

# Cognitive Function and the Costs of Alzheimer Disease

## An Exploratory Study

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**Objective:** To estimate the dollar savings in costs attainable from drug or other treatments for Alzheimer disease (AD) that stabilize or reverse patients' cognitive decline.

**Methods:** Medical and other disease-related utilization data were collected from the caregivers of 64 patients diagnosed as having probable AD. The quantities of utilization were priced at national levels to generate measures of illness costs. Costs per patient were then estimated as regression functions of scores on the Mini-Mental State Examination (MMSE), which was used as an index of patient cognitive function. Potential savings in illness costs were estimated by comparing predicted costs at various baseline and intervention-level values of the patient's MMSE score.

**Results:** The potential savings in illness costs attainable from treatment are small for mildly and very severely demented patients with AD. However, for moderately to severely demented home-dwelling patients having, say, an MMSE score of 7 at baseline, prevention of a 2-point decline in the score would save about \$3700 annually, and a 2-point increase in an MMSE score rather than a 2-point decline would save about \$7100.

**Conclusions:** Large savings in the costs of caring for moderately to severely demented home-dwelling patients with AD may be achievable from disease interventions that have minor effects on patients' cognitive status.

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**A**LZHEIMER DISEASE (AD) is an exceptionally costly disease whose social burden approaches \$100 billion annually in the United States.<sup>1</sup>

Although AD is not a curable illness, the drug tacrine hydrochloride recently has become available as the first approved AD medication, and other drugs for treating the disease are sure to be introduced in the future. The clinical efficacy of any new drug will be measured by its ability to stabilize or reverse the decline in patients' cognitive functioning. However, determining whether the drug also is cost-effective depends on 3 factors: the price of the drug, its ability to stabilize or improve patients' (and caregivers') quality of life, and its effect on caregiving costs. We addressed the third question. In particular, even if a drug or other treatment of AD raises patients' cognitive status above an expected or baseline level, it remains to be seen whether this change in cognitive functioning also lowers medical and other caregiving costs.

The illness costs of persons with AD or other dementing conditions and illnesses have been estimated from sample

data in several studies.<sup>2-9</sup> Most of these studies have reported that direct or indirect (ie, unpaid caregiver time) costs increase significantly as the patient's cognitive impairment increases. However, none

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of them explicitly attempted to estimate the quantitative relation between costs and the level of cognitive impairment. To our knowledge, this study is the first to estimate a functional association between AD illness costs and a measure of patients' cognitive status.

### RESULTS

It is evident from Table 2 that mean direct cost per patient is lower for home-

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## SUBJECTS AND METHODS

### DATA

The primary data for the study were collected by the Aging Clinical Research Center (ACRC), a geriatric research institute affiliated with the Department of Veterans Affairs Medical Center Hospital of Palo Alto, Calif, and the Stanford University School of Medicine, Stanford, Calif. For more than a decade, the ACRC has maintained a longitudinal database on patients with AD. Criteria for entry into the database are (1) a clinical diagnosis of probable AD by standards of the National Institute of Neurological and Communicative Disorders and Stroke-Alzheimer's Disease and Related Disorders Association<sup>10</sup> and (2) stable physical health (eg, no recent history of cancer or congestive heart failure, and hypertension and hypothyroidism under control). Clinical workups follow the recommendations by McKhann et al,<sup>10</sup> and diagnoses are based on the consensus of an interdisciplinary team including 1 to 3 physicians. Patients are seen at intervals of 4 or more months, so that multiple data points are routinely recorded for clinical and cognitive measures. Typically, patients are followed up until their scores on the Mini-Mental State Examination (MMSE) are zero on 2 consecutive evaluations.

In the winter of 1994 to 1995, the caregivers of 64 ACRC patients reported their own and patients' use of medical and other illness-related goods and services during periods varying from the previous 6 months (for hospital care) to the previous week (for paid and unpaid in-home care). Through outreach efforts, we were able to include service utilization information on patients who had not received cognitive (MMSE and other) testing for several months to several years because they were institutionalized outside the area, had moved, or had scored zero on the MMSE on 2 consecutive evaluations. In this way, utilization records were collected for patients with AD who represented the continuum of cognitive decline.

