

**Consensus Report**

**Review of Scientific Evidence Addressing Prevalence,**

**Documented Needs, and Interdisciplinary Research:**

**Persons in Early Stage Alzheimer's Dementia**

***Including Recommendations from the Panel of Experts***

**Submitted to:**

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## **A. Estimates of early-stage AD and future predictions**

Approximately 4.5 million people have Alzheimer's disease (AD) in the United States. It is estimated that by the year 2030, the rate will be 7.7 million, with an anticipated 13.2 million by 2050 (Hebert, et al., 2003). Overall prevalence of AD appears to double for every 5-year age group beyond age 65 (NIA, 2005). The prevalence of early stage AD is not clear. This relates, in part, to a historic lack of clarity in the terms, definitions, diagnostic criteria and methods that have been used for distinguishing early stage AD. Mild cognitive impairment (MCI) has been the most commonly used term to define the transition from normal cognition to probable AD. As the body of literature on MCI has developed, the parameters and limits of this diagnosis have become increasingly ambiguous (Winblad, Palmer, Kivipelto, et al., 2004) and considerable methodologic differences in defining MCI have been demonstrated (Luis, Loewenstein, Acevedo, Barker, & Duara, 2003).

Methodological variability in epidemiologic studies has made it difficult to determine prevalence, incidence and conversion rates to dementia of persons diagnosed with cognitive impairments (Luis, et al, 2003). In the last few years, considerable effort has been made to study and identify specific subtypes that will better distinguish and more accurately diagnosis MCI linked to early AD. Overall prevalence of MCI in population-based epidemiological studies has ranged from 3% to 19% in those 65 and older (Ritchie, 2004). More than half of these cases progress to dementia within a five year period. The Amnesic subtype of mild cognitive impairment (MCI with memory problems) has consistently demonstrated a high risk of progression to dementia, particularly dementia of the Alzheimer type (Gauthier, Reisberg, Zaudig, et al., 2006).

Some investigators consider MCI to be an early stage of AD (Morris, Storandt, Miller, et al., 2001), contending that in patients with amnesic MCI, followed longitudinally, the early changes of AD are present (Markesbery, Schmitt, Kryscio, Davis, Smith, & Wekstein, 2006). A revision of current diagnostic criteria is being suggested by some investigators to specifically diagnose early AD, including those individuals considered mildly cognitively impaired for whom the cognitive impairment represents the earliest clinical symptoms of AD (amnesic subtype of MCI) (Morris, 2006). There are investigators who believe that a revision of diagnostic criteria would permit the diagnosis of and thereby facilitate earlier intervention for early stage AD (Markesbery, et al, 2006; Morris).

Individuals most at risk for developing AD are those 85 and older. Relating to substantial decreases in mortality among the older population, we are seeing more people survive to ages where AD is more common as well as more people surviving after they are diagnosed with AD (NIA, 2005). Familial history is linked to the more uncommon early onset AD, developing in persons 30-60 years of age. For AD occurring in those over age 60 (the more common type), no familial link is evident (NIA, 2006).

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## **B. Documented Needs of Persons with Early Stage AD**

### **Search Method**

The literature search took place between November 11, 2006 and January 26, 2007. Databases used in the search include PubMed, CINAHL, PsychInfo, Web of Science, SportDISCUS, and the Cochrane Database of Systematic Reviews and included studies back to 1995 unless there were articles of an earlier date that provided insights with no more recent studies. The following terms were used initially: dementia; early stage; Alzheimer's Disease; dementia, multi-infarct; dementia, senile; limited to research. Mesh terms were cross referenced such as early stage dementia and needs, early stage dementia and interventions, MH program development, MH community programs, MH program evaluation, MH program implementation, MH program planning, MH program instruction and MH psychotherapy. Studies which looked primarily at caregivers were excluded from this search. When a citation was found, links to related studies from a study to be included in the review were also explored. Further searches were done on the names of authors in research articles found in the initial search as well as on the names of their projects. In addition searches were done on noted experts in the field. Professionals working in the field contributed lists of references on early stage Alzheimer's disease interventions as well. Once articles were included in this search, further references were found using the ancestry method. Our initial search results produced over 500 articles, 334 were selected for review, and 54 were determined to fit inclusion criteria.

### **Inclusion Criteria**

All research articles addressing need for persons with early stage dementia in some way were included. Since many studies defined their subject group as Mild Cognitive Impairment (MCI), yet upon review their inclusion criteria were the same as or overlapped the inclusion criteria this group used for early stage AD, these studies were included.

In this literature review, particularly when using the search term early stage, it became evident that there are few studies that focus exclusively on early stage. More often studies report a diagnostic parameter such as the MMSE or CDR, or combination of tools in their data, but often don't consider it as a variable in analysis, thus making stage specific interventions and needs difficult to ferret out. Further, frequently studies report the mean MMSE with standard deviation which demonstrates a range that goes from early stage to moderate stage, blending results as dementia as a whole and not specific to stage. Similar results are reported when the CDR is used. It is our feeling that to ignore this body of research would exclude many articles that have information relative to early stage dementia. Identification of needs for persons with AD (PwAD) in early stages was often implicit in the studies, and we chose to include that information in this review.

There is a need to determine whether or not MCI is an accepted diagnostic category or if those persons should be included in early stage discussions, since many of those "MCI" people will eventually be diagnosed with dementia.

### **Awareness in Persons with Early Stage Dementia**

Although not directly related to a need, the growing body of evidence concerning retained awareness in persons with early stage AD serves as background for the identification of evidenced-based needs. For several decades, it has been assumed that persons with AD, even in the early disease stages, were unaware of their disease, the implications of the disease for their lives, and disease-related losses. However, a growing body of evidence supports the existence of awareness in persons with AD. Awareness is relevant in the identification of needs, as needs associated with retained awareness may be appropriately identified. With retained awareness, a broader range of needs are evident such as needs related to protection of self-esteem, managing responses to the disease, personal control, education, and support. Retained awareness allows persons with AD the opportunity to share their perspective and, in some ways, to help determine their own quality of life (Burgener, Twigg & Popovich, 2005; evidence grade: C1; Clare, Markova, Merhey, & Kenny, 2005; evidence grade: A1). Clare and Wilson (2006; evidence grade: C1) have found that awareness of persons with AD persists long into the dementia process with no association between discrepancy scores (measure of awareness) and MMSE scores over time.

Knowledge regarding retained awareness in persons with AD impacts on program design and content, including the target of support programs. The caregiver has traditionally been the identified target for education, support, and intervention trials, based on the longstanding belief that the onset and progression of dementia is accompanied by disintegration of awareness. Although a study by Onor and colleagues (2006; evidence grade: C1) supports some decline in awareness, awareness can still be objectively assessed. Further, studies have indicated that caregiver assessments varied from the person with AD, even regarding awareness of caregiver emotions (Derouesne, 1999; evidence grade: C1; Starkstein, 1997; evidence grade: C1; Vasterling, 1997; evidence grade: C1). The perpetuation of awareness has implications for program development, content, and assessment of outcomes. This recent evidence supports that programs and assessments that rely on caregiver learning and evaluation are limited and may not adequately represent the person with AD. Many programs and studies preclude participation if a person with AD does not have a reliable informant, a practice that is no longer supported.

Further support for awareness of persons with AD comes from research targeted at the transition to AD. In a review of studies, Jonker and colleagues (2000; evidence grade: A1) evaluated the predictive value of memory complaints, indicating self-awareness of memory loss. The reviewers found that subjective memory is predictive of cognitive decline and dementia, particularly in individuals who already have some cognitive decline. Findings indicate the greater the subjective memory, the slower the decline and disease progression. These findings are supported by a more recent study by Jorm and colleagues (2005; evidence grade: C1). Higher levels of awareness are also related to better outcomes in cognitive rehabilitation interventions (Clare, Wilson, Carter, Roth, & Hodges, 2004; evidence grade: C1).

### **Need for Early Diagnosis**

The implications for need for early diagnosis are multifold. The earlier dementia is differentially diagnosed, the earlier both pharmacologic and non-pharmacological interventions are possible.

It is important to track changes over time with sensitive tools so that interventions may be targeted at regaining or compensating for failing skills or to minimize losses (Farias, Mungas, Reed, Harvey, Cahn-Weiner, & DeCarli, 2006; evidence grade: C1; Salmon & Lane, 2001; evidence grade: A1). Because of the growing emphasis on early detection and intervention in dementia care, the need for a clear evidence base for cognitive training and cognitive rehabilitation is increasingly needed (Woods, Moniz-Cook, Orrell, & Spector, 2006, Cochrane report; evidence grade: A1). Not only is there a need for early diagnosis, but the need for a more accurate diagnosis has been identified. Several studies have found that there are more than just cognitive changes that are evident in early stage, supporting the need to assess a variety of cognitive and functional domains (Artero & Ritchie, 2003; evidence grade: C1; Backman, Jones, Berger, Laukka, & Small, 2004; evidence grade: A1; Richards, Moniz-Cook, Duggan, Carr, & Wang, 2003; Evidence grade C1; Salmon & Lange, 2001; evidence grade: A1).

An early, correct diagnosis and treatment may also have a positive impact on the caregiver. Early interventions often include education and caregiver (CG) training. These types of programs are associated with reduction of CG burden and stressors as well as better outcomes for the person with AD. Both outcomes have been shown to decrease premature institutionalization (Doody, et al, 2001; evidence grade: B1; Farina, et al, 2006; evidence grade: C1; Gaugler, Kane, Kane, Newcomer, 2005; evidence grade: C1; Geldmacher, 2004; evidence grade: D; Zarit, Femia, Watson, & Rice-Oschger, 2004; evidence grade: C1).

Changes that progress beyond what is considered normal aging include not only memory impairment, particularly episodic memory, but research points to the occurrence of neuropsychological behavioral symptoms (NPBD) as mild cognitive impairments begin. The study by Lyketsos and colleagues (Lyketsos, Lopez, Jones, Breitner, DeKosky, 2002; evidence grade: C1) demonstrated that with the onset of dementia symptoms, more than 80% of persons with dementia or their caregivers report one or more NPBD symptoms, with about 50% of those with mild cognitive impairments. Along with the occurrence of these symptoms, there is greater report of caregiver depression. As there is more ADL dependence upon caregivers, caregiver burden also increases (Geldmacher, 2004; evidence grade: D; Lyketsos, et al, 2002; evidence grade: C1; Knopman, Boeve, & Peterson, 2003; evidence grade C1). This is further supported by the work of Richards and colleagues (2003; evidence grade: C1) who demonstrated that measures of psychosocial distress were more meaningful than measures of cognition alone when evaluating outcomes for community dwelling persons with dementia.

Farias and colleagues (2006; evidence grade: C1) conducted a study of the everyday functioning of three groups; a normal group, a group with MCI, and a group with AD. They found that while there was a change between groups in each variable measured, the changes were significant in the MCI group compared to the normal group. Of primary importance, this study adds to the body of knowledge that indicates a need for early diagnosis and that persons with mild cognitive impairments have sufficient functional impairments as to benefit from interventions. Even when people don't demonstrate adequate symptoms to meet DSM IV criteria, impairments impact their lives in important areas such as safety, work related functioning, and planning issues. Their functional deficits are significantly worse than unimpaired individuals (Knopman, Boeve, & Peterson, 2003; evidence grade C1). Researchers concur that impairments exhibited early in the

disease course affect more than memory. Other abilities affected may include: writing checks; paying bills; balancing the checkbook; assembling tax records; managing business affairs or papers; shopping alone for personal items, household goods, or groceries; heating water; working at the stove; preparing a balanced meal; remembering appointments, family events, or holidays; adhering to medication schedules; and/or traveling out of the neighborhood and driving.

The findings of these and other studies point to the needs of persons with MCI and early stage dementia related to memory, planning and language. Many of the tasks identified could be addressed through adaptive interventions. Program development is indicated for learning compensatory tools for memory and language skills, for example, memory tools such as notes, lists, cueing, calendars, simple directions, task breakdown, assistance with money management, long term planning and health care, work implications, driving implications, and safety implications. Professionals must consider that each person is at a different place in their decline and their abilities, so it takes knowing the person to adequately plan interventions. Group interventions are not always effective because of the participants' different functional levels.

In their evidenced-based review, Doody et al (2001; evidence grade: B1) found support for use of cholinesterase inhibitors early in the disease process. Early and accurate diagnoses may impact positively on appropriate medication prescription and usage. Clinical trials indicate that cholinesterase inhibitors have the potential to impact positively on a variety of outcomes, including cognition, global function, and ADLs. Some studies also indicate there is an effect on neuropsychological and behavior symptoms as well (Doody et al, 2001; evidence grade: B1; Gelmacher, 2004; evidence grade: D).

While there is a need for early diagnosis to help persons prepare and maintain abilities for as long as possible, it is also critical that the person in early stage AD does not become 'medicalized'. This type of medicalization of AD results in the person with dementia becoming lost in the diagnosis and pharmacological treatment. When this occurs, the focus of helping the person with dementia to maintain personhood is lost (Penrod, Yu, Kolanowski, Fick, et al., 2007; evidence grade: D). Penrod and colleagues describe the need for a combination of biophysical and personhood interventions based on lived experiences with dementia to assure quality of life and humane care.

### **Need for Accessible Service and Knowledgeable Providers**

Currently 25% of elders in the U.S. live in a rural community, either alone or with their spouse. Rural health care services are less accessible, less specialized and more costly to deliver than those in urban areas. The access of rural elders to a range of health care services is narrower than in urban areas, and fewer community-based services are available to them. Lack of community based services has resulted in a higher utilization rate of nursing home services for rural elders (Coward, Netzer & Mullins, 1996; evidence grade: C1). Lack of services also results in a less-than-complete assessment and diagnosis with fewer interventions for problems with cognition.

The increasing numbers of older persons will increase the demands for mental health services that are already sorely lacking. This increase in demand has led to projections of severe shortages of specialized, highly educated professionals to meet the increasing mental health needs of the

changing population. There is a need to have qualified health care professionals to meet the needs of persons in early stages of dementia. Because most of what is the current practice in dementia care was unknown ten years ago, the supply of qualified health professionals has not kept pace with the demand for specialized assessment and treatment services.

### **Need for Assessment of Individual Losses and Strengths to build Individualized Plans of Care**

Persons with dementia suffer different losses at different stages of the disease and therefore accurate assessment of abilities and losses is critical to assist the person in planning for their future and care needs. There is a need to tailor programs to retained skills and not assume all persons with dementia are the same over a changing and unpredictable clinical course (Garand, Buckwalter & Hall, 2000; evidence grade: D; Salmon & Lange, 2001; evidence grade: A1).

The Mini-Mental State Exam (MMSE) is relatively insensitive to very mild, but significant cognitive decline in highly educated persons, and has floor effects in tracking persons with severe dementia. The MMSE provides a valuable screening tool, but is less useful for tracking progression over time. Neuropsychological assessment provides a reliable means of detecting dementia in its earliest stages and of tracking the progression of cognitive decline (Salmon & Lange, 2001). Assessment of everyday behavior is significant for diagnosing and predicting disease progression in AD. Memory, IADLs, mood and social behavior have a linear deterioration as the disease progresses. However, this is not true for behavioral symptoms, which may fluctuate overtime, and their severity does not systematically increase with disease progression (Blasi, Brubacher, Zehnder, Monsch, Berres, et al ,2001; evidence grade: B1). There is a need for accurate assessment to focus on the information provided about impaired and spared abilities so that the retained abilities can be capitalized upon and impaired abilities supplemented. This is especially important for communication. Prediction with the use of standardized tests can be made about functions that are likely to decline and interventions can be implemented to sustain those functions for as long as possible (Tomoeda, 2001; evidence grade: A1). Individual assessment and individualized plans may also identify coping strategies to enhance well being and self esteem of PwAD in early stages (Clare, 2002).

Awareness of persons with AD in early stages has implications for assessment and individualizing care. As noted earlier, Clare and colleagues (2004, 2006) found that awareness persists long into the dementia process. This awareness affects the caregiver/person with dementia dyad in important ways. The perpetuation of awareness has implications for assessment instruments that rely on caregiver report versus self-report, as the caregiver may introduce bias based on many factors. Using caregiver ratings only may not give a clear picture to health care providers and is an important consideration when doing assessments to meet the needs of the person in early stage AD. Obtaining assessments only from caregivers of the needs and strengths of the person with AD increases the likelihood that educational and support programs may fall short of adequately addressing the actual needs of the person with the disease. The need for individualized, person-centered programming may only be met in the perceptions of the person with AD are taken into account and valued.

### **Need for Psychosocial Support:**

The need to provide early psychosocial support for persons newly diagnosed with dementia and their caregivers (soon after receiving even the tentative diagnosis) has been identified. Early support has been related to better outcomes (Brodaty, Gresham & Luscombe, 1997; evidence grade: C1; Moniz-Cook, Gibson, Win, & Wang, 1998; evidence grade: B2). In the study by Moniz-Cook and colleagues, the intervention group received intensive verbal and written information on the diagnosis. An average of four consecutive contacts was used to “break the news” followed by: 1) information on the interactive role of caregiver and person with dementia, 2) counseling regarding feelings of loss associated with the disability and potential progression of the disease with an emphasis on preserved abilities and skills, 3) prevention of crisis, and 4) maintenance of social activity. Persons in the treatment group had more positive outcomes. Persons in the control group without this intense focus on psychosocial support dropped the occasional support they received, had not read the information, did not follow through with the suggested cognitive exercises, and had increased institutionalization rates. The support is a necessary prerequisite to planning and working on improving or retaining memory ability.

### **Need for Information and Knowledge**

Information must be given in such a way that persons with dementia will use it. When given brochures with encouragement to read, persons with dementia will not read or use the information. It often takes an extended period of time for persons who have received the diagnosis to begin to process and try to understand the implications of the diagnosis, so timing of the information and the way in which it is shared is critical (Moniz-Cook, et al, 1998; evidence grade: B2; Zarit, Femia, Watson, Rice-Oeschger, & Kakos, 2004; evidence grade: C1).

Zarit and colleagues (2004) tested the intervention of a 10-session Memory Club program to provide information about memory loss and resources for coping for person in the early stage of dementia and their care partners. The rationale for doing the intervention what that dementia in the early stages presents an opportunity for examining the immediate and long-term consequences of the illness at a point when the individual with memory loss can participate. In addition to providing information, the group’s purpose was to strengthen both the person with dementia and their care partner’s ability to cope and to support one another. A preliminary evaluation of the project indicated positive response from both members of the dyad. While the primary purpose of the intervention was not health promotion, enhancing coping, support and control promotes improved health.

### **Need for Education of Health Providers to the Perspectives and Maintained Awareness of Persons with Dementia**

Evidence-based reports have described the perceptions of PwAD participating in early stage support groups (Dyck, 2003; evidence grade: D). Participants shared a feeling that they are being marginalized through their loss of independence, treatment by care providers, and public and media portrayals. Persons with dementia emphasize the need to belong, to feel important, to be a part of something bigger, e.g. some sort of collective action or self advocacy, and the need for support groups. These needs for recognition and participation in care support findings from additional studies by Lawton (1994; evidence grade: D), Burgener and Dickerson-Putman,

(1999; evidence grade: C1), and Clare (2002; evidence grade: C1) which identifies that PwAD need psycho-social support, programs and supportive contacts to encourage maintenance of self esteem, and caregiver understanding. Clare also identifies key areas in which interventions may identify coping strategies and enhance well-being and self esteem. The identified strategies may help people cope, but they must be relevant and specific to the individual.

Understanding that persons with dementia have awareness of their disease, including losses, may assist health providers and the general public to become more sensitive to the needs of persons with dementia (Clare, 2004; evidence grade: A1). Providers, both formal and informal, need to recognize that awareness persists well into disease progression. Persons with dementia are capable of perceiving and responding to negative feedback and interactions of other's expressed negative emotions. These negative interactions have a direct impact on outcomes of PwAD (Burgener & Dickerson-Putman, 1999; evidence grade: C1). Health providers knowledgeable regarding retained awareness in AD may be more likely to include the person in planning care, obtain information directly from the person, and develop individualized care plans tailored to the person's self-identified health-related needs.

### **Need to be Heard**

The published research describing the self-identified needs of the person with early stage AD is limited, although growing (Cotrell & Schulz, 1993; evidence grade: D; Zarit, et al, 2004; evidence grade: C1). Most published reports in this area are based on personal stories or are qualitative in nature; therefore they are not included in this body of work. Some of the work on loss of personhood in dementia was described earlier (Clare, 2004; Burgener & Dickerson-Putman, 1999). These studies build on the work of Lawton (1994; evidence grade: D) describing the "stripping" of personhood and the need of persons with dementia to be listened to. These collective findings support that persons with dementia are very much aware of the changes and losses inherent in the disease. Findings also support that the person's perceptions remain stable over time (in the 6 month time frame studied). A strong relationship was found between negative caregiver feelings toward the person with dementia and the person's productive behaviors/outcomes (Burgener & Dickerson-Putman). These findings supporting the need for interventions targeted toward increasing the caregiver's understanding of the person's needs to improve the caregiver/PwAD relationship. Increasing caregiver knowledge and understanding of awareness in persons with dementia may translate that into the inclusion of the person in decision making and conversations. Persons with AD need to have their self esteem protected by valuing their perspectives.

In a study by Zarit and colleagues (2004; evidence grade: C1), PwAD found it helpful to talk with other persons in early stage AD and their care partners. The following are the issues regarding the self-identified need to be heard in participants in a memory club. These concerns are shared by the PwAD and their care partners:

- To understand the diagnosis and its implications,
- To explore feelings of loss, grief, and sadness as well as hope, love and fortitude,
- To maintain or retain feeling connected to one's self and to the larger community of family, friends, and peers,
- To strive for emotional and physical well-being: avoid excess disability,

To balance increasing dependence and the need to maintain independence,

To plan for the future but focus on living in the present (p. 265).

Zarit also points out that most educational programs and literature are targeted at middle to late stage dementia. Few materials exist that are focused on the needs of PwAD in earlier stages.

### **Need for Recognition and Treatment of Depression**

Clinically significant levels of depressive symptoms are generally found in 15-30% of persons with AD although they often do not meet the diagnostic criteria for major depression. A 4- year longitudinal study evaluated factors related to the development of depressive symptoms in 410 persons with AD (Gilley, Wilson, Bienias, Bennett, & Evans, 2004; evidence grade: C1). The researchers found greater cognitive impairment resulted in a small reduction in depressive symptoms and a modest increase in somatic symptoms. They also found that younger persons with AD had more intense depressive symptoms. Pre-morbid personality also influenced the degree of depression. These findings support that persons with early stage AD are more likely to have depressive symptoms and individual assessment is needed. Because depression is treatable, it is essential that it be recognized in persons with AD in early stages to maximize their ability to retain and regain abilities. (See non-cognitive section for additional information about depression).

### **Need for Managing Cognitive Losses: Memory**

Memory difficulties are a defining feature of AD and are one of the main problems experienced by persons in the early stages. A number of cognitive abilities, such as visual and auditory discrimination and the ability to learn and retain motor skills, are unaffected until the very late disease stages. The focus of assistance to persons with early stage AD needs to be on losses such as memory and using retained skills to regain or minimize losses (Salmon & Lange, 2001).

For the person with dementia, memory difficulties can have a major impact on self-confidence, and can lead to anxiety, depression, and withdrawal from activities. Withdrawal can result in a general increase in symptoms, including memory loss. This increase in symptoms beyond those attributable to the disease process is an example of what has been termed “excess disability” (Reifler, 1990; evidence grade: D). In early stage dementia, the difficulties lie primarily in taking in new information and forming new memories (Christensen, 1998; evidence grade: C1). Needs related to cognitive losses in early stage AD include optimizing retained memory and finding ways of compensating for difficulties. The person with AD may optimize remaining abilities by identifying the best ways of taking in important information or carrying out essential, real-live practical skills. Compensating for difficulties may be accomplished through such use of memory aids or adjusting the environment so that the demands on memory are reduced.

### **Needs Associated to Non-Cognitive Symptoms or Behavioral Psychological Symptoms of Dementia (BSPD)**

Non-cognitive symptoms in dementia are common in nearly 80-95% of PwAD. Persons with AD develop at least one neuropsychological symptom over the course of their disease, and the incidence of BSPD begins with evidence of cognitive impairment (Aalten, de Vugt, Jaspers,

Jolles, & Verhey, 2005; evidence grade: C1; Lyketsos, et al, 2002; evidence grade: C1; Manning, 2004; evidence grade: D). BPSD or non-cognitive symptoms include (but are not limited to): depression, agitation, apathy, delusions, hallucinations, anxiety, irritability, euphoria, disinhibition, aberrant motor disturbances, night-time and sleep disturbances, and appetite and eating disorders. These symptoms have been found to be correlated to adverse effects for both the care providers and PwAD, especially affecting quality of life, rapid decline, and early institutionalization (Aalten et al, 2005; evidence grade: C1; Burgener & Twigg, 2002; evidence grade: C1; Lyketsos et al , 2002; evidence grade: C1).

Apathy and depression were the most common BSPD reported in early stage AD (Aalten et al, 2005; evidence grade C1; Manning, 2004, evidence grade D). The prevalence and severity of depression has an inverse relationship to disease progression (more progressed=less depression), while apathy has the opposite relationship, showing increasing prevalence and severity as the disease worsened (more progressed=more apathy). Aberrant motor behavior occurred less frequently but followed the same pattern as apathy. The study by Aalten and colleagues also revealed that pharmacological treatment did not influence the course of neuropsychiatric symptoms in dementia. In contrast, Woodhead and colleagues (2005; evidence grade: C1) found that PwAD that participated in engaging activities demonstrated a significant decline in behavior problems and an increase in positive behaviors. Farina and colleagues (2006; evidence grade: B2) demonstrated a significant reduction in disruptive behavior and a reduction in overall behavior symptoms when a combination of caregiver education and support was provided in recreational and occupational therapies in their sample of community dwelling PwAD. This multimodal, multidisciplinary approach also reduced the caregiver's negative responses. In general, research findings support the use of non-pharmacological interventions for BSPD. While outcomes show decreased use of psychotropic medications, improved nutrition, and caregiver satisfaction, these results are found through continuous programming, individually developed according to retained abilities, interest and preference of PwAD, and incorporate a balance of stimulation and rest (Kolanowski, Litaker, & Buettner, 2005; evidence grade A2; Kovach, et al, 2004; evidence grade A2; Volicer, Simard, Pupa, Medrek, & Riordan, 2006; evidence grade: C1). Evidence from other non-pharmacological interventions demonstrates diverse findings dependent on the intervention. Support for these interventions is described in other sections of this review.

Since evidence has supported the early institutionalization of persons with PwAD with high levels of BPSD, intervening on the day-to-day frequency of behavioral disturbances may assist with maintenance in the home setting. Derouesne and colleagues (1999; evidence grade: C1) found that while most persons with AD were aware of their cognitive deficits, they were unable to appraise the severity and consequences of their deficits on everyday life, thus leading to more caregiver burden. Findings by Onor and colleagues (2006; evidence grade: C1) supports the evidence that even though behavioral disturbances may be mild, persons in early AD stages were less aware of their cognitive and behavioral deficits. These perceptions also vary from those of their caregivers. This discrepancy may disrupt the relationship between caregiver and person with AD, contributing further to institutionalization. Collectively, these findings support the need for programs that address behavioral symptoms in early stage AD.

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## **Need for Safety**

Cognitive deficits pose inherent threats to safety. Difficulties in processing, task breakdown, memory, sequencing, and decision making are among the deficits that engender safety concerns. Onor and colleagues (2006; evidence grade: C1) found that not only are persons with AD less aware of their behavioral and cognitive deficits, but they also do not update their self-perceptions of performance. Further evidence suggests that although awareness persists in dementia, persons with AD may be unable to appraise the severity and consequences of their deficits in everyday life (Derouesne et al, 1999; evidence grade: C2). Nygard and Stakhammar (2003; evidence grade: C2) examined difficulties in telephone usage for persons with AD living in the community. They found persons with AD have difficulty in using the phone effectively and in communicating concerns during use. These factors contribute to issues of safety for the persons with AD.

Multiple needs and appraisal limitations may contribute to an increase in safety concerns. Findings from a study by Gaugler, Kane, Kane, and Newcomer (evidence grade: C1) demonstrated that persons with two or more unmet needs are more likely to suffer adverse consequences such as falls, discomfort, injuries, pressure ulcers, They also found that unmet needs tended to occur in multiple domains and that the person with AD was more likely to die from the consequences of adverse outcomes.

A cohort that has not been evaluated separately, though unique needs are evident, are persons with AD who live alone. Persons with dementia who live alone experience a higher rate of institutionalization (Newhouse, Niebuhr, Stroud, & Newhouse, 2001; evidence grade: D; Tuokko, 1999; evidence grade: C1). Tierney and colleagues (2004; evidence grade: C1) developed a predictive model for institutionalization which included perceptions of fewer social resources, poorer MMSE scores (MMSE  $21.4 \pm 3.8$ ), and presence of COPD. The researchers also identified a pattern of self neglect where the person with AD neglected to provide themselves with food, drink, and personal hygiene. This cohort also sought emergency medical interventions due to failure to follow instructions and/or solicit healthcare. These poor health outcomes and increased institutionalization rates may be indicative of the need to identify persons with AD living alone as a distinct cohort requiring interventions to assist in remaining safe in the community.

In their Home Safety/Injury model, Hurley and colleagues (2004; evidence grade: D) provide examples of risky behavior that are related to actions of commission or omission. These actions are implicitly hazardous and include: getting lost, falls, becoming exposed to elements, burns, abrasions, medication mismanagement, inability to recognize objects or sounds, and apraxia. Increased frailty of persons with AD was also identified as a risk factor for injury. The authors conclude that safety may be enhanced by making home and environmental modifications, improving caregiver competence and knowledge, and increase provision of social supports.

Safety remains an important need consideration in persons with AD especially as they transition through the early disease stages while adapting to the changes of declining cognition and function. The cohort of persons with AD who live alone is especially vulnerable. This cohort may especially benefit from community support programs beneficial to the care management process.

## **Need for Health Promotion**

No studies were identified that specifically identified the need for health promotion, although the need for services and programs that decrease excess disability and early institutionalization may be considered as having a health promotion focus. Although not specific to persons with AD, findings from one study indicated that older adults were more likely to participate in health promotion activities when they were supported by Medicare. These findings have implications for health promotion activities for persons in early stage dementia (Lave, Ives, Traven, & Kuller, 1996; evidence grade: B1). Persons in early stage AD may also be more willing and able to participate in health promotion activities if funding for these services was available.

