "Qualidem" 1999-2006) estimated that 9% of the elderly older than 65 years suffered from dementia¹⁴. Based on the national statistics of the Belgian population that would mean nearly 170 000 elderly people who suffer from dementia.

1.2.4 Types of dementia in Europe

Several large scale studies analysed the types of dementia in Europe:

- A collaborative study by Lobo and colleagues found Alzheimer's disease the most common cause of dementia (53.7% of the cases), followed by vascular dementia (15.8% of the cases) and less common causes (e.g. dementia with Lewy bodies, fronto-temporal dementia)¹⁰;
- A study from Austria found that among 1110 old demented patients (90% over age 70), Alzheimer's disease accounted for dementia in over 40% of the cases and pure vascular dementia in 10.8%¹¹.
- The BrainNet Europe Consortium Experience (survey within brain banks) found that that 53.3% of the 3,303 individuals with dementia had a diagnosis of mixed dementia^{4,12}.

I.3 RESEARCH QUESTION

This systematic review addresses the effectiveness of non-pharmacological interventions for patients with dementia in home and residential settings. The list of non-pharmacologic interventions for dementia included in this report is provided in 2.1.1.2.

2 METHODS

2.1 INCLUSION CRITERIA

2.1.1.1 *Population*

Publications had to include patients or caregivers eligible for a non-pharmacologic intervention for dementia. The systematic review included all types of dementia based on indexing of online databases of the literature (see appendix 6.1). Diagnoses (and criteria) and stages of dementia were reported when documented by authors. Mild cognitive decline was excluded. However the absence of reporting did not prevent the inclusion of the study.

The setting was the context of community care either at home or in nursing homes. Hospitalised patients were excluded. Home and residential care settings were included, because their populations are relatively comparable and usually included together in the available scientific literature. The setting was reported for every included study in the data extraction tables (see appendices 6.5 and 6.9).

2.1.1.2 *Interventions*

Interventions under study

The interventions (and their combinations) considered as eligible for inclusion are the following ones^a:

INTERVENTIONS PRIMARILY FOCUSED ON THE PATIENT

1. Cognition:
 - Reality orientation;
 - Cognitive stimulation or training;
 - Patient counselling;
 - Montessori activities;
2. Emotion:
 - Reminiscence therapy;
 - Validation therapy;
 - Self-maintenance;
 - Individualised instructions;
3. Sensory enhancement:
 - “Snoezelen”;
 - Massage;
 - Aromatherapy;
 - Simulated presence;
 - Acupuncture;
 - Music therapy;
 - Light therapy;
 - Integrated experience-oriented support (“Geïntegreerde belevingsgerichte ondersteuning”);

^a “Humanitude” has been proposed by experts during the study. “Humanitude” has been described as “autonomic power to develop one’s knowledge, emotional space and wishes over time and to exchange this in dialogue in therapy”¹⁵. This concept has been later excluded from the review as it is more a philosophy than an intervention.

4. Daily activities:
 - Activity therapy;
 - ADL rehabilitation care;
5. Physical activity;
6. Communication/Interaction/relationship;
7. Environmental changes:
 - Environmental adaptation;
 - Special care units;
 - Milieu therapy;
8. Nutrition;

INTERVENTIONS PRIMARILY FOCUSED ON THE CAREGIVER:

9. Staff education;
10. Respite care;

INTERVENTIONS FOR PATIENTS AND THEIR INFORMAL CAREGIVERS:

11. Psychoeducation / psychosocial interventions;
12. Interventions to delay institutionalisation.

“Dementia care mapping” was mentioned by the experts at the end of the study. This observation and intervention tool is defined as “a method of implementing person-centred care underpinned by the social psychological theory of personhood in dementia »¹⁶. One RCT recently published¹⁶ did not show any relevant clinical impact on the patient QOL or agitation. Trials about dementia care mapping are ongoing (see <http://www.trialregister.nl/trialreg/admin/rctview.asp?TC=2314>).

Classification of interventions

In this review, the interventions are categorised:

- Based on the primarily targeted group (patient and/or caregiver), even if all interventions might have an impact on both target groups;
- Based on different domains affecting the patient e.g. neuropsychiatric and other symptoms, behaviour, mental status, daily activities (ADL), quality of life (QOL).

This classification is in line with other systematic reviews on mixed interventions and in particular with the previous KCE report ¹. It is however quite arbitrary. Interventions as for example special care units also have an effect on the patient whose life environment changes. In the same way interventions that improve the patient might also have an impact on the caregiver outcomes such as burden of care.

The former KCE report also mentioned “interventions to delay institutionalisation” as separate interventions, based on the available systematic reviews on this topic. That is the reason why this intervention has been also considered apart in this search strategy. The results show that many interventions might delay institutionalisation. This point will be handled in the discussion.

2.1.1.3 *Comparators*

Other interventions, waiting list or usual care (as defined by the authors).

2.1.1.4 Outcomes

Clinically relevant symptoms and/or behaviour changes measured by validated outcome measurement tools such as:

- Change in behaviour (e.g. assessed by the Agitated Behaviours in Dementia Scale or Behavioural Symptoms of Dementia);
- Patient depression, stress and quality of life;
- Activities of daily living (e.g. assessed by Alzheimer's disease assessment scale-activities of daily living);
- Cognition (e.g. assessed by Alzheimer's disease assessment scale-cognitive subscale);
- Caregiver quality of life;
- Caregiver burden and depression (e.g. assessed by Caregiver Activity Schedule, Care Assessment of Difficulties Index).

Studies reporting only costs, laboratory outcomes or other outcomes without direct clinical relevance were excluded.

2.1.1.5 Language

Databases were searched for publications in English, French, Dutch or German.

2.1.1.6 Design

Selection criteria were set up for systematic reviews as for RCTs as explained in chapter 2.3.

2.2 LITERATURE SEARCH STRATEGY

The wealth of research literature in this particular therapeutic area made a de novo systematic review of the primary studies impractical. The project was segmented into two phases. Phase I was a systematic review of existing systematic reviews published since the former KCE report. Phase II was a search for RCTs associated with a low risk of bias.

2.2.1 Phase I : systematic reviews

Using the search terms detailed in Appendix 6.2, the following databases were first systematically searched in August 2010 for systematic reviews (SRs) of non-pharmacological interventions for dementia. The searches were designed to be comprehensive and to capture all relevant systematic reviews.

- The Cochrane Library
- OVID Medline
- OVID EMBASE
- Psychinfo
- CRD HTA

Additional hand searching was also undertaken to ensure that no potentially relevant studies were missed. The reference lists of retrieved articles and existing systematic reviews were scanned and websites of INAHTA members were checked (see Appendix 6.3 for a full list of websites checked in detail).

Systematic reviews were eligible as evidenced by the description of a systematic search of one or more electronic databases. The date limit was a publication after 2007, the search dates of the last KCE report¹(see 1.1). The most recent review with low risk of bias was used as a starting point for a de novo systematic review of RCTs.

2.2.2 Phase II : randomised controlled trials

Using the search terms detailed in appendix 6.7, the following databases were systematically searched in January 2011 from 2008 onwards for RCTs^b:

- Cochrane Central Register of Controlled Trials (Clinical Trials)
- OVID Medline
- OVID EMBASE
- Psycinfo

Additional hand searching of reference lists was also undertaken to ensure that no potentially relevant studies were missed.

Only RCTs were eligible as evidenced by a reference to randomisation and to a control/comparator treatment. RCTs with a mixed population were only included if they included more than 30 patients, with >75% of patients with dementia.

2.3 ASSESSING METHODOLOGICAL QUALITY AND RISK OF BIAS

2.3.1 Systematic reviews

The methodological quality of selected reviews and associated risk of bias were rated using the SIGN tool^c. The assessment of the risk of bias in the included SR was conducted by three reviewers (JB, MK, FA). In order for publications to be included, four of the five following criteria had to be rated as “well covered” or “adequately addressed”:

- Appropriate and clearly focussed study question,
- Description of methodology: number and types of databases searched and description of search terms used,
- Sufficiently rigorous literature searches: inclusion of at least Medline and Cochrane databases,
- Quality and methodological strengths and weaknesses of identified data assessed and taken into account: description of a quality appraisal of the included studies using a clearly defined tool,
- Study type was described and included: RCTs, (quasi-)experimental studies, or controlled before-after studies.

The results of the quality appraisal are in appendix 6.4.

^b The intervention « nutrition » has been suggested by the experts at the end of the phase on systematic reviews. This term has only been included in the RCT phase. In addition, four reviews were identified on nutrition, but these were not systematic reviews and were therefore not included.

^c <http://www.sign.ac.uk/methodology/checklists.html>

2.3.2 Randomised controlled trials

The methodological quality of selected RCTs was rated using a modified version of the SIGN tool. The assessment of the risk of bias in the included RCTs was conducted by three reviewers (SGS, MK, FA). Each reviewer assessed one third of the RCTs and then blindly assessed a different third. The reviewers then discussed discrepancies. In order for publications to be included, three of the four following criteria had to be rated as “adequately addressed”:

- Randomisation: with a description of the method,
- Blinding and the mention of the blinded groups i.e. patients or assessors: blinding of therapists was hardly possible,
- Treatment groups comparable at baseline,
- Description of dropouts and withdrawals and possible inclusion in the analysis.

The results of the quality appraisal are in appendix 6.8.

The quality of the evidence has been rated according to the GRADE criteria⁸⁵.

2.4 DATA EXTRACTION

For each phase, quality appraisal and data extraction were performed using a specifically designed data extraction template (DET) in order to summarise key design features and results. The DET for systematic reviews (see 6.5) captured the following information; reference, risk of bias, details of searches, details on treatments, (including target of patient and/or caregiver, comparators), treatment setting (home or community-based care or residential), population (e.g. type of dementia and criteria for diagnosis), and results.

The DET for RCTs (see 6.9) captured the following information: reference, country, setting, number of patients, patient characteristics including type of dementia and criteria for diagnosis, details of intervention, details of comparator, outcome, time of follow-up, effect between groups and interpretation of results.

Data extraction of the SR and RCT judged to have a low risk of bias were performed by a reviewer (SGS) into a pre-prepared Excel® spreadsheet. A second reviewer (MK) reviewed the publication in full in order to check the extracted information and any additional information that had not been extracted by the first reviewer. Any discrepancies were resolved through discussion with an independent third party (FA). Discrepancies could involve consistency of reporting outcomes, reporting of clinical effectiveness or interpretation of effectiveness by the researchers. Standard rules (such as reporting of statistical significance and time of follow-up) were adopted to determine clinical meaning of effect.

3 RESULTS

3.1 METHODOLOGICAL CONSIDERATIONS

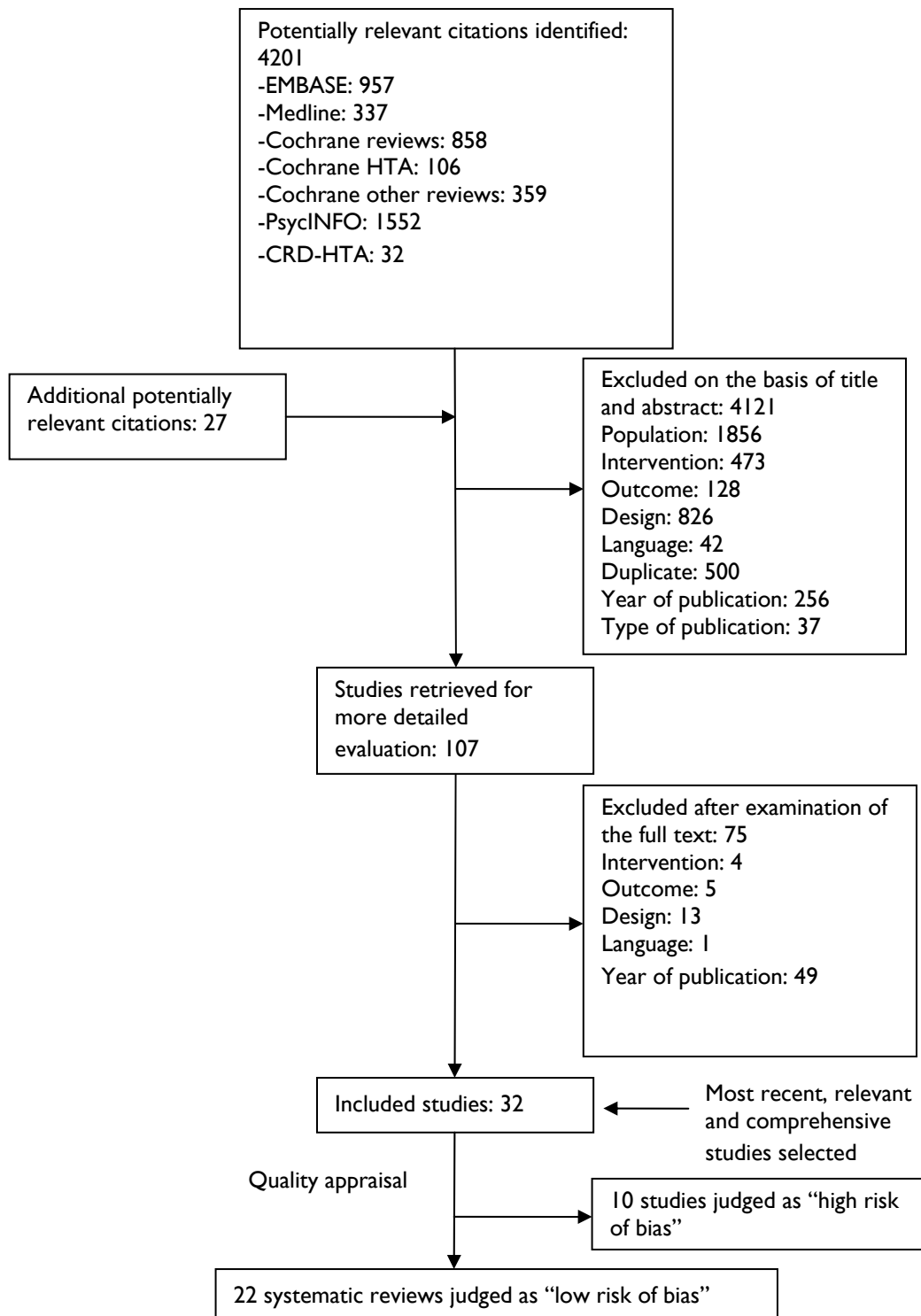
3.1.1 Systematic reviews

3.1.1.1 *Number of included systematic reviews*

The initial search identified 4201 citations (Figure 1). The supplementary searches of INAHTA member websites and handsearching yielded 27 additional references. The majority of citations were excluded on the basis of title and abstract (based on e.g. language, drug interventions or incorrect patient population); the other papers (n=107) were retrieved in full and reviewed in more detail.

On the basis of the full text, 81 reviews were included. As this number was much larger than expected, the most recent reviews were prioritised for extraction. A cut-off of 2008 was selected as the existing KCE publication¹ already presented reviews published up to 2007. Therefore the researchers performed the quality appraisal of the 32 reviews published in 2008, 2009 and 2010.

Figure 1 Results of searches and selection of systematic reviews



3.1.1.2 Quality of systematic reviews

The majority of studies (n=22) were judged to be of high quality and at a low risk of bias (see 6.4). Some of them failed to address the quality of included studies but performed better against other methodological markers and were judged to be more reliable²⁷⁻²⁹.

Ten studies were judged to have been undertaken using less rigorous methods and were labelled as “high risk of bias”. The most frequent reason was that none of these reviews adequately addressed the quality and associated biases of included studies¹⁷⁻²⁶. These studies are summarised in appendix 6.6 but are not discussed further.

Several reviews of high quality only included RCTs: Nocon 2010²⁷, Olazaran 2010³⁰, Kong 2009³¹, Forbes 2009³², Forbes 2008³³, IQWiG 2009³⁴, Nguyen 2008³⁵, Lee 2009³⁶, Rieckmann 2009²⁸, Weina 2009³⁷. The other reviews included also other types of study design: controlled clinical trials (CCTs), (quasi)-experimental studies, controlled before-after studies.

3.1.1.3 *Interventions analysed in systematic reviews*

Among the 22 systematic reviews with a low risk of bias, 8 studied specific interventions (see appendix 0) and 14 studied mixed interventions (see appendix 0). These last ones did not confine their review to one specific intervention and defined the interventions to be included more broadly as “non-pharmacological”^{31,34,38}, “psychosocial interventions”^{39,40}, “interventions to support caregivers”⁴¹, “communication intervention/strategies”⁴². Two systematic reviews had even larger concepts (“care interventions”⁴³ and “any theoretically based, nonchemical, focused, and replicable intervention, conducted with the patient or the caregiver, which potentially provided some relevant benefit”³⁰).

Two studies that used a broad definition to define the scope of included interventions further addressed separately the different interventions^{40,43}.

3.1.1.4 *Intervention setting in systematic reviews*

Seven reviews included studies with residential care setting and nine reviews included mixed settings. Three reviews did not specify the setting. The three reviews that used the home setting analysed interventions specifically designed for informal caregivers (e.g. respite care, psychosocial support).

3.1.1.5 *Diagnosis and stage of dementia in systematic reviews*

The reviews published in the Cochrane library specified a diagnosis, according to criteria included in the Diagnostic and Statistical Manual of Mental Disorders, the ICD-10, the National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer’s Disease and Related Disorders Association. Most reviews lamented the lack of a confirmed diagnosis in the included studies without making it an inclusion or exclusion criteria. Only a few reviews report on the stage of dementia of the included patients (e.g. Olazaran³⁰: Global Deterioration Scale stages 3-7).

3.1.2 *Randomised controlled trials*

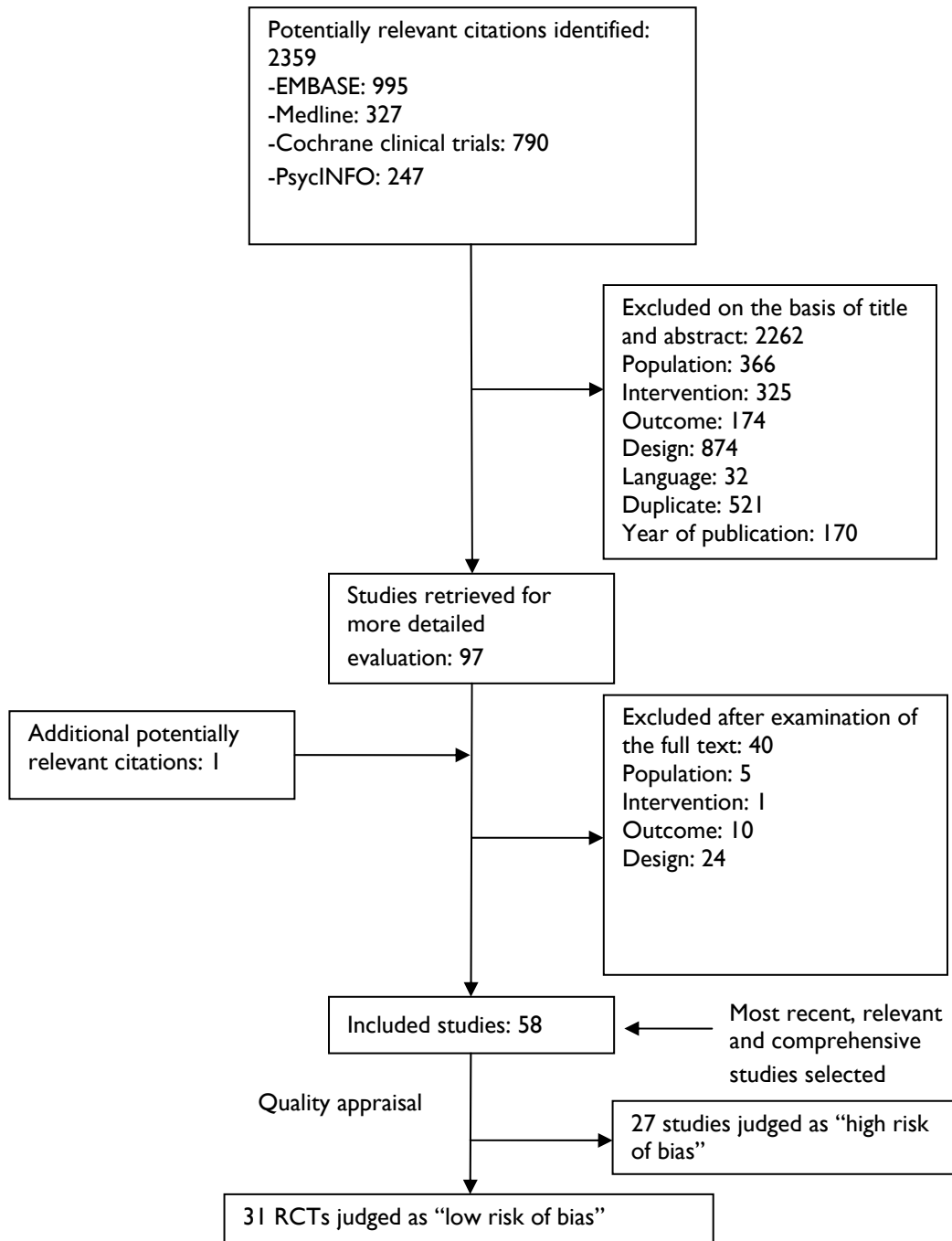
3.1.2.1 *Number of included RCTs*

The search performed in January 2011 identified 2359 citations (Figure 2). Hand searches of reference lists provided an additional RCT published between 2008-present that was not identified in the database searches⁴⁴. The majority of citations were excluded on the basis of title and abstract; the other papers (n=97) were retrieved in full and reviewed in more detail.

On the basis of the full text, 58 RCTs were included. After quality appraisal of the papers, only 31 RCTs with a low risk of bias were extracted in full.

The tables in appendix 6.8 summarise the quality appraisal for all included and excluded RCTs. The data extraction table of the 31 selected RCTs published in 2008, 2009 and 2010 is in appendix 6.9.

Figure 2 Results of searches and selection of RCTs



3.1.2.2 Study quality of RCTs

The majority of studies (n=31) were judged to be at a low risk of bias according to the criteria detailed in 0 (see appendix 0). Twenty-seven studies were judged to have been undertaken using less rigorous methods, with “high risk of bias”. Authors regularly did not report methods sufficiently and particularly baseline characteristics were not often similar between study arms. In addition, investigator blinding was often not reported or not possible at all. The quality appraisal of these studies is in appendix 0 but they are not discussed further.

3.1.2.3 Setting, sample size and follow-up in RCTs

Most RCTs with low risk of bias were undertaken in Europe (n=18) and the US (n=9). Four studies were performed in China / Hong Kong and two in Australia (some studies recruited patients in multiple countries).

The settings of the studies were often long term institutions, except when the intervention specifically targeted a caregiver (and patient) at home. Twelve RCTs (n=12) used the home setting and 19 RCTs were performed in residential care setting (e.g. nursing homes or memory clinics).

Overall, the included studies had sample sizes between 32 to 1131 participants. Some studies used cluster randomisation to group participants that lived in residential care institutions: it was checked that these cluster studies used appropriate randomisation methods and provided adequate treatment allocation.

Follow-up time was sometimes short: measurements were often taken just after treatment. Some follow-ups were long term (up to 24 months).

3.1.2.4 Interventions and outcomes in RCTs

Interventions primarily focused on the patient

Thirteen RCTs were in this category, two only in the home setting⁴⁵⁻⁵⁷. The nature, length and frequency of intervention and follow-up were usually well described. The effects of the interventions were measured using various scales and scoring systems for outcomes in several clinical domains e.g. Mini Mental State Examination score, mood, depression, disturbing behaviour, sleep and activity. Scores after follow-up were compared with baseline scores; with the change over time vs. comparator arms; or with both.

Interventions primarily focused on the caregivers

Eighteen papers studied interventions targeted at the (in)formal caregivers of patients with dementia⁵⁸⁻⁷⁵. A common caregiver-targeted intervention was caregiver training, which will be described in more detail in section 3.2.9. Outcomes of caregiver interventions were symptom improvements in patients or changes in caregiver wellbeing (e.g. burden, depression or quality of life) using scoring systems. While some RCTs focussed the intervention on caregivers, the outcomes of the study often involved often both the caregiver and the patient.

3.1.2.5 Diagnosis and stage of dementia in RCTs

Patients did not always have a clear diagnosis at study entry^{50, 58, 60, 61, 66}. The difficulty to diagnose subtypes of dementia e.g. Alzheimer’s disease was given as a reason in the study by Charlesworth et al⁶¹. Studies that diagnosed patients at study entry used several scales e.g. DSM-IV (Diagnostic and Statistical Manual of Mental Disorders, Diagnostic criteria for Dementia), NINCDS (National Institute of Neurological and Communicative Disorders and Stroke). Stage of dementia was sometimes defined (e.g. using Clinical Dementia Rating).

3.2 RESULTS BY INTERVENTION

The evidence described in the following sections, aims to list the outcomes of all non-pharmacological interventions found in the selected literature. The first sections address the interventions that more specifically target the patient (section 3.2.1 - 3.2.8) while the last sections (3.2.9) address more specifically caregivers.

Each section begins with a description of the intervention under consideration. For most interventions no uniform and generally accepted definition exists. Consequently different systematic reviews may classify the same studies in different intervention categories. Even within one type of intervention, there is a considerable diversity of intervention parameters and outcome measures.

Results of the systematic reviews have been pooled with those of the RCTs. Moreover it is also reported for each intervention when evidence was found in the previous KCE report¹. The effects described as “positive” have a statistically significant effect on reported outcomes.

3.2.1 Cognition

3.2.1.1 *Reality orientation*

Reality orientation is based on a general philosophy that states that confusion would result from understimulation of the patient e.g. care providers’ lack of insistence or expectation that the patient would perform normal behaviours; and care providers’ non-reinforcement of desired behaviours when they are performed⁷⁶.

Four reviews specifically addressed this therapy. Two reviews (Nocon 2010, Rieckmann 2009) included two publications on reality orientation^{27,28}. In both publications positive outcomes were found on cognition, and in one study on quality of life. The authors of the reviews conclude that due to lack of robustness of the study methodology, there was not enough clinical evidence of effectiveness to warrant treatment recommendations. Fisher-Terworth (2008) cite another review, in which three out of 14 included RCTs showed significant improvements on cognition. The Swedish SBU review cite the review from Spector et al. that evaluated reality orientation: SBU concluded that evidence was insufficient because the included studies in this review had a poor quality.

Summary: the conclusion of this systematic review on reality orientation is similar to the conclusion of the previous KCE report i.e. a lack of studies of high quality (low level of evidence) for this intervention.

3.2.1.2 *Cognitive stimulation or training*

Cognitive stimulation involves themed activities to orientate and actively stimulate cognition through e.g. association and categorization, while cognitive training focuses on teaching of strategies (e.g. mental imagery) to improve verbal learning and other cognitive functions. Seven reviews included cognitive stimulation or training.

The previous KCE report stated that cognitive stimulation / training were promising therapies, given that at least 2 well-conducted RCTs found positive outcomes. However, further confirmation of these results was considered necessary given the diversity of interventions and outcome measures used.

Positive results from three systematic reviews and two RCTs

Two of the most recent and best reviews (cf. appendix 6.4 (quality appraisal) and appendix 0) calculated pooled effect sizes of the studies that they included: they found convincing evidence for a mild effect of cognitive training or stimulation^{30,34}.

The first systematic review by Olazaran (2010) reported cognitive interventions either targeting specific abilities (cognitive training, 14 included RCTs including one combining it with donepezil) or more general stimulation (cognitive stimulation, 10 included RCTs) in either a group or individual setting³⁰. It could also be a multicomponent intervention including cognitive stimulation (five included RCTs).

