

SOCIO-ECONOMIC ISSUES IN ALZHEIMER'S DISEASE. RESILIENCE AND ALZHEIMER'S DISEASE CAREGIVERS

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ABSTRACT

Alzheimer's Disease (AD) is the most common form of dementia in the old population, carrying a major negative influence upon society and caregivers, as its socio-economic implications are enormous. The devastating impact of AD is also due to the fact that the diagnosis is difficult to be established in an early stage, and in spite of the advances made in medicine, the new symptomatic and disease modifying therapies have still only a mild though promising positive effect. Caregivers are exposed to increased risk of disease themselves, due to the high burden which predisposes them to stress related psychological, behavioral or cognitive disorders. Greater caregiver resilience can predict lower levels of depression. Also a strong external support system was associated with increased resilience. Establishing a pattern for the behavioral and psychological manifestations in dementia can have as direct effect developing better coping strategies in order to reduce stress and the burden of the caregivers. Some data regarding the economic and social impact of AD, as well as facts and numbers from our local centers will be described in the following pages.

Keywords: dementia, Alzheimer's Disease, social, economics, caregiver, burden

INTRODUCTION

Alzheimer's Disease is a disease that manifests by a progressive damage in both cognitive fields and emotional abilities, leading to a negative interaction with the life of the patient. When thinking about AD, it easily comes to mind that the risk of developing the illness is increasing with age, especially after the age of 65. Since 2010 it is considered that in half of the cases of persons over 70 years, having significant memory loss, the reason being AD (Bird & Miller, 2010). Also, actual statis-

tics reveal another negative scenario for the year 2050: there will be a new AD case every 33 seconds only in America (Alzheimer's Association, 2012)!

Other than age itself, there is also a lot of other of risk factors to be considered, such as: a low level of education, repeated/severe head trauma, female sex (also including mothers of children with Down's syndrome), familial predispositions and APOE ε4 susceptibility gene (Nima, 2007). Not only that, but throughout the last decades it became obvious that cerebrovascular disease and vascular

disease risk factors: history of stroke, hypertension, hyperlipidemia and diabetes also increase the risk for developing AD (Bird & Miller, 2010).

In spite of the new treatment development attempts, the prevalence of AD continued to increase throughout the years, the worse direct effect being the average life expectancy and quality of life (QoL), actual therapy showing only mild improvement, such as preventing a faster evolution of the disease, and obtaining a few years delay of the progression.

The devastating social and economic impact of AD starts especially from the difficulty in early establishing a diagnosis (Mummenthaler & Mattle, 2004), even in spite of some efforts made lately.

SOCIAL AND HEALTH ECONOMIC ASPECTS

In 2012 there were approximately 5 million prevalent cases of AD only in the USA (3 million diagnosed and only 1/3 receiving treatments) and the Alzheimer's Association concluded the same year that in America an individual develops AD every 68 seconds (Zabar, 2012; Alzheimer's Association, 2012). Around the same year, more than 15 million Americans provided care for a person suffering either from AD or other forms of dementia (Sørensen, Pinquart, Duberstein, 2002). The total number of people with dementia is expected to double every 20 years (65.7 million in 2030) and 115.4 million in 2050 (Price, Bryce, Albanese, Wimo, Riberio, Ferri, 2013), context in which population aging seems to be a problem becoming more pressing in both developed and developing countries.

Alzheimer's Association considered AD being the sixth cause of death in patients older than 65, and published numbers such as 17.4 billion hours of care for AD patients with an estimated cost at \$210 billion (Jones et al., 2014). Also, it is estimated that caring for only one AD patient in an advanced stage of illness means more than \$50000 (Bird & Miller, 2010). Also, earlier in 2010 the worldwide cost of dementia was close to \$604 billion (70% of it in Western European countries and in North America) (Wimo, Jonsson, Bond, Prince, Winblad, 2013).

All this data reveals the picture of the massive worldwide economic impact that AD is responsible for. Although focused primarily on direct costs, economists can also consider three main components of costs: direct costs (such as medical costs, paid home help and nursing costs home); indirect costs (productivity losses due to missed work or

other productive activities); pain and suffering (agitation, stress, depression).

