

# Economic Evaluation of an Integrated Diagnostic Approach for Psychogeriatric Patients

## Results of a Randomized Controlled Trial

Claire A. G. Wolfs, PhD; Carmen D. Dirksen, PhD; Alfons Kessels, MD, MSc;  
Johan L. Severens, PhD; Frans R. J. Verhey, PhD, MD

**Context:** Because of the increasing number of elderly people with dementia, the costs of dementia and dementia care are expected to grow rapidly in the coming decades. Cost-effectiveness results are relevant for decision making about new strategies in dementia care.

**Objective:** To evaluate the cost-effectiveness of an integrated multidisciplinary diagnostic facility for diagnosing dementia in ambulatory psychogeriatric patients.

**Design:** Randomized controlled trial with an economic evaluation component.

**Setting:** The Maastricht Evaluation of a Diagnostic Intervention for Cognitively Impaired Elderly, Maastricht University Hospital, Maastricht, the Netherlands.

**Patients:** A total of 137 patients who received care in the multidisciplinary diagnostic facility and 93 who received usual care.

**Main Outcome Measures:** Quality-adjusted life-years (QALYs) as the main outcome measure and cognition and behavioral problems as secondary outcome measures.

**Results:** Compared with patients receiving usual care, patients who visited the diagnostic facility gained a mean 0.05 QALY at the extra cost of €65. The incremental cost per QALY amounted to €1267. This point estimate lies beneath commonly accepted thresholds and is within an acceptable range of uncertainty. With regard to the secondary analyses, cost-effectiveness results showed a substantial amount of uncertainty and were therefore indecisive.

**Conclusion:** On the basis of the main cost-per-QALY analysis, the use of the integrated multidisciplinary diagnostic facility is cost-effective for the diagnosis and management of dementia in ambulatory patients.

**Trial Registration:** clinicaltrials.gov Identifier: NCT00402311

*Arch Gen Psychiatry.* 2009;66(3):313-323

### Author Affiliations:

Department of Clinical Epidemiology and Medical Technology Assessment, University Hospital Maastricht, Maastricht, the Netherlands (Drs Wolfs, Dirksen, Kessels, and Severens); and Departments of Psychiatry and Neuropsychology (Drs Wolfs and Verhey) and Health Organization, Policy and Economics (Dr Severens), Maastricht University, Maastricht.

**D**EMENTIA IS AN EXPENSIVE condition, and the costs of dementia contribute significantly to the total health care expenditures.<sup>1-3</sup> Because of the increasing number of individuals with dementia, the costs of dementia care are expected to increase considerably in the coming years. People affected by dementia also pay a high price in terms of their quality of life. Studies focusing on dementia and dementia care are therefore of great importance. Although many studies on this topic have been conducted, randomized studies are rare and economic evaluations even more so.<sup>2</sup> Economic evaluations aim to support decision making about new strategies in dementia care but are often laden with methodologic problems.<sup>4</sup> To our knowledge, no randomized studies concerning an integrated approach to dementia and dementia care with a full economic evaluation have previously been performed.<sup>5,6</sup>

This article reports on an economic evaluation of a multidisciplinary integrated approach to the diagnosis and management of dementia alongside a randomized controlled trial. Results of this randomized controlled trial showed that such an integrated approach improves dementia care.<sup>7,8</sup> An economic evaluation was performed in which care through the Diagnostic Observation Centre for Psychogeriatric Patients (DOC-PG) was compared with usual care in the Netherlands.

## METHODS

### STUDY PARTICIPANTS AND RANDOMIZATION

The Maastricht Evaluation of a Diagnostic Intervention for Cognitively Impaired Elderly (MEDICIE study) was approved by the medical ethics committee at Maastricht University Hospital, Maastricht, the Netherlands. The study was conducted from July 2002 until August 2004

in 70 general practices. General practitioners (GPs) were asked to refer all patients suspected of having dementia or a cognitive disorder. The inclusion criteria were age 55 years or older, suspicion of dementia or cognitive disorder, no referral to other local/regional services in the past 2 years, and availability of a proxy (visiting the patient at least once a week). Exclusion criteria were presence of acute disorders that required prompt therapeutic intervention and residence in a nursing home.