### MEASUREMENT OF COSTS

Insofar as possible, the costs of AD care were specified as (economic) opportunity costs.<sup>11</sup> The opportunity cost of a resource is the resource's highest market value in any use other than its current use. The opportunity-cost concept is standard in cost-of-illness studies, including those of AD.<sup>1,4,12,13</sup> The costs of an illness are classified as direct and indirect. Direct costs are money payments for medical care and all other goods and services used because of the illness. Indirect costs are the imputed market values of unpaid medical and health care and of resources that are lost due to the illness. There are 3 main types of indirect illness costs: those of morbidity (patients' lost labor services), premature death, and unpaid caregiver services. Because all patients in the study were disabled but living, the first 2 costs were invariant with respect to cognitive status, so they were excluded. The only indirect cost considered was the cost of unpaid caregiver services.

Because many caregivers did not possess or were not aware of payment records—for example, some were HMO members of a health maintenance organization—we collected data only on patient utilization. Prices or unit costs were then assigned to the reported rates of utilization, and patients' illness costs were defined as the products of these prices or unit costs and physical quantities of utilization. The types of illness-related goods and services used by patients and caregivers are given, with the assigned prices or unit costs, in **Table 1**.<sup>14-25</sup>

The assumptions underlying the price and cost assumptions are as follows: First, from the societal perspective, it can be shown that the appropriate working definition of the direct opportunity cost of any commodity is the minimum payment for the commodity that is necessary to induce the producer to go on providing it in the long run. Payments in excess of the minimum signify producer waste or inefficiency, monopoly returns, or other distortions such as tax effects, and none of these is an opportunity cost. This definition was applied herein as far as was feasible.

When payment rates (ie, provider average revenues) could not be obtained, deduced, or reliably estimated, unit accounting cost estimates were used instead. An effort was made to scale the estimates of prices and unit costs at national levels from 1992 to 1993 (the most recent years for which some of the data were available) to make them representative of the United States as a whole. Because the prices actually paid by caregivers and patients may differ from our estimates of the national minimums, the observed illness costs of AD in any given community may be higher or lower than the costs derived here.

Per diem hospital use was priced at the average national reimbursement rate for Medicare services in 1993. It was assumed that a hospitalized patient would receive 1 physician visit per inpatient day. Because AD-related hospitalizations are unlikely to involve surgery (except possibly for problems such as injuries indirectly due to the disease), no estimates of surgical costs were considered. However, the total per diem cost of hospital and physician services may be understated insofar as it omits surgical and diagnostic workup costs. Because it was slightly higher than the mean per diem reimbursement rate, the statewide mean per diem cost for California long-term care facilities was used as the national unit cost of nursing home care. The per diem nursing home cost for California Medi-Cal (Medicaid) patients<sup>16</sup> was almost identical to the national average for Medicaid patients,<sup>26</sup> suggesting that the mean cost for all California nursing homes also was similar to the national average. The mean Medi-Cal per diem cost was not used because many patients with AD might require and be housed in facilities furnishing a higher level of care than that provided by Medicaid facilities. Because no national rates for residential care were available, the residential care rate was approximated as mean per diem total nursing home cost in California minus the mean per diem cost of nursing care.<sup>16</sup>

Because emergency department services are regularly cross-subsidized by hospitals so that payments for emergency department services probably understate their opportunity

dwelling than institutionalized patients, and that mean indirect cost per patient is higher. Moreover, both differences are statistically significant below the 5% level. Because the likelihood of institutionalization increases as MMSE falls (below), this pattern suggests that a decline in MMSE may not cause direct and indirect costs to change in the same

direction, and, accordingly, that its effect on total costs need not be readily predictable. These considerations led us to estimate annualized direct, indirect, and total costs as separate functions of MMSE.