One specific study aimed at testing a health promotion activity was conducted by Fitzsimmons and Buettner (2003; evidence grade: C1). This was a pilot study of an experimental 10-week college course for individuals with newly diagnosed dementia. The course focused on teaching methods for promoting and maintaining optimal health. The course was designed to provide information on the disease process and on healthy behaviors designed to prevent problems that are common later in the course of the disease. Underlying the development of the course was the evidence from a number of studies supporting formal education for individuals with cognitive impairment. Findings point to the need to change lifestyles and habits while the person is still in the early stages of the disease. Following participation in the course, persons with AD demonstrated lower depression and perceived stress and improved self-esteem. Self-efficacy remained stable. This study not only addresses the need for health promotion programs, but demonstrates a unique and successful way to offer such a program.

Often, following the diagnosis of AD, the focus of attention is on the disease diagnosis and medical management. Little attention or effort is given to promoting healthy lifestyles contributing to quality of life, maintenance of function, and prevention of excess disabilities. Evidence exists for the need to assist persons with early stage AD with health promotion to sustain their function, quality of life, and prevent premature institutionalization. Additionally, programs testing unique and effective health promotion interventions have been tested, providing models for widespread dissemination.

## **Conclusions**

A variety of empirically based needs have been identified for persons in the early stages of dementia. With the growing body of evidence supporting the maintenance of self-awareness in persons with AD, identified needs include supportive and educational programs that are individualized to the person's self-identified needs. The need for programs that take into account preserved self-awareness was identified, including programs that address preservation of self-esteem, maintenance of abilities, management of behavioral symptoms including depression, and health promotion. The need for early and accurate diagnosis of dementia was identified, given the effectiveness of medications and non-pharmacological interventions in the slowing of disease progression. Safety concerns were also identified. Collectively, this review of needs for persons in early stage AD may be used to inform program development. The evidence for tested interventions that follows provides further guidance for support and program development for this growing population of persons with AD.

## Rating Summary

Grading Score	Number	%
A	9	17%
B	4	8%
C	29	55%
D	11	20%
Total Reviewed	53	100%

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## **C. Introduction to Interdisciplinary Research Review**

The comprehensive review of the research literature resulted in an evaluation of research examining domains of concerns for persons in early-stage dementia. The review resulted in an analysis of studies conducted internationally and was multidisciplinary in breadth.

### **General Search Strategies and Categories**

General search strategies included the review of databases containing the majority of health and well-being multidisciplinary literature: Medline (PubMed), Cumulative Index for Nursing and Allied Health Literature (CINAHL), and PsychInfo, representing studies of a psycho/social nature. No date restrictions were applied to allow for the capturing of early seminal studies as well as the latest research reports. In some reviews, only studies published in English were reviewed. In domains known to be studied extensively in other countries (exercise interventions, cognitive therapies), some studies were translated from both Spanish and French. Specific restrictions for each search are briefly described within the domain. Definitions of early-stage dementia were used to guide the selection and review of studies. Several studies, however, were included when the studies were conducted using persons in the early-middle disease stages and the results were deemed as representing useful knowledge regarding transition across stages or slowing of disease progression. These ‘transitional’ studies were viewed as offering knowledge useful to persons with Alzheimer’s disease (PwAD) in the early disease stages. A table summarizing the review findings is included as Table 1. The strength of each domain may be assessed by reviewing the ratings for reviewed studies. Comments by the Expert Panel regarding the strengths and weaknesses of each domain add further support the domain’s overall contributions to improving outcomes for PwAD.

### **Criteria for Grading the Strength and Consistency of Evidence**

This guideline was developed from a systematic review and synthesis of current evidence. Research findings and other evidence, such as guidelines and standards from professional organizations, case reports and expert opinion were critiqued, analyzed and used as supporting evidence. The practice recommendations were assigned an evidence grade based upon the type and strength of evidence from research and other literature.

The grading schema used to make recommendations in this evidence-based review is:

- A1= Evidence from well-designed meta-analysis or well-done systematic review with results that consistently support a specific action (e.g. assessment, intervention, or treatment)
- A2= Evidence from one or more randomized controlled trials with consistent results
- B1= Evidence from high quality evidence-based practice guideline
- B2= Evidence from one or more quasi experimental studies with consistent results
- C1= Evidence from observational studies with consistent results (e.g. correlational, descriptive studies)
- C2= Inconsistent evidence from observational studies or controlled trials
- D= Evidence from expert opinion, multiple case reports, or national consensus reports

## **Reliability Assessment**

To assure reliable and consistent ratings of research reports, the assistants conducting the majority of the review met with a program faculty member weekly during month two of the evaluation project. Prior to the meeting, each assistant and the faculty would rate at least 2 research reports included in the review. If inconsistencies across ratings were found, the raters would discuss the rationale for their rating and a consensus of the appropriate ratings would be reached. This process helped assure consistency in the evaluation of the research reports.

## **Inclusion of Persons with Lewy Body and Frontal-Temporal Lobe Dementia in Studies**

Persons with two related, yet distinctive, forms of dementia are often included in studies of dementia. These dementia types include Lewy Body dementia (LBD) and Frontal-Temporal Lobe dementia (FTD). In past studies, rarely have researchers differentiated subjects by type of dementia, although this trend is changing given new diagnostic techniques that more accurately classify dementia type. The clinical and pathological features of both AD variants distinguish the type of dementia. Clinical features also assist in defining optimal treatments. For example, persons with LBD most commonly present with core features including fluctuating cognition characterized by variations in attention and alertness, recurring visual hallucinations, and spontaneous features of Parkinsonism, most markedly gait disturbances. Persons with LBD are also noted to have severe sensitivity to neuroleptic drugs. Together, these pronounced features of LBD lead to variant-specific treatment approaches, including non-pharmacological interventions. To date, studies of non-pharmacological interventions to ameliorate symptoms in persons with LBD are lacking (Boeve, 2005; McKeith, Dickson, Lowe, et al., 2005).

Similarly, FTD presents in a markedly different manner than AD. The prefrontal cortex is primarily affected in FTD. Therefore, persons with FTD often have preserved memory but remarkable changes in executive function including disinhibition, loss of initiative, extreme personality changes, and inability to modify their behavior (Stewart, 2006). In fact, persons with FTD often present with near-normal MMSE scores, when changes in MMSE are a common feature in persons with AD. Persons with either FTD or LBD have difficult attending and may not be good candidates for group interventions such as support programs or cognitive stimulation programs. While both groups may respond to exercise interventions, lack ability to attend and gait disturbances in persons with LBD may make participation more difficult, affecting the possible positive benefits of exercise programs. Although persons with LBD or FTD may be included in the studies included in this review, no attempt was made to differentiate the study outcomes by these AD-variant diagnostic categories.

## **Theories Underlying Studies**

Generally, an analysis of the theoretical framework used to guide the study was not included in the review, as the majority of studies did not utilize a pre-designated theoretical model. To assist in understanding theories common in defining variables associated with outcomes in PwAD, the following is a brief review of the theories often utilized in the study of interventions for PwAD.

Several middle-range theories have been developed and tested to increase understanding of variables associated with positive outcomes in PwAD. The Progressively Lowered Stress Threshold (PLST) model focuses on the interaction between environmental stimuli, a lowered capacity for stress management in PwAD, and behavioral symptoms. This model is useful in identifying common stressors which lead to excess disability including: misleading or inappropriate stimuli, excessive external demands, physical stressors, and changes in the environment, routine, or caregiver (Hall & Buckwalter, 1987; Hall, 1994). Fatigue and excessive internal demands are also thought to contribute to behavioral symptoms, but are internal to the person. Interventions derived from this model focus on reducing, eliminating, or controlling the timing of stressors and/or increasing the capacity of PwAD to manage stress.

Multiple theories have identified the importance of person-environment fit in optimizing functioning and quality of life (QOL) in PwAD. Lawton's (1983, 1997) formulations of QOL evolved from his work with PwAD. According to Lawton, QOL includes the four domains: 1) psychological well-being, consisting of the person's affective states, including depression; 2) behavioral competence, including person factors such as social behavior, personal control, physical health, self esteem, and cognition, along with the more complex domains of time use; 3) the objective environment, consisting of structured events and interactions including health services utilization; and 4) subjective evaluations of QOL. All of the QOL domains are likely to be amenable to intervention, with a number of studies having supported the relationships outlined in Lawton's model.

Dawson and colleagues (1993) developed the Enablement Model of dementia care which rejects strictly biomedical explanations of declining function and QOL for PwAD. Similar to models of care posited by Kitwood (1997) and Lyman (1989), the Enablement Model focuses on supporting the intact or remaining abilities of PwAD and avoiding excess disability.

More recently, the Need-Driven Dementia-Compromised Behavior Model (NDB) has been used to conceptualize behavioral symptoms in PwAD as the result of background and proximal factors (Algase et al., 1996; Kolanowski, 1999). The NDB model conceptualizes disruptive or disturbing behaviors as potentially understandable needs. If these needs are responded to appropriately, quality of life will be enhanced (Kolanowski, 1999). A model described by Kolanowski, (1999) explained need-driven dementia-compromised behavior as individual characteristics that are moderately constant along with inconsistent environmental factors, which together trigger the behavior. Needs-driven behaviors expressed by individuals with cognitive impairment are the most meaningful and integrated responses they can communicate given the restrictions of the dementing illness, the portions of their character and abilities that are still intact, and other supportive or restrictive factors in the environment (Kolanowski, 1999). Need-driven behaviors are those behaviors that display an expression of a need or are stemming from the pursuit of a goal (Colling, 1999). Factors of the NDB:

- ◆ Background factors: These are relatively stable aspects of the client that may influence behavior but are more difficult to change.
  - Neurological: pathophysiological changes in the brain associated with the dementing illness and any other neurological disorder such as Parkinson's disease.

- Cognitive: Includes all areas of cognition such as attention, memory, aphasia, apraxia, and agnosia
  - General Health: Past and current diagnoses such as diabetes, cancer, arthritis, cardiovascular conditions and hypothyroidism.
  - Psychosocial elements such as gender, education, past occupation, personality type, and history of responses to stress
- ◆ Proximal factors: Current situational variables including the following three categories:
1. Physiological Needs: Current physical factors such as hunger or thirst, elimination, pain, discomfort, or sleep disturbances.
  2. Physical environment: The quality of the living areas of the client: light level, noise, temperature, or other items or persons present in the treatment area.
  3. Social Environment: The qualities of the persons who come into contact with the client such as staff mix, staff stability, program/unit ambiance, presence of others.
  4. Psychological Needs: Current psychosocial factors such as loneliness, fear, depression.
  5. Functional Impairments: Current functioning such as feeding, bathing, ambulation, transferring.

Both the PLST and NBD models have been used primarily to investigate specific behavioral symptoms in PwAD; that is, to identify antecedents to behavioral symptoms and develop interventions to positively affect outcomes. Although these models are effective for this stated purpose, focusing primarily on behavioral symptoms may limit researchers in their attempts to more broadly identify interventions to affect a variety of outcomes, including maintenance of function and slowing of disease progression.

Theories evolving from the physical sciences are exciting and promising as they offer support for interventions designed to assist PwAD to maintain function and/or slow disease progression. Specifically, theories of neurological functioning and regeneration guide many of the multimodal intervention studies included in the Exemplar domain. Research primarily using animal models suggests that the brain, despite injury, is capable of extensive reorganization, termed brain "plasticity." The results of animal studies have been reported since the mid-1980s providing evidence of the brain's capacity to respond structurally to external stimuli (Black, Sirevaag & Greenough, 1987; Fillit, Butler, O'Connell, et al., 2002). Early studies in mice provide evidence of the environmental effects on neuronal density and synapses per neuron. Turner & Greenough (1985) found increased synapses per neuron in the occipital cortex of rats reared in enriched environments. Enriched environments typically include: 1) structured exercise beyond that which is baseline; 2) multiple environmental stimuli such as sensory stimuli, music, cognitive tasks. Enriched environments were directly related to increased neuronal density and synapses per neuron. In senescent mice, living in an enriched environment, defined as opportunities for social interaction, exploration, and physical activity, resulted in neurogenesis in the hippocampus, an area of the brain essential to memory formation (Kempermann, Kuhn, & Gage, 1997, 1998). Research testing the effects of exercise in animals has demonstrated increased spatial learning and long-term potentiation in exercised mice compared to controls. Results indicate that some forms of physical activity can regulate neurogenesis and synaptic plasticity and improve learning (VanPraag, Christie, Sejnowski & Gage, 1999). Findings have not been consistent across studies,

however. Increased numbers of neurons have been found post-injury in animal studies (rats). However, differences in cell proliferation between the groups (complex environment, exercise, or control) have not been consistently found (Briones, Suh, Jozsa, et al., 2005; Briones, Suh, Hattar, & Wadowska, 2005). In adult primates (macaques), new neurons have been found to develop in three areas of the brain essential to cognitive functioning: prefrontal, inferior temporal, and posterior parietal cortex (Guld, Reeves, Graziano, & Gross, 1999). Collectively, studies using animal models suggest the existence of a use-dependent neuroplasticity in the older brain, although findings are lacking in consistency (Briones, Suh, Hattar & Wadowska; Siervaag, Black, Shafron, & Greenough, 1988; Soffie, Hahn, Terao, & Eclancher, 1999).

In humans, the production of new neurons has been shown to continue even into later years. Based on animal studies and clinical trials in humans, plasticity theory suggests that both rehabilitative and pharmacological interventions may facilitate neuronal reorganization and recovery of function (Albensi & Janigro, 2003; Bach-y-Rita, 2003a,b). Within the rehabilitative framework, studies using humans as subjects have begun to test the effectiveness of enriched environments on preservation of neuronal function, including the slowing of cell death inherent in progressive dementia, such as AD (Bach-y-Rita, 2003b). Robertson & Murre (1999) conducted a review of studies regarding brain plasticity in humans and concluded that the adult brain can undergo dramatic changes in neural structures, including dendritic and axonal sprouting. Studies testing the effects of stimulating and rehabilitative activities on neurogenesis support the multimodal interventions designed to stimulate the brain using varied, intense stimuli. These exemplar studies particularly hold promise as a model of intervention design for persons in the early stages of AD.

### **Definitions of Early-Stage Dementia**

For purposes of this review, consistent with the scholarly literature, early stage AD was defined by any of the following criteria:

- Mini-Mental State Exam (MMSE) scores of >17 (Folstein, Folstein, & McHugh, 1985)
- Clinical Dementia Rating (CDR) Scale scores of 0.5 to 2.0 (Hughes, et al., 1982)
- Global Deterioration Scale (GDS) scores of 2.0 or less

Most reviewed studies used one of the three criteria noted above as in defining early-stage AD. If a study did not give the criteria for inclusion, the study was not evaluated if it was conducted in a long-term care setting, although this was a rare occurrence. If studies were conducted in the home or community setting, such as adult day care centers, and no stage criteria were provided, the study was included if reference was made to 'early-stage' AD, etc.

### **Definition of Key Terms**

- *Agnosia*: Loss of comprehension of auditory, visual, or other sensations although the sensory sphere is intact. Can be seen as auditory, finger, optic, or tactile inability to distinguish or interpret information (Venes & Thomas, 2001).
- *Apathy*: A lack of motivation that is not attributable to diminished level of consciousness, cognitive impairment, or emotional distress. Apathy has several components: lack of initiation and perseverance, lack of emotional expression, and lack of goals. The apathy spectrum includes decreases in interest, motivation, spontaneity, affection, enthusiasm, and emotion (Marin, 1991; Levy et al., 1998).

- *Aphasia*: Absence or impairment of the ability to communicate through speech, writing, or signs due to dysfunction of brain centers (Venes & Thomas, 2001).
- *Apraxia*: Inability to perform purposeful movement although there is no sensory or motor impairment. Inability to use objects properly (Venes & Thomas, 2001).
- *Delirium*: An acute, reversible organic mental disorder characterized by reduced ability to maintain attention to external stimuli and disorganized thinking as manifested by rambling, irrelevant or incoherent speech. There is also a reduced level of consciousness, sensory misperception, and disturbance of the sleep wakefulness cycle and level of psychomotor activity, disorientation to time, place or person and memory impairment. Delirium may be caused by a large number of conditions resulting in derangement of cerebral metabolism, including systemic infection, poisoning, drug intoxication or withdrawal, seizures or head trauma and metabolic disturbances such as hypoxia, hypoglycemia, fluid, electrolyte or acid base imbalances or hepatic or renal failure (On-line Medical Dictionary, 2002).
- *Dementia*: “Nonspecific but lasting deterioration of intellectual functioning characterized by failing memory, distractibility, impairment in judgment and abstraction, reduced language facility, alterations in mood and affect, and disturbance of orientation. Accompanied by changes in personality and ways of relating to others.” (Austin, 2001, p. 21). Dementia is a syndrome in which a main symptom is loss of memory. There are many forms and causes of dementia some are reversible.
- *Behavioral Symptoms*: Through a concept analysis, patterns of behaviors were described as disrupting symptoms because they interfere with functional abilities and quality of life. (Colling, 1999; Kolanowski, 1995).
- *Diversional activities*: Activities used to divert attention or entertain the individual. A volunteer, family member or others can provide these. The goal may simply be to attend the activity (Buettner & Martin, 1995).
- *Exercise*: Performed activity of the muscles, voluntary or otherwise, especially to maintain fitness. Active exercise means the individual performs voluntary contraction and relaxation of the muscles. Assistive exercise means the individual performs the movement with the aid of a therapist. Passive exercise is carried through by the therapist with no assistance from the individual. Therapeutic exercise is movement performed with supervision for the purpose of restoring normal function to diseased or injured tissues (Venes & Thomas, 2001).
- *Functional ability*: What people are capable of doing, aside from activities of daily living, in their own environments (Ross & Burdick, 1991).
- *Global Deterioration Scale*: This scale provides an estimation of cognitive function for clients with dementia. This scale is broken down into stages of the disease process (Reisberg, Ferris, Leon, & Crook, 1982).
- *Mini-Mental State Examination*: This is a commonly used tool used with older adults, to screen for cognitive functioning (Folstein, Folstein, & McHugh, 1975).
- *Passive behavior*: Often distinct changes in a personality pattern that is exemplified by a diminished ability to be open, conscientious and extroverted. Passivity is demonstrated as decreased activity, loss of interest, and apathy (Colling, 1999).

- *Recreational therapy*: Therapeutic Recreation is the provision of Treatment Services and the provision of Recreation Services to persons with illnesses or disabling conditions. The primary purposes of Treatment Services, which are often referred to as Recreational Therapy, are to restore, remediate or rehabilitate in order to improve functioning and independence as well as reduce or eliminate the effects of illness or disability. The primary purposes of Recreational Services are to provide recreation resources and opportunities in order to improve health and well being. Therapeutic Recreation is provided by professionals who are trained and certified, registered and/or licensed to provide Therapeutic Recreation (ATRA, 2002).
- *Relaxation* A state of relative freedom from both anxiety and skeletal muscle tension. (Online Medical Dictionary, 2002).
- *Self-determination*: Refers to "acting as the primary casual agent in one's life and making choices and decisions regarding one's quality of life free from undue external influence or interference" (Wehmeyer, 1994).
- *Sensorimotor activities*: Activities involving both senses and motor skills (Ross, 1991).
- *Sensory integration*: Skill and performance required in the development and coordination of sensory input, motor output, and sensory feedback. Includes sensory awareness, visual spatial awareness, body integration, balance, bilateral motor coordination, visual-motor integration, praxis, and other components (Ross & Burdick, 1991).
- *Sensory stimulation*: Activities that have properties that affect the central nervous system (CNS) (Ross & Burdick, 1991).
- *Standards of Practice*: Developed by a profession, the Standards reflect levels of service provision for professionals. Using the standards established by a profession assists the health professional in assuring the systematic provision of quality evidence based services.
- *Therapeutic activities*: Individualized activities with specific outcomes for the client involved. A therapist provides these after a recreational therapy assessment and planning is completed. (Buettner & Martin, 1995).

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## **Literature Review of Delirium Outcomes and Prevention in Early Stage Alzheimer's Disease**

### **Significance of delirium superimposed on dementia in early AD**

Delirium is a disorder of acute onset, with fluctuating symptoms, inattention, disorganized thinking, and altered level of consciousness. Delirium superimposed on dementia is when delirium occurs on top of an existing dementia. The pathogenesis of delirium is poorly understood and, even though clinically and methodologically we often separate delirium and dementia, they often occur together and are probably highly interconnected. Even though the presence of dementia has been shown to be an independent risk factor for delirium (Inouye, 2006), many studies exclude persons with dementia (PWD). Several studies have reported higher rates of hospitalization in PWD compared to persons without dementia which may put them at risk of developing delirium (Chodosh et al., 2004; Fick, Kolanowski, Waller, & Inouye, 2005). Delirium often occurs in the hospital setting but may occur even more frequently in community-living PWD. The prevalence of delirium superimposed on dementia (DSD) ranges from 22%-89% in both hospital and community settings (Fick, Agostini, & Inouye, 2002). The onset of delirium is associated with poor outcomes including functional decline, increased hospitalizations, increased healthcare utilization, nursing home placement, and death (Baker, Wiley, Kokmen, Chandra, & Schoenberg, 1999; Fick & Foreman, 2000; Fick, Kolanowski, Waller, & Inouye, 2005; McCusker et al., 2001; O'Keeffe & Lavan, 1999). As increasing numbers of persons are diagnosed with dementia at earlier stages, increased attention to the outcomes of and prevention of delirium will be important issues for this growing population. The purpose of this systematic review is to critically review papers published since 1990 addressing interventions for delirium superimposed on dementia in early Alzheimer's disease (AD) and to set an agenda for future research on delirium in persons with early AD.

### **Search Method**

We searched the literature from January 1, 1990 through January 15, 2007 from the following databases; MEDLINE, CINAHL, PsychInfo, and Cochrane databases for studies with primary sources of data on prevention models for delirium in persons with dementia. We searched using the key terms dementia, delirium, delirium superimposed on dementia, delirium and early Alzheimer's disease, delirium, prevention, controlled trials, and intervention. Mesh terms were cross-referenced where appropriate. Other sources reviewed included reference lists of published papers, and personal communication. We reviewed and categorized abstracts of 225 journal articles.

### **Criteria for Inclusion**

Inclusion criteria included intervention studies with primary data on delirium in persons with dementia and early AD. We included delirium studies with an analysis or sub-analysis of patients with delirium. We eliminated review articles, case studies, case reports, and letters to the editors. We reviewed seven intervention studies that included persons with dementia.

## **Definitions**

Most studies used Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision (DSM-IV-TR) criteria or the Confusion Assessment Method (CAM) for the diagnosis of delirium (Inouye, 1990).

## **Evidence in support of delirium prevention programs for early stage Alzheimer's disease**

There is an expanding body of evidence examining delirium in persons with dementia but only a few controlled trials of interventions for the prevention and management of DSD. Many intervention studies in the past ten years have not included PWD, did not measure or report dementia status, or did not have sufficient power to analyze PWD separately (Britton & Russell, 2004; Fick, Agostini, & Inouye, 2002; Lundstrom et al., 2005; Naughton et al., 2005; Milisen et al., 2005). A few of the studies did do a sub-analysis of persons with dementia in the intervention group compared to usual care. None of the published studies we found examined treatment effectiveness or delirium outcomes that were specific to persons with early stage AD.

Many of these delirium prevention models focused on multi-component interventions including consultation by a geriatrician, early mobilization, hydration, decreasing psychotropic medication, and nursing care interventions. Most of these models are targeted towards hospitalized older adults. At least one of these delirium models, Hospitalized Elder Life Program (HELP), is being disseminated nationally and internationally and relies on hospital volunteers to deliver many program components (Inouye, Baker, Fugal, & Bradley, 2006). A 1999 controlled clinical trial by Inouye (Inouye et al., 1999) that included PWD found that fewer patients in the treatment group (22/128, 17%) developed DSD compared to the usual care group (40/125, 32%). The most effective part of their intervention for persons with dementia was the non-pharmacological sleep protocol. In a randomized trial by Cole et al. (2002), over 50% of the sample had dementia in both the control and treatment group, but no differences were found in delirium or mental status scores between groups. In a randomized trial to reduce delirium after hip fracture surgery, geriatric consultation decreased the incidence of delirium in the intervention group compared to usual care, but the intervention showed little or no benefit in persons with dementia. The dementia groups were too small to detect significance (Marcantonio, Flacker, Wright, & Resnick, 2001). Pitkala and colleagues (2006) found symptoms were alleviated faster in persons with DSD but there were no differences in mortality or nursing home placement between the intervention and control group.

## **Conclusions**

In conclusion, despite poor outcomes associated with DSD, only a few studies have analyzed the prevention of delirium in persons with dementia, and the results of those studies have been mixed. These mixed results may be due to methodological and setting issues or may indicate that we need to address different risk factors and intervention models for delirium in persons with dementia. No studies have addressed delirium in persons with early AD. The overall evidence for delirium prevention models in early AD is weak (level C) due to a low number of randomized trials with inconsistent results (Atkins, et al., 2004). Delirium models specific to early AD are urgently needed. In addition, future studies of DSD should address: (1) the impact of delirium

episodes on the trajectory of cognitive decline for persons with early AD; (2) which interventions are most effective for the prevention of delirium in early AD; (3) how delirium impacts the quality of life of the person with early stage AD and their caregiver; and (4) which risk factors are most important for delirium in early AD. Prospective studies that test current and future intervention models for AD will aid the understanding of the needs of persons with AD across care settings and allow evidence-based guidelines to be developed for delirium in early AD.

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## **Literature Review of Support Groups and Psychotherapy Interventions for Persons in Early Stage Alzheimer's Disease**

Models for the development of support and psychotherapeutic groups for persons in the early stages of dementia have been published since the late 1980's. However, the development and implementation of support and psychotherapeutic groups for persons with AD has lagged behind the offering of support programs for their caregivers. Support and psychotherapy groups targeting persons in the early disease stages may be efficacious for several reasons. One, persons with AD are adjusting to the diagnosis of dementia at a time when they are most acutely aware of the significance of the diagnosis and changes in their selves. Recent studies have provided evidence of retained self-awareness in persons in the early disease stages, despite changes in cognitive ability (Clare, 2003). Secondly, persons in the early disease stages are more likely to actively engage in a support program and benefit from the interactions and information shared. Social skills generally remain intact well into the middle disease stages, allowing for increased enjoyment and social engagement through support group interactions. Although support programs are viewed as positive interventions for persons with dementia, systematic evaluation of the effects of support programs are lacking. A literature review of support and psychotherapeutic programs was conducted to identify effective support programs for persons in early stage AD.

### **Search Method**

The literature search took place between December 5, 2006 and January 16, 2007. Databases utilized in the search include PubMed, CINAHL, PsychInfo, and the Cochrane Database of Systematic Reviews. The following terms were used: dementia, support groups, support, psychotherapy, and Alzheimer's disease. Mesh terms were cross-referenced, such as dementia and support groups to narrow the search. When a citation was found, links to related studies from a study to be included in the review were also explored. Further searches were done on the names of authors of research articles found in the initial search as well as on the names of their projects. Additional searches were performed on the names of researchers known for their work with people in early stage dementia. Professionals working in the field contributed lists of references on early stage Alzheimer's disease interventions. Once articles had been pulled for inclusion in this review, further references were found using the ancestry method.

### **Inclusion Criteria**

All research articles testing a support group or psychotherapy group were included in the review. This review focuses on early stage Alzheimer's disease, defined as having a diagnosis of early stage Alzheimer's disease with either an MMSE score of 18 or higher, a CDR score of 2.0 or less or a GDS of 2 or less. Only research reports written in English were reviewed. Reports based on undocumented opinion were excluded.

### **Definitions**

Support Groups: Support groups are generally defined as emphasizing a supportive and nurturing relationship among the group participants and leaders. The group process emphasizes each

member, the group, the leaders, and the group activity or work. Many support groups follow the early publication by Yale (1991) and are topical in nature. Group formats vary, with some groups allowing for time with the caregiver or family member being present, while other groups are intended solely for the person with dementia. Support groups are often led by health professionals with experience in care of persons with dementia.

Psychotherapeutic Groups: Psychotherapeutic groups are designed specifically to meet the psychological and emotional needs of persons with dementia. Most psychotherapeutic groups provide direct counseling, with a variety of counseling approaches being used (i.e., milieu therapy, anxiety management, resolution therapy, Rogerian counseling skills). Psychotherapeutic groups require a skilled, professional leader.

### **Evidence in support of support and psychotherapy programs for early stage Alzheimer's disease**

The search produced 9 articles testing the effects of support group participation on a variety of outcomes. An additional 4 studies of psychotherapeutic groups were found, although these interventions often represented 'mixed' approaches, including validation, reminiscence, and psychodynamic techniques.

### **Evidence for Support Groups**

The Memory Club is a 10-session support program that includes dyadic participation (Zarit et al., 2004, Evidence Grade = C1). The central program goals are to empower care partners to problem solve and plan for the future. Positive support for the marital relationship is also inherent in the Memory Club format. Typical MMSE scores for participants are > 25, indicating early stage dementia. Outcomes from the program have been evaluated by program participants using questionnaires and interviews. Positive outcomes include positive ratings of the program's content, the benefits of a shared experience with other group members, and increased social support.

The Alzheimer's Café (Morrissey, M.V., 2006; Netherlands, Evidence Grade: D) is a support program designed to provide a relaxed forum in a café-like environment for people with dementia and their family caregivers. The Café provides a milieu for exchanging ideas while increasing social interactions. The goals of the Café are to: provide information, talk openly with other newly diagnosed people with dementia and caregiver partners, and prevent isolation. Using casual observations as a method of evaluation, outcomes support the positive benefits of the Café including: positive interactions (it was noted that it was difficult to identify the people with dementia and caregiver), decrease of loneliness, increase of social interaction, increase of living skills and self esteem, and gain of insight. Participation is open-ended, allowing for ongoing participation. About 60 Cafes are currently functioning throughout the Netherlands, with participation being open-ended.

