# Economic considerations of Alzheimer's disease and related disorders

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ABSTRACT. Economic analyses of geriatric syndromes are seldom performed. However, demographic and epidemiological imperatives have led to significant interest in the evaluation of AD-related costs. Over 300 papers devoted to economic considerations of Alzheimer's disease have been published in peer-reviewed journals, within the last five years. In these papers, the chosen perspective (costs to society or to specific payers) is important. Analytical methods are still evolving and remain complex. Unresolved methodological issues will need to be addressed to further our understanding of long-term economic consequences. At present, it is clear that diagnostic and drug costs are low compared to the major cost of institutionalization. Thus, directing efforts at early diagnosis and delaying nursing home placement are two key cost-containment interventions. In this respect, the need to support informal care should not be underestimated.

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# "Dementia is certainly one of the most dramatic medical and economic challenges that our society will face in the coming vears"(1)

This strong statement by Souêtre recognizes the interaction between world-wide demographic changes and the particular nature of dementing conditions. Population aging has resulted in a doubling of the population over 60 years of age over the past century in developed countries. This phenomenon is occurring at accelerated rates in developing countries, which will undergo a similar demographic change over less than 3 decades (2). In most countries, the prevalence of dementia varies between 6 and 8% for individuals aged 65 years or more, and rises dramatically with age. For each decade after the 6<sup>th</sup>, the number of affected people doubles so that an estimated 30% of the 85+ population is affected by dementia (3, 4). In a recent prevalence study performed in Geneva, 5.6% of the population over the age of 65 suffered from dementia: however, the rate of the disease varied from 2.6% in women in the 65-70 years age group to 28.1% in men in the over 90 years group (5). In the United States, in 1994 dementia ranked 9<sup>th</sup> in incidence (959,000 cases/year), and 8<sup>th</sup> in prevalence (7,082,000 cases) (6). The number of individuals with dementia will double between 1990 and 2005 in many developing countries. such as Brazil, India, and Nigeria (7). These demographic and epidemiological considerations have major economic consequences. Until a few years ago, the economic impact of chronic conditions such as dementia suffered a lack of theoretical and empirical development (8). However, over 300 papers devoted to economic aspects of Alzheimer's disease (AD) have been published in peer reviewed journals within the last five years. In these papers, the chosen perspective (costs to society or to specific payers) is important to consider. The societal perspective includes global costs, while that of specific payers (e.g., patients, families, insurance companies, municipality, county, etc.) may stress costs for which they themselves are responsible (9).

#### COST OF THE ILLNESS FOR SOCIETY

The economic burden of dementia borne by society includes all relevant costs regardless of the payers, and is closely related to the rapidly increasing number of demented patients (9, 10). Calculating such costs requires complex analyses, however, some data are available (9).

Key words: Cost analysis of AD, informal care, institutionalization, pharmacoeconomics, trade-off analysis of AD.

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In Switzerland, global dementia-related costs reached \$ 1.9 billion for 50,000 affected individuals in 1998 (11). In the Netherlands, in 1994 dementia ranked 3<sup>rd</sup> in total health care costs (5.6% of the total budget, 7.4% for women and 2.9% for men), 1st in the 65-84 years age group health care costs (9.5% of the budget of this age group), and 1st in the over 85 years age group (22.2% of the health care costs) (12). In the US, the annual direct costs of treating AD were estimated to be \$21.0 billion in 1991 (13), and \$ 29.8 billion in 1998 (14). This 42% difference is indicative of the dramatic increases in health care costs related to dementia. The US Health Care Finance Administration has forecast an 80% increase in total health care expenditures (to over \$ 2 trillion annually) between 1997 and 2007. The US government has expressed significant concern that these costs could threaten budgetary stability without any evidence of pertinent outcomes or improvement in patients' and families' quality of life (15). Although cost of illness analyses can be crucial to direct social and health policies, they do not provide information pertinent to individual patients and carers.

## COST ANALYSIS OF VARIOUS CARE STRATEGIES OF DEMENTED PATIENTS

Cost perspectives from a specific payer's point of view (e.g., patients, families, insurance companies, municipality, county, etc.) may include only selected costs (9). Cost evaluations of various care strategies include "cost description" and "cost analysis".