Randomization took place at the level of the general practice to prevent contamination on both the patient level and the GP level. The random allocation sequence was concealed for most of the participants. The MEDICIE study is described elsewhere in more detail.<sup>7</sup>

## INTERVENTIONS

### The DOC-PG

The function of the DOC-PG is to provide multidisciplinary assessment and advice through somatic screening, psychogeriatric assessment, and evaluation of the required levels of care for the patient and the patient's caregiver. The diagnostic screening conducted by the DOC-PG consists of a home visit by the community mental health team (CMHT) and 2 visits to the University Hospital Departments of Geriatric Medicine and Geriatric Psychiatry. In addition, a computed tomographic scan and various blood tests are performed. The results are then discussed at a weekly interdisciplinary meeting in which a definitive diagnosis is made and a treatment plan is formulated. Correspondence is sent to the referring GP in which a summary of the assessments, the multi-axis diagnosis, and recommendations for treatment and management are described.<sup>7</sup>

### Usual Care

Usual care was provided by the GP. This means that either the diagnosis was made by the GP or the GP referred the patient to one of the existing separate regional services, such as the Maastricht Memory Clinic,<sup>9</sup> geriatric medicine clinic, or the Department of Mental Health for the elderly of the CMHT.

### Cost-effectiveness Analysis

An economic evaluation conducted alongside the randomized controlled trial compared 1-year costs and consequences of the DOC-PG with those of usual care from a societal perspective.<sup>10-12</sup> The main incremental cost-effectiveness ratio (ICER) was calculated by dividing the difference in costs by the difference in quality-adjusted life-years (QALYs). Furthermore, 2 secondary ICERs were calculated by dividing the difference in costs by the difference in changes in cognition and by dividing the difference in costs by the difference in changes in behavioral problems.

### Effectiveness

Health-related quality of life (HRQoL) was chosen as the primary outcome. The EuroQoL-5D (EQ-5D) was used to measure patients' HRQoL at baseline and at 6 and 12 months of follow-up and was filled out by each patient's proxy (ie, we measured the proxy's perception of the patient's health). The EQ-5D instrument was developed and validated in a number of European countries, including the Netherlands,<sup>13-15</sup> and it has been validated in patients with dementia.<sup>16,17</sup> The EQ-5D describes health status according to 5 dimensions of 3 levels each, which yields 243 potential combinations of health states. Each com-

ination leads to a utility score by means of an additive function derived from the UK general population.<sup>18,19</sup> The utility scores of our population were used to calculate QALYs by means of the following formula:  $\{[(\text{utility score at baseline} + \text{utility score at 6 months})/2] \times 0.5\} + \{[(\text{utility score at 6 months} + \text{utility score at 12 months})/2] \times 0.5\}$ . Patients who had died during the year covered by the evaluation were given a utility score of 0 from the exact time of death.

Because cognition and behavioral problems are 2 important cost drivers in dementia and are not explicitly covered by the EQ-5D,<sup>20-22</sup> these characteristics were included as secondary outcomes. The Mini-Mental State Examination (MMSE)<sup>23,24</sup> was used to assess the severity of cognitive decline, and the Neuropsychiatric Inventory (NPI)<sup>25,26</sup> was used to appraise patients' behavioral and psychological problems. Both instruments were also administered at baseline and at 6 and 12 months of follow-up.

### Costs

The cost analysis was performed according to Dutch guidelines.<sup>12</sup> Costs were calculated by multiplying volumes of resource use during follow-up by the cost price per resource unit. Health care costs and costs outside the health care sector were included. All costs were expressed in euros at 2005 values (at that time, €1.00 was equivalent to US \$1.32 and British £0.68). Whenever necessary, cost prices were converted to this reference year by means of price index numbers. All cost prices were adopted from Oostenbrink et al<sup>12</sup> unless stated otherwise. The costs of the patients who had died during follow-up were set at 0 from the exact time of death.

