

Cyclical Health Patterns in Alzheimer's Patients and Caregivers

By

Christopher Schneider

Research Project

Submitted to the School of Health Sciences

Eastern Michigan University

In partial fulfillment of the requirements

for the degree of

MASTER of SCIENCE

in

Clinical Research Administration

December 17, 2015

Ypsilanti, Michigan

Abstract

The purpose of this review is to assess the existence of support in existing peer reviewed literature for a cyclical relationship between the health of Alzheimer's patients and their caregivers. While Alzheimer's disease has long been understood to have detrimental effects on those who have the responsibility of caring for the ill, caregiver health may have implications for the quality of the care environment provided to the patient, resulting in patterns of change in health of Alzheimer's disease patients themselves. Current research strongly supports the existence of real and measurable effects of specific patient symptoms and behaviors on psychological burden felt by caregivers. Caregiver burden also correlates with deterioration in the physical and mental health of caregivers. Rare, though not nonexistent is research suggesting that the presence of illness or burden in caregivers are may contribute to the progression of symptoms and problematic behaviors in Alzheimer's disease patients.

Table of Contents

Abstractii

Chapter 1: Introduction and Background1

Chapter 2: Methods5

Chapter 3: Results6

Chapter 4: Discussion8

The Effects of Patient Health on Caregiver Burden8

The Effects of Caregiver Burden on Caregiver Health.....9

The Effects of Caregiver Health on Quality of Care12

The Effects of Quality of Care on Patient Health14

Chapter 5: Conclusion.....16

References.....17

Introduction and Background

Alzheimer's disease poses a serious health problem to society on multiple levels. Individuals who develop the disease are those most obviously affected by the condition, but they are not alone. Loss of memory and cognitive abilities rob patients of the ability to live and function as independent members of society, leading to dependence on those around them. These caregivers, often spouses, children or other family members, are charged with providing an ever increasing amount of time and attention to patients as their symptoms worsen over time.

Alzheimer's disease is thought to account for up to 80 percent of dementia cases (Alzheimer's Disease Association, 2015). Long before problems with memory and thinking become noticeable to doctors, family members or the patient themselves, changes at the cellular level occur in the brain. Two distinct proteins suspected of possible causal relationships to the progression of the disease are known as beta-amyloid and tau. Beta amyloid molecules form into plaques in the space between nerve cells in the brain. Tau molecules form fibers within brain cells. The pathophysiology of the disease and the roles of these two proteins are not completely understood, however magnetic resonance imaging (MRI) and positron emission tomography (PET) have allowed visualization of these structures and a correlation to be established between their presence and frequency and the symptoms displayed by Alzheimer's patients (Alzheimer's Disease Association, 2015). Clinically, these biological changes manifest as the symptoms that are associated with Alzheimer's disease. These symptoms are often separated into two broad categories. The first category includes problems with both memory and thinking abilities which together are considered cognitive symptoms. Behavioral symptoms are the second category, which includes agitation, aggression, wandering and disturbances to normal sleep and appetite patterns. Distinctions between these groupings of symptoms are relevant as the causes and

effects of Alzheimer's disease are often evaluated for association with either behavioral or cognitive symptoms.

Caring for an Alzheimer's patient has long been known to place significant burden on those charged with the task (Alzheimer's Disease Association, 2015). The burden felt and reported by caregivers increase as the disease progresses and with no disease modifying treatments yet available, the outlook for many caregivers is grim (Covinsky, et al, 2003, Ornstein et al., 2013). In 2015 it is estimated that 5.3 million American's are living with the disease. The Alzheimer's Association estimated that in 2014, friends and family of Alzheimer's patients in the United States provided 17.9 billion hours of unpaid care (Alzheimer's Disease Association, 2015). Caregiver burden however is not measured only in time. Research shows that the stress of acting as a caregiver is correlated with an increased risk of physical and mental illness (Richardson et al., 2013). Caregiver burden is by its nature, both variable and subjective, but definitions have been applied to it. It has been described as a multidimensional response in a caregiver resulting from the stresses of caring for someone who is ill. The multiple dimensions of the response include physical, emotional, psychological and economic effects (Carretero et al., 2009). The burden associated with this progressive neurodegenerative disease has been associated with both mental and physical health problems that manifest at an increased frequency in caregivers, including depression, anxiety, hypertension and diabetes (Richardson et al. 2013, Mausbach et al., 2013, Laks et al., 2015). While Alzheimer's itself is not contagious, effects spread nonetheless to those closest to the patients, leading to incredible burdens within family and social circles and to the public health.