- For the outcome “cognitive function”, they found homogeneous evidence (grade B) from low-quality RCTs, with a pooled effect size of 0.59 (95%CI 0.05-1.14; three RCTs, moderate effect) for cognitive training group sessions, and 0.40 (95%CI 0.09-0.72; seven RCTs, mild effect) for cognitive training individual sessions. They found a pooled effect size of 0.44 (95%CI 0.20-1.69; 6 RCTs, mild effect) for cognitive stimulation group sessions. Multicomponent interventions including cognitive stimulation had a pooled effect size of 0.31 (95%CI 0.04-0.58); five RCTs, mild effect).
- For the outcome “ADL functioning” they mentioned three RCTs from multimodal stimulation including cognitive training, with a pooled effect size of 0.37 (95%CI 0.06-0.68); three RCTs, mild effect).
- For the outcome “behaviour” three RCTs from group cognitive stimulation as well as another two RCTs from multimodal stimulation including cognitive training had moderate effects (pooled effect size 0.61 (95%CI 0.09-1.12) resp. 0.61 (95%CI 0.18-1.03)).
- For the outcome “mood” three RCTs from multimodal stimulation including cognitive training had mild effects (pooled effect size 0.38 (95%CI 0.07-0.69)). The outcome “caregiver well-being” was reported by 2 RCTs on cognitive group stimulation, with mild effects as well.

The second review of high quality from IQWiG (Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen)³⁴ included eight RCTs (of which seven of poor quality). They found for mild dementia patients positive effects on cognitive outcome, with an effect size of half a standard deviation, and a 95% Confidence Interval of 0.23-0.80. There was no effect on ADL activities. IQWiG added that the clinical relevance and effectiveness in daily practice remained to be studied.

A third review by Fischer-Terworth⁷⁷ (2008) reported on three reviews and three RCTs that describe diverse types of cognitive training interventions and outcome measures which make pooling difficult. They conclude that a moderate level of evidence supports the effectiveness of cognitive training, and especially group training (based on the RCT by Spector 2003), in stabilizing cognition in mild to moderate dementia patients.

One additional RCT evaluated cognitive training in addition to donepezil using 45 minute individual sessions for ten weeks in Chinese patients (mild to moderate Alzheimer disease). This RCT showed significant efficacy of cognitive stimulation on MMSE score and for lowering apathy and depression⁵³.

A second additional RCT evaluated a one hour individualised intervention addressing personally meaningful goals such as face-name learning and techniques for stress management over a period of eight weeks. This trial found that cognitive rehabilitation produced significant improvement in ratings of goal performance and satisfaction, whereas scores in the two control groups did not change. Behavioural changes in the intervention group were supported by fMRI data for a subset of participants⁴⁶.

Lack or conflicting of evidence in other systematic reviews

Four systematic reviews did not find evidence for cognitive stimulation or training. The two first ones only rely on two other publications from 2003. The two last reviews were more specific for communication interventions.

A Canadian HTA reported on a Cochrane review (2003) based on 9 RCTs. The authors' report state that that this review reported no significant positive effects of cognitive training on cognitive function of dementia patients⁴⁰. However when looking at this primary source the conclusions of the Cochrane authors concluded that: “there is still no indication of any significant benefits from cognitive training...Some gains resulting from intervention may not be captured adequately by available standardized outcome measures. It is not possible at present to draw conclusions...due to the lack of any RCTs in this area.” The same Canadian HTA also mentioned one RCT on cognitive stimulation (Spector 2003) with positive results. It concluded moderate to low quality of evidence for benefits on cognitive functioning.

The Swedish SBU (2008) included the same sources from 2003. They conclude that the Cochrane review found no study with statistically significant effect. They summarize the RCT from Spector et al as having had a significant effect on cognitive function and quality of life measurements, but not on behaviour.

Two reviews (Vasse 2010, McGilton 2009) studied the effect of communication interventions on dementia e.g. individual communication therapy or assisted “walking and conversations” (see also 3.2.6). These two reviews included ten primary studies. One author pooled the data in a meta-analysis: the overall effect on communication measures and on behavioural symptoms was not significant. One study not included in the meta-analysis did show positive results. The authors concluded that more evidence is needed to draw conclusions about the effectiveness of these communication interventions^{42, 78}.

Summary

There is moderate quality of evidence for cognitive training/stimulation based on two recent meta-analyses (and two additional RCTs). Both meta-analyses found evidence for a mild to moderate effect of cognitive training/cognitive stimulation therapy individually or in group sessions on specific outcomes: cognitive function, ADL, behaviour, mood, caregiver wellbeing. The authors point methodological weaknesses of the included studies, concomitant use of drugs and short term follow-up. The other reviews had conflicting or inconclusive results.

3.2.1.3 *Counselling or training of the patient for behavioural problems*

Three systematic reviews mention counselling / training for behavioural problems. However their conclusions are based on RCTs that target either the patient or the caregiver or both: separate conclusions for the patient are therefore not possible.

- Olazaran (2010) included one high quality (with family members) and four low-quality RCTs. They analysed behavioural interventions for moderate to severe dementia patients, e.g. distraction techniques to mitigate aggressive periods. Pooling of three of these studies (N=167) showed a moderate effect (effect size 0.57 (95%CI 0.21-0.92)).
- SBU (2008) included one of these RCTs that targeted the dyad patient-caregiver. and reported a positive effect on depression.
- Fischer-Terworth (2008) included two other reviews and several primary studies dealing with behavioural interventions for dementia patients, often including a caregiver targeted intervention as well. The authors reported significant effects of these interventions on behavioural and psychopathological symptoms.

Summary: There is no evidence for behavioural interventions with the patient only: most RCTs included the caregiver as well.

3.2.1.4 *Montessori activities*

Montessori activities were originally developed for children as self-directed learning activities. Examples of activities include reading groups and memory games. They have been proposed by clinicians for patients with dementia. The previous KCE report and this systematic review did not identify any relevant publication for that target group.

3.2.2 Emotion

3.2.2.1 *Reminiscence therapy*

Reminiscence therapy is a group therapy that helps to boost self-esteem and to remember events that happened in a person's life prior to developing dementia by recalling intact memories from the past⁷⁹. The previous KCE report concluded that there were conflicting results and low level of evidence for reminiscence therapy.

Six reviews described studies on reminiscence therapy.

- Nocon et al²⁷ concluded from five RCTs that there was not enough evidence of effectiveness to warrant treatment recommendations because in most studies there was no significant positive effect on cognition, behaviour or quality of life.
- Two of RCTs included in the previous review were also included by Rieckmann et al.²⁸ with the same conclusion.
- The review by IQWIG (2009) concluded from two RCTs that insufficient evidence was available to support or reject the therapy³⁴.
- Olazaran et al. included six RCTs with high risk of bias on reminiscence therapy. Some of them showed positive results on cognitive function, behaviour and ADL. Because a lack of homogeneous results Olazaran et al. concluded that this therapy cannot be recommended³⁰.
- Fischer-Terworth⁷⁷ and the review by SBU⁴³ included one Cochrane review (based on 4 small, low-quality RCTs) with statistically significant results on cognitive function and on behaviour difficulties. Two additional RCTs included in Fischer-Terworth had the same results⁷⁷.

No eligible additional RCTs were identified for this intervention.

Summary: several studies included in systematic reviews on reminiscence therapy show positive results on cognition, behaviour and ADL (low evidence level). Nevertheless, due to weaknesses of the underlying studies and the lack of homogeneous results, most reviews conclude that this therapy cannot be recommended.

3.2.2.2 *Validation therapy*

The basic concept of validation therapy is a reciprocated communication of respect: the other's opinions are acknowledged, respected, heard, and (regardless whether or not the listener actually agrees with the content), they are being treated with genuine respect as a legitimate expression of their feelings⁸⁰.

The previous KCE report concluded that there was low level of evidence for validation therapy. No additional RCT has been found but seven reviews addressed this therapy.

- Two systematic reviews^{27, 28} did not find evidence for a clear difference between intervention and control groups for the outcomes "behaviour" and "overall functioning". These conclusions were based on 3 RCTs.
- One of these RCTs was also included by the IQWIG review and by O'Connor et al^{34, 39} with the same conclusions.
- Olazaran et al.³⁰ included 2 RCTs. One had positive results on behaviour and mood, but they conclude that there is not enough evidence to recommend this therapy.
- Fisher-Terworth et al.⁷⁷ and the SBU review⁴³ found no evidence in 3 RCTs from a Cochrane review. Fisher-Terworth et al still note positive results on behaviour and mood in 2 non-randomized studies.

Summary: most RCTs included in the reviews on validation therapy showed no difference between groups for an effect on behaviour or mood outcomes.

3.2.2.3 *Self-maintenance therapy*

The aim of self-maintenance therapy is to maintain the sense of personal identity, continuity and coherence for as long as possible. The therapy combines methods from milieu therapy, validation therapy and reminiscence therapy.

The previous KCE report and this systematic review did not identify any relevant publication in patients with dementia.

3.2.2.4 *Individualised special instruction*

Individualized specialised instruction is an intervention that focuses individual attention and participation in an activity appropriate for each individual. The previous KCE report concluded, based on one small pre-post study in one review, that there was low level of evidence for individualised special instruction.

One additional review (2008) was identified in this systematic review. The paper analysed this intervention for vocally disruptive behaviour¹⁹ but it was excluded given a high risk of bias (see appendix 0). No eligible RCTs were identified for this intervention.

Summary: This review confirms the results of the previous KCE report i.e. there is a lack of evidence for this intervention.

3.2.3 *Sensory enhancement*

3.2.3.1 *“Snoezelen” / multisensory stimulation*

“Snoezelen” (multisensory stimulation) can be defined as an approach which actively stimulates the senses of hearing, touch, vision and smell in a resident-oriented, non-threatening environment. A moderate effect on behaviour was found in the previous KCE report.

Five reviews specifically addressed multisensory stimulation/“snoezelen”:

- Three reviews concluded that there was not enough clinical evidence (i.e. no significant differences between intervention and control groups) on the effectiveness of any of the interventions^{27, 30, 39}.
- One review mentions two RCTs that found significant effects of “snoezelen” on depression, agitation and apathy⁷⁷.
- SBU found one study showing no effect, while two studies showed effects on mood, behaviour and cognition from some components of interventions (light and aromatherapy). However those studies were not comparable with respect to the type of intervention. They also suggest that multisensory stimulation would work in later stages of dementia⁴³.

No eligible additional RCTs were identified for this intervention.

Summary: Three of the four reviews concluded that the available evidence is not sufficient to support this intervention.

3.2.3.2 *Massage and aromatherapy*

The previous KCE report concluded that there was insufficient evidence for other sensory stimulations but some results were promising. Five additional systematic reviews have studied this topic:

- Nguyen et al.³⁵ evaluated the impact of aromatherapy. Lemon balm, lavender and oil blends were evaluated. In the largest of 11 included studies, lemon balm was superior to placebo in improving agitation but the result was not significant.
- Several RCTs in the review by Kong et al. reported beneficial effects of sensory interventions (aromatherapy, thermal bath and hand massage). Agitation was reduced by hand massages in one study and by aromatherapy in another included study. When combining these effects in meta-analysis, these studies were however associated with significant heterogeneity³¹.

- Fischer-Terworth et al. (2009) found the same results as Kong based on the same studies⁷⁷.
- O'Connor et al. (2009) concluded that the results of aromatherapy on reducing agitation were promising but this statement was based on the same source study as Kong et al.³⁹.
- More recently, Olazaran et al. did not find evidence on massage in patients with dementia³⁰.

One additional RCT found significant effects of therapeutic touch on restlessness and morning cortisol levels in patients with moderate to severe dementia⁵². These effects were only measured at five days post-treatment.

Summary: Three reviews based on the same trials concluded that aromatherapy was a promising intervention to reduce agitation in dementia: positive but not clinically significant effects have been noted. The studies on massage do not allow drawing conclusions about this intervention.

3.2.3.3 *Simulated presence therapy*

Simulated presence therapy is a video/audiotape prepared by an established caregiver, family member, participant's spouse, psychologist or 'surrogate' family member for use by the dementia patient²⁹. Material for the tapes includes positive experiences from the patient's life and shared memories involving family and friends. The previous KCE report concluded that the literature for this therapy had a low level of evidence.

A meta-analysis by Zetteler et al. combined four studies, from which 2 RCTs²⁹. They yielded a statistically significant difference on challenging behaviour outcome versus no treatment. O'Connor included the same RCTs³⁹ but concluded that there was conflicting evidence. A last review by Kong et al³¹ included one of both RCTs: they concluded that no effect had been demonstrated.

Summary: There is conflicting evidence for simulated presence therapy.

3.2.3.4 *Acupuncture*

The previous KCE report similarly concluded that there was insufficient evidence for acupuncture in dementia. No eligible RCTs were identified for this intervention.

Needle acupuncture was reviewed by Lee et al.³⁶: acupuncture was the sole treatment or an adjunct to other treatments. Trials comparing different forms of acupuncture and those with no or insufficient clinical data for comparison were excluded. All trials originated from China and their methodological quality was universally poor. The evidence was inconsistent: the authors concluded that the effectiveness of acupuncture for Alzheimer's disease had yet to be demonstrated.

Two other systematic reviews that included this topic did not report any result given the absence of good quality studies:

- A Cochrane review³⁷ did not identify any RCT in the searches;
- Olazaran et al³⁰ found only one RCT of poor quality.

Summary: All reviews conclude that there is no evidence to support the therapeutic use of acupuncture in patients with dementia.

3.2.3.5 *Music therapy*

The previous KCE report found moderate evidence for music therapy in patients with dementia. Five additional reviews have been identified for this topic but their results are inconsistent.

- Kong et al. concluded that there are some beneficial effects found on aggression and agitation. However these effects are not significantly different between groups who listened to music and those who did not³¹.
- Decreased levels in agitation were also found in another review, but only as short term effects⁷⁷.
- No effect was found in O'Connor's review³⁹.
- Olazaran and the SBU review concluded to a need for more evidence because results are inconsistent between studies^{30 43}.

One additional RCT concluded that participation in a 40-minute live music intervention, three times a week for eight weeks, did not significantly affect levels of depression and QOL in older people with dementia⁴⁷.

Summary: five reviews and one RCT all conclude that the clinical evidence is not sufficient to draw conclusions about music therapy: studies are of poor quality and their results are conflicting.

3.2.3.6 *Bright-light therapy*

The previous KCE report did not find any evidence on light therapy.

A Cochrane review by Forbes et al. (2009) investigated specifically light therapy administered from a Brite-Lite™ box³². The alternative method was a Dawn-Dusk Simulator™, an overhead halogen lamp placed behind a diffusing membrane behind the patients' bed. The treatment groups received light therapy ranging from 2,500 to 10,000 lux whereas the comparator groups received dim red light or dim, low-frequency blinking light, of less than 300 lux. Eight studies were identified but there was no evidence of the effectiveness of light therapy in managing cognition, sleep, function, behaviour, or psychiatric disturbances associated with dementia. Three other systematic reviews did not either find any evidence of positive effects of light therapy^{30, 31, 43}.

Two additional RCTs were identified for this intervention^{45, 54}. Burns et al. (2009) found no evidence to support the conclusion that bright light therapy is "a potential alternative to drug therapy in people with dementia who are agitated." Riemersma van der Lek et al. (2009) was excluded as light therapy was combined with the administration of melatonin.

Summary: all the evidence found for light therapy conclude that this intervention has no demonstrated effect in dementia.

3.2.3.7 *Geïntegreerde belevingsgerichte ondersteuning*

"Geïntegreerde belevingsgerichte ondersteuning" ("Integrated experience-oriented support") aims to stimulate useful and experience-oriented communication on an integrative way i.e. discussing therapeutic options with patients rather than just telling the caregiver or patient what to do⁸¹. This intervention was not mentioned in the previous KCE report and no relevant publication was identified in this review.

3.2.4 Daily activities

ADL rehabilitative care aims to maintain or regain the abilities to perform the most basic every-day activities (e.g. eating and washing) as goal of therapy, while activity therapy uses certain (more advanced) activities, e.g. solving puzzles to improve symptoms.

The labelling of interventions is difficult. As an illustration a German HTA included five RCTs on “ergotherapie”. They mentioned e.g. ADL rehabilitative care in the definition but none of the 5 included RCT analysed this intervention. Three trials analysed home environmental interventions. The two RCTs about occupational therapy had conflicting results²⁸.

3.2.4.1 Activity therapy (e.g. puzzles, bicycles)

The previous KCE report found inconsistent and low level of evidence for activity therapy. Two reviews included this intervention:

- The SBU review based on one RCT found that activities combined with multisensory stimulation had some effects on quality of life and social behaviour such as spontaneous speech and talking initiative⁴³.
- The review from Olazaran et al. did not find any effect for recreational activities (four trials) without multisensory stimulation³⁰.

Four additional RCTs studied activity programmes. The first one was already included in the review from Olazaran et al.⁵⁰.

- A second RCT did not find any significant difference of clinical meaning between groups⁵⁶.
- The two last RCTs studied walking and hand-motor activities, but neither found significant effects^{48,49}.

Summary: The studies identified on activity therapy did not find any conclusive evidence.

3.2.4.2 ADL rehabilitative care e.g. eating dressing, bathing

The previous KCE report suggested that interventions addressing patient’s ADL activities such as feeding were promising.

The Olazaran review found positive results in reducing urinary incontinence, finding the dining room and eating independently comparing ADL training to a usual-care control group in four identified RCTs³⁰. The SBU review had a similar conclusion but based on one study only⁴³.

Conversely, another review also based on another RCT (not included in the Olazaran review) found no significant difference³¹.

A German review found four RCTs with conflicting results for ADL training³⁴.

No eligible RCTs were identified for this intervention.

Summary: There is conflicting evidence between systematic reviews about the effect of ADL training on ADL outcomes.

3.2.5 Physical activity

3.2.5.1 Exercise therapy

The KCE report concluded in 2008 that there was a lack of evidence for this intervention. The review from Forbes et al. (2008) also concluded that there is insufficient evidence to conclude whether or not physical activity is beneficial for people with dementia. The authors investigated specifically the effect of physical activity defined as aerobic exercise training or physical activity programs offered over any length of time. The aim of these programs was to improve cognition, function, behaviour, depression, and mortality in older persons with dementia and/or family caregiver health, quality of life, or to decrease caregiver mortality, and/or use of health care services³³.

Olazaran et al³⁰ did find conflicting results in nine RCTs on physical activity:

- Positive results were found in three out of five trials for the cognition and physical domains;
- One trial found a positive effect on mood;
- No effect has been found for ADL activities (2 trials) and QOL (one trial).

Two reviews concluded that physical activity has a positive effect in patients with dementia:

- The SBU review summarised a meta-analysis and five studies on walking or exercise programmes⁴³. It concluded that those programmes are effective in promoting wellbeing, functional ability and positive emotional mood in patients with dementia.
- A report from the Ontario Medical Advisory Secretariat analysed physical activity with seniors suffering from mild to moderate dementia⁴⁰. They reported the results of the same meta-analysis and another systematic review. The conclusion was that physical exercise under the supervision of occupational therapists is effective for improving physical functioning.

Two additional RCTs with small sample sizes had contradictory results. The first one included 38 patients in a nursing home. The authors found positive effects of 15 weeks of physical activity (i.e. walking exercises) on walking and cognition, although these effects may have been overestimated by increased interpersonal contact during intervention⁵¹. The second one studied the effects of exercise on depression and mood: it did not find significant differences but the three subgroups were very small (12 patients in the control group)⁵⁷.

Summary: Three systematic reviews concluded that there is evidence for a positive effect of exercise programmes on wellbeing, functional ability, physical functioning and mood. Studies with positive results were conducted in home and nursing home settings, some of them under the supervision of a professional. The fourth review and two RCTs with poor quality did not find evidence to support this intervention.

3.2.6 Communication/interaction/relationship interventions

Non-convincing effects were found in the previous KCE report for this intervention. In particular, no study had been found for interpersonal therapy, a form of psychotherapy originally developed for depression.

As stated in 3.2.1.2, two reviews from Vasse and McGilton studied the effect of communication interventions on dementia e.g. individual communication therapy or assisted “walking and conversations”. They concluded that more evidence is needed to draw major conclusions^{42, 78}.

Fisher-Terworth found positive effects of having an animal companion on agitation and aggression, but this result was based on another review with high risk of bias⁷⁷.

No eligible RCTs were identified for communication therapy.

Summary: there is a lack of evidence on the effectiveness of communication interventions, including the effects of an animal companion on behaviour symptoms.

3.2.7 Environmental changes

3.2.7.1 *Environmental adaptation*

Environmental adaptation assists dementia patients in the house. This intervention is focussed on assistance and maintaining everyday functioning. The previous KCE report did not find enough evidence on environmental adaptations. Four systematic reviews also studied this intervention:

- A Cochrane review (Martin 2009) targeted patient-focussed smart home technologies (e.g. social alarm) but failed to find any eligible studies for inclusion⁸².
- The Olazaran review included two studies. In a first study the home environment was adapted to match patient capabilities alongside continuous counselling and support to the caregiver; this improved significantly caregiver and patient quality of life. A second study in which patients received the intervention less frequently, assessed the caregiver's quality of life: the results were not significant³⁰.
- Another review, based on positive results from two out of three controlled trials, concludes that there is moderate evidence for effectiveness of environmental adaptation (e.g. visualized day schedules) on cognitive functioning and general well-being⁷⁷.
- The SBU concludes that too few studies are available to conclude on interventions affecting the care environment. Only one of two studies showed postponed institutionalization⁴³.

No additional eligible RCTs were identified for this intervention.

Summary: Only a limited number of studies is available on environmental adaptation strategies, and these studies address different care settings and different types of adaptation. The overall results are inconsistent, and need further confirmation.

3.2.7.2 *Special care unit*

The previous KCE conclusion was in accordance mentioned that conclusions were conflicting. One recent Cochrane review evaluated special care units for patients with dementia⁸³. In this review a special care unit must have three of the five following criteria, as defined in one of their included study:

- a geographically distinct area;
- a locked and secured unit;
- specialised activities programming;
- specially trained staff and/or enriched staffing pattern;
- diagnosis-specific admission and/or discharge criteria.

They did not identify any eligible RCT and no evidence of benefit from the available non-RCTs.

The SBU review reported that one study showed that dementia special care units resulted in less patient discomfort than a traditional long-term setting but that another study found no difference in patient outcomes. Neither show the results of this systematic review evidence of benefits from special care units for the informal caregivers⁴³.

The review by Olazaran included one study on special care units; it stated that more studies are needed before drawing conclusions.

No additional eligible RCTs were identified for this intervention.

Summary: There is not enough evidence on the clinical effectiveness of specialised care units for patients with dementia but their definition vary between studies.

3.2.7.3 *Milieu therapy*

Milieu therapy aims to manipulate the environment so that all aspects of the patient's experience is considered as a therapy. In this environment, patients are expected to learn adaptive coping, interaction and relationship skills that can be generalized to other aspects of their life. Some reviews discussed environmental adaptation but they did not include specific studies about milieu therapy. No eligible RCTs were identified for this intervention.

Summary: This review and the previous KCE report did not find specific studies for milieu therapy.

3.2.8 Nutrition

One review included two studies (non RCTs) about nutrition. They found an effect on body weight, but they were not comparable with respect to intervention details⁴³.

One additional RCT was identified for this intervention⁵⁵. This RCT used a nutritional drink with vitamins and fatty acids for 12 weeks as intervention and control drinks as placebos. Positive significant effects on memory were observed at 12 weeks, but these effects were not sustained at 24 weeks follow-up.

Summary: No conclusion can be formulated on nutrition for patients with dementia. Only one RCT financed by a food company has been identified with positive results.

3.2.9 Interventions primarily focused on caregivers

The previously listed interventions, listed from 3.2.1 onwards, were patient focussed. The following interventions primarily focus on the caregivers.

3.2.9.1 *Staff education*

The previous KCE report found positive results for staff education in residential care but the interventions were diverse in nature. It was concluded that this type of interventions was promising, but more evidence was needed to draw conclusions.

Four systematic reviews with contradictory results

Four reviews with interventions for professional caregivers were included. The caregiver education or training programme varied, as well as the content and frequency^{30, 34, 43, 78}.

Based on two RCTs, Olazaran et al. found that health professionals' training avoided the use of restraint in institutional settings, compared with usual care. There was no difference in falls, mobility and use of psychotropic drugs although one study reported an increase in agitation in the experimental group. They also found that training nursing home professionals in dementia knowledge, behaviour management and communication techniques improved the person with dementia's behaviour. This conclusion was based on a meta-analysis of four RCTs of which two were positive; 5 other RCTs on professional training found no positive outcome for behaviour measurements. Finally, professional caregiver training showed no effect on ADL activities in four RCTs.

Vasse (2009) included 9 studies (of which 4 RCTs, 2/4 RCTs also included in Olazaran). They concluded that training of residential care staff in communication techniques had positive effects on communication outcome measures (although only 1/4 RCTs had positive results) during daily care activities and on their relationship with the persons with dementia, whereas effects on behavioural outcomes were not clear.

The Swedish review included seven quantitative studies (of which one RCT, neither included by Olazaran nor by Vasse) and one qualitative study on health professionals' education and training. Most included studies were of low quality: the authors concluded that insufficient evidence was available to judge on effect.

The IQWiG (2009) review discussed caregiver education, but the authors did not analyse education of professional and non-professional caregivers separately.

Randomised controlled trials

Three RCTs with low risk of bias studied staff education as intervention^{63, 70, 75}.

- Two studies (not included by Olazaran), found positive effects of staff training on the use of restraints, without increase in falls or use of psychoactive drugs^{70, 75}.
- One study found positive effects on patient behavioural symptoms⁶³.

Summary: There is moderate quality of evidence that staff education and training results in a positive effect on the use of restraints. One RCT reported negative effects (increased agitation). Results for the other outcomes are not conclusive but more research is necessary: the training that professional caregivers received was of diverse nature and differences between studies make identification of a particular effective training programme difficult.

3.2.9.2 Respite care

Respite care is the provision of short-term, temporary relief to informal caregivers. No evidence was found in the previous KCE report and no additional eligible RCTs were identified for this intervention.

Four systematic reviews addressed respite care or special care units^{30, 40, 43, 84}.

- The Ontario HTA concluded that the assessment of evidence was difficult for this intervention⁴⁰: there is limited evidence from RCTs whilst qualitative studies abundantly describe the benefits perceived by the caregivers. Furthermore the effect would depend on the fact that the intervention is tailored to the caregiver's needs.
- Schoenmakers et al. pooled the results of two RCTs to analyse the effect of respite care on burden⁸⁴. They concluded that respite care increased the feeling of burden among caregivers, a finding that is contradictory with the supposed positive effect of this intervention. Reasons would include caregiver's concern about nursing quality and uncomfortable feeling about the sudden time-off.
- The SBU included respite care in its broader analysis of caregiver support programs. The included systematic reviews found no or little effects of respite care on caregivers' outcomes as for example well-being, burden, physical health⁴³.
- Olazaran et al.³⁰ included two RCTs on respite care: none effect has been found on mood and the effect on psychological being was conflicting.

Summary: The available limited evidence on respite care suggests little or no effect of this intervention on caregivers' outcomes.

3.2.10 Interventions for the informal caregivers and patients at home

3.2.10.1 Psychoeducation/psychosocial interventions for informal caregivers

The Swedish systematic review defined psychoeducational and psychosocial interventions as "interventions to maintain and improve the emotional well-being of caregivers". The three major components are counselling, support group participation and ad hoc education⁴³.

