

# Caregiver burden and psychosocial services in patients with early and late onset Alzheimer's disease

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## ABSTRACT

**INTRODUCTION:** The purpose of the study was to analyse caregiver burden and consumption of psychosocial services in a consecutive group of patients with early onset Alzheimer's disease (EOAD) compared with a matching group with late onset Alzheimer's disease (LOAD).

**MATERIAL AND METHODS:** This was a case-control study with 42 patients who were matched according to disease severity at the time of diagnosis. Caregivers in both groups were interviewed using the Neuro Psychiatric Inventory (NPI), the Activities of Daily Living (ADL) scale and the Resource Utilization in Dementia scale. The quantitative outcomes were compared statistically.

**RESULTS:** The EOAD group had a significantly higher ADL score than the LOAD group. There was a trend towards caregivers in the LOAD group spending more time helping the patients, and they needed more social services than the EOAD group. NPI scores were not significantly different, but a tendency towards a higher caregiver burden in the EOAD group was observed.

**CONCLUSION:** The higher caregiver burden in patients with EOAD – despite a better ADL function than LOAD patients – suggests that the existing psychosocial services might be particularly insufficient for caregivers in EOAD.

**FUNDING:** The study was funded by a three-month scholarship grant from the research fund at Roskilde Hospital.

**TRIAL REGISTRATION:** not relevant.

Alzheimer's Disease (AD) is the most common dementia disorder. Its prevalence increases with age, and more than 25% of the population above 85 years of age has AD [1]. About 1-2% of all AD cases present before the age of 65 years (early onset AD (EOAD)), and the disease is autosomal dominant hereditary in about 10% of these patients; three relevant genes have been identified (presenilin 1 (PSEN1), amyloid precursor protein and presenilin 2 (PSEN2)). Previously, EOAD was recognized as being rare, but following the revision of the diagnostic criteria for AD published in 1984 [2], the disease is no longer exclusively considered to be related to old age [3]. New research criteria have recently been published and they are finding an ever wider application as clinical criteria in specialized settings [4]. Overall, the incidence of AD continues to grow [1], probably mainly because of the rising mean age in the general population. Addition-

ally, owing to improved diagnostic tools, we may expect an increase in the number of patients who will be diagnosed with EOAD in years to come.

Besides a gradual deterioration of episodic memory, the classic symptoms of AD are progressive deterioration of other cognitive domains that clinically affect language, executive functions, praxis and visuospatial functions. Within a few years, the disease will limit the patient's abilities through an increasing weakening of cognitive functions, progressive neuropsychiatric symptoms and a weakening of regular daily functions.

There is currently no curative treatment, but pharmaceutical treatment has a modest symptomatic effect and sometimes has the potential to stabilize the progression of the disease for a limited period of time.

Previous studies have shown that the clinical symptoms in EOAD often present differently to those of late onset AD (LOAD). Several studies have LOAD defined as AD with symptom onset more than 65 years of age. The clinical picture of LOAD is dominated by episodic amnesia, whereas the symptoms in EOAD to a greater extent involve primary attention problems, apraxia and visual dysfunction [5].

It has previously been reported that EOAD patients have a lower mean Neuro Psychiatric Inventory (NPI) score, which suggests fewer behavioural and psychosocial symptoms than in a matching group of LOAD patients [6], and one previous study indicated that the NPI score was a better predictor of caregiver burden than other measures including cognition and global disease severity [7]. However, previous studies that have investigated the caregiver burden in EOAD report a considerable burden and also a high occurrence of depression among caregivers [8]. Furthermore, only one published

## ORIGINAL ARTICLE

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Dan Med J  
2013;60(7):A4649



The large caregiver burden in younger demented patients indicates the need for additional psychosocial support.

study has shown a significant difference in caregiver burden between patients with EOAD and LOAD [9]. A review article concluded that the subject is poorly investigated because most studies are small and very heterogeneous in terms of design, methods, and inclusion and exclusion criteria [10].

Another area that has received only limited attention is the socioeconomic consequences of AD. It has been suggested that the derived economic expenses of early onset dementia are almost the same as those caused by late onset dementia, but studies in the field are limited and the costs may be higher than previously reported [11].

The purpose of this study was to uncover the degree of caregiver burden and the use of social services in a well-defined and consecutive group of EOAD patients, and to compare these parameters with a strictly matched group of LOAD patients.