Two United Kingdom support groups (N=11) were evaluated using videotapes of support group sessions and semi-structured interviews with group participants (Mason, Clare, & Pistrang, 2005; Evidence grade: C1). The average MMSE score for participants was 24, with MMSE scores

ranging from 19 to 29. Group interactions were rated for content with the highest category of participant responses being 'information giving' with the second highest being 'self-disclosure'. Group facilitators' responses were primarily of a questioning nature, following by information giving and an impersonal question. The majority of participant responses were not as 'helpful' to other group members. Analysis of the interview data revealed that participants identified benefits of group participation as useful and seeing that one is not alone, although negative aspects of participation were also identified. Quantitative outcome measures were lacking.

A Canadian program, Circle of Care, is similar to the support group format using an 8-week structured agenda (Goldsilver & Gruneir, 2001; Evidence Grade: C1). The 75-minute sessions focus on positive coping and problem-solving, increase in living skills, and managing grief and loss. Using casual observations and evaluation, outcomes of the program include positive feelings of affirmation, increased confidence, and decreased helplessness. MMSE scores for participating persons with dementia range from 18 to 30. No systematic evaluation of outcomes has been conducted. Participation is limited to the 8-week program.

Snyder and colleagues (1995, Evidence grade: C1) used a grounded theory method to study 15 family units (caregiver/person with dementia) who were coping with the stress of dementia. The pairs attended a weekly 90-minute, eight-week supportive seminar group. The group was led by a social worker and a nurse. Participants were encouraged to discuss a specific topic each week. During the first hour of each session, the participant and caregiver met separately; for the final 30 minutes of the session, the family unit would reconvene and share highlights from their discussions. Group leaders recorded statements made by the participants; the 93 statements were content-analyzed for reoccurring themes. Four raters validated the themes. The qualitative data collected described four positive themes: purposefulness, gratification, belonging, and surviving. Negative themes included: helplessness, devaluation and unpredictability. The positive comments were focused on the weekly topic intervention process and/or the interaction of the group. The negative comments were not directly linked to the seminar topics. Qualitative comments were not collected from the caregiver group.

An early study by Robyn Yale (1991; Evidence Grade: B2) formed the basis for later studies of support groups for persons with dementia. Persons in the early disease stages (N=13) were assigned to either an 8-week educational/emotional support group or an 'usual-care' control group. The support sessions ranged from one to 1.5 hours. Although verbal reports of the group's benefits were positive, no differences were found in the quantitative outcome measures, including depression. Positive benefits included a decrease in feelings of isolation, assistance with the grieving process, and an opportunity to exchange ideas and support.

Two reports were found describing the outcomes of an eight-session support group program, Project Esteem, developed and tested by LaBarge and colleagues (1995, 1998; Evidence grade = D). The program goals were to provide opportunities for persons with Alzheimer's dementia to share thoughts and feelings with each other and program facilitators. An additional goal was to provide an opportunity to enjoy each other; in other words, just have fun. No specific measurement for cognition was used for inclusion in the support group. However, participants (N=10) were interviewed to determine conversational ability and understanding of their memory problems. Participants were judged to be only mildly to moderately impaired based on interview

performance, ability to participate in a group setting and family report. No cognitive evaluation tool was administered prior to inclusion. Documented observations by the group facilitators were used to evaluate program outcomes. Additionally, an eleven question yes/no satisfaction questionnaire along with three open ended questions were answered by participants. Responses to the open ended questions were both audio and video recorded. Responses revealing feelings of anger, anxiety, stress, acceptance and frustration were shared by participants. The second report included an analysis of themes that emerged from the audio and video observations from Project Esteem. The expressed emotions of persons with dementia were evaluated. The findings suggest that persons with early stages of AD are very aware of their deficits and the changes that the disease brings to their lives and relationships with others. Once participants became comfortable with each other, sharing of feelings and emotions increased. Laughter was evident during most sessions and appeared to relieve stress. The researchers concluded that although persons with AD have an awareness of loss of functional capability, social enjoyment continues. Conclusions also included the observed ability of persons with AD to appropriately share emotions in a group setting.

Using qualitative methods, Morhartdt and Menne (2001; Evidence grade = C1) examined responses of participants in a support group. Face-to-face interviews were conducted with six persons in early stages of AD and their family members. The interview was designed to assess the responses of the participants to the conduct of the group and positive benefits from participation. The interview responses were analyzed for consistent themes. The major themes included: 1) Reaction to group dynamics and leader; 2) A sense of the commonalities in the participants' experiences; 3) Reaction to a variety of symptoms and to different levels of functioning experienced among group members; and 4) Techniques and education found to be helpful in facilitating coping with the disease.

### **Evidence for Psychotherapeutic Groups**

An early review of the literature of psychotherapeutic work included 26 published studies of psychotherapeutic interventions with persons with dementia (Cheston, 1998; Evidence grade: B2). No search criteria for the review were stated, and the quality of the studies was not evaluated. The findings included a summary of adaptations to the psychotherapeutic interventions for persons with dementia, content of the therapeutic interventions, group dynamics and characteristics, and evaluation data. The author concludes that psychotherapeutic groups may be appropriate for persons with specific issues or problems as well as providing a more general, supportive intervention appropriate to all persons with a dementia diagnosis. Psychotherapeutic interventions were noted to be particularly helpful in assisting the person with dementia to 'make sense of their experiences'. A lack of systematic studies and research evidence also led to the conclusion that more outcome studies are required before formal psychotherapeutic interventions can be recommended as a priority in care of persons with dementia. It should be noted, however, that the review included studies of general support groups, validation groups, and case study reports, not just research reports of psychotherapeutic interventions.

Group psychotherapy sessions have been offered for persons with dementia in Great Britain (Cheston, Jones, & Gilliard, 2003; Evidence Grade: B2). The group is led by a trained therapist,

with participants (N=42) having a mean MMSE score of 23. The group focused on a sharing of experiences of dementia, with participants being asked to discuss 'what it's like when your memory isn't as good as it used to be'. Using a pre-post test design, positive benefits from participation were decreased depression, with slight, non-significant improvements in anxiety. Due to high attrition, n=19 completing all three project phases, conclusions of the benefits of the group are difficult to determine.

Using a group format similar to the format described in the 2003 Cheston report, the authors described the effects of psychotherapy group participation, focusing on changes in awareness in one group participant, Robert (Watkins, Cheston, Jones, & Gilliard, 2006; Evidence Grade: C1). From analysis of transcripts of Robert's comments during the groups, changes in awareness were evident from the first session through session ten. Robert was able to move from a stance of feeling different or removed from the group, lessening the implications of his own diagnosis, to acknowledgement of his diagnosis and the short- and long-term consequences. Robert's anxiety and depression rose during the 10-session group, with anxiety nearing baseline at the group's termination. Overall, this study represents an in-depth analysis of the possible positive benefits of psychotherapy group participation on acceptance of the diagnosis of dementia.

A review of psychological interventions was conducted by Scott and Clare (2003; Evidence grade = A1). The group interventions reviewed included: reality orientation, validation therapy, reminiscence therapy, cognitive stimulation, memory training, psychotherapy, cognitive behavior therapy and support groups. The authors concluded that most studies testing psychological interventions have small numbers of participants and lack formal outcome measures. The authors recommend that future studies include large participant numbers, a comparison group, and evaluation of both individual and group outcomes.

## **Conclusions**

Support and psychotherapy programs generally include an educational and social support component. Although the format, content, and program goals vary, most support programs are from 8 to 10 weeks in length, with each program lasting from 1.25 to 1.5 hours. Most programs target persons with early stage dementia, although some programs utilize dyadic participation with the caregivers present as well. Research examining the effects of support programs has been carried out in the United States, Canada, Great Britain, and the Netherlands. Studies of support programs lack a quantitative design and systematic outcome evaluation and are hampered by small sample sizes, typically 8 to 20 participants. Also, no studies were found that included an age-matched control group. One particularly problematic aspect of these support programs is the 'termination' of the participant at the end of the formal sessions. With the exception of the 'Alzheimer's Café' in the Netherlands, the programs ended after a pre-determined time period. No discussion was found regarding additional follow-up or need for support following the program's termination. As persons may stay in the early disease stages from anywhere from 1 to 5 or 6 years, the need for on-going support programs is evidenced.

## **Recommendations**

Based on the review of evidence, further studies are needed to determine the optimal format, length, and evaluation of support and group psychotherapy programs. As no studies were found using a no-treatment control group, conclusions regarding the treatment (group participation) effects are tenuous at best. The majority of studies examining the effects of support groups were rated in the C and D category, indicating the lowest strength of the evidence. Termination of the group at a pre-determined time (usually 8 to 10 weeks) raises concerns regarding the long-term benefits of participation. The possible benefits of ‘open enrollment’ compared to limited participation is one recommendation for future studies. In the meantime, open enrollment is recommended for support and psychotherapy group structures.

## **Rating Summary**

### **1. Support Groups**

Grading Score	Number	%
B	1	12%
C	5	55%
D	3	33%
Total Reviewed	9	100%

### **2. Psychotherapy Groups**

Grading Score	Number	%
A	1	25%
B	2	50%
C	1	25%
Total Reviewed	4	100%

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## **Literature Review of Non-Pharmacological Cognitive Enhancement Interventions for Persons in Early Stage Alzheimer’s Disease**

A literature review of non-pharmacological cognitive enhancement programs was conducted to identify effective means of supporting, maintaining, and improving cognitive functioning in early stage AD.

### **Search Method**

The search for evidence to support interventions effecting primarily cognitive outcomes took place between December 26, 2006 and January 20, 2007. Multiple databases were utilized, including PubMed, CINAHL, and the Cochrane Database of Systematic Reviews. The following terms were used: early stage Alzheimer’s disease, cognition, Alzheimer’s disease therapy, reality orientation, Alzheimer’s disease, Alzheimer’s disease prevention, psychosocial factors, cognitive therapy, brain plasticity, enriched environments, and memory training. Mesh terms were combined when indicated to narrow the search, such as Alzheimer’s disease and cognitive therapy. When a citation was found, links to related studies from a study to be included in the review were also explored. Further searches were done on the names of authors of research articles found in the initial search as well as on the names of their projects. The table of contents of the Cochrane Database of Systematic Reviews—Cochrane Dementia and Cognitive Impairment Group was also searched for research reports on this topic. Additional searches were performed on the names of researchers known for their work with people in early stage dementia. Professionals working in the field contributed lists of references on early stage Alzheimer’s disease interventions. Once research reports had been reviewed for inclusion, additional citations were obtained using the ancestry method. A search was also performed research reports on including persons with Lewy body and frontal temporal lobe dementia. No studies were found that specifically addressed cognitive therapies for persons with these Alzheimer’s variants.

### **Criteria for Inclusion**

All research reports written after 1984 addressing cognitive therapies were included in the review. The reviewed studies focused on reports of the efficacy of techniques that could be used to improve cognition. Studies testing a cognitive intervention for other outcomes, such as depression, were not included, such as the early study by Teri and Gallagher-Thompson (1991). This review focuses on early stage Alzheimer’s disease, defined as having a diagnosis of early stage Alzheimer’s disease with either an MMSE score of 18 or higher, a CDR score of 2.0 or less or a GDS of 2 or less. Articles written in English or Spanish were reviewed. Articles which were based on undocumented opinion or were solely descriptive in nature were excluded.

### **Definitions in Non-pharmacological Cognitive Enhancement Programs**

Cognitive training (CT) refers to any non-pharmacologic intervention designed to improve cognitive functioning, regardless of mechanism of action. Typically, CT interventions focus on specific domains of cognitive functioning (such as memory, attention, and problem solving), but more general, cognitive mediated domains of functioning, such as basic and instrumental activities of daily living (ADLs and IADLs, respectively), social skills, and behavioral

disturbances can also be targeted. CT strategies can be divided into two sub categories: Compensatory strategies and restorative techniques. Compensatory strategies teach new ways of performing tasks by “working around” cognitive deficits. Examples of compensatory strategies include internal strategies such as organizing information by visualization or categorizing, encoding through multiple sensory channels, asking questions during learning, and focusing on a single task. Compensatory interventions also use external strategies such as memory notebooks, environmental cues, and calendars. Restorative strategies are used to re-train persons with Alzheimer’s disease to perform tasks using practice, drills, spaced retrieval, and a variety of other techniques.<sup>1</sup>

Cognitive rehabilitation is a term used mostly in European studies to describe interventions used for cognitive training.

Cognitive stimulation is defined as non-regimental involvement in activities which require mental functioning. Cognitive stimulation can be either active, as in a group discussion of current events or solving a crossword puzzle, or passive which is more observational in nature. Examples of passive cognitive stimulation include listening to a poetry reading, watching a play, or listening to music. Cognitive stimulation is much less formal programming than cognitive training/cognitive rehabilitation.

Dual cognitive support involves the provision of cues and the enhancement of saliency and organization of the to-be-remembered information at both acquisition and retrieval of the information.<sup>2</sup>

Errorless learning is a learning approach that avoids, or at least limits, errors during the acquisition phase of learning, thereby reducing the chance of reinforcement of incorrect information.

Errorful learning is a learning approach that focuses on the correction of mistakes made during the acquisition phase of learning.

Explicit memory is the type of memory that is encoded through rote memorization, verbally oriented means, and is purposeful. This type of memory is one of the first areas of impairment in AD. Explicit learning happens when people use rote memorization and verbally oriented learning in a conscious process to create a memory or learn a skill.

Implicit memory is non-verbal and observational, and may be accomplished during the course of an activity unrelated to what is being learned. It is considered to be “automatic” and is not done on a conscious basis. Practice of motor skills is a type of implicit learning. This type of memory remains intact the longest during the course of AD. Implicit memory is enhanced through the use of environmental cues in learning.

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<sup>1</sup> Sitzer D.I., Twamley E.W., & Jeste D.V. (2006). Cognitive training in Alzheimer’s disease: a meta-analysis of the literature. *Acta Psychiatrica Scandinavica*, 114(2), 75-90.

<sup>2</sup> Lowenstein D. (2004). Cognitive rehabilitation of mildly impaired Alzheimer disease patients on cholinesterase inhibitors. *American Journal of Geriatric Psychiatry*, 2(4), 395-402.

Memory rehabilitation: A variety of learning techniques can be applied to improve the memory skills of participants. Memory rehabilitation is based on the hypothesis that memory loss in AD results from defective encoding and storage of information rather than forgetting information.<sup>3</sup> It focuses on encoding information in areas of the brain that are less impaired by AD. Cognitive training and cognitive rehabilitation differ from memory training and rehabilitation in three ways. First, the memory interventions specifically target encoding of memory and recall, while the cognitive therapies target many different areas of cognition, sometimes within the same therapy. Secondly, the cognitive approaches usually offer a milieu of therapies within a study while the reviewed studies in memory rehabilitation typically look at one method per study. Third, current memory research is based upon the location of active pathology within the brains of persons with AD, targeting therapies to the functions coordinated in the least impaired parts of the brain.

Montessori method is a technique pioneered in Rome for improving the lives of children. Research is now looking at its use with people with dementia. “Each lesson is first presented at its simplest level and each subsequent lesson, increasing in complexity, is a variation of previously mastered skills or concepts.” Learning materials are used from the every day environment, tasks are broken down into small steps that are mastered and then sequenced. The method involves immediate feedback, high probability of success, and repetition.<sup>4</sup>

Procedural memory training: This type of memory training requires involvement of the motor system--“learning by doing.”

Neuropsychological rehabilitation (NR) is “a process of active change aimed at enabling people, who are disabled by injury or disease, to achieve an optimal level of physical, psychological, and social function.” NR is used across a whole range of areas including physical health, psychological well being, daily living skills, and social relationships. “NR applied to persons with AD aims to optimize functions, minimize excessive disability risk, and prevent the development of negative social psychology.”<sup>5</sup> NR can be implemented within an interdisciplinary context.

Prospective memory is the type of memory that refers to the timely execution of a previously formed intention.<sup>6</sup>

Reality orientation (RO): Reality orientation is a specific form of cognitive training first described by Taulbee and Folsom in 1966 as a technique to improve the quality of life of confused elderly people. RO consists of relating information to a confused person regarding

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<sup>3</sup> Metzler-Baddely C., & Snowden J.S. (2005). Brief report: errorless versus errorful learning as a memory rehabilitation approach in Alzheimer’s disease. *Journal of Clinical and Experimental Neuropsychology*. 27(8), 1070-9.

<sup>4</sup> Camp C.J., Judge K.S., Bye C.A., Fox K.M., Bowden J., Bell M., et al. (1997). An intergenerational program for persons with dementia using Montessori methods. *The Gerontologist*, 37(5), 688-692.

<sup>5</sup> Avila R., Bottino C.M.C., Carvalho I.A.M., Santos C.B., Seral C., & Miotto E.C. (2004). Neuropsychological rehabilitation of memory deficits and activities of daily living in patients with Alzheimer’s disease: a pilot study. *Brazilian Journal of Medical and Biological Research* 37(11), 1721-1729.

<sup>6</sup> Kixmiller J.S. (2002). Evaluation of prospective memory training for individuals with mild Alzheimer’s disease. *Brain and Cognition*, 49(2), 237-41.

memory and orientation, such as person, place, and time. RO can be done continually or as a classroom technique. During continual orientation, the confused person is involved in reality-based communication with every contact throughout their day. In classroom RO, groups meet on a regular basis to engage in orientation-related activities.<sup>7</sup>

Spaced retrieval is a learning technique using repeatedly recalled information over increasingly longer retention periods to encourage memory formation.

Therapeutic recreation interventions: Recreation is used as a treatment modality to improve the biopsychosocial well being of participants. In cognitive enhancement, therapeutic recreation draws upon the interests and abilities of the person with AD to design approaches to maintain or improve cognitive functioning.

### **Evidence in support of cognitive enhancement programs for persons in early stage AD**

The search produced 60 research reports of cognitive enhancement programs in early stage AD. Eighteen reports were excluded either because research subjects did not meet inclusion criteria (progressed past early-stage) or because the articles were not research based. The reviewed articles supported a variety of interventions for improving outcomes in persons with early stage AD, including cognition. For clarity, the evidence is divided into several categories: 1) Background studies supporting brain plasticity; 2) Learning in early-stage AD; 3) Cognitive training and cognitive rehabilitation; 4) Cognitive stimulation using combined therapies; 5) Memory rehabilitation/training; 6) Neuropsychological rehabilitation; and 7) Reality orientation.

#### **1. Background Studies Supporting Brain Plasticity**

Bach-Y-Rita (2003, evidence grade=A2) reviewed several studies which support the theory that the human brain can reorganize after damage and result in functional improvement. One of the mechanisms through which this can happen is non-synaptic neurotransmission in which communication between cells does not take place through connected synapses, but through the release of neurotransmitters from sites that may be remote from the target receptors. Therefore, it is possible for receptors in various parts of the brain to have a variety of tasks, rather than specific ones limited by synaptic connectivity. Multiplexing in the brain consists of the multiple uses of neurons and fibers so that they are involved in a variety of functions. Implications from this study are evident for persons with early stage AD as findings imply that even though part of the brain is injured, another part of the brain may be involved in a function regulated in the injured part of the brain and can be trained to assume further responsibility for that function. Further evidence for brain plasticity is found in results that support that new neuronal connections may form with rehabilitation.

Use of functional magnetic resonance imaging (fMRI) is being used to study how functioning is recovered in a several types of neurological conditions, including AD. Rocca and Filippi (2006, evidence grade=B2) note that studies using the fMRI have shown increased activation of several

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<sup>7</sup> Spector A., Davies S., Woods S., & Orrel M. (2000). Reality orientation for dementia: A systematic review of the evidence of effectiveness from randomized controlled trials. *The Gerontologist*, 40(2), 206-212.

cortical areas in the brains of persons with early AD during cognitive tasks, which indicates functional compensation for neuronal loss.

Increased understanding of human brain functioning is resulting in strategies to utilize that knowledge for the purpose of improving cognition and quality of life of persons with AD. Swaab, Dubelaar, Scheder, van Someren, and Verwer (2003, evidence grade= B2) examined evidence from a variety of studies that indicate that neurons don't die in AD, but atrophy instead. The clinical implication is that the cells may be able to be stimulated. Also, an increasing body of evidence indicates that metabolic impairment may contribute to neuronal dysfunction and atrophy in AD. Therefore, stimulation of neurons both pharmacologically and non-pharmacologically is a promising strategy in the treatment of AD.

Environmental enrichment is a non-pharmacological strategy used for neuronal stimulation. Jankowsky and colleagues (2005, evidence grade A2) described a study using a mouse model of AD. Enrichment of the environments of mice, by providing cages with access to novel objects, exercise wheels, and interaction with a large number of cage mates, resulted in significant improvement in brain functioning compared to animals housed in standard cages. The overall result of the studies reviewed in this work was that even in the face of Alzheimer's related pathological lesions, the function of the nervous system can be substantially influenced by environmental factors.

The term "cognitive reserve" is used to explain how two people with similar neurodegenerative changes can vary considerably in cognitive abilities and clinical dementia. Whalley, Deary, Appleton, and Starr (2004, evidence grade=A1) reviewed the research literature pertaining to cognitive reserve and concluded that there is no evidence to support a simple threshold model for pathology leading to impaired cognitive function. The authors also concluded that impaired cognitive function is a product of more than pathology. The biggest factors in cognitive impairment appear to be intelligence, occupation, level of education, work environment, personal management of stressful experiences, choice of cognitively stimulating leisure pursuits, better use of health services, and perhaps implementation of health education resulting in healthier lifestyles.

Stern (2006, evidence grade=A1) conducted a systematic review of research on cognitive reserve and concluded that individual differences in how tasks are processed may result in a reserve against brain pathology and age related changes. These conclusions have implications for persons with AD, including the existence of cognitive reserve allowing for potential treatment prior to the onset of symptoms. These early treatments and enhancement of cognitive reserves has the potential to prolong the onset of cognitive impairment for an indefinite time.

## **2. Learning in Early-Stage AD**

Before cognition can be improved in early stage Alzheimer's disease, it must first be shown that people with dementia can still learn. Many studies have shown that it is possible to learn during early stage AD. One study also demonstrated that increased awareness of deficits increases the likelihood that a person can benefit from cognitive rehabilitation. There are two main hypotheses in evaluating learning in Alzheimer's disease. The first comes from recent evidence of that

neuronal regeneration is possible as a result of stimulation of the areas of the brain that have been damaged. The second hypothesis is that the human brain is adaptable enough for one area of the brain to assume the tasks and memories that were lost during the disease process that occurred in another part of the brain. These studies are based on research that the plaques and tangles characteristic of AD are present in predictable patterns in the brain, causing predictable deficits and leaving predictable areas relatively unharmed in the early stages of AD. The mechanism of learning in AD is to transfer lost data and functions to the less impaired portion of the brain. A variety of techniques are used, including implicit learning, emotional priming, error free learning, use of props and environmental cues, and external memory devices. All techniques show some promise. Most of these studies were conducted in outpatient clinics in Great Britain.

Bozoki, Grossman, and Smith (2006, Evidence grade=A2) demonstrated that while persons with AD are not able to learn categories explicitly due to impairment in the medial-temporal lobe of their brains, mediated by the hippocampal system, they are able to learn categories implicitly. Learning to classify items into categories according to common features is how children learn about the world and how adults refine their knowledge. This study consisted of 40 people with AD and 40 control subjects. Findings demonstrated that persons with AD can learn categories, but probably use a different combination of implicit memory and working memory than people without AD. This article specifically describes the content of the intervention.

Davis (2005, evidence grade=B1) conducted a review of the different interventions identified for enhancing cognition of persons with dementia, examining the literature supporting the use of each intervention. Davis concluded that it is possible to for persons with AD to learn and recommended that rehabilitation professionals advocate for the use of therapies for this group. The author makes specific recommendations regarding the approaches the interdisciplinary team should use in treating people with early stage dementia. These interventions include the use of implicit learning techniques, error free learning strategies, use of external props and environmental manipulation to facilitate conversation and memory, and the incorporation of reality orientation and reminiscence into therapeutic sessions to increase orientation and positive behaviors.

LaBar and colleagues (2005, evidence grade=A2) examined the effects of emotion on retained memories in persons in early AD. In a controlled study of three different groups, a young adult group (n=25), a middle aged adult group (n=22), an older adult group (n=25) and a group diagnosed with early stage AD (N=10), the researchers found support for the preservation of emotional enhancement of priming magnitude in healthy aging and early stage AD. They also demonstrated that the emotional priming effect could not be attributed to explicit memory. These findings have relevance for the design of the content of interventions to enhance memory.

In a study of six participants with early stage AD, Clare and colleagues (2000, evidence grade=C1) found that errorless learning techniques were beneficial in improving every day memory tasks. Errorless learning techniques were also used to re-learn face-name associations in another study by Clare and colleagues (2002, evidence grade=C1). Twelve participants with early stage AD were trained in face-name association using an errorless learning method. The intervention resulted in improved recall of the trained items, which was maintained without

training for six months. However, not all participants benefited from the use of errorless learning. Those who were aware of their diagnosis and deficits and had higher scores on the MMSE benefited the most from using the errorless learning approach.

Clare, Wilson, Carter, Roth, and Hodges (2004, evidence grade=C1) examined the relationship between awareness of cognitive deficits and achievement in cognitive rehabilitation in a sample of persons with early-stage AD. In a cognitive rehabilitation intervention of face-name training, the authors demonstrated that the more awareness there is of personal deficits, the more effective are cognitive rehabilitation interventions.

### **3. Cognitive training and cognitive rehabilitation**

These two terms are used in the literature to describe the same types of formal interventions to improve cognition of persons with early-stage AD. The reviewed literature demonstrates that the earlier the diagnosis is made, the greater the impact cognitive training and cognitive rehabilitation can have on cognition. Some studies evaluated one specific technique while others evaluated a variety of techniques within the same study. All studies support the usefulness of cognitive training/rehabilitation during the early stages of AD, especially in combination with cholinergic drugs. The majority of these studies took place in Italy and England in outpatient clinics.

#### Computer based training

Computer based training was used to instruct four patients with early to middle stage AD in functional tasks appropriate to their lifestyle (Hofmann, Hock, & Muller-Spahn, 1996; Evidence grade=C1). Photographs were taken of the steps in tasks to be learned and were scanned into a computer. Persons with AD then used the touch screen of the computer to sequence the tasks. A facilitator was present to offer advice, but participants were encouraged to work as independently as possible. All four participants' training performance improved substantially, but training did not result in overall cognitive improvement.

#### Cognitive rehabilitation/training in combination with cholinergic drugs

Bottino and colleagues (2005, Evidence grade=A2) examined the effects of a cognitive rehabilitation intervention combined with medications and medications alone in 13 persons with mild AD. Six were randomized to a treatment group that received cognitive rehabilitation and rivastigmine and seven to a control group that received rivastigmine only. All participants were stabilized on the cholinergic drug for two months prior to the beginning of the study. The cognitive rehabilitation group received group sessions once a week for 90 minutes at a time for five months. The control group received no systematic intervention. The rehabilitation consisted of orientation to time and place, the use of compensatory memory strategies, and the use of external memory aids. Errorless learning techniques were utilized to teach those strategies and the use of the memory aids. In addition, the intervention group was involved in reminiscing, socialization, and even took trips to the museum or to see a movie. They also received procedural training in ADLs, such as shopping and making an appointment. Simultaneously, their caregivers attended a support group and were instructed to repeat some of the cognitive rehabilitation

exercises at home, at least three times a week. The cognitive rehabilitation group showed improvement in their MMSE score from an average of 23.50 to 24.33 at the end of the five months. The control group's average MMSE score declined from 21.29 to 19.86.

Using a case studies design, one man in the early stages of AD was taught, on a one to one basis, mnemonics and practiced remembering names in conjunction with photographs of faces through an errorless learning strategy (Clare, Wilson, Carter, & Hodges, 2003; Evidence grade=D). The participant was stabilized on rivastigmine for several months prior to the study. In addition to the sessions with the researchers, practice took place at home on a daily basis. The focus of the intervention was to improve memory of the names of the 13 members of the participant's support group. Prior to memory training, the participant was not able to recall names of 12 of the group members and was successful in recalling the 13<sup>th</sup> name about 30% of the time. At the end of three months, he was able to recall nearly all of the names in the first subset of names he was given. After an additional three months, the participant showed marked forgetting. The authors concluded that although the errorless learning showed immediate positive benefits, the effects were not sustained over time.

Cognitive rehabilitation was compared with cognitive stimulation (called mental stimulation in this article) in a three month, randomized study of 44 persons with mild AD (Lowenstein, 2004, Evidence grade=C1). All participants were also stabilized on a cholinergic drug. Forty-one participants were taking donepezil and the remaining three were taking either rivastigmine or galantamine. Participants were randomly assigned to either the cognitive rehabilitation group or to the mental stimulation group. All participants were required to take part in 24 individual training sessions, each lasting 45 minutes. The training sessions took place twice a week for a period of 12 to 16 weeks. The cognitive rehabilitation group received spaced retrieval, dual cognitive support, and procedural memory training. The mental stimulation group worked with commercially available computer games that required the subject to match pairs of letters, numbers, or designs from memory, exercises such as "hangman," tasks that required the subject to find words distributed in an array of letters, topic of the day discussions (reminiscence), and review and discussion of homework. The cognitive rehabilitation group showed improvement in a variety of measures with improvements being maintained at a 3 month follow-up, despite no further training. The mental stimulation group showed continued deterioration. The authors concluded that the cognitive rehabilitation intervention, in conjunction with cholinergic medications, was effective in memory maintenance.

#### Comparisons of types of cognitive training/rehabilitation

Davis, Massman, and Doody (2001, evidence grade=A2) used a combination of interventions designed to improve memory. One intervention included spaced-retrieval in which participants are taught information and then were repeatedly tested on it over repeated trials. When a successful retrieval was completed, the interval until the next test was then increased. When a retrieval failure occurred, the participant was given the correct response and asked to repeat it. The second tested intervention was a cognitive stimulation program. The third tested intervention was training in face-name associations. This study used a randomized, placebo-controlled design of 37 early stage persons with AD. Initially, 19 were assigned to the 5 week intervention group and received training in the above interventions. After the 5 weeks, participants were asked to

continue in the intervention in the home for 30 minutes per day, six days per week. The remaining participants were involved in a 5 week placebo program that consisted of watching general health videos, interviews with the investigators, and unstructured conversations. After the initial five week treatment, participants were re-assessed and the placebo group then received the 5 week intervention. The intervention groups improved in the areas in which they received training; however, these gains did not translate to improved quality of life or overall neuropsychological functioning.