Moderate level of evidence was found in the previous KCE report for a positive effect of several forms of psychosocial interventions and psychoeducation on informal caregiver depression and stress. Four additional systematic reviews and eleven RCTs were added in this study.

Positive effect found in systematic reviews

Parker et al concluded that the effects of psychosocial interventions (not administered as part of a multicomponent intervention) on psychosocial morbidity and caregiver burden were positive ⁴¹.

Olazaran et al. analysed 33 RCTs on caregiver education and 8 RCTs on caregiver support³⁰. Interventions using telephone or computer support improved caregiver mood and psychological status. Caregiver education including e.g. problem-solving, cognitive restructuring techniques, coping skills also had an effect on caregivers' mood. The response was higher when the caregiver suffered from psychological problems. However some programs (e.g. focusing on family interactions, information) had no effect on caregiver mood. Finally, psychosocial interventions had a positive effect on caregiver mood, well-being and quality of life when combined in multicomponent interventions.

The Swedish report⁴³ included moderate and high quality studies for psychosocial programs. They conclude that isolated interventions had no effect on the caregiver depression but their combination had an impact on the caregiver psychological well-being. However it is difficult to identify which component is most effective in multifaceted interventions and that the length of intervention needed to have an impact on the outcome.

Schoenmakers et al concluded that psychosocial interventions have a slight but not significant effect on the caregiver burden⁸⁴. The authors emphasized the difficulty to interpret the results because of:

- Various components of these interventions that teach caregivers (with various profiles) about how to cope with specific situations;
- The range of duration and frequencies of the interventions.

Randomised controlled trials

Eleven RCTs studied psychoeducational/psychosocial interventions for informal caregivers ^{60-62, 64, 66-69, 71-74}.

- One large RCT in France (Nourhashemi, 2010) used a “comprehensive assessment” for patients and their caregiver⁷⁴. There was no difference between groups in terms of functional decline, admission rates and mortality. However the intervention was poorly described and combined with drugs. The control groups (“usual care”) were managed differently between the study centres.
- A Spanish RCT with 10 month follow-up found that a psychoeducational program (4 months) reduced caregiver burden and improved their quality of life and perceived health ⁷³.
- A UK RCT studied the effect of a local befriending scheme for caregivers ^{60, 61}. The role of the befriending volunteer was to provide emotional support for the carer. There was no effect on the carer's mood (depression and anxiety level) and health related quality of life at 15 months follow-up.
- Another RCT from the UK (Dias 2008) found positive effects of a multicomponent intervention including caregiver education and support, referral to psychiatrists, networking of families (versus education only). on the caregiver distress and mental health⁶⁴. This study was included in the IQWiG review mentioned above.
- One RCT in Russia (Gavrilova, 2009) analysed the effect of caregiver training sessions during five weeks. At six months large positive effects were found for caregiver burden but not for distress and quality of life outcomes ⁶⁷.

Three RCTs conducted in the US found positive results at the end of the intervention (4 months) but the effect decreased or disappear later on:

- The first study by Gitlin et al. included 10 sessions with an occupational therapist: an effect was noted at 4 months (functioning and caregiver well being) but not at 9 months⁶⁸.
- The second study by the same author was a caregiver training that targeted behaviours that upset them. An effect was found for caregiver and patient outcomes at the end of the intervention (4 months) but this effect decreased at 6 months follow-up⁶⁹.
- The third RCT studied the effect of a 16 weeks “coping with caregiving programme”. The effect was positive for several outcomes (e.g. depression, stress) at the end of the intervention⁶⁶.

Three last RCTs were conducted in Hong Kong. The transferability of these results has to take account of possible cultural differences^{62, 71, 72}.

- The first RCT by Chien et al. delivered dementia care management programme tailored to the patient’s needs. The authors found positive effects on caregivers (burden and QOL) and on the patient (symptoms, institutionalisation) at 6 and 12 months follow-up⁶². This study was included in the Olazaran and IQWIG reviews.
- The second study by Lam et al. found positive effects on patient depression and skills only when the intervention (skills training) was patient-tailored⁷¹.
- The third RCT by the same author analysed the effect of a case manager with regular home visits during 4 months. At 12 months the study found no significant effects on caregiver burden, but caregivers tended to seek more external support⁷².

Summary: This systematic review confirms the results of the previous KCE report. There is moderate quality of evidence of evidence that psychosocial interventions have an effect on caregivers outcomes: psychological well-being, mood, quality of life, burden. Results are positive for multicomponent interventions but conflicting in case of isolated interventions. There is a wide variety in the nature, duration and intensity of the effective interventions and conclusions about the optimal interventions are not possible. The time for measurement (at the end of the intervention versus long term) also influences the interpretation of the effects.

3.2.10.2 *Interventions to delay institutionalisation*

All but one interventions to delay institutionalisation included caregivers (and the patient), except one study with patients living in assisted home facilities⁵⁸.

The previous KCE report found some positive findings, particularly counselling for spouse-caregivers showed long-term benefits¹.

The Olazaran review reported the pooling of three high quality RCTs. Significant benefits were associated with multicomponent caregiver interventions. The essential components reported by Olazaran et al. were individual assessment, information, counselling and support³⁰.

Spijker et al.³⁸ performed a meta-analysis on the effectiveness of nonpharmacological interventions in delaying the institutionalization of patients with dementia. Thirteen multicomponent programs were included. The meta-analysis showed an impact of the interventions on the odd for and time to institutionalization. A further analysis of the best-quality studies also found positive results for the odds of institutionalization but the impact on time to institutionalization was not longer significant. The active involvement of caregivers for the treatment’s choice was a key for the effectiveness of the program.

The SBU report concluded that there was insufficient evidence to conclude that day care, caregiver support or case management could delay institutionalisation⁴³. They included ten RCTs, but most of them were of low quality and had non significant results.

Three RCTs published afterwards were identified for this intervention^{58, 59, 65}.

- One RCT studied the effect of a multicomponent intervention for spouses caregivers: family care coordinator, geriatrician, goal oriented support groups and individualized services for the couples⁶⁵. The significant impact on institutionalisation found at 1.6 years (11 versus 25%) but the effect did not longer last at 2 years. Other positive outcomes were noted for community services use and expenditures.
- A second RCT found no effect on time to institutionalisation by counselling spouse caregivers⁵⁹. Yet the intervention was minimal: only five sessions in a mean of 5.4 years follow-up, in three different health care contexts.
- Bellantonio et al. studied a geriatrics team intervention in patients living in assisted home facilities⁵⁸. Participants randomised to the intervention received only four systematic, multidisciplinary assessments conducted by a geriatrician or geriatrics advanced practice nurse, a physical therapist, a dietician, and a medical social worker during the first nine months of their residence in assisted living. No significant effects on relocation to a permanent nursing home were found.

Summary: There is moderate quality of evidence for multicomponent interventions to delay institutionalisation.

4 SUMMARY OF THE MAIN FINDINGS

This systematic review analyse the available evidence for non-pharmacological interventions at home and in long term care facilities. The quality of the evidence has been rated according to the GRADE criteria⁸⁵.

4.1 QUALITY OF EVIDENCE: SUMMARY TABLE

The table below summarize the interventions for the patient or the caregiver:

- The existence of RCTs (either analysed in other good systematic reviews or in this one);
- Quality of evidence for a given intervention, based on the GRADE classification⁸⁵;
- Results of most studies: positive (+), negative (-), conflicting results (+ and -).

None of the interventions under study can be rated as 'high quality of evidence': all of them are based on systematic reviews with conflicting results and/or RCTs with limitations. This is due to some extent to nature and heterogeneity of the interventions and to the nature of the disease.

Six interventions (five with with positive results) have a moderate quality of evidence based on the following criteria:

- Results differ between the systematic reviews, but those ones with the highest quality (e.g. based on a meta-analysis, inclusion of RCTs only) are positive;
- And/or the systematic reviews with positive results mentioned that an underlying evidence of poor quality;
- And/or the RCTs on this topic have major limitations.

Interventions primarily focused on the patient

	RCT	Quality Of Evidence	Result: effect	Comments
Cognition				
Reality orientation	Yes	Low	Positive	More studies needed
Cognitive stimulation / training	Yes	Moderate	Positive	Mild to moderate dementia; mostly mild effect*; long-term effect not known
Patient behaviour interventions	Yes	-	-	Systematic reviews included RCTs that targeted also caregivers
Montessori	No	-	-	No RCT
Emotion				
Reminiscence	Yes	Low	Conflict	More studies needed
Validation	Yes	Low	Conflict	More studies needed
Self-maintenance	No	-	-	-
Individualised instruction	No	-	-	
Sensory enhancement				
"Snoezelen"	Yes	Low	Conflict	More studies needed
Massage	I	Low	(+)	More studies needed
Aromatherapy	Yes	Low	Conflict	More studies needed
Simulated presence	Yes	Low	Conflict	More studies needed
Acupuncture	Yes	Low	No effect	More studies needed
Music therapy	Yes	Low	Conflict	More studies needed
Light therapy	Yes	Low	No effect	More studies needed
Integrated experiential support	No	-	-	-

Daily activities				
Activity therapy	Yes	Low	Conflict	More studies needed
ADL rehab care	Yes	Moderate	Conflict	More studies needed
Physical activity (under supervision)	Yes	Moderate	Positive	Mild to moderate dementia
Communication Interaction Relationship	Yes	Low	No effect	More studies needed
Environmental changes				
Environmental adaptation	Yes	Low	Conflict	Different types of interventions and few RCTs for each intervention
Special care unit	Yes	Low	Conflict	More studies needed
Milieu therapy	No	-	-	-
Nutrition	I	Low	(+)	More studies needed

* effect on cognition, behaviour, mood, ADL functioning, caregiver well-being

Interventions primarily focused on the caregiver

	RCT	Quality Of Evidence	Result: effect	Comments
Staff education	Yes	Moderate	Positive	Effect on use of restraints
Respite care	Yes	Low	Conflict	Various effects* according to studies

* Negative effects even described for burden: authors hypothesize that the effects would depend on the fact that intervention would be tailored to the caregiver's needs

Interventions for the caregivers and the patients at home

	RCT	Quality Of Evidence	Result: effect	Comments
Psychoeducation Psychosocial intervention	Yes	Moderate	Positive	Only if multicomponent intervention
Interventions to delay institutionalisation	Yes	Moderate	Positive	

* Negative effects even described for burden but the effects would depend on the fact that intervention would be tailored to the caregiver's needs

The results have been submitted to the experts who rated the strength of recommendation according to the GRADE classification⁸⁵ ("strong" or "weak"). After two rounds they unanimously agreed on a strong recommendation for psychoeducation/psychosocial interventions (I B). Opinion was divided for the other interventions, mainly depending on the experts' profile.

4.2 MODERATE QUALITY OF EVIDENCE FOR SIX GROUPS OF INTERVENTIONS

Five interventions with a moderate quality of evidence had a positive effect:

- Cognitive stimulation/training,
- Physical activity,
- Staff education,
- Multicomponent psychoeducation/psychosocial interventions for caregivers,
- Multicomponent interventions for caregivers to delay institutionalisation.

The sixth intervention with moderate quality of evidence was ADL rehabilitative care but the studies had conflicting results.

The effective interventions are presented below (in decreasing order) according to the number of experts who gave them a strong level of recommendation. The results for two multicomponent interventions will be further grouped because they have a common content and the impact on institutionalisation is an outcome.

4.2.1 Multicomponent psychoeducation/psychosocial interventions : impact on caregivers outcomes and on institutionalisation

Effective caregiver training and psychosocial support included a range of interventions to develop their skills with the following aims: to control stress, to develop strategies for handling their relative's behavioural problems, to decrease their burden and to increase their satisfaction with life.

Some publications had conflicting results but multicomponent interventions had usually a significant impact on caregivers' outcomes (psychological well-being, mood, quality of life, burden.) and on the delay / risk for institutionalisation.

Successful multicomponent interventions with caregivers always included spouse counselling (30 to 90 minutes sessions). The other components of the interventions varied, as underlined in the systematic review of Schoenmakers et al.⁸⁴: they encompassed support groups, various teaching strategies to handle specific situations and improve well-being. The skills of the included health professionals also varied between studies. The multicomponent interventions were tailored to the patient and caregivers' specific situation. A low frequency and/or number of sessions did not produce significant effects on institutionalisation.

All experts (and validators later on) agreed on a strong level of recommendation (1B) for multicomponent psychoeducational/psychosocial interventions for caregivers.

4.2.2 Physical activity

Most studies were positive about the effect of physical activity programs on patients with dementia. They included walking or exercise programs. The target group might be important as one positive review focused on patients with mild or moderate dementia. The supervision by a professional could also have an added value.

Most consulted experts agreed on a strong level of recommendation (1B)

4.2.3 Staff education

Effective training of staff in nursing homes included programmes on how to manage these patients. They aimed to modify the resident's outcomes (e.g. to reduce aggressive behaviours) and to minimise restraint use. Successful interventions had an effect on restraint use: they ran for at least 8 weeks and were implemented by experienced educators. More studies are needed to confirm the impact of staff education on other outcomes as behaviour, communication, ADL outcomes.

Most consulted experts agreed on a strong level of recommendation (1B).

4.2.4 Cognitive stimulation / training

The effectiveness of cognitive stimulation/training interventions was characterised by high intensity and frequency of the intervention (i.e. one hour sessions over eight weeks or more). Successful individual interventions were tailored to the needs of the dementia patient and carried out by a trained therapist.

Cognitive stimulation/training was the intervention with the lowest agreement among experts for the strength of recommendation: many studies have negative results and some experts further raised concerns about possible side effects i.e. a stress upon the patient by the relatives.

4.3 LOW QUALITY OF EVIDENCE FOR SIXTEEN INTERVENTIONS

The quality of evidence was low in the selected literature for sixteen interventions: no recommendation can therefore be formulated.

- Low quality of evidence, positive effect: reality orientation;
- Low quality of evidence, no effect: acupuncture, light therapy, communication/interaction;
- Low quality of evidence, conflicting results: reminiscence therapy, validation therapy, “snoezelen”, aromatherapy, simulated presence therapy, music therapy, activity therapy, special care units, environmental adaptation, respite care;
- One RCT for massage and nutrition respectively.

4.4 NO RCT FOR SIX INTERVENTIONS

This review did not identify any systematic review or RCT for six interventions: Montessori activities, self-maintenance therapy, behaviour intervention with the patient individualised instruction, “geïntegreerde belevingsgerichte ondersteuning”, milieu therapy.

5 DISCUSSION

This systematic review addresses the effectiveness of non-pharmacological interventions in patients with dementia and their (in)formal caregivers in the context of family and community care.

5.1 STRENGTHS OF THE SYSTEMATIC REVIEW

The major strength is the identification of four groups of interventions that have an impact on the patients (e.g. symptoms, institutionalisation) and/or caregivers (e.g. depression, psychological well-being, quality of life): psychosocial support of caregivers, physical activity, staff training and cognitive stimulation/rehabilitation.

This conclusion relies on a strict methodology including a priori-defined inclusion criteria and quality appraisal tools. A similar systematic review of high quality has been published during the course of this study by Olazaran et al.³⁰. The combination of the search strategy of this review with the publications included in Olazaran et al. For Alzheimer's disease provided a comprehensive list of all non-pharmacological therapies that are usually considered.

5.2 LIMITATIONS IN THE INTERPRETATION OF RESULTS

Some limitations must be considered in the interpretation of the results:

- Many included systematic reviews were based on the same source RCTs. This may account for double counting and was noted where possible.
- The design of the included RCTs did not always allow to draw firm conclusions. The nature of non-pharmacological interventions differed between studies that analysed the same intervention. Moreover the trials did not take account of personal characteristics of the patients (preferences, physical condition) that could have an impact on the success of the therapy (for example music therapy). In addition, patient populations could be highly selective in some studies, because the recruitment was supported by the institutions.
- The inclusion and exclusion of RCTs based on methodological grounds was not always straightforward as study designs were often poorly reported.
- Long term post-treatment effects were not often analysed: this could overestimate the clinical relevance of the interventions.

Finally, the cost-effectiveness of the interventions was out of scope in this study. It would be particularly difficult to analyse it given the heterogeneity of interventions that yield positive results.

5.3 LACK OF EVIDENCE: SOME HYPOTHESES

The lack of evidence for many non-pharmacological interventions might be explained by other factors than methodological limitations:

- Differences between the comparator and the intervention are frequently small. The comparator "usual care" still encompasses interventions from the caregivers, in particular in RCTs where people are interested by the care to people with dementia (selection bias). For example comparator groups' in trials on communication still benefit from positive interactions with the caregivers, even if not in an intervention group.
- There is also a difficulty in defining a comparator that is well-matched to the active treatment and ethically acceptable. For instance, in case of special care units, it is difficult to randomly allocate patients to a special care unit versus 'usual care', whatever 'usual care' means.
- Conclusions are difficult for one "standard" intervention. As stated above RCTs differ in terms of setting, supervision, content and duration;

- Some interventions benefited earlier from trials with conflicting results. The same trials are included by all systematic reviews but updates show that the researchers do not invest anymore in their analysis (for example reality orientation, reminiscence therapy).

5.4 RESULTS: APPLICABLE TO ALL PATIENT SUBGROUPS ?

The limitations detailed in the previous paragraph (heterogeneity of interventions, study design, length of the follow-up) explain some discrepancies between the studies. However, as stated in the previous paragraph, one specific intervention might have an impact in subgroups of dementia patients, according to their personal characteristics, diagnosis or disease severity. One illustration is the systematic review that showed an effect of physical activity in a specific population of seniors with mild to moderate dementia. However, a mixed population of diagnoses and severity grades is the mirror of the situation in the clinical practice of the GP or geriatric specialist.

When the trials analysed the results in specific subgroups, the sample sizes were often too small to detect any difference between groups (as for example the RCTs on physical activity).

5.5 RESULTS APPLICABLE TO ALL SETTINGS ?

This study focused on patients who stay at home or in residential facilities but conclusions for a specific setting are not possible for two reasons.

First, for the interventions that targeted primarily the patient, just two primary studies were conducted in home settings. The first one on activity therapy⁵⁰ and the second one by Clare et al.⁴⁶ on cognitive rehabilitation. The systematic reviews included populations from mixed settings and most primary studies that targeted the patient were conducted in residential facilities.

Second, a successful intervention in one setting (home or residential care) does not necessarily transfer to a different setting:

- Patients at home may represent a population with a different profile (e.g. milder form of dementia) than those in residential care settings.
- Patients at home may also be more isolated: one intervention could have a larger effect on these people than on those living in a care facility, having more interpersonal contact.
- The training of caregivers at home is more difficult than the training of health professionals. The implementation at home of any intervention tested in institutions (with a motivated and trained staff) needs therefore caution.

5.6 INTERVENTIONS TAILORED TO THE PATIENT AND INFORMAL CAREGIVER ARE MORE SUCCESSFUL

Some authors concluded that successful interventions had to be tailored to patient and his/her caregiver. Illustrations are:

- Psychoeducation/psychosocial interventions for informal caregivers^{50, 62, 71};
- Respite care⁴⁰;
- Interventions to delay institutionalisation^{30, 38}.

5.7 ADAPTATION TO THE CULTURAL AND HEALTH CARE CONTEXT

This systematic review did not exclude any study on the basis of the cultural context; On one hand it might be hypothesized that at least a part of the findings from other countries might be applicable to people with dementia in Belgium. On the other hand, some interventions (in particular in nursing homes) might produce different results in Belgium than in other European or non European countries.

The health care context also plays a role. An illustration is the lack of evidence in the literature for special care units. The criteria selected by the Cochrane review and the included studies do not take account for example of the size of these units: this factor might well have an impact on people with dementia. Special care units currently developed in Belgium rely on specific criteria and some of them (for example the small size of care units) were not present in the studies from the international literature⁸³.

5.8 PERSPECTIVES

Health care contexts are important but the recent European conference⁸⁶ on the quality of life of people with dementia highlighted the importance of implementing interventions that have been shown effective in other contexts.

The conclusion of this conference also underlined the need for interventions beyond the framework of health services and in particular: the recognition and support of the close informal carer, the continuity of care, a patient-oriented care and the cooperation between all caregivers. These elements are underlined in this report under the terms of “psychosocial support” and “multicomponent tailored intervention”.

Those findings will foster non-pharmacological care tailored to the needs of the patient and his/her caregivers, at home or in nursing homes. A Belgian study recently confirmed the importance of the consumption of antipsychotics by elderly people⁸⁷ (from 9 to 35% in nursing homes). Opting for selected non-pharmacological treatments could diminish this consumption by replacing those medications by non dangerous, potentially efficacious alternative treatments.

5.9 SUGGESTIONS FOR FURTHER RESEARCH

Non-pharmacological interventions in dementia require further research to determine their clinical effectiveness with more certainty. However the nature of these interventions without commercial interest calls for alternative sources of funding e.g. with the following objectives:

- To set up high quality studies with large sample sizes and homogeneous populations;
- To target specific populations according to their characteristics (e.g. severity of disease, past experience and preferences);
- To compare different frequencies and durations of a given effective intervention;
- To give a blind assessment of the results;
- To use uniform outcome measures across interventions;
- To analyse the long term effects of the interventions.

6 APPENDICES

6.1 APPENDIX 1 MESH TERM : DEMENTIA

Dementia

AIDS Dementia Complex
 Alzheimer Disease
 Aphasia, Primary Progressive
 Primary Progressive Nonfluent Aphasia
 Creutzfeldt-Jakob Syndrome
 Dementia, Vascular
 Dementia, Multi-Infarct
 Diffuse Neurofibrillary Tangles with Calcification
 Frontotemporal Lobar Degeneration
 Frontotemporal Dementia
 Primary Progressive Nonfluent Aphasia
 Huntington Disease
 Kluver-Bucy Syndrome
 Lewy Body Disease
 Pick Disease of the Brain

6.2 APPENDIX 2 SEARCH STRATEGIES SYSTEMATIC REVIEWS

Cochrane Library

06/08/2010 by Abacus International																																											
Database	Cochrane Library (Cochrane reviews, other reviews, and health technology assessments)																																										
Search Strategy	<table border="0"> <tr> <td>#1</td> <td>MeSH descriptor Dementia explode all trees</td> <td>3088</td> </tr> <tr> <td>#2</td> <td>dement*</td> <td>8224</td> </tr> <tr> <td>#3</td> <td>alzheimer*</td> <td>4456</td> </tr> <tr> <td>#4</td> <td>lewy* bod*</td> <td>127</td> </tr> <tr> <td>#5</td> <td>huntington*</td> <td>449</td> </tr> <tr> <td>#6</td> <td>cerebrovascular</td> <td>5705</td> </tr> <tr> <td>#7</td> <td>wernicke*</td> <td>94</td> </tr> <tr> <td>#8</td> <td>CADASIL or cerebral dominant arteriopathy</td> <td>20</td> </tr> <tr> <td>#9</td> <td>korsakoff syndrome</td> <td>42</td> </tr> <tr> <td>#10</td> <td>delerium</td> <td>1</td> </tr> <tr> <td>#11</td> <td>Kluver bucy</td> <td>6</td> </tr> <tr> <td>#12</td> <td>pick* disease</td> <td>345</td> </tr> <tr> <td>#13</td> <td>arteriosclerosis</td> <td>1</td> </tr> <tr> <td>#14</td> <td>ischemic white matter</td> <td>33</td> </tr> </table>	#1	MeSH descriptor Dementia explode all trees	3088	#2	dement*	8224	#3	alzheimer*	4456	#4	lewy* bod*	127	#5	huntington*	449	#6	cerebrovascular	5705	#7	wernicke*	94	#8	CADASIL or cerebral dominant arteriopathy	20	#9	korsakoff syndrome	42	#10	delerium	1	#11	Kluver bucy	6	#12	pick* disease	345	#13	arteriosclerosis	1	#14	ischemic white matter	33
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#11	Kluver bucy	6																																									
#12	pick* disease	345																																									
#13	arteriosclerosis	1																																									
#14	ischemic white matter	33																																									

#15	CJD or JCD or creutzfeldt jakob	67
#16	(memory adj2 (complaint* or impair* or problem*))	19
#17	head trauma	977
#18	MeSH descriptor Craniocerebral Trauma, this term only	278
#19	HIV adj3 dementia	5
#20	MeSH descriptor HIV, this term only	247
#21	parkinson*	3460
#22	MeSH descriptor Parkinsonian Disorders explode all trees	1963
#23	vascular dementia	768
#24	(NOS or not otherwise specified) and dementia	159
#25	(#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24)	19375
#26	MeSH descriptor Psychotherapy explode all trees	11134
#27	Cognitive Therapy or behavioural therapy or Behavior Therapy	23203
#28	Psychotherapy or Multiple Psychotherapy or Imagery or Group Psychotherapy or Brief Psychotherapy or Rational-Emotive Psychotherapy	6599
#29	Reality Therapy or reality orientation	435
#30	signposting	2
#31	Interpersonal Relations or interpersonal communication	1541
#32	MeSH descriptor Interpersonal Relations explode all trees	2998
#33	unlocking doors	4
#34	group living or group homes	42465
#35	MeSH descriptor Group Homes explode all trees	41
#36	validation therapy	1187
#37	standard therapy	29686
#38	alternative therapy	13133
#39	MeSH descriptor Complementary Therapies explode all trees	9970
#40	alternative medicine	6324
#41	art therapy	5775

#42	MeSH descriptor Art Therapy explode trees 1 and 2	27
#43	Music Therapy	753
#44	MeSH descriptor Music Therapy explode trees 1 and 2	339
#45	massage or touch	2818
#46	white noise	199
#47	natural elements	266
#48	reminiscence therapy	74
#49	MeSH descriptor Occupational Therapy explode all trees	412
#50	activity therapy	27884
#51	complementary therapy	2299
#52	aromatherapy	172
#53	MeSH descriptor Aromatherapy explode trees 1, 2 and 3	79
#54	Phototherapy or bright-light therapy	1149
#55	MeSH descriptor Phototherapy explode all trees	1606
#56	Physical Stimulation or Hydrotherap* or multisensory approach* or Sensory Art Therap*	2600
#57	multisensory stimulation	40
#58	Photic Stimulation	871
#59	MeSH descriptor Photic Stimulation explode all trees	808
#60	MeSH descriptor Relaxation Therapy explode all trees	1111
#61	snoezelen	35
#62	MeSH descriptor Sensory Art Therapies explode all trees	1170
#63	cognitive-behavioural therapy	3121
#64	cognitive-behavioural therapy	3121
#65	cognitive training	2613
#66	physical touch	287
#67	interpersonal therapy	1274
#68	self maintenance therapy	1095
#69	simulated presence therapy	97
#70	acupuncture	5644
#71	exercise therapy	16623
#72	MeSH descriptor Exercise Therapy explode all trees	4061
#73	kinesiotherapy	181