"Cost description" is an economic analysis that is restricted to one type of treatment or care; it does not include comparisons with alternative types of treatment or care (16).

"Cost analysis" compares different therapies and treatments, but does not compare their effects. A large majority of economic studies of dementia care are of this type, and many have their origin in local projects or programs. Methodological strategies include detailed cost analysis, average costs, longitudinal cost analysis of patient care, and cost comparisons with other types of care (10).

Both cost description and cost analysis include costs linked to organizations operating within the health sector. These costs can be distinguished in direct and indirect costs.

Direct costs include:

- Direct medical costs: outpatient visits (general practitioners, specialists, physical therapists, occupational therapists), laboratory investigations, diagnostic tests, drug costs, home care, social services and hospitalization, as well as costs related to insti-

tutional care, which vary markedly within the same country (depending on the staff number and competence), and from one country to another (9, 16).

 Direct non-medical costs: rent for housing, light, heat, food, out-of-pocket expenses, patient and family involvement in care.

*Indirect costs* are essentially composed of:

- Medical costs linked to behavioral and psychiatric disturbances, co-morbidities and drug side effects (17).
- Community costs including the loss of productivity as a result of time lost from work.
- Intangible costs corresponding to psychological consequences such as an AD patient's pain and suffering. These costs also include the family's burden, and are closely related to the nature of the family; they have changed over time as a result of modifications in family composition, and the increasing participation of women in the work force. Inter-generation patterns of informal care also need to be considered when attempting to estimate intangible costs (18).

Methodological differences, lack of consensus concerning the exact components of direct and indirect costs, the difficulty inherent in the comparison of different care systems, and differences between countries explain, in part, the discrepancies among international cost evaluations. However, the important impact of formal care on costs has been demonstrated. In a recent comparison of dementia costs in three different countries (19), the annual costs of illness ranged from \$52,000 (in the USA) to \$23,600 (in Sweden), and \$6,000 (in England); these marked cost variations were related to cross-national differences in the ratio of formal to informal care which was 1/1 in the USA, 1/2 in Sweden, and 1/6 in England.

- "Formal care" is defined either as care by a health professional, or care by paid persons whatever their competence. It is simpler to consider formal care as an equivalent to "paid care" (20). The main component of formal care is institutional care. In a Swedish study of dementia, less than 1% of the national heath care system's annual costs were devoted to diagnostic procedures, 1% to drugs, and another 1% to day care; however, 67% of the yearly costs were linked to institutional care (19).
- "Informal care" can then be considered as an equivalent of "unpaid care". In New York City, half of the patients received informal care only (7.2 hours per day), a quarter of them formal care only (9.8 hours per day), and one third received both kinds of care (14.6 hours per day) (21). There are two different methods to evaluate informal costs. The first is the "replacement cost method", which values each informal care hour at the equivalent hourly wage of a

professional; the second method gauges the carer's cost in terms of having to give up paid employment, or to pass up the opportunity for career advancement (22).

Dementia-related costs vary during the course of the

At the early stage of the disease, direct costs, linked to diagnostic consultations, neuropsychological evaluations and testing procedures, are predominant (1, 23). The time interval between the first symptoms and the first medical consultation is approximately 1.5-years (23). Currently, only 10 to 30% of demented individuals are investigated. Thus, direct costs related to this process should increase considerably if all individuals with cognitive impairment could benefit from a diagnostic evaluation (19).

It is important to note that each decrease of one point in the MMSE score increases the annual dementia costs by 4%. Moreover, costs are also related to concomitant disease, behavioral disturbances and psychiatric symptoms (21, 24). Thus, early intervention has the potential to decrease disease-related costs.

In severely demented patients, non-medical costs, linked to caring time spent by a third party (housework, custodial care...) or to institutionalization are largely superior to medical costs (1). In Canada, institutionalization is the largest component of cost, accounting for 84% of the cost for people with severe dementia (25). In the USA, nursing home care represents 71% of US long-term care expenditures that reached \$ 90.9 billion in 1995 (26).

In a British cross-sectional study, non-institutionalized patients with AD (N=128), their caregivers (N=128), and 56 non-demented matched controls were interviewed once to establish resource use. Over a three-month period, the mean cost per control subject (387 £) was less than that incurred by patients with mild (6616 £), moderate (10,250 £) and severe (13,593 £) AD. Indirect cost, mainly time spent by caregivers, was the main cost component in all groups (68.6%), followed by direct medical costs (24.7%)(27).