Farina and colleagues (2002, evidence grade=C1) compared the efficacy of two different types of cognitive training programs on a total of 22 persons with mild to moderate AD. The first group received “procedural” memory training, which involved direct training of 24 different ADLs. Group two received “training of residual cognitive functions,” which consisted of activities aimed to stimulate attention, improve short term memory and improve language. At the end of the training, both groups showed improvement in functional abilities, with the group receiving the procedural memory training showing the most marked improvement.

Cognitive training effects were compared with cognitive stimulation effects by Farinamd, and colleagues (2006, evidence grade=B2). Participants included 32 persons with early-stage AD. Participants were divided into either a “global stimulation” or “cognitive-specific” group for six weeks. The global stimulation group received stimulation activities in the form of recreation— conversation, singing, dancing, party games, and creative pursuits. The cognitive specific group received a combination of procedural memory training on activities of daily living and neuropsychological rehabilitation of residual functions. Participants receiving cognitive specific treatment improved only on the scale that evaluated functional competence in daily living while the global stimulation group evidenced more improvement in behavioral disturbances and functional abilities.

A meta-analysis of studies testing cognitive training interventions for early stage AD completed and published between 1840 and 2004 was conducted by Sitzer, Twamley, and Jeste (2006, evidence grade=A1). Findings from the analysis supported the effectiveness of cognitive training interventions with medium effect sizes for learning, memory, executive functioning, activities of daily living, general cognitive problems, depression, and self-rated general functioning. Despite variations in the content of the training interventions, positive effects for a variety of cognitive and functional outcomes were found across studies, supporting the general effectiveness of cognitive interventions.

Cotelli, Calabria, and Zanetti (2006, Evidence grade=D) reviewed studies (N=13) testing the efficacy of two different types of non-pharmacological treatment in AD. No specific criteria were given for evaluation of the reviewed studies, resulting in a summary of the research literature rather than a critical analysis. The first category of interventions consisted of reality orientation, reminiscence therapy, and validation therapy. The second intervention group included cognitive training methods. Findings from the meta-analysis included positive effects for reality orientation on cognition. The reviewers were unable to draw conclusions about validation therapy and reminiscence. The reviewers also concluded that the evidence supporting the effects cognitive methods was not strong enough to draw conclusions about the efficacy of cognitive rehabilitation and training on cognitive outcomes in persons with AD.

#### 4. Cognitive stimulation using combined therapies

Cognitive stimulation interventions are used globally and across care settings with the rationale that the brain is the same as other muscles: “use it or lose it.” Findings document that the use of cognitive stimulation in early AD stages will at least maintain cognitive abilities, and, in some cases, the persons receiving cognitive stimulation improve as demonstrated by higher MMSE scores compared to baseline. Two of the studies in this category took place in an adult day center in Spain. One study took place in an outpatient clinic at the University of Texas.

Requena, Ibor, Maestu, Campo, Ibor, and Ortiz (2004, evidence grade=A2) conducted a one year randomized, controlled study of 86 clients of an adult day center in Spain with mild AD. The researchers tested the use of both a cholinergic drug (donepezil) and cognitive stimulation on cognitive outcomes. This 4-group experimental study included: a group receiving donepezil and cognitive stimulation, a group receiving the drug alone, another group receiving the cognitive stimulation alone, and a control group receiving no drug or cognitive stimulation. Participants in the combined therapy improved their average MMSE score from a 22.95 to a 24.45. Participants in the second treatment group that received cognitive stimulation alone also showed an increase in average MMSE score while the drug only group showed a decline from an average score of 21.17 to 17.80. The control group’s baseline average MMSE score was 19.39. At the end of the year long study, the average MMSE for the control (no treatment) group was 13.11. Findings include support for the efficacy of combined (cognitive stimulation and medication) therapies compared to single-therapy treatments.

Requena, Ibor, Maestu, Campo, Ibor, Ortiz (2006, evidence grade=A2) continued the evaluation of the randomized trial. The researchers maintained the group placement of participants and assessed outcomes to determine if the intervention’s effects would continue for a second year. During the second year, all four groups declined, with the fastest decline being seen in the group that received no therapies at all. The slowest decline was seen in the group that received both cholinergic drugs and cognitive stimulation, with their MMSE scores at the end of two years significantly higher than those of the control group. One concern regarding this longitudinal study is the ethical considerations in designating a ‘no treatment’ group, given the collective evidence of that cholinergic medications provide some benefits, especially in the early disease stages.

Chapman, Weiner, Rackley, Hynan, and Zientz (2004, evidence grade=B2) compared the effects of cognitive stimulation in combination with donepezil and donepezil alone in a group of 54 persons with mild to moderate AD (median MMSE score at baseline was 20.87). The participants were divided into two groups, the cognitive stimulation + donepezil group (n=26) and the donepezil-only group (n=28). The combined therapy group was treated in subgroups of six or seven participants each by a licensed speech-language pathologist and three master’s level speech-language pathology students. Training consisted of education on AD, communication techniques, and instruction on how to create a Life Stories Book. These groups met once a week for eight weeks in sessions that lasted for an hour and a half. Outcomes included a slower decline in MMSE scores, less irritability, less apathy, and improved quality of life in the combined therapy group compared to outcomes for the donepezil alone group. The effect lasted past the

two month stimulation period as demonstrated by better scores on evaluations at months eight and twelve post-intervention. Overall, findings support the long-term effects of a combined intervention beyond those accounted for by medications alone.

## **5. Memory rehabilitation/training**

Studies in this area seek to prove that the memory skills of persons with early stage AD can be improved through the use of modified encoding techniques. The most successful studies utilized implicit memory encoding approaches. The research supports the hypothesis that memory skills can be improved, however, the rehabilitation must be provided in a systematic way with reinforcement at home. The research suggests that when less rigorous the memory rehabilitation techniques were used, positive outcomes were not achieved. Memory rehabilitation programs can be found in England, Ireland, Spain, Italy, and Brazil. The participants in these studies reside at home, usually with a caregiver. Most studies were conducted at outpatient clinics or in adult day centers.

### Explicit learning strategies

Backman, Josephsson, Herlitz, and Stigsdotter (1991, evidence grade=C2) used a mnemonics technique to improve face-name recall with 8 participants, 6 of whom were in the early stages of AD, The technique proved useful to one of the participants.

Cohn-Weiner, Malloy, Rebok, and Ott (2003, evidence grade=A2) studied 34 persons with mild AD who were taking cholinergic drugs. Participants were enrolled in this six week program of memory training with n=17 participants in the intervention group and n=17 in the control group. The memory training was based upon the explicit learning strategies of Advanced Cognitive Training for Independent and vital Elderly (ACTIVE) program, which consists of practice of mnemonics, organization of items to be recalled into categories, and visualizing and associating memories. Efficacy of the memory training intervention was determined through a questionnaire completed by the significant others of the participants regarding the participants' memory and abilities to perform ADL's. Questionnaires were completed as a baseline, after six weeks, and as a follow-up, after eight weeks. No significant differences were found between the two groups at any assessment point. The study does suggest that modest gains can be made in learning and memory; however, these gains may not transfer to functioning in every day life.

### Errorless learning strategies

Haslam, Gilroy, Black, and Beelsey (2006, evidence grade: C2) examined errorless learning techniques in supporting memory in persons with AD. The researchers tested errorless learning in three different studies to examine the effects of this intervention on both high level (very general) and low level (very specific) knowledge levels. Errorless learning prevents or at least reduces the reinforcement of incorrect responses during learning. By preventing errors during learning, they are not available to be reinforced. Therefore, only the correct response is reinforced, which increases accurate associations. The purpose of Study One was to determine the benefit of errorless learning over errorful learning. It compared three persons with AD with 8 control participants who did not have AD, matched to the AD patients as closely as possible on

age and education. Both groups participated in one to one memory training using an errorless learning approach and an error free learning approach. The control group performed better than the group with AD in both interventions. Errorless learning improved recall of low level knowledge in both groups more than in high level knowledge. In the second study, a man and a woman, both diagnosed with probable AD, were exposed to the same type of intervention as the first study. The aim of this study was to separate the effect of familiarity based judgment from positive effects of errorless learning. Then, if that was successful, to again evaluate the effectiveness of errorless learning over errorful learning, this time at a higher level of knowledge. The researchers were able to eliminate the effects of familiarity based judgment from the study by using higher level knowledge testing. However, once eliminated, there was no significant difference in the efficacy of either errorful or errorless learning. The third study was done with persons with mixed dementia and severe memory impairment, so findings will not be included. Results from the first two studies indicate that errorless learning interventions can be effective in cognitive training as part of a comprehensive program.

Errorless versus errorful learning was evaluated in a study of four persons with AD, three with MMSE scores of 21 or greater, one with an MMSE score of 11 (Metzler-Baddeley & Snowden, 2005; Evidence grade=C2). The four participants were taught both novel and familiar materials using errorful and errorless learning techniques. All four learned some of the material presented, with errorless learning techniques resulting in modestly better memory outcomes than errorful techniques.

Kixmiller (2002, Evidence grade=A2) trained five persons with mild AD, using an errorless learning method, in a prospective memory task. Two persons with mild AD served as a control group, receiving instruction in the prospective memory task without the use of errorless learning. The intervention group performed significantly better in the prospective memory task than the control group, supporting the effects of the errorless learning approach. The small sample size in this study limits the significance and generalizability of the findings, however.

### Implicit learning strategies

Following a review of the research literature, an evidence based model for memory training is proposed by Camp and colleagues (1993; Evidence grade = D) called, “The E-I-E-I-O Model.” The model is used to guide practitioners in the choice of tools and therapies to improve the memories of persons with early stage AD. The acronym stands for, “explicit, implicit, external, internal—OH!” and gives several concrete, evidence based examples for each strategy. Testing of the intervention model was not included.

Procedural memory training was tested by Zanetti, Binetti, Magni, Rozzini, Bianchetti, and Trabucchi (1997, evidence grade=A2). Ten normal elderly participants were used as a control group, with 10 persons with mild to mild-moderate AD in the intervention group (N=20). The intervention group was divided in half and trained, during the course of three weeks, on a total of 20 daily activities. Five people learned one half of the 20 activities; the other five learned the rest of the activities. Training sessions were done in a rehabilitation facility that included kitchen, dining room, and bathroom areas. Training, which emphasized the motor skills of each activity, was conducted in the appropriate room for each task. After the three weeks of training, the

intervention groups improved significantly in the trained activities, but also in the non-trained activities, which were closely related to the untrained activities. Control group participants evidenced no improvement in motor skills.

### Compensating strategies using memory aids

Oriani and colleagues (2003, Evidence grade=C1) examined the use of an electronic memory aid (EMA) to support prospective memory in early to mid stages of AD. Five persons, four of which had an MMSE score of 18 or greater, were trained in the use of the electronic memory aid. The EMA is an electronic device which uses vocal recordings for appointments or tasks. The EMA can be programmed with dates and times for appointments, using an alarm system to alert the user to a message regarding an appointment or task. The user pushes a button and then receives the recorded message. The EMA was compared within each of the 5 participants to two other conditions: 1) recall using a written list, and 2) recall without any external memory aid. Results revealed that the use of the EMA yielded significantly better results on recall than either of the other two methods.

A digital clock and a memory book for activities of daily living were utilized in a case study of a person with early stage AD by Quittre, Olivier, and Salmon (2005, Evidence grade=C1). The authors utilized a spaced retrieval method of teaching the use of these devices. All interventions were also reinforced at home by the participant's caregiver. At the end of the three month training period, even though the participant's MMSE score declined, functional abilities improved.

The efficacy of an interactive computer program, MULTITASK, was tested by Schreiber and colleagues (1999; Evidence grade = A2) in persons in the early and middle stages of AD or vascular dementia (N=14). Participants in the treatment group (n=7) were trained with the computer program through 10, 30-minute sessions. Control group participants engaged in an 'attention control' conversation with a psychologist. The MULTITASK program includes training for immediate and delayed recall of objects and routes. Following training, treatment group participants displayed improvements in immediate recall of objects and immediate and delayed recall of routes in their environment. Control group participants showed no increase in recall.

### Reviews of memory rehabilitation studies

A comprehensive review of the literature was conducted by DeVreese and colleagues (2001, evidence grade=A1). Conclusions from the review indicated that memory rehabilitation can result in performance gains over time with long-term retention. Rehabilitation interventions were most effective if performed in a systematic way by a skilled professional in cooperation with a relative or caregiver who reinforces the memory rehabilitation at home. The researchers suggested standards or practice in memory rehabilitation. Suggested standards include: 1) a full neuropsychological assessment to determine which processes are impaired and which remain intact; 2) the methodology used in the intervention be based upon the findings of the assessment; 3) the intervention be based on the interests of the person with AD and their caregiver to increase motivation for practice; 4) caregivers reinforce memory rehabilitation through exercises at home;

and 5) the person with AD be observed and assessed by a therapist at regular intervals throughout the intervention to adjust therapy as needed.

## **6. Neuropsychological Rehabilitation**

Two studies conducted outside the United States tested neuropsychological rehabilitation interventions on outcomes in persons with early stage AD. Participants lived in the home with caregivers and were recruited as outpatients of two different memory clinics, one in Brazil and one in Italy.

Long term effects of neuropsychological rehabilitation were reviewed in the case study of one man with AD by Fernandez, Manoiloff, and Monti (2006, evidence grade=D1) over the course of two years and ten months. During this longitudinal study, the person was treated at different times with two different cholinergic drugs at different times, serving as his own control. The participant was involved in neuropsychological rehabilitation for part of the study period and was not involved in neuropsychological rehabilitation (cross-over treatment design). The participant did decline over the study period, but at a much slower rate than his projected decline had he not been receiving non-pharmacological therapy and the cholinergic drugs. The participant was most stable during rehabilitation phases, and even showed initial improvement in cognition and functioning at the onset of neuropsychological interventions.

A 14-week neuropsychological rehabilitation program was tested with 5 persons with mild AD (Avila, Bottino, Carvalho, Santos, Seral, & Miotto, 2004; Evidence grade=C1). The participants had been stabilized on rivastigmine prior to the study. The neuropsychological rehabilitation program consisted of memory training, repeated motor movements, verbal associations and categorization, and activities of daily living training. All 5 participants demonstrated statistically significant improvement in cognition and performance of activities of daily living.

## **7. Reality Orientation**

Reality orientation in the United States is generally not used in the care of persons with early stage AD, especially not in a classroom setting. This approach has the reputation of being applied insensitively. In Europe, however, classroom reality orientation programs for the treatment of early stage AD have been applied sensitively with positive results on cognition. The majority of reviewed studies were conducted at a memory specific day hospital in Italy, with participants being recruited from the outpatient centers. The reality orientation intervention in one of the studies was performed at home by the participants' caregivers after the caregivers were instructed in the technique.

Metitieri and colleagues (2001, Evidence grade=B2) conducted a retrospective study of 74 persons with early stage AD, mean MMSE=18. Participants were enrolled in at least one cycle of reality orientation therapy (ROT) from 1994-1998. Comparisons were made between the 46 participants (treatment group) who completed at least two to ten ROT cycles with 28 participants (control group) who completed only one ROT cycle. Outcomes that were compared included cognitive decline, defined as a loss of at least four points on the MMSE; functional decline,

defined as the appearance of urinary incontinence as reported by the primary caregiver; institutionalization; and death. The median time from baseline to cognitive decline was seven months longer in the treatment group than in the controls. Participants in the treatment group remained at home on the average of six months longer than control group participants. No statistical differences between groups were found for rate of functional decline or death.

Onder and colleagues (2005, Evidence grade=A2) compared the treatment effects of donepezil alone with reality orientation therapy in combination with donepezil. Participants included 79 (total N=156) persons with mild AD. All participants were being treated with donepezil. Participants were randomly assigned to either a reality orientation treatment group or medication-only control. Caregivers of the treatment group participants were required to offer the program at home three days per week for 30 minutes per day for 25 consecutive weeks. Findings included gains of .2 in MMSE scores for the treatment group, a slight improvement, while the control group evidenced a decline of 1.1 points on their median MMSE score over the same time period.

In a controlled study of reality orientation therapy, Zanetti and colleagues (1995, evidence grade=A2) demonstrated that persons with mild to moderate AD may benefit from the intervention. The group of 16 participants who received cycles of one month reality orientation therapy classes with breaks of five to seven weeks between cycles improved in verbal fluency in comparison with the control group. At the end of the 8 month study, the reality orientation therapy group also demonstrated mild improvement in their median MMSE score (0.68) while the control group declined (-2.58).

A meta-analysis of 6 randomized controlled trials with a total of 125 participants of classroom reality orientation (RO) was performed by Spector, Davies, Woods, and Orrell. (2000, Evidence grade=A1) demonstrating a positive effect of RO on cognition. The largest study found a 2.1 point benefit on MMSE scores for the treatment group compared to the control group. Variation among the operationalization of control groups was found. Some studies used a 'no treatment' control group, while others provided control group participants with some type of social therapy ('time-control'). The results of this analysis indicated no effects on outcomes from differences in control groups, suggesting that the qualities of RO rather than the effects of social interaction influenced the outcomes.

## **Conclusions**

Current scientific research examining brain plasticity and neuronal regeneration clearly supports the possible efficacy of non-pharmacological interventions for the treatment of AD, despite the progressive nature of the disease. Studies collectively support that persons in early AD stages are capable of learning and that this learning results in improved cognitive outcomes.

This comprehensive literature review clearly demonstrates that non-pharmacological therapies for cognitive enhancement are effective in the treatment of AD. A range of cognitive stimulation interventions have been tested with positive results. Overall, outcomes of cognitive stimulation programs include: improved memory and mental status, errorless learning achievement, improved executive functioning, improved functioning in activities of daily living, decreased

depression, and decreased general cognitive impairment. Studies of the long-term benefits of cognitive therapies have shown gains were maintained as long as 3 months following the intervention's termination. In longitudinal studies where a control group was used, persons with AD who received a cognition enhancement intervention maintained higher MMSE scores compared with the control group for up to two years following the intervention.

The strongest evidence supports the effectiveness of structured therapies: cognitive training and rehabilitation, memory rehabilitation, and reality orientation as opposed to less-defined approaches, although a well-done study conducted in Spain demonstrated that cognitive stimulation is capable of maintaining and improving cognition for a year. Cognitive stimulation with combined therapies has also produced significant benefits for memory and other cognitive functions. Neuropsychological rehabilitation interventions show promise, although few studies were found and sample sizes were small, N=1 to 5. Cognitive stimulation may be a very effective approach in the treatment of AD, but only three empirical studies could be found to support this intervention. The remainder of the literature on cognitive stimulation was descriptive and anecdotal. Interventions utilizing memory rehabilitation interventions should be based upon the known losses related to a specific pathological process and residual abilities in persons with AD.

### Recommendations

Further studies are needed testing cognitive therapies for other types of dementia, i.e., frontal-temporal and Lewy body dementia. Head-to-head studies of the varying types of cognitive therapies are also indicated to provide evidence of the most efficacious intervention. Also, standardized content for each type of cognitive therapy should be defined to serve as the 'model' intervention for the head-to-head studies.

### Rating Summary

<b>Intervention or Process Tested:</b>	<b>% rated As "A"</b>	<b>% rated As "B"</b>	<b>% rated As "C"</b>	<b>% rated As "D"</b>
Support for brain plasticity (n=6)	67	33	0	0
Learning in Alzheimer's disease (n=6)	33	17	50	0
Cognitive training and rehabilitation (n=9)	33	11	33	23
Cognitive stimulation using combined therapies (n=3)	67	33	0	0
Memory rehabilitation (n=11)	45	0	45	10
Neuropsychological rehabilitation (n=2)	0	0	50	50
Reality orientation (n=4)	75	25	0	0
Total: N = 41	19	6	12	4

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## Literature Review of Exercise Interventions for Persons in Early Stage Alzheimer's Disease

Although a large body of research exists testing exercise interventions with older adults, research testing exercise interventions specifically in persons with early-stage Alzheimer's disease (AD) is lacking. Exercise studies in persons with AD are typically conducted in long-term care settings with persons who have more advanced disease and are focused on balance, strength and range-of-motion exercises (Heyn, et al., 2004). Therefore, despite a growing body of basic science findings and empirical studies supporting the positive outcomes of exercise interventions, particularly the beneficial effects of aerobic exercise interventions on brain plasticity and cognition, the effects of exercise interventions in persons with early stage AD are less robust. Using a prospective design, following a cohort of older adults, persons who exercised three or more times/week were less likely to develop AD than those who exercised at lower levels or did not exercise at all. The protective effects of exercise were attributed to the observed delay in the onset of dementia (Larson, Wang, Bowen, et al., 2006).

The beneficial effect of exercise on brain function is increasingly supported by basic science findings supporting neuronal plasticity and the effects of enriched environments, including exercise, on neuronal function and vitality. Cerebral neuropathological changes in AD include cerebral atrophy, decreased blood flow and metabolism, and decreased number of working neurons, synapses, and neurotransmitters in multiple cortical and subcortical regions of the brain. (Reisberg, Franssen, Souren, Auer, & Kenowsky, 1998). Exercise, especially aerobic exercise may be particularly robust for improving cognition and function in persons with early-stage AD since their brains remain plastic to some extent. Such an assumption is supported by findings in animal models. Exercise was found to delay or reverse cerebral structural and functional changes in transgenic mice with AD pathology in the brain. Recently, exercise has been reported to delay  $\beta$ -amyloid accumulation and improve memory in transgenic mice (Adlar, Perreau, Pop, & Cotman, 2004; Lazarov, Robinson, Tang, et al., 2005). Exercise might further help persons with early stage AD through sparing brain tissue loss and increasing cerebral vasculature and blood flow which were most noticeable in the frontal, parietal, and temporal cortices (Kramer, Bherer, Colcombe, Dong & Greenough, 2004).

Additionally, exercise effects are attributed, in part, to increased levels of brain-derived neurotrophic factor (BDNF), a neurotrophin associated with learning, cell health and survival, and protection from injury. Additionally, exercise affects vascular factors contributing to cognitive decline, including hyperinsulinemia and insulin resistance, both of which increase the risk of AD (Fillit, et al., 2002; Ott et al, 1999; Peila, Rodriguez, & Launer, 2002). Exercise moderates the effects of aging on dopamine levels in the brain, and decreased dopamine levels are associated with age-related neurological disorders (Ball & Birge, 2002). Exercise increases the oxygen-transport capacity and resulting blood circulation to the brain, potentially increasing performance and neuronal preservation. (Fillit et al.) Importantly, in animal studies, the type of exercise that produced greater benefits for neurogenesis and synaptic plasticity was acrobatic exercise, requiring motor learning, compared to forced exercises, such as running or exercise on a treadmill (Ball & Birge). These findings suggest that exercise forms that require attention of motor learning, such as Taiji, might have larger impact on improving cognitive functioning than other exercise forms.

## **Search Method**

The literature search took place between December 12, 2006 and January 16, 2007. Databases utilized in the search include PubMed, CINAHL, PsychInfo, and the Cochrane Database of Systematic Reviews. The following terms were used: dementia, exercise, health promotion, and Alzheimer's disease. Mesh terms were cross-referenced, such as dementia and exercise to narrow the search. When a citation was found, links to related studies from a study to be included in the review were also explored. Further searches were done on the names of authors of research articles found in the initial search as well as on the names of their projects. Additional searches were performed using the names of researchers known for their work with people in early stage dementia. Professionals working in the field contributed lists of references on early stage Alzheimer's disease interventions. Once articles had been pulled for inclusion in this review, further references were found using the ancestry method.

## **Inclusion Criteria**

All research articles testing an exercise intervention in persons in early stage AD were included in the review. This review focuses on early stage AD, defined as having a diagnosis of early stage Alzheimer's disease with either an MMSE score of 18 or higher, a CDR score of 2.0 or less, or a GDS of 2 or less. Studies including mixed groups, persons at early AD stages and persons more progressed in AD, were also included if the results were applicable to early stage AD. Only research reports written in English and French (translator available) were reviewed. Reports based on undocumented opinion were excluded.

## **Definitions**

Aerobic exercise: also known as endurance exercise, refers to exercises that involve continuous and rhythmic use of large muscles for at least 15 minutes three or more times per week and increase resting heart rate by at least 60% of heart rate reserve (American College of Sports Medicine 1986).

Exercise: Performed activity of the muscles, voluntary or otherwise, especially to maintain fitness. Active exercise means the individual performs voluntary contraction and relaxation of the muscles. Assistive exercise means the individual performs the movement with the aid of a therapist. Therapeutic exercise is movement performed with supervision for the purpose of restoring normal function to diseased or injured tissues (Venes & Thomas, 2001).

## **Evidence in support of exercise interventions for persons with early stage AD**

The search produced 11 data-based articles testing the effects of exercise interventions on a variety of outcomes. An additional dissertation (grey literature) testing a strength training program was found, but not included in the review due to difficulty accessing the study report.

## **Multi-modal interventions including exercise**

Teri and colleagues (2003, Evidence grade = A2) completed a multimodal intervention study testing the effectiveness of home-based exercises and caregiver training in behavior

management. Using a randomized, experimental design, the study was conducted in the home setting with persons (N=140) in the early to early middle AD stages (mean MMSE = 17.6) and their family caregivers. Caregivers/persons with AD dyads in the treatment group received 12 hours of instruction in the home, followed by follow-up visits to answer questions and assess outcomes. Exercises included aerobic/endurance activities, strength training, balance, and flexibility training, with a goal of maintaining 30 minutes of moderate-intensity exercise daily. Post-intervention outcomes included improved physical role functioning scores, less depression, and fewer days of restricted activity for the treatment group. Outcomes were maintained at 2-year post-intervention, with a trend toward lower institutionalization rates for treatment group subjects. The strength of this bimodal intervention is supported by the long-term positive outcomes in addition to immediate gains.

Burgener, Gilbert, and Mathy (2006, Evidence grade=A2) examined the effects of a multimodal intervention, including Tai Chi exercises. Using brain plasticity theory as a basis for the intervention, an experimental design was used to test the multimodal intervention. Subjects, who were in the early stage of AD, were randomly assigned to either a treatment (n = 24) or control (n = 19, delayed treatment) group. Baseline mean MMSE scores were 22.5 for all subjects. A 20-week multimodal intervention consisting of: 1) Tai Chi exercises; 2) Cognitive/behavioral therapies, and 3) A support group was offered to the treatment group. Post-intervention MMSE scores varied significantly between the groups (increased for the treatment group), while baseline scores did not differ, indicating a treatment effect. Improvements in executive functioning were also evident in the treatment group after 20 weeks. Treatment group subjects demonstrated improved balance, while a decline in balance was seen in the control group. Between group differences were also evident for self-esteem at 20 weeks, although no baseline differences were found. A stabilization effect was found for depression and illness, with treatment group subjects increasing by only 0.4 points and the control group increasing by 1.7 points on illness ratings.

Tai chi, body work and cognitive work is a multi-modal intervention tested with persons with AD and other related cognitive impairments in an adult day care (Sanglier, Sarazin, & Zinetti, 2004; Evidence grade = C1). Participants (N=20) initially attended 3 days a week for 4 months of orientation, including a weekly 60-minute course. The multi-modal intervention was completed in three 20-minute sessions per week. The multidisciplinary team included orthophonists, massage therapists, and ergonomic specialists. Each session began with self-massage to connect participants with their bodies, to warm up and get centered, and to identify the different body parts. Exercises and short sequences of movements were successfully performed. Each session ended with a short self-massage with each body part being named as it was massaged including the different parts of the face and sense organs. The study was conducted over a three year time period. Due to the observed progress in year 2, the researchers decided to add daily 20-minute Tai Chi exercise to the intervention in year 3. Year 4 plans included adding Tai Chi classes for staff, teaching family members Tai Chi exercises with the goal of enjoying shared exercises at home, and the addition of outreach classes to build relationships with community-dwelling older adults. Staff observation of participants engaged in Tai Chi informed treatment decisions in other areas. Staff observed marked improvement in participants' behavior including increased calm, concentration, balance, and overall quality of life.

An exercise and diet supplement dual intervention was tested using an experimental design in a residential care facility with persons (N=191) in the early to middle AD stages (mean MMSE = 17.8) (Rosendahl et al., 2006; Evidence grade = B2). The exercise intervention was conducted by physiotherapists and included high-intensity functional exercises consisting of tasks to improve leg strength, postural stability, and gait ability. Exercises were based on identified functional deficits and individualized for each subject. The nutritional intervention consisted of a high-protein energy supplement. It was hypothesized that the energy supplement would increase the training effects if consumed immediately after exercising. The intervention included 29 sessions over a 3-month time period. Positive effects included improvements in physical functioning (improved self-paced gait, balance, and lower-leg strength) for the treatment group. No effects were found for the addition of the nutritional supplement.

The combined effects of exercises and cognitive and social stimulation were tested by Arkin (2003, Evidence grade = B2) in a small (N=24) community-based study. Persons in the early AD stages (MMSE range 15-29) participated in 16 to 20 exercise sessions and 10 activity sessions for 2 to 8 semesters. The exercise sessions were supervised by students with the assistance of caregivers. Exercises included stretching and balance, about 30 minutes of aerobic activity, and 30 minutes of upper- and lower-body strength training using resistance machines. In addition to the exercises, 50% of the weekly sessions also included memory and language stimulating activities. Cognitive stimulation activities were varied and included such tasks as story recall, word associations, traveling bingo, and object descriptions (selected from about 14 activities). Compared to age-matched health older adults, treatment group subjects evidenced gains in the six-minute walk test, mood, and a slowing in cognitive decline. The positive benefits of using students to supervise the intervention, including motivation and cost-effectiveness, are described.

### **Exercise-only intervention studies**

Thomas and Hageman (2003; Evidence grade = B2) utilized a pre/post-test design to test an exercise intervention in community-dwelling persons with AD (mean MMSE = 17.8) attending an adult daycare facility. The exercise intervention consisted of moderate-intensity resistance training of the hip extensors, abductors, knee extensors and flexors, and dorsiflexors using a Theraband resistance method. Subjects participated in exercises 3 days/week for a 6-week time period. Subjects exercising at least 2 x weekly experienced gains in quadriceps and handgrip strength, gait speed, and sit-to-stand time. Benefits for daycare attendees are evidenced by this exercise intervention.