#74	MeSH descriptor Physical Therapy Modalities explode all trees	10229
#75	Rehabilitation or rehabilitative care	20594
#76	MeSH descriptor Rehabilitation explode all trees	10060
#77	Activities of Daily Living or daily life activity	7282
#78	MeSH descriptor Activities of Daily Living explode all trees	3052
#79	therapy	285570
#80	(#78 AND #79)	1873
#81	communication	6903
#82	MeSH descriptor Communication explode tree 1	3274
#83	interpersonal communication	403
#84	social interaction	1947
#85	intervention	79453
#86	(#81 OR #82 OR #83 OR #84)	10302
#87	(#85 AND #86)	4265
#88	environmental manipulation	83
#89	mirror*	629
#90	(#88 AND #89)	1
#91	staff education	1727
#92	MeSH descriptor Inservice Training explode all trees	427
#93	MeSH descriptor Education, Nursing, Continuing explode all trees	213
#94	MeSH descriptor Education, Nursing explode all trees	498
#95	structured activity	3925
#96	montessori	8
#97	electroconvulsive therapy	732
#98	MeSH descriptor Electroconvulsive Therapy explode all trees	457
#99	ECT	779
#100	Transcutaneous electric* nerve stimulation or TENS	18182
#101	MeSH descriptor Transcutaneous Electric Nerve Stimulation explode trees 1 and 2	542
#102	non-pharmacologic* or nonpharmacologic* or pharmacologic*	5226
#103	caregiv*	3240

	#104 restraint adj2 free	3
	#105 dog assist*	59
	#106 psychosocial adj2 intervention*	78
	#107 behavioural therapy	9489
	#108 behaviour therapy	13866
	(#26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32 OR #33 OR #34 OR #35 OR #36 OR #37 OR #38 OR #39 OR #40 OR #41 OR #42 OR #43 OR #44 OR #45 OR #46 OR #47 OR #48 OR #49 OR #50 OR #51 OR #52 OR #53 OR #54 OR #55 OR #56 OR #57 OR #58 OR #59 OR #60 OR #61 OR #109 #62 OR #63 OR #64 OR #65 OR #66	173204
	OR #67 OR #68 OR #69 OR #70 OR #71 OR #72 OR #73 OR #74 OR #75 OR #76 OR #77 OR #80 OR #87 OR #89 OR #90 OR #91 OR #92 OR #93 OR #94 OR #95 OR #96 OR #97 OR #98 OR #99 OR #100 OR #101 OR #102 OR #103 OR #104 OR #105 OR #106 OR #107 OR #108)	
	#110 (#25 AND #109)	8120
	#111 (#110)	1615
Note	1615 includes protocols which were excluded from the reviews, breakdown of hits from each relevant database as follows: Cochrane systematic reviews: 858 Cochrane HTA: 106 Cochrane other reviews: 359 Total relevant to this project= 1323	

EMBASE

Date	10/08/2010 by Abacus International
Database	OVID EMBASE 1980 to 2010 Week 3
Search Strategy	1 Delirium/ or Dementia/ or Organic Brain Syndrome/ or Cognitive Defect/ (112697) 2 Alzheimer Disease/ (85089) 3 Wernicke Encephalopathy/ (1504) 4 Huntington Chorea/ (12164) 5 Creutzfeldt Jakob Disease/ (7437) 6 Korsakoff Psychosis/ (1202) 7 Brain Infarction/ (26595) 8 Binswanger Encephalopathy/ or Cadasil/ or Cerebrovascular Disease/ or Autosomal Dominant Disorder/ (47636) 9 Kluver Bucy Syndrome/ (144) 10 Pick Presenile Dementia/ (787) 11 dement*.mp. (81897) 12 alzheimer*.mp. (97772) 13 "lewy* bod*".mp. (6446) 14 huntington*.mp. (14030) 15 cerebrovascular.mp. (94953) 16 wernicke*.mp. (3067) 17 (CADASIL or "cerebral autosomal dominant arteriopathy").mp. (1011) 18 korsakoff syndrome.mp. (599)

19	delerium.mp. (36)
20	Kluver bucy.mp. (260)
21	"pick* disease".mp. (3407)
22	arteriosclerosis.mp. (3)
23	"ischemic white matter".mp. (106)
24	(CJD or JCD or "creutzfeldt jakob").mp. (8278)
25	(memory adj2 (complaint* or impair* or problem*)).mp. (11790)
26	head trauma.mp. or head injury/ (32619)
27	HIV.mp. or Human immunodeficiency virus/ (210224)
28	parkinson.mp. or Parkinson disease/ (68186)
29	("not otherwise specified" or NOS).mp. (22467)
30	vascular dementia.mp. or multiinfarct dementia/ (7345)
31	27 or 28 or 29 (300486)
32	1 and 31 (8923)
33	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 30 or 32 (373586)
34	cognitive therapy/ or behavior therapy/ or psychotherapy/ or behavioural therapy.mp. (101325)
35	reality orientation.mp. (214)
36	signposting.mp. or interpersonal communication/ (80434)
37	"unlocking doors".mp. (2)
38	group living.mp. (523)
39	validation therapy.mp. or validation therapy/ (75)
40	standard therapy.mp. (7454)
41	alternative therapy.mp. or alternative medicine/ (25712)
42	alternative therapy.mp. (2706)
43	art therapy/ (1491)
44	music therapy/ or music.mp. (13090)
45	(massage or touch).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer] (29371)
46	"white noise".mp. (2724)
47	"natural elements".mp. (43)
48	reminiscence therapy.mp. (106)
49	activity therapy.mp. (85)
50	complementary therapy.mp. (723)
51	aromatherapy.mp. or aromatherapy/ (1074)
52	phototherapy/ or bright-light therapy.mp. (11529)
53	multisensory stimulation/ or sensory stimulation/ or learning/ or education/ or multisensory approaches.mp. or auditory stimulation/ (340958)
54	relaxation training/ or behavior therapy/ or sensory stimulation/ or occupational therapy/ or snoezelen.mp. or snoezelen/ (57051)
55	brief psychotherapy.mp. (392)
56	cognitive-behavioural therapy.mp. (1533)
57	cognitive stimulation.mp. (219)
58	cognitive training.mp. (438)
59	physical touch.mp. (34)
60	interpersonal therapy.mp. (235)
61	self maintenance therapy.mp. (4)
62	simulated presence therapy.mp. (11)
63	acupuncture/ or acupuncture.mp. (22594)
64	exercise therapy.mp. or kinesiotherapy/ (18069)
65	rehabilitation care/ or rehabilitation/ or rehabilitative care.mp. (32377)
66	daily life activity/ or ADL.mp. (42450)
67	therapy/ (598422)
68	66 and 67 (488)
69	communication.mp. or interpersonal communication/ (265023)

70	social interaction.mp. or social interaction/ (19895)
71	relationship.mp. (607215)
72	intervention.mp. (280993)
73	69 or 70 or 71 (869050)
74	72 and 73 (21263)
75	environmental factor/ or environmental manipulation.mp. (44654)
76	mirror\$.mp. (20081)
77	67 and 76 (289)
78	staff education.mp. or staff training/ (7047)
79	structured activity.mp. (72)
80	montessori.mp. (59)
81	34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48 or 49 or 50 or 51 or 52 or 53 or 54 or 55 or 56 or 57 or 58 or 59 or 60 or 61 or 62 or 63 or 64 or 65 or 68 or 74 or 75 or 77 or 78 or 79 or 80 (726754)
82	exp Meta Analysis/ (49851)
83	((meta adj analy\$) or metaanalys\$.tw. (38331)
84	(systematic adj (review\$I or overview\$I)).tw. (27868)
85	or/82-84 (84751)
86	cancerlit.ab. (565)
87	cochrane.ab. (18472)
88	embase.ab. (15039)
89	(psychlit or psyclit).ab. (895)
90	(psychinfo or psycinfo).ab. (3606)
91	(cinahl or cinhal).ab. (5572)
92	science citation index.ab. (1419)
93	bids.ab. (350)
94	or/86-93 (26999)
95	reference lists.ab. (6238)
96	bibliograph\$.ab. (10505)
97	hand-search\$.ab. (2851)
98	manual search\$.ab. (1585)
99	relevant journals.ab. (567)
100	or/95-99 (19616)
101	data extraction.ab. (8135)
102	selection criteria.ab. (16016)
103	101 or 102 (22899)
104	review.pt. (1626187)
105	103 and 104 (15038)
106	letter.pt. (695656)
107	editorial.pt. (351454)
108	animal/ (1619737)
109	human/ (11829165)
110	108 not (108 and 109) (1230590)
111	or/106-107,110 (2265572)
112	85 or 94 or 100 or 105 (108083)
113	112 not 111 (103273)
114	electroconvulsive therapy.mp. or electroconvulsive therapy/ (12980)
115	ECT.mp. (5956)
116	transcutaneous nerve stimulation/ or transcutaneous electric* nerve stimulation.mp. or TENS.mp. (9847)
117	(non-pharmacologic* or nonpharmacologic* or non pharmacologic*).mp. (8608)
118	caregiv*.mp. (36296)
119	(restraint adj2 free).mp. (81)
120	dog assist*.mp. (9)
121	(psychosocial adj2 intervention*).mp. (2847)
122	Behavior Therapy/ or behavior?ral therapy.mp. (34721)
123	81 or 114 or 115 or 116 or 117 or 118 or 119 or 120 or 121 or

	<p>122 (784493)</p> <p>124 33 and 113 and 123 (943)</p> <p>125 from 124 keep 1-775 (775)</p> <p>126 33 and 123 (33842)</p> <p>127 psychotherapy/ or art therapy/ or autogenic training/ or behavior contracting/ or behavior modification/ or behavior therapy/ or cognitive behavioral stress management/ or cognitive rehabilitation/ or cognitive therapy/ or family therapy/ or gestalt therapy/ or group therapy/ or guided imagery/ or milieu therapy/ or music therapy/ or pet therapy/ or psychodrama/ or relaxation training/ or role playing/ or sociotherapy/ or therapeutic community/ or validation therapy/ (145672)</p> <p>128 123 or 127 (814089)</p> <p>129 33 and 113 and 128 (957)</p> <p>130 from 129 keep 1-957 (957)</p>
Note	

Medline

Date	06/08/2010 by Abacus International
Database	Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R) 1950 to Present
Search Strategy	<p>1 Delirium, Dementia, Amnestic, Cognitive Disorders/ or Dementia, Vascular/ or Dementia, Multi- Infarct/ or Dementia/ (41484)</p> <p>2 Alzheimer Disease/ (52119)</p> <p>3 Delirium/ or Wernicke Encephalopathy/ (5403)</p> <p>4 Delirium, Dementia, Amnestic, Cognitive Disorders/ (8461)</p> <p>5 Huntington Disease/ (7656)</p> <p>6 Lewy Bodies/ (1189)</p> <p>7 Creutzfeldt-Jakob Syndrome/ (5117)</p> <p>8 Korsakoff Syndrome/ (200)</p> <p>9 Cerebral Infarction/ or CADASIL/ or Cerebrovascular Disorders/ (57215)</p> <p>10 Kluver-Bucy Syndrome/ (58)</p> <p>11 "Pick disease of the brain"/ (322)</p> <p>12 Brain Ischemia/ (28888)</p> <p>13 dement*.mp. (71744)</p> <p>14 alzheimer*.mp. (74143)</p> <p>15 "lewy* bod*".mp. (4757)</p> <p>16 huntington*.mp. (10643)</p> <p>17 cerebrovascular.mp. (97236)</p> <p>18 wernicke*.mp. (3022)</p> <p>19 (CADASIL or "cerebral autosomal dominant arteriopathy").mp. (704)</p> <p>20 korsakoff syndrome.mp. (524)</p> <p>21 delerium.mp. (19)</p> <p>22 Kluver bucy.mp. (194)</p> <p>23 "pick* disease".mp. (2228)</p> <p>24 arteriosclerosis.mp. (2)</p> <p>25 "ischemic white matter".mp. (86)</p> <p>26 (CJD or JCD or "creutzfeldt jakob").mp. (6280)</p> <p>27 (memory adj2 (complaint* or impair* or problem*)).mp. (9548)</p> <p>28 head trauma.mp. or Craniocerebral Trauma/ (20421)</p> <p>29 HIV.mp. or HIV/ (214345)</p> <p>30 parkinson.mp. or Parkinson Disease/ (48025)</p> <p>31 ("not otherwise specified" or NOS).mp. (19966)</p> <p>32 vascular dementia.mp. or Dementia, Vascular/ (4768)</p> <p>33 Cognitive Therapy/ or behavioural therapy.mp. or Behavior Therapy/ (31257)</p> <p>34 psychotherapy.mp. or Psychotherapy/ or Psychotherapy, Multiple/</p>

	<p>or "Imagery (Psychotherapy)"/ or Psychotherapy, Group/ or Psychotherapy, Brief/ or Psychotherapy, Rational-Emotive/ (55404)</p> <p>35 Reality Therapy/ or reality orientation.mp. (340)</p> <p>36 signposting.mp. (27)</p> <p>37 Interpersonal Relations/ or interpersonal communication.mp. (44742)</p> <p>38 "unlocking doors".mp. (2)</p> <p>39 Psychotherapy, Group/ or group living.mp. or Group Homes/ (11825)</p> <p>40 validation therapy.mp. (37)</p> <p>41 standard therapy.mp. (6025)</p> <p>42 alternative therapy.mp. or Complementary Therapies/ (13428)</p> <p>43 alternative medicine.mp. (4368)</p> <p>44 art therapy.mp. or Art Therapy/ (1088)</p> <p>45 Music Therapy/ or Music/ or music.mp. (11704)</p> <p>46 (massage or touch).mp. (28922)</p> <p>47 "white noise".mp. (2555)</p> <p>48 "natural elements".mp. (41)</p> <p>49 reminiscence therapy.mp. (83)</p> <p>50 Occupational Therapy/ or activity therapy.mp. (8616)</p> <p>51 complementary therapy.mp. (580)</p> <p>52 aromatherapy.mp. or Aromatherapy/ (609)</p> <p>53 Phototherapy/ or bright-light therapy.mp. (4568)</p> <p>54 Physical Stimulation/ or Hydrotherapy/ or multisensory approaches.mp. or Sensory Art Therapies/ (16558)</p> <p>55 multisensory stimulation.mp. or Photic Stimulation/ (38392)</p> <p>56 Relaxation Therapy/ or snoezelen.mp. or Sensory Art Therapies/ (5322)</p> <p>57 cognitive-behavioural therapy.mp. (1034)</p> <p>58 cognitive stimulation.mp. (177)</p> <p>59 cognitive training.mp. (349)</p> <p>60 physical touch.mp. (26)</p> <p>61 interpersonal therapy.mp. (154)</p> <p>62 self maintenance therapy.mp. (2)</p> <p>63 simulated presence therapy.mp. (6)</p> <p>64 Acupuncture Therapy/ or Acupuncture/ or acupuncture.mp. (14428)</p> <p>65 exercise therapy.mp. or Exercise Therapy/ (20468)</p> <p>66 Physical Therapy Modalities/ or kinesiotherapy.mp. (21977)</p> <p>67 Rehabilitation/ or rehabilitative care.mp. (15132)</p> <p>68 "Activities of Daily Living"/ or daily life activity.mp. (40763)</p> <p>69 therapy.mp. (1349590)</p> <p>70 68 and 69 (6049)</p> <p>71 Communication/ or communication.mp. (177022)</p> <p>72 interpersonal communication.mp. (591)</p> <p>73 social interaction.mp. (4337)</p> <p>74 relationship.mp. (959494)</p> <p>75 intervention.mp. (235145)</p> <p>76 71 or 72 or 73 or 74 (1129733)</p> <p>77 75 and 76 (18858)</p> <p>78 environmental manipulation.mp. (197)</p> <p>79 mirror\$.mp. (22103)</p> <p>80 69 and 79 (1132)</p> <p>81 Inservice Training/ or staff education.mp. or Education, Nursing, Continuing/ or Education, Nursing/ (56221)</p> <p>82 staff training.mp. (1332)</p> <p>83 structured activity.mp. (61)</p> <p>84 montessori.mp. (51)</p> <p>85 Meta-Analysis as Topic/ (10499)</p> <p>86 meta analy\$.tw. (31556)</p>
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87	metaanaly\$.tw. (981)
88	Meta-Analysis/ (25719)
89	(systematic adj (review\$1 or overview\$1)).tw. (24624)
90	exp Review Literature as Topic/ (5019)
91	or/85-90 (66114)
92	cochrane.ab. (15455)
93	embase.ab. (12898)
94	(psychlit or psyclit).ab. (822)
95	(psychinfo or psycinfo).ab. (4026)
96	(cinahl or cinhal).ab. (4950)
97	science citation index.ab. (1211)
98	bids.ab. (294)
99	cancerlit.ab. (485)
100	or/92-99 (24011)
101	reference list\$.ab. (5809)
102	bibliograph\$.ab. (8864)
103	hand-search\$.ab. (2561)
104	relevant journals.ab. (441)
105	manual search\$.ab. (1462)
106	or/101-105 (17165)
107	selection criteria.ab. (13448)
108	data extraction.ab. (6477)
109	107 or 108 (18870)
110	Review/ (1546084)
111	109 and 110 (12424)
112	Comment/ (439492)
113	Letter/ (700700)
114	Editorial/ (269352)
115	animal/ (4623573)
116	human/ (11356227)
117	115 not (115 and 116) (3432541)
118	or/112-114,117 (4448485)
119	91 or 100 or 106 or 111 (85954)
120	119 not 118 (79721)
121	29 or 30 or 31 (282138)
122	electroconvulsive therapy.mp. or Electroconvulsive Therapy/ (9233)
123	ECT.mp. (4781)
124	(Transcutaneous electric* nerve stimulation or TENS).mp. or Transcutaneous Electric Nerve Stimulation/ (8391)
125	(non-pharmacologic* or nonpharmacologic* or non pharmacologic*).mp. (6749)
126	caregiv*.mp. (28863)
127	(restraint adj2 free).mp. (76)
128	dog assist*.mp. (7)
129	(psychosocial adj2 intervention*).mp. (2252)
130	Behavior Therapy/ or behavioural therapy.mp. (21928)
131	behavioral therapy.mp. (3058)
132	33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48 or 49 or 50 or 51 or 52 or 53 or 54 or 55 or 56 or 57 or 58 or 59 or 60 or 61 or 62 or 63 or 64 or 65 or 66 or 67 or 70 or 77 or 78 or 80 or 81 or 82 or 83 or 84 or 122 or 123 or 124 or 125 or 126 or 127 or 128 or 129 or 130 or 131 (442363)
133	1 and 121 (2527)
134	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 32 or 133 (293259)
135	120 and 132 and 134 (335)
136	from 135 keep 1-334 (334)

	<p>137 132 and 134 (14313)</p> <p>138 psychotherapy/ or animal assisted therapy/ or aromatherapy/ or art therapy/ or autogenic training/ or behavior therapy/ or dance therapy/ or feedback, psychological/ or biofeedback, psychology/ or feedback, sensory/ or gestalt therapy/ or hypnosis/ or "imagery (psychotherapy)"/ or music therapy/ or nondirective therapy/ or psychoanalytic therapy/ or psychotherapeutic processes/ or psychotherapy, brief/ or psychotherapy, multiple/ or psychotherapy, rational-emotive/ or reality therapy/ or socioenvironmental therapy/ or milieu therapy/ or psychotherapy, group/ or residential treatment/ (97493)</p> <p>139 132 or 138 (464267)</p> <p>140 120 and 134 and 139 (337)</p>
Note	

PsyclINFO

Date	August Week 5 2010, by KCE
Database	PsyclINFO
Search Strategy	<p>1 dementia/ or aids dementia complex/ or dementia with lewy bodies/ or exp presenile dementia/ or senile dementia/ or vascular dementia/ or delirium/ or huntingtons disease/ or korsakoffs psychosis/ or kluver bucy syndrome/ or parkinson's disease/ or Alzheimer's Disease/ or cerebrovascular accidents/ or cerebrovascular disorders/ or exp cerebral ischemia/ or traumatic brain injury/ or exp cerebral ischemia/ (65183)</p> <p>2 (dement* or vascular dementia or "lewy* bod*" or huntington* or cerebrovascular or wernicke* or CADASIL or "cerebral autosomal dominant arteriopathy" or korsakoff syndrome or delirium or Kliver bucy or "pick* disease" or arteriosclerosis or "ischemic white matter" or (CJD or JCD or "creutzfeldt jakob") or (memory adj2 (complaint* or impair* or problem*)) or parkinson or ("not otherwise specified" or NOS) or alzheimer*).tw. (68471)</p> <p>3 Creative Arts Therapy/ or Art Therapy/ or dance therapy/ or music therapy/ or recreation therapy/ or alternative medicine/ or acupuncture/ or exp Aromatherapy/ or phototherapy/ or rehabilitation/ or cognitive rehabilitation/ or occupational therapy/ or exercise/ or photopic stimulation/ or exp relaxation therapy/ or animal assisted therapy/ or autogenic training/ or guided imagery/ or behavior therapy/ or brief psychotherapy/ or client centered therapy/ or cognitive therapy/ or group psychotherapy/ or reality therapy/ or rational emotive behavior therapy/ or gestalt therapy/ or hypnosis/ or exp psychoanalysis/ or psychotherapeutic processes/ or rational emotive behavior therapy/ or reality therapy/ or milieu therapy/ or interpersonal relationships/ or group homes/ or physical contact/ or reminiscence/ or biofeedback/ or neurotherapy/ or electroconvulsive shock therapy/ or inservice training/ or mental health inservice training/ or nursing education/ (162256)</p> <p>4 (psychotherapy or reality orientation or signposting or "unlocking doors" or group living or validation therapy or standard therapy or Complementary Therap\$ or alternative therapy or alternative medicine or art therapy or music or (massage or touch) or "white noise" or natural elements or reminiscence therapy or activity therapy or Aromatherapy or bright-light therapy or Physical Stimulation or Hydrotherapy or multisensory approaches or multisensory stimulation or Photic Stimulation or snoezelen or Sensory Art Therapies or cognitive-behavioural therapy or cognitive stimulation or cognitive training or physical touch or interpersonal therap\$ or self maintenance therapy or simulated presence therapy or acupuncture or exercise therapy or Physical Therapy Modalities</p>

	<p>or kinesiotherapy or rehabilitative care or staff education or staff training or structured activity or montessori or electroconvulsive therapy or ECT or (Transcutaneous electric* nerve stimulation or TENS) or (non-pharmacologic* or nonpharmacologic* or non pharmacologic*) or feedback, psychological or residential treatment).tw. (118949)</p> <p>5 daily life activity.tw. or exp "activities of daily living"/ (3132)</p> <p>6 therap\$.mp. (326229)</p> <p>7 5 and 6 (510)</p> <p>8 interpersonal communication/ or interpersonal communication.tw. or communication/ or communication.tw. or social interaction.tw. (105650)</p> <p>9 intervention.mp. (114880)</p> <p>10 8 and 9 (6686)</p> <p>11 exp Meta Analysis/ (3011)</p> <p>12 (meta analy\$ or metaanaly\$ or systematic review? or systematic overview?).tw. or (cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or cinhal or science citation index or bids or cancerlit).ab. or reference list\$.ab. or bibliograph\$.ab. or relevant journals.ab. or hand-search\$.ab. or manual search\$.ab. (2696885)</p> <p>13 "literature review"/ (21814)</p> <p>14 data extraction.ab. (359)</p> <p>15 selection criteria.ab. (1199)</p> <p>16 14 or 15 (1545)</p> <p>17 13 and 16 (31)</p> <p>18 11 or 12 or 17 (2696889)</p> <p>19 3 or 4 or 7 or 10 (248126)</p> <p>20 1 or 2 (89118)</p> <p>21 19 and 20 (6487)</p> <p>22 11 or 12 or 17 (2696889)</p> <p>23 21 and 22 (6438)</p> <p>24 limit 23 to yr="1950 -Current" (6370)</p> <p>25 *dementia/ or *aids dementia complex/ or *dementia with lewy bodies/ or exp *presenile dementia/ or *senile dementia/ or *vascular dementia/ or *delirium/ or *huntingtons disease/ or *korsakoffs psychosis/ or *kluver bucy syndrome/ or *parkinson's disease/ or *Alzheimer's Disease/ or *cerebrovascular accidents/ or *cerebrovascular disorders/ or exp *cerebral ischemia/ or *traumatic brain injury/ or exp *cerebral ischemia/ (59930)</p> <p>26 *Creative Arts Therapy/ or *Art Therapy/ or *dance therapy/ or *music therapy/ or *recreation therapy/ or *alternative medicine/ or *acupuncture/ or exp *Aromatherapy/ or *phototherapy/ or *rehabilitation/ or *cognitive rehabilitation/ or *occupational therapy/ or *exercise/ or *photopic stimulation/ or exp *relaxation therapy/ or *animal assisted therapy/ or *autogenic training/ or *guided imagery/ or *behavior therapy/ or *brief psychotherapy/ or *client centered therapy/ or *cognitive therapy/ or *group psychotherapy/ or *reality therapy/ or *rational emotive behavior therapy/ or *gestalt therapy/ or *hypnosis/ or exp *psychoanalysis/ or *psychotherapeutic processes/ or *rational emotive behavior therapy/ or *reality therapy/ or *milieu therapy/ or *interpersonal relationships/ or *group homes/ or *physical contact/ or *reminiscence/ or *biofeedback/ or *neurotherapy/ or *electroconvulsive shock therapy/ or *inservice training/ or *mental health inservice training/ or *nursing education/ (144188)</p> <p>27 25 or 2 (87364)</p> <p>28 26 or 4 or 7 or 10 (233664)</p> <p>29 27 and 28 (5833)</p> <p>30 22 and 29 (5792)</p>
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	31	limit 30 to yr="1999 -Current" (3948)
	32	25 and 26 (2834)
	33	22 and 32 (2799)
	34	limit 33 to yr="1950 -Current" (2796)
	35	limit 34 to yr="1999 -Current" (2054)
	36	11 or 13 (24723)
	37	21 and 36 (58)
	38	(meta-analysis or search:).tw. (51897)
	39	21 and 38 (189)
	40	(risk: or search:).tw. or exp treatment/ (628857)
	41	21 and 40 (5234)
	42	(control: or effectiveness or risk:).tw. (559155)
	43	21 and 42 (1956)
	44	limit 43 to yr="1999 -Current" (1552)
Note		

6.3 APPENDIX 3. WEBSITES ADDITIONAL HANDSEARCHING

- Agence d'Évaluation des Technologies et des Modes d'Intervention en Santé
- Agencia de Evaluación de Tecnologías Sanitarias
- Andalusian Agency for Health Technology Assessment
- L'Agenzia nazionale per i servizi sanitari regionali (Agency for Regional Healthcare)
- Agency for Healthcare Research and Quality
- Adelaide Health Technology Assessment
- Agency for Health Technology Assessment in Poland
- Australian Safety and Efficacy Register of New Interventional Procedures - Surgical
- Galician Agency for Health Technology Assessment
- Canadian Agency for Drugs and Technologies in Health
- Catalan Agency for Health Technology Assessment and Research
- Center for Drug Evaluation
- Comité d'Évaluation et de Diffusion des Innovations Technologiques
- Centro Nacional de Excelencia Tecnológica en Salud Reforma
- Committee for New Health Technology Assessment
- Centre for Reviews and Dissemination
- College voor Zorgverzekeringen
- Danish Centre for Evaluation and Health Technology Assessment
- German Agency for HTA at the German Institute for Medical Documentation and Information
- Secretaria de Ciència, Tecnologia e Insumos Estratégicos, Departamento de Ciència e Tecnologia
- Danish Institute for Health Services Research
- Department of Quality and Patient Safety of the Ministry Health of Chile
- Finnish Office for Health Care Technology Assessment
- GÖG - Gesundheit Österreich GmbH
- Gezondheidsraad
- Haute Autorité de Santé
- Health Information and Quality Authority
- Health Services Assessment Collaboration
- Israel Center for Technology Assessment in Health Care