# TRADE-OFF ANALYSIS BETWEEN CARE COSTS AND DEFINED/SUPPOSED **OUTCOMES**

Previously described cost evaluations do not take into account a care strategy's results. Trade-off analysis, on the contrary, also considers defined or assumed outcomes; it includes cost-minimization, cost-benefit, cost-effectiveness and cost-utility analyses. In its strictest sense, pharmacoeconomics can also be included among these types of analyses.

"Cost-minimization" analysis (CMA): Assuming equivalent effects of two treatments or two care strategies, CMA corresponds to a comparison between the two, simply on the basis of costs with a final recommendation to use the cheaper one. However, it is rarely used.

"Cost-benefit" analysis (CBA) and "Cost-effectiveness" analysis (CEA) correspond, respectively, to the same monetary and non-monetary analysis of all costs linked to a therapy or care strategy with a precise expected outcome. CEA shows the relationship between all the resources used for a particular intervention, and the health benefit achieved (28). Thus, CEA can be used to assess the value of informal care, and take into account the patient's quality of care (29).

'Cost-utility" analysis (CUA) addresses the cost of a particular treatment or care strategy considering a single important outcome, such as the patient's "Quality of life" (30). CUA shows the relationship between weights or utility weights (quality-adjusted life years or QUALY) for a particular outcome and quality of life (31). The use of generic scales allows comparisons between different diseases. However, specific scales may help define an optimal level of care (9).

Pharmacoeconomics, a new area of health economics, emerged in the late 70s from concerns about the relative effectiveness and costs of different medications (32, 33). Pharmacoeconomics, in its strictest sense, can be included among the previous types of analysis, but it also encompasses the analysis of "cost consequences", which correspond to consumer preferences and satisfaction with regard to outcomes and costs of a specific treatment or health service (34). For example, the cost-effectiveness of the new anti-dementia drugs (such as acetylcholinesterase inhibitors) includes not only the price of the drug, but also its ability to stabilize and improve patients' (and caregivers') quality of life, and reduce caregiver burden (35). This kind of analysis appears complex because it includes data and costs that constantly vary such as delay in institutionalization and reduction in the number of hours of informal care required by the patient, as well as improvement in the patients' and caregivers' quality of life, and need to be compared with societal trends and progress (1).

In the context of trade-off analysis, numerous evaluations have been performed to compare one strategy of care to another, or to appreciate the impact of one drug in comparison with another.

- Cost of Alzheimer's disease and related dementia in managed care

In the US, the high prevalence of dementia among the oldest, coupled with total costs of up to \$ 195,000

for each case of AD (36), create very significant clinical and financial incentives for managed care plans to improve the care of members suffering from dementia (37). Whatever the type of Health Care Organization (HMO), it appears that people diagnosed with dementia have 1.5- to 1.9-fold higher health care utilization and costs than enrolees without dementia (p<0.001) (37, 38). This variability is related to different adjustments for co-morbidity, and the fact that case managers differ significantly by site in how they prioritize tasks, functions, and goals, viewing themselves along a continuum from a clinical approach to one that emphasizes service management (39); the higher costs among demented cases were always linked to inpatient expenses (2/3 of the costs) (37, 38).

- How to reduce nursing home care and dementia costs?

Institutionalization is the largest component of cost, accounting for more than 2/3 of the cost for people with severe dementia. Providing support to informal carers, proposing substitutes for nursing homes (day or residential care), and postponing the requirement for institutionalization through the use of newer "anti-dementia" drugs can significantly lengthen the time spent by demented individuals in their own home (40-43). This not only has obvious quality of life implications, but can also have a significant positive impact on costs.

Assisted Care Facilities (ACF) combine housing and supportive services for individuals who require assistance with the tasks of daily living, but who do not need the level of skilled nursing care provided in nursing homes (NH) (44). Several recent studies have shown that ACF costs were lower than NH costs, and ACFs have been promoted as a substitute for nursing home placement, when appropriate, for individuals who can no longer live in their own home (26, 45-47).