The burden and associated health problems seen in caregivers have been recognized as a serious public health problem and a significant amount of research has been devoted to it in

recent years. The severity of burden has been correlated with specific outcomes and aspects of the progression of the disease in the patient (Mohamed et al., 2010, Ferreira de Oliveira et al., 2015). Characteristics of patients and caregivers alike have been evaluated, measured and found to be associated with burden and health outcomes in the caregiver (Brodaty et al., 2014). Less understood is how the characteristics, abilities and health of caregivers affect the quality of the care provided to patients.

The picture of the relationship between the health of the caregiver and patient is a complex one. As the disease progresses and symptoms worsen, the patient relies upon the caregiver for assistance with activities of daily life and eventually the more basic human needs. Patients may rely upon their caregiver for financial support, meal preparation, transportation, monitoring of personal hygiene and health among other needs (Schmidt et al., 2009). While the dependence of the patient upon the caregiver is obvious, less obvious is the dependence of the caregiver upon the patient. With health outcomes of the caregiver tied to the severity of symptoms exhibited by the patient, the caregivers own health may rely upon the preservation of independent function in the patient through the quality of care that they provide. Caregiver personality and coping strategies have been shown to have an effect on the rate of cognitive decline (Tschanz et al., 2013, Norton et al., 2013). Behavioral symptoms of dementia such as repetitive questioning, wandering, and constant restlessness or talkativeness have been shown to be associated with caregiver characteristics including depression, level of burden and the number of hours spent giving care each week (Sink et al., 2006, Gitlin et al., 2014). As the caregiver can affect the status and outcomes for the patient and the patient can affect the status and outcomes for the caregiver, the basis for a cyclical relationship between the healths of the two parties involved can be defined. By more closely examining the relationship between caregiver and

patient, evidence of specific cause and effect dynamics between patient health, caregiver burden, caregiver health and quality of care were sought to support the theory of a cyclical relationship between caregiver and patient health outcomes.

Methods

A review of peer-reviewed articles in scholarly journals was conducted by search of the PubMed database. Primary keywords of “Alzheimer’s” “Caregiver” linked with secondary key words of “Burden” “Depression”, “Characteristics” and “Health Outcomes” were used to identify relevant primary research. Research which measured and compared specific measures of physical or mental health and characteristics of patients and/or caregivers was selected. Articles were categorized based on study objective into one of four categories. The four categories were; the effect of Alzheimer’s disease patient health on caregiver burden, the effects of caregiver burden on caregiver health, the effects of caregiver health on quality of care, and the effects of quality of care on patient health. Each article was reviewed for findings based on the category it was assigned to in order to establish a relationship between the two aspects of each category. By reviewing the literature on relationships between patient health, caregiver burden, caregiver health and the quality of the care provided to the patient; evidence for the presence of cyclical relationship between these factors will be either be supported or opposed by recent research. Furthermore, areas of need and opportunities for further investigation into the caregiver-patient relationship may be identified.

Results

The results of the review of the literature showed that a majority of research on caregivers of patients with Alzheimer’s disease is focused on the effects of patient health and symptoms on caregiver burden. The results of the literature search are described and categorized in Table 1. Columns dedicated to individual keywords represent all relevant articles identified with the keyword. Some articles were identified with 2 or more keywords and are included in multiple keyword columns. In total, 124 unique results were identified, with 56 being relevant articles to at least one category. Burden as a keyword returned the most results, at 100, with 49 of them being relevant according to review criteria. The category’ “Effects of AD patient health on caregiver burden”, had the most articles assigned to it at 43. Each of the 4 keywords generated results of this category more frequently than the other 3. None of the other 3 categories had more than 6 relevant studies identified.

