

Patients With Alzheimer's Disease Living at Home in France: Costs and Consequences of the Disease

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ABSTRACT

Alzheimer's disease (AD) creates a substantial burden on human and financial resources. However, there are few data relating to the cost of AD in France. This retrospective study assesses the total costs of caring for home-based patients with mild to moderate AD. Pattern of care, sociodemographic data, caregiver burden, and estimated net costs of caring for AD patients were assessed in a stratified sample of 50 untreated AD patients. The net costs of caring for all AD patients who completed all study parameters increased with decreasing cognitive ability. Unpaid assistance was the most costly component of the total cost of care. Mini-Mental State Examination scores correlated strongly with functional status, and instrumental activities of daily living scores were a robust indicator of the magnitude of behavioral, cognitive, and dependence problems. This study suggested a significant link between costs of caring for an AD patient at home and disease severity.

Keywords: ADLs; Alzheimer; cognition; costs; burden

Alzheimer's disease (AD) is a chronic, progressive neurodegenerative disorder and the commonest cause of dementia in the elderly. It produces cognitive and functional disturbances that lead to a gradual but relentless loss of autonomy as well as severe behavioral problems.¹⁻³ The average duration of AD from onset to death is 5–10 years,^{1,4-6} and symptomatic progression in AD requires increasing levels of care. Spouses and relatives can provide adequate care in the early stages of the disease, but nursing home and psychiatric hospital care often become necessary when the home carers are no longer able to cope. Currently, the overall prevalence of AD in industrialized societies is estimated at 2.6% to 11.2% in those aged >65 years^{7,8} and 50% to 60% in those aged ≥80 years.⁹ AD therefore poses a substantial human and financial burden on caregivers, their relatives, health care systems, and society in general.

Moreover, as the incidence of AD increases exponentially with the growing worldwide elderly population, so too will economic pressure on the provision of health care.

Costs involved in caring for AD patients can be distinguished as both direct and indirect. Direct costs include hospitalization, physician visits, paid home care, drugs, laboratory testing, and institutionalization, the latter of which is often found the largest component of the direct costs of AD. The nature of indirect costs in the case of dementia may differ among studies, especially as far as informal care is concerned. It is usually accepted at present to consider informal care as a substitute to professional home care and to include it as a direct cost. Indirect costs may then include emotional and psychological consequences for families such as stress, sleeplessness, fatigue, anxiety, social isolation, and poor quality of life, as well as associated medical consumption.^{10,13}

Although economic data on dementia are relatively sparse, sociodemographic studies have shown variations between countries in the overall economic impact of AD, reflecting differences in health care organization and unit costs as well as differences in cultural and social factors that may have an effect on rates of institutionalization.¹⁴ Beside these factors, evaluation methods may also largely differ between studies that make the national estimates difficult to compare.¹⁵⁻¹⁹

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AD is considered to be a major public health issue in France, where the overall incidence is up to 60 per 1000 person years, depending on age.²⁰ Only one French socioeconomic study of AD has been reported to date, in which the annual estimated cost per case in 1991 was found to range between \$5156 (Euros 5304) and \$8400 (Euros 8641) depending on disease severity.²¹ Here, we describe a 6-month, retrospective analysis of 50 untreated AD patients living at home, designed to examine further the direct and indirect costs of caring for AD patients in France in connection with disease severity.

METHODS

The design of this observational study was cross-sectional and retrospective. The study took place at the Broca Geriatric Day Care Hospital, which is a memory clinic located in Paris for patients suffering from AD and related disorders. The eligible population was composed of a stratified random sample of outpatients who met the *Diagnostic and Statistical Manual of Mental Disorders* (4th ed.)²² and NINCDS-ADRDA criteria for probable AD.²² At study enrollment, patients were stratified into 1 among 4 groups in relation to baseline Mini-Mental State Examination (MMSE) score as follows: <10, 11 to 15, 16 to 20, >21. Other inclusion and exclusion criteria were the following: patients were required to be living at home alone or with a host family and to be accompanied during outpatient consultation by the principal caregiver who was also willing to complete a questionnaire. AD patients receiving specific treatment for dementia at inclusion, such as the cholinesterase inhibitors tacrine, donepezil, or rivastigmine, or suffering from other severe medical conditions or living in a medical institution were excluded from the study. The population of eligible patients selected may then be considered as a population visiting for the first time a specialized clinic before starting a specific treatment. The evaluation procedure consisted of detailed recording of medical history, physical and neurological examinations, psychiatric and cognitive evaluations, and all imaging procedures and laboratory tests having been performed in the past 6 months. Laboratory tests included complete blood cell count and differential; serum electrolytes and glucose, liver, and renal function tests; thyroid hormones; Venereal Disease Research Laboratory test; vitamin B12; folate levels; and an electrocardiogram (ECG). Patients and/or their caregivers gave informed consent to participate in the study.