In our country the main problem in dealing with dementia-related pathology, is the low compliance that patients and their families show to medical recommendations, as well as low addressability to specialized medical services. We are dealing dementia by an interdisciplinary approach, based on a teamwork constituted by neurologist-psychiatrist-geriatrics collaboration. The neurology clinic tends to deal more with vascular, mixed or PD dementia, on the other hand the psychiatric clinic gets to treat AD more often. Geriatric clinics may come across all sorts of dementia, including AD more often.

Related strictly to Alzheimer's disease, in 2012 a number of 27 patients received treatment and in 2013 there were 13 AD patients that received treatment in our local services. These cases are highlighted out of 132 cases of treated patients suffering from different types of dementia in 2012, respectively 92 in 2013, related only to the dynamics of cases in one dedicated facility. For the year 2013, our statistics reveal 3 cases of AD with early onset (before 65 years) currently receiving treatment. The decrease of the number of patients is only due to an administrative change in this particular department's destination towards only palliative care.

SHORT OVERVIEW OF PATHOLOGY, QOL AND FUTURE PERSPECTIVES

Dementia is a clinical syndrome that is caused by neurodegeneration as a pathophysiologic process. Neurodegeneration is closely followed by progressive deterioration and a decline in cognitive abilities and perturbing main aspects of daily living (Price, Bryce, Albanese, Wimo, Riberio, Ferri, 2013).

There are many types of dementia, but the most common form is AD, with hallmark abnormalities consisting in β -amyloid plaques and tau tangles (Fig. 1). The vascular type often occurs post-stroke or because of brain injuries (microscopic bleeding and blood vessel blockage); both AD and vascular dementia can be present at the same time (Sørensen, Pinquart, Duberstein, 2002).

When Lewy bodies, DLB, (abnormal aggregations of the protein α -synuclein) are present at the cortex level, dementia occurs. Brain modifications alone can cause dementia, but they can also coexist with AD or vascular dementia. When this happens, we talk about the mixed dementia form, which represents the association of any of the 3 forms from above (Sørensen, Pinquart, Duberstein, 2002).