- Institute for Clinical Effectiveness and Health Policy
- Institute of Health Economics
- International Network of Agencies for Health Technology Assessment
- Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen
- Belgian Federal Health Care Knowledge Centre
- Ludwig Boltzmann Institut für Health Technonoly Assessment
- Health Technology Assessment Section, Ministry of Health Malaysia
- Medical Advisory Secretariat
- Medicare Services Advisory Committee
- Medical Technology Unit - Swiss Federal Office of Public Health
- National Coordinating Centre for Health Technology Assessment
- Quality Improvement Scotland
- National Horizon Scanning Center
- Norwegian Knowledge Centre for Health Services
- Basque Office for Health Technology Assessment
- Swedish Council on Technology Assessment in Health Care
- Unidad de evaluación Tecnologías Santarias
- HTA Unit in A.Gemelli University Hospital
- State Health Care Accreditation Agency under the Ministry of Health of the Republic of Lithuania
- VA Technology Assessment Programme
- The Medical and Health Research Council of The Netherlands
- Clinical Guidelines / Pymont [Australia]: Medical Journal of Australia - 2005
- CMA Infobase / Ottawa [Canada]: Canadian Medical Association (CMA)
- Guidelines / Canberra [Australia]: National Health and Medical Research Council - 2008
- Guidelines and Reports of the New Zealand Guidelines Group / Wellington [New Zealand]: New Zealand Guidelines Group Inc. - 2007
- NHG-richtlijnen / Utrecht [The Netherlands] : Nederlands Huisartsen Genootschap (NHG) - 2008
- NICE guidance / London [UK]: National Institute for Health and Clinical Excellence (NICE) - 2008
- Recommandations professionnelles de la Haute Autorité de Santé (HAS) /paris [France] : Haute Autorité de Santé (HAS) - 2008
- Richtlijnen (CBO) / Utrecht [The Netherlands]: Kwaliteitsinstituut voor de Gezondheidszorg (CBO) - 2008
- SIGN Guidelines / Edinburgh [UK] : Scottish Intercollegiate Guidelines Network (SIGN) - 2001
- National Guideline Clearinghouse/AHRQ [USA]: <http://www.guideline.gov/>
- The “Dementia in Europe” Yearbook (2009)

6.4 APPENDIX 4 QUALITY APPRAISAL FOR INCLUDED SYSTEMATIC REVIEWS

Study	Internal validity					Overall assessment		Type of study included		
	Appropriate and clearly focussed question?	Is a description of methodology used included?	Are the literature searches sufficiently rigorous to identify all the relevant studies?	Is study quality assessed and taken into account?	Enough similarities to make combining reasonable (if combined for analysis)?	Bias minimisation?	If coded as + or - what is the likely direction in which bias might affect results?	Types of study	Research question answered?	Risk of bias
Fischer-Terworth 2008 ⁷⁷	Poorly addressed	Adequately addressed	Adequately addressed	Adequately addressed	N/A	+	Mixed type of evidence for mixed symptom improvements allow no good comparison between therapies	RCTs, systematic reviews, controlled studies	No	Low
Forbes 2008 ³³	Adequately addressed	Well covered	Well covered	Adequately addressed	Adequately addressed	++		RCTs	Yes	Low
Forbes 2009 ³²	Adequately addressed	Well covered	Well covered	Adequately addressed	N/A	++		RCTs	Yes	Low
IQWIG 2009 ³⁴	Well covered	Adequately addressed	Adequately addressed	Well covered	Adequately addressed	++		RCTs	Yes	Low
Kong 2009 ³¹	Adequately addressed	Well covered	Well covered	Adequately addressed	Poorly addressed	++		RCTs	Yes	Low
Lai 2009 ⁸³	Well covered	Adequately addressed	Well covered	Adequately addressed	Adequately addressed	++		RCTs and other non RCTs	Yes	Low
Lee 2009 ³⁶	Well covered	Adequately addressed	Well covered	Adequately addressed	Adequately addressed	++		RCTs	Yes	Low
Martin 2009 ⁸²	Adequately addressed	Well covered	Well covered	Adequately addressed	N/A	++	No results	RCTs, quasi-experimental studies, controlled before and after studies	No	Low
McGilton 2009 ⁴²	Adequately addressed	Adequately addressed	Well covered	Well covered	N/A	++		RCTs or quasi experimental	No	Low
Napoles 2010 ²³	Adequately addressed	Adequately addressed	Adequately addressed	Not addressed	N/A	+	Only useful for specific ethnic groups	Any study type	Partly	High
Nguyen 2008 ³⁵	Adequately addressed	Poorly addressed	Adequately addressed	Adequately addressed	N/A	++		RCTs in English language only	No	Low
Nocon 2010 ²⁷	Adequately addressed	Adequately addressed	Adequately addressed	Not addressed	N/A	+	Only studies with more than 30 patients were included	RCT; English and German papers	Partly	Low

O'Connor 2009 ³⁹	Adequately addressed	Adequately addressed	Well covered	Well covered	N/A	++		High quality experimental studies	Yes	Low
Olazaran 2010 ³⁰	Adequately addressed	Adequately addressed	Adequately addressed	Well covered	Adequately addressed	++		RCTs	Yes	Low
Ontario 2008 ⁴⁰	Well covered	Well covered	Well covered	Not addressed	N/A	++		Systematic reviews, meta-analyses and RCTs	Yes	Low
Parker 2008 ⁴¹	Adequately addressed	Well covered	Well covered	Adequately addressed	Adequately addressed	++		Systematic reviews, meta-analyses and primary studies	Yes	Low
Perkins 2008 ²⁵	Adequately addressed	Adequately addressed	Adequately addressed	Poorly addressed	N/A	++		All types, except reviews, case studies, viewpoints, editorials and opinions	No	High
Powell 2008 ²⁶	Adequately addressed	Adequately addressed	Adequately addressed	Not addressed	N/A	++		RCTs, non-RCTs, cohort studies, pre- and post-test studies and interrupted time series	No	High
Rieckmann 2009 ²⁸	Adequately addressed	Well covered	Well covered	Not addressed	N/A	-		RCTs or other best evidence (case-control as a minimum)	Yes	Low
Schoenmakers 2010 ⁸⁴	Well covered	Adequately addressed	Well covered	Well covered	Poorly addressed	++		RCT and CCT	Yes	Low
Skingley 2010 ¹⁷	Adequately addressed	Adequately addressed	Poorly addressed	Not addressed	N/A	-	Included only studies available in full text for free	Qualitative studies only (not further defined)	No	High
Spijker 2008 ³⁸	Adequately addressed	Well covered	Adequately addressed	Adequately addressed	Adequately addressed	++		Controlled clinical trials (CCTs)	Yes	Low
The Swedish Council on Technology Assessment in Health Care 2008 ⁴³	Adequately addressed	Adequately addressed	Adequately addressed	Adequately addressed	N/A	+		Systematic reviews, meta-analyses and primary studies	Yes	Low
Tucker 2010 ¹⁸	Adequately addressed	Poorly addressed	Adequately addressed	Not addressed	N/A	-	Single case study only	Any study type	No	High
Van Mierlo 2010 ²⁴	Adequately addressed	Adequately addressed	Well covered	Not addressed	N/A	+		Any study type	Yes	High
Vasse 2010 ⁷⁸	Adequately addressed	Well covered	Well covered	Well covered	Adequately addressed	++		RCT or CCT	Yes	Low

Verbeek 2009 ²²	Adequately addressed	Adequately addressed	Adequately addressed	Not addressed	N/A	++		All study types in Dutch, English and German language, only small patient groups (15 or less)	No	High
Von Gunten 2008 ¹⁹	Adequately addressed	Poorly addressed	Adequately addressed	Not addressed	N/A	-		Any type	No	High
Wall 2010 ²⁰	Adequately addressed	Adequately addressed	Poorly addressed	Not addressed	N/A	+		Any study type	Yes	High
Weina 2009 ³⁷	Adequately addressed	Adequately addressed	Adequately addressed	Not addressed	N/A	+		No studies met the inclusion criteria (no RCTs identified)	No	low
Wu 2009 ²¹	Poorly addressed	Adequately addressed	Adequately addressed	Not addressed	N/A	-		Any type	Yes	High
Zettler 2008 ²⁹	Adequately addressed	Adequately addressed	Adequately addressed	Not addressed	Poorly addressed	-		Quasi- experimental design, RCT, controlled trial, within subject experimental design	No	Low

6.5 APPENDIX 5 DATA EXTRACTION TABLE FOR INCLUDED SYSTEMATIC REVIEWS (WITH A LOW RISK OF BIAS)

Systematic reviews for specific interventions (n=8)

Reference	Risk of bias	Inclusion criteria						Results summary
		Intervention			Population			
		Treatments included	Treatment target (patient or caregiver)	Additional information	Setting (residential or home)	Type of dementia	Criteria for diagnosis	
Forbes 2008 ³³	Low	Physical activity	Patient and caregiver	Aerobic exercise training or physical activity programs offered over any length of time with the aim to improve cognition, function, behaviour, depression, and mortality in older persons with dementia and/or family caregiver health, quality of life, or to decrease caregiver mortality, and/or use of health care services. Trials were included where the only difference between groups was the physical activity intervention	Mixed	Not specified	A diagnosis of dementia according to accepted criteria such as the Diagnostic and Statistical Manual of Mental Disorders, the National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Disorders Association or ICD-10	There was insufficient evidence to be able to say whether or not physical activity programs are beneficial for people with dementia.
Forbes 2009 ³²	Low	Light therapy	Patient	Light therapy was usually administered from a Brite-Lite™ box placed approximately one metre from the participant's head. The alternative method was Dawn-Dusk Simulator™ which included an overhead halogen lamp placed behind participants' bed. The treatment groups received light therapy ranging from 2,500 to 10,000 lux.	Residential care	Alzheimer's disease, Dementia with Lewy Bodies, Vascular Dementia, or dementia due to another cause)	A diagnosis of dementia according to accepted criteria such as the Diagnostic and Statistical Manual of Mental Disorders, the National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Disorders Association or ICD-10	No adequate evidence of the effectiveness of light therapy in managing cognition, sleep, function, behaviour, or psychiatric disturbances associated with dementia is available.

Reference	Risk of bias	Inclusion criteria						Results summary
		Intervention			Population			
		Treatments included	Treatment target (patient or caregiver)	Additional information	Setting (residential or home)	Type of dementia	Criteria for diagnosis	
Lai 2009 ⁸³	Low	Special care unit	Patient	Special care unit characterised as 1.admission of residents with dementia and most often with AD, 2.special selection, training, and supervision of staff members, 3.specially designed activity programming, 4.family involvement, and 5.a specially designed physical environment that is segregated from other areas	Residential care	A confirmed diagnosis of dementia or Alzheimer's disease or related disorders	A diagnosis of dementia according to accepted criteria such as the Diagnostic and Statistical Manual of Mental Disorders, the National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Disorders Association or ICD-10	There were no identified RCTs found and no strong evidence of benefit from the available non-RCTs. It is probably more important to implement best practice than to provide a specialized care environment.
Lee 2009 ³⁶	Low	Needle acupuncture with or without electrical stimulation	Patient	Trials were included if they employed acupuncture as the sole treatment or as an adjunct to other treatments. Trials comparing two different forms of acupuncture and those in which no clinical data or insufficient data for comparison were reported were excluded.	Not specified	Alzheimers disease	Not specified	The existing evidence does not demonstrate the effectiveness of acupuncture for Alzheimers disease
Martin 2009 ⁸²	Low	Smart home technologies	Patient	Smart home technologies include: social alarms, electronic assist devices, telecare social alert platforms, environmental control systems, automated home environments and 'ubiquitous' homes (telemedicine and remote monitoring studies were excluded)	Home care	Not specified	Not specified	Smart home technology has not yet been assessed for patients with dementia

Reference	Risk of bias	Inclusion criteria						Results summary
		Intervention			Population			
		Treatments included	Treatment target (patient or caregiver)	Additional information	Setting (residential or home)	Type of dementia	Criteria for diagnosis	
Nguyen 2008 ³⁵	Low	Aromatherapy	Patient and caregiver	Lemon balm, lavender oil, blends. Concurrent medication was allowed	Residential care (or not specified)	Patients with behavioural and psychological symptoms of dementia	CMAI and other scales were used to score symptoms; or observation of behaviour	Data supporting the efficacy of aromatherapy are scarce; available studies reported mixed outcomes for both people with dementia and their caregivers. The side-effect profile of commonly used oils is virtually unexplored.
Weina 2009 ³⁷	Low	Acupuncture	Patient	Patients with vascular dementia	Home or residential care setting	Patients with vascular dementia	"according to accepted criteria" "Diagnosis by other means such as scores on the HIS could be used in older trials"	No RCTs were identified
Zettler 2008 ²⁹	Low	Simulated presence therapy	Patients	Audiotape prepared by established caregiver, family member, participant's spouse, psychologist or 'surrogate' family member Videotape prepared by family members or research team	Residential care (or not specified)	Not specified	Not specified	When combined, the four included studies yielded a statistically significant difference versus no treatment (0.70, 95% CI 0.38–1.02, p<0.001), although there was also evidence of significant heterogeneity (I ² =71%). Some support for the use of simulated presence therapy

Systematic reviews for mixed interventions (n=14)

Reference	Risk of bias	Inclusion criteria					Summary	
		Intervention			Population			
		Treatments included	Treatment target (patient or caregiver)	Additional information	Setting	Type of dementia		Criteria for diagnosis
Fischer-Terworth 2008 ⁷⁷ [German]	Low	Psychological interventions	Patient and caregiver	1. Environmental modification therapy 2. Cognitive stimulation therapy 3. Cognitive behavioural therapy 4. Music therapy 5. Reminiscence therapy Sensory stimulation e.g. 6. Aromatherapy, 7. Snoezelen and 8. Hand massage 9. Animal-guided therapy 10. Validation therapy Specific therapies for patients with both dementia and anxiety disorders were also discussed	Mixed	Alzheimers disease and related disorders	Discussed in introduction, but not specified for inclusion	There was convincing evidence to recommend the use of cognitive behavioural therapy. There was moderate evidence to recommend environmental modification therapy, cognitive stimulation therapy and music therapy there was not enough evidence for recommendation of the other therapies
IQWiG 2009 ³⁴ [German]	Low	Non-pharmacological interventions	Patient and caregiver	1. Caregiver training 2. Emotion-orientated interventions 3. Cognitive training procedures 4. Activity based interventions 5. Other	Mixed	Alzheimers disease or mixed type including Alzheimers	Not specified	No long-term benefits of strategies have been found
Kong 2009 ³¹	Low	Non-pharmacological interventions	Patient and caregiver	1. Aromatherapy 2. Thermal bath 3. Calming music and hand massage 4. Simulated presence 5. Pet therapy 6. Rocking chair therapy 7. Therapeutic recreational activities 8. Morning bright light therapy 9. Behaviour management techniques 10. Abilities focused morning care 11. Stimulation-retreat programme 12. Activities of daily living intervention 13. Way finding intervention	Mixed	Not specified	Not specified	A review of high quality studies that demonstrated effectiveness only for sensory interventions (albeit in association with significant heterogeneity)

Reference	Risk of bias	Inclusion criteria					Summary	
		Intervention			Population			
		Treatments included	Treatment target (patient or caregiver)	Additional information	Setting	Type of dementia		Criteria for diagnosis
McGilton 2009 ⁴²	Low	Communication interventions	Patient and caregiver	1. Behaviour management training 2. Communication techniques (inc personalised memory books) 3. Assisted walking 4. Snoezelen	Residential care	Not specified	Not specified though 3/4 included studies showed that patients had behavioural disturbances as well as dementia	Absence of results for relevant subpopulation preclude summary
O'Connor 2009 ³⁹	Low	Psychosocial interventions	Patient and caregiver	Treatments included (but not prospectively specified) were: 1. Music 2. Carer education 3. Sensory enrichment 4. Simulated family presence 5. Novel bathing techniques 6. Aromatherapy 7. Recreation 8. Relaxation 9. Validation therapy	Residential care	Not specified	Not specified	High quality studies indicate that aromatherapy, bed baths, one-to-one social interaction, simulated family presence and muscle relaxation therapy all reduced behavioural symptoms. Validation therapy significantly reduced agitation.
Ontario Medical Advisory Secretariat 2008 ⁴⁰	Low	Respite care Psychosocial interventions Multicomponent interventions	Caregiver	Respite care: defined as a break or relief for the caregiver usually provided in the home, through day programs or at institutions (usually 30 days or less). Respite services will vary in delivery and duration. A number of individuals may carry out respite care including paid staff, volunteers, family, or friends. Psychosocial interventions: Psychosocial interventions encompass a broad range of interventions including psychoeducational interventions, counseling, supportive therapy, and behavioural management interventions, as well as a host of other supportive services	Homecare	Not specified	Not specified	Respite care: poor-quality and inconclusive evidence from RCTs for the effectiveness of respite care services. Psychosocial interventions: good quality evidence suggests that individual behavioural interventions (≥ 6 sessions), directed at the caregiver (or combined with the patient) are effective in improving psychological health in dementia caregivers. Multicomponent intervention: There is good quality evidence that

Reference	Risk of bias	Inclusion criteria					Summary	
		Intervention			Population			
		Treatments included	Treatment target (patient or caregiver)	Additional information	Setting	Type of dementia		Criteria for diagnosis
				Multicomponent intervention: 2 or more psychosocial interventions				multicomponent interventions improve caregiver psychosocial health and may impact rates of institutionalization of dementia patients
Ontario Medical Advisory Secretariat 2008 ⁴⁰	Low	Physical activity Non-pharmacologic and non-exercise interventions	Patient	Non-pharmacologic and non-exercise interventions: Cognitive training - Guided practice on a set of standard tasks designed to improve particular cognitive functions (e.g., memory, attention, problem solving) Cognitive rehabilitation - Individualized approach to help people with cognitive impairments in which those affected, and their families, work together with health care professionals to identify personally relevant goals and devise strategies for addressing these. Emphasis is not on enhancing performance on cognitive tasks, but on improving functioning in the everyday context	Mixed	Not specified beyond mild to moderate disease	Not specified	Physical activity: Physical exercise is effective for improving physical functioning in patients with dementia Non-pharmacologic and non-exercise interventions: the evidence is inconsistent and are in the "artisan" stage (moving to becoming more evidence-based)
Parker 2008 ⁴¹	Low	Interventions designed to support caregivers in their role	Caregiver	1 Interventions designed to support caregivers in their role • Skills training • Education to assist in caring for a person living with dementia • Support groups/programs 2 Interventions of formal approaches to care designed to support caregivers in their role • Care planning • Case management • Specially designated members of the healthcare team – for example dementia nurse specialist or volunteers	Homecare	Alzheimer's disease, vascular dementia, frontotemporal dementia, dementia with Lewy bodies, Wernicke Encephalopathy, CJD and Korsakoff Syndrome	Not specified	There is evidence to support the use of well-designed psychoeducational or multi-component interventions for caregivers of people with dementia who live in the community.

Reference	Risk of bias	Inclusion criteria					Summary	
		Intervention			Population			
		Treatments included	Treatment target (patient or caregiver)	Additional information	Setting	Type of dementia		Criteria for diagnosis
				trained in caring for someone with dementia 3 Multi-component interventions that involve any of the above				
Spijker 2008 ³⁶	Low	Non-pharmacological interventions	Patient and caregivers	Included components in interventions: A Psychoeducation B Cognitive behavioural therapy C Respite care D Environmental modification E Skills training/problem solving F Case management G Person with dementia focussed memory training H General support U Unknown or multicomponent interventions	Mixed	Alzheimer's disease or dementia	Not specified	The analysis of the intervention characteristics showed that actively involving caregivers in making choices about treatments distinguishes effective from ineffective support programs.
The Swedish Council on Technology Assessment in Health Care 2008 ⁴³	Low	Care interventions (Non-medical, non-pharmacological, psychosocial interventions)	Patient and caregivers	The authors describe a care intervention as an overarching concept that includes nursing, physical therapy, occupational therapy, music therapy, etc. Previously the term non-pharmacological intervention was common. However, that would suggest that normal intervention is pharmacological. Pharmacological and care interventions are appropriate on different occasions and often in combination.	Mixed	Not specified	Dementia diagnosed according to DSM III-IV, ICD 9-10, ADRS, NINDS, NINCDSADRDA or Lundman-Mancheter, or any of the following rating scales: MMSE, GBS or GDS	Evidence of the efficacy of care interventions was difficult to prove, the included evidence did not show any scientific evidence for the efficacy of interventions. Many studies were rejected due to methodological inadequacy. Qualitative methods Show that it is possible to communicate with people who have severe dementia in a way that brings out latent abilities.

Reference	Risk of bias	Inclusion criteria						Summary
		Intervention			Population			
		Treatments included	Treatment target (patient or caregiver)	Additional information	Setting	Type of dementia	Criteria for diagnosis	
Nocon, 2010 [German] ²⁷	Low	Validation therapy Multisensory stimulation Reality orientation therapy Reminiscence therapy	Patient	N/A	Not specified	Not specified	Not specified	There is not enough clinical evidence that the 4 studied interventions are effective therapies (only some cognitive improvements found) for patients with dementia

Reference	Risk of bias	Inclusion criteria					Summary	
		Treatments included	Treatment target (patient or caregiver)	Intervention	Population			
				Additional information	Setting	Type of dementia		Criteria for diagnosis
Olazaran 2010 ³⁰	Low	"Any theoretically based, nonchemical, focused, and replicable intervention, conducted with the patient or the caregiver, which potentially provided some relevant benefit"	Patient and caregiver	For patients: 1. Cognitive training 2. Behavioural interventions 3. Cognitive stimulation 4. TENS 5. Physical exercise 6. Use of music 7. Reminiscence 8. ADL training 9. Massage and touch 10. Recreation therapy 11. Use of light 12. Multisensory stimulation 13. Support and psychotherapy 14. Validation 15. Acupuncture Transcranial magnetic stimulation, muscle relaxation, multicomponent For caregivers: 16. Caregiver education 17. Caregiver support 18. Case Management 19. Respite care 20. Multicomponent Other interventions: 21. Multicomponent for patient and caregiver 22. Professional caregiver training 23. Special units	Mixed	Alzheimers disease and related disorders	Not specified	The majority of studies were poor quality and many of the analyses included heterogenous studies but most interventions were associated with significant improvements in the outcomes assessed

Reference	Risk of bias	Inclusion criteria						Summary
		Intervention			Population			
		Treatments included	Treatment target (patient or caregiver)	Additional information	Setting	Type of dementia	Criteria for diagnosis	
Rieckmann 2009 ^{28,.....}		Sensory stimulation, reality orientation, reminiscence, validation, emotion-oriented care, ergotherapy, relaxation techniques.	Patient	Interventions were pre-specified as previously described	Not specified	Not specified	Not specified	Few methodologically robust studies were available. There was not enough evidence for efficacy of any of the interventions. More studies are needed.
Schoenmakers 2010 ⁸⁴	Low	Active psychosocial intervention in a care home (in order to support the family caregiver)	Caregiver (family member)	Psychosocial care grouped into 6 subtypes: 1. CBT or group therapy (psychosocial) 2. respite care 3. telephone/internet support 4. case management 5. physical exercise 6. communications skills	Home care	Not specified	Not specified	Heterogeneity in design, delivery and recipients of psychosocial limit generalisation. Most interventions were associated with small non-significant short-term improvements, respite care and exercise therapy increased caregiver burden by causing disruption in daily activities
Vasse 2010 ⁷⁸	Low	Communication strategies (defined as sharing information by speaking, writing, body movements or other signalling behaviour)	Patient and caregiver	Communication intervention/session for residents (included a walking programme combined with conversation, group validation therapy, life review programmes, cognitive stimulation therapy, and activity therapy) Training in communication techniques for care staff (communication techniques and multicomponent training programmes including communication techniques)	Residential care (or studies with at least 80% residents or stratified results)	Not specified	Not specified	Communication between carers and patients can be improved but with limited effect on neuropsychiatric symptoms

6.6 APPENDIX 6 SYSTEMATIC REVIEWS EXCLUDED (HIGH RISK OF BIAS)

Reference	Risk of bias?	Inclusion criteria						Results summary
		Intervention			Population			
		Treatments included	Treatment target (patient or caregiver)	Additional information	Setting (residential or home)	Type of dementia	Criteria for diagnosis	
Perkins 2008 ²⁵	High	Dog-assisted therapy	Patient	Patient interaction with dog was studied. Dogs were either visiting or residential dogs	Mixed	Old patients (>60 years) with dementia	Several studies used presence of challenging behaviour and prior positive relationships with animals; 1 study used MMSE; 1 study independently verified the diagnosis of dementia	There was methodological variability and confounding factors that make it difficult to draw conclusions, research suggests that dog contact ameliorates BPSD in patients with dementia
Powell 2008 ²⁶	High	Networked ICT interventions	Caregiver	Interventions: 1. ComputerLink 2. AlzOnline 3. Caring for Others 4. TLC: computer-mediated automated telephone support system 5. CTIS: computerised system using Spanish and English text and voice screen phones [Telephone-only interventions were excluded]	Non-institutional settings	Alzheimers disease and dementia	Not specified	Findings were inconsistent and suggested moderate effects.
Skingley 2010 ¹⁷	High	Music or singing interventions	Patient	Caregiver singing Background music Preferred music (identified by carers) 'Music therapy' studies were specifically excluded	Mixed (dementia unit, nursing home, 'restrained hospitalised patients', home care)	Not specified	Not specified	A small number of limited studies suggest a musical intervention reduced agitation whilst improving interaction and cooperation
Wall 2010 ²⁰	High	Music therapy	Patient	N/A	Not specified	Not specified	Not specified	Limited evidence on positive effects of music therapy for agitation

Reference	Risk of bias?	Inclusion criteria					Summary	
		Intervention			Population			
		Treatments included	Treatment target (patient or caregiver)	Additional information	Setting	Type of dementia		Criteria for diagnosis
Napoles 2010 ²³	High	Any psychosocial support intervention used in the USA	Caregiver	Looked specifically at African American, Latino and Chinese (Asian) American caregivers using psychosocial interventions Treatments included: 1. Multicomponent psychoeducational and problem solving 2. Skills training 3. Screen telephone support access system 4. Structural ecosystems therapy 5. Psychoeducational programme 6. Behavioural management programme 7. Occupational therapist visit 8. Peer mentoring 9. Yoga-meditation programme	Mixed	Not specified	Not specified	The limited studies including specific ethnic groupings showed some evidence of effectiveness for multicomponent skills training and social support intervention in reducing burden, upset, depression and negative coping amongst other outcomes
Tucker 2010 ¹⁸	High	Non-pharmacological interventions (pharmacologic interventions were also included but are not discussed)	Patient	Patients exhibiting inappropriate sexual behaviours	Mixed	Not specified	Not specified	No evidence available on non-pharmacological interventions specifically for inappropriate sexual behaviours
Van Mierlo 2010 ²⁴	High	All psychosocial interventions studies for patients living in the community and in care	Patient and caregiver	Community-based interventions included: 1. Reminiscence therapy 2. Music/video memory lane 3. Multisensory stimulation 4. Progressive muscle relaxation 5. Cognitive stimulation/support 6. Errorless learning intervention 7. Reality orientation therapy 8. Prosthetic memory aid 9. Student-led rehabilitation 10. Therapeutic recreation intervention 11. Meeting centres support programme	Mixed	Not specified	Not specified	Positive (significant) effects from community-based interventions were mostly in mild to severe dementia not otherwise specified and mild to moderate Alzheimers disease. Positive (significant) effects from institutionally based interventions were seen in patients with moderate to severe dementia, severe to very severe dementia, and patients with behavioural problems

Reference	Risk of bias?	Inclusion criteria					Summary	
		Intervention			Population			
		Treatments included	Treatment target (patient or caregiver)	Additional information	Setting	Type of dementia		Criteria for diagnosis
				12. Animal companion/therapy 13. Reducing Disability in Alzheimers disease (RDAD) 14. Caregiver training 15. Nighttime Insomnia Treatment and Education for Alzheimers Disease (NITEAD) 16. Prince Henry Hospital dementia caregivers training programme 17. video respite therapy 18. individualised learning/ activities 19. Dementia special care unit 20. Person-centred showering 21. Towel bath 22. Memory/Sensory stimulation activities 23. Simulated presence therapy 24. Resident dog 25. Music during bathing 26. Psychomotor Activation Programme 27. Student-led rehabilitation 28. Reminiscence therapy 29. Skill elicitation 30. Life review programme 31. Snoezelen 32. Environmental barriers 33. Closet modification 34. Morning bright light therapy plus others not listed here				

Reference	Risk of bias?	Inclusion criteria						Summary
		Intervention			Population			
		Treatments included	Treatment target (patient or caregiver)	Additional information	Setting	Type of dementia	Criteria for diagnosis	
Verbeek 2009 ²²	High	Small, homelike care interventions	Patient	Psychological care; normalisation of home living; maximising independence; integrated staff; personalised care etc.	Nursing homes that reflect a homelike environment	Not specified	Not specified, but ADL capacities, behavioural disturbances and level of dementia were analysed	More details are required about the patient characteristics before firm conclusions can be drawn
Von Gunten 2008 ¹⁹	High	Psychosocial interventions for vocally disruptive behaviour	Patient and caregiver	Patient-focused interventions: Split into 1. common-sense approaches, 2. specific care attitudes or environments, 3. reinforcement strategies Caregiver-focused interventions	Not specified	Not specified	Not specified (displaying vocally disruptive behaviours)	The limited available evidence is largely of poor quality and unconvincing of the benefits associated with intervention
Wu 2009 ²¹	High	Psychosocial interventions using information and communication technologies.	Caregiver	The evaluation of the impact of the intervention had to either concern the psycho affective state of the carer (measure of burden, feeling of competence) or the technology used (questionnaires about useability, satisfaction)	N/A	Alzheimer's disease or related	Not specified	Telephone and internet interventions appear to be as effective to face-to-face measures and may be used to support carers, who experience a lot of stress.