The initial regression results are shown in **Table 3**. Respectively, the dependent variables in the tables are the

costs, we approximated the national cost per emergency department visit as the mean cost per visit in Los Angeles County deflated by the factor 1.28. The deflation factor was derived from the Los Angeles-Long Beach health care price index, which was about 28% higher than the national average in the early 1990s.<sup>27</sup> Adult day care was priced at (unit-cost) rates reported in 3 recent studies.<sup>19-21</sup> Paid in-home health, housekeeping, and other care was priced at the mean national hourly rate of home health care workers, and the (indirect opportunity) cost of unpaid in-home patient care was priced at the same hourly rate. The direct and indirect costs of purchased meals (meals-on-wheels) were placed at \$4.50 and \$1.76 per meal, respectively. The indirect cost estimate was based on a report of 0.22 hours of volunteer preparation and delivery time per meal,<sup>22</sup> which was priced at the mean national hourly rate of residential care workers.<sup>24</sup> Because it was almost negligibly small, the cost of volunteers' time was included in the estimate of direct caregiving costs. Drug prices were assumed to be the minimum of Medicare and lowest wholesale prices. A pharmacist determined whether each drug was likely to be used for an acute or a chronic condition. Medications for chronic conditions were assumed to be used for an entire year; medications for acute conditions were assumed to be used for a single month.

Several respondents reported caring for their patients 168 h/wk, presumably because they considered themselves continuously available for caregiving. Because many primary caregivers of home-dwelling patients with AD must be continuously available for caregiving unless they have assistance, we were left with 2 options: accept 168 hours as the weekly norm for unassisted primary caregiver hours (which would cause indirect caregiving costs to be fixed and independent of the patient's cognitive status), or adopt a procedure for estimating the number of active caregiving hours. We chose the second alternative and assumed that no caregiver would spend more than 16 hours per day in patient care. The weekly number of active caregiving hours by the primary caregiver was therefore defined as the minimum of the reported number of hours and 112. This reduced the sample mean total weekly number of unpaid caregiving hours for home-dwelling patients from 60.7 to 51.0. We then tested a range of upper bounds on the caregiver's weekly hours (from 84-168) and found in each instance that total unpaid caregiver hours—and hence unpaid caregiving costs—were not significantly related to the patient's measured cognitive status. Last, no effort was made to delete the costs of comorbid conditions because of the impracticality of identifying utilization due to these conditions from caregivers' responses. Thus, the total cost estimates may be exaggerated, but there is no reason to think that estimates of the marginal effect of patient cognitive status on caregiving costs also are biased upward.

#### MEASUREMENT OF PATIENT COGNITIVE DYSFUNCTION

In general, the patient's most recently recorded MMSE score before the date of cost collection was used as the measure of

cognitive status. For the most part, the dates of MMSE scores preceded the dates of the cost data by 0 to 4 months. We used MMSE scores for 21 patients that were recorded after the date of cost data collection. Among the latter, 6 scores were obtained more than 3 months after the date of cost data collection, and 1 of the 6 was obtained 7 months afterward. These errors in measuring MMSE scores at the time costs were incurred tend to bias the ordinary least squares (OLS) regression estimators of the coefficient on MMSE score in the illness cost functions. Accordingly, we also estimated the functions as errors-in-variables models with YRSAD (the time in years from the onset of symptoms to 1995) as the instrument for MMSE. The instrumental variable (IV) estimates of the functions are shown and discussed herein.

The mean (SD) patient costs, MMSE scores, and the values of other explanatory variables are given in **Table 2**. Family income data were unavailable at the time the study analysis was undertaken, and, except for several patients who were covered by both Medicare and Medi-Cal (Medicaid), the entire sample had Veterans Affairs benefit coverage, Medicare coverage (in most instances with a supplemental package), or both. Consequently, family income and indicators of health insurance coverage were both omitted as predictors of costs.

#### COST FUNCTION ESTIMATION

One of the 65 caregivers reported a zero utilization of both paid and unpaid services, and because there was no way to verify the accuracy of the response, we deleted the caregiver's patient from the sample. All cost functions were estimated for users of services only. Inasmuch as medical expenditure data frequently appear to be log-normally distributed,<sup>28,29</sup> we specified the cost functions in the semi-log form

$$\ln(C_i) = \alpha + \beta \text{MMSE}_i + \gamma Z_i + u_i,$$

where  $i$  is the patient index,  $C_i$  denotes the annualized direct, indirect, or total cost of caring for the  $i$ -th patient,  $Z_i$  denotes other explanatory variables,  $u_i$  is a disturbance, and  $\alpha$ ,  $\beta$ , and  $\gamma$  are parameters. The estimated (expected) cost for the  $i$ -th patient is obtained from