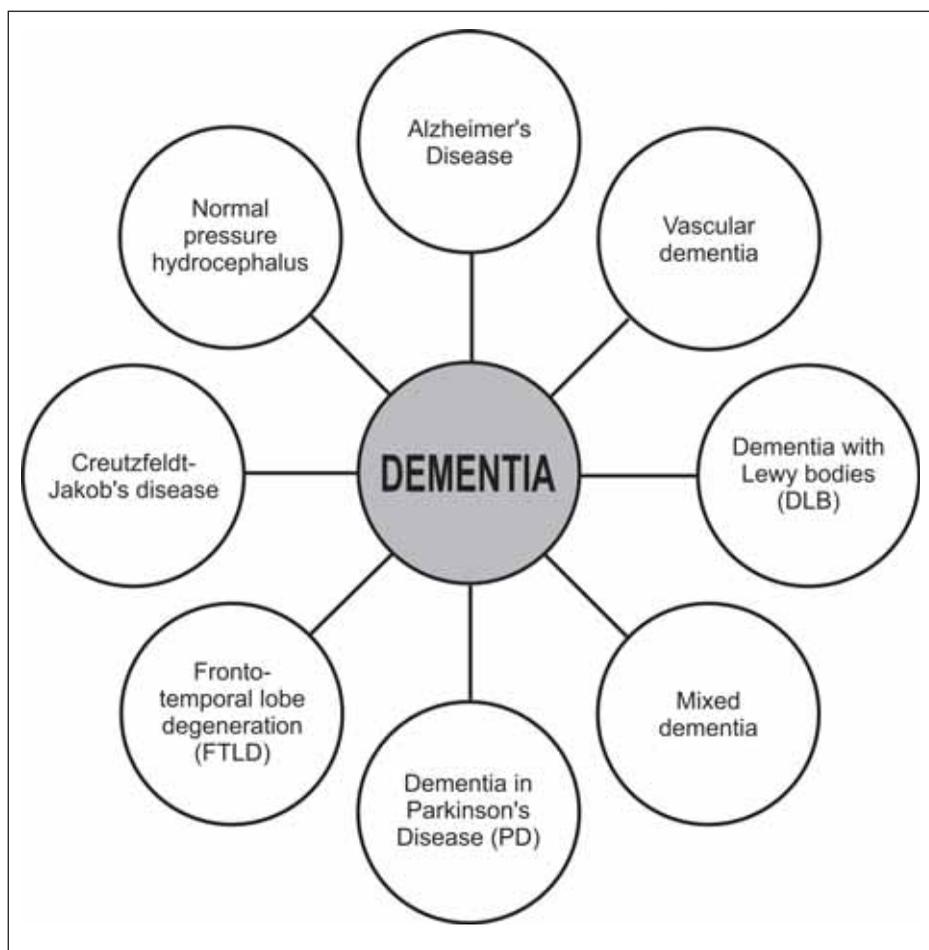


FIGURE 1. Types of dementia

Lewy Bodies or AD, a frequent symptom in this case being the early installed movement disorder), (Fronto-temporal lobe degeneration – behavioral form, Pick’s disease or progressive supranuclear palsy; manifested by changes in the personality field, behavior or language difficulties), in Creutzfeldt-Jakob disease (due to prion infection) or the normal pressure hydrocephalus (surgically solved by placing a shunt to drain excess fluid) (Sørensen, Pinquart, Duberstein, 2002).

Dementia may also be present in pathologies as PD (dementia similar to Dementia with There are several mechanisms involved in developing AD. These are: A β generation and tau hyperphosphorylation, oxidation, inflammation, glutamate excitotoxicity, insulin dysfunctions, all of these contributing to neuronal cell death. Disease modifying treatments target these mechanisms in the attempt of obtaining results that would be noticeable for several years, slowing down the natural course of the disease.

Alzheimer’s disease is a disorder with an important genetic component (Karch, Cruchaga, Goate, 2014). Commonly the disease onset occurs after the age of 65 (late-onset form – LOAD) but in 1% of

cases the disease manifests before 65 years of life (early-onset form – EOAD) (Kima, Yeo, Park, Choi, Lee, 2014). Genetic studies have shown that in patients with early onset the disease is autosomal dominant transmitted and is caused by mutations in three major genes involved in amyloid processing, APP, PSEN1, and PSEN2 (Medway, Morgan, 2014). Most cases of Alzheimer’s disease were late-onset form in whose etiology are involved age, environmental factors and genetic factors (Medway, Morgan, 2014). By 2009 the only genetic risk factor identified was allele ϵ 4 of apolipoprotein E (APOE) (Medway, Morgan, 2014). Only 50% of individuals with LOAD show APOE ϵ 4 mutations suggesting that there are other genetic factors that contribute to the risk of developing the disease. Since 2009 started the era of genome-wide association studies and so far there have been identified 20 new susceptible loci: CASS4, CELF1, FERMT2, HLA-DRB5/HLA-DRB1, INPP5D, MEF2C, NME8, PTK2B, SLC24A4/RIN3, SORL1, ZCWPW1, CR1, BIN1, CD2AP, EPHA1, CLU, MS4A6A, PICALM, ABCA7 (Mitsui, Tsuji, 2014). These newly identified loci confer an increased risk of AD only 0.10 fold to 0.15-fold, so that APOE ϵ 4 still

remains the major genetic risk factor (Mitsui, Tsuji, 2014).

There are four drugs approved for the treatment of AD (Donepezil, Rivastigmine, Galantamine and Memantine), but other therapeutic strategies may also prove their utility in building up a better therapeutic strategy for these patients: gama-secretase inhibitors, RAGE inhibitor, antioxidants (vitamins, coenzyme Q10, alpha lipoic acid, omega 3 fatty acids), immunization, Insulin etc.

The non-pharmacological cognitive training (CT) or active music therapy (AMT) also shows promising results: CT has proven facilitation of control and memory functions, and AMT is believed to enhance well-being especially in terms of socialization, both techniques improving cognition and behavior.

Primary prevention continues to be the most promising therapy, and this can be possible only by early improvement of life. This means association between controlling cardiovascular risk factors with a healthy diet and antioxidant, vitamin supplementation, all these contributing to developing a healthy life style, based on both physical and mental activity and involvement in socio-professional activities.