6.7 APPENDIX 7 RCT SEARCH STRATEGIES

EMBASE

Date	28-01-2011
Database	EMBASE OVID <1980 to 2011 Week 03>
Search Strategy (attention, for PubMed, check « Details »)	<ol style="list-style-type: none"> 1 cognitive therapy/ or behavior therapy/ or psychotherapy/ or behavioural therapy.mp. (104210) 2 reality orientation.mp. (217) 3 signposting.mp. or interpersonal communication/ (83421) 4 "unlocking doors".mp. (2) 5 group living.mp. (554) 6 validation therapy.mp. or validation therapy/ (78) 7 standard therapy.mp. (8131) 8 alternative therapy.mp. or alternative medicine/ (26573) 9 alternative therapy.mp. (2856) 10 art therapy/ (1577) 11 music therapy/ or music.mp. (13566) 12 (massage or touch).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer] (30421) 13 "white noise".mp. (2800) 14 "natural elements".mp. (46) 15 reminiscence therapy.mp. (110) 16 activity therapy.mp. (88) 17 complementary therapy.mp. (759) 18 aromatherapy.mp. or aromatherapy/ (1124) 19 phototherapy/ or bright-light therapy.mp. (12082) 20 multisensory stimulation/ or sensory stimulation/ or learning/ or education/ or multisensory approaches.mp. or auditory stimulation/ (351177) 21 relaxation training/ or behavior therapy/ or sensory stimulation/ or occupational therapy/ or snoezelen.mp. or snoezelen/ (58630) 22 brief psychotherapy.mp. (394) 23 cognitive-behavioural therapy.mp. (1654) 24 cognitive stimulation.mp. (241) 25 cognitive training.mp. (484) 26 physical touch.mp. (35) 27 interpersonal therapy.mp. (248) 28 self maintenance therapy.mp. (4) 29 simulated presence therapy.mp. (11) 30 acupuncture/ or acupuncture.mp. (23610) 31 exercise therapy.mp. or kinesiotherapy/ (18698) 32 rehabilitation care/ or rehabilitation/ or rehabilitative care.mp. (33752) 33 daily life activity/ or ADL.mp. (44198) 34 therapy/ (617321) 35 33 and 34 (548) 36 communication.mp. or interpersonal communication/ (272647) 37 social interaction.mp. or social interaction/ (21104) 38 relationship.mp. (630729) 39 intervention.mp. (300834) 40 36 or 37 or 38 (900555) 41 39 and 40 (22808) 42 environmental factor/ or environmental manipulation.mp. (46861) 43 mirror\$.mp. (21127) 44 34 and 43 (342) 45 staff education.mp. or staff training/ (7340) 46 structured activity.mp. (76) 47 montessori.mp. (62) 48 electroconvulsive therapy.mp. or electroconvulsive therapy/ (13344)

	<p>49 ECT.mp. (6194)</p> <p>50 transcutaneous nerve stimulation/ or transcutaneous electric* nerve stimulation.mp. or TENS.mp. (10347)</p> <p>51 (non-pharmacologic* or nonpharmacologic* or non pharmacologic*).mp. (9128)</p> <p>52 caregiv*.mp. (38146)</p> <p>53 (restraint adj2 free).mp. (82)</p> <p>54 dog assist*.mp. (11)</p> <p>55 (psychosocial adj2 intervention*).mp. (3029)</p> <p>56 Behavior Therapy/ or behavio?ral therapy.mp. (35837)</p> <p>57 psychotherapy/ or art therapy/ or autogenic training/ or behavior contracting/ or behavior modification/ or behavior therapy/ or cognitive behavioral stress management/ or cognitive rehabilitation/ or cognitive therapy/ or family therapy/ or gestalt therapy/ or group therapy/ or guided imagery/ or milieu therapy/ or music therapy/ or pet therapy/ or psychodrama/ or relaxation training/ or role playing/ or sociotherapy/ or therapeutic community/ or validation therapy/ (149483)</p> <p>58 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 35 or 41 or 42 or 44 or 45 or 46 or 47 or 48 or 49 or 50 or 51 or 52 or 53 or 54 or 55 or 56 or 57 (842344)</p> <p>59 Clinical trial/ (825675)</p> <p>60 Randomized controlled trial/ (287964)</p> <p>61 Randomization/ (53288)</p> <p>62 Single blind procedure/ (13776)</p> <p>63 Double blind procedure/ (101029)</p> <p>64 Crossover procedure/ (29994)</p> <p>65 Placebo/ (173674)</p> <p>66 Randomi?ed controlled trial\$.tw. (58992)</p> <p>67 Rct.tw. (6352)</p> <p>68 Random allocation.tw. (1015)</p> <p>69 Randomly allocated.tw. (15091)</p> <p>70 Allocated randomly.tw. (1690)</p> <p>71 (allocated adj2 random).tw. (681)</p> <p>72 Single blind\$.tw. (10675)</p> <p>73 Double blind\$.tw. (115546)</p> <p>74 ((treble or triple) adj blind\$).tw. (231)</p> <p>75 Placebo\$.tw. (154363)</p> <p>76 Prospective study/ (162093)</p> <p>77 or/59-76 (1113824)</p> <p>78 Case study/ (10975)</p> <p>79 Case report.tw. (196147)</p> <p>80 Abstract report/ or letter/ (767143)</p> <p>81 or/78-80 (970591)</p> <p>82 77 not 81 (1081533)</p> <p>83 caregiver.mp. or exp CAREGIVER/ (30092)</p> <p>84 58 or 83 (842344)</p> <p>85 exp DEMENTIA/ or dementia.mp. (171891)</p> <p>86 82 and 84 and 85 (3075)</p> <p>87 limit 86 to yr="2008 -Current" (995)</p>
Note	

Medline

Date	28-01-2011
Database	Database: Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R) <1948 to Present>
Search Strategy (attention, for PubMed, check « Details »)	<p>1 Cognitive Therapy/ or behavioural therapy.mp. or Behavior Therapy/ (31338)</p> <p>2 psychotherapy.mp. or Psychotherapy/ or Psychotherapy, Multiple/ or "Imagery (Psychotherapy)"/ or Psychotherapy, Group/ or Psychotherapy, Brief/ or Psychotherapy, Rational-Emotive/ (55321)</p> <p>3 Reality Therapy/ or reality orientation.mp. (340)</p> <p>4 signposting.mp. (29)</p> <p>5 Interpersonal Relations/ or interpersonal communication.mp. (45086)</p> <p>6 "unlocking doors".mp. (2)</p> <p>7 Psychotherapy, Group/ or group living.mp. or Group Homes/ (11778)</p> <p>8 validation therapy.mp. (37)</p> <p>9 standard therapy.mp. (6111)</p> <p>10 alternative therapy.mp. or Complementary Therapies/ (13489)</p> <p>11 alternative medicine.mp. (4428)</p> <p>12 art therapy.mp. or Art Therapy/ (1120)</p> <p>13 Music Therapy/ or Music/ or music.mp. (11863)</p> <p>14 (massage or touch).mp. (29032)</p> <p>15 "white noise".mp. (2598)</p> <p>16 "natural elements".mp. (42)</p> <p>17 reminiscence therapy.mp. (81)</p> <p>18 Occupational Therapy/ or activity therapy.mp. (8629)</p> <p>19 complementary therapy.mp. (591)</p> <p>20 aromatherapy.mp. or Aromatherapy/ (619)</p> <p>21 Phototherapy/ or bright-light therapy.mp. (4608)</p> <p>22 Physical Stimulation/ or Hydrotherapy/ or multisensory approaches.mp. or Sensory Art Therapies/ (16481)</p> <p>23 multisensory stimulation.mp. or Photic Stimulation/ (38392)</p> <p>24 Relaxation Therapy/ or snoezelen.mp. or Sensory Art Therapies/ (5313)</p> <p>25 cognitive-behavioural therapy.mp. (1071)</p> <p>26 cognitive stimulation.mp. (184)</p> <p>27 cognitive training.mp. (358)</p> <p>28 physical touch.mp. (27)</p> <p>29 interpersonal therapy.mp. (158)</p> <p>30 self maintenance therapy.mp. (2)</p> <p>31 simulated presence therapy.mp. (6)</p> <p>32 Acupuncture Therapy/ or Acupuncture/ or acupuncture.mp. (14740)</p> <p>33 exercise therapy.mp. or Exercise Therapy/ (20493)</p> <p>34 Physical Therapy Modalities/ or kinesiotherapy.mp. (21821)</p> <p>35 Rehabilitation/ or rehabilitative care.mp. (15152)</p> <p>36 "Activities of Daily Living"/ or daily life activity.mp. (40587)</p> <p>37 therapy.mp. (1356008)</p> <p>38 36 and 37 (6033)</p> <p>39 Communication/ or communication.mp. (179256)</p> <p>40 interpersonal communication.mp. (609)</p> <p>41 social interaction.mp. (4402)</p> <p>42 relationship.mp. (961126)</p> <p>43 intervention.mp. (239044)</p> <p>44 39 or 40 or 41 or 42 (1133497)</p> <p>45 43 and 44 (19277)</p> <p>46 environmental manipulation.mp. (203)</p> <p>47 mirror\$.mp. (22950)</p> <p>48 37 and 47 (1147)</p> <p>49 Inservice Training/ or staff education.mp. or Education, Nursing, Continuing/ or Education, Nursing/ (56592)</p> <p>50 staff training.mp. (1343)</p>

	<p>51 structured activity.mp. (65)</p> <p>52 montessori.mp. (51)</p> <p>53 electroconvulsive therapy.mp. or Electroconvulsive Therapy/ (9248)</p> <p>54 ECT.mp. (4828)</p> <p>55 (Transcutaneous electric* nerve stimulation or TENS).mp. or Transcutaneous Electric Nerve Stimulation/ (8644)</p> <p>56 (non-pharmacologic* or nonpharmacologic* or non pharmacologic*).mp. (6886)</p> <p>57 caregiv*.mp. (29513)</p> <p>58 (restraint adj2 free).mp. (78)</p> <p>59 dog assist*.mp. (8)</p> <p>60 (psychosocial adj2 intervention*).mp. (2301)</p> <p>61 Behavior Therapy/ or behavioural therapy.mp. (21835)</p> <p>62 behavioral therapy.mp. (3142)</p> <p>63 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 38 or 45 or 46 or 48 or 49 or 50 or 51 or 52 or 53 or 54 or 55 or 56 or 57 or 58 or 59 or 60 or 61 or 62 (445049)</p> <p>64 psychotherapy/ or animal assisted therapy/ or aromatherapy/ or art therapy/ or autogenic training/ or behavior therapy/ or dance therapy/ or feedback, psychological/ or biofeedback, psychology/ or feedback, sensory/ or gestalt therapy/ or hypnosis/ or "imagery (psychotherapy)"/ or music therapy/ or nondirective therapy/ or psychoanalytic therapy/ or psychotherapeutic processes/ or psychotherapy, brief/ or psychotherapy, multiple/ or psychotherapy, rational-emotive/ or reality therapy/ or socioenvironmental therapy/ or milieu therapy/ or psychotherapy, group/ or residential treatment/ (97310)</p> <p>65 caregiver.mp. or exp Caregivers/ (19829)</p> <p>66 63 or 64 or 65 (466935)</p> <p>67 Randomized controlled trials as Topic/ (69288)</p> <p>68 Randomized controlled trial/ (295289)</p> <p>69 Random allocation/ (69268)</p> <p>70 Double blind method/ (106498)</p> <p>71 Single blind method/ (14313)</p> <p>72 Clinical trial/ (454121)</p> <p>73 exp Clinical Trials as Topic/ (232670)</p> <p>74 or/67-73 (747202)</p> <p>75 (clinic\$ adj trial\$1).tw. (154141)</p> <p>76 ((singl\$ or doubl\$ or treb\$ or tripl\$) adj (blind\$3 or mask\$3)).tw. (106622)</p> <p>77 Placebos/ (28794)</p> <p>78 Placebo\$.tw. (127917)</p> <p>79 Randomly allocated.tw. (12611)</p> <p>80 (allocated adj2 random).tw. (664)</p> <p>81 or/75-80 (322595)</p> <p>82 74 or 81 (851677)</p> <p>83 Case report.tw. (161144)</p> <p>84 Letter/ (707425)</p> <p>85 Historical article/ (266371)</p> <p>86 Review of reported cases.pt. (0)</p> <p>87 Review, multicase.pt. (0)</p> <p>88 or/83-87 (1125400)</p> <p>89 82 not 88 (827326)</p> <p>90 dementia.mp. or exp Dementia/ (115412)</p> <p>91 66 and 89 and 90 (1364)</p> <p>92 limit 91 to yr="2008 -Current" (327)</p>
Note	

Cochrane Library

Date	28-01-2011		
Database	Database: Cochrane library – Clinical trials		
Search Strategy (attention, for PubMed, check « Details »)	ID	Search	Hits
	#1	MeSH descriptor Dementia explode all trees	3193
	#2	dement*	8483
	#3	(#1 OR #2)	9182
	#4	MeSH descriptor Psychotherapy explode all trees	11635
	#5	Cognitive Therapy or behavioural therapy or Behavior Therapy	24176
	#6	Psychotherapy or Multiple Psychotherapy or Imagery or Group Psychotherapy or Brief Psychotherapy or Rational-Emotive Psychotherapy	6915
	#7	Reality Therapy or reality orientation	461
	#8	signposting	2
	#9	Interpersonal Relations or interpersonal communication	1662
	#10	MeSH descriptor Interpersonal Relations explode all trees	3148
	#11	unlocking doors	4
	#12	group living or group homes	43750
	#13	MeSH descriptor Group Homes explode all trees	41
	#14	validation therapy	1264
	#15	standard therapy	30949
	#16	alternative therapy	13634
	#17	MeSH descriptor Complementary Therapies explode all trees	10496
	#18	alternative medicine	6640
	#19	art therapy	6016
	#20	MeSH descriptor Art Therapy explode trees 1 and 2	31
	#21	Music Therapy	788
	#22	MeSH descriptor Music Therapy explode trees 1 and 2	371
	#23	massage or touch	2924
	#24	white noise	204
	#25	natural elements	282
	#26	reminiscence therapy	85
	#27	MeSH descriptor Occupational Therapy explode all trees	424
	#28	activity therapy	28890
	#29	complementary therapy	2424
	#30	aromatherapy	179
	#31	MeSH descriptor Aromatherapy explode trees 1 , 2 and 3	83
	#32	Phototherapy or bright-light therapy	1199

#33	MeSH descriptor Phototherapy explode all trees	1676
#34	Physical Stimulation or Hydrotherap* or multisensory approach* or Sensory Art Therap*	2705
#35	multisensory stimulation	40
#36	Photic Stimulation	919
#37	MeSH descriptor Photic Stimulation explode all trees	857
#38	MeSH descriptor Relaxation Therapy explode all trees	1153
#39	snoezelen	38
#40	MeSH descriptor Sensory Art Therapies explode all trees	1225
#41	cognitive-behavioural therapy	3303
#42	cognitive-behavioural therapy	3303
#43	cognitive training	2725
#44	physical touch	302
#45	interpersonal therapy	1382
#46	self maintenance therapy	1157
#47	simulated presence therapy	101
#48	acupuncture	5690
#49	exercise therapy	17299
#50	MeSH descriptor Exercise Therapy explode all trees	4432
#51	kinesiotherapy	210
#52	MeSH descriptor Physical Therapy Modalities explode all trees	10898
#53	Rehabilitation or rehabilitative care	21467
#54	MeSH descriptor Rehabilitation explode all trees	10716
#55	Activities of Daily Living or daily life activity	7486
#56	MeSH descriptor Activities of Daily Living explode all trees	3180
#57	therapy	294210
#58	(#56 AND #57)	1962
#59	communication	7160
#60	MeSH descriptor Communication explode tree I	3422
#61	interpersonal communication	434
#62	social interaction	2037
#63	intervention	83022
#64	(#59 OR #60 OR #61 OR #62)	10683
#65	(#63 AND #64)	4475
#66	environmental manipulation	86
#67	mirror*	648
#68	(#66 AND #67)	1
#69	staff education	1795

	#70 MeSH descriptor Inservice Training explode all trees	441
	#71 MeSH descriptor Education, Nursing, Continuing explode all trees	221
	#72 MeSH descriptor Education, Nursing explode all trees	527
	#73 structured activity	4130
	#74 montessori	9
	#75 electroconvulsive therapy	768
	#76 MeSH descriptor Electroconvulsive Therapy explode all trees	465
	#77 ECT	787
	#78 Transcutaneous electric* nerve stimulation or TENS	18648
	#79 MeSH descriptor Transcutaneous Electric Nerve Stimulation explode trees 1 and 2	573
	#80 non-pharmacologic* or nonpharmacologic* or non pharmacologic*	5457
	#81 caregiv*	3255
	#82 restraint adj2 free	3
	#83 dog assist*	62
	#84 psychosocial adj2 intervention*	84
	#85 behavioural therapy	9927
	#86 behaviour therapy	14496
	#87 (#4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32 OR #33 OR #34 OR #35 OR #36 OR #37 OR #38 OR #39 OR #40 OR #	178949
	#88 (#87 AND #3), from 2008 to 2011	790
Note		

PsycINFO

Date	03-02-2011
Database	PsycINFO 1806 to January Week 4 2011
Search Strategy	<p>1 exp Dementia/ (39567)</p> <p>2 exp Alzheimer's Disease/ (23783)</p> <p>3 1 or 2 (39567)</p> <p>4 Creative Arts Therapy/ or Art Therapy/ or dance therapy/ or music therapy/ or recreation therapy/ or alternative medicine/ or acupuncture/ or exp Aromatherapy/ or phototherapy/ or rehabilitation/ or cognitive rehabilitation/ or occupational therapy/ or exercise/ or photopic stimulation/ or exp relaxation therapy/ or animal assisted therapy/ or autogenic training/ or guided imagery/ or behavior therapy/ or brief psychotherapy/ or client centered therapy/ or cognitive therapy/ or group psychotherapy/ or reality therapy/ or rational emotive behavior therapy/ or gestalt therapy/ or hypnosis/ or exp psychoanalysis/ or psychotherapeutic processes/ or rational emotive behavior therapy/ or reality therapy/ or milieu therapy/ or interpersonal relationships/ or group homes/ or physical</p>

	<p>contact/ or reminiscence/ or biofeedback/ or neurotherapy/ or electroconvulsive shock therapy/ or inservice training/ or mental health inservice training/ or nursing education/ (165928)</p> <p>5 (psychotherapy or reality orientation or signposting or "unlocking doors" or group living or validation therapy or standard therapy or Complementary Therap\$ or alternative therapy or alternative medicine or art therapy or music or (massage or touch) or "white noise" or natural elements or reminiscence therapy or activity therapy or Aromatherapy or bright-light therapy or Physical Stimulation or Hydrotherapy or multisensory approaches or multisensory stimulation or Photic Stimulation or snoezelen or Sensory Art Therapies or cognitive-behavioural therapy or cognitive stimulation or cognitive training or physical touch or interpersonal therap\$ or self maintenance therapy or simulated presence therapy or acupuncture or exercise therapy or Physical Therapy Modalities or kinesiotherapy or rehabilitative care or staff education or staff training or structured activity or montessori or electroconvulsive therapy or ECT or (Transcutaneous electric* nerve stimulation or TENS) or (non-pharmacologic* or nonpharmacologic* or non pharmacologic*) or feedback, psychological or residential treatment).mp. [mp=title, abstract, heading word, table of contents, key concepts] (149674)</p> <p>6 exp "activities of daily living"/ (3222)</p> <p>7 daily life activity.mp. (20)</p> <p>8 therap\$.mp. (335271)</p> <p>9 6 or 7 (3237)</p> <p>10 8 and 9 (526)</p> <p>11 interpersonal communication/ (11963)</p> <p>12 interpersonal communication.tw. (2351)</p> <p>13 communication/ (12852)</p> <p>14 communication.tw. (92824)</p> <p>15 social interaction.tw. (12079)</p> <p>16 intervention.mp. (120239)</p> <p>17 11 or 12 or 13 or 14 or 15 (109262)</p> <p>18 16 and 17 (7044)</p> <p>19 exp Caregivers/ (14007)</p> <p>20 4 or 5 or 10 or 18 or 19 (278843)</p> <p>21 (Random* and trial*).mp. [mp=title, abstract, heading word, table of contents, key concepts] (24530)</p> <p>22 3 and 20 and 21 (248)</p>
Note	Only 247 citations captured in Library from KCE

6.8 APPENDIX 8 QUALITY APPRAISAL FOR RCTS

RCTs with low risk of bias (included)

Study	Appropriate and clearly focussed question?	Internal validity						Overall assessment			
		Randomised?	Observer blinded?	Allocation concealment?	Patient group comparable?	Dropouts and intervals described?	Analyses conducted in ITT population?	Bias minimisation?	If biased, how would bias affect results?	Research question answered?	Risk of bias
Bellantonio 2008 ⁵⁸	Adequately addressed	Adequately addressed	Not reported	Not addressed	Adequately addressed	Adequately addressed	Not addressed	Control subjects lived in same facility so may have been influenced by intervention	May favour control group	partly	low
Clare 2010 ⁴⁶	Adequately addressed	Adequately addressed	Adequately addressed	Adequately addressed	Well covered	Adequately addressed	Not addressed	Low likelihood of bias	-	yes	low
Deudon 2009 ⁶³	Adequately addressed	Poorly addressed	Adequately addressed	Not addressed	Adequately addressed	Adequately addressed	Not addressed	MD in nursing home allocated patients to study so not truly randomised : possible selection bias. Some differences between intervention and control group	Differences in CMAI scale became similar after baseline measurements	yes	low
Eggermont 2009 ⁴⁸	Adequately addressed	Adequately addressed	Adequately addressed	Not addressed	Adequately addressed	Adequately addressed	Poorly addressed	Low likelihood of bias	-	yes	low

Study	Appropriate and clearly focussed question?	Internal validity						Overall assessment			
		Randomised?	Observer blinded?	Allocation concealment?	Patient group comparable?	Dropouts and intervals described?	Analyses conducted in ITT population?	Bias minimisation?	If biased, how would bias affect results?	Research question answered?	Risk of bias
Brodsky 2009 ⁵⁹	Well covered	Poorly addressed	Adequately addressed	Not reported	Adequately addressed	Well covered	No (modified, 3 patients excluded)	Due to nature of interventions some bias may exist, no allocation concealment reported.	Bias may have occurred during the short intervention but long follow up period. Results may favour treatment arm	Yes	low
Burns 2009 ⁴⁵	Adequately addressed	Adequately addressed	Adequately addressed	Poorly addressed	Adequately addressed	Adequately addressed	Yes	Low likelihood of bias	-	Yes	Low

Study	Appropriate and clearly focussed question?	Internal validity						Overall assessment			
		Randomised?	Observer blinded?	Allocation concealment?	Patient group comparable?	Dropouts and intervals described?	Analyses conducted in ITT population?	Bias minimisation?	If biased, how would bias affect results?	Research question answered?	Risk of bias
Charlesworth 2008 (HTA) ⁶¹	Well covered	Well covered	Adequately addressed	Adequately addressed	Well covered	Well covered	Yes	Recruitment bias as carers volunteered for the study after having initial information given therefore potential bias here as these carers may have had specific need for a befriender. Additionally carer contacts were given to the BF who then contacted the carer; the pilot of this study waited for carers to contact the BF, which they declined to do.	Results could favour the intervention	Yes	low

Study	Appropriate and clearly focussed question?	Internal validity						Overall assessment			
		Randomised?	Observer blinded?	Allocation concealment?	Patient group comparable?	Dropouts and intervals described?	Analyses conducted in ITT population?	Bias minimisation?	If biased, how would bias affect results?	Research question answered?	Risk of bias
Charlesworth 2008b ⁶⁰	Adequately addressed	Well covered	Adequately addressed	Adequately Addressed	Adequately addressed	Well covered	No	Participating subjects could not be blinded due to the nature of the intervention therefore some bias may exist	Results may favour treatment arm	Yes	low
Chien 2008 ⁶²	Adequately addressed	Poorly addressed	Adequately addressed	Not reported	Adequately addressed	Well covered	Yes	Due to nature of interventions some bias may exist, no allocation concealment reported	Results may favour treatment arm	Yes	low
Cooke 2010 ⁴⁷	Well covered	Adequately addressed (crossover trial)	Adequately addressed	Not addressed	Well covered	Well covered	Yes	Good crossover design and investigator blinding	Negligible effect on outcomes	Yes	low
Dias 2008 ⁶⁴	Adequately addressed	Well covered	Adequately addressed	Adequately addressed	Adequately addressed	Well covered	Not reported	Participating subjects could not be blinded due to the nature of the intervention, therefore some bias may exist	Results may favour treatment arm	Yes	low