Table 1. Results of PubMed literature search

| | A. | B. | C. | D. | E. | |
|----|---------------------------------------|-----------|------------|-----------------|-----------------|----------|
| | Unique Results (any of 4 key words) | Burden | Depression | Characteristics | Health Outcomes | |
| 1. | Results returned | 124 | 100 | 45 | 25 | 16 |
| 2. | AD Patient Health on Caregiver Burden | 43 | 37 | 19 | 8 | 4 |
| 3. | Caregiver Burden on Caregiver Health | 6 | 6 | 3 | 2 | 0 |
| 4. | Caregiver Health on Quality of Care | 2 | 3 | 2 | 1 | 1 |
| 5. | Quality of Care on Patient Health | 5 | 3 | 1 | 2 | 0 |
| 6. | Relevant | 56 | 49 | 25 | 13 | 5 |

Depression as a keyword generated the second most results, with 25 of 45 results returned being relevant. "Characteristics" and "Health Outcomes" returned 13 and 5 relevant results respectively.

Discussion

The Effects of Patient Health on Caregiver Burden

Recent research strongly supports the concept that the decline in health of Alzheimer's patients has a direct correlation to the level of burden felt by the caregiver (Ryan et al., 2012, Yu et al., 2015). While the diagnosis alone may be enough to burden a caregiver, there are specific problems that manifest in the disease that correlate more strongly with caregiver burden, though there is no consensus on what the most important factor is. Patient depressive symptoms have been shown to have a possible correlation with the presence of depressive symptoms in the caregiver (Ornstein et al., 2013). Other symptoms such as sleep disturbances, anxiety, hallucinations and unusual motor behaviors have been studied and shown to be highly correlated with caregiver burden (Allegri et al., 2006).

Further validating the effect of patient symptoms on caregiver burden are studies involving treatment of patient symptoms. These treatments include pharmacologic and behavioral interventional strategies. Pharmacologic treatment of Alzheimer's disease with cholinesterase inhibitors such as donepezil hydrochloride and galantamine have been shown to decrease caregiver reported burden (Nakamura et al., 2014, Hashimoto et al., 2009, Monsch & Giannakopoulos, 2004). A possible explanation for the decreased burden reported by caregivers is the preservation of the ability of patients to complete normal every day activities, leading to less time demanded of the caregiver and lower levels of caregiver stress.

In addition to the specific characteristics, behaviors or cognitive deficits that have been recognized as influencing caregiver burden, the duration and severity of the dementia experienced by the patient correlates with the amount of burden felt and reported by the caregiver. Given the degenerative nature of the disease, it can be expected that over time as the

disease progresses in the patient, burden felt by the caregiver will increase as well. The prevalence of burden in caregivers at the time of diagnosis has been measured at 50%, rising to nearly 58% at 12 months (Brodaty et al., 2014). Many studies have sought to evaluate the correlation between behavioral and psychological symptoms, and it is largely agreed upon that as patients exhibit a worsening of symptoms, caregiver burden worsens as well (Kanaan et al., 2011, Kamiya et al., 2014).

Given that patient symptoms are going to worsen and with the worsening of those symptoms, the burden felt by the caregiver will increase, the first step in the proposed cycle can be identified. Patient health, through the worsening of behavioral and cognitive symptoms has a negative effect on burden experienced by caregiver. Though the link is not completely understood and varies in individual situations, there is evidence of a link between the emotional health of the caregiver and the symptoms seen in the patient (Ferreira de Oliveira et al., 2015).

The dynamics of the relationship between patient and caregiver health are significant and support the first step in a cyclical relationship between health outcomes of patient and caregiver. The link between them is real and measurable, but does not give a complete picture of how the health and behaviors of each party affect the other.