$$\hat{E}(C_i) = \exp(\alpha + \beta \text{MMSE}_i + \gamma Z_i + \sigma^2/2),$$

where circumflex denotes estimates,  $\sigma$  is the variance of  $u_i$ , and  $\sigma^2/2$  is the conventional correction factor.<sup>30</sup> Annualized costs were defined as estimated costs over the relevant reporting periods inflated to annual rates (eg, by the factor 2 for hospital care recorded over the previous 6 months and 52 for in-home care recorded over the previous week). Each patient was assumed to live in his or her current residence continuously throughout the year. The parameter  $\beta$  in the cost function model can be interpreted as the (instantaneous) growth rate of total caregiving costs with respect to MMSE score. That is,  $\beta$  is proportional change in costs  $dC/C$  induced by a small increase  $d\text{MMSE}$  in the MMSE score.

natural logarithms of the patient's annualized direct (DCOST), indirect (ICOST), and total (TCOST) costs. Four regression equations are given in Table 3. The explanatory variables in the equations and the sample statistics are given in the left column. For example, the dependent variable in all 4 regressions for direct cost is the

natural logarithm of direct cost per patient (LDCOST). In equation 3, LDCOST was regressed on MMSE score, AGE, MALE, EDUC, and WH. The interaction variables  $\text{MMSE} \times \text{HOME}$  and  $\text{MMSE} \times (1 - \text{HOME})$  were omitted. The estimated regression coefficients on the explanatory variables and their  $t$  ratios are shown opposite

**Table 1. Unit Cost Estimates**

Type of Good/Service	Unit of Good/Service	Unit Cost, \$	Reference Source
Acute hospital	Inpatient day	759	14
Physician hospital	Visit	58	15
Physician office or outpatient	Visit	64	15
Nursing home	Inpatient day	84	16
Residential care	Inpatient day	47	16
Ambulance	Trip	130	17
Emergency department	Visit	85	18
Adult day care	Hour	6.50	19-21
Paid in-home care	Hour	10.41	22
Purchased meals	Meal	6.26	23, 24
Unpaid in-home care	Hour	10.41	22
Medications	Prescriptions	Varies	25

the variable names. The values of  $R^2$  adjusted for degrees of freedom ( $\bar{R}^2$ ), the F statistic (F), and the sample size (number of patients) are entered at the bottom of Table 3.

Equations 1, 3, and 4 in each table were estimated by OLS. Equations 2 were estimated by the IV method with YRSAD used as the instrument. If MMSE is measured with errors of the classical type, the OLS estimators of the coefficient on MMSE in equations 1 are biased toward zero but the IV estimators in equations 2 are not.<sup>31</sup> Thus, one test, albeit a crude one, for bias consists of comparing the OLS and IV estimates of the coefficient. If the second set of estimates is much larger in absolute value than the first, it is prima facie cause for suspecting measurement-error bias. In the LDCOST regressions, the OLS and IV estimates 1 and 2 suggest bias. In the regressions for natural

**Table 2. Variables Studied\***

Variable	Definition	Mean (SD)
AGE	Age of patient in 1995, y	74.64 (7.35)
EDUC	Patient's highest educational attainment, 1-6	5.05 (1.40)
MALE	1 if patient is male, 0 otherwise	0.39 (0.49)
WH	1 if patient is white, 0 otherwise	0.92 (0.27)
YRSAD	Years (dated from 1995) since first dementia symptoms	9.57 (5.07)
HOME	1 if patient lives at home, 0 otherwise	0.61 (0.49)
MMSE	Patient's MMSE score, 0-30	8.23 (7.74)
	MMSE score of patient living at home	12.21 (6.90)
	MMSE score of patient living away from home	2.04 (4.06)
Cost, \$		
TCOST	Estimated annual total cost of caring for patient	35 287 (21 730)
DCOST	Estimated annual total direct cost of caring for patient	15 275 (14 773)
ICOST	Estimated annual total indirect cost of caring for patient	20 012 (21 730)
	Estimated total annual cost of patient living at home	33 316 (25 719)
	Estimated total annual cost of patient living away from home	38 360 (13 872)
HDCOST	Estimated total annual direct cost of patient living at home	5854 (7207)
NOHCOST	Estimated total annual direct cost of patient living away from home	30 284 (10 273)
	Estimated total annual indirect cost of patient living at home	27 662 (24 640)
	Estimated total annual indirect cost of patient living away from home	6076 (5895)

\*Sixty-four observations: 39 on patients living at home; 25 on patients living away from home. MMSE indicates Mini-Mental State Examination.