Outcome Measurements

A series of clinically validated scales were used to assess patients' cognitive and functional impairment and degree of behavioral dysfunction at inclusion. These included the MMSE²⁴ for cognitive function, the results of which were used for stratification. Additional measures

included the Global Deterioration Scale (GDS)²⁵ as well as the Katz Activities of Daily Living (ADL)²⁶ and Lawton instrumental activities of daily living (IADL)²⁷ scales to assess the severity of the patient's functional disability. The NeuroPsychiatric Inventory (NPI)²⁸ was used to assess frequency and severity of behavioral disturbances, and the impact of the disease on the caregiver was rated using both the 12-item General Health Questionnaire (GHQ)²⁹ and the Zarit scale.³⁰ The latter 2 scales provide subjective and objective measures of the "burden" of caring for an AD patient and include parameters such as somatic symptoms, psychological well-being, finances, social dysfunction, and relationship between caregiver and patient. In addition, sociodemographic information on patients and caregivers, the patient's conditions of life and job before retirement, and the caregiver's age, gender, job, relationship to the patient, home distance from the patient, and whether it was intended to institutionalize the patient, and so forth, was obtained using a questionnaire that was filled in at the end of the inclusion visit.

Estimating the Costs of AD

This study considered only direct costs of dependence and medical expenditure incurred retrospectively over a 6-month period in AD patients. Informal unpaid care provided by caregivers was considered as a substitute to paid care and valued as a direct cost. Cost items then included in the study were paid and unpaid informal assistance, general medical consumption, and the cost of temporary accommodation in nonmedical institutions, such as day centers.

The items of medical consumption recorded included medical consultations, physiotherapy, speech therapy, occupational therapy, memory stimulation, visiting nurses during the past month, and hospitalizations during the past 6 months. They were obtained from questionnaires completed by the caregiver. Caregivers were also asked to report the number of times formal care or paid nonmedical services (eg, home health aid, attendant, housekeeper, food delivery) were received in the past 4 weeks and the average number of hours and minutes per visit. These values were extrapolated to the 6-month period. Informal care—the amount of time spent by the primary or other caregiver in a typical day on bathing, dressing, dinner fixing, feeding, medications administration, supervision, housekeeping, transportation, and other tasks—was estimated by the caregivers in hours and minutes. A list was made of all individuals who helped with an individual patient's care, and the average daily amount of care provided was estimated.

Caregiver time was valued in a conservative manner at Euros 8.4/hour at the average rate for housekeeping work, and paid assistance was valued Euros 13/hour, as the average rate for professionals involved in these services. Some items of medical consumption, such as pharmacy

charges, and procedures (imaging and biological testing) could not be recorded directly for practical reasons. For unit costs of the items of medical consumption, such as general practitioner (GP) or specialist visit, we used current French tariffs and costs per disease-related group for inpatient care. Costs estimated in the present study were net costs, arrived at by subtracting the costs due to consumption of resources (aid, care) in a reference population without AD. For general medical consumption, we used the estimates from the National Household Survey^{31,32} in the same age group (>70 years) as a reference value. For paid and unpaid care at home, no external reference values were available, and we then used the subgroup of patients with an MMSE score of 30 within this study as the reference group.