RESILIENCE AND ALZHEIMER'S DISEASE CAREGIVERS

Most often the AD patient has to receive help from a family member, known as a "caregiver". The impact of the caregiving process has been described as caregiver burden.

Caregivers provide all sorts of helping activities: supervising the intake of medications, bathing, dressing, managing incontinence, transferring from bed to chair, taking care of medical appointments and other services such as home-nursing, and overall helping the AD patient avoid dangerous or unsafe situation (Sørensen, Pinqart, Duberstein, 2002). These activities may vary within the different forms of dementia and AD stages and may also mean dealing with aggressive behavior or withdrawal and apathy, a stressful situation for caregivers (Williamson & Schulz, 1990). In such cases the patient's illness can provide anger, frustration or guilt for the care provider (Pinqart & Sørensen, 2003).

These are reasons why people taking care of patients with dementia carry a higher risk for psychiatric illness (O'Rourke, 2003), especially the ones living together with the AD patients having higher depression scores (Pinqart & Sørensen, 2003).

Care might be as well influenced by attitudes, religious beliefs or cultural aspects, especially in informal caregivers (Yektatalab, Sharif, Kaveh, Fallahi Khoshknab & Petramfar, 2013), scheduling of care being necessary (Yektatalab Sh, Kaveh M.H., Sharif F., Fallahi Khoshknab M., Petramfar P., 2012).

Depressed feelings, sadness, frustration, loss of interest or pleasure, chronic fatigue, sleep changes, difficulty in concentration or decision making and a disruption in social participation can be found in caregivers, placing a great burden on them (George & Gwyther, 1986). A more profound analysis of the caregiver's burden would have to include the family as well, for obtaining a larger view among the effects of caregiving (Zhu C.W., Scarmeas N., Ornstein K., et al, 2014). Caregiving can have negative impacts on family the most common being difficulties in communication between family members and between caregiver and care recipient (Speice, Shields, & Bliezner, 1998).

Longitudinal results from the Predictors Caregiver Study help us visualize both the typical caregiver and the care recipient. Therefore the typical caregiver in this case was statistically found as a 65 years white female, college graduate (16 years of schooling), relatively healthy (most reported chronic condition: hypertension) whereas the typical care recipient was 76 years white female (15 years of schooling) with chronic conditions other than dementia, especially hypertension and depression (Zhu C.W., Scarmeas N., Ornstein K., et al, 2014).

Resilience is generally described as the ability to successfully adapt regardless of adverse conditions (Norman, 2000) or as the process of individuals coping with adversities that result in positive outcomes (Richardson, 2002).

Three measures scale of resilience have been used in the resilience research studies (The Resilience Scale, The Resilience Scale for Adults, and the New Connor-Davidson Resilience Scale). The Resilience Scale measures resilience as a personality characteristic in which the focus is on personal competence and acceptance of self and life thus leading to a successful adaptation (Wagnild & Young, 1990; Wagnild & Young, 1993). Resilience Scale for Adults in which the focus is on personal strength, social competence, structured style, family cohesion, and social resources was proposed by Friborg, Hjemdal, Rosenvinge, Marinussen, and Flaten, 2006. Connor and Davidson, 2003 created the Connor-Davidson Resilience Scale (CDRSC), a self-report with 25 items. The CDRSC measures resilience as a measure of successful stress-coping ability (Connor and Davidson, 2003).

Few resilience studies have been conducted within the Alzheimer's disease caregiver. Garity (1997) examined the relationships among stress level, learning style, resilience factors, and ways of coping among Alzheimer's caregivers. He believes that resilience was a personality characteristic that moderates the negative effects of stress, and recommends more specified educational interventions for caregiver support groups (Garity, 1997).

A relationship between personal characteristics, coping behaviors and resilience was found by Ross, Holliman, & Dixon, 2003. Indicators associated with resilient caregivers were distancing from the caregiver role, participating in physical exercise, hobbies, religion, humor, and having a good support system (Ross, Holliman, & Dixon, 2003).

Gaughler, Kane, and Newcomer (2007) examined the relationship between resilience, perceived demands, and institutionalization. The study indicates that Alzheimer's caregivers with low resilience and high caregiver demands are more likely to place loved ones in the nursing home (Gaughler, Kane, and Newcomer, 2007).