## MATERIAL AND METHODS

The Memory Clinic at Roskilde University Hospital is a multidisciplinary outpatient clinic under the Department of Neurology. The Memory Clinic evaluates approximately 250 new patients annually of whom 10-15% of new referrals are under the age of 65 years. Patients are typically treated and followed in the Memory Clinic for a minimum of six months from the time of the diagnosis.

### Methods

This was a case-control study in which two groups of patients with EOAD and LOAD, respectively, were compared with regard to a series of parameters. As part of the study, patients were invited for an extra follow-up visit at the clinic. The patients' closest caregiver accompanied them to the extra study visit. All journals were reviewed beforehand to obtain information about cognitive and neuropsychiatric test scores at the time of the diagnosis.

During the study visit, the history and information regarding educational status, pharmaceutical treatment and co-morbidity was registered. A neurological examination was performed, and the following cognitive tests were carried out: Mini Mental Status Examination (MMSE) [12] and Addenbrooke's Cognitive Examination (ACE) [13]. Furthermore, a depression score was obtained using the Hamilton Scale of Depression (Ham-D 17) [14].

The caregivers were interviewed by the specialist nurse, who recorded systematic questions about the caregivers' perception of the patients' behavioural symptoms using the NPI [15]. Additionally, information about how the patient coped with everyday activity using the Activities of Daily Living inventory from the Alzheimer's Disease Cooperative Study instrument protocol (ADCS-ADL) [16] was recorded. Finally, a questionnaire regarding the consumption of social services and the caregivers' role was completed using the Resource Utilization in Dementia (RUD) [17]. Any co-morbidity thought to be relevant to cognitive health was registered (i.e. cerebrovascular disease, head trauma, CNS infections, etc.). Each registered co-morbidity was quantitated with a score of 1 using an arbitrary scale. Eventually, the average co-morbidity score was statistically compared group-wise (EOAD versus LOAD).

The project was approved by the ethic and scientific committee (SJ-222) and reported to the Danish Data Protection Agency.

### Inclusion criteria

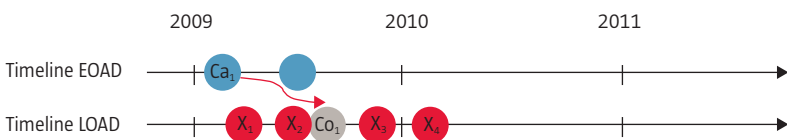
Regardless of their age, all patients were diagnosed with AD using the NINCDS-ADRDA criteria for "probable AD" [2]. Patients aged 65 years or less at the time of diagnosis were included in the EOAD group. Patients eligible for the LOAD group were selected pairwise using a strict randomization algorithm: for each EOAD patient, a LOAD "match" was identified as the next patient downstream over the age of 70 years at the time of diagnosis who had an MMSE score within  $\pm 2$  points and an ACE score within  $\pm 5$  points from the respective EOAD patient (**Figure 1**). All patients should have been treated with anti-dementia drugs since the time of diagnosis. The diagnosis should have been made more than six months prior to the project follow-up visit.

### Exclusion criteria

The following exclusion criteria were applied: An MMSE score below 18 or an ACE score below 50 at the time of the diagnosis, inability to cooperate, e.g. due to sight or hearing impairment, amputation or other major handicaps, legal incompetence or cognitive impairment to a degree that would prohibit informed consent, patients with known psychiatric diseases other than well treated

**FIGURE 1**

Randomization algorithm for matching "cases" (EOAD) with "controls" (LOAD).



Ca<sub>1</sub> (case 1) – MMSE 25, ACE 76

X<sub>1</sub> – first control candidate down the timeline (but MMSE score 19, ACE score 61)

X<sub>2</sub> – second control candidate down the timeline (MMSE score 26, ACE score 74 – but age 68 years)

Co<sub>1</sub> (control 1) – first match down the timeline with an MMSE score within the 23-27 interval and an ACE interval (71-81) and age 81 years (> 70 years)

ACE = Addenbrooke's Cognitive Examination. MMSE = Mini Mental Status Examination. EOAD = early onset Alzheimer's disease. LOAD = late onset Alzheimer's disease.

depression, patients with known neurological or medical diseases that might contribute to cognitive impairment, patients treated with antipsychotic medication or neuroleptics three months prior to inclusion, patients with a history of drug or alcohol abuse, patients with known prior head trauma or central nervous system infection that was known to contribute to the cognitive impairment, patients who had received electroconvulsive therapy less than three months prior to inclusion.