The Effects Caregiver Burden on Overall Health

The first step in the proposed cycle led from patient symptoms to caregiver burden. The next step is the effect of caregiver burden on the health of the caregiver. Depression which correlates very strongly with caregiver burden is not the only ailment seen in increased frequency. Other diseases occur in the Alzheimer's caregiver population at an increased frequency. Just as an increase in the severity of dementia has been shown to increase caregiver

burden, an increase in caregiver burden is shown to increase the frequency and severity of other health problems in the caregiver. In recognizing these two links, the beginning of a pattern can be established and a cause and effect relationship inferred.

The effects of caregiving are measurable in many ways, though not all are apparent to even an astute observer of caregivers. That is because the effects are not just psychological, but also biological. At the cellular level, changes occur that correlate with the stresses of acting as a caregiver and shed possible light on some of the health risks that are seen at a greater frequency in this population. Caregiving has been shown to over time lead to chronic elevations in C-Reactive Protein (CRP), a biomarker of inflammation in the body which has been shown to be an independent risk factor for cardiovascular disease (Von Kanel et al., 2012). Other important biomarkers, including IL-6, another pro-inflammatory messenger and D-Dimer, which promotes coagulation, have been observed to be elevated in caregiver populations (Von Kanel et al., 2006). The most pronounced effects seen in caregivers however are those reported and observed in the clinical setting.

While a wide variety of health problems are seen at an increased rate in this population, the most commonly studied are depression and anxiety. Just as caregiver burden has been shown to increase with both severity and duration of dementia, anxiety and depression too follow this trend (Garcia-Alberca et al., 2011). Along with anxiety and depression, rates of hospitalization and emergency room usage have been measured in the Alzheimer's caregiver population. Again, a strong correlation is seen with symptom severity, with caregivers of severely impaired patients being hospitalized and visiting the emergency room at rates greater than double those of caregivers of patients with mild symptoms (Kannan et al., 2011). Aside from the health problem

necessitating utilization of health resources and in particular hospitalization, these occurrences can lead to increased financial strain and reduce availability to function as an effective caregiver.

While the increase in health resource utilization by caregivers is measurable, there is no consensus as to the particular circumstances experienced by either caregiver or patient that lead to the increase. Shaw et al. (1997) evaluated caregiver health outcomes, at the same time measuring two variables in the Alzheimer's patient population, requirement of assistance with the activities of daily life, and the presence of behavioral and psychological symptoms. In this study, involving 150 caregivers, it was found that caregiver health was dependent on the preservation of patient ADL function, and independent of the presence of behavioral and psychological symptoms. Similar research has confirmed the effects of loss of ADL function on caregiver health but has found additional correlations with behavioral and psychological symptoms (Schubert et al, 2008). Though each of these studies have shown a correlation between symptoms of Alzheimer's disease associated with caregiver burden, neither directly measured caregiver burden for comparison against caregiver health outcomes. Though measurement of health utilization in relation to patient symptomology is more common, increased caregiver burden has been shown to independently predict increases in health resource utilization and associated costs for caregivers (Miller et al., 2010, Miller et al., 2012).

The relationship thus far can be traced, from progression and worsening of patient symptoms, to increased caregiver burden and to a decline in caregiver health. On its own, this chain of events is a problem to both individual and public health. Though the changes so far have been linear, a caregiver whose health is in decline still has the responsibilities of caregiving. Through increased burden and associated health changes, patients still need care, and the question can be asked whether the caregiver is still capable of providing the same quality of care

as they could previously, when they were healthier, less burdened or when the patient was more independent or lucid.

Changes in Caregiver Health and their Effects on Quality of Care

Here then is the beginning of a cyclical shape to this relationship. With caregiver health compromised, the essential tasks that a caregiver is charged with may too be compromised. Caregivers who suffer from depression and other serious health conditions may not be able to provide the quality of care needed for patients. While Alzheimer's patients and their caregivers are frequently studied, the abilities, appropriateness and adequacy of their caregiver are not often evaluated.

Also confounding to the understanding of changing caregiver abilities is the incredible variety of caregivers that exist in society. While the typical caregiver may be a similarly aged spouse or an adult child, for patients requiring frequent assistance, the caregiver may be a combination of varied individuals. There is also no consensus as to whether the relationship between caregiver and patient is a determinant in burden felt. Spousal relationships in some cases have been found to be more likely to increase caregiver burden. (Kim et al., 2012) Other research has found that adult children acting as caregivers for their parents are the more burdened group (Molyneaux et al., 2008).