- Impact of new medications for Alzheimer's disease therapy

The lack of long-term data on resource use and drug efficacy has led various authors to apply theoretical models to forecast the impact of cholinesterase inhibitors on the course of AD. A decision analysis model predicts a possible cost reduction of \$9,250 for each patient if treatment with tacrine is used from the time of diagnosis (36). A "modelling approach" based on disease progression suggests that the largest long-term cost savings is obtained with treatment of mild AD (MMSE > 20). However, if a patient's life expectancy is expected to be less than 2 years, cost savings are increased by prioritizing patients with moderate AD (20 > MMSE > 11) (48). In an "incremental

cost-effectiveness theoretical model" comparing the impact of Donepezil vs no treatment on quality-adjusted life-years gained, drug costs appeared to be partially offset. The model predicts that for mild AD, the drug would pay for itself in terms of costs (47). But the positive impact of these results is attenuated by the application of a "Markov model". By estimating the 5-year cost-effectiveness of adding Donepezil (5 mg/d) to the usual care in the management of patients with mild to moderate AD (10 < MMSE < 26) in Canada, the overall cost savings reached CA\$ 882 per patient on Donepezil; patients not receiving Donepezil were predicted to spend 2.21 years in non-severe dementia, while treated AD patients were predicted to spend 2.41 years (49).

## **CONCLUSIONS**

Economic analyses of geriatric syndromes are seldom performed. However, demographic and epidemiological imperatives have led to significant interest in the evaluation of AD-related costs. Dementia is a chronic disease with far reaching implications. Analytical methods are still evolving and remain complex. Unresolved methodological issues will need to be addressed to further our understanding of long-term economic consequences. At present, it appears clear that diagnostic and drug costs are low compared to the major cost of institutionalization. Thus, directing efforts at early diagnosis, and delaying nursing home placement are two key cost containment interventions; in this respect, the need to support informal care should not be underestimated

### **REFERENCES**

- Souêtre E.J., Qing W., Vigoureux I.: Economic analysis of Alzheimer's disease in outpatients: impact of symptom severity. In: Giacobini E., Becker R. (Eds.), Alzheimer's disease: therapeutic strategies. Birkhauser, Boston, 1994, pp. 470-480.
- Kalache A.: Ageing world-wide. In: Ebrahim S., Kalache A. (Eds.), Epidemiology in old age. British Medical Society Publishing Group, London, 1996, pp. 22-31.
- Khatchaturian Z.S., Radebaugh T.S.: Alzheimer Disease: Where are we now? Where are we going? Alzheimer Dis. Assoc. Disord. 12 (Suppl. 3): S24-S28,1998.
- Ritchie K., Kildea D.: Is senile dementia "age related" or "aging related"? Evidence from a meta-analysis of dementia prevalence in the oldest old. *Lancet* 346: 931-934, 1995.
- Herrmann F.: Prevalence of Dementia in Switzerland (Unpublished data).
- Murray C.J., Lopez A.D.: Summary: the global burden of disease. Cambridge Mass., Harvard University Press, 1997, p. 43.
- 7. Henderson A.S., Jorm A.F.: Definition, and epidemiology of dementia. In: Maj M., Sartorius N. (Eds.), Dementia. John Wil-