### Statistical analysis

In regards to the quantitative or semi-quantitative data (MMSE, ACE, NPI and ADL), both parametric (Welch's two-sample t-test) and non-parametric (Wilcoxon rank-sum test) statistic comparisons of the EOAD group in relation to the LOAD group were performed.

*Trial registration:* not relevant.

## RESULTS

### Demographic data

All patients had sporadic AD, except for one EOAD patient with a known PSEN1 mutation. The mean age, MMSE scores, mean duration of the follow-up period and gender distribution for both patients and caregivers are provided in **Table 1**.

For the scores relating to activities of daily living (ADL) and NPI, see **Table 2**. The EOAD group had a significantly higher ADL score than the LOAD group, whereas there were no significant differences between the groups in regards to behavioural and psychiatric symptoms (NPI). In contrast, there was a tendency towards a higher caregiver burden among the caregivers in the EOAD group, although this was not statistically significant.

### Caregiver time consumption

Compared with the EOAD group, caregivers in the LOAD group consumed more time helping patients at home with the following daily tasks eating, getting dressed, taking walks, housekeeping, economy and surveillance (**Table 3**), but this trend was only significant when measuring the single parameters.

### Social resources

There was a tendency towards a higher consumption of social resources, i.e. home nursing care, home care, transportation and day centre use in the LOAD than in the EOAD group (**Table 3**).

## DISCUSSION

We investigated a consecutive group of patients with early clinical AD compared with a randomized algorithmically selected group with onset of AD after the age of

**TABLE 1**

Demographic data.

Group	Age, project visit, years, mean $\pm$ SD	Gender, M/F, n	MMSE score, time of diagnosis, mean $\pm$ SD	ACE score, time of diagnosis, mean $\pm$ SD
EOAD patients	60.1 $\pm$ 2.8	7/14	23.1 $\pm$ 3.6	70.4 $\pm$ 16.8
EOAD caregivers	57.0 $\pm$ 12.5	12/9	–	–
LOAD patients	79.6 $\pm$ 3.7	12/9 <sup>a</sup>	24.0 <sup>a</sup> $\pm$ 4.5	69.0 <sup>a</sup> $\pm$ 16.5
LOAD caregivers	68.1 $\pm$ 13.1	5/16	–	–

ACE = Addenbrooke's Cognitive Examination. EOAD = early onset Alzheimer's disease. LOAD = late onset Alzheimer's disease. MMSE = Mini Mental Status Examination. SD = standard deviation.

a) Non-significant.

**TABLE 2**

ADL-functions, neuropsychiatric symptoms, caregiver burden and co-morbidity.

Group	ADL score $\pm$ SD	NPI score, behavioural symptoms $\pm$ SD	NPI-Q score, caregiver burden $\pm$ SD	Co-morbidity score $\pm$ SD
EOAD	65.5 $\pm$ 7.6	4.6 $\pm$ 6.8	9.5 $\pm$ 12.9	0.9 $\pm$ 0.6
LOAD	54.2 $\pm$ 11.3	4.5 $\pm$ 3.9	8.4 $\pm$ 7.8	1.0 $\pm$ 0.7
p-value	< 0.001	NS	NS	NS

"The Neuropsychiatric Inventory is an instrument designed to assess behavioural symptoms and personality changes (neuropsychiatric symptoms (BPSD)) as well as caregiver burden in various conditions. The scale is divided into 12 domains, and for each domain (i.e. agitation) the presence (score 0-1), the frequency (score 1-4) and severity (score 1-3) can be applied, that is – the total NPI score can vary from 0 to 144 points. The NPI-Q is a questionnaire in which the caregiver rates severity and burden for each of the 12 domains (score 0-3), yielding a total score from 0 to 36 points" [15].

ADL = activities of daily living. BPSD = behavioural and psychological symptoms in dementia. EOAD = early onset Alzheimer's disease. LOAD = late onset Alzheimer's disease. NPI = neuropsychiatric inventory. NPI-Q = neuropsychiatric inventory questionnaire. NS = non-significant. SD = standard deviation.

65 years. We used the date of diagnosis as a parameter to separate the two age groups, as this date is better defined than the date for symptom onset. Thus, the groups were clearly separated in regards to mean age, and they were carefully matched on disease severity at the time of diagnosis. We invited all eligible patients to an extra follow-up visit in the clinic. In this article, we primarily focus on reporting information from the caregivers. The purpose was to determine whether the two groups differed with regard to functional level, psychosocial resource consumption and caregiver burden.