Caregivers, though frequently burdened have an opportunity to profoundly influence the lives of those they care for. The often observed deterioration of their physical, psychological or emotional health has not been evaluated to measure the impact on the environment they provide for patients. The review of available literature found very little research investigating the abilities of caregivers or the quality of the care environment they provided. A recently published

literature review had similar finding, with only one relevant study identified, which only tangentially evaluated care quality (Hazzan et al., 2015). Patients may require the assistance of caregivers for achievement of activities of daily life, but they also rely on them for social interaction, cognitive stimulation, conversations and continued communication. AD patients may not have any disease modifying therapies available to them, but the environment provided by their caregivers can have an effect on their symptoms (De Vugt et al., 2004). Specific strategies adopted by caregivers for dealing with behavioral problems exhibited by Alzheimer's patients are associated with the frequency of behavioral problems, but there is no tool or score to rate the quality of the environment provided by the caregiver.

Caregiver characteristics and management strategies have been tested, studied to find correlation between them and the symptoms exhibited by patients. These studies aim to test whether or not caregiver behaviors can influence these symptoms. Cognitively stimulating activities have been shown to preserve cognitive function, which strengthens the importance of the environment provided by the caregiver (Treiber et al., 2011). Coping strategies adopted by caregivers to deal with the burden of caregiving also have the potential to influence the symptoms seen in Alzheimer's patients. Positive coping strategies, such as a problem-focused strategy have been observed to be associated with slower cognitive and functional decline in patients (Tschanz et al., 2013). With the role of and the environment provided by the caregiver identified as strong correlates of patient outcomes, the importance of the caregiver in the preservation of patient health is reinforced. There is evidence that those patients with a closer relationship to their primary caregiver actually show slower symptom progression in both cognitive and functional domains (Norton et al., 2009). The physical, mental and economic components contributing to burden experienced by caregivers are worth examination not only as

an effect of the symptoms displayed by AD patients, but as a cause, influencing symptoms through the quality of care provided.

The Effects of Quality of Care on Patient Health

Burden and the associated mental and physical health symptoms experienced by caregivers have been recognized as being correlated with the symptoms of dementia experienced by patients, but the potential downstream effects these symptoms have on the abilities of the caregiver are not well understood. While health problems such as cardiovascular disease and hypertension, and an overall increase in utilization of health resources, it is possible that physical health problems experienced by caregivers could have a negative effect on the quality of care provided to the patient.

Though quality of care was not measured directly in any studies or found to be relevant to effects on patient symptoms, caregiver burden was linked to symptom development and progression and Alzheimer's patients. In the absence of a valid scale or test that can be used to evaluate the care environment, burden and other measurable characteristics of caregivers have been used to evaluate this link. Burden has been identified as a predictor of nutrition related problems, such as eating disorders and weight loss in patients (Bilotta et al., 2010, Riviere et al., 2003). While these are not commonly recognized symptoms, changes in appetite are recognized as a problematic behavior observed at increased frequency in Alzheimer's disease. Burden has also been linked to earlier patient institutionalization and even death, with use of professional caregiving services actually being recognized as a protective factor (Hirono et al., 2002). One study was identified that specifically sought to explore the role of the caregiving environment in the survival of patients. Caregiver coping methods employed by caregivers were identified to be

associated with patient survival times, with negative coping skills linked to a shorter survival time for patients (McClendon, Smyth & Neundorfer, 2004).

While the close relationship between patient and caregiver contains many interconnected cause and effect dynamics, this review did not identify a clear cyclical relationship between the symptoms experienced by the patient and the care provided by the caregiver. In addition to the severity and duration of the disease, individual symptoms experienced by the patient, both in the behavioral and cognitive domains are understood to impact the burden felt by caregivers. Caregiver burden however is a complex phenomenon, influenced strongly by characteristics intrinsic to individual caregivers such as age, race and patient relationship and situational factors such as, education level, economic status and the amount of time spent caregiving. Despite, or perhaps because of the complexity, the experience of the caregiver is frequently studied and these downstream effects of Alzheimer's patient symptoms are recognized.