In all these studies was emphasized the importance of external support systems for caregivers, having a strong external support system was associated with increased resilience (Ross, Holliman & Dixon, Greene, 2002).

A known fact today is that greater caregiver resilience can predict lower levels of depression, possible especially if caregivers have the possibility of focusing on specific interventions in order to prevent a negative impact on both their health and income, especially the unpaid caregivers (Sørensen, Pinquart, Duberstein, 2002).

Sørensen et al, 2002 mentioned 4 types of beneficial interventions (Fig. 2), useful in preventing the caregivers become patients as well, due to the burden their assumed mission means (Sørensen, Pinquart, Duberstein, 2002).

The psycho-educational type is based on lectures and discussions while the supportive one mainly represents a context in which all sorts of problems and feelings caregiving involves are being discussed. Psychotherapy also involves communication as it focuses on aspects like time management, emotions and involvement in positive activities. The multicomponent approach realizes a mix of interventions combined with technological approaches. All these four types are led by specialized professionals (Sørensen, Pinquart, Duberstein, 2002).

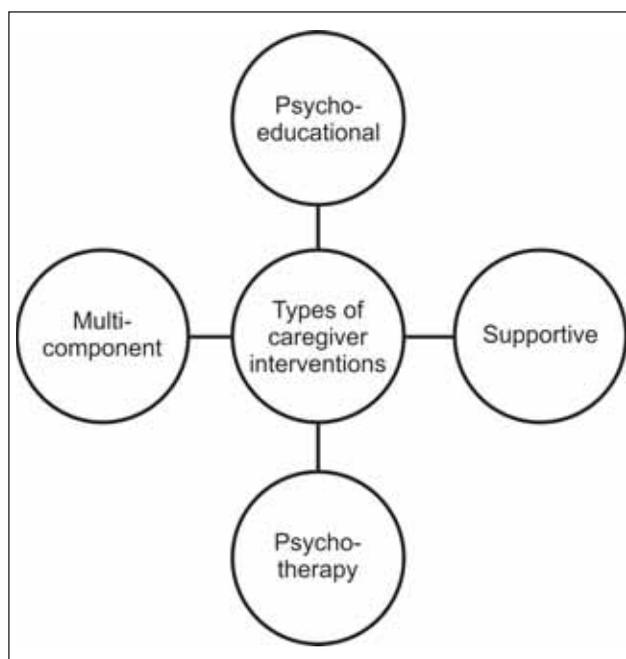


FIGURE 2. Types of beneficial interventions

These activities will eventually lead to an increase of resilience, having as a probably but desired result, a decrease of the caregiver's burden (Zhu C.W., Scarmeas N., Ornstein K., et al, 2014; Gonzalez E.W., Polansky M., Lippa C.F., Gitlin L.N., Zauszniewski J.A., 2014). More than that, there is also evidence that a multicomponent intervention that is adapted to the individual risk profiles, can result in an increase of the quality of life among different ethnically caregivers (Belle S.H., Burgio L., Burns R., Coon D., Czaja S.J., Gallagher-Thompson D., et al, 2006). Home skills building programs based on occupational therapy also show benefits (Gitlin L.N., Hauck W.W., Dennis M.P., Winter L., 2005).

CouldQoLbe considered to be an important though subjective tool for quantifying a certain drug's effectiveness? (Schwam E.M., Abu-Shakra S., del Valle M., Townsend R.J., Carrilo M.C., Fillit H., 2007). A recent research evaluated the effect of increasing the dose of Donepezil from 5 mg daily to 10 mg daily and measure AD patient's behavior during a 16 week study: the increased dose had a benefic effect on improving the impaired swallowing function, improved dementia's severity and also decreased caregiver burden. By contrast with a temporarily improvement of symptoms, it is difficult to influence the progression of AD by simply increasing Donepezil dosage; also the decrease of the caregiver's burden is only temporarily as well, long term support for both the patient and the caregiver being most necessarily (Nakamura K., Watanabe N., Ohkawa H., et al, 2014).