**Table 3. Logarithm of Cost per Patient**

Variable	Cost per Patient*							
	Direct				Indirect			
	1	2†	3	4	1	2†	3	4
Constant	10.03 (53.11)‡	10.48 (14.99)‡	10.63 (6.81)‡	9.93 (56.60)‡	9.18 (22.27)‡	8.38 (13.48)‡	9.12 (4.90)‡	9.10 (39.82)‡
MMSE	-0.133 (7.92)‡	-0.187 (2.28)‡	-0.135 (7.42)‡	...	0.016 (0.78)	0.113 (1.54)	0.010 (0.45)	...
AGE	...	...	0.003 (0.18)	...	...	...	-0.004 (0.17)	...
MALE	...	...	-0.036 (0.13)	...	...	...	0.037 (0.11)	...
EDUC	...	...	-0.203 (1.95)	...	...	...	0.271 (2.24)‡	...
WH	...	...	0.237 (0.42)	...	...	...	-1.072 (1.65)	...
MMSE×HOME	...	...	...	-0.136 (8.83)‡	...	...	...	0.018 (0.85)
MMSE×(1-HOME)	...	...	...	-0.017 (0.37)	...	...	...	-0.056 (0.92)
$\bar{R}^2$	0.503	0.064	0.502	0.582	-0.007	0.022	0.030	0.002
F	62.70‡	5.20‡	18.32‡	43.44‡	0.58	2.37	1.38	1.08
No. of patients	62	62	62	62	62	62	62	62

\*Dependent variable in all 4 equations is the natural logarithm of cost (direct, indirect, or total) per patient. Absolute t ratios are given in parentheses. Abbreviations are given in Table 2.  $\bar{R}^2$  indicates  $R^2$  adjusted for degrees of freedom.

†Instrumental variable estimate.

‡Significantly different from zero at or below 5% level.

logarithm of indirect cost per patient (LICOST) and natural logarithm of total cost per patient (LTCOST), they do not. Nevertheless, because YRSAD may not be an adequate instrument for MMSE, we do not rule out the possibility that the estimates of caregiving costs have been distorted by measurement errors.

Equations 3 include 4 background variables: patient age, male sex, race indicators, and educational attainment (used as a proxy for the family's caregiving preferences). Except for EDUC in the LICOST equation, none of the variables significantly influences caregiving costs. On balance, the estimates of equations 1, 2, and 3 indicate that a decline in the patient's cognitive status increases direct costs, has no significant effect on indirect costs, and increases total costs only through its effect on direct costs. In conjunction with the result that institutionalization significantly affects the means of direct and indirect costs (Table 2), this finding indicated that declining cognitive function might influence caregiving costs mainly or exclusively by raising the probability of the patient's institutionalization. To explore that hypothesis further, we reestimated the logarithms of costs as functions of MMSE conditional on the patient's place of residence—home or institutional (nursing home, residential care, or similar) facility. The estimates, which are shown as equations 4 in Table 3, only partly confirm the hypothesis. As indicated by the *t* ratios of the coefficients on MMSE×HOME and MMSE×(1-HOME), MMSE has no significant effect on indirect costs for home-dwelling or institutionalized patients, and it has no significant effect on direct or total costs if the patient has been institutionalized (Table 3). However, direct costs and total costs are significantly and negatively associated with MMSE if the patient lives at home.

These conclusions caused us to revise the initial cost function model as follows: Let  $p(\text{HOME}|\text{MMSE})$  denote the probability that the patient lives at home conditional on MMSE score. Then the patient's expected direct cost conditional on MMSE was respecified as

$$(1) E(\text{DCOST}|\text{MMSE}) = p(\text{HOME}|\text{MMSE}) \times E(\text{HDCOST}|\text{MMSE}) + [1 - p(\text{HOME}|\text{MMSE})] \times E(\text{NDCOST}|\text{MMSE}).$$