Study	Appropriate and clearly focussed question?	Internal validity						Overall assessment			
		Randomised?	Observer blinded?	Allocation concealment?	Patient group comparable?	Dropouts and intervals described?	Analyses conducted in ITT population?	Bias minimisation?	If biased, how would bias affect results?	Research question answered?	Risk of bias
Eggermont 2009b ⁴⁹	Adequately addressed	Poorly addressed (cluster randomization)	Adequately addressed	Not addressed	Adequately addressed	Adequately addressed	Yes and PP	Bias minimised by blinding of investigators but some selection bias as cluster randomisation with individuals chosen for participation by nursing staff based on their motivation	Results may favour the intervention	Yes	low
Eloniemi-Sulkava 2009 ⁶⁵	Well covered	Well covered	Poorly addressed	Adequately addressed	Adequately addressed	Adequately addressed	Yes	Bias possibly due to no investigator blinding and inability to blind participants	Results may favour the intervention	Yes	low
Gallagher-Thompson 2008 ⁶⁶	Adequately Addressed	Adequately Addressed	Adequately Addressed	Adequately Addressed	Adequately Addressed	Adequately Addressed	Yes	Long period between initial contact and start of study caused 47 (20%) to decline to continue, this may have introduced selection bias.	Results may not be applicable to all carers if only the more motivated caregivers remain in the study	Yes	low

Study	Appropriate and clearly focussed question?	Internal validity						Overall assessment			
		Randomised?	Observer blinded?	Allocation concealment?	Patient group comparable?	Dropouts and intervals described?	Analyses conducted in ITT population?	Bias minimisation?	If biased, how would bias affect results?	Research question answered?	Risk of bias
Gavrilova 2009 ⁶⁷	Poorly addressed	Well covered	Adequately addressed	Not addressed	Adequately addressed	Adequately addressed	Reported as intention to treat, but only for those who completed 6 month follow-up	Bias minimised by Investigator blinding. Differences in baseline demographics, more need for 'care much of the time', in control.	Results were adjusted for difference in baseline but may favour the intervention	Yes	low
Gitlin 2008 ⁵⁰	Well covered	Adequately addressed	Adequately addressed	Adequately addressed	Poorly addressed	Adequately addressed	No	Participating subjects could not be blinded due to the nature of the intervention, therefore some bias may exist	Results may favour treatment arm	Yes	low
Gitlin 2010 ⁶⁸	Poorly addressed	Well covered	Adequately addressed	Well covered	Well covered	Adequately addressed	No	Bias minimised by investigator blinding but unable to blind participants. Baseline differences for agitated behaviour and education	Results may favour the intervention. Baseline difference may favour control group	Yes	low

Study	Appropriate and clearly focussed question?	Internal validity						Overall assessment			
		Randomised?	Observer blinded?	Allocation concealment?	Patient group comparable?	Dropouts and intervals described?	Analyses conducted in ITT population?	Bias minimisation?	If biased, how would bias affect results?	Research question answered?	Risk of bias
Gitlin 2010b ⁶⁹	Poorly addressed	Well covered	Poorly addressed	Adequately addressed	Adequately addressed	Adequately addressed	No	Some chance of bias as not possible to blind caregiver to intervention/control and no mention made of investigator blinding	Results may favour the intervention	Yes	low
Kemoun 2010 ⁵¹	Adequately addressed	Adequately addressed	Not addressed	Not addressed	Adequately addressed	Adequately addressed	Not addressed	Bias may occur due to no blinding.	Results may favour the intervention	Yes	low
Kuske 2009 ⁷⁰	Adequately addressed	Adequately addressed	Adequately addressed	Adequately addressed	Adequately addressed	Well covered	Not addressed	Differences in baseline characteristics between participants	Effect may be overestimated because of higher knowledge among control group caregivers	No clear conclusion	low
Lam 2010 ⁷²	Well covered	Well covered	Adequately addressed	Adequately addressed	Well covered	Well covered	Yes. Adequately addressed	Participating subjects and case managers could not be blinded due to the nature of the intervention therefore some bias may exist	Results may favour the treatment arm	Yes	low

Study	Appropriate and clearly focussed question?	Internal validity						Overall assessment			
		Randomised?	Observer blinded?	Allocation concealment?	Patient group comparable?	Dropouts and intervals described?	Analyses conducted in ITT population?	Bias minimisation?	If biased, how would bias affect results?	Research question answered?	Risk of bias
Lam 2010b ⁷¹	Adequately addressed	Poorly addressed	Adequately addressed	Poorly addressed	Adequately addressed	Adequately addressed	Yes	Adequate patient and investigator blinding; baseline differences in education only	Negligible effects from bias	Yes	low
Lynn Woods 2009 ⁵²	Adequately addressed	Adequately addressed	Adequately addressed	Not addressed	Adequately addressed	Not reported	Not addressed	Patients were given the choice of a 'little shoulder rub' and potentially did not all receive the same number of treatments	The effect would be in favour of the control group	yes	low
Martin-Carrasco 2009 ⁷³	Well covered	Well covered	Not addressed	Not addressed	Well covered	Adequately addressed	Not addressed	Bias may exist as neither allocation concealment nor blinding were mentioned.	Bias is likely to favour the treatment arm	Yes	low
Niu 2010 ⁵³	Adequately addressed	Adequately addressed	Adequately addressed	Not addressed	Adequately addressed	Adequately addressed	Yes	Investigator blinding, some chance of selection bias and very small cohort	Negligible effects on outcomes	Yes	low

Study	Appropriate and clearly focussed question?	Internal validity						Overall assessment			
		Randomised?	Observer blinded?	Allocation concealment?	Patient group comparable?	Dropouts and intervals described?	Analyses conducted in ITT population?	Bias minimisation?	If biased, how would bias affect results?	Research question answered?	Risk of bias
Nourhashemi 2010 ⁷⁴	Well covered	Adequately addressed (Cluster randomization)	Not addressed	Not addressed	Well covered	Well covered	Yes	No attempt to blind subjects or investigators. Strong possibility of bias	Results may favour either arm depending on investigator response to protocols	Yes	low
Pellfolk 2010 ⁷⁵	Well covered	Well covered	Poorly addressed	Poorly addressed	Adequately addressed	Adequately addressed	Adequately addressed	Some bias may exist as the article is not clear on blinding and allocation concealment	Results may favour the treatment arm	Yes	low
Riemersma-van der Lek 2008 ⁵⁴	Well covered	Adequately addressed (Cluster randomization + further randomization of subjects)	Adequately addressed	Not addressed	Adequately addressed	Well covered	No	Low likelihood of bias	Negligible effect on outcomes	Yes	low
Scheltens 2010 ⁵⁵	Adequately addressed	Well covered	Adequately addressed	Adequately addressed	Adequately addressed	Adequately addressed	Adequately covered	Very little bias exists in this study	Bias may favour the treatment arm as only patients with very mild disease were included in the study	Yes	low

Study	Appropriate and clearly focussed question?	Internal validity						Overall assessment			
		Randomised?	Observer blinded?	Allocation concealment?	Patient group comparable?	Dropouts and intervals described?	Analyses conducted in ITT population?	Bias minimisation?	If biased, how would bias affect results?	Research question answered?	Risk of bias
Schwenk 2010 ⁵⁶	Adequately addressed	Adequately addressed	Not addressed	Adequately addressed	Adequately addressed	Adequately addressed	Adequately addressed	Very little bias exists in this study. Some may result from having included only mild to moderate dementia patients	This may favour the treatment arm	Yes	low
Williams 2008 ⁵⁷	Adequately addressed	Adequately addressed	Adequately addressed	Not addressed	Adequately addressed	Adequately addressed	Yes	Small sample size could lead to bias. Significant difference in baseline MMSE scores and treatment intensity acknowledged by author	Unclear	Yes	low

RCTs with high risk of bias (excluded)

Burgener 2008 ⁸⁸	Adequately addressed	Poorly addressed	Not reported	Not addressed	Well covered	Adequately addressed	Not addressed	Method of randomisation not reported. Patients could self-refer into the study – possible selection bias?	-	yes	high
Connell 2009 ⁸⁹	Adequately addressed	Poorly addressed	Not reported	Not addressed	Adequately addressed	Adequately addressed	Not addressed	No specific minimisation	-	No clear conclusion	high
Donath 2010 ⁹⁰	Well covered	Poorly addressed	Not addressed	Not addressed	Not addressed	Poorly addressed	No	Cluster randomization of GMP's rather than patients. Baseline demographics of patients not addressed, drop outs of GMP's not addressed. No blinding reported	Generally poor study protocol, high likelihood of bias, therefore not extracted	Yes	high
Dowling 2008 ⁹¹	Well covered	Poorly addressed	Poorly addressed	Not addressed	Adequately addressed	Not reported	Not reported	No information regarding randomization procedure or concealment, blinding seemed to only to part of the intervention, drop outs not addressed, differences in baseline	High likelihood of bias therefore not extracted	Yes	high

								demographics			
Elliott 2010 ⁹²	Well covered	Poorly addressed	Not addressed	Not addressed	Adequately addressed	Not reported	Not addressed	Due to the nature of the intervention, bias is likely to arise. Blinding and allocation concealment were not specifically mentioned	The results would be biased in favour of the intervention	Yes	high
Fortinsky 2009 ⁹³	Adequately addressed	Poorly addressed	Poorly addressed	Not addressed	Poorly addressed	Adequately addressed	Poorly addressed	Sample size was too small ;underpowered study; intervention group was older		No	high
Fritsch 2009 ⁹⁴	Adequately addressed	Not reported	Not reported	Not addressed	Poorly addressed	Not addressed	Not addressed	Researchers were unable to identify in advance which special care unit residents would provide data and they were unable to limit their observations to residents who were only exposed to the TS intervention.. Additionally no pre-test observations were made,	The results would be biased as observations could not be limited to residents who were only exposed to the TS intervention. This bias could go either direction	No. Can't assess the impact of a program if you have not measured outcome variables prior to the intervention.	high

								only post –test.			
Gallagher Thompson 2010 ⁹⁵	Adequately addressed	Poorly addressed	Not reported	Not addressed	Adequately addressed	Adequately addressed	Not addressed	Small sample size and intervention (watching DVD) was self – reported so may not be reliable	Could influence treatment or control group	No	high
Gaugler 2009 ⁹⁶	Well covered	Adequately addressed	Not addressed	Not addressed	Poorly addressed	Adequately addressed	Not applicable	Some bias may exist due to the nature of the intervention. Allocation concealment was not mentioned. Imbalance in patient baseline characteristics.	Some bias may exist in favour of the treatment arm as there was no allocation concealment; however, this may be balanced by the fact that the 'usual care' group may have accessed more services than persons outside of the study.	Yes	high
Hawranik 2008 ⁹⁷	Adequately addressed	Poorly addressed	Adequately addressed	Not addressed	Adequately addressed	Not addressed	Not addressed	Investigators and practitioners were aware of the intervention group	Could favour intervention	No	high
Hicks-Moore 2008 ⁴⁴	Adequately addressed	Poorly addressed	Not addressed	Not addressed	Not addressed	Not addressed	Not addressed	The authors only addressed	Unknown	Yes	high

								that residents were randomly assigned to treatment or control groups, but overall, the authors did not address any other methods to minimise bias			
Kessels 2009 ⁹⁸	Adequately addressed	Poorly addressed	Not addressed	Not addressed	Adequately addressed	Not addressed	Not addressed	No information on randomization method or concealment of allocation.No blinding possible due to nature of intervention. No reference to drop outs Single task performed so maybe no drop outs and ITT analysis)	NA	Yes	high
Kurz 2010 ⁹⁹	Adequately addressed	Poorly addressed	Adequately addressed	Not addressed	Adequately addressed	Poorly addressed	Not addressed	Little information regarding randomization procedure, diff in baseline demographics. No information regarding drop outs	Not extracted as poor quality and likelihood of bias	Yes	high
Lin 2009 ¹⁰⁰	Well covered	Poorly	Adequately	Not addressed	Adequately	Not	Not	Some bias may	This may	Yes	high

		addressed	addressed		addressed	addressed	addressed	exist as randomisation was not described and dropouts were not mentioned.	favour treatment as if randomisation was not appropriate the already existing sampling bias may be increased.		
Lin 2010 ¹⁰¹	Adequately addressed	Poorly addressed	Adequately addressed	Not addressed	Poorly addressed	Adequately addressed	Not addressed	Cluster randomization lead to differences in baseline ADL which could bias results	SR group had highest ADL score therefore results could favour this intervention	Yes	high
Logsdon 2010 ¹⁰²	Not addressed	Poorly addressed	Not addressed	Not addressed	Poorly addressed	Adequately addressed	Yes	Little information on randomization, cluster method used. No blinding. Differences in baseline demographics	High likelihood of bias therefore not extracted	No	high
Neely 2009 ¹⁰³	Adequately addressed	Poorly addressed	Not addressed	Not addressed	Poorly addressed.	Poorly addressed	Poorly addressed	At baseline, verbal fluency test, control dementia significantly worse than collaborative group	Could favour collaborative group over dementia only group	No clear conclusions	high
Nourhashemi 2008 ¹⁰⁴	Adequately addressed	Adequately addressed	Not reported	Not addressed	Adequately addressed	Not addressed	Not addressed	Patients in the control group	The authors were aware	No	high

								had a higher baseline MMSE score – study shows interim results, follow up will be reported in later publications	of the effect and took it into account		
Moniz-Cook 2008 ¹⁰⁵	Adequately addressed	Poorly addressed	Not addressed	Not addressed	Adequately addressed	Adequately addressed	Not addressed	This study has high potential for bias as blinding and allocation concealment were not mentioned in the article	Bias would be likely to favour the treatment arm, but this could have been balanced out by the CMHNs not adhering to the protocol	Yes	high
Raglio 2008 ¹⁰⁶	Well Covered	Poorly addressed	Poorly addressed	Adequately addressed	Adequately addressed	Adequately addressed	Not addressed	There may be some bias present in this study.	Bias may favour the treatment arm as patients who showed negative acceptance were excluded from the study and assessment for communication (MTCS) was done	Yes	high

									only for the experimental group		
Rowe 2010 ¹⁰⁷	Well covered	Poorly addressed	Not addressed	Not addressed	Adequately addressed	Adequately covered	Poorly addressed	Some bias may exist as no allocation concealment mentioned. Also, participants initially randomised to the experimental group were switched to the control group.	Bias would be likely in the direction of the treatment	Yes	high
Salva 2009 ¹⁰⁸	Adequately addressed	Poorly addressed	Not addressed	Not reported	Adequately addressed	Not addressed	Yes	No specific minimisation	-	No clear conclusion	high
Spector 2010 ¹⁰⁹	Poorly addressed	Poorly addressed	Adequately addressed	Not addressed	Adequately addressed	Not addressed	Not addressed	Analysis of results from an earlier study, protocol may be better described earlier. Little information on randomization method, no information of drop outs	Due to lack of pertinent information bias cannot be ruled out in this study therefore not extracted.	Yes	high
Testad 2010 ¹¹⁰	Adequately addressed	Poorly addressed	Adequately addressed	Adequately addressed	Poorly addressed	Adequately addressed	Not addressed	Statistically significant diff between study groups: use of antipsychotics, restraints and	Differences between baseline characteristic could influence	yes	high

									CMAI score (higher in intervention group) could confound results	results towards or against intervention group		
Williams 2010 ¹¹¹	Adequately addressed	Poorly addressed	Poorly addressed	Not addressed	Poorly addressed	Well covered	No		Alternate allocation, not true randomization. No blinding. Significant differences in base line demographics	High likelihood of bias so not extracted	Yes	high
Visser 2008 ¹¹²	Adequately addressed	Poorly addressed	Not addressed	Not addressed	Adequately addressed	Poorly addressed	Poorly addressed		There is high level of bias in this study	The high attrition rate in the education only group and the subsequent removal of that group from follow-up analyses may bias results in favour of the other arms	No	high
Zhao 2009 ¹¹³	Adequately addressed	Adequately addressed	Not reported	Adequately addressed	Adequately addressed	Poorly addressed	Not addressed		Bias does exist in this study	There is an almost 20% drop out rate and observer blinding was not described/	Yes	high

									discussed. The paper does not qualify which groups the drop-outs came from therefore making it difficult to say which treatment arm would be favoured		
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6.9 APPENDIX 9. DATA EVIDENCE TABLES FOR THE 30 INCLUDED RCTS

Reference, Country	Setting	Number of patients	Patient characteristics and type of dementia	Patients diagnosed? If yes, criteria for diagnosis	Details of intervention	Details of comparator	Outcome	Time of follow up	Effect between groups?	Abacus' interpretation of value of RCT for decision making
Bellantonio 2008 ⁵⁸ United States	Dementia-specific assisted living facilities	100 Intervention=48 Control=52	Type of dementia not reported but was not a high-risk dementia population.	Not stated	Four systematic, multidisciplinary assessments conducted by a geriatrician or geriatrics advanced practice nurse, a physical therapist, a dietician, and a medical social worker during the first 9 months of their residence in assisted living	Usual clinical care consisted of a medical evaluation conducted by the resident's primary care physician 30 days before move-in or within 7 days of admission.	Permanent relocation (transition) to a nursing facility, emergency department (ED) visits, hospitalizations, and death.	Independent assessment occurred at Days 7, 30, 120, and 320 after admission.	The intervention reduced the risk of all transition types, although none reached statistical significance.	No strong conclusions can be gained from this study. A diagnosis of dementia was not confirmed. In addition, the intervention may have been implemented too infrequently to have an effect.

Reference, Country	Setting	Number of patients	Patient characteristics and type of dementia	Patients diagnosed? If yes, criteria for diagnosis	Details of intervention	Details of comparator	Outcome	Time of follow up	Effect between groups?	Abacus' interpretation of value of RCT for decision making
Brodsky 2009 ⁵⁹ Australia, United Kingdom, United States	Outpatients and spouse caregivers	158 patient/ care giver dyads Treatment: UK=27 USA=26 Australia=26 Control: UK=24 USA=26 Australia=26	Alzheimer's disease, GDS score of 4-5	NINCDS-ADRDA and DSM-IV criteria for probable Alzheimer's.	Donepezil (24 months), plus 5 counselling sessions based on the NYU intervention for caregivers and family with a theme of emotional support and assistance for the spouse. Additional ad hoc counselling by telephone + usual care	Donepezil (24 months) + usual care	Caregiver depression (BDI-II) and social support. Patient assessment (MMSE; GDS; ADSC-Cog; ADSC-ADL; RMBPCL. Care givers rated patient physical health using OARS; time to nursing home placement	Every 3 months in the first year and every 6 months in the second year then periodic contact for up to 8.5 years (mean 5.4 SD 2.4 years)	No difference in time to nursing home placement between groups except in Australia (P=0.044). No difference in time to mortality	Showed no changes in time to NH placement or mortality with additional spouse counselling, however only 5 sessions in a mean of 5.4 years follow up is only a minimal intervention
Burns 2009 ⁴⁵ United Kingdom	Two nursing homes for patients with dementia	Total N=48. Bright light therapy (BLT) N=22; Control N=26	Dementia with sleep disruption and agitated behaviours	WHO (1993)	BLT 1000 Lux for 2 hours per day (light box) with a nurse chatting/distracting patient to help them remain for the two hours	Two hours of standard light (100 Lux) in a light box with nurse chatting/distracting	MMSE; CSDD; MOUSEPAD; CRBRS; sleep charts; Mean activity counts per hour (10 most active hours and 5 least active hours in 24 hour period) using an activwatch.	Assessments at baseline, 4 and 8 weeks	Limited evidence of reduction in agitation. Non-significant improvements in sleep duration in both groups. No significant effects on change in MMSE score.	Data do not allow supporting conclusion that BLT is "a potential alternative to drug therapy in people with dementia who are agitated." No significant difference in agitation vs control group, possibly due to low sample size
Charlesworth 2008 (HTA) ⁶¹ United Kingdom	Carers who cohobited with community dwelling dementia	N=116 intervention; N=120 control	Primary progressive dementia	No specific diagnosis although Alzheimer's patients	Usual care plus access to an employed befriender (BF) and offer of contact	Usual care, typically diagnostic clinics (memory clinics);	Depression, anxiety(HADS); loneliness; QOL (for QALYs EQ-5D); positive and	6, 15 and 24 months	No evidence of effectiveness or cost-effectiveness from the primary analysis of ITT	Potentially limited use as some recruitment bias and mixed population. Protocol changed

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	sufferers and provided at least 20 hours/week of care			probably included; the difficulty in making a specific diagnosis is cited as a reason not to make AD an inclusion criteria	with a volunteer befriender for at least 6 months. BF provided companionship and conversation for emotional support of carer. Limited informational support	community support for challenging behaviours (Community psychiatric nurses); Short and long term respite care; assistance with washing, dressing and eating for the more dependent patients. Carer information and support groups; lunch clubs	negative affectivity (PANAS); Objective burden (CADI); relationship quality (MCBS); perceived loss of companionship; social support (PANT scale); perceived social support (MSPSS); coping (COPE); life events (LTE); resource use (CSRI, CTQ, CAS, RUD)		population. Some evidence approaching significance for a reduction in depression (HADS) for those carers who befriended the facilitator for 6 months or more	from an 'opt in' arrangement to proactive contact from BF due to low uptake in pilot. Hard to pin point what the BF scheme was offering over and above the usual care that is stated. Authors conclude that BF is neither effective nor cost-effective.
Charlesworth 2008b ⁶⁰ United Kingdom	Outpatients and family caregivers in community setting	N=116 intervention; N=120 control	Primary progressive dementia	Not reported	Local befriending scheme (BECCA), offering emotional support through companionship and conversation. Plus usual care	Usual care by health, social or voluntary services including community psychiatry; day hospitals/centres; home, personal and respite care; carer's information and support groups	Carer's wellbeing HADS; EuroQOL VAS; PANAS; MSPSS. Institutionalisation and death of patient	6, 15 and 24 month follow up with data at 15 months being the main outcome data	No evidence for a benefit of intervention over control at any time point	Befriending scheme has been shown of low value, possibly due to low uptake as high levels of family support already available in this trial

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Chien 2008 ⁶² Hong Kong	Family caregivers of outpatients in dementia care centres	44 pairs in intervention and control groups Dementia care management program (N=44) Standard care (N=44)	80% were early 'ambulatory' stage with moderate levels of impairment	Diagnosed as having a type of dementia caused by Alzheimer's disease, according to DSM-IV criteria	Dementia care management programme: education and support group delivered by case managers to tailor needs specifically to each patient	Standard care plus 6 monthly education sessions	QOL and service use for carers and patients	6 and 12 months	Significant between group differences in: Care givers burden and QOL; Patient symptom severity; Frequency and length of institutionalisation; Family service utilization	Useful but cultural differences have to be considered. Lack of clarity of nature of intervention provided.
Clare 2010 ⁴⁶ United Kingdom	Outpatient, community-based	69 Cognitive rehabilitation (CR) (n=23) Relaxation therapy (n=24) No treatment (n=22)	Alzheimer's disease early stage; MMSE>18 and be on AChEI medication for 4 weeks	NINCDS	Patients identified 5 personally relevant goals using the COPM tool with the help of a research assistant. Cognitive rehabilitation (CR) (n=23) involved 8 1 hr weekly sessions addressing personal goals.	2 patient groups: Relaxation therapy (n=24) and no treatment (n=22)	COPM at 7 days Secondary outcome s: Rivermead Behavioural Memory test II; verbal fluency; map search, elevator counting, and elevator counting with distraction subtests from the Test of Everyday Attention; Independent Living Scales, Health and Safety subtest HADS; QoL-AD scale self-and informant ratings. Instrumental Activities of Daily Living Scale and Physical Self-Maintenance Scale and the (MARS)	8 weeks and 6 months (all groups)	Patients in the CR group showed significant improvement in ratings of goal performance and satisfaction on the COPM scale, with large effect sizes (Cohen's d ≥0.8) in comparison with both an active control and treatment as usual.	CR showed benefits in patients with early stage Alzheimer's disease possibly due to the programme being tailored around individual goals. Study was powered to detect a large effect size, despite small sample size

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							Memory Functioning and Memory Performance subscales. World Health Organization Quality of Life Assessment, short version; General Health Questionnaire-12; HADS; and Relatives' Stress Scale			
Cooke 2010 ⁴⁷ Australia	2 mixed gender age care facilities with both low and high assistance patients	N=47 allocated. Arm 1 intervention control n=24; arm 2 control then intervention n=23	Confirmed dementia or probable dementia or features consistent with Alzheimer's disease	DSM-IV and MMSE 12-24	Music sessions led by a musician, 40 minutes 3 times/wk. Live group interactions, singing, dancing and playing instruments to familiar songs	Reading session led by a research assistant, interactive reading of books, local news etc, jokes and quizzes	Severity of dementia MMSE; Dementia quality of life DQOL; depression GDS;	8 weeks x 8 weeks crossover with 5 week washout period between	The control/ reading group reported significantly higher mid-point feelings ($p<0.05$) of QOL belonging than the music group. When the first reading group crossed over into music their QOL scores decreased. When the first music group crossed over to reading their QOL scores increased	Well conducted study but small sample size and few significant results favouring either treatment. Treatments are not really compared, but concluded as both having an effect on improving self-esteem, belonging and depression.
Eggermont 2009 ⁴⁸ Netherlands	Nursing homes	97 Intervention=51 Control=46	A diagnosis of dementia, ≥ 70 years of age, being able to walk for short distances	DSM-IV criteria	30 minute walks at self-selected speed, with rest if required, conducted 5 times	Control group received social visits in the same frequency and duration.	Following tests were evaluated: Face recognition, picture recognition, eight	Baseline, post-intervention (day after 6 weeks of	No difference was found between the intervention and control groups	No value can be inferred from this RCT.

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			with or without a walking aid		a week for 6 weeks.		words test, digit span, category fluency, letter fluency.	intervention) and again after 6 weeks without treatment		
Eloniemi-Sulkava 2009 ⁶⁵ Finland	Spouses caring for a partner with dementia and living at home	125 couples; N=63 couples intervention; N= 62 couples control	Dementia minimum score 1.0 on CDR and maximum score 23 on MMSE	Etiological diagnosis of dementia based on specialist's examinations and CT or MRI of brain	Multi component support program with a Family Care Coordinator, a geriatrician, support groups for care givers and individualised services	Usual care from municipal or private sector plus information and referrals to community services and an opportunity to share feelings with the study nurse at each assessment	Time from enrolment to long term institutionalisation; use of services and service expenditure	Screening, baseline, 6 months, 12 months and 24 months	At 2 years the difference between groups for those in long term institutions was not significant but it had been at 1.6 years. Intervention led to significantly decreased use of community services and expenditures (p=0.03).	Interesting: long follow-up. There is an impact at 1.6 years on all outcomes under study, but disappears at 2 years.
Eggermont 2009b ⁴⁹ Netherlands	Nursing home residents	66 randomized; intervention N=34; control N=32	Dementia and >70 years	DSM-IV	Hand motor activity: 30 minutes 5 x per week performing hand movements designed for this population with a group instructor	Reading of books by a leader and general conversation	Assessment of cognitive function, 1) memory (RBMT). 2) Executive function (WMS-R). 3) Assessment of mood (GDS). 4) Assessment of the rest-activity rhythm (actiwatch)	6 weeks intervention then 6 weeks follow up	In mixed model analyses no significant group x time interactions were found on either cognitive, mood, or rest activity domains (ITT). In the PP analysis mood improved only in the intervention group (p=0.012 vs baseline)	Weak results but authors suggest that this intervention has a positive effect on mood.