Statistical Analysis

The various resource consumption measures as well as the cognitive, functional, and behavioral outcome scores were analyzed using descriptive statistical methods, calculated and stored using Microsoft Excel 97 software. Exponential and linear regression analyses were used to evaluate relationships between outcome measures and net costs of care, and Pearson's correlation coefficients were calculated. For comparisons involving parameters that were not normally distributed, Wilcoxon's signed rank test or Mann and Whitney's U test were performed.

RESULTS

Subjects

The study population consisted of 39 women (78%) and 11 men (with a mean age of 80.9 ± 6.3 and 80.2 ± 4.4 years, respectively). The educational level was 1 (primary school) for 41% of patients, 2 (secondary school) for 37%, and 3 (higher education) for 22% of patients. Most patients (58%) lived alone, while 34% lived with a spouse and 8% with parents or children. The caregiver sample was predominantly female (75%), with an average age of 60 years, and two thirds (66%) of the care was provided by a child of the patient, 32% by a spouse, and 2% by a sibling. In 62% of cases, the principal caregiver was the only person available to assist and care for the patient, which was dependent on the caregiver's professional status. Most caregivers either lived with the patient (40%) or nearby (38%), with 10% residing more than 100 km from the patient's home. Plans to institutionalize the patient were under consideration by 46% of caregivers. This was dependent on both the distance between the patient's and caregiver's homes (but not the latter's professional status) as well as to the patient's level of cognitive (MMSE: $P = .0182$; GDS: $P = .015$), functional (IADL: $P = .042$), and behavioral (NPI: $P = .0028$) dysfunction. However, we found no association between the intention to institutionalize the patient and the general health status or level of caregiver burden.

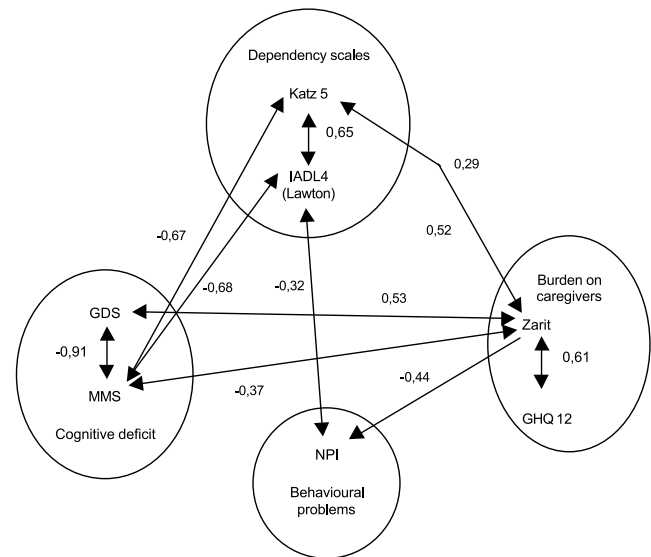


Figure 1. Relationships between cognitive, functional, and behavioral outcome measures. Arrows denote interrelationships. Numbers next to each arrow show the respective Pearson's correlation coefficients.

Relationship Between Cognition, Functional Capacity, and Behavioral Disturbances

The relationships between the cognitive and behavioral outcome measures, disability assessment scores, and the scores for scales measuring the impact of the disease on the caregiver are shown in Figure 1. There was a strong correlation between the loss of basic and instrumental ADLs, as measured on the Katz ADL and IADL scales, and cognitive deterioration, as measured by the MMSE (-0.67 and -0.68 , respectively). Interestingly, while behavioral disturbances were independent of severe functional disability, a correlation was observed between IADL scores and behavior (-0.32) measured by the NPI. Of the 2 instruments used to measure caregiver burden, the Zarit, but not the GHQ-12 score, correlated strongly with all measures of cognition (-0.37 and 0.53 on the MMSE and GDS scales, respectively), functional disability (0.29 and 0.52 on the Katz and IADL scales, respectively), and behavioral impairment (-0.44).