$p(\text{HOME}|\text{MMSE})$  was next estimated as a logistic regression of MMSE on all 64 observations. The estimated probability was

$$p(\text{HOME}|\text{MMSE}) = [1 + \exp(1.2897 - 0.2804\text{MMSE})]^{-1}, \quad (2.82) \quad (4.17)$$

where the figures in parentheses beneath the parameter estimates are absolute (asymptotic) *t* ratios. The estimated expected direct cost of a home-dwelling patient given MMSE,  $\hat{E}(\text{HDCOST}|\text{MMSE})$  was obtained by regressing LDCOST on MMSE for home-dwelling patients and transforming the OLS log regression into natural numbers. The regression estimate was

$$\hat{E}(\text{HDCOST}|\text{MMSE}) = \exp(9.0339 - 0.07990\text{MMSE}), \quad \text{SEE} = 1.05605 \quad (24.58) \quad (3.07)$$

We then tested the revised model (1) for selectivity bias. Selectivity bias invalidates (1) if the probability of nursing home placement is related in some unobservable nonrandom way to nonnursing home direct costs. The tests, which used the Heckman-Lee and generalized selectivity-bias correction factors,<sup>32</sup> failed to show significant evidence of bias, and expected direct costs therefore were estimated without adjustment from equation 1. Because there was also no significant evidence that indirect costs vary with MMSE score, we set the estimated direct cost of an institutionalized patient given MMSE,  $\hat{E}(\text{NDCOST}|\text{MMSE})$  equal to the sample mean of direct costs for institutionalized patients, and we assumed that changes in total caregiving costs conditional on changes in MMSE were identical to changes in direct caregiving costs.

The cost savings resulting from AD treatments can be estimated under various assumptions. For example, it can be supposed that the treatment increases the patient's MMSE score above some pretreatment level, prevents it from declining below that level, or causes it to fall only by some positive fraction less than 1 of the decline that would occur without treatment. Table 4 gives illustrative annual dollar savings in direct caregiving costs generated by the revised cost-function model under the first 2 of these 3 scenarios. Initial or baseline values of the patient's MMSE score, including the sample mean scores of home-dwelling (12.21) and institutionalized (2.04) patients, are shown in the left column of Table 4. The dollar estimates of savings presume that the treatment effect lasts 1 year. A 6-month effect would halve the savings, and a 2-year effect would double the savings before discounting. If the treatment prolongs the patient's life by, say, the length of the treatment effect, the result of the treatment is essentially to defer costs by the length of the effect. In that case, savings would accrue only because of the time discounting of the deferred costs.

As Table 4 indicates, the cost savings that follow from a small improvement or the prevention of a small decline in the patient's initial MMSE score generally increase as the patient's initial score falls, and become quan-

Total			
1	2†	3	4
10.60 (62.36)‡	10.43 (20.39)‡	10.52 (7.63)‡	10.58 (61.24)‡
-0.056 (3.72)‡	-0.035 (0.59)	-0.060 (3.69)‡	...
...	...	0.002 (0.10)	...
...	...	-0.071 (0.28)	...
...	...	0.154 (1.71)	...
...	...	-0.831 (1.74)	...
...	...	...	-0.057 (3.74)‡
...	...	...	-0.024 (0.53)
0.169	-0.011	0.185	0.163
13.80‡	0.34	3.86‡	7.13‡
64	64	64	64

**Table 4. Estimated Annual Savings in Direct and Total Costs per Patient With Alzheimer Disease by Changes in Mini-Mental State Examination Scores\***

Initial MMSE Score	Savings if MMSE Score Is Raised by Average Annual Point Totals, \$				Savings if MMSE Score Is Prevented From Falling by Average Annual Point Totals, \$			
	+10	+5	+2	+1	-1	-2	-5	-10
20	1965	1242	587	312	356	765	2424	7537
15	3666	2424	1186	638	744	1611	5113	13733
12	5630	3805	1876	1008	1164	2494	7407	16125
7	11213	7407	3418	1770	1846	3706	8718	...
5	13733	8619	3706	1860	1806	3494	7429	...
2.04	16111	8733	3219	1526	1324	2434	...	...