The results show that patients in the LOAD group on average have a significantly lower ADL function than patients in the EOAD group, and on isolated parameters they have a significantly higher caregiver time consumption (**Table 3**). Thus, it would be expected that the caregivers in the LOAD group would report a higher psychosocial burden (NPI caregiver burden, see **Table 2**). Surprisingly, despite the lack of any significant difference between the groups with regard to behavioural and neuropsychiatric symptoms evaluated by the NPI, a larger, though not statistically significant, degree of burden was registered among the caregivers in the EOAD group.

TABLE 3

Caregivers' time consumption and patients' need for social resources.

	Caregivers EOAD, mean $\pm$ SD	Caregivers LOAD, mean $\pm$ SD	p-value
<i>Caregivers' consumption of time</i>			
Eating, dressing, walks	0.3 $\pm$ 1.2 h/day	0.4 $\pm$ 0.7 h/day	NS
	4.3 $\pm$ 10.8 days/ month	7.3 $\pm$ 13.0 days/ month	NS
Housekeeping, transportation, economy	1.3 $\pm$ 1.5 h/day	2.5 hours $\pm$ 2.0 h/ day	< 0.05
	21.4 $\pm$ 12.4 days/month	23.9 $\pm$ 11.7 days/ month	NS
Surveillance	1.5 $\pm$ 5.2 h/day	2.4 $\pm$ 6.6 h/day	NS
	8.2 $\pm$ 13.0 days/ month	10.6 $\pm$ 14.3 days/ month	NS
<i>Social health-care resources</i>			
Home nursing	6 $\pm$ 26.1 visits/ month	2 $\pm$ 6.5 visits/ month	NS
Homecare	8.6 $\pm$ 27.1 visits/ month	14.8 $\pm$ 31.8 visits/ month	0.08
Food delivery	1.4 $\pm$ 6.6 visits/ month	6.1 $\pm$ 20.4 visits/ month	NS
Day-center	1.4 $\pm$ 3.9 visits/ month	3.6 $\pm$ 5.9 visits/ month	0.10
Transportation	1.1 $\pm$ 3.1 visits/ month	3.0 $\pm$ 7.4 visits/ month	NS

EOAD = early onset Alzheimer's disease; LOAD = late onset Alzheimer's disease; NS = non-significant; SD = standard deviation.

We can therefore not confirm the results from an earlier study, which recorded lower NPI scores among patients with EOAD than among patients with LOAD. In that study, the disease severity in the two groups was similar, but the groups had very different sizes and the disease severity as such could have been different to that of our study [18].

The lower ADL score we recorded in the LOAD was expected due to normal aging not directly related to AD. Taking into account all relevant co-morbidity, we saw no significantly higher degree of co-morbidity in the LOAD group. The presence and severity of neuropsychiatric symptoms was on average lower than reported in most previous studies of AD, regardless of the age group. We have no obvious explanation for this finding.

A difference in the demography or other characteristics of the caregivers might partly explain the observed trend towards a heavier burden in the EOAD group. However, the proportion of even-aged spouses was similar in the two groups in our material, and we did not observe any other relevant demographic differences between the two groups of relatives.

## CONCLUSION

This study indicates the existence of a difference in caregiver burden in a consecutive group of patients with

EOAD compared with a carefully matched group of patients with LOAD. The trend towards a heavier caregiver burden in the EOAD group despite lack of differences in neuropsychiatric symptoms, significantly less time consumption among caregivers and a higher mean ADL score, suggests that current support to caregivers of younger demented patients is highly insufficient. One recently suggested area of priority with an impact on caregiver burden is individually tailored psycho-educational interventions [19].

Given the limited study size, the results should be assessed with caution, but our findings may provide important inspiration for larger, controlled randomized studies.

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ACCEPTED: 10 April 2013

**CONFLICTS OF INTEREST:** Disclosure forms provided by the authors are available with the full text of this article at [www.danmedj.dk](http://www.danmedj.dk).

**ACKNOWLEDGEMENTS:** We would like to express our gratitude to our Memory Clinic secretary, Jane Liin, who handles many of the practical issues related to this study with great enthusiasm and devotion. Also, we wish to thank the research fund at Hospital Nord, Region Zealand, Denmark, for a 3-month research scholarship.

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