Medical and Paramedical Care Consumption

Of the 50 patients enrolled in the study, resource utilization data were available from 48. In the last 6 months, 12 patients were hospitalized for a mean duration of 36.5 days, with the percentage of patients hospitalized greatest in the MMSE <10 group. The majority (80%) of patients enrolled into the study consulted at least one doctor, in the main a GP (82.5%), in the month preceding the initiation of the study. Paramedical care, which included physiotherapy, speech therapy, occupational therapy, memory stimulation, and visiting nurses, was received by 21 (42%)

Table 1. Mean Monthly Costs per Alzheimer Patient Living at Home According to Cognitive Deficit (Euro 1996 Value)

Mini-Mental State Examination Score	Medical Consumption ^a (x)		Paid Assistance (y)		Unpaid Assistance ^b (z)		Total Cost (x) + (y) + (z)		Total Net Cost (x) + (y) + (z) - (A)
	Cost	%	Cost	%	Cost	%	Cost	%	
≤10	522.9	11.8	900.5	20.3	3,015.0	67.9	4,438.4	100%	4,104.8
11–15	432.3	26.1	280.6	21.3	939.7	52.6	1,652.6	100	1,319
16–20	375.6	37.9	141.8	14.3	474.7	47.8	992.1	100	658.5
≥21	296.4	56.4	52.6	10	176.2	33.6	525.2	100	191.6
Reference population	216.2	64.2	26.4	7.8	91.0	28	336.6	100 (A)	—

a. Drugs and procedures (diagnostic imaging, laboratory tests) not included.

b. Based on a rate of Euros 8.4 per hour.

of the AD patients. Costs for pharmacy and additional charges such as diagnostic imaging and laboratory tests for the AD patients could not be estimated directly and were supposed identical in all subgroups.

Paid and Unpaid Assistance

The majority (62%) of patients in this study received paid (formal) assistance at home. This consisted of a housemaid (48%), a home health aid (29%), an attendant (13%), or a housekeeper (13%). The mean number of weekly paid and unpaid (informal) hours was estimated to be 7.4 (16%) and 39.2 (84%), respectively. Using exponential regression analysis, a statistically significant correlation was observed between patients' MMSE scores and the total time for weekly assistance, as well as with the monthly cost of paid and unpaid home care.

Reference Costs (Non-AD Patients) and Net Costs of Care for AD Patients

The general population older than 70 years of age was used in the present study as a reference group for medical care consumption. The mean monthly value of health expenditure taken for the reference population was estimated at Euros 274 from the results of a general household survey projected to 1996 values. Net costs of paid and unpaid assistance were calculated by subtracting those costs of the patient with an MMSE score of 30 taken as a reference group, that is, 0.47 hours/week of paid assistance and 2.51 hours/week of unpaid assistance equating to Euros 26 and Euros 89, respectively, per month.

The net monthly costs incurred by patients with AD by the 4 subgroups of patients with MMSE scores from ≥21 to ≤10 are shown in Table 1. At an MMSE score >20, monthly costs of care of an AD patient were estimated at Euros 191.6, rising to Euros 4,104.8 for MMSE scores ≤10.

DISCUSSION

The results of this study indicate that the total costs of caring for a patient with AD at home are greater than those incurred in looking after an elderly non-AD person

and, most significantly, that these costs increase rapidly as cognitive function declines. Data from this study not only suggest that the overall costs increase steeply in relation to disease severity but also that the largest component (one half to two thirds) of the total cost of caring for AD patients in the home is unpaid assistance. In addition, this study suggests that IADL score is a good synthetic indicator of the patient's level of cognitive, functional, and behavioral impairment and that the Zarit scale provides a valuable indicator of the effect of the patient's cognitive and behavioral symptoms on the caregiver.

Present Data and Previous Evidence: Cost of Informal Care

These findings are consistent with the results of a number of other cost-of-illness studies conducted worldwide on resource utilization in AD.^{33–37} In all these studies, the cost of unpaid or informal care emerges as a significant proportion of the total direct costs even when government or health insurance schemes cover direct health care costs. In common with the results presented here, these studies also demonstrate that caregiving costs increase as cognitive functioning declines, especially in patients being cared for in the home.