An earlier study by Teri and colleagues was also conducted in the home setting (1998; Evidence grade = B2). This small (N=3), non-experimental study utilized caregiver-directed exercise activities for persons in the early to middle AD stages (mean MMSE = 17.8). Exercises were individualized and included walking, strength training, and balance and flexibility exercises. Outcomes included physical measures, health status, and caregiver reports of restricted activity days, disability days, falls, and exercise participation before and after the 12-week treatment. Although the physical outcome data were not reported, adherence rates were high for compliance with the exercise treatments and completion of all assigned exercises (33%). The lack of a full description of the measured outcomes lessens the contribution of this study to the exercise literature.

Palleschi and colleagues (1996; Evidence grade = B2) examined the effects of an aerobic (ergocyclometer) exercise with 15 male participants (MMSE range: 18-21). The aerobic exercise intervention was conducted for a three-month period, 3 days/week for 20 minutes using ergocyclometer at a submaximal intensity of 70% of maximal heart rate. A pharmacological wash out period of at least three weeks took place prior to the study's initiation. Mean MMSE scores increased from 19.40 +/- 1.06 to 21.73 +/-1.33. Tests of verbal span and supra-verbal span demonstrated significant increases post-treatment.

One additional study included home-dwelling persons (N=23) at both early and late disease stages, with a mean MMSE score of 16 and a range of 1 to 23 (Rolland, Rival, Pillard, Lafont, Rivere, Albarede & Vellas, 2000; Evidence grade = B2). The exercise intervention included 5 to 12 weeks of endurance exercises (walking, exercise bicycle) adapted to the person's individual exercise capacity. No control group was included, with participants serving as their own control for pre- and post-treatment measures of the intervention's effects. Positive treatment effects were nutritional status and cognitive ability (improved MMSE scores) with reductions in risks for falls and behavioral problems. Although family members assisted with the exercise intervention, they did not experience an increase in workload. Although this study was conducted with a mixed participant group (early and later disease stages), the positive outcomes support the potential of an individualized, home-based exercise program on persons in the early AD stages.

A study of persons at varying levels of dementia, including early stages, was conducted to examine the relationship of exercise participation on depression (Regan, Katona, Walker, & Livingston, 2005; Evidence grade=C1). Persons with AD and their caregivers (N=224) living in the community (United Kingdom) were assessed regarding their exercise levels: absent, moderate, and vigorous. The sample included 30% of persons in early stage AD, compared to 41% with moderate AD and 29% with advanced AD. Persons who exercised were significantly less likely to be depressed (17%) compared to persons with AD who did not exercise (44%). Exercise participation was most strongly associated with depression, even more so than taking part in hobbies and other interests. Findings support the potential benefits of exercise participation for protection of depression in early stage AD.

A meta-analysis of exercise interventions for persons with cognitive impairment and dementia was conducted by Heyn and colleagues (2004; Evidence grade = A1). Although not all of the 30 included studies were directed to persons with AD or those in the early disease stages, MMSE scores were >18 in 10 of the 30 studies. The results from the meta-analysis included moderate, positive effects on cognitive performance (ES = .57), strength (ES = .75), physical fitness (ES = .69), and functional performance (ES = .59). Gains in flexibility (ES = .91) and cardiovascular effects (ES = .62) were also identified. The exercise interventions included in this meta-analysis consisted mostly of mobility exercises (primarily walking), isotonic and isometric strength-resistance exercises, light aerobic exercises, endurance and balance exercises, and cardiovascular training. The overall mean effect for differences between exercisers and non-exercisers was .62, supporting the positive effects of exercise on a variety of outcomes in persons with dementia.

## **Conclusions**

Studies examining the effects of exercise in persons with AD demonstrate improvements primarily in cognition, physical and functional ability, depression, and behavioral symptoms in exercisers compared to non-exercisers. The type of tested exercise form has varied, with home-based aerobic/endurance activities, strength training, balance and flexibility training being most common. The research evidence for the positive effects of exercise has also been conducted using more rigorous study designs, with the majority (>80%) being rated at A or B level.

Although only two studies of Tai Chi as a specific exercise form for persons with AD were found, Tai Chi may be an appealing exercise alternative for older adults with AD. In two reviews of the research regarding Tai Chi, the reviewers (Klein & Adams, 2004; Khalsa, 1998) described the multiple benefits of Tai Chi over other exercise forms for older adults including improved physical function, pain management, balance, immune response, flexibility, and reduced risk of falls. Tai Chi uniquely utilizes a moderate intensity, slow movement to capitalize on gains in balance and strength to improve physical and functional outcomes. Tai Chi is a particularly salient exercise form for persons with AD as it supports the development of a memory for movement and a relaxation response. The variety of Tai Chi forms, slow movements, and inclusion of relaxation/mediation (Qi-Gong) exercises reinforces learning, facilitating the performance of Tai Chi movements by persons with AD. The American Geriatrics Society has recommended Tai Chi as the most beneficial form of exercise for fall prevention.

Aerobic exercise is another exercise form worthy further exploring in persons with early stage AD. (Yu, Kolanowski et al. 2006) Other than supports from basic science of its positive effects on brain plasticity, aerobic exercise has been shown in a meta-analysis to improve cognition, particularly executive functioning in older adults who participated in moderate aerobic exercise three times a day for even a short duration of 8 weeks (Colcombe & Kramer, 2003). Although improvements in specific cognitive domains were not measured, improvements in global cognition have been observed in the three studies that have aerobic exercise components. Therefore, these collective benefits support that Tai Chi and aerobic exercise merit further testing as interventions in persons with early stage AD at least.

## Recommendations

The collective evidence for the efficacy of multi-modal interventions including an exercise component supports these intervention combinations as an effective intervention for a variety of outcomes for persons in early stage AD. Evidence for the positive effects of exercise interventions alone is strong. Therefore, therapies including exercise are strongly recommended for persons in early stage AD.

## Rating Summary

Grading Score	Number	%
A	3	27%
B	6	55%
C	2	18%
Total Reviewed	11	100%

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## **Literature Review of Exemplar Programs for Persons in Early Stage Alzheimer’s Disease**

A literature review exemplar programs was conducted to identify effective means of supporting, maintaining, and improving independent functioning in early stage Alzheimer’s disease. Exemplar programs represent those studies that substantially advance the science of interventions appropriate for persons in the early AD disease stages. Exemplar interventions are distinguished from other interventions by their effects on a variety of outcomes, including improved overall quality of life. Exemplar programs do not just address specific symptoms, but instead have broad effects.

### **Search Method**

The search for evidence to support exemplar programs took place between December 26, 2006 and January 21, 2007, utilizing PubMed, Cochrane, and CINAHL databases. The following terms were used: Alzheimer’s disease therapy, Alzheimer’s disease prevention and control, psychosocial factors, programs for AD, behavioral interventions in AD. When a citation was found, links to related studies from a study to be included in the review were also explored. Further searches were done on the names of authors of research articles found in the initial search as well as on the names of their projects. Additional searches were performed on the names of researchers known for their work with people in early stage dementia. Professionals working in the field contributed lists of references on early stage Alzheimer’s disease interventions. Once articles were analyzed for this review, additional studies were identified using the ancestry method. Web sites were also searched for efficacy work done on individual programs. A researcher in the field was contacted for information yet to be published on one intervention program.

### **Criteria for Inclusion**

All research articles written after 1984, examining broad-based outcomes were included in the review. This review focuses on early stage Alzheimer’s disease, defined as having a diagnosis of early stage Alzheimer’s disease with either an MMSE score of 18 or higher, a CDR score of 2.0 or less or a GDS of 2 or less. Only research studies that evaluated interventions related to outcomes of persons in early stage AD were included. Articles written in English were reviewed. Reports which were based on undocumented opinion or were solely descriptive in nature were excluded.

### **Definitions within Exemplar Programs**

Cognitive-linguistic stimulation—cognitive-linguistic activities typically involve “different aspects of cognition, including language, problem solving, memory, and reasoning” to keep patients engaged in using skills that can deteriorate if not used.<sup>8</sup> It is a type of multi modal intervention.

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<sup>8</sup> Mahendra, N. (2001). Direct interventions for improving the performance of individuals with Alzheimer’s disease. *Seminars in Speech and Language* 22(4),291-304.

Cognitive training, “CT refers to any non-pharmacologic intervention designed to improve cognitive functioning, regardless of mechanism of action. Typically, CT interventions focus on specific domains of cognitive functioning (such as memory, attention, and problem solving), but more general, cognitive mediated domains of functioning, such as basic and instrumental activities of daily living (ADLs and IADLs, respectively), social skills, and behavioral disturbances can also be targeted.” CT strategies can be divided into two sub categories: Compensatory strategies and restorative techniques. Compensatory strategies teach new ways of performing tasks by “working around” cognitive deficits. Examples of compensatory strategies include internal strategies such as organizing information by visualization or categorizing, encoding through multiple sensory channels, asking questions during learning, and focusing on a single task. Compensatory interventions also use external strategies such as memory notebooks, environmental cues, and calendars. Restorative strategies are used to re-train people with Alzheimer’s disease to perform tasks using practice, drills, spaced retrieval, and a variety of other techniques.<sup>9</sup>

Cognitive rehabilitation—this term is used mostly in Europe to describe the same interventions used in cognitive training.

Cognitive stimulation—for the purpose of this review, cognitive stimulation is defined as non-regimental involvement in activities which require mental functioning. Cognitive stimulation can be either active, as in a group discussion of current events or solving a crossword puzzle or passive, which is observational in nature. Examples of passive cognitive stimulation include listening to a poetry reading, watching a play, or listening to music. Cognitive stimulation is much less formal than cognitive training/cognitive rehabilitation.

Managed care—the use of health information and support services as a means of reducing excessive utilization, preventing crisis episodes, and helping patients emotionally cope with their illnesses.<sup>10</sup>

Memory rehabilitation—a variety of learning techniques are applied to improve the memory skills of participants. Memory rehabilitation is based on the hypothesis that memory loss in Alzheimer’s disease results from defective encoding and storage of information rather than forgetting information.<sup>11</sup> It focuses on encoding information in areas of the brain that are less impaired by Alzheimer’s disease. Cognitive training and cognitive rehabilitation differ from memory training and rehabilitation in three ways. First, the memory interventions specifically target encoding of memory and recall, while the cognitive therapies target many different areas of cognition, sometimes within the same therapy. Secondly, the cognitive approaches usually offer a milieu of therapies within a study while the reviewed studies in memory rehabilitation typically look at one method per study. Third, current memory research is based upon the location of active pathology within the brains of people with Alzheimer’s disease, targeting

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<sup>9</sup> Sitzer DI, Twamley EW, Jeste DV. (2006). Cognitive training in Alzheimer’s disease: a meta-analysis of the literature. *Acta Psychiatrica Scandinavica*, 114(2), 75-90.

<sup>10</sup> Clark PA, Bass DM, Looman WJ, McCarthy CA, Eckert S. (2004). Outcomes for patients with dementia from the Cleveland Alzheimer’s Managed Care Demonstration. *Aging & Mental Health*, 8(1), 40-51.

<sup>11</sup> Metzler-Baddely C., & Snowden J.S., (2005). Brief report: errorless versus errorful learning as a memory rehabilitation approach in Alzheimer’s disease. *Journal of Clinical and Experimental Neuropsychology*, 27(8), 1070-9.

therapies to the functions coordinated in the parts of the brain with the least amount of impairment.

Multi-modal interventions—for the purpose of this review, multi-modal therapy is defined as at least two techniques, tested within the same study, aimed at improving one or more aspect of the life of the person with Alzheimer’s disease.

## **Evidence Support for Exemplar Programs**

Some excellent studies and evidence-based programs were found that appear to improve the lives of persons with early stage AD. Inherent in these programs are multimodal interventions, including exercise interventions combined with other therapies; the Center for Positive Aging; sleep enhancement; managed care programs; and technology-based interventions. The need for research testing intensive programming for persons in the early stages of AD was examined by Zarit and Leitsch<sup>12</sup> with recommendations for mechanisms to prove efficacy.

### **1. Multimodal Interventions**

The most common type of approach in the non-pharmacological treatment of early stage AD is to use a variety of interventions to improve quality of life, enhance cognition, and promote functional independence. The strength of these interventions is that they are based on one of the strongest theories supporting interventions with persons with dementia: the theory of the effects of enriched environments on neuronal regeneration. Multimodal interventions are designed to provide a variety of stimuli, affecting neuronal activity and responses through varying mechanisms.

Teri and colleagues (2003, Evidence grade = A2) completed a multimodal intervention study testing the effectiveness of home-based exercises and caregiver training in behavior management. Using a randomized, experimental design, the study was conducted in the home setting with persons (N=140) in the early to early middle AD stages (mean MMSE = 17.6) and their family caregivers. Caregivers/persons with AD dyads in the treatment group received 12 hours of instruction in the home, followed by follow-up visits to answer questions and assess outcomes. Exercises included aerobic/endurance activities, strength training, balance, and flexibility training, with a goal of maintaining 30 minutes of moderate-intensity exercise daily. Post-intervention outcomes included improved physical role functioning scores, depression, and fewer days of restricted activity for the treatment group. Outcomes were maintained at 2-years post-intervention, with a trend toward lower institutionalization rates for treatment group subjects. The strength of this bimodal intervention is supported by the long-term positive outcomes in addition to immediate gains.

Olazaran and colleagues (2004, Evidence grade=A2) implemented a 12 month, randomized controlled study of cognitive/motor intervention. Eighty-four persons with dementia were enrolled, 40 in the control group and 44 in the treatment group. All participants were stabilized on cholinergic medications prior to their entry into the study. The intervention was conducted

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<sup>12</sup> Zarit S.H., & Leitsch S.A., (2001). Developing and evaluating community based interventions for Alzheimer’s patients and their caregivers. *Aging & Mental Health*, 5(Supplement 1), S84-S98.

twice weekly and consisted of reality orientation techniques, cognitive exercises, training of activities of daily living, a coffee break, psychomotor exercises or workshop, and a conclusion. Cognitive ability in both groups declined after an initial improvement in cognitive ability in the intervention group. Cognitive loss was more rapid in the control group. A long term mood benefit was seen in treatment group participants.

Burgener, Gilbert, and Mathy (2006, Evidence grade=A2) examined the effects of a multimodal intervention on a variety of outcomes in persons in early stage AD. Using brain plasticity theory as a basis for the intervention, an experimental design was used to test the multimodal intervention. Participants, who were in the early stage of AD, were randomly assigned to either a treatment (n = 24) or control (n = 19, delayed treatment) group. Baseline mean MMSE scores were 22.5 across groups. The 20-week intervention consisted of: 1) Taiji exercises; 2) Cognitive/behavioral therapies, and 3) a support group were offered to the treatment group. The control group received an attention-control intervention of monthly educational programs and supportive phone contacts. Post-intervention MMSE scores varied significantly between the groups (increased for the treatment group), while baseline scores did not differ, indicating a treatment effect. Improvements in Exit 25 scores were also evident in the treatment group after 20 weeks. Treatment group participants demonstrated improved balance, while a decline in balance was seen in the control group. Between group differences were also evident for self-esteem at 20 weeks, although no baseline differences were found. A stabilization effect was found for depression (Geriatric Depression Scale) and illness (Cumulative Illness Rating Scale), with treatment group participants increasing by only 0.4 points and the control group increasing by 1.7 points on illness ratings.

An exercise and diet supplement dual intervention was tested using an experimental design in a residential care facility with persons (N=191) in the early to middle AD stages (mean MMSE = 17.8) (Rosendahl et al., 2006; Evidence grade = B2). The exercise intervention was conducted by physiotherapists and included high-intensity functional exercises consisting of tasks to improve leg strength, postural stability, and gait ability. Exercises were based on identified functional deficits and individualized for each subject. The nutritional intervention consisted of a high-protein energy supplement. It was hypothesized that the energy supplement would increase the training effects if consumed immediately after exercising. The intervention included 29 sessions over a 3-month time period. Positive effects included improvements in physical functioning (improved self-paced gait, balance, and lower-leg strength) for the treatment group. No effects were found for the addition of the nutritional supplement.

The combined effects of exercises and cognitive and social stimulation were tested by Arkin (2003, Evidence grade = B2) in a small (N=24) community-based study. Persons in the early AD stages (MMSE range 15-29) participated in 16 to 20 exercise sessions and 10 activity sessions for 2 to 8 semesters. The exercise sessions were supervised by students with the assistance of caregivers. Exercises included stretching and balance, about 30 minutes of aerobic activity, and 30 minutes of upper- and lower-body strength training using resistance machines. In addition to the exercises, 50% of the weekly sessions also included memory and language stimulating activities. Cognitive stimulation activities were varied and included such tasks as story recall, word associations, traveling bingo, and object descriptions (selected from about 14 activities). Compared to age-matched health older adults, treatment group subjects evidenced gains in the

six-minute walk test, mood, and a slowing in cognitive decline. The positive benefits of using students to supervise the intervention, including motivation and cost-effectiveness, are described.

The Elder Rehab program was developed at the University of Arizona's Department of Speech & Hearing Sciences and utilizes students to work with persons in early-stage AD in an outpatient setting (Mahendra & Arkin, 2003; Evidence grade=B2). Programs offered included physical exercise, pairing of students on a one to one basis with participants to supervise them in 10 weekly, 2-hour sessions consisting of either volunteer service or other meaningful community activity. Students also administered structured verbal fluency and conversational stimulation. The students used their own motor vehicle to transport themselves and their participant partner to and from the center and to all volunteer and community service projects. Twenty-four persons in early-stage AD started the four-year program. Four participants completed the program and were assessed throughout the project. All four remained stable in most measures throughout the study, contrary to the expected decline seen in AD.

## **2. Southwest Florida Interdisciplinary Center for Positive Aging**

Its mission is to provide interdisciplinary education, training, research, and service within a university environment and in varied urban, rural, and reservation community environments for the varied needs of the older persons in Charlotte, Collier, Glades, Hendry, and Lee counties to enhance overall quality of life. Programs for people with memory loss are aimed at education, therapies, and psychosocial assistance for the entire family. Preventative programs are offered for those with memory loss. Research at the Center for Positive Aging has focused on treating cognition, depression, quality of life, functional abilities, and behaviors in Alzheimer's disease through the use of therapeutic recreation interventions.

Buettner (2006, evidence grade=B2) examined outcomes in 40 persons diagnosed with early AD who participated in programs of their choice at the Center for Positive Aging. A control group consisted of 40 participants who also had a diagnosis of early AD but did not attend the Center. MMSE scores for the treatment group improved from a mean score of 20.5 at baseline to a mean score of 21.52 after six months of participation. The score did decline somewhat (20.08) 12 months after baseline measurement. Depression scores also improved for treatment group participants, with significant improvements at both the 6 and 12-month assessments. Depression improved somewhat for control group participants, but did not reach significant levels. Quality of life scores also improved for the treatment group, with declines noted in the control group. Trends were also found for improved self-esteem and lower stress for treatment group participants, although these trends were not found in the control group. Collectively, these findings support the effectiveness of comprehensive community-based interventions on a variety of outcomes in persons in the early AD stages.

A complimentary report of the benefits of participation in community-based recreational activities utilized interview data to assess benefits from participation (Buettner & Fitzsimmons, 2006; Evidence grade = C1). Participants and family members were interviewed at 6-month intervals to evaluate satisfaction and perceived stress. Findings included: 90% of participants experienced health benefits; 97% reported having made 3 or more close friends due to participation; 92% developed new leisure activities and increased opportunities for community

participation; and 97% reported extremely high satisfaction levels with the program. The multiple benefits of this comprehensive, community-based program are evident in both the positive qualitative and quantitative outcomes for persons in the early AD stages.

### **3. Sleep enhancement**

Common problems in AD, even in the early disease stages, are sleep disturbances such as day/night confusion, getting up repeatedly during the night, and having nightmares and hallucinations. One line of study is showing promise in treating this prevalent care issue. Although this study was conducted using persons in more advanced AD stages as participants, the fact that the study was conducted in the home setting, involved caregiver support and education, and represents translational research merits its inclusion as an exemplary line of research.

McCurry, Gibbons, Logsdon, Vitiello and Terri (2005, Evidence grade: A2) developed a sleep program for persons in home setting at the middle disease stages (mean MMSE 11.8). NITE-AD is a program consisting of sleep hygiene education, daily walking, and increased light exposure all directed at improving sleep. Participants resided in the home for this community-based study. This study was a six-month randomized controlled trial of NITE-AD with 36 participants: 17 in the experimental group, and 19 in the control group. The control group received general dementia education and caregiver support, but no specific sleep interventions. At the end of the three month treatment, treatment group participants demonstrated significantly greater reductions in the number of nighttime awakenings, total time awake at night, and depression with increases in weekly exercise days compared to controls. At a six-month follow-up evaluation, treatment gains were maintained and additional significant improvements in the reduction of night awakenings was evident. NITE-AD participants also reported less sleepiness during the day and less time in bed during daytime hours than the control group. The significant and continuing positive effects of this community-based study merit further investigations with larger samples.

### **4. Managed Care**

The primary purpose of managed care is to control health care costs, however, there can be some related benefits for participants as well. A study was found that examined outcomes in persons with AD.

Clark, Bass, Looman, McCarthy, and Eckert (2004, Evidence grade: A2) examined the effects of a participant-based form of managed care. This study utilized a 12-month randomized controlled investigation of the effects of care consultation with the person with AD on the person's psychosocial well-being and appropriate utilization of health care resources. The care consultation process involved the person with AD in the assessment of all strengths, including caregivers, and needs of the participant. After the assessment, the care consultant, together with the participant, devised a plan of care for treatment of their AD, referring the person to Alzheimer's Association services and to traditional health care opportunities. The control group did not receive care consultation, but had all traditional resources of the Alzheimer's Association and the health care community available to them, but had to seek these services themselves. Findings suggested that treatment group participants felt less isolated because of their disease

and experienced less difficulty in coping than the control group. Findings included outcomes for the treatment group such as: participants more severe impairment (yet still living in the community) had fewer physician visits, were less likely to have an emergency department visit or hospital admission, and experienced less depression and strain.

## **5. Technology-Based Interventions**

Research has been conducted using a variety of technology-based interventions as a means to deliver care or provide assistance to persons in early-stage AD. These studies, although in their infancy, hold potential to increase the scope of available services in the community setting. As technology-based interventions often minimize the need for professional support services, can be utilized by family caregivers, and can often be offered for minimal costs, their potential for widespread dissemination is also optimized as a method of delivering cognitive training to persons with Alzheimer's disease.

Computer based training was used to instruct four participants with early to middle stage AD in functional tasks appropriate to their lifestyle (Hofmann, Hock, & Muller-Spahn, 1996; Evidence grade=C1). Photographs were taken of the steps in tasks to be learned and were scanned into a computer. Persons with AD then used the touch screen of the computer to sequence the tasks. A facilitator was present to offer advice, but participants were encouraged to work as independently as possible. All four participants' training performance improved substantially, but training did not result in significant cognitive improvement.

Oriani and colleagues (2003, Evidence grade=C1) examined the use of an electronic memory aid (EMA) to support prospective memory in early to mid stages of AD. Five persons, four of which had an MMSE score of 18 or greater, were trained in the use of the electronic memory aid. The EMA is an electronic device which uses vocal recordings for appointments or tasks. The EMA can be programmed with dates and times for appointments, using an alarm system to alert the user to a message regarding an appointment or task. The user pushes a button and then receives the recorded message. The EMA was compared within each of the 5 participants to two other conditions: 1) recall using a written list, and 2) recall without any external memory aid. Results revealed that the use of the EMA yielded significantly better results on recall than either of the other two methods.

A digital clock and a memory book for daily life activities were utilized in a case study of a person with early-stage AD by Quittre, Olivier, and Salmon (2005, evidence grade=C1). The authors utilized a spaced retrieval method of teaching the use of these devices. All interventions were also reinforced at home by the person's caregiver. At the end of the three month training period, even though the participant's MMSE score did decline, her functional abilities improved.

Poon, Hui, Dai, Kwok, and Woo (2005, Evidence grade= C1) compared the administration of cognitive assessment and cognitive training using video conferencing and face-to-face methods. A total of 12 sessions were conducted via both methods. Twenty-two participants with early-stage AD were randomized into two groups (n=11). Following the cognitive intervention, both groups improved MMSE scores significantly. Significant improvement of both groups was also seen in the areas of attention, memory, and language, with no difference in outcomes in either

group. However, in spatial construction ability, only the face to face group improved. As outcomes were similar for both groups, support was evidenced for the efficacy of video conferencing methods as an alternative to face-to-face interventions.

## Conclusions

A variety of approaches show promise in improving the lives of persons with dementia. These exemplar studies have resulted in a variety of positive outcomes, including improved cognition and physical abilities, lessened depression, heightened self-esteem, and enhanced communication ability. Although some areas have received minimal testing (sleep enhancement and managed care programs), the potential of these developing areas of study to affect broad outcomes merits their inclusion as an exemplar program. Support for technology-based intervention studies is hampered somewhat by the small sample sizes and limited outcomes measured. However, technology-based programs offer strong promise for the future as an exemplary method to: minimize the need for professional support services, be utilized by family caregivers, be offered for minimal costs, and be widely disseminated.

## Recommendations

Multimodal interventions demonstrate great promise and should receive support for further investigation. These interventions are exemplar programs for several reasons, including the power of the intervention, the effects on a variety of outcomes including cognitive, functional, and affective behaviors, and the fit of the intervention with the most powerful theory supporting therapies for persons with AD. These interventions are particularly promising in the treatment of early stage AD. Many intervention studies are designed to affect one or two symptoms. The more powerful multimodal interventions hold the promise of actually interfering with the course of the disease through their effects on neuronal functioning, producing widespread positive benefits.

## Rating Summary

Topic of Study	% graded As "A"	% graded As "B"	% graded As "C"	% graded As "D"
Multi-Modal Interventions, n=6	50	50	0	0
Center for Positive Aging, n=2	0	50	50	0
Sleep Enhancement, n=1	100	0	0	0
Managed Care, n=1	100	0	0	0
Technology-Based Interventions, n=4	0	0	100	0
Total = 14	5	4	5	0

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## **Literature Review of Health Promotion Interventions for Persons in Early Stage Alzheimer's Disease**

In reviewing interventions for health promotion for persons in the early AD stages, several categories of intervention studies were apparent: sleep disorders management, nutritional support programs, falls prevention, and college courses for persons with AD. The research evidence for interventions across these broad categories varies, with some areas (falls prevention, sleep disorders management) having more substantial intervention studies than others (college courses). Each category will be reviewed separately, including an evaluation of the strength of each focused area.

### **Search Method**

The literature search took place between December 27, 2006 and January 16, 2007. Databases utilized in the search include PubMed, CINAHL, PsychInfo, and the Cochrane Database of Systematic Reviews. The following terms were used initially: dementia, health promotion, and Alzheimer's disease. Mesh terms were cross-referenced, such as dementia and health promotion to narrow the search. Once studies focusing on health promotion were identified, the search was narrowed to the identified topic. For example, dementia, Alzheimer's disease, and falls prevention were then cross-referenced for each database to fully search within each category. When a citation was found, links to related studies from a study to be included in the review were also explored. Further searches were done on the names of authors of research articles found in the initial search as well as on the names of their projects. Professionals working in the field contributed lists of references on early stage Alzheimer's disease interventions. Once articles were included in this review, further references were found using the ancestry method.

### **Inclusion Criteria**

All research articles addressing health promotion interventions (within the 5 identified categories) for persons in early-stage AD were included in the review. This review focuses on early stage AD, defined as having a diagnosis of early stage Alzheimer's disease with either an MMSE score of 18 or higher, a CDR score of 2.0 or less or a GDS of 2 or less. Only research reports written in English were reviewed. Reports based on undocumented opinion were excluded.

### **Definitions**

Antioxidant—a substance that reduces damage due to oxygen such as the damage done by free radicals, which are chemicals that react very easily with other molecules by capturing electrons and thus altering the molecule's molecular structure. Dietary antioxidants include fruits and vegetables.

Falls: A fall is defined as 'an event reported either by the faller or a witness, resulting in a person inadvertently coming to rest on the ground or another lower level, with or without loss of consciousness or injury' (Rubenstein, Robbins, Josephson, Schulman, & Osterweil, 1990)

Oxidative stress—a harmful cellular condition caused by exposure to damaging molecules.

REM sleep: REM is a sleep stage characterized by rapid eye movements and is affected by cholinergic systems, a system impaired in AD.

Sleep disturbances: Sleep disturbances are defined as disruptions to normal sleep including insomnia, hypersomnia, excessive nocturnal motor activity, and hallucinations or behavioral disturbances.

### **1) Evidence supporting sleep disorders management in early stage AD**

Although sleep disorders often occur in the early stages of dementia, studies examining factors associated with sleep disorders or testing interventions to improve sleep outcomes have been conducted primarily in institutional settings with persons at later disease stages. Also, some medications for treatment of AD, including the cholinesterase inhibitors, contribute to sleep disturbances through the development of ‘night terrors’ – a common side effect. Although minimal, a few studies were found that examined sleep disorders in persons in early stage AD. A total of 8 studies were included in this review.

#### **Supporting Evidence**

A two-year longitudinal study by Hatfield and colleagues (2003; Evidence grade = C1) compared disturbed sleep cycles and cortisol rhythms in home-dwelling persons with AD. A total of N=46 participants were included with n=19 in the control group, n=13 in the early AD stages (mean MMSE = 24.1), and n=14 in more progressed disease stages (mean MMSE = 13). Results indicated that circadian rhythms in early stage AD participants were comparable to the control group. However, actimetric data obtained from a wrist-mounted activity monitor indicated that deterioration of activity/rest cycles was common and occurred early in the disease. Activity/rest cycle disturbances were also found to be progressive, increasing with disease progression. Overall, findings provide evidence of activity/rest cycle disturbances in persons in early stage AD, despite stable circadian rhythms.

The relationship between anxiety and nighttime disturbances was examined in a descriptive study conducted by McCurry, Gibbons, Logsdon, and Teri (2004, Evidence grade = C1). Using a sample of community-dwelling persons with probable AD (N=153), caregiver ratings of nighttime disturbances were evaluated. Findings included moderate frequency of awakenings, reported by 29% of caregivers. Anxiety and physical function impairment were significantly associated with nighttime awakenings, with the presence of anxiety doubling the odds of persons with AD waking their caregivers. Findings support the prevalence of nighttime disturbances and suggest that interventions directed at lowering anxiety may decrease disordered sleep.