\*MMSE indicates Mini-Mental State Examination.

titatively important below an initial score of about 10 to 12. For example, at MMSE=7, a year-long 2-point increase in the score would produce an estimated saving in direct and total costs of \$3418 per patient, and a treatment that prevented a 2-point fall in the score over a year would yield an estimated saving of \$3706 per patient. If, instead of experiencing a 2-point decline in MMSE score over the year, the same patient were to gain 2 points, the estimated saving would be \$7124 (\$3418+\$3706). In each instance, the average saving results partly from the improvement in MMSE given that the patient is home-dwelling and partly from the reduction in the probability of institutionalization.

#### COMMENT

We estimated functional relations between the costs of AD and patient cognitive status. The estimated relations were then used to project the potential savings in societal costs attainable from treatments for AD that stabilize or reverse the rate of patients' cognitive decline. As far as possible, we priced patients' resource utilization at national opportunity cost levels in 1993. In many geographic areas or at higher resource utilization rates, the cost savings will be somewhat greater than those we have estimated.

The results indicated that, even when the treatment effect is small, the savings seem to be numerically significant for moderately to severely demented patients who live at home. Direct and indirect costs were not related to MMSE scores for institutionalized patients. Hence, improvements in institutionalized patients' cognitive functioning would not reduce either component of total costs.

Nevertheless, the research described herein should be described as exploratory, mainly because of the nature of the patient sample. There were few study subjects and all were located in a suburban area of northern California. Ideally, a study of this kind requires a large, geographically diverse sample of patients that is demonstrably representative of the AD population.

For example, the limited availability and accessibility of community and family resources has been reported to increase the risk of institutionalization among

the rural elderly with higher levels of impairment.<sup>33</sup> This suggests that the direct costs given MMSE scores of rural patients may be higher (due to institutionalization) than our estimates indicate, and hence that the savings attainable from palliative AD treatments also may be higher. Whether or not AD costs vary significantly with the types and supplies of local caregiving services is a question that awaits future research.

Estimates of the costs of AD care also differ markedly among studies. In research on patients with AD and other dementia carried out in the late 1980s, the reported annual rates of direct costs were slightly lower or much lower than those derived herein.<sup>3,6,7</sup> Conversely, another study conducted in northern California from 1989 to 1990 found a mean total cost per patient one third higher than the estimate obtained herein.<sup>4</sup> To what extent these differences in costs are due to geographic differences in the prices of AD care or to other factors is unclear. The patterns of AD care and utilization may vary with family characteristics that we were unable to observe, such as income, patient and caregiver health status, religious background, and patient-family emotional relationships. Large differences in sample composition for any of these characteristics could account for the between-sample differences in AD costs that otherwise seem due to differences in geographic location. In any event, the causes of the reported differences in AD costs are unlikely to be ascertained until a more comprehensive, large-sample study of the cost of AD care is undertaken.

Finally, we were surprised to find that indirect costs were not significantly associated with patients' MMSE scores. The result seems implausible, and 2 other studies have shown that indirect caregiving costs increase as cognitive functioning declines, at least among home-dwelling patients with dementia.<sup>3,8</sup> The exact nature of the indirect cost-cognitive status relation therefore merits further research attention, especially in view of the AD family caregiver's heavy time and emotional burden and the possibility that palliation of the disease might not only lower direct AD costs but also reduce this burden.

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#### REFERENCES

- Ernst RL, Hay JW. The US economic and social costs of Alzheimer's disease revisited. *Am J Public Health*. 1994;84:1261-1264.
- Hu T, Huang L, Cartwright WS. Evaluation of the costs of caring for the senile demented elderly: a pilot study. *Gerontologist*. 1986;26:158-163.