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Dias 2008 ⁶⁴ United Kingdom	Community dwelling dementia sufferers and their principal caregiver	N=41 pairs intervention and N= 40 pairs control	Mild and moderate dementia (severe dementia excluded)	DSM IV and CDR	Home Care Advisors provided education about dementia and management of behaviours; support to the caregiver; referral to psychiatrists; networking of families; advice about government schemes for elderly	Education and information only	Caregiver mental health (GHQ); Zarit Burden Score; NPI-D; NPI-S; EASI; deaths	3 and 6 months	Treatment significantly affected GHQ and NPI-D (net reduction) at 6 months follow-up	Two out of five outcomes (caregivers) have significant differences between groups
Deudon 2009 ⁶³ France	Nursing homes	Intervention=158 Control=114	A mixture of Alzheimer's disease, vascular dementia, mixed dementia, dementia with Lewy bodies, frontotemporal dementia, non-specific dementia had an MMSE score ≤ 24 and BPSD at least once/week	Yes, ICD criteria	8 week staff education and training programme based on cards with guidelines on how to deal with BPSD and mini interventions.	Routine care in control nursing homes	CMAI and Observation scale	Baseline, week 8 (end of intervention period) and week 20	There was a significant decrease in the global CMAI score between baseline and week 8 (-7.8; $p > 0.01$) and between baseline and week 20 (-6.5; $p > 0.01$) in the intervention group but not in the control group. Similar pattern seen in OS.	Randomisation of care homes is appropriate when the intervention is directed at staff. Lack of clarity in the control arm. Further study of this intervention with longer term follow up is needed.
Gallagher-Thompson 2008 ⁶⁶ United States	At home caregivers of elderly relatives	184 care givers (95 NHW and 89 HL) Intervention N= 50 NHW and 47 HL:	Alzheimer's disease or other dementia divided into Non-Hispanic White (NHW) and Hispanic-Latino	Not reported	Coping with Caregiving (CWC) 13-16 week protocol driven treatment package. 4-8 caregivers per	Control is Telephone Support Condition (TSC), 13-16 week protocol	Depressive symptoms (CESD); Perceived psychological Stress (PSS-10); Conditional	Approx. 4 months intervention with follow up at approx. 6 months	CWC showed significantly greater improvement from pre to post results on measures of depressive	Well conducted study with caregivers showing a positive effect. Limitations: only female caregivers

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		Control N= 45 NHW and 42 HL	(HL) women by ethnicity		group met weekly for 2 hour sessions following a detailed treatment manual based on cognitive behaviour principles.	driven treatment package. Empathic support provided over the telephone for 15-20 minutes each week; total of 7 calls + educational materials etc	Bother (RMBPC-CB); Skill utilization (CBT)		symptoms, overall life stress and care giving specific stress than TSC regardless of ethnicity. Tests for mediation suggest that effective skill utilization may mediate the effect of treatment on outcome	from one ethnic group does not prove generalisation. Long term effects at different follow-up times needed.
Gavrilova 2009 ⁶⁷ Russia	Community dwelling patients and family/friend caregivers	60 couples, N= 30 intervention; N= 30 control	Dementia and aged 65 or over	DSM-IV	10/66 Caregiver training intervention. Five weekly 30 minute sessions focused on the caregiver. 3 modules, 1= assessment, 2= education, 3= training on problem behaviours + usual care	Waiting list (usual care at local Mental Health Research Centres) + usual care	Care Giver: Care giver burden (ZB); Care giver mental health (SRQ 20); Care giver QOL (WHOQOL-BREF). Patient : Behavioural and psychological symptoms of dementia (NPI-Q); QOL (DEMQOL)	6 months follow-up after 5 weeks of sessions	Intervention caregivers reported large and statistically significant net improvements in burden vs. control ; no differences in caregiver psychological distress and patient or care giver QOL	Reasonably well conducted study but small sample size may limit usefulness. The control group received medical care as usual, which was not further clarified
Gitlin 2010 ⁶⁸ United States	Community dwelling dementia patients with family	237 dyads randomized, N= 117 intervention, N= 120 control	Dementia	NINCDS/ADRD or MMSE <24	COPE program. Up to 10 sessions over 4 months with occupational therapists and two	Three telephone calls from research assistants using scripts and	Patients: Functional Independence (FIM); QOL (QOLAD);	Baseline, 4 months and 9 month assessments	Significant differences in intervention group at 4 months vs. control in functional dependence;	Convincing "perceived" short term results but questionable evidence for long

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	caregivers				sessions with an advance practice nurse. Assessment of patient capabilities and deficits, trained families in home safety, simplifying tasks and stress reduction.	educational materials	Activity engagement (5 item scale); Agitated behaviour (ABDS). Care giver: Wellbeing (PCI); Caregiver confidence, care giver evaluation of the study		improved engagement. Caregivers had improved wellbeing and confidence. There were no observed differences at 9 months for patients but there were perceived benefits for intervention care givers	term benefit of this intervention
Gitlin 2010b ⁶⁹ United States	Caregiver/patient dyads, carers live at home with patient	272 randomized, N=137 intervention; N=135 control	Diagnosed dementia, MMSE <24 and reporting upset >5 on a 10 point scale	MMSE	Advanced caregiver training (ACT) seeks to identify and then modify potential behaviour triggers to help caregivers eliminate, reduce or prevent the behaviours. 16 weeks with up to 9 occupational therapy (OT) sessions plus 2 nursing sessions, then 3 OT telephone contacts from 16 to 24 weeks	No treatment control	Patient: frequency of the targeted behaviour targeted by the caregiver as most distressing. Caregiver: caregiver upset and confidence in managing the targeted behaviour (scale 1-10); Wellbeing (ZB scale; CES-D,PCI), skill enhancement (TMSI); perceived benefit of study	16 weeks active intervention then 8 weeks follow up	At 16 weeks significantly more intervention caregivers reported improvement in targeted problem behaviour vs. control; Significant results in 8 other outcomes for patients and caregivers. Benefits were also seen at week 24, but for less outcomes then at 16 weeks (e.g. not significant for depression and need for simplification strategies)	This intervention with caregivers had a positive effect although it was not reported if investigators and caregivers were blinded, ACT showed significant improvements over control in "perceived benefit" in several behavioural outcomes both for caregivers as for persons with dementia. In addition, problematic

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										behaviour at follow-up may not be the same behaviour as before.
Gitlin 2008 ⁵⁰ United States	Community dwelling dementia sufferers and their principal caregiver who lived with them	30 pairs in each group	Dementia, MMSE <24	Not reported	Tailored Activity Program (TAP); 6x 90min home visits and 2x 15min phone calls by occupational therapists over 4 months. Written plan with target activities developed for patient and stress management for carers	Not stated, placed on waiting list for intervention	Frequency of occurrence of 24 behaviours in the patient recorded by carer (16 from ABDS, 2 from RMBPC and 4 others). CSDD for carer and patient. Activity engagement. Caregiver perception of QOL in patient using 12 item QOL-AD. Caregiver burden (Zarit Burden Scale); Care giver depression (CES-D); confidence; skill enhancement (TMSI)	4 months after baseline TAP, then after 4 months reassessed	Patient outcomes: treatment effect for frequency of behavioural occurrences; Greater activity engagement and ability to keep busy. Carer outcomes: Fewer hours doing things for patients, fewer hours 'on duty'; greater mastery; enhanced self-efficacy using activities; greater use of simplification techniques vs control. No difference in subjective burden	Positive conclusions of authors but patients ill-defined, lack of clarity of control, small sample size. Beneficial effects are not significantly different vs control
Kemoun 2010 ⁵¹ France	Nursing home inhabitants	38 patient included; N=20 intervention; N=18 control	Alzheimer type dementia	DSM-IV; MMSE<23; ability to walk 10m without assistance	Physical activity programme, 3 x 1 hour sessions per week for 15 weeks of 40 minutes exercise- walking,	Usual care and activities (no physical activities)	Walking assessment (Bessou Locomotor and SATEL software); Cognitive	19 weeks (assessments two weeks before and two weeks after 15	ERFC results significantly improved for intervention whilst control decreased (p<0.01). Intervention	Lack of blinding and small sample size; there was no additional one to one attention paid to control subjects

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					stamina, equilibrium through differing activities		assessment (French ERFC)	weeks of activities)	improved walking parameters significantly	which may overestimate effect in intervention group.
Kuske 2009 ⁷⁰ Germany	Six nursing homes for patients with dementia	Caregivers N=134; intervention (IG)=89; relaxation (RG)=90; control (CG)=94 Residents N=321 (IG= 107; RG=104; CG=110)	Dementia. (All staff from the targeted wards were invited to participate)	CDR \geq 1	Training modules for nursing home staff to improve caregivers knowledge. Focus on sensitisation to the experience of residents with dementia, communication competencies and special and adjuvant care methods requiring little effort (IG)	Two controls. 1) Relaxation group (care givers received relaxation training) RG 2) Wait list control (CG)	Patient assessment: 1) use of physical restraints; 2) use of sedative drugs. Caregiver assessment: 1) knowledge and competencies (GEROLF; MHQ); 2)level of burnout (MBI-D); 3) level of health complaints (BL)	Assessments at baseline, immediately after training and six months after training	Significant positive effects of programme immediately after; and at 6 months on the use of physical restraints. Overall competence improved in IG and RG groups. No effect on care-giver burnout, health complaints or use of sedative drugs in residents. RG better than IG in reducing care-givers' health complaints	Prolonged effect on the use of physical restraints even after cessation of the intervention; results cannot be extrapolated to another training program.
Lam 2010 ⁷² Hong Kong	Community dwelling	CM group, N=59 control group, N=43	Psychiatric and geriatric outpatients with mild dementia (Chinese). 65 years old or above.	Yes. Chinese Mini-Mental State examination scored 15 or above	Subjects assigned to a case manager (trained occupational therapist) for 4 months and regular home visits were carried out. Included assessment and advice, home based	One home visit for home safety performed by the same occupational therapist with the control trial at the beginning of the trial. Subjects had no access to case	Zarit Carer Burden Interview. General Health Questionnaire and the Personal Well-Being Index for adults. Use of Social care support. Burden of family caregivers. MMSE	Assessments occurred at baseline and at the 4 th and 12 th month after recruitment	At 4 th month – there were no significant changes in PWI-A, ZBI and GHQ scores in both groups. . No change in PWI-ID was observed in both groups At 12 th month – the caregivers of the	Although the primary objective was to decrease caregiver burden this did not seem to change significantly. However, family caregivers did seem to seek external support more readily

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					program on cognitive stimulation and case management (n=59)	management. (n=43)			CM group showed no significant changes in ZBI and PWI-A, but GHQ scores were increased (p=0.03 vs baseline). Use of domestic helpers and day care was greater in CM group at 4 th and 12 th month follow-up (p<0.05 vs baseline). MMSE did not differ between groups, but was decreased in both groups (p<0.05 vs baseline)	Depressive mood improved in the short term but benefit was not sustained. Helpful study, but in conducted in Hong Kong
Lam 2010b ⁷¹ Hong Kong	Social Centres and old age Homes in Hong Kong	74 randomized: N=37 intervention; N=37 control (ITT)	Mild to moderate dementia; CDR (1 or 2)	DSM-IV	Functional Enhancement Program; tailor made (chosen by the principle investigator (PI) based on the results of a pre-randomization questionnaire) functional and skills training from an occupational therapist (OT). 45 minute sessions	Skills training from OT (45 minutes twice weekly) in a mixed group with the intervention but their skill assignment was randomly chosen by the PI	Functional abilities (Chinese DAD and AMPS); Depressive mood (CSDD, NPI); Global cognitive function (Cantonese MMSE); General medical burden (CIRS)	8 weeks training and assessment at 1 month and 4 months after training completion	At 1 month both groups showed significant improvement in AMPS (p<0.05); at 4 months the intervention group showed significant further reduction in CSDD (p=0.02). Group difference in functional scores and mood changes were not significant	Reasonably well conducted study showing some benefits for teaching a tailor made skill program rather than just general skill training, but no comparison with a control having no training.

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					twice weekly.					
Lynn Woods 2009 ⁵² United States	Three nursing homes for patients with dementia.	65 participants. Treatment N=22; Placebo N=21; Control n=21 (1 drop out)	Moderate to severe dementia with behavioural symptoms (BSD)	DSM-IV; score ≥ 15 on BARS; MMSE < 25	Therapeutic Touch (TT), contact on the neck and shoulders twice daily (5-7 minutes). Two separate treatment phases of 3 days with 5 days between them and 5 days post treatment	Placebo (mimic treatment that looked identical to TT to the untrained eye) and control (usual care)	Behaviour observed and recorded by a trained research assistant for 10 hours per day (8am to 6pm). Salivary cortisol levels (on waking, 30mins later, 6 hours later, 12hours later)	20 days for entire protocol, measurements at 5 days post-treatment	Restlessness was significantly decreased in the intervention group compared to control during the second intervention period. There was a significant difference in morning cortisol variability among groups across time periods	Well conducted study but results show only slight evidence of an effect vs. control and are not significant vs. placebo (due to low sample size).
Martin-Carrasco 2009 ⁷³ Spain	Hospitals and non-hospital psychiatric outpatient clinics across Spain.	115 Intervention n=60 Control n=55	Participants were male or female caregivers living in the community with a patient, was aged 18 and over and directly cared for the patient for a minimum of 4 hours per day. The care recipient had to have been on treatment with rivastigmine at a dose of > 6mg/day for over 6 mths	Yes. Clinical diagnosis of AD (DSM-IV-TR criteria, mini-mental score = 10-26). Functional impairment (Lawton and Brody Scale and Katz Index)	Standard care, and psycho educational Intervention Program (PIP) consisting of 8 individual 90 min sessions, at 1-2 wk intervals over 4 months. The program incorporated elements of cognitive – behavioural guidance, such as training in the control of activation, cognitive	Standard care consisting of general information on how AD progressed, individualized information about the patient, both in person and over the telephone 'on demand', information leaflets about AD and information	Primary: Caregiver burden. Secondary: caregiver quality of life and caregiver mental health status, general health questionnaire, use of healthcare and social resources by caregiver and patient	Evaluation visits took place at 4 months (once PIP finished) and 10 months after the start of the study.	Caregiver burden as measured by the Zarit scale had a significantly larger reduction in the intervention group. (These differences were not statistically significant at 4 and 10 months). Caregiver quality of life was measured by the SF-36 questionnaire was significantly higher for the intervention group. However, for mental health, as	This intervention showed beneficial results in reducing caregiver burden which appears to extend to improvement in quality of life

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					restructuring techniques, problem solving and increasing rewarding activities.	about resources directed at caregivers available in their community. (n=55)			assessed by the GHQ-28, mean scores were lower in the IG than in the control group at 10 month follow-up ($p=0.0004$).	
Niu 2010 ⁵³ China	Military Sanatorium, Beijing	N=16 intervention; N= 16 control	Probable Alzheimer's Disease taking donepezil for at least 3 months at a stable dose	NINCDS-ADRDA. MMSE 10-24	Continued donepezil and twice weekly, 45 minute individual session with a trained activity therapist providing cognitive stimulation therapy based on a set of defined tasks	Continued donepezil and sessions (controlled for time and attention) with a caregiver for general conversation	Neuropsychiatric Inventory and MMSE	After the 10 weeks of intervention	NPI scores showed significant improvement vs a slight decline in control. MMSE significantly improved in treatment group (with 0.81) and declined in control (with -0.19)	Useful study, well conducted, but small sample size and population, (patients in a military sanatorium) may not translate to the general populace. The change in MMSE might not be have a clinical significance
Nourhashemi 2010 ⁷⁴ France	Memory Clinics in University and General hospital, community dwelling	N=574 intervention patients; N=557 control patients. N= 26 intervention hospitals; n=24 control hospitals	Probable or possible Alzheimer's disease; mild to moderate disease	NINCDS-ADRDA. MMSE 12-26	Six monthly comprehensive assessment and then standardised management protocols that could be initiated when necessary based on the assessment. Non-drug and drug interventions. The non-drug interventions were	Managed according to each centre's usual practice	Decline in functional capacities according to ADCS activities of daily living; rate of admission to institutionalised care and mortality	12 and 24 months assessment	Functional decline, risk of being admitted or mortality did not differ significantly between the two groups over two years. Admission in the intervention group was mostly due to reasons related to the caregiver whereas in the	The lack of clarity of interventions and usual care in control arm makes it difficult to perceive what the difference in care was

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					not specified. Package of written support material for carers				control group it was mostly due to worsening health of the patient	
Pellfolk 2010 ⁷⁵ Sweden	Nursing units	40 units. Staff 346. Residents – 353 Intervention group: 20 units Staff, n=205 Residents, n=192 Control group: 20 units Staff, n=188 Residents, n=163	Type of dementia was not outlined. As intervention was targeted to staff, patient characteristics were given as means	Yes. MDDAS, was used, but no ranges were given.	Education program for nursing staff conducted for 6 months (six 30 minute video-taped lectures). Staff = 184 Residents = 191	Not reported/ no education program. Staff = 162 Residents = 162	Staff - Use of physical restraints. Residents – Wandering behaviour and cognition. Falls	1 month after the education program	Staff – In the intervention group they were less prone to use physical restraints (p=0.001), and their estimated knowledge of dementia had increased significantly. Residents – In the analyses including all residents present at baseline and follow-up, cognitive levels were significantly different between the intervention and control groups. In residents present at baseline and follow-up, there was no significant difference between or within the proportion of fallers during a period 1 month	Very little conclusive evidence regarding cognitive and behavioural outcomes in residents can be drawn from this study based on video-taped lectures. The study does suggest that a decrease in use of restraints does not increase the proportion of falls experienced by residents Cognitive and behavioural outcomes were discussed in this study as a byproduct of the use of restraints and not necessarily as secondary outcome

Reference, Country	Setting	Number of patients	Patient characteristics and type of dementia	Patients diagnosed? If yes, criteria for diagnosis	Details of intervention	Details of comparator	Outcome	Time of follow up	Effect between groups?	Abacus' interpretation of value of RCT for decision making
									before and after the intervention. The same was found for residents present only at baseline or follow-up	in its own right.
Riemersma-van der Lek 2008 ⁵⁴ Netherlands	Residents of open care homes	Light, n= 49; Melatonin, n= 46; Light + melatonin, n= 49; Double placebo n= 45. 12 facilities and 189 total participants. 2x2 factorial design	Elderly patients with various diagnoses; 63% probable Alzheimer's; 11% vascular dementia; 13% other dementia; 8% other medical/psychosocial reasons for care + (8 subjects with insufficient data for diagnosis)	NINCDS-ADRDA; DSM-IV	Bright light therapy: increased illumination to +/- 1000 Lux between 10am and 6pm ; 2.5mg melatonin	Lighting similar to usual light intensity (new fixtures added to ensure staff blinding), +/-300 Lux; Placebo tablet	Cognitive and non-cognitive symptoms; functional abilities; sleep quality estimates. MMSE; CSDD; PGCMS; PGCARS; MOSES; NPI-Q; CMAI; NI-ADL. Actigraph recordings for 14 days	Up to 3.5 years, Mean 15 (SD 12) months	Light attenuated cognitive deterioration on MMSE (0.9 points relative 5%, p=0.04), depressive symptoms on CSDD (1.5 points relative 19%) and the increase in functional abilities NI-ADL (1.8 points per year relative 53%). Melatonin shortened sleep onset latency by 8.2 minutes and increased sleep duration by 27 minutes. Side effects of melatonin were seen on mood, but improved in the group receiving light	Useful well conducted study into this treatment modality in a mixed population with dementia. Results on sleep are clinically meaningful (+27 minutes/night) but side effects noted; More studies on melatonin warranted.
Scheltens 2010 ⁵⁵ The Netherlands,	AD treatment centres in the Netherlands,	225 patients 113 allocated to	Patients with very mild disease, 50 years and older;	Yes. Diagnosis of probable AD according	Souvenaid drink (containing fatty acids and vitamins)	Control product drink in a 125 ml	Cognitive functions	6, 12 and 24 weeks. With other visits	After substituting the planned mixed model analysis of 12	As only patients with mild disease were recruited, the

Reference, Country	Setting	Number of patients	Patient characteristics and type of dementia	Patients diagnosed? If yes, criteria for diagnosis	Details of intervention	Details of comparator	Outcome	Time of follow up	Effect between groups?	Abacus' interpretation of value of RCT for decision making
Germany, Belgium, United Kingdom, and United States	Germany, Belgium, United Kingdom and United States	active product 112 allocated to control product	with current status as an outpatient. Also 2 years postmenopausal or surgically sterile and Geriatric Depression Scale score of 4 or less on a 15- item scale	to criteria of National Institute of Neurological and Communicative Disorders and Stroke – AD and Related Disorders Association; MMSE score of 20-26 and a recent magnetic resonance imaging or computed tomography scan compatible with AD	in a 125 ml tetrapackage (choice of 2 flavours) to be taken each day at breakfast and consumed within the hour	tetrapackage (choice of 2 flavours) to be taken each day at breakfast and consumed within the hour	Primary: Delayed verbal recall test of the of the WMS-r and the 13 item modified ADAS-cog. Secondary: 24 week change from baseline on ADAS-cog and WMS-r delayed verbal task recall.	and phone calls to encourage protocol adherence.	week data with non-parametric analysis, a statistically significant improvement in WMS-r delayed recall was observed in the active group but not in the control group. At 12 weeks, 40% of the patients in the active group showed an improvement in WMS-r delayed recall compared to 24% in the control group. During this period, the modified ADAS – cog scores did not change in either group. No differences in secondary outcome measures were observed between groups.	clinical significance of the improved WMS-r improvement (but no improvement in ADAS-cog) is not clear, the value of this RCT is questionable Effect on one scale only out of two measurements. Possible conflict of interest (unrestricted funding and second author from a food company)
Schwenk 2010 ⁵⁶ Germany	Geriatric institution in Germany	61 Intervention=26 Control=35	Mild to moderate dementia. Geriatric patients	Yes. National Institute for Neurological and Communicative Disorders and Stroke – AD and Related Disorders Association; MMSE score of 20-26 and a recent magnetic resonance imaging or computed tomography scan compatible with AD	Specific dual task training and progressive resistance and functional balance	Supervised motor placebo group training , 2 times a week for one hour.	Gait analysis, cognitive performance (number of correct	Baseline and after 12 weeks of intervention	An insignificant trend of reduced DTC in gait speed and stride length was observed in the	Some value may be inferred from this RCT but results should be considered with

Reference, Country	Setting	Number of patients	Patient characteristics and type of dementia	Patients diagnosed? If yes, criteria for diagnosis	Details of intervention	Details of comparator	Outcome	Time of follow up	Effect between groups?	Abacus' interpretation of value of RCT for decision making
				e Disorders and Stroke-Alzheimer's Disease and Related Disorders Association. National Institute of Neurological Disorders and Stroke Association Internationale pour le Recherche en L'Enseignement en Neurosciences	training exercises, performed in groups of 4 to 6 persons for 12 weeks (2 hours, twice a week) and supervised by a qualified trainer. (n= 26)	Typical activities were flexibility exercise, callisthenics and ball games while seated. (n=35)	calculations), (assessed by CERAD)		IG, but it remained unchanged in the CG. Patients in the IG significantly improved in dual task motor performance compared to patients in the CG. For all cognitive domains assessed by CERAD, group x time interactions was not significant.	caution: as there is conflicting evidence on whether and how physical training shows effects on general cognitive performance in patients with dementia
Williams 2008 ⁵⁷ United States	Residents of long term care facilities	N=45. Exercise=16 Walking=17 Attention control=12	Patients with Alzheimer's disease and depression	NINCDS-ADRDA; CSDD (score 7 or above)	Comprehensive exercise plan or supervised walking. Interventions provided in individual sessions 5 days a week for a period increased until 30 min max reached	Attention control group (Social conversation) (Three arm study)	Effect of exercise on depression (CSDD)and mood (DMAS; AMS); Affect (OAS)	16 weeks	Depression was reduced in all three groups on CSDD and improvements also in most other tests. No evidence of significant improvements in either of the exercise groups over attention control	Very small sample size of the subgroups.

Abbreviations: ABD: Agitated Behaviour in Dementia; ABDS: Agitated Behaviours in Dementia Scale; ACT: Advancing Caregiver Training; ADAS-cog: Alzheimer's disease Assessment Scale – cognitive subscale; ADCS-ADL: Alzheimer's disease Cooperative Study – Activities of Daily Living; AMPS: Assessment of Motor and Process Skills; AMS:

Alzheimer's Mood Scale; BARS: Brief Agitation Rating Scale; BDI-II: revised Beck Depression Inventory; BECCA: Befriending and Costs of Caring; BL: Berchwerdeliste (Zerssen 1976); BSD: Behavioural Symptoms of Dementia; CADL: Carers Assessment of Difficulties Index; CAS: Caregiver Activity Schedule; CDR: Clinical Dementia Rating; CESD: Centre for Epidemiological Studies Depression Scale; CES-D: Centre for Epidemiological Studies Depression Scale; CIRS: Cumulative Illness Rating Scale; CMAI: Cohen-Mansfield Agitation Index; COPE: Brief Coping Orientation for Problem Experience; CRBRS: Crichton Royal Behaviour Rating Scale; COPM: Canadian Occupational Performance Measure; CSDD: Cornell Scale for Depression in Dementia; CSRI: Client Service Receipt Inventory; CTQ: Caregiver Time Questionnaire; DAD: Disability Assessment for Dementia; DEMQOL: Dementia specific health related quality of life; DMAS: Dementia Mood Assessment Scale; DQOL: Dementia Quality of Life; DSM IV: Diagnostic criteria for Dementia (American Psychiatric Society); EASI: Every Day Abilities Scale for India; Ed-FED: Edinburgh Feeding Evaluation in Dementia; EQ-5D: Euro-QoL 5 Dimensions; ERFC: Rapid Evaluation of Cognitive Function; FIM: Functional Independence Measure; GDS: Geriatric Depression Scale; GDS: Global Deterioration Scale; GEROLF: German benchmarking instrument to measure quality of life of geronto-psychiatric residents in nursing homes: (one for staff, one for patients); GHQ: Global Health Questionnaire; HADS: Hospital Anxiety and Depression Scale; HAS: Hamilton Anxiety Scale; MBI-D: Maslach Burnout Inventory; MCBS: Mutual Communal Behavioural Scheme; MHQ: Penn State Health Care-giving Questionnaire; MMSE: Mini-Mental Stated Examination; MNA: Mini-Nutritional Assessment; MOSES: Multi Observational Scale for Elderly Subjects; MOUSEPAD: Manchester and Oxford Universities Scale for the Psychological Assessment of Dementia; MSPSS: Multidimensional Scale of Perceived Social Support; MTCS: Music Therapy Coding Scheme; NIADL: Nurse Informant Activities of Daily Living; NPI-D: Neuropsychiatric Inventory (perceived distress by care giver); NPI-Q: Neuropsychiatric Inventory (Questionnaire); NPI-S: Neuropsychiatric Inventory (Severity of behaviours); NYU: New York University intervention; OAS: Observed Affect Scale; PANAS: Positive and Negative Affectivity Scale; PANT: Practitioner Assessment of Network Type scale; PCI: Perceived Change Index; PGCARS: Philadelphia Geriatric Centre Affect Rating Scale; PGCMS: Philadelphia Geriatric Centre Morale Scale; PSS-10: Perceived Stress Scale; QOLAD: Quality of Life in Alzheimer's disease scale; RBMT: Rivermead behavioural Memory Test; RMBPC: Revised Memory and Behavioural Problem Checklist (CB Conditional Bother); RMBPC: Revised Memory and Behaviour Problem Checklist; RMBPCL: Revised Memory and Behaviour Problems Checklist; RUD: Resource Use in Dementia; SRQ 20: Self Reporting Questionnaire 20; TMSI: Task Management Strategy Index; TT: Therapeutic Touch; WMS-R: Wechsler Memory Scale- Revised; ZB: Zarit Burden

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