Nighttime disturbances in persons in the early AD stages paired with their caregivers (n=25) were compared to an age-matched comparison group (n=18) (Pollak & Stokes, 1997; Evidence grade = B2). The purpose of the study was to determine the correlates of nighttime disturbances in persons with AD and their caregivers and the control group. Participant pairs kept daily sleep logs and recorded wrist motor activity every .5 minute for 9 days. Findings were somewhat

surprising in that persons with AD were not significantly more active at night than their caregivers. Persons with AD were significantly less active in the daytime than were their caregivers. Cognitively-intact older persons (comparison group) were significantly more active at night than their caregivers and were as active by day as their caregivers. The caregivers of persons with AD and control group caregivers had similar rest-activity patterns. The researchers concluded that the decreased daytime activity in persons with AD may have resulted from deficient physical stimulation or frailty. The shared variations in activity for the participant pairs indicated that caregivers interacted mainly with the person with AD at bedtime and at rising time in the morning.

Vitiello and colleagues (1990; Evidence grade: C1) assessed sleep disturbances in 44 persons with mild AD compared to 45 controls (non-impaired). Participants were living in the home at the time of the study. Findings included increased time awake and number of awakenings for persons with AD compared to controls. Slow wave sleep was also reduced in persons with AD, indicating disturbances in sleep cycles. These descriptive findings identify specific sleep disturbances in persons with AD, including disruptions to the phases inherent in the sleep cycle.

Related reports of assessment of sleep quality examined differences in persons with AD and a control group on both sleep apnea and sleep quality, including REM sleep, outcomes. Alterations in the rapid eye movement (REM) sleep phase was examined in 28 persons in early stage AD (mean MMSE=18) and 28 age- and gender-matched controls (Bliwise, Tinklenberg, Yesavage, et al., 1989; Evidence grade: C1). All participants were living in the home setting during the study. Sleep stages were assessed in a sleep laboratory (one night) using polysomnography measures. The percent of time spent in REM sleep did not vary between the groups, although some REM qualities differed between groups. Participants with AD were found to have overall poorer sleep quality, lower percentages of deep sleep (Stages 3 and 4), and a high percentage of light sleep (Stage 1). Findings support variations in sleep quality in persons with early-stage AD compared to non-impaired age-matched controls. From this same sample, Bliwise and colleagues (1989; Evidence grade = C1) reported findings of sleep apnea variations between the two groups. Findings included no differences in occurrence or frequency of sleep apnea in persons with AD compared to controls. Persons with AD who experienced oxygen deprivation during sleep experienced increased confusion upon awakening.

#### Studies using participants transitioning into middle AD stages (MMSE: 12-16)

Two studies were found that included persons in the early middle AD stages, a time of transition in the disease process. Although the studies do not meet the strict criteria for inclusion (early stage AD), findings may be relevant to persons in the early AD stages.

A common problem in AD, even in the early disease stages, is sleep disturbances such as day/night confusion, getting up repeatedly during the night, and having nightmares and hallucinations. One line of study is showing promise in treating this prevalent care issue (McCurry, Gibbons, Logsdon, Vitiello & Teri, 2005). Although this study was conducted using persons in more advanced AD stages, the fact that the study was conducted in the home setting, involved caregiver support and education, and represents translational research merits its inclusion in this review.

Three groups comprised the sample in a descriptive study examining sleep rhythm disturbances across early (n=10; mean MMSE=16), middle (n=8; mean MMSE=13.3), and late (n=16; mean MMSE=4.4) AD stages (van Someren, Hagebeuk, Lijzenga, et al., 1996; Evidence grade = C1). A control group (n=11) was also included. Participants in early and middle AD stages were residing in the home, while persons at later disease stages were in institutional settings. Measures of indoor light were taken to assess the relationship of light exposure to sleep rhythm disturbances. Findings included the highest level of rest/activity disturbances in institutionalized participants – the most progressed in AD. Stability of rest/activity rhythms was associated with high levels of daytime activity and environmental light, including seasonal variations and indoor illumination. Disturbed rest/activity rhythms were associated with low levels of daytime activity. Finally, night-time activity was found to be highest when days were shorter (low light) and lower when days were longer (more light). The findings support the relevance of environmental factors (light) and daytime activity levels on rest/activity disturbances.

McCurry, Gibbons, Logsdon, Vitiello and Teri (2005, Evidence grade: A2) developed a sleep program for persons in home setting at the middle disease stages (mean MMSE 11.8). NITE-AD is a program consisting of sleep hygiene education, daily walking, and increased light exposure all directed at improving sleep. Participants resided in the home for this community-based study. This study was a six-month randomized controlled trial of NITE-AD with 36 participants: 17 in the experimental group, and 19 in the control group. The control group received general dementia education and caregiver support, but no specific sleep interventions. At the end of the three month treatment, treatment group participants demonstrated significantly greater reductions in the number of nighttime awakenings, total time awake at night, and depression with increases in weekly exercise days compared to controls. At a six-month follow-up evaluation, treatment gains were maintained and additional significant improvements in the reduction of night awakenings was evident. NITE-AD participants also reported less sleepiness during the day and less time in bed during daytime hours than the control group. The significant and continuing positive effects of this community-based study merit further investigations with larger samples.

## **Conclusions**

Studies of sleep disturbances in persons in early stage AD have been primarily descriptive in nature. Outcomes have provided evidence for variations in sleep quality and disturbances in persons with AD compared to controls. Persons with AD have generally demonstrated: 1) variations in sleep cycles; 2) rest/activity disturbances related to daytime activity and light exposure; 3) increased nighttime awakenings; and 4) increasing sleep disturbances with disease progression. Increased sleep disturbances were also found to be associated with higher anxiety levels and physical functional impairment. Only one study tested an intervention to improve sleep outcomes, and this study included persons at the early-middle disease stages. Overall, research testing interventions are lacking, especially interventions targeting persons in the early AD stages.

## **Recommendations**

As the effects of sleep disturbances are well-supported in persons in early stage AD, further studies of interventions to enhance sleep are merited. To date, some evidence supports the

effectiveness of sleep hygiene interventions for sleep enhancement in the home setting. As this intervention was carried out with the assistance of the family caregiver, the intervention has the potential to be widely disseminated with minimal costs. Further studies are needed, however, to support the effectiveness of this intervention and others across stages of AD and ethnically and geographically diverse populations.

### **Rating Summary**

Score	Number	%
A	1	12.5%
B	1	12.5%
C	6	75%
Total Reviewed	8	100%

## **2) Evidence supporting nutritional interventions for persons in early stage AD**

The physiological mechanisms underlying neuronal damage suggests that disease is caused by the same type of stress and environmental factors that cause aging in the rest of our bodies. Some people live to be over 90 years old and maintain normal cognitive functioning, while some people develop neurodegenerative diseases, such as AD, in their late 50's. The reason for the difference is extremely complex, involving the interaction of genetics and environment. Treatments for neurological diseases such as AD are focused on these two different aspects of brain aging. This review will focus on the environmental aspect. The environment can be manipulated to promote positive brain aging, by introducing substances such as pharmaceuticals or nutrients to the brain to counteract negative effects of aging and promote neuronal integrity. Nutritional interventions, then, have the potential to affect neuronal integrity and possibly disease onset and progression.

### **Supporting Evidence**

The search produced only epidemiological studies testing nutritional interventions for persons in early-stage AD. Studies testing nutritional interventions for persons with AD included persons in the later disease stages and were conducted primarily in long-term care settings. Therefore, this review includes a sampling of 8 research reports of nutritional interventions, mostly systematic reviews of the research literature, for prevention of neurodegeneration and preservation of neuronal function. The reviewed studies provide some support for nutritional practices that can be used as treatment modalities for AD. For clarity, the evidence is divided into three categories: 1) Dietary restriction, 2) Antioxidants, and 3) Mediterranean diet. Due to ethical considerations in testing some nutritional interventions, such as dietary restriction, many studies have used animal models, with translational research being non-existent.

#### **1. Dietary restriction**

In a review of the literature, Mattson, Chan, and Duan (2002, evidence grade=A1) cite many studies that show a variety of effects of dietary restriction. Animal studies show that rodents fed a restricted diet compared with a control group of rodents who were allowed unlimited access to food revealed changes in gene expression in brain cells during aging and that dietary restriction can control those changes. Additional animal studies showed that dietary restriction has a positive impact at the neuronal level on prevention of neurodegeneration and also demonstrated a positive impact on actual neurodegeneration in the hippocampal and cortical areas, resulting in a positive effect on learning and memory.

Mattson, Duan, Chan, Cheng, Haughey, & Gary, et al. (2002, evidence grade=A1) conducted a review of 125 research articles on the cause, prevention, and treatment of neuronal damage in the brain and found that because two different areas of the brain contain neural stem cells capable of producing new neurons and glial cells, it is possible for the brain to repair itself after being damaged. They also found evidence that the extent of neuronal death in early stage Alzheimer's disease may not be as great as initially thought and that neurons may instead be dysfunctional, but capable of revival. A variety of substances and strategies have been found to facilitate the

protection and repair of neurons, including dietary restriction, ingestion of antioxidants, behavioral therapy.

Mattson (2002; Evidence grade = A2) observed that dietary restriction provides protection to neurons from oxidative stress by decreasing the amount of neurotoxic substances in the brain. Further work indicated that dietary restriction actually increased the amount of newly generated neural cells in the adult brain, suggesting that this dietary manipulation can increase the brain's capacity for plasticity and repair. The data obtained from animal studies extrapolated to humans suggests that moderate levels of dietary restriction (1800-2200 calories/day) can dramatically reduce the incidence and severity of Alzheimer's disease, Parkinson's disease, and stroke.

Pasinetti and colleagues (2007, evidence grade=A1) conducted a review of the literature on AD and nutrition. Based on their findings, the researchers conducted further studies using animals as subjects (mice) to determine the role of various nutritional strategies on AD. In these experimental studies, they found that high caloric intake based on saturated fat promotes AD type  $\beta$ -amyloidosis while dietary restriction based on reduced carbohydrate intake plays a preventive role in the onset of AD.

## **2. Antioxidants**

Research indicates that our cells become more vulnerable to oxidative stress as we age, which leaves us more vulnerable to the expression of neurodegenerative diseases such as AD. Further, epidemiological human and controlled animal and human studies are showing that introducing more antioxidants into our diets can reduce oxidative stress to our cells, thereby preventing and even reversing observable signs of neurodegeneration.

Joseph and colleagues (2000, Evidence grade=A2) reviewed animal and human studies of antioxidant effects on cellular vulnerability to oxidative stress. The researchers concluded that antioxidants in both laboratory and in vitro experiments were effective in reducing oxidative stress on cells. Further, the team determined that ingestion of foods replete with antioxidants, such as blueberries, spinach, and strawberries, produced these same cellular protective effects and actually reversed signs of neurodegeneration in aged rodents.

Further support for the role of antioxidants as neural protectors at the cellular level was found in a large review of studies by Gonzalez-Gross, Marcos, and Pietrzik (2001, Evidence grade=A1). The researchers called for further clinical studies to determine the link between nutrient intake/nutritional status with cognitive impairment and to determine if it is possible to inhibit or delay the onset of dementia using nutritional interventions.

Another review of almost 300 research articles (Esposito, Rotilo, DiMatteo, DiGiulio, Cacchio, & Algeri, 2002; Evidence grade=A1) confirmed the positive role antioxidants play in protecting neurons from damage by free radicals and reactive oxygen. The researchers called for further research on the neuroprotective role of antioxidants in humans, especially using a combination of antioxidants.

In a review of over 100 studies on a variety of nutritional interventions in AD, Luchsinger & Mayeux (2004, Evidence grade=A1) determined there was insufficient evidence to permit specific recommendation on diet for the prevention and treatment of AD. While in vitro studies show promise for a variety of diet modifications, very few human studies have been done to confirm those results. Also, contradictory findings require further clarification before dietary recommendations can be made.

A review of the literature by Martin (2003, Evidence grade=B2) demonstrates a relationship between dietary intake of foods containing antioxidants and reduced incidence of AD. The review examined epidemiological studies of humans and in vitro animal studies.

An overview of the relationship between dementia and nutrition, which consisted of a literature review, (Salerno-Kennedy & Cashman, 2005, Evidence grade=A1) indicated that free radicals and oxidative stress play a role in neurodegenerative diseases and suggest that the consumption of antioxidants, particularly folate and vitamins B6 and B12 can be used to prevent AD. The authors also recommend a diet with less saturated fat, and, based on the relationship between polyunsaturated fatty acid intake and lower risk for AD, greater consumption of fish and seafood.

Epidemiological studies support the relationship between reduced levels of vitamin B12 and high levels of the folate marker homocysteine and higher incidence of AD. Morris and colleagues (2005, Evidence grade B2) found a relationship between dietary intake of tocopherol (Vitamin E) with a reduced incidence of AD and other types of cognitive impairment in the 1993-2002 Chicago Health and Aging Project (n=1141 persons aged 65 or older). A study of 321 men receiving services through the Boston Veterans Affairs Medical Center concluded that intake of vitamins B6 and B12 and dietary folate all resulted in cognitive improvement, (Tucker, Qiao, Scott, Rosenberg, and Spiro, 2005; Evidence grade=B2).

Another epidemiological study of 228 people being seen in a Swiss memory clinic compared levels of blood homocysteine, folate, and vitamin B12 in relation to incidence of dementia. Quadri and colleagues (2004, Evidence grade=B2) compared the blood levels of these three substances in persons who had no dementia (n=55), persons who had mild cognitive impairment with a CDR of .5 (n=81), and 92 persons with mild dementia and with a clinical diagnosis of AD (n=74) or vascular dementia (n=18). It was found that persons with the least amount of folate had significantly higher odds for mild cognitive impairment or dementia. In participants with a CDR of .5, the mean MMSE score was significantly lower in the group that had the highest levels of homocysteine than in the lowest group. The group concluded that folate deficiency may precede AD and vascular dementia.

In a longitudinal study, the Nun Study, the researchers examined predictors of AD incidence and severity (Snowdon, Tully, Smith, Riley, & Markesbery, 2000; Evidence grade=B2). Finding related to nutritional intake demonstrated a strong association between low serum folate and the atrophy of the cerebral cortex (N=30).

Ellinson, Thomas, and Patterson (2004, Evidence grade=A1) conducted a systematic review of published studies on the relationship between serum vitamin B12, folate, and total homocysteine and cognitive function in elderly persons. A total of three case controlled studies were reviewed

and found that serum homocysteine was significantly higher in cases of cognitive impairment when compared with controls. However, there was a wide variation for both serum vitamin B12 and folate. In fact, one case study found a relationship between increased levels of vitamin B12 and decreasing cognitive functioning scores. The authors conclude that no dietary recommendation for the prevention or treatment of Alzheimer's disease can be made in this area until further studies are done.

### **3. Mediterranean Diet**

The diet of people who live in the Mediterranean area of Europe is rich in virgin olive oil, which is high in antioxidants. Other components of the Mediterranean diet are fish, red wine, and cereals. Epidemiological studies show that in countries where this diet was the norm, such as Spain, Greece, and Italy, there are lower incidence rates of cancer and cardiovascular disease. The high amounts of antioxidants in this diet are expected to play a neuroprotective role, thereby reducing the incidence of Alzheimer's disease as well.

A review of the literature completed by Solfrizzi, D'Introno, Colacicco, Capurso, Del Parigi, & Capurso et al. (2005, Evidence grade=A2) concluded that, based on lack of definitive evidence, no dietary recommendations on fish, vegetables, or unsaturated fat can be made for the treatment of Alzheimer's disease because of the lack of clear clinical evidence that this type of diet is an effective treatment. However this type of diet is still recommended for lowering the risk of cardiovascular disease, obesity, diabetes, and hypertension.

Another review of the literature by Panza Solfrizzi, Colacicco, D'Introno, Capurso, & Torres et al. (2004, Evidence grade=A1) provides support for the Mediterranean diet as protective against cognitive decline, when moderate amounts of olive oil, at least 100 g per day, are consumed as part of that diet.

A study focusing on the chemicals found primarily in fish was conducted by Tully and colleagues (2003, Evidence grade=B2) to determine if there was a relationship between low serum cholesteryl ester-docosahexaenoic acid (DHA) levels and the severity of clinical dementia. The 119 subjects had a mean MMSE score of 19.5. The control group (n=45) did not have dementia. They found serum cholesteryl ester-DHA levels were progressively reduced with the severity of dementia.

### **Conclusions**

Strong evidence supports that in both animals and humans reducing the number of calories ingested while maintaining adequate nutrition results in longer life and reduced risk for many different types of diseases, including AD. An emerging strategy for the prevention of AD and the treatment of early stage AD is to limit caloric intake without decreasing nutrition. However, one associated phenomenon with AD is weight loss, so this strategy needs further study before a recommendation can be made.

While many epidemiological studies have been done to show that various nutrients can prevent or treat AD, there are few randomized controlled trials with humans as subjects. Before a

definitive dietary recommendation can be made, translational research studies need to be conducted. The body of evidence to support nutritional interventions in the prevention and treatment of AD is growing and has potential as a treatment modality following translational studies.

### **Recommendations**

Based on animal research and descriptive studies in humans, support for some dietary modifications can be found including fat and carbohydrate reduction and assuring adequate Vitamin E, B6, and B12 levels.

### **Rating Summary**

<b>Topic of Study</b>	<b>% graded As “A”</b>	<b>% graded As “B”</b>	<b>% graded As “C”</b>	<b>% graded As “D”</b>
Dietary restriction: n= 4	4			
Antioxidants: n=11	6	5		
Mediterranean diet: n=2	2			
Total:	17			

### 3) Evidence in support of interventions for fall prevention

The search produced 6 data-based articles describing interventions for falls prevention, including one review of the literature. Three additional community-based studies were found including persons just below the early disease stages (mean MMSE scores from 16.2 to 16.9)

#### Supporting Evidence

One descriptive study utilized a review of medical records of community-dwelling persons with AD (N=153) admitted to the hospital following a fall (Rowe & Fehrenbach, 2004; Evidence grade = C1). Although no MMSE scores or ranges were provided, the community-dwelling sample typifies persons in the early disease stages. Injuries were high from the fall, including 96% of persons admitted. The most common reasons for the injury included falling against an object (31% of injuries), losing balance, and falling out of bed. Tripping over an object and falling on the stairs were the next two highest reasons for the fall. The bedroom was the most common site of the injury (40.5%), followed by bathroom and kitchen (15.9% and 14.5% respectively). One alarming finding was the high rate of institutionalization following the injury, 64.6% of persons with AD were discharged to an institution rather than going back home. Overall, findings are helpful in understanding the etiology for falls in the home setting.

An intervention study was conducted by Manckoundia and colleagues (2006, Evidence grade = B2) to examine the effects of a cognitive task on static posture on persons in the early AD stages (N=13) compared to non-impaired health controls (N=17). The range of MMSE scores for the AD group was 21 – 28.5, supporting the early stage nature of the group. It was hypothesized that a dual task (cognitive + mobility) would result in greater postural instability in persons with AD compared to age-matched healthy controls. The cognitive task included the watching of a 30 second video sequence, then answering questions about the sequence during the postural measures using a force platform. This hypothesis was supported by increased sway in the AD group following a cognitive task compared to no change in the healthy controls. These findings have implications for positive environments (less distraction) that might lessen risk for falls in persons in early AD stages.

A review of the research regarding falls and cognitive impairment was conducted by Shaw (2002; Evidence grade: D). The author did not evaluate the research literature, but rather reported the epidemiology of falls in persons with dementia and causes for falls. Across studies, the most common causes of falls included: postural instability; medication side effects; neurocardiovascular instability including orthostatic hypotension and carotid sinus hypersensitivity; environmental factors; and type of dementia. Studies examining interventions for fall prevention were reviewed, although the majority of studies included persons in the later AD stages, with many being conducted in institutional environments. The author concluded that studies testing interventions for fall prevention were sparse, with more attention being needed to risk factors for fall, improving compliance with interventions that modify risk factors, and studies testing interventions to modify cardiovascular and neurocardiovascular instability.

Franssen and colleagues (1999, Evidence grade = C1) examined balance and coordination in 365 community-residing persons at various stages of dementia, with 33% (n=138) of the sample

being in the early disease stages (mean MMSE: 23, GDS stage 3 to 4). Compared to persons with no cognitive impairment (MMSE 29.2; GDS stage 1 and 2 indicating mild cognitive impairment [MCI]), persons at GDS stages 3 and 4 displayed decreased performance on balance and coordination measures. No gender differences were found for any outcome measures. The authors conclude that persons with mild AD may be at greater risk for falls than persons with MCI.

One additional study included home-dwelling persons (N=23) at both early and later disease stages, with a mean MMSE score of 16 and a range of 1 to 23 (Rolland, Rival, Pillard, Lafont, Rivere, Albarede & Vellas, 2000; Evidence grade = B2). The exercise intervention included 5 to 12 weeks of endurance exercises (walking, exercise bicycle) adapted to the person's individual exercise capacity. No control group was included, with participants serving as their own control for pre- and post-treatment measures of the intervention's effects. Positive treatment effects were nutritional status and cognitive ability (improved MMSE scores) with reductions in risks for falls and behavioral problems. Although family members assisted with the exercise intervention, they did not experience an increase in workload. Although this study was conducted with a mixed participant group (early and later disease stages), the positive outcomes support the potential of an individualized, home-based exercise program targeting fall prevention for persons in the early AD stages.

A description of the literature provided a summary of common reasons for falls in persons in early disease stages (Shaw & Kenny, 1998; Evidence grade = D). The most common reasons found for falls were: medications, particularly benzodiazepines, phenothiazines, and anti-depressants; cardiovascular disease, and environmental hazards. Recommendations for multi-disciplinary interventions for falls prevention were given, including the modification of medications and environmental hazards.

## **Conclusions**

Evidence exists for the negative outcomes, including increased mortality, from falls in persons with early stage AD. Falls in persons with early stage AD have been found to be associated with increased cognitive impairment, environmental hazards, changes in balance and equilibrium, and distractions while walking or performing a task. Few studies have been conducted testing interventions for fall prevention. Overall, most studies have been descriptive in nature. Tested interventions include endurance exercises and elimination of distractions.

## **Recommendations**

Given the strong evidence regarding the negative effects of falls and descriptive studies identifying risks for falls, future studies are needed to identify a variety of interventions to be implemented in the home setting. Given the increased environmental hazards in the home, studies conducted with the assistance of the family caregiver have the potential to significantly reduce fall risks. Although studies are limited, the positive effects of exercise on fall risk reduction also merit further investigation and dissemination of exercise interventions to those identified at highest risk for fall.

### Rating Summary

Score	Number	%
A		%
B	2	33%
C	2	33%
D	2	34%
Total Reviewed	6	100%

#### **4) Evidence supporting college courses for health promotion in early stage AD**

Only one study was found that examined the effects of college course participation on outcomes in persons in early-stage AD. Although limited, the strength of this line of research rests on the multiple positive benefits of participation on health outcomes and overall quality of life.

##### **Supporting Evidence**

Fitzsimmons and Buettner (2003; Evidence grade: C1) developed and tested an experimental college course for persons newly diagnosed with AD. The course focused on interventions for promotion and maintenance of optimal health and included such topics as: physical and cognitive fitness, nutrition, recreation, communication, understanding the disease process, depression, coping, relationships, and driving concerns. Community-dwelling participants were included in the 10-week college course. Pre- and post-course outcome measures included stress, depression, self-efficacy, and self-esteem, with positive effects found following the course. The emphasis on teaching new health habits and lifestyle changes early in the disease process holds promise for fewer health-related problems with disease progression.

##### **Conclusions**

Although only one study was found that tested college-based interventions for health promotion, the positive nature of the intervention and benefits to participants merit further study. Given the high rates of depression in persons in early stage AD, this type of intervention may be especially appealing due to the positive effects on depression anxiety, and self-esteem.

##### **Summary Recommendations for Health Promotion**

Beginning support has been found for interventions to promote health behaviors (college course), reduce falls (exercise and risk reduction), improve sleep outcomes, and promote nutritional health. Collectively, improvement in these health-related factors has the potential to significantly impact on overall functioning and health benefits for persons in early stage AD. As descriptive studies and animal studies regarding nutrition have provided a basis for translational research, the groundwork has been laid for the appropriate next step for intervention development.

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## **Literature Review of ‘Other’ Interventions Persons in Early Stage Alzheimer’s Disease**

In reviewing interventions for persons in the early AD stages, studies related to outcomes of persons with early-stage AD that did not fall logically into another category were placed in the ‘other’ section. Within this category, studies were found related to the following areas: driving safety; volunteer work programs; life story writing and other writing interventions; technology-based interventions; art and creative activities; dance therapies; neural stimulation (TENS & vagal stimulation); and narrow areas of study such as telephone support programs and teaching persons with AD to use cell phones, etc. The research evidence for interventions across these broad categories is varied, with some areas (driving safety; art and creative activities) having more substantial intervention studies than others (dance therapies, stress management, and narrowly-focused interventions). Each category will be reviewed separately, including an evaluation of the strength of each area.

### **Search Method**

The literature search took place between December 10, 2006 and January 16, 2007. Databases utilized in the search include PubMed, CINAHL, PsychInfo, and the Cochrane Database of Systematic Reviews. The following terms were used initially: dementia, interventions, treatment, and Alzheimer’s disease. MESH terms were cross-referenced, such as dementia and interventions to narrow the search. Once studies focusing on a variety of interventions (~ 560) were identified, the entire database was reviewed to identify ‘miscellaneous’ areas of study. As general categories were identified, MESH terms were again cross-referenced for each category. For example, dementia, Alzheimer’s disease, and driving were cross-referenced for each database to fully search within each category. When a citation was found, links to related studies from a study to be included in the review were also explored. Further searches were done on the names of authors of research articles found in the initial search as well as on the names of their projects. Once articles were included in this review, further references were found using the ancestry method.

### **Inclusion Criteria**

All research articles addressing general interventions not falling into the other 6 search categories (cognitive therapies, support and psychotherapeutic interventions, exercise interventions, health promotion, exemplar programs, and delirium in early-stage dementia) were included in the ‘other’ category. This review focuses on early stage AD, defined as having a diagnosis of early stage AD with either an MMSE score of 18 or higher, a CDR score of 2.0 or less or a GDS of 2 or less. Only research reports written in English were reviewed. Reports based on undocumented opinion were excluded.

### **Definitions**

Montessori Method is a technique pioneered in Rome for improving the lives of children. Research is now looking at its use with persons with dementia. “Each lesson is first presented at its simplest level and each subsequent lesson, increasing in complexity, is a variation of previously mastered skills or concepts.” Learning materials are used from the every day

environment, tasks are broken down into small steps that are mastered and then sequence. The method involves immediate feedback, high probability of success, and repetition.<sup>13</sup>

On-road testing: Tests of driving safety that included actual driving performance under the supervision of an expert in safe driving behaviors.

Transcutaneous electrical nerve stimulation (TENS): TENS is the clinical application of an electrical current through electrodes attached to the skin. TENS is used to treat a variety of conditions, most commonly pain.

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## **1. Driving safety in early stage AD**

### **Significance**

The inclusion of interventions for driving safety goes beyond the significance of these studies for persons in early stage AD. While studies were conducted with this population, findings hold meaning for family caregivers, professional providers, and the community at large. This area of study has been developing since the early 1990s and provides a background for assessment and decisions regarding driving safety for this population.

### **Supporting Evidence**

Following the search techniques described previously, 17 studies of driving safety were identified, including one systematic review of the literature. For clarity, the research reports will be organized into four categories: 1) Neuropsychological assessment, simulator testing, and on-road testing comparison studies; 2) Factors associated with driving performance and cessation; 3) Provider and self-evaluations of driving performance; and 4) Review of safe driving studies.

#### **A. Neuropsychological assessment and simulator testing studies**

Three studies describing appropriate neuropsychological assessments for persons in early stage AD were published from 1994 to 1998. Rebok and colleagues (1994; Evidence grade = C1) compared the testing results of persons with probable AD (n=10; mean MMSE = 22) and 12 health, age-matched controls. At the time of testing, the majority of the sample (16) was driving, with the remaining subjects having terminated driving in the previous year. Using well-developed driving performance measures, including assessment of reaction time, decision-making, and perceptual-motor tracking, and neuropsychological assessments, persons with AD took longer to react and committed more driving errors. Persons with AD self-appraised their driving ability as equal to controls, however. Persons with AD also performed poorer on all neuropsychological tests. MMSE scores and category fluency tests were most strongly associated with driving behaviors. Conclusions include the effects of impaired mental status on driving performance and the lack of insight of persons with AD into their own driving ability.

These early findings were supported through subsequent studies by Brashear and colleagues (1998; Evidence grade = C1) and Carr and colleagues (1998; Evidence grade = C1). Sample sizes for both studies were larger. The study by Brashear and colleagues also included an unimpaired control group (n=47) and 37 drivers with dementia (mean MMSE scores: 22; CDR: 0.7). Recognition of 10 common road signs was analyzed for both groups. Persons with early stage AD failed the sign test (identifying at least 7 of the 10 signs) at higher rates than controls (57% and 11% respectively). Of particular concern was the failure of 76% of persons with AD to recognize a 'STOP' sign and 45% failing to identify a 'No Passing Zone' sign. The study by Carr and colleagues tested the reliability of a 39-sign recognition test with 38 very mildly impaired, 30 mildly impaired, and 12 moderately impaired persons with AD. A comparison group of 66 intact older adults was also included. From the 39 items, 10 items were selected to distinguish subjects with and without cognitive impairment. Using subject responses to the sign recognition test, 74% of persons with combined mild and moderate AD and 97% of the comparison group

subjects were correctly classified. Conclusions from both studies support the effectiveness of a brief sign recognition test as a screening tool for driving safety.

Two studies examined the relationship of simulated driving tests to outcome measures, including current driving status, cognition, and presence of cognitive impairment. Shua-Haim and Gross (1996; Evidence grade = C1) examined cognitive performance and simulated driving in 41 persons with early stage AD. Performance on the driving test predicted to degree of cognitive impairment, with significantly more persons scoring < 22 on the MMSE failing the test. No person with an MMSE score of <19 successfully completed the driving test. A later study by Cox and colleagues (1998; Evidence score = C1) compared driving performance in 45 persons with AD and 62 non-impaired controls. Of the AD group, < 50% (n=17) of the AD group were able to complete the simulated driving course, with MMSE scores being significantly related to total driving scores,  $r = -0.40$ . As 2 persons with mild AD performed equal to controls, the authors conclude that a dementia diagnosis alone was not a determining factor in driving safety.