3. Coughlin TA, Liu K. Health care costs of older persons with cognitive impairments. *Gerontologist*. 1989;29:173-182.
4. Rice DP, Fox PJ, Max W, et al. The burden of caring for Alzheimer's disease patients. In: *Proceedings of the 1991 Public Health Conference on Records and Statistics*. Washington, DC: US Dept of Health and Human Services; 1992: 119-224.
5. Welch HG, Walsh JS, Larson EB. The cost of institutional care in Alzheimer's Disease: nursing home and hospital use in a prospective cohort. *J Am Geriatr Soc*. 1992;40:221-224.
6. Weinberger M, Gold DT, Divine GW, et al. Expenditures in caring for patients with dementia who live at home. *Am J Public Health*. 1993;83:338-341.
7. Stommel M, Collins CE, Given BA. The costs of family contributions to the care of persons with dementia. *Gerontologist*. 1994;34:199-205.
8. Max W, Webber P, Fox P. Alzheimer's disease: the unpaid burden of caring. *J Aging Health*. 1995;7:179-199.
9. Souëtre EJ, Qing W, Vigoureux I, et al. Economic analysis of Alzheimer's disease in outpatients: impact of symptom severity. *Int Psychogeriatr*. 1995;7: 115-122.
10. 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.
11. Alchian A. Cost. In: Sills DL, ed. *International Encyclopedia of the Social Sciences*. New York, NY: Macmillan Publishing Co Inc; 1988:404-415.
12. Hodgson TA, Melners M. Cost of illness methodology: a guide to current practices and procedures. *Milbank Q*. 1982;60:429-462.
13. Rice DP, Hodgson TA, Kopstein AN. The economic costs of illness: a replication and update. *Health Care Financing Rev*. 1985;7:61-80.
14. US Dept of Health and Human Services. *Health Care Financing Review: Statistical Supplement, 1995*. Baltimore, Md: US Dept of Health and Human Services; 1995.
15. Gonzalez ML, ed. *Socioeconomic Characteristics of Medical Practice 1995*. Chicago, Ill: American Medical Association; 1995.
16. California Office of Statewide Health Planning and Development. *Individual Long-Term Care Facility Financial Data for California, December 31, 1992-December 30, 1993*. Sacramento: California Office of Statewide Health Planning and Development; 1995.
17. US Congress, Senate, Committee on Appropriations. *Hearing on Ambulance Costs Under Medicare*. Washington, DC: US Government Printing Office; 1995.
18. California Office of Statewide Health Planning and Development. *Individual Hospital Financial Data for California, June 30, 1992-June 29, 1993*. Sacramento: California Office of Statewide Health Planning and Development; 1994.
19. Connis RT, Hedrick SC, Ries LM. Adult day health care organizational and program characteristics. *Med Care*. 1993;31(suppl):SS26-SS37.
20. Ehrlich J, Chapko M, Hedrick SC. Cost of VA adult day health care programs and their effect on utilization of services. *Med Care*. 1993;31(suppl):SS50-SS61.
21. Cox NJ, Reiffer BV. Dementia care and respite services program. *Alzheimer Dis Assoc Disord*. 1994;8(suppl 3):113-121.
22. Sensenig AL, Heffer SK, Donham CS. Health care indicators. *Health Care Financing Rev*. 1995;17:277-317.
23. US Congress, Senate, Committee on Labor and Human Resources, Subcommittee on Aging. *Hearing on Reauthorization of Senior Nutrition Programs Under Title III of the Older Americans Act, March 21, 1995*. Washington, DC: US Government Printing Office; 1995.
24. US Bureau of Labor Statistics. *Employment, Hours, and Earnings, 1990-95*. Washington, DC: US Government Printing Office; 1995.
25. *1995 Drug Topics Red Book*. Montvale, NJ: Medical Economics Books; 1995.
26. US Department of Commerce. *Statistical Abstract of the United States, 1995*. Washington, DC: US Government Printing Office; 1995.
27. US Department of Commerce. *Statistical Abstract of the United States, 1991*. Washington, DC: US Government Printing Office; 1991.
28. Duan N, Manning W, Morris C, et al. *A Comparison of Alternative Models for the Demand for Medical Care*. Santa Monica, Calif: RAND; 1983. Technical Report R-254-HHS.
29. Culler SD, Callahan CM, Wolinsky FD. Predicting hospital costs among older decedents over time. *Med Care*. 1995;33:1089-1105.
30. Ramanathan R. *Introductory Econometrics With Applications*. 2nd ed. Fort Worth, Tex: Dryden Press; 1992.
31. Maddala GS. *Introduction to Econometrics*. 2nd ed. New York, NY: Macmillan Publishing Co Inc; 1992.
32. Maddala GS. *Limited-Dependent and Qualitative Variables in Econometrics*. New York, NY: Cambridge University Press; 1983.
33. Dwyer JW, Barton AJ, Vogel WB. Area of residence and the risk of institutionalization. *J Gerontol*. 1994;49:S75-S84.