The caregiver's burden can be objectively measured by evaluating the patient's dependence, and also subjectively, by relating to the way in which caregiving interferes with everyday life's activities, some of the latest conclusions showing that the patient's disability and the volume of care received (the patient is considered primary determinant) have only secondary impact on the caregiver (Schwam E.M., Abu-Shakra S., del Valle M., Townsend R.J., Carrilo M.C., Fillit H., 2007).

QoL is difficult to quantify, this is why treatments should be considered effective if they improve cognition, function or behavior in spite of an inefficient improvement of QoL (Schwam E.M., Abu-Shakra S., del Valle M., Townsend R.J., Carrilo M.C., Fillit H., 2007).

Caregiver's burden may also be influenced indirectly by cost. It is estimated that as the disease progresses, costs also increase, from approximately \$9,239/year in early stages to \$19,925/year in later stages, nevertheless, costs being lower for people staying at home than institutionalized, however emotional and physical costs to caregivers being enormous. Interventions for caregivers may alleviate some of the cost and burden related. (Nichols L.O., Chang C., Lummus A., Martindale-Adams J., Graney M.J., Coon D.W., et al, 2008).

Caregiving can be an important "route to self-discovery" (Mac Rae, 1995), a potentially positive and growth-enhancing experience (Acton & Wright, 2000; Sherrell, Buckwalter, & Morhardt, 2001).

Caregivers have the opportunity to learn more about themselves and become aware of strengths they did not know they had (Noonan et al., 1996). Caregivers may develop feelings of achievement in their responsibility of caring for a loved person at home (Cohen, Pringle, & LeDuc, 2001). Emotional connection between caregiver and care receiver, love, affection, feeling of being useful, learning to be more tolerant, learning to become resilient will be beneficial for maintaining the health of caregivers. Resilience will not solve the problems, but can give them the ability to get over problems, to be optimistic in their resolution, and to find enjoyment in life. Another positive feature of a caregiver is that in spite of difficult situations they will find the people who are there for them in good and bad times.

Educating, supporting caregivers can be a key factor in increasing the quality of life in individuals living with AD, therefore in the future it is necessary to identify strategies of social policies that have the potential to enhance caregiver resilience (Luthar, 2006).

Further comparative studies between formal and informal caregivers could also be beneficial in establishing different approaches regarding interventions, as the increasing interest towards the relationship between the severity of AD, caregiver burden and costs will continue to attract more research in this field, with hope of better management strategies for this global health issue AD represents.

CONCLUSIONS

AD is a major health problem for both the patient and the caregiver, with major effect on the patient's quality of life, and also carrying a negative effect among care providers. An increasing interest towards the severity of AD and costs has been going on for the last years as the level of dependence of these patients is also associated with increased costs.

The various dementia diagnostics, and especially AD, require different approaches, caregivers playing a major role in the process of care for these patients. Nevertheless, they are exposed to and increased risk of disease themselves, due to the high burden which predisposes them to stress related psychological, behavioral or cognitive disorders.

Thus the need of establishing intervention strategies for caregivers, as involvement in social activities with desired results in improving physical state and preserving mental health, which will also have a benefit among the care receivers.

Establishing a pattern for the behavioral and psychological manifestations in dementia can have as direct effect developing better coping strategies in order to reduce stress and the burden of the caregivers. An improvement in the quality of life for the patient is also desirable, another main objective being represented by the delay as much as possible of the evolution of the case towards institutionalization.