- ley & Sons LTD, Chichester, 2000, pp. 1-33.
- 8. Whitehouse P.J.: Pharmacoeconomics of dementia. Alzheimer Dis. Assoc. Disord. 11 (Suppl. 5): S22-S33,1997.
- 9. Winblad B., Hill S., Beermann B., Post S.G., Wimo A.: Issues in the economic evaluation of treatment for dementia. Position paper from the International Working Group on Harmonization of Dementia Drug Guidelines. Alzheimer Dis. Assoc. Disord. 11 (Suppl. 3): 39-45, 1997.
- 10. Wimo A., Ljunggren G., Winblad B.: Costs of dementia and dementia care: a review. Int. J. Geriatr. Psychiatry 12: 841-856, 1997.
- 11. Volz A., Monsch A.U., Zahno A., Wettstein A., Staehelin H.B.: Was kostete die Schweiz die Alzheimer-Krankheit 1998?: Eine präliminäre. Analyse Praxis 89: 803-811, 2000.
- 12. Meerding W.J., Bonneux L., Polder J.J., Koopmanschap M.A., van der Mass P.J.: Demographic and epidemiological determinants of healthcare costs in the Netherlands: cost of illness study. BMJ 317: 111-115, 1998.
- 13. Ernst R.L., Hay J.W.: The U.S. economic and social cost of Alzheimer's Disease revisited. Am. J. Public Health 84: 1261-1264, 1994.
- 14. Menzin J., Lang K., Friedman M., Neumann P., Cummings J.L.: The economic cost of Alzheimer's Disease and related dementia to the California Medicaid Program ("Medi-Cal") in 1995. Am. J. Geriatr. Psychiatry 7: 300-308, 1999.
- 15. Neumann P., Kuntz K.M., Leon J.L., Araki S.S., Hermann R.C., Hsu M.A., Weinstein M.C.: Health utilities in Alzheimer's Disease: a cross sectional study of patients and caregivers. Med. Care 37: 27-32, 1999.
- 16. Drummond M., Stoddart G.L., Torrance G.E.W.: Methods for the economic evaluation of health care programmes. Oxford University Press, Oxford, 1987.
- 17. Nagaratnam N., Lewis-Jones M., Scott D., Palazzi L.: Behavioral and psychiatric manifestations in dementia patients in a community: caregiver burden and outcome. Alzheimer Dis. Assoc. Disord. 12: 330-334, 1998.
- 18. Cavallo M.C., Fattore G.: The economic and social burden of Alzheimer Disease on families in the Lombardy region of Italy. Alzheimer Dis. Assoc. Disord. 11: 184-190, 1997.
- 19. Wimo A., Karlson G., Jönsson B., Winblad B.: The Health Economics of dementia. John Wiley & Son, London, UK,
- 20. Fox P.J.: Service use and cost outcomes for persons with Alzheimer Disease. Alzheimer Dis. Assoc. Disord. 11 (Suppl. 6): 125-134, 1997.
- 21. Albert S.M., Sano M., Bell K., Merchant C., Small S., Stern Y.: Hourly care received by people with Alzheimer's Disease: results from an urban community survey. Gerontologist 38: 704-714, 1998.
- 22. Knapp M., Wilkinson D., Wigglesworth R.: The economic consequences of Alzheimer's disease in the context of new drug developments. Int. J. Geriatr. Psychiatry 13: 531-543, 1998.
- 23. Trabucchi M., Govoni S., Bianchetti A.: Socio-economic aspects of Alzheimer's disease treatment. In: Giacobini E., Becker R. (Eds.), Alzheimer's disease: therapeutic strategies. Birkhauser, Boston, 1994, pp. 459-463.
- 24. Trabucchi M., Ghisla K.M., Bianchetti A.: CODEM: a longitudinal study on Alzheimer disease costs. In: Becker R., Giacobini E. (Eds.), Alzheimer's disease: From molecular biol-