Responses from a survey of neuropsychologists were used to compile a battery of tests to measure driving skills (Sylyk, Myers, Ahang, Wetzel & Shapiro, 2002; Evidence grade = C1). Tests included evaluation of attention and concentration, memory, visual spatial reasoning, visual tracking, and executive function. Using a small sample (N=22), persons were placed in either an impaired (mean MMSE = 20) and intact (mean MMSE = 28) group. After completing the 12 neuropsychological tests, drivers in the impaired group drive significantly slower and had more difficulties in lane boundary crossings than the control group. Drivers in the impaired group also drove less frequently. Overall, studies examining neuropsychological assessments and simulated driving performance have been effective in detecting driving errors in persons with early-stage AD, as well as reliably assessing safe driving behaviors.

## **2. Factors associated with driving performance and cessation**

Several studies examined driving performance and driving cessation in persons with early-stage AD. A longitudinal study by Duchek and colleagues (2003; Evidence grade = C1) included 58 healthy controls, 21 subjects with very mild AD (CDR = 0.5), and 29 persons with mild AD (CDR = 1). Evaluations of driving behaviors were conducted at 6-month intervals over 4 assessment points, or approximately 2 years following entry into the study. Progression into a 'not safe' driving category was fastest for the mild AD group compared to both groups, and for the very mild AD group and the healthy controls. The greatest change in specific driving behaviors was found in lane change and signal use behaviors and degree of impairment. Authors noted that with repeated testing, some participants in both the very mild and mild AD groups continued to retain safe driving skills, supporting the findings of the study by Cox and colleagues.

In a South American study, 56 persons with AD (mean MMSE = 18.5) and 31 controls (mean MMSE = 28.5) were evaluated using a semi-structured interview to assess driving behaviors (Zuin, Ortiz, Boromei, & Lopez, 2002; Evidence grade = C1). The number of motor vehicle crashes (MVC) and abnormal driving behaviors (ADB) were the outcome variables. Medical and neurological symptoms were also compared between the two groups, with the early AD group evidencing higher levels of abnormal gait compared to controls. Persons with AD had

significantly more multiple MVCs, with a trend toward higher ADBs. When gender was included in the analysis, males were found to have more multiple MVCs than women, with presence of dementia and gender being the strongest predictors of ADB, MVC, and multiple MVCs.

Adler and Kuskowski (2003, Evidence grade = C1) assessed driving history, habits, and expectations using a 44-item questionnaire in 53 persons with AD (mean baseline MMSE = 23.1) and informants, with reevaluation of driving behaviors by informants 25 to 39 months after the baseline assessment. On the follow-up evaluation, 46% of persons with AD continued to drive consistently, with 53.5% of the sample having ceased driving, mostly due to care provider recommendations. Using univariate logistic regression, both baseline MMSE scores and age were significant predictors of driving cessation. In the United Kingdom, Talbot and colleagues (2005, Evidence grade = C1) used a retrospective study design to examine driving cessation in 430 consecutive patients (mean MMSE = 19, with 73% of subjects having a dementia diagnosis) referred to a memory clinic for evaluation over 21 months. Caregivers (informants) completed a 16-item questionnaire addressing driving frequency, location (urban or rural), living arrangements, accident history, importance of driving, decision maker for driving cessation, and subjective opinion regarding driving safety of the person with AD. Both cognition and functional ability predicted significantly to persons with AD who continued driving. After controlling for cognitive and functional status, age (older) predicted to higher rates of driving cessation. Persons with AD most likely to continue driving were those living in cities and living alone. Consistent findings across studies and broad geographic locations support the relevance of cognitive impairment (MMSE) and increased age in predicting driving cessation.

Fitten and colleagues (1995; Evidence grade = C1) examined driving behavior in two cognitively impaired groups, AD and vascular dementia, with persons with diabetes, an age-matched control, and younger control group, N=80 total. (n=15 AD, mean MMSE=23.2; n=12, vascular dementia; mean MMSE =25.4) Lower drive scores were found in both cognitively impaired groups compared to controls, with persons with AD scoring lowest. Short-term memory impairment, visual tracking, and MMSE scores were most strongly associated with safe driving behaviors. Conclusions include that type and degree of cognitive impairment (AD and vascular) were better predictors of safe driving behaviors than medical diagnosis or age.

### **3. Provider and self-evaluations of driving performance**

Two related reports describe the outcomes of evaluations of driving performance by clinicians, experienced neurologists, and professional driving instructors. Both cross-sectional and longitudinal data are reported from the studies (Brown, Ott, Papandonatos, Sui, Ready & Morris, 2005; Evidence Grade = C1; Ott, Anthony, Papandonatos, E'Abreu, Burock, Curtin, et al., 2005; Evidence Grade = C1). Cross-sectional analysis included the comparison of neurologist and driving instructor ratings of driving ability to an on-road driving score (N=75; 50 persons with AD; n=33 very mild AD, mean MMSE = 24.9; n=17 mild AD, mean MMSE = 21.5). Participant self-ratings and informant ratings of driving ability were collected prior to physician ratings (blinded to ratings and on-road tests) and driving instructor on-road driving test (blinded to diagnosis and previous ratings). Of the three ratings, only the neurologist's ratings were related

to the on-road driving score. Driving instructors were less likely than the neurologist or the informant to rate the driving behavior as 'safe'.

Wild and Cottrell (2003; Evidence grade = C1) examined self-ratings of driving performance in persons with AD (n=15; mean MMSE = 22.3) and non-impaired controls to ratings from a driving test conducted by an independent evaluator (driving rehabilitation specialist). Using expert ratings, persons with AD were rated poorer on 9 of the 10 driving performance indicators. However, persons with AD rated themselves better than the specialist on 7 of the 10 indicators, while non-impaired elders rated themselves better on only 1 of 10 indicators. Results indicate that persons with AD are less reliable in their self-evaluations of driving performance and overestimate their driving ability.

Findings from an Australian study supported the association of mental status (N=19; MMSE range 20 to 25) to driving performance (Fox, Bowden, Bashford & Smith, 1997; Evidence grade = C1). Using a standardized medical examination, neuropsychological testing, and driving evaluation, only the person's MMSE score predicted to successful passing of the on-road driving evaluation (12 failed; 7 passed). The physician's assessment, neuropsychological test scores, and psychologist's predictions all failed to predict success in the driving evaluation. Findings support the need for an on-road evaluation to successfully predict safe driving behaviors in persons with early-stage AD.

Using 10 focus groups, Perkinson and colleagues (2005; Evidence grade = D) assessed beliefs and perceptions regarding driving behaviors of persons with AD. Health professionals, transportation and law-enforcement professionals, current and former, drivers with AD, and family caregivers comprised the focus groups. Results included the belief that a diagnosis of mild AD alone did not substantiate termination of driving. Family members were viewed as being most responsible to monitor driving safety. Each professional group also acknowledged their role in monitoring and assessing driving. Implications for education for family caregivers regarding the need to monitor driving and make appropriate referrals were identified.

#### **4. Review of safe driving studies**

In a review of 11 studies of driving behaviors in persons with AD, Adler, Rottunda and Dysken (2005; Evidence grade = A1) concluded that further studies were needed to support the reliability of neuropsychological tests in predicting safe driving behaviors. Fewer than 50% of studies using neuropsychological tests also utilized road tests to confirm the evaluation results. Variability in the road tests also contributes to a lack of consensus regarding the reliability of driving evaluations. Road tests tended to be based on routine driving situations rather than demanding evaluations. In 5 studies, persons with AD performed more poorly on driving tests, although the tests were unable to distinguish unsafe drivers. The authors recommend that all driving evaluations also include measures of visual spatial skills, attention, and reaction time. Also, although no consensus was found in the reviewed studies, Duchek and colleagues (2003) recommend testing every 6 months for persons with AD, a recommendation Adler and colleagues support.

#### **Conclusions**

Studies examining safe driving behaviors have been largely descriptive in nature. Evidence has been found for the efficacy and accuracy of on-road driving tests compared to neuropsychological evaluations and provider recommendations. Inaccuracies in self-reports of driving compared to on-road testing have also been identified, with persons in the early AD stages being found to over-estimate driving ability. Lower MMSE scores, perceptual inaccuracies, and overall memory impairment have been consistently associated with poorer driving performance. Family caregivers have been identified as the group to monitor driving safety by professional providers, although family members have also tended to over-estimate safe driving ability in persons with early-stage AD. The presence of AD alone has not been supported as an indicator for driving cessation, as some persons continue to evidence safe driving behaviors.

### **Recommendations**

Descriptive studies support the efficacy of on-road driving evaluations as an effective means of determining safe driving behaviors in persons with AD. Given the consistent findings from descriptive studies, studies testing interventions to improve driving behaviors and assist the persons with AD and family in termination of driving are the next logical step in this area of study. Driving evaluations at 6-month intervals following the disease diagnosis are recommended.

### **Rating Summary**

Grading Score	Number	%
A	1	6%
B	0	0%
C	15	88%
D	1	6%
Total Reviewed	17	100%

## **2) Evidence supporting volunteer work programs**

### **Significance**

The rationale for investigating benefits of volunteer work for persons with early stage AD is based on outcomes reported in several studies in healthy older adults with AD (Hunter & Linn, 1981) as well as a theoretical approach of providing opportunities to reintroduce some responsibility and control that is often diminished with the diagnosis and associated changes. Volunteer opportunities may include activities that match the individual's prior interests and hobbies such as dog walking, baby cuddling, animal assisted therapy, and visiting nursing home patients (Mahendra & Arkin, 2004).

### **Methods**

We searched the literature from January 1, 1990 through January 15, 2007, from the following databases; MEDLINE, CINAHL, PsychInfo, and Cochrane databases for studies with primary sources of data on prevention models for delirium in persons with dementia. We limited our search to English and Human studies. We searched using the key terms dementia, early Alzheimer's disease, volunteering, volunteer work and AD, prevention, controlled trials, and intervention. Mesh terms were cross-referenced where appropriate. Other sources reviewed included reference lists of published papers, and personal communication. We reviewed and categorized abstracts of 116 journal articles. We included 4 studies with primary data sources and early AD patients. We eliminated review articles, case studies, case reports, and letters to the editors.

### **Supporting Evidence**

A study by Arkin (1996; Evidence grade = B2) tested the effects of participation in a volunteer program that paired speech therapy students with 12 persons with early stage AD. This study utilized a convenience sample and pre- and post-test study design. Students supervised the volunteer participants in 1- weekly, 2-hour sessions of volunteer services or other meaningful community activity. The sessions also included student-directed structured verbal fluency and conversational stimulation for 30 to 50 minutes. Findings included improvements in memory and language post-intervention for 7 of the 12 participants. Eight participants also showed improvement in their descriptions of pictures and interpretation of proverbs.

Mahendra and Arkin (2003, 2004; Evidence grade = B2) conducted a longitudinal (4-year) that included testing a three-part intervention that included volunteer activities as part of the comprehensive cognitive-linguistic treatment. Participants included N=24 community dwelling persons in the early AD stages (8 men, 16 women) with a mean MMSE of 23.4. The intervention consisted of physical fitness training using a treadmill and stationary bicycle, supervised community volunteer services, and cognitive-linguistic activities. Volunteer activities were done in conjunction with an undergraduate student. Volunteer activities included: reading to preschool children, visiting nursing home residents, and assisting at a food bank. Positive effects were found for maintained or improved performance on discourse outcome measures. Caregiver reports were also evaluated, with 75% of the caregivers reporting they thought the person with

AD benefited from participation in volunteer programs. Subject patient measures of mood and physical fitness were collected for the other intervention components but not for the volunteer participation component of the intervention.

The Canada Alzheimer's Society (2006; Evident grade = C1) reported findings from a program of engaging persons with early stage AD in the work of the Association. This report described benefits of participation for N=9 volunteers. Findings also included responses from staff members working with AD volunteers. Ninety-five percent of staff members agreed that persons with AD would benefit from volunteering in the society.

## **Conclusions**

In summary, few studies have examined the effects of volunteer programs on outcomes in persons in early AD stages. Using pre- and post-test and descriptive designs, findings include benefits such as increased language and memory skills, and positive caregiver perceptions of volunteer work for persons with AD. These studies however, are limited by several caveats including non-experimental designs, convenience samples, a lack of objective patient outcome measures, and small sample sizes. In addition, most studies have investigated volunteering as part of a multi-component intervention and have not assessed the individual contribution of volunteering to participant outcomes. Prospective, controlled studies are needed to further test volunteer work models for early stage AD to make informed recommendations for these programs.

## **Recommendations**

Given the positive nature of volunteer activities and identified benefits to persons in early stage AD, the development of volunteer programs is supported. Community programs may be adapted to include opportunities for volunteer participation. Utilization of students to supervise the volunteer activity, consistent with the research reviewed, will minimize the costs associated with volunteer programs. Maintaining positive activity in early stage AD has the potential to affect a variety of outcomes, increasing the support for this intervention.

## **Rating Summary:**

Grading Score	Number	%
A	0	0%
B	1	33%
C	2	67%
Total Reviewed	3	100%

### **3) Evidence supporting writing programs**

#### **Significance**

Activities including a writing component may provide benefits for persons in early stage AD may provide the person with creative outcomes for expression of feelings, documentation of a 'life story' or personal history, and as a clue (recorded) for significant past events. Writing activities are varied including creative writing and poetry, life stories, memory books, and journaling. Positive effects from creative activities, such as writing, include stimulation of parts of the brain that may be affected by AD. This varied stimulation may affect areas damaged by AD -- providing multiple benefits for persons in the early disease stages.

#### **Evidence**

Sierpina & Cole (2004; Evidence grade = C1) describe the observed benefits from participation in a variety of creative activities, including writing, for persons in early stage AD. Creative interventions have been offered at the University of Texas Center for Health, Humanities, and the Human Spirit for community-residing elders, many of whom are in the early AD stages. The 'Life Story Writing Workshops' have been offered for persons with AD for over 7 years. This workshop is held weekly for 8 weeks. The 2-hour sessions allow participants to read their work and receive feedback from group leaders and other participants. The group is led by trained facilitators. The life stories are narratives written in a variety of literary forms including letters, poems, personal narrations, and self-reflective writings. Positive benefits from participation include personal growth through self-exploration and group interactions, improved self-confidence, and memory enhancement for persons with AD.

A personal account of the benefits of creative activities for a person with early stage AD is given by a professional, Ph.D. prepared, diagnosed with AD (Truscott, 2004; Evidence grade = D). The author describes a variety of leisure and creative activities in which she engages, including creative writing and poetry. The author also used memory books and daily journals as an outlet for writing. Memory books were theme-based, generally centering on an event or person. Memory books and journals also serve as reminders of coming events and past activities. Self-described benefits of writing include enjoyment of the writing process and outcomes, sharing of personal reflections with family, reminders of happy times, and provision of a lasting record of life experiences to be shared with others (life stories).

#### **Conclusions**

Published accounts of the benefits of writing interventions are sparse and are descriptive in nature. The benefits of writing interventions are supported by these reports, however. One advantage of writing interventions is the ease of implementation across settings, including the home. Writing interventions are largely offered in the home or community setting. In a group setting, the writing intervention has the additional advantage of providing social support and positive reinforcement for maintaining writing skills. Although systematic studies are lacking, writing interventions merit further study, given the potential for positive benefits for persons in the early AD stages and ease of implementation.

## Recommendations

Evidence-based support for the positive effects of writing interventions is lacking. However, given the benign nature of this intervention and the ability to implement the intervention in a variety of settings, including day care programs, this intervention merits further study.

### Rating Summary:

Grading Score	Number	%
A	0	0%
B	0	0%
C	1	50%
D	1	50%
Total Reviewed	2	100%

#### **4) Evidence supporting technology-based interventions**

##### **Significance**

Technology-based interventions for persons in early stage AD represent a growing area of study. Although studies are limited, the cost-effectiveness of technology-based interventions and potential positive outcomes in terms of increasing autonomy in the home setting support the significance of this line of inquiry.

##### **Supporting Evidence**

Computer based training was used to instruct four participants with early to middle stage AD in functional tasks appropriate to their lifestyle (Hofmann, Hock, & Muller-Spahn, 1996; Evidence grade=C1). Photographs were taken of the steps in tasks to be learned and were scanned into a computer. Persons with AD then used the touch screen of the computer to sequence the tasks. A facilitator was present to offer advice, but participants were encouraged to work as independently as possible. All four participants' training performance improved substantially, but training did not result in significant cognitive improvement.

Oriani and colleagues (2003, Evidence grade=C1) examined the use of an electronic memory aid (EMA) to support prospective memory in early to mid stages of AD. Five persons, four of which had an MMSE score of 18 or greater, were trained in the use of the electronic memory aid. The EMA is an electronic device which uses vocal recordings for appointments or tasks. The EMA can be programmed with dates and times for appointments, using an alarm system to alert the user to a message regarding an appointment or task. The user pushes a button and then receives the recorded message. The EMA was compared within each of the 5 participants to two other conditions: 1) recall using a written list, and 2) recall without any external memory aid. Results revealed that the use of the EMA yielded significantly better results on recall than either of the other two methods.

A digital clock and a memory book for daily life activities were utilized in a case study of a person with early-stage AD by Quittre, Olivier, and Salmon (2005, evidence grade=C1). The authors utilized a spaced retrieval method of teaching the use of these devices. All interventions were also reinforced at home by the person's caregiver. At the end of the three month training period, even though the participant's MMSE score did decline, her functional abilities improved.

Poon, Hui, Dai, Kwok, and Woo (2005, Evidence grade= C1) compared the administration of cognitive assessment and cognitive training using video conferencing and face-to-face methods. A total of 12 sessions were conducted via both methods. Twenty-two participants with early-stage AD were randomized into two groups (n=11). Following the cognitive intervention, both groups improved MMSE scores significantly. Significant improvement of both groups was also seen in the areas of attention, memory, and language, with no difference in outcomes in either group. However, in spatial construction ability, only the face to face group improved. As outcomes were similar for both groups, support was evidenced for the efficacy of video conferencing methods as an alternative to face-to-face interventions.

The efficacy of an interactive computer program, MULTITASK, was tested by Schreiber and colleagues (1999; Evidence grade = A2) in persons in the early and middle stages of AD or vascular dementia (N=14). Participants in the treatment group (n=7) were trained with the computer program through 10, 30-minute sessions. Control group participants engaged in an ‘attention control’ conversation with a psychologist. The MULTITASK program includes training for immediate and delayed recall of objects and routes. Following training, treatment group participants displayed improvements in immediate recall of objects and immediate and delayed recall of routes in their environment. Control group participants showed no increase in recall.

A comprehensive in-home technology support system, the SAFE House system, was tested in persons in more advanced disease stages (moderate and severe). Although this system was not tested in persons in the early disease stages, it is included here as an example of the effects of a continuous monitoring system on safety outcomes (Kinney, Kart, Murdoch, & Conley, 2004; Evidence grade = C1). The SAFE House system consists of camera and sensors that are routed through a controlled unit to a web site accessed with a broadband-connected computer. Caregivers are alerted via text messages from the web site regarding any activity that may indicate an unsafe activity in the home of the person with AD. Caregivers receive training in the use of the system prior to installation. In a study of 19 families, the positive benefits from using the system outweighed the negative effects. Positive benefits included peace of mind in caregivers, increased compassion in caregivers, and allowed family members more free time.

In Europe, a computer-based multimedia program, the Picture Gramophone, has been tested in day centers across the United Kingdom and Scandinavia (Topo, Maki, Saarikalle, et al., 2004; Evidence grade = C1). This intervention was tested with persons at the early (35% of the sample) and later disease stages. The Gramophone is similar to karaoke in that participants can choose from a list of artists, themes, or types of music. Lyrics are displayed on the computer screen, along with images specific to each choice of music. This program enables the person to sing along with the music while providing a relaxing and stimulating activity. Using observations by staff members, positive benefits from the program included improved mood, increased social interaction, and singing or humming with the music.

## **Conclusions**

Support for technology-based interventions is hampered somewhat by the small sample sizes and limited studies to date. The range of outcomes measured has been limited as well. Studies to date have also been largely descriptive in nature, with only one study utilizing a comparison group. However, technology-based programs offer strong promise for the future as an exemplary method to: minimize the need for professional support services, be utilized by family caregivers, be offered for minimal costs, and be widely disseminated. Technology-based interventions also may influence cognitive abilities by stimulating activity and functions specifically affected by AD, increasing the potential for neuronal preservation and regeneration.

## **Recommendations**

Although limited, the potential for technology interventions to increase safety in the home, decrease caregiver burden, and reduce total costs of care provides support for further development of technology-based interventions. While the current cohort of persons with AD may be uncomfortable with technological devices, persons representing future cohorts of older adults have become accustomed to technology and should readily adapt to this intervention format. Hand-held devices and in-home systems that are easy to use may be especially beneficial for the person with AD and family caregivers.

### **Rating Summary**

Grading Score	Number	%
A	1	14%
B	0	0%
C	6	86%
Total Reviewed	7	100%

## **5) Evidence for art and creative activity interventions**

### **Significance**

Very little research exists to support the assertion that art and creative activity interventions can have a positive impact on the functional abilities, cognition, or quality of life of persons with AD. However, given research into learning in Alzheimer's disease, brain plasticity, neuronal regeneration, and the phenomenon of cognitive reserve, this area has enormous potential. As art and creative activities may stimulate areas of the brain affected by AD, this type of intervention may provide multiple benefits for persons in the early disease stages.

### **Search Method**

Utilizing the same databases and search strategies as discussed earlier in this review, art and creative therapies in early stage AD were researched. A total of 33 research reports were found. All but three reports were excluded. The major reason for exclusion was the progressed level of participants, with a majority of studies being carried out in institutional settings. Other reports were excluded if they were based solely upon the authors' opinions, undocumented by research. The search produced three studies which met criteria for inclusion in this review.

### **Supporting Evidence**

Rentz (2002, evidence grade=C1) described the Memories in the Making© program used in the Cincinnati area to promote quality of life of people with dementia. A total of 41 participants diagnosed with early to moderate stage AD in adult day centers, an assisted living facility, and one nursing home participated in the program. During the sessions, an artist guided art experiences using watercolors, acrylics, paper, and canvas. Well-being was assessed through observer measurement of participants' engagement in the projects, expressions of pleasure during the sessions, behavioral and verbal expressions of self esteem and expression of emotions and feelings. Overall, observations indicated that participants experienced improved quality of life during their Memories in the Making© participation.

A program of recreation therapy with emphasis on art and other creative expression was studied for its effect on quality of life of fifteen persons with AD residing in a dementia specific assisted living facility (Zeltzer, Stanley, Melo, & LaPorte, 2003, evidence grade=D). The study sample included participants at various levels of disease progression with 20% of the participants with mild dementia. The remainder of the sample included persons in the moderate to severe disease stages. Quality of life was assessed through a scale developed by the director of nursing at the assisted living facility. Approximately four therapy sessions were conducted per week for sixteen weeks. Residents were assessed at baseline and at unspecified times throughout the intervention. Results of this study indicate that the use of recreation therapy improved overall lifestyle patterns in the participants.

Sezaki and Bloomgarden (2000, evidence grade=D) reported a case study of a man with AD and his wife who participated in a home based art therapy project with the first author. Utilizing art

as a medium, the therapist and wife reported improved communication between the person with AD and his wife as well as expressions of enjoyment by both during the art therapy sessions.

### **Conclusions and Recommendations**

No conclusions regarding the efficacy of art and creative therapies can be drawn based upon the limited amount of evidence available. Further research is needed to evaluate art and creative therapy specifically for persons in the early stages of AD and living in the home setting.

### **Rating Summary:**

Grading Score	Number	%
A	0	0%
B	0	0%
C	1	33%
D	2	67%
Total Reviewed	3	100%

## **6) Evidence for dance therapies**

### **Significance**

Therapies that combine physical exercise and movement with social interaction may increase the total power of the intervention. Dance therapies contain exercise, movement, and social interaction components, all of which have the potential to reduce physical decline and improve overall outcomes, including improved quality of life. While the majority of studies of dance interventions have been conducted with persons at more advanced disease stages, studies including participants at early and later disease stages provide support for the potential effectiveness of these interventions.

### **Search Method**

Utilizing the same databases and search strategies as discussed earlier in this review, databases were searched for research reports of dance therapy interventions in early stage AD. The search resulted in seven citations. Upon further review, one study pertained to the interpretation of non-verbal communication during dance therapy sessions in persons in advanced AD stages. Across studies, the majority of participants were in moderate to severe AD stages as opposed to mild AD stages. However, the evidence provided by these studies overwhelmingly supports that even in more advanced AD stages, dance therapy may assist in preventing the cognitive decline inherent in AD. Also, the social and physical benefits of this type of light exercise may also have implications for persons in the early disease stages. Therefore, this review includes studies of persons in the middle disease stages, representing data relevant to transitioning across disease stages for persons in early AD stages. All reviewed studies took place in Western Europe.

### **Supporting Evidence**

Palo-Bengtsson, Winblad, and Ekman (1998, evidence grade=D) examined social dancing as a nursing intervention in their work with persons with dementia. In the nursing home where this study takes place, all residents have one staff person who is their primary contact, called their “carer.” Social dances are arranged once a month and are intended for all residents and their carers. The study group was comprised of six persons with AD, four of whom lived in the nursing home and two who attended the adult day center attached to the nursing home. Results of the study supported the effects of social dancing on increased physical activity in participants. The social dancing also stimulated participants to talk with one another.

In 2002, Palo-Bengtsson & Ekman (evidence grade=C1) reported on a small study (n=6) of the effect of dance and walks on the emotional well-being of people with moderate AD living in a nursing home. Outcomes included smiles, signs of tenderness between caregiver and persons with AD, and non-verbal expressions of pleasure.

Dance therapies were used to test the ability of persons with moderate AD to learn new motor skills using procedural memory (Rosler, Seifritz, Krauchi, Spoerl, Brokuslaus, & Prospero et al., 2002, evidence grade=C1). Five participants with moderate AD were age matched with non-impaired older adults (n=5) with depression. The intervention consisted of 12, 30-minute dance

lessons. Comparing the findings between groups, participants in the AD group made substantial progress in learning the dance steps in contrast with the participants with depression.

A study of dance movement therapy evaluated the effects of a 4-month, weekly dance movement therapy intervention on verbal, behavioral, and cognitive outcomes (Hokkanen, Rantala, Remes, Harkonen, Viramo, & Winblad, 2003; Evidence grade C1). Participants (N=4) at varying levels of disease severity were included, with some persons at moderate disease levels. The intervention was conducted over a four month period. The intervention was conducted for 30 to 45 minutes for each of the sixteen sessions. Participant MMSE scores remained stable, even one month following the intervention, an important finding considering the progressive nature of AD. The study group showed initial improvement in verbal abilities, but this effect diminished toward the end of the study. Behavioral symptoms also remained stable.

### **Conclusions**

Studies to date examining the effects of dance therapies on persons with early stage AD are limited. Studies conducted with mixed samples (varying levels of disease progression) have been descriptive in nature and included very small samples. Outcomes to date have been modest, although this type of intervention holds promise due to the possible physical, functional, and cognitive benefits.

### **Recommendations**

Given the support for positive outcomes from dance therapies in persons in the moderate disease stages, research testing this intervention for persons in early stage AD is recommended. The potential balance, strength, and social engagement benefits from dance therapies make it an appropriate intervention format for persons earlier in the disease process. Combined with other therapies, such as cognitive training, dance therapies may be an attractive alternative to more traditional exercise programs.

### **Rating Summary**

Grading Score	Number	%
A	0	0%
B	0	0%
C	3	75%
D	1	25%
Total Reviewed	4	100%

## **7) Evidence for neural stimulation (TENS & vagal stimulation) interventions**

### **Significance**

Stimulation of neurons through electrical (TENS) and vagal stimulation is hypothesized to alter the activity of various neurotransmitters or through direct increase in brain activity. Both mechanisms may slow neuronal degeneration and stimulate regenerative processes, consistent with theories of brain plasticity. When used in persons with AD during sleep, applications of TENS may also alleviate sleep disorders associated with dementia. Generally, TENS units are applied to the back of the head during treatments. Most studies of the application of TENS for persons with AD have been conducted in Europe, primarily in the Netherlands.

### **Supporting Evidence**

Scherder (2002; Evidence grade = A2) has conducted a series of studies of the effects of TENS applications on a variety of outcomes in persons with AD. Samples have been varied, with some studies including primarily persons in the early disease stages. In one randomized, double-blind trial of a 6-week treatment, participants (N=18) included 9 persons in the early AD stages (mean MMSE = 18.3) and 9 persons in the control group. Electrodes were clipped to the ear and activated for 30 minutes/day, 5 days/week for 6 weeks. Control group participants received the TENS placement with no current administered. Although no negative outcomes were noted, the application of the TENS did not produce positive benefits for treatment group participants for any outcome including cognitive evaluations, depression, and symptoms.

An earlier study by Scherder, Bouma, and Steen (1995; Evidence grade = B1) examined the effects of a TENS application on memory and affective outcomes in persons in early stage AD (n=16), with mean Short Portable Mental Questionnaire scores of 10.6 supporting early stage AD. The TENS electrodes were attached to the participant's back for the treatment group and to the back of the hand for control group participants. The TENS stimulation was applied for 6 hours/day along with 30 minutes of tactile stimulation throughout the 6-week study. Positive outcomes for the treatment group included improved verbal and visual short and long-term memory. Affective outcomes included a more cheerful outlook, more active and alert behaviors, and less irritable and dejected feelings. Treatment group participants also were more outgoing and interested in social interactions. Overall, the benefits of treatment and lack of negative effects support the efficacy of a TENS intervention for persons in the early AD stages.

In a later study, Scherder and colleagues (2003; Evidence grade = A2) examined the effects of TENS applications using the same methods and time frames as described in previous studies. Participants were in the early AD stages, as evidenced by cognitive testing. Outcomes examined included benefits of TENS applications for sleep activity rhythms. Results included improved (stabilized) sleep activity rhythms in treatment group participants compared to controls. Collective findings suggest that TENS applications may provide sleep, affective, memory, mood, and cognitive benefits for persons in the early AD stages.