TOTAL COSTS, COGNITIVE DEFICIT, AND FUNCTIONAL DECLINE IN AD

Comparisons with the only other cost-of-illness study to have been carried out in France are also in agreement with these findings. The net monthly medical expenditure of Euros 353 for AD patients with MMSE scores of 20 in this study compares with a value of Euro 296, after adjusting to 1996 prices, reported from the other French study: an 18% difference.²¹ Corresponding expenditures for those with MMSE scores of 9 were Euros 521 and Euros 477, respectively: an 8% difference. In both studies, the net annual cost per patient with AD rises as MMSE score declines, and net annual costs of caring for an AD patient at home were significantly higher in patients with low MMSE scores.

COSTS AND SYMPTOMATIC PROGRESSION

Interestingly, 2 recently published cost-of-illness studies show no significant association between caregiver unpaid assistance and MMSE score.^{38,39} However, although Bianchetti and colleagues found the MMSE score to be unrelated to indirect caregiving costs, their study did show a strong link between indirect costs of AD and functional status as measured by the IADL.³⁹ The Italian Co-Dem study also found that the number of IADLs lost was the principal predictor of costs of home care.³⁸ In the present study, cognitive deterioration correlated strongly with functional status as measured by both the Katz ADL and IADL. In particular, the IADL emerged as a fair indicator of the overall magnitude of behavioral, cognitive, and dependence problems of the patient, and it suggests that the model described here provides a satisfactory link between costs incurred in caring for an AD patient and disease severity.

Disease Severity and Caregiver Burden

The present study also showed that there was a strong correlation on all measures of cognitive, functional, and behavioral impairment with the Zarit scale, which measures caregiver burden and stress. In addition to measurable costs, caring for an AD patient at home involves enormous personal and social-economic burdens that are difficult to quantify, such as social isolation, fatigue, disruptions to family life, and poor quality of life.⁴⁰ Severity of cognitive and functional impairment, and especially neuropsychiatric symptoms, appear to be the strongest predictors of the scale of this burden.⁴¹

CAREGIVER BURDEN: A PREDICTOR OF INSTITUTIONALIZATION

Caregiver burden has been identified as a predictor of institutionalization of elderly demented patients.⁴² In the present study, there was a strong correlation between intention to institutionalize patients with declining levels of cognitive impairment. Despite this, however, most of the caregivers in the present study preferred to keep the patient at home for longer. There are distinct variations between countries in the overall economic impact of AD on society. This reflects differences in health care organization and costs as well as differences in cultural and social factors that may have an effect on rates of institutionalization. A high level of home-based care is common in many other European countries, notably Italy, where a substantial share of the cost of caring for the patient is absorbed by the caregiver.¹⁴ Interestingly, in countries such as Sweden and the Netherlands, where rates of institutional care have traditionally been high, there is now a growing trend toward more home-based care for AD patients.⁴³

CONCLUSION

The present study was designed to address the lack of systematic studies to estimate the economic consequences of caring for AD patients in the home in France. The study investigated how the care of AD patients is organized (eg, formal and informal caregiving time, medical and paramedical consultations, hospitalizations, day care center use), the relationship between a patient's cognition and functional capacity, and behavioral disorders and their impact on costs. The results presented here show that there is an additional burden on caregivers in looking after AD patients at home in comparison with a non-AD elderly population, and these costs grow rapidly as cognitive, behavioral, and functional status declines.

Overall costs of caring for patients with AD increase steeply in relation to cognitive decline, as measured by clinical cognitive rating scales. The largest component (one half to two thirds) of the total cost of caring for AD patients in the home is unpaid assistance cost.

The use of clinical rating scales that measure personal and social-economic burdens of caregivers can show a strong correlation between the degree of cognitive, functional, and behavioral impairment of AD patients and caregiver burden and stress.

Although a large amount of patient, caregiver, and economic data was generated to perform this analysis, the size of the patient sample used was small. Costs of medical care and time spent by caregivers and professional home assistance were assessed by extrapolating from interviews of caregivers on a limited retrospective time period. This method is subject to some error and bias, especially concerning the estimates of time spent by spouses of the patients. It is difficult and sometimes impossible for them to separate time of supervision and time devoted to active care. The separate comparison of AD and non-AD patient populations can present problems due to differences in comorbid medical conditions and living conditions and availability of caregivers. The extent to which recently available agents for the symptomatic treatment of patients with mild to moderate AD influence care placement and the quality of life of both the patient and caregiver is an issue that needs to be addressed in future studies.