REFERENCES

1. **Acton G.J. & Wright K.B.** Self-transcendence and family caregivers of adults with dementia. *Journal of Holistic Nursing*, 2000, 18, 143-158
2. **Allam G.J., Baker R.A.**, (coord.), 2nd ed. *Netter's Neurology*. Philadelphia: Elsevier Saunders, pp. 221-234
3. **Alzheimer's Association.** Alzheimer's disease facts and figures. *Alzheimers & Dementia*, 2012, 8, 131-168
4. **Belle S.H., Burgio L., Burns R., Coon D., Czaja S.J., Gallagher-Thompson D., et al.** Enhancing the quality of life of dementia caregivers from different ethnic or racial groups: a randomized, controlled trial. *Ann Intern Med.*, 2006, 145, 727-738
5. **Bird T.D., Miller B.L.** Alzheimer's Disease and other Dementias. In: Hauser S.L., Josephson S.A., (coord.), 2nd ed. *Harrison's Neurology in Clinical Medicine, McGraw-Hill Medical* 2010, pp. 298-319
6. **Cohen C., Pringle D. & LeDuc L.** Dementia caregiving: The role of the primary care physician. *Canadian Journal of Neurological Science*, 2001, 28, S72-S76
7. **Connor K. & Davidson J.** Development of a new resilience scale: The Connor Davidson Resilience Scale (CD-RISC). *Depression and Anxiety*, 2003, 18, 76-82
8. **Friborg O., Hjemdal, Rosenvinge J., Martinussen M. & Flaten M.** Resilience as a moderator of pain and stress. *Journal of Psychosomatic Research*, 2006, 61, 213-219
9. **Garity J.** Stress, learning style, resilience factors and ways of coping in Alzheimer family caregivers. *American Journal of Alzheimer's Diseases*, 1997, 171
10. **Gaughler J., Kane R., Newcomer R.** Resilience and transitions from dementia caregiving. *Journal of Gerontology: Psychological Sciences*, 2007, 62B, 38-P44
11. **George L.K., Gwyther L.P.** Caregiver well-being: a multidimensional examination of family caregivers of demented adults. *Gerontologist*, 1986, 26, 253-259
12. **Gitlin L.N., Hauck W.W., Dennis M.P., Winter L.** Maintenance of effects of the home environmental skill-building program for family caregivers and individuals with Alzheimer's disease and related disorders. *J Gerontol A Biol Sci Med Sci.*, 2005, 60, 368-374
13. **Gonzalez E.W., Polansky M., Lippa C.F., Gitlin L.N., Zauszniewski J.A.** Enhancing resourcefulness to improve outcomes in family caregivers and persons with Alzheimer's disease: a pilot randomized trial. *Int J Alzheimers Dis.*, 2014, 2014: 323478
14. **Jones R.W., Romeo R., Trigg R., Knapp M., Sato A., King D., et al.** Dependence in Alzheimer's disease and service use costs, quality of life, and caregiver burden: The DADE study. *Alzheimers & Dementia*, pii: S1552-5260(14)00107-1, 2014
15. **Karch C.M., Cruchaga C.V., Goate A.M.** Alzheimer's Disease Genetics: From the Bench to the Clinic. *Neuron*, 2014, 83, 11-26
16. **Kima D.H., Yeo S.H., Park J.M., Choi J.Y., Lee T.H.** Genetic markers for diagnosis and pathogenesis of Alzheimer's disease. *Gene*, 2014, 545, 185-193
17. **Luthar S.S.** Resilience in development: A synthesis of research across five decades. In D. Cicchetti & D.J. Cohen (Eds.), *Developmental psychopathology: Vol. 3. Risk, disorder, and adaptation* (2nd ed., pp. 739-795). New York: Wiley, 2006
18. **MacRae H.** Women and caring: Constructing self through others. *Journal of Women and Aging*, 1995, 7, 145-167
19. **Medway C., Morgan K.** The genetics of Alzheimer's disease; putting flesh on the bones. *Neuropathology and Applied Neurobiology*, 2014, 40, 97-105
20. **Mitsui J., Tsuji S.** Genomic aspects of sporadic neurodegenerative diseases. *Biochemical and Biophysical Research Communications*, 2014, 452, 221-225
21. **Mumenthaler M., Mattle H.** 4th ed. *Neurology*, Georg Thieme Verlag, 2004, pp. 367-369
22. **Nakamura K., Watanabe N., Ohkawa H., Ando M., Ogura Y., Funabiki S., et al.** Effects on caregiver burden of a donepezil hydrochloride dosage increase to 10 mg/day in patients with Alzheimer's disease. *Patient Prefer Adherence*, 2014, 8, 1223-1228