With the significant health and economic problems associated with caregiving, to further evaluate the connection between the specific components of burden experienced by caregivers and the symptoms exhibited by patients, an instrument for measurement of quality of care should be developed. Recent studies identifying the potential of caregivers to influence symptoms and outcomes for patients validate for better understanding of the care environment provided to these patients. Such an instrument could be used to evaluate the effect that the care environment provided to patients has on the presence of symptoms in both the behavioral and cognitive domains, differentiating those symptoms that could be influence by the caregiver from those that could not. The quality of care could also be compared with caregiver burden, to explore which facets of burden affect only the caregiver and which carry through to influence the quality of care provided to the patient.

Conclusion

The exploration of the relationship between caregivers and patients is limited and heavily biased toward the effects felt by and seen in caregivers as a result of symptoms or behaviors expressed by patients. Though this review identified no particular reason for the imbalance in the focus of research, it did demonstrate a gap in the understanding of the effects that caregivers have on those with Alzheimer's disease. Opportunities exist for research into the downstream effects of caregiver burden and health on both caregiver behaviors and patient outcomes. In particular, scales or clinical tools which serve to evaluate the abilities of caregivers and quality of the care environment are worthy of developing, not only to identify those patient for which the care provided is inadequate, but also to identify the practices and characteristics of caregivers providing a superior level of care. Measurement and evaluation of caregivers of patients with Alzheimer's disease may lead to the development of new standards, practices and resources for caregivers, which may ultimately benefit both caregiver and patient alike.

References

Allegri, et al. (2006). Neuropsychiatric Symptoms as a predictor of caregiver burden in Alzheimer's disease. *Neuropsychiatric Disorders Treatment*, 2(1), 105-110.

Alzheimer's Association. (2015). [Facts and figures regarding prevalence, mortality, caregiver impact and cost]. Retrieved from <http://www.alz.org/facts/overview.asp#prevalence>

Bell, Chaim M., et al. (2001). The Association Between Caregiver Burden and Caregiver Health-Related Quality of Life in Alzheimer Disease. *Alzheimer Disease and Associated Disorders*, 15(3), 129-136.

Bilotta, Claudio, et al. (2010). Caregiver Burden as a short-term predictor of weight loss in older outpatients suffering from mild to moderate Alzheimer's disease: A three months follow-up study. *Aging & Mental Health*, 14(4), 481-488.

Brodsky, Henry, et al. (2014) Prevalence and Predictors of Burden in Caregivers of People with Dementia. *American Journal of Geriatric Psychiatry*, 22(8), 756-765.

Carretero, S., et al. (2009). The informal caregiver's burden of dependent people: Theory and empirical review. *Archives of Gerontology and Geriatrics*, 49(1), 74-79.

Covinsky, Kenneth E., et al. (2003) Patient and Caregiver Characteristics Associated with Depression in Caregivers of Patients with Dementia. *Journal of Geriatric Internal Medicine*, 18, 1006-1014

Danhauer, S, et al. (2004). Do Behavioral Disturbances in Persons With Alzheimer's Disease Predict Caregiver Depression Over Time? *Psychology and Aging*, 19(1), 198-202.

De Vugt, Marjolein E., et al. (2004) Do Caregiver Management Strategies Influence Patient Behavior in Dementia? *International Journal of Geriatric Psychiatry*, 19, 85-92.

Ferreira de Oliveira, Fabricio, et al. (2015) Correlations Among Cognitive and Behavioural Assessments in Patients with Dementia Due to Alzheimer's Disease. *Clinical Neurology and Neurosurgery*, 135, 27-33.

Gainey, Randy R., Payne, Brian K. (2006). Caregiver Burden, Elder Abuse and Alzheimer's Disease: Testing the Relationship. *Journal of Health and Human Services Administration*, 29(1), 245-259

Garcia-Alberca, JM, Lara, JP, Berthier, ML. (2011). Anxiety and Depression in Caregivers are Associated with Patient and Caregiver Characteristics in Alzheimer's Disease. *International Journal of Psychiatry and Medicine*. 41(1), 57-69.