References

1. American Psychiatric Association. Practice guideline for the treatment of patients with Alzheimer's disease and other dementias of late life. *Am J Psychiatry* 1997; 154(5):1?39.
2. Galasko D, Edland SD, Morris JC, et al. The Consortium to Establish a Registry for Alzheimer's Disease (CERAD). Part XI. Clinical milestones in patients with Alzheimer's disease followed over 3 years. *Neurology* 1995; 45:1451?1455.
3. Finkel S, Costa E, Silva J, et al. Behavioral and psychological signs of symptoms of dementia: a consensus statement on current knowledge and implications for research and treatment. *Int J Geriatr Psych Neurol* 1997; 12:1060?1061.

4. Barclay LL, Zemcov A, Blass JP, Sansone J. Survival in Alzheimer's disease and vascular dementias. *Neurology* 1985; 35:834?840.
5. Knopman D, Kitto J, Deinhard S, Heiring J. Longitudinal study of death and institutionalization in patients with primary degenerative dementia. *J Am Geriatr Soc* 1988; 36:108?112.
6. Small GW, Rabins PV, Barry PP, et al. Diagnosis and treatment of Alzheimer's disease and related disorders: consensus statement of the American Association for Geriatric Psychiatry, and Alzheimer's Association, and the American Geriatrics Society. *J Am Med Assoc* 1997; 278:1363?1371.
7. Rocca WA, Hofman A, Brayne C, et al. Frequency and distribution of Alzheimer's disease in Europe: a collaborative study of 1980-1990 prevalence findings. The EURODEM-Prevalence Research Group. *Ann Neurol* 1991; 30(3):381?390.
8. Ernst RL, Hay JW. Economic research on Alzheimer's disease: a review of the literature. *Alzheimer Dis Assoc Dis* 1997; 11:135?145.
9. Fratiglioni L. Epidemiology. In: Wimo A, Jonsson B, Winblad B, eds. *Health economics of dementia*. Chichester, UK: John Wiley & Sons, 1998:13?31.
10. Baumgarten M. The health of persons giving care to the demented elderly: a critical review of the literature. *J Clin Epidemiol* 1989; 42:1137?1148.
11. Kiecolt-Glaser JK, Dura JR, Speicher CE, et al. Spousal caregivers of dementia victims: longitudinal changes in immunity and health. *Psychosom Med* 1991; 53:345?362.
12. Schmall VL. Dealing with Alzheimer's disease: caregiver issues. *Consult Pharm* 1996; 11(suppl E):25?31.
13. Bauer ME, Vedhara K, Perks P, et al. Chronic stress in caregivers of dementia patients is associated with reduced lymphocyte sensitivity to glucocorticoids. *J Neuroimmunol* 2000; 103(1):84?92.
14. Trabucchi MO. An economic perspective on Alzheimer's disease. *J Geriatr Psychiatry Neurol* 1999; 12:29?38.
15. Ernst RL, Hay JW. The US economic and social costs of Alzheimer's disease revisited. *Am J Pub Health* 1994; 84:1261?1264.
16. Ostbye T, Crosse E. Net economic costs of dementia in Canada. *Can Med Ass J* 1994; 151:1457?1464.
17. Wimo A, Karlsson G, Sandman PO, et al. Cost of illness due to dementia in Sweden. *Int J Geriatr Psych* 1997; 12:857?861.
18. Gray A, Fenn P. Alzheimer's disease. The burden of illness in England. *Health Trends* 1993; 25:31?37.
19. Hay J. The costs and social burdens of Alzheimer's disease: what can and should be done? *Alzheimer Dis Assoc Dis* 1997; 11(4):181?183.
20. Letenneur L, Commenges D, Dartigues JF, et al. Incidence of dementia and Alzheimer's disease in elderly community residents in South-Western France. *Int J Epidemiol* 1994; 23:1256?1261.
21. Sou  tre EJ, Qing W, Vigoureux I, et al. Economic analysis of Alzheimer's disease in outpatients: impact of symptom severity. *Int Psychogeriatrics* 1995; 7(1):115?122.