- ogy to therapy. Birkhauser, Boston, 1996, pp. 561-565.
- 25. Hux M.J., O'Brien B.J., Iskedjian M., Goeree R., Gagnon M., Gauthier S.: Relation between severity of Alzheimer's disease and costs of caring. Can. Med. Assoc. J. 159: 457-465, 1998.
- 26. US Congress General Accounting Office: Alzheimer's disease: estimates of prevalence in the United States [GAO pub. No.HEHS-98-16]. Washington, DC, US Government Printing Office, 1998.
- 27. Souêtre E., Thwaites R.M., Yeardley H.L.: Economic impact of Alzheimer's disease in the United Kingdom. Cost of care and disease severity for non-institutionalised patients with Alzheimer's disease. Br. J. Psychiatry 174: 1-5, 1999.
- 28. Neumann P.J., Hermann R.C., Berenbaum P.A., Weinstein M.C.: Methods of cost-effectiveness analysis in the assessment of new drugs for Alzheimer's Disease. Psychiatr. Serv. 48: 1440-1444, 1997.
- 29. Busschbach J.J., Brouwer W.B., van der Donk A., Passchier J., Rutten F.F: An outline for a cost-effectiveness analysis of a drug for patients with Alzheimer's disease. Pharmacoeconomics 13: 21-34, 1998.
- 30. Torrance G.W.: Utility approach to measuring health related quality of life. J. Chronic Dis. 40: 593-603, 1987.
- 31. Albert S.M., Del Castillo-Castaneda C., Sano M., Jacobs D.M., Marder K., Bell K., Bylsma F., Lafleche G., Brandt J., Albert M., Stern Y.: Quality of life in patients with Alzheimer's Disease as reported by patients proxies. J. Am. Geriatr. Soc. 44: 1342-1347, 1996.
- 32. Bootman J.L., Townsend R.J., McGhan W.F.: Principles of pharmacoeconomics, ed. 2. Harvey Whitney Books, Cincinnati, 1996.
- 33. Spilker B.: Adopting higher standards for quality of life trials. Quality of life and pharmacoeconomics in clinical trials, ed. 2. Lippincott-Raven, Philadelphia, 1996.
- 34. Withehouse P.J.: Pharmacoeconomics of dementia. Alzheimer Dis. Assoc. Disord. 11 (Suppl. 5): S22-S33, 1997.
- 35. Ernst R.L., Hay J.W.: Economic research on Alzheimer Disease: a review of the literature. Alzheimer Dis. Assoc. Disord. 11 (Suppl. 6): 135-145, 1997.
- 36. Schumock G.T.: Economic considerations in the treatment and management of Alzheimer's Disease. Am. J. Health Syst. Pharm. 55 (Suppl. 2): S17-S21, 1998.
- 37. Gutterman E.M., Markowitz J.S., Lewis B., Fillit H.: Cost of Alzheimer's Disease and related dementia in managed medicare. J. Am. Geriatr. Soc. 47: 1065-1071, 1999.
- 38. Weiner M., Powe N.R., Anderson G.F.: Medicare expenditures for beneficiaries with dementia of the Alzheimer's type (Letter). J. Am. Geriatr. Soc. 47: 1276, 1999.
- 39. Arnsberger P., Fox P., Zhang X.: Case manager-defined roles in the Medicare Alzheimer's Disease Demonstration: relationship to client and caregiver outcomes. Care Manag. J. 1: 29-37, 1999.
- 40. Wimo A., Wallin J.O., Lundgren K., Ronnback E., Asplund M., Mattson B., Krakau I.: Impact of day care on dementia patients - costs, well-being and relatives' views. Fam. Pract. 7: 279-287, 1990.
- 41. Wimo A., Mattson B., Krakau I., Eriksson T., Nelvig A.: Cost-effectiveness analysis of day care for patients with dementia disorders. Health Econ. 3: 395-404, 1994.
- 42. Knopman D., Schneider L., Davis K., Talwalker S., Smith F., Hoover T., Gracon S.: Long term tacrine (Cognex) treatment: effects on nursing home placements and mortality.

- Neurology 47: 166-177, 1996.
- 43. Thal L.J., Thomas R.G., Sano M.: Tacrine and nursing home placement. *Neurology* 49: 897-899, 1997.
- Leon J., Moyer D.: Potential cost savings in residential care for Alzheimer's disease patients. Gerontologist 39: 440-449, 1999.
- 45. Lewin V.H.I.: National study of assisted living for the frail elderly: literature review update. Report prepared for HHS/ASPE under contract no. DHHS-100-94-0024. Research Triangle Institute, 1996.
- Mollica R.L., Snow K.I.: State assisted living policy 1996. A report prepared for HHS/ASPE under contract no. DHHS-100-94-0024 Portland, ME. National Academy for State

- Health Policy, 1996.
- Neumann P.J., Herrmann R.C., Kuntz K.M., Araki S.S., Duff S.B., Leon J., Berenbaum P.A., Goldman P.A., Williams L.W., Weinstein M.C.: Cost-effectiveness of Donepezil in the treatment of mild or moderate Alzheimer's Disease. *Neu*rology 52: 1138-1145, 1999.
- Fenn P., Gray A.: Estimating long-term cost savings from treatment of Alzheimer's Disease. A modelling approach. *Pharmacoeconomics* 16: 165-174, 1999.
- O'Brien B.J., Goeree R., Hux M., Iskedjian M., Blackhouse G., Gagnon M., Gauthier S.: Economic evaluation of Donepezil for the treatment of Alzheimer's Disease in Canada. *J. Am. Geriatr. Soc.* 47: 570-578, 1999.