23. **Nichols L.O., Chang C., Lummus A., Burns R., Martindale-Adams J., Graney M.J., et al.** Resources for Enhancing Alzheimer's Caregivers Health II Investigators, The cost-effectiveness of a behavior intervention with caregivers of patients with Alzheimer's disease. *J Am Geriatr Soc.*, 2008, 56, 413-420
24. **Nima M.** Syndromes of cognitive dysfunction. In: Nima M., Flemming K.D. *Neurology Board Review. An Illustrated Study Guide*, Canada: Mayo Clinic Scientific Press, 2007, pp. 297-330
25. **Noonan A., Tennstedt S., Rebelsky F.** Making the best of it: Themes of meaning among in formal caregivers to the elderly. *Journal of Aging Studies*, 1996, 10, 313-327
26. **Norman E.** Resiliency enhancement: Putting the strengths perspective into social work practice. Columbia University: New York, 2000
27. **O'Rourke N.** Equivalence of French and English Language Versions of the Center for Epidemiologic Studies-Depression Scale (CES-D) among Caregivers of Persons with Dementia. *Canadian Journal on Aging*, 2003, 22, 323-329
28. **Pinquart M., Sörensen S.** Associations of stressors and uplifts of caregiving with caregiver burden and depressive mood: a meta-analysis. *The Journals of Gerontology Series B: Psychological Sciences and Social Sciences*, 2003, 58, 112-128
29. **Prince M., Bryce R., Albanese E., Wimo A., Ribeiro W., Ferri C.P.** The global prevalence of dementia: a systematic review and meta-analysis. *Alzheimer's & Dementia*, 2013, 9, 63-75
30. **Richardson G.E.** Metatheory of resilience and resiliency. *Journal of Clinical Psychology*, 2002, 58, 307-321
31. **Ross L., Holliman D., Dixon D.R.** Resiliency in family caregivers: Implications for social work practice. *Journal of Gerontological Social Work*, 2003, 40, 81-96
32. **Schwam E.M., Abu-Shakra S., del Valle M., Townsend R.J., Carrillo M.C., Fillit H.** Health economics and the value of therapy in Alzheimer's disease. *Alzheimers Dement.*, 2007, 3, 143-51
33. **Sherrell K., Buckwalter K., Morhardt D.** Negotiating family relationships: Dementiacare as a midlife development task. *Families in Society*, 2001, 82, 383-392
34. **Sörensen S., Pinquart M., Duberstein P.** How effective are interventions with caregivers? An updated meta-analysis. *Gerontologist*, 2002, 42, 356-372
35. **Speice J., Shields C. & Blieszner R.** The effect of family communication patterns during middle-phase Alzheimer's disease. *Families, Systems and Health*, 1998, 16, 233-248
36. **Wagnild G. & Young H.** Resilience among older women. *Journal of Nursing Scholarship*, 1990, 22, 252-255
37. **Wagnild G. & Young H.** Development and psychometric evaluation of the resilience scale. *Journal of Nursing Measurement*, 1993, 1, 165-178
38. **Williamson G.M., Schulz, R.** Relationship orientation, quality of prior relationship, and distress among caregivers of Alzheimer's patients. *Psychology and Aging*, 1990, 5, 502-509
39. **Wimo A., Jonsson L., Bond J., Prince M., Winblad B.** Alzheimer Disease International. The worldwide economic impact of dementia 2010. *Alzheimer's & Dementia*, 2013, 9, 1-11
40. **Yektatalab S., Sharif F., Kaveh M.H., Fallahi Khoshknab M., Petramfar P.** Living with and caring for patients with Alzheimer's disease in nursing homes. *J Caring Sci.*, 2013, 2, 187-195

41. **Yektatab S., Kaveh M.H., Sharif F., Fallahi Khoshknab M., Petramfar P.** Characteristics of care and caregivers of Alzheimer's patients in elderly care homes: a qualitative research. *Iran Red Crescent Med J.*, 2012, 14, 294-299
42. **Zabar Y.** Dementia: Mild Cognitive Impairment, Alzheimer Disease, Lewy Body Dementia, Frontotemporal Lobar Dementia, Vascular Dementia. In: Royden J.H., Srinivasan J., Allam G.J., Baker R.A., Eds. 2nd ed. *Netter's Neurology*. Philadelphia: Elsevier Saunders, 221-234, 2012
43. **Zhu C.W., Scaemeas N., Ornstein K., Albert M., Brandt J., Blacker, D., et al.** Health-care use and cost in dementia caregivers: Longitudinal results from the Predictors Caregiver Study, *Alzheimers Dement.* 2014 Mar 15. pii: S1552-5260(14)00007-7