22. American Psychiatric Association. *Diagnostic and statistical manual of mental disorders*. 4th ed., rev. Washington, DC: American Psychiatric Association, 1994:133?155.
23. McKhann G, Drachman D, Folstein M, et al. Clinical diagnosis of Alzheimer's disease: report of the NINCDS-ADRDA work group under the auspices of the Department of Health and Human Services Task Force on Alzheimer's Disease. *Neurology* 1984; 34:939?944.
24. Folstein MF, Folstein SE, McHugh PR. "Mini-Mental State": a practical method for grading the cognitive state of patients for the clinician. *J Psych Res* 1975; 12:189?198.
25. Reisberg B, Ferris SH, de Leon MJ, Crook T. The global deterioration scale for assessment of primary degenerative dementia. *Am J Psychiatry* 1982; 139:1136?1139.
26. Katz A, Ford AB, Moskowitz RW, et al. Studies of illness in the aged. The index of ADL: a standardized measure of biological and psychosocial function. *J Am Med Assoc* 1963; 185:914?919.
27. Lawton MP, Brody EM. Assessment of older people: self-maintaining and instrumental activities of daily living. *Gerontologist* 1969; 9(3):179?186.
28. Cummings JL, Mega M, Gray K, et al. The Neuropsychiatric Inventory: comprehensive assessment of psychopathology in dementia. *Neurology* 1994; 44:2308?2314.
29. Goldberg DP. *The detection of psychiatric illness by questionnaire*. Mandsley Monograph No 21. Oxford, UK: Oxford University Press, 1972.
30. Zarit SH, Orr NK, Zarit JM. *The hidden victims of alzheimer's disease: families under stress*. New York: New York University Press, 1985.
31. Com-Ruelle L, Dumesnil S. Determinants de la consommation m  dicale de ville en 1992. CREDES no 1200: Tome 3, Les auxiliaires m  dicaux, 1997.
32. Dumesnil S, et al. Sant  , soins et protection sociale en 1996. CREDES no 1204.
33. Coughlin TA, Liu K. Health care costs of older persons with cognitive impairments. *Gerontologist* 1989; 29:173?182.
34. Max W, Webber P, Fox P. Alzheimer's disease. The unpaid burden of caring. *Journal of Aging Health* 1995; 7(2):179?199.
35. Clipp EC, Moore MJ. Caregiver time use: an outcome measure in clinical trial research on Alzheimer's disease. *Clin Pharmacol Ther* 1995; 58:228?236.
36. Ernst RL, Hay JW, Tinklenberg J, et al. Cognitive function and the costs of Alzheimer's disease. *Arch Neurol* 1997; 54:687?693.
37. Hux MJ, O'Brien B, Iskedjian M, et al. Relation between severity of Alzheimer's disease and costs of caring. *Can Med Assoc J* 1998; 159:457?465.
38. Trabucchi M, Ghisla MK, Bianchetti A. CODEM: a longitudinal study on Alzheimer disease costs. In: Giacobini E, Becker R, eds. *Alzheimer's disease: therapeutic strategies*. Boston: Birkhauser; 1996:561?565.
39. Bianchetti A, Frisoni GB, Ghisla KM, et al. Clinical predictors of the indirect costs of Alzheimer's disease. *Arch Neurol* 1998; 55:130?131.
40. Teri L. Behavior and caregiver burden: behavioral problems in patients with Alzheimer's disease and its association with caregiver distress. *Alzheimer Dis Assoc Dis* 1997; 11(4):S35?S38.
41. Winblad B, Wimo A. Assessing the societal impact of acetylcholinesterase inhibitor therapies. *Alzheimer Dis Assoc Dis* 1999; 13(2):S9?S19.
42. Liebermann MA, Kramer JH. Factors affecting decisions to institutionalize demented elderly. *Gerontologist* 1991; 31:371?374.
43. Wimo A, Winblad B, Grafstrom M. The social consequences for families with Alzheimer's disease patients: potential impact of new drug treatment. *Int J of Geriatr Psych* 1999; 14:338?347.