Gitlin, Laura N. et al. (2014). Factors Associated with Caregiver Readiness to Use Nonpharmacologic Strategies to Manage Dementia-related Behavioral Symptoms. *International Journal of Geriatric Psychiatry*, 29(1), 91-102.

Hashimoto, et al. (2009). Impact of donepezil hydrochloride on the care burden of family caregivers of patients with Alzheimer's disease. *Psychogeriatrics*, 9(4), 196-203.

Hazzan, Afeez Abiola, et al. (2015). Caregiver perceptions regarding the measurement of level and quality of care in Alzheimer's disease. *BioMedCentral Nursing*, 14(54).

Hirono N, et al. (2002). Predictors of Long-Term Institutionalization in Patients with Alzheimer's disease: Role of Caregiver Burden. *No To Shinkei*, 54(9), 812-818.

Iavarone, Alessandro, et al. (2014). Caregiver Burden and Coping Strategies in Caregivers of Patients with Alzheimer's Disease. *Neuropsychiatric Disease and Treatment*, 10, 1407-1413.

Kamiya, M., et al. (2014). Factors Associated with Increased Caregiver's Burden in Several Cognitive Stages of Alzheimer's Disease. *Geriatric Gerontology International*, 14(2), 45-55.

Kannan, Hema et al. (2011) The Association Between Alzheimer's Disease Symptom Severity and Careiver Outcomes: A Cross Sectional Study. *The Primary Care Companion for CNS Disorders*, 13(3).

Kim, H et al. Predictors of Caregiver burden in caregivers of individuals with dementia. *Journal of Advanced Nursing*. (2012) Volume 68, issue 4, 846-55.

Laks, J. et al. (2015) Caregiving for Patients with Alzheimer's disease or dementia and its association with Psychiatric and Clinical Comorbidities and other Health Outcomes in Brazil. *International Journal of Geriatric Psychiatry*, 10, 1002.

Mahoney, DF, et al. (2003). The Caregiver Vigilance Scale: Application and validation in the Resources of Enhancing Alzheimer's Caregiver Health (REACH) Project. *American Journal of Alzheimer's Disease and Other Dementias*, 18(1), 39-48

Mausbach, Brent T., et al. (2013) A Comparison of Psychosocial Outcomes in Elderly Alzheimer's Caregivers and Non-Caregivers. *American Journal of Geriatric Psychiatry*, 21(1).

McClendon, M, Smyth, K, Neundorfer, Marcia. (2004). Survival of Persons with Alzheimer's Disease: Caregiver Coping Matters. *The Gerontologist*, 44(4), 508-519.

Miller, Edward A. et al. (2012). Caregiver burden, health utilities, and institutional service use in Alzheimer's Disease. *International Journal of Geriatric Psychiatry*, 27(4), 382-393.

Miller, Edward Alan, et al. (2010). Caregiver Burden, Health Utilities and Institutional Service Costs among Community-Dwelling Patients with Alzheimer's Disease. *Alzheimer's Disease and Associated Disorders*, 24(4), 380-389.

Mittelman, M. et al. (2008). A 3 Country Randomized Controlled Trial of a Psychosocial Intervention for Caregivers Combined with Pharmacological Treatment for Patients with Alzheimer's Disease: Effects on Caregiver Depression. *American Journal of Geriatric Psychiatry*, 16(11), 893-904.

Mohamed, Somaia, et al. (2010) Caregiver Burden in Alzheimer's Disease: Cross Sectional and Longitudinal Patient Correlates. *American Journal of Geriatric Psychiatry*, 18(10), 917-927.

Molyneaux, GJ, et al. Prevalence and predictors of carer burden and depression in carers of patients referred to an old age psychiatric service. *International Psychogeriatrics*. (2008) Volume 20, Issue 6. 1193-202.