Van Someren and colleagues (1998; Evidence grade = A2) examined the effects of TENS applications on rest-activity rhythms in N=14 persons with early stage AD. Six participants were

in the treatment group, with n=8 participants in the control group. The 6-week study included placement of TENS units between the shoulder blades for 30 minutes/day and 5 days/week. Actigraph measures were taken to monitor rest-activity rhythms. Positive effects were found for one of the three rest-activity measures. Results support the benefits of TENS for stabilization in Circadian rhythms in persons with AD.

## **Conclusions**

Studies examining the effects of electrical stimulation have found positive effects for persons in the early AD stages. Measured outcomes include primarily sleep and rest-activity rhythms, although benefits have also been evidence for positive effects on mood; cognitive functions, including memory; and social engagement. Across studies, only one negative effect of the TENS treatment was reported – a burning sensation in one participant. Limitations of this line of inquiry include small sample sizes, with the majority of studies being conducted in one research center in Holland.

## **Recommendations**

Findings do support further testing of neuronal stimulation using TENS applications with larger samples across care settings, including the home environment.

## **Rating Summary:**

Grading Score	Number	%
A	3	75%
B	1	25%
C		0%
D		0%
Total Reviewed	4	100%

## **8) Other: Evidence for narrowly focused areas of study: telephone support programs; teaching persons with AD to use cell phones**

### **Montessori methods**

Camp, Judge, and Fox (1997, evidence grade=C1) tried to reduce apathy through the use of an intergenerational Montessori program, with the people with Alzheimer's disease acting as teachers to the children. Twelve persons with early stage AD (median score on MMSE of 18) were paired with a child for a total of 75 sessions which lasted 30 to 45 minutes each. Skills of the persons with AD improved and they were able to teach an average of 22.3 lessons total.

### **Telephone support services**

Keady and colleagues (1999; Evidence grade = C1) reported the descriptive findings from a British telephone support service for home-dwelling persons with AD, the DIAL-log study. Findings include the most common reasons for calling the telephone support service including direct requests for information and the need to share the experience of memory loss and the diagnostic process. During the telephone support conversation, additional issues and concerns were identified, including the need for information regarding disease progression, strategies to cope with forgetfulness, and information about the diagnostic process. Concerns regarding future possibilities of increased burden on family members were also discussed. Findings suggest that persons in the early AD stages may benefit and seek information and support outside the home setting.

### **Decreasing learned helplessness**

A description of a proposed psychosocial rehabilitation intervention to decrease learned helplessness in persons with AD was described by Flannery (2002; Evidence grade = D). The intervention, Project SMART, is designed to assist persons with AD through increasing stress-resistance and problem solving. The project has been used with other clinical populations, including persons with mental illnesses, but has not been used with persons with AD. The Project SMART program consists of 10 weekly, 90 minutes sessions in groups of 8 to 10 participants. In addition to stress-management, the program includes a reduction of dietary stimulants and relaxation and aerobic exercises. The author concludes that this intervention may provide benefits for persons in early stage AD similar to benefits for other populations.

### **Training in mobile phone use**

A case study approach was used to examine the outcomes of training two persons in the early AD stages (mean MMSE = 21.5) to use a mobile phone (Lekeu, Wojtasik, Van der Linden, & Salmon, 2002; Evidence grade = D). Training sessions were conducted as part of a 3-month rehabilitation program for 45 minutes/day and 1-2 days/week. The intervention included attaching an instruction card to the back of the phone that described a step-by-step method for making and answering calls. Participants were trained in general phone usage using spaced-retrieval methods with expanded intervals of 0, 10, 20, 40, 60 seconds until 240 seconds were reached. Actual practice exercises of phone usage were also included in the training. At the end

of the 3-month training, both participants demonstrated a decrease in their consultation of the phone cared instructions and sustained ability to correctly place a call. The authors conclude that these findings, although evidenced with a very small sample, provide support for the effectiveness of combined learning techniques for improving autonomy for persons with early stage AD.

### **Conclusions and Recommendations**

Studies examining narrowly focused interventions and outcomes have largely been descriptive in nature and have been tested with very small samples (N=2 to N=12). Some interventions, such as teaching persons with AD to use cell phones, have the potential to increase independent functioning in the home and empower the person with additional self-care abilities. These interventions, despite their narrow focus, may have wider benefits and merit further testing.

### **Rating Summary:**

Grading Score	Number	%
A	0	0%
B	0	0%
C	2	50%
D	2	50%
Total Reviewed	4	100%

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Table 1

Summary of Research Evidence (N=155) for Programs and Interventions in Persons in Early Stage AD

Research Domain	Ratings Summary (%)	Major Strengths (S)/Weaknesses (W)
(Number of Studies Included in the Review)		
<b>1. Early Stage Support Groups (13)</b>		
Support Groups: n=9	A: 0	W: Time-limited programs; no method to
	B: 1 (12%)	Continue participation
	C: 5 (55%)	W: Lacks rigorous testing
	D: 3 (33%)	
Psychotherapeutic Groups: n=4	A: 1 (25%)	S: Have been tested on using 1:1 therapies
	B: 2 (50%)	
	C: 1 (25%)	
<b>2. Cognitive Training and Enhancement Programs (41)</b>		
A. Support for brain plasticity: n=6	A: 4 (67%)	S: A variety of outcomes have been tested including cognitive
	B: 2 (33%)	functioning
B. Learning in AD: n=6	A: 2 (33%)	
	B: 1 (17%)	S: More rigorous studies have been
	C: 3 (50%)	conducted
C. Cognitive training and rehabilitation: n=9	A: 3 (33%)	S: Studies have been conducted in the home and institutional setting
	B: 1 (11%)	
	C: 3 (33%)	
	D: 2 (23%)	
D. Cognitive stimulation using combined therapies: n=3	A: 2 (67%)	
	B: 1 (33%)	
E. Memory rehabilitation: n=11	A: 5 (45%)	
	B: 0	W: Lack of consistency in content of intervention tested
	C: 5 (45%)	
	D: 1 (10%)	
F. Neuropsychological Rehabilitation: n=2	C: 1 (50%)	
	D: 1 (50%)	
G. Reality orientation: n=4	A: 3 (75%)	W: Time-limited programming
	B: 1 (25%)	

Research Domain	Ratings Summary (%)	Major Strengths (S)/Weaknesses (W)
<b>3. Exercise Programs (11)</b>		
	A: 4 (36%)	S: Affects broad outcomes, such as strength, balance, cognition, mood, functional ability
	B: 6 (55%)	
	C: 1 (9%)	
<b>4. Exemplar Programs (14)</b>		
A. Multi-modal interventions: n=6	A: 3 (50%)	S: Affects multiple, broad outcomes
	B: 3 (50%)	S: Not just symptom-specific
B. Center for Positive Aging: n=2	B: 1 (50%)	S: Broad range of activities and multiple positive outcomes
	C: 1 (50%)	
C. Sleep Enhancement: n=1	A: 1 (100%)	
D. Managed Care: n=1	A: 1 (100%)	
E. Technology Inter: n=4	C: 4 (100%)	S: Decreased support needs
<b>5. Health Promotion (32)</b>		W: Lack of rigorous studies in home and community settings
A. Sleep Management: n=8	A: 1 (12.5%)	
	B: 1 (12.5%)	
	C: 6 (75%)	
B. Diet/Nutrition: n=17		
Dietary restrictions: n=4	A: 4 (100%)	
Antioxidant use: n=11	A: 6 (55%)	
	B: 5 (45%)	
Mediterranean diet: n=2	A: 2 (100%)	
C. Falls Prevention: n=6	A: 0	
	B: 2 (33%)	
	C: 2 (33%)	
	D: 2 (34%)	
D. College Courses: n=1	C: 1 (100%)	

Research Domain	Ratings Summary (%)	Major Strengths (S)/Weaknesses (W)
<b>5. Other Domains (40)</b>		
A. Driving Safety: n=17	A: 1 (6%)	S: Exceptional descriptive studies on driving safety
	B: 0	S: Intervention studies merited
	C: 15 (88%)	
	D: 1 (6%)	
B. Volunteer Programs: n=3	A: 0	S: Multiple benefits
	B: 1 (33%)	S: Low-cost intervention
	C: 2 (67%)	
C. Writing Interventions: n=2	C: 1 (50%)	S: Can be easily implemented across settings
	D: 1 (50%)	
D. Technology-Based Support Programs: n=5	A: 1 (14%)	S: Some programs require minimal equipment/costs
	B: 0	S: Easily disseminated
	C: 6 (86%)	
E. Art and Creative Activities: n=2	C: 1 (50%)	W: Few programs have been tested in persons in early AD stages
	D: 1 (50%)	
F. Dance Therapies: n=4	C: 3 (75%)	S: Multiple benefits
	D: 1 (25%)	S: Alternative exercise form
G. Neural Stimulation: n=4	A: 3 (75%)	
	B: 1 (25%)	
H. Other Narrowly Focused Programs: n=4	C: 2 (50%)	
	D: 2 (50%)	

## Recommendations

The recommendations derived from the evidence in this report are organized around three major imperatives related to program initiatives for persons with early stage dementia: 1) global recommendations focused on the imperative for a *national focus* on early dementia intervention practice and research; 2) recommendations based on the results from this critical analysis and the imperative for *significant research evidence of best practice* in programming; and 3) recommendations addressing the imperative for a *national research agenda* to rapidly advance the evidence base underpinning best practice in programming in this population.

### **1. The Imperative for a National Focus on Early Dementia Intervention Research and Program Development.**

By 2030, approximately 7.7 million Americans and their families will face the diagnosis of AD. The nation has a demographic and moral imperative to act with conviction and compassion to relieve the suffering of this population. The following recommendations reflect responsive national-level priorities considered essential by this expert group:

**Recommendation 1.1:** That the Alzheimer’s Association lead a **National Information Campaign on Early Stage Dementia** to raise public awareness of the exponential rise in services needed for persons with early stage dementia that is critical to support dignified, person-centered care and quality of life.

**Recommendation 1.2:** That the development of community-based early dementia programs be identified as a **National Healthcare Priority** within Federal funding agencies and private foundations supporting health-related research.

**Recommendation 1.3:** That a **National Symposium** on Interventions for Early Stage Dementia and Best Practices in Programming, with sponsorship from the Alzheimer’s Association and major stakeholders from public policy and the health care industry, be held in the US within 18 months.

**Recommendation 1.4:** That the **critical perspectives of persons with early stage dementia** and those at high risk of developing the disease be given prominence in the national agenda and discourse on early stage dementia care.

### **2. The Imperative for the Early Adoption of Existing Best Practices in Programming [meeting the stringent criteria of this review]**

The substantial body of research evidence for interventions for persons in early stage dementia includes > 150 research reports. The findings are centered around six major domains, in addition to a statement regarding the need for intervention studies on delirium in early stage dementia. The evidence presented in this report reflects a scope of intervention development and testing for use in early stage dementia that is impressive. This highlights the concern felt in the practice and research community for robust intervention options tailored to meet individual

needs. The interventions with the strongest support for positive outcomes include (listed in order of strength of evidence and positive outcomes):

1. Physical exercise, preferably aerobic exercises if tolerated. If aerobic exercises cannot be tolerated, then exercises that are less-strenuous yet promote strength, balance, and coordination, such as Tai Chi, are recommended.\*
2. Cognitive therapies, preferable therapies that use cognitive training and rehabilitation or memory rehabilitation as the focus of the training.\*
3. Comprehensive recreational therapies, including such activities as art, writing, social engagement, individualized hobbies.\*
4. Support group participation\*
5. Sleep hygiene programs, such as NITE-AD
6. Driving evaluations at least every 6 months, including an on-road test with an experienced driving specialist
7. Individualized instruction and training in activities to promote independence such as phone cell usage, computer e-mail programs, etc.
8. Electronic reminder and monitoring support programs (costs may be prohibitive for this intervention)

\*Continuous, not time-limited. Termination of participation should be determined by the person's ability and met needs.

Therapies should not be time-limited, but should be continuous for optimal benefit. Participation with a close family member may increase adherence to the therapies and improve outcomes as well. Optimally, therapies should involve at least two of the three interventions, such as exercise and cognitive therapies or exercise and recreational therapies. Combined therapies produce greater effects, with a combination of exercise and cognitive or recreational therapy producing the strongest long-term positive outcomes.

Some limitations of the research evidence are apparent, with most domains having few studies that reach the highest level of evidence (A). At this time in the development of theory-driven, empirically tested interventions for this group, it is critical to support the broader implementation of interventions with strong potential to provide benefit. The following recommendations reflect the concern of the expert group that promising interventions be rapidly translated into practice.

**Recommendation 2.1:** Those barriers **to the implementation of promising programs** be systematically identified and addressed by a **national panel of experts** convened by the Alzheimer's Association in collaboration with other stakeholders.

**Recommendation 2.2:** That significant attention be given to strategies designed to minimize the **social stigma and medicalization of dementia** and increase the normalization of persons with early stage dementia by **embedding promising programs** in accessible community-based settings.

**Recommendation 2.3:** That the **evidence base** affirming the potential of certain types of interventions identified in this review be **widely circulated** to stakeholders in summary form in multiple media.

**Recommendation 2.4:** That funding agencies be broadly canvassed to **commit funds** for the immediate implementation of a series of competitive community-based best practice **demonstration projects** emerging from the identified high-evidence project pool in this report [Domains 3, 4 and 5] and leading to the submission of funding for **large-scale, multi-site trials**.

**Recommendation 2.5:** That high priority is given in all program implementation to the necessity for **ongoing program continuity** to provide sufficient cohesive and sensitive support to maintain older adults in their homes at a high level of well being.

**Recommendation 2.6:** That all program implementation initiatives meet the **criteria for the inclusion** of those with early onset disease, persons living in rural and remote areas, persons from culturally and linguistically diverse backgrounds, indigenous people and those who live alone.

### **3. The Imperative for a Research Agenda to Rapidly Advance the Evidence Base.**

Many of the reviewed studies show promise, but do not yet reach the level of evidence necessary to be considered robust enough to move forward into clinical trials. It is essential that our approach to intervention be broad-based to include all potentially promising intervention strategies until sound research provides evidence to the contrary. It is essential that a national agenda for research in this area is developed, promulgated, and recognized as a national priority. A ‘rapid advance’ strategy is necessary for the nation to have any realistic possibility of providing responsive intervention programming for the next generation of those with early stage dementia.

**Recommendation 3.1:** That, as an extension of this report, a **5-10 year priority-driven research agenda related to early dementia** be developed, widely publicized, and presented to leadership in major funding agencies by experts.

**Recommendation 3.2:** That funding bodies be appraised of [recognize] the necessity for **longer term funding** to support continuity in priority programs.

**Recommendation 3.3:** That the scope and strength of **interdisciplinary collaboration** in research teams seeking funding for early dementia intervention projects be closely considered in decisions made by funding bodies.

**Recommendation 3.4:** That **priority** in research funding is given to studies with strong **theoretical underpinnings** that compare interventions **head to head**, including comparisons of non-pharmacological and pharmacological interventions.

**Recommendation 3.5:** That **priority** be given to studies that describe the prevalence of early stage dementia and/or further explicate the trajectory, characteristics and rates of conversion from mild cognitive impairment to early dementia.

**Recommendation 3.6:** That **early technology-based interventions** that show promise be promoted via special funding mechanisms since they have the unique capacity to make a difference in the lives of persons with early stage dementia who are isolated from treatment options by distance or other factors.

**Recommendation 3.7:** That a **Consortium of Intervention Researchers in Early Dementia** be formed with the express purposes of extending and connecting the corpus of scholars committed to this endeavor and giving an organized voice to the research agenda.

## Sample Protocols: Mild Cognitive Impairment and Early Stage AD

### A. Treatment Protocol: Mild Cognitive Impairment (MCI):

A comprehensive diagnostic evaluation is necessary to confirm the diagnosis and rule out other causes of cognitive impairment. Most diagnostic centers equipped to complete a full diagnostic exam have a multidisciplinary team that includes a neurologist, geriatrician, neuropsychologist, trained evaluators, social workers, and possibly an advanced practice nurse specializing in geriatrics (G.N.P.). The standard for diagnostic testing includes no less than:

1. History and physical examination
2. CAT or MRI scan
3. Thyroid dysfunction tests, urinalysis, and blood chemistry
4. Neuropsychological testing

Once a confirmed MCI diagnosis has been reached, the following non-pharmacological therapies are recommended to protect cognitive health:

1. Physical exercise, preferably aerobic exercises if tolerated. If aerobic exercises cannot be tolerated, then exercises that are less-strenuous yet promote strength, balance, and coordination, such as Tai Chi, are recommended.\*
2. Cognitive therapies, preferable therapies that use cognitive training and rehabilitation or memory rehabilitation as the focus of the training.\*
3. Comprehensive recreational therapies, including such activities as art, writing, social engagement, individualized hobbies.\*
4. Dietary modifications including foods that are rich in antioxidants such as blueberries, spinach, and strawberries. Replacement of cooking oils (canola, vegetable, corn) with olive oil.

Therapies should not be time-limited, but should be continuous for optimal benefit. Participation with a close family member may increase adherence to the therapies and improve outcomes as well.

\*Optimally, therapies should involve at least two of these three interventions, such as exercise and cognitive therapies or exercise and recreational therapies. Combined therapies have been found to produce greater effects, with a combination physical therapy, such as exercise, and cognitive or recreational therapy producing positive outcomes.

## B. Treatment Protocol: Early stage Alzheimer's disease (AD):

A comprehensive diagnostic evaluation is necessary to confirm the diagnosis and rule out other causes of cognitive impairment. Most diagnostic centers equipped to complete a full diagnostic exam have a multidisciplinary team that includes a neurologist, geriatrician, neuropsychologist, trained evaluators, social workers, and possibly an advanced practice nurse specializing in geriatrics (G.N.P.). The standard for diagnostic testing includes no less than:

1. History and physical examination
2. CAT or MRI scan
3. Thyroid dysfunction tests, urinalysis, and blood chemistry
4. Neuropsychological testing

Early stage AD is defined as: 1) Mini-Mental State Exam (MMSE) score of 18 or higher; 2) Clinical Dementia Rating Scale (CDR) score of 2.0 or less; or 3) Global Deterioration Scale (GDS) score of 2 or less. Once a confirmed diagnosis of early-stage AD has been reached, the following non-pharmacological therapies are recommended to protect, promote, and continue functioning, assist with independence, and maintain cognitive health:

1. Physical exercise, preferably aerobic exercises if tolerated. If aerobic exercises cannot be tolerated, then exercises that are less-strenuous yet promote strength, balance, and coordination, such as Tai Chi, are recommended.\*
2. Cognitive therapies, preferable therapies that use cognitive training and rehabilitation or memory rehabilitation as the focus of the training.\*
3. Comprehensive recreational therapies, including such activities as art, writing, social engagement, individualized hobbies.\*
4. Support group participation (continuous, not time-limited)
5. Sleep hygiene programs, such as NITE-AD
6. Dietary modifications including foods that are rich in antioxidants such as blueberries, spinach, and strawberries. Replacement of cooking oils (canola, vegetable, corn) with olive oil.
7. Driving evaluations at least every 6 months, including an on-road test with an experienced driving specialist
8. Individualized instruction and training in activities to promote independence such as phone cell usage, computer e-mail programs, etc.
9. Electronic reminder and monitoring support programs (costs may be prohibitive for this intervention)

Therapies should not be time-limited, but should be continuous for optimal benefit. Participation with a close family member may increase adherence to the therapies and improve outcomes as well.

\*Optimally, therapies should involve at least two of the three interventions, such as exercise and cognitive therapies or exercise and recreational therapies. Combined therapies produce greater effects, with a combination of exercise and cognitive or recreational therapy producing positive outcomes.

## Panel of Experts

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Adjunct Faculty, College of Nursing  
The University of Iowa

Ms. Bossen is part of the Adult and Gerontology area of study in the College of Nursing. She is currently Co-PI and project coordinator for an Administration on Aging Alzheimer Demonstration Grant through the Iowa Department of Elder Affairs. This project is working to enhance the capacity for care of persons with dementia in Adult Day Services and Respite care in rural Iowa. This is the 7<sup>th</sup> year of funding from the Administration on Aging. Ms. Bossen's research interests are care of persons with dementia and their caregivers, and promotion of dementia specific education. Her education is from the University of Iowa. In addition to nursing degrees, Ms. Bossen is certified in informatics and global health with interests in global aging.

Sarah Boyne is a Registered Nurse currently working on her master's degree in nursing at the University of Southern Maine (USM), specializing as a Family Nurse Practitioner. She is the graduate research assistant focusing on health promotion programs for older adults with early stage dementia.

4. Kathleen Coen Buckwalter, PhD, RN, FAAN  
Sally Mathis Hartwig Professor of Gerontological Nursing Research  
The University of Iowa

Dr. Kathleen Buckwalter, University of Iowa, was named Associate Provost for Health Sciences from 1997-2004. In addition to her primary academic appointment as professor of nursing, she is Director of the John A. Hartford Center for Geriatric Nursing Excellence, Co-Director of the

University's Center on Aging, Associate Director of the Gerontological Nursing Interventions Research Center, Co-Director of the National Health Policy and Resource Center. She has secondary appointments in the College of Medicine Departments of Psychiatry and Internal Medicine, and College of Law. She was appointed to the State of Iowa Commission of Elder Affairs in 2004. Dr. Buckwalter is recognized internationally for her research in psychiatric nursing, aging and long term care, and has a sustained record of private and federal support related to the evaluation of clinical nursing interventions for geropsychiatric populations. Her particular interest is in behavioral management strategies for rural caregivers of persons with dementia and the effectiveness of community programs to prevent, minimize, and treat psychiatric problems in the rural elderly. With support from the NIMH and Administration on Aging, Dr. Buckwalter headed the Mental Health of the Rural Elderly Outreach Project. She also served as principal investigator of the PLST Model: Effectiveness for Rural ADRD Caregivers funded by NINR.

5. Linda Buettner, Ph.D., CTRS  
Professor of Health Science  
College of Health Professions  
Florida Gulf Coast University

Linda L. Buettner is a Gerontologist and Recreational Therapist who specializes in therapeutic programs for persons with dementia. Originally from Upstate New York, she received her Ph.D. from Penn State University in 1994. Her credentials also include: Florida Dementia Trainer Level I and II, and Delta licensed Pet Partner Instructor and Team Evaluator. Dr. Buettner is the author of *Therapeutic Recreation in the Nursing Home* and co-author of *Dementia Practice Guidelines for Recreational Therapy*. She has served a board member for the American Therapeutic Recreation Association, Alzheimer's Association, Dr. Piper Center, Sr. Friendship Center of SW FL, and is the editor for the *American Journal of Recreational Therapy*. She is on the editorial board of the *American Journal of Alzheimer's Disease*. She is a member of the Alzheimer's Association Early Stage Task Force.

6. Sandy C. Burgener, Ph.D., APRN-BC, F.A.A.N.  
Associate Professor  
University of Illinois College of Nursing  
Adjunct Clinical Professor of Neurology  
Southern Illinois University Center for ADRD

Dr. Burgener has been conducting studies of predictors of quality of life in persons with dementia for over 20 years. Certified as a Gerontological Nurse Practitioner, Dr. Burgener developed and directed the Geriatric Nurse Practitioner program at the University of Illinois from 2000 to 2005. Dr. Burgener's program of research includes R0-1 funding from the National Institute for Nursing Research and National Institute for Aging, National Institutes of Health. Dr. Burgener is a fellow in both the American Academy of Nursing (2003) and the Geriatric Society of America, Psychological Sciences Section (2002). Current funded studies and education-dissemination grants focus on the development and testing of wellness-focused interventions for persons with dementia (funded through the Midwest Roybal Center for Health Promotion, National Institutes of Health) and the development and dissemination of educational programs

designed to increase competence in geriatric care: ‘Increasing Competence in Geriatric Care’ Health and Human Service; Health Resources Service Administration (2003-2006) and ‘Creating Clinical Expertise Across Geriatric Care Settings’ (2006-2009) also funded by HRSA.

7. Donna Fick, Ph.D., APRN-BC  
Associate Professor, School of Nursing  
The Pennsylvania State University

Dr Fick received her B.S. in Nursing Science from Berea College in Berea, KY, her M.S.N. at the University of Cincinnati, and her Ph.D. from the University of California, San Francisco. She holds national certification as a clinical nurse specialist in gerontological nursing and has over 20 years of clinical experience with older adults across all care settings. Her research expertise is in delirium in persons with dementia and inappropriate medication use in older adults, including the inappropriate use of central nervous system active medications in persons with dementia. Dr. Fick was principal investigator of the updated Beer’s Criteria for inappropriate medication use in older adults which was published in Archives of Internal Medicine in December 2003. These criteria have been adopted by the Centers for Medicare & Medicaid Services (CMS) and as part of a 2006 HEDIS® quality measure. She has over 30 publications on health outcomes in medication use, and delirium in older adults. She is also principal investigator on a National Institute of Aging funded study on Delirium in Persons with Dementia through 2008.

8. Suzanne Fitzsimmons, M.S., APRN-BC  
Clinical Director, Center for Positive Aging  
Florida Gulf Coast University

Ms. Fitzsimmons is a geriatric nurse practitioner with a certificate in recreational therapy. Originally from Ithaca, NY, she attended graduate school at Binghamton University. Ms. Fitzsimmons has worked with older adults with dementia across care settings. She has been involved in many research projects examining interventions for depression and disturbing behaviors of dementia. She is currently involved in early interventions for older adults in early stages of dementia and for older adult without precursors of dementia. Ms. Fitzsimmons has presented at numerous local, regional, and national conferences and has published several articles and books.

9. Ann Kolanowski, Ph.D., F.A.A.N.  
Professor, School of Nursing  
The Pennsylvania State University

Dr. Ann Kolanowski is Professor of Nursing at Penn State University School of Nursing. For the past two decades, she has conducted research on factors associated with behavioral symptoms exhibited by persons with dementia. Her work has been supported by grants from the National Institute of Health, the Alzheimer’s Association and the Neuroscience Nursing Foundation. She is currently the principal investigator on a 4-year NIH funded project, “A Prescription for Enhancing Resident Quality of Life.” This study will test the efficacy of recreational activities for responding to behavioral symptoms in nursing home residents with dementia. Dr. Kolanowski has published extensively and was recently awarded the first Fran and Holly

Soistman Award for innovation in health services research by the College of Health & Human Development at Penn State University. She is a fellow in the American Academy of Nursing and the Gerontological Society of America.

10. Nancy E. Richeson, Ph.D., CTRS  
Associate Professor, College of Nursing and Health Professions  
University of Southern Maine

Dr. Richeson graduated with her PhD from the University of Nebraska in 2001. She is a Recreational Therapist and Gerontologist with an interest in advancing the geriatric recreational therapy practice. Dr. Richeson is a Certified Therapeutic recreation Specialist and is registered as a therapy dog tester and observer through Therapy Dogs, Inc.

11. Karen Rose, PhD, RN  
Assistant Professor of Nursing  
University of Virginia

Dr. Rose's research interest is working with family caregivers to delay institutionalization of their loved one with AD or a related dementia. Dr. Rose's current research focus is in the area of reducing the sleep disturbances often exhibited by caregivers. Dr. Rose was a John A. Hartford Foundation Pre-doctoral Scholar in the *Building Academic Geriatric Nursing Capacity* program. Dr. Rose studied at both the University of Iowa and the University of Virginia.

12. Andrea Schreiner, Ph.D.  
Research Associate, Department of Health Policy and Administration  
College of Health and Human Development  
The Penn State University  
Adjunct Assistant Professor, Department of Nursing  
The University of Vermont,

Dr. Schreiner teaches about and conducts health services research in the area of Gerontology. She is interested in the care of older adults across a variety of health services settings from nursing homes to home health agencies to private homes. Some of Dr. Schreiner's research has examined family caregivers of persons with dementia as well as nursing homes and paid caregivers, focusing on how to improve quality of care and quality of life through management practices and organizational design. Currently, Dr. Schreiner is interested at looking at ways to improve the quality of home health care on the policy level.

13. Janet K. Pringle Specht, PhD, RN, FAAN  
Associate Professor, College of Nursing  
The University of Iowa

Dr. Specht is in the Adult and Gerontology area of study in the College of Nursing. Dr. Specht is currently Co-PI for an Administration on Aging Alzheimer Demonstration Grant through the Iowa Department of Elder Affairs to enhance the capacity for care of persons with dementia in Adult Day Services and Respite care in rural Iowa. This is the 7<sup>th</sup> year of funding from the

Administration on Aging. Dr. Specht's research interests are in the areas of urinary incontinence, care of persons with dementia and their caregivers, and implementation of evidence based practice in nursing homes. Dr. Specht and her partner, Dr. Meridean Maas, developed and operated a successful alternative living facility for persons with dementia for five and one half years. They were awarded an Edgerunner's Award for this endeavor from the American Academy of Nursing, December, 2006. Dr Specht currently is co-owner of a nurse care management business, HomeSafe, aimed at assisting older persons including persons with dementia to remain in the living environment of their choice.

14. Fang Yu, Ph.D.  
Assistant Professor, School of Nursing  
University of Minnesota

Dr. Yu received her BSN in China and completed her MSN as a Gerontological Nurse Practitioner in 2002 and PhD in Gerontological Nursing in 2003 at the University of Pennsylvania. She was awarded the John A. Hartford *Building Academic Geriatric Nursing Capacity* Postdoctoral Fellowship in 2004. While pursuing higher education, Dr. Yu had worked in a variety of clinical settings as staff nurse, clinical educator, and nurse supervisor which helped her to recognize the clinical importance of functional independence in older adults, particularly in those with dementia. Her program of research, thus, focuses on developing non-pharmacological interventions for improving cognition and function in older adults with AD. Her dissertation study showed that despite their greater degree of functional dependence at baseline, older adults with cognitive impairment were able to achieve significant and comparable functional gain to those with intact cognition from a comprehensive outpatient rehabilitation program. Her postdoctoral work further suggested that the exercise component of rehabilitation, particularly aerobic exercise, might account for her dissertation findings and be robust for improving cognition and function in older adults with AD. Recent basic science findings further suggest that aerobic exercise delays the neuropathological changes of AD and improves memory in transgenic mice. Currently, Dr. Yu has obtained several grants to support the testing of the effects of aerobic exercise on cognition and function in older adults with AD.