Monsch, AU, Giannakopoulos, P. (2004) Effects of galantamine on behavioural and psychological disturbances and caregiver burden in patients with Alzheimer's disease. *Current Medical Research and Opinion*, 20(6), 931-938.

Nakamura, K, et al. (2014). Effects on caregiver burden of a donepezil hydrochloride dosage increase to 10 mg/day in patients with Alzheimer's disease. *Patient Preference and Adherence*, 15(8), 1223-8.

Norton, Maria C. et al. (2013). Caregiver Personality Predicts Rate of Cognitive Decline in a Community Sample of Persons with Alzheimer's Disease. The Cache County Dementia Progression Study. *International Psychogeriatrics*, 25(10), 1629-1637.

Norton, Maria C., et al. (2009) Caregiver-Recipient Closeness and Symptom Progression in Alzheimer's Disease. The Cache County Dementia Progression Study. *The Journals of Gerontology*, 64(5), 560-568.

Ornstein, K., et al. (2013) The Differential Impact of Unique Behavioral and Psychological Symptoms for the Dementia Caregiver: How and why do Patients' Individual Symptom Clusters Impact Caregiver Depressive Symptoms. *American Journal of Geriatric Psychiatry*, 21(12).

Reed, Catherine et al. (2014). Caregiver Burden in Alzheimer's Disease: Differential Associations in Adult-Child and Spousal Caregivers in the GERAS Observational Study. *Dementia and Geriatric Cognitive Disorders*, 4, 51-64.

Richardson, Todd, et al. (2013) Caregiver Health: Health of Caregivers of Alzheimer's and Other Dementia Patients. *Current Psychiatry Reports*, 15(367).

Riviere, S, et al. (2003). Cognitive Function and Caregiver Burden: Predictive Factors for Eating Behaviour Disorders in Alzheimer's disease. *International Journal of Geriatric Psychiatry*, 17, 950-955.

Ryan, Kelly A. et al. (2012). Neuropsychiatric Symptoms and Executive Functioning in Patients with Mild Cognitive Impairment: Relationship to Caregiver Burden. *Dementia and Geriatric Cognitive Disorders*, 34, 206-215.

Schmidt, Karen L. et al. (2009). Verbal Communication among Alzheimer's Disease Patients, their Caregiver, and Primary Care Physicians during Primary Care Office Visits. *Patient Education Counseling*, 77(2), 197-201.

Schubert, Cathy et al. Acute Care utilization by Dementia Caregivers Within Urban Primary Care Practices. *Journal of General Internal Medicine*. (2008) Volume 23, issue 11, 1736-40.

Shaw, William, et al. Longitudinal Analysis of Multiple Indicators of Health Decline Among Spousal Caregivers. *Annals of Behavioral Medicine*. (1997) Volume 19, Issue 2, 101-9.

Sink, Kaycee M, et al. (2006) Caregiver Characteristics Are Associated with Neurophychiatric Symptoms of Dementia. *Journal of the American Geriatrics Society*, 54, 796-803.

Treiber, Katherine A., et al. (2011) Cognitive Stimulation and Cognitive and Functional Decline in Alzheimer's Disease: The Cache County Dementia Progression Study. *Journals of Gerontology*, 66(4), 416-425.

Tschanz, JoAnn T., et al. (2013) Caregiver Coping Strategies Predict Cognitive and Functional Decline in Dementia: The Cache County Dementia Progression Study. *American Journal of Geriatric Psychiatry*, 21(1), 57-66.

Von Kanel, R, et al. (2006). Effect of Alzheimer Caregiving Stress and Age on Frailty Markers Interleukin 6, C-Reactive Protein and D-dimer. *The Journals of Gerontology*, 61(9), 963-69.

Von Kanel, R, et al. (2012). Effect of Alzheimer Caregiving on Circulating Levels of C-Reactive Protein and Other Biomarkers Relevant to Cardiovascular Disease Risk: A Longitudinal Study. *Gerontology*, 58(4), 354-65.

Yu, H, et al. Measuring the Caregiver Burden of Caring for Communit-residing People with Alzheimer's Disease. *PLos One*. (2015) Volume 10, Issue 7.