### Volumes of Resource Use and Costs

The hospital information system, the electronic patient files of the local CMHTs, the registries of local pharmacies, an informal care survey, and cost diaries were used to determine the volumes of resource use for each participating patient (**Table 1**). The hospital information system (designated "A" in Table 1) was used to determine, per patient, the number of days in the hospital, of visits to the outpatient departments, and of all diagnostic and therapeutic interventions. The CMHT costs (B in Table 1) were collected from the electronic patient files maintained by the RIAGG (Regionaal Instituut voor Ambulante Geestelijke Gezondheidszorg [CMHT]) Maastricht and the Prins Claus Centre in Sittard. The pharmacists were asked to provide us with medication overviews (C in Table 1) during the time a patient participated in the MEDICIE study. The cost diaries were used to calculate medication costs when no overview was available.

With respect to informal care activities, a survey was used that had been developed for the measurement and valuation of informal care (D in Table 1).<sup>27,28</sup> In the survey, informal caregivers were asked to indicate the average time spent on 16 different informal care tasks per week, at baseline and at 6 and 12 months of follow-up. It was used to determine the costs of informal care and out-of-pocket costs (such as telephone costs and traveling expenses) for the informal caregiver, home care, day care, institutionalization, and housekeeping. The time devoted to informal care was valued against the wage rate of a paid housekeeper for all 16 tasks.<sup>12</sup>

Cost diaries completed by the proxy of the patient (E in Table 1) were used to determine the costs made outside the hospital that could not be gathered from the hospital or pharmacist's registrations. Cost diaries are an accepted method to assess resource use in cost-effectiveness studies.<sup>29</sup> In these diaries, we asked the proxies to document visits to the GP, visits

**Table 1. Costs per Unit**

	Costs per Unit, € (2005)	Source of Costs <sup>a</sup>	Source of Volume Information <sup>b</sup>
<b>Hospital</b>			
Outpatient	102.91/Visit	1	A
Inpatient	489.86/d	1	A
Intervention (various) <sup>c</sup>	Various	2	A
Parking	2.50/Visit	1	A
<b>CMHT</b>			
All contacts	127.60/Contact	1	B
<b>Medication</b>			
Various <sup>c</sup>	Various/DDD	3	C, E
<b>Admission<sup>d</sup></b>			
Home for elderly persons	87.47/d	1	D
Nursing home	212.00/d	1	D
<b>Home care<sup>d</sup></b>			
Domestic help	22.33/h	1	D
Nursing	41.58/h	1	D
<b>Day care</b>			
In community center	5.13/d	4	D
In home for elderly persons	49.89/d	4	D
In nursing home	124.52/d	1	D
<b>General practitioner</b>			
Practice	20.79/Contact	1	E
Home	41.58/Contact	1	E
Telephone	10.39/Contact	1	E
<b>Health care professionals</b>			
Psychiatrist	78.21/Contact	1	E
Psychologist	75.00/Contact	4	E
Physical therapist	23.41/Contact	1	E
Occupational therapist	23.67/Contact	1	E
Speech therapist	25.73/Contact	1	E
Dietitian	59.60/Contact	4	E
Podiatrist	38.00/Contact	4	E
Audiologist	53.40/Contact	4	E
Pedicurist	15.00/Contact	4	E
Dentist	18.40/Contact	4	E
<b>Alternative professionals</b>			
Reflexologist	32.00/Contact	4	E
Magnetizer	40.00/Contact	4	E
<b>Informal care<sup>d</sup></b>			
Various	8.54/h	1	D
Paid housekeeper	8.54/h	1	E
<b>Resources/aids bought</b>			
Consumable goods <sup>e</sup>	9.85/4 wk	5	E
Durable goods <sup>f</sup>	480.00/y	5	E
Traveling expenses <sup>g</sup>	0.17/km	1	A, E
Patient (meals brought to the patient's home, etc)	Various	6	E
Proxy (telephone, gasoline, etc)	Various	6	D

Abbreviations: CMHT, community mental health team; DDD, daily defined dose.

<sup>a</sup> 1 indicates Oostenbrink et al<sup>12</sup>; 2, unit costs of Maastricht University Hospital and the hospital in Sittard, the Netherlands; 3, the Genees-en hulpmiddelen Informatie Project databank (<http://www.gipdatabank.nl>); 4, various professionals contacted for an indication of price; 5, various Web sites, eg, <http://www.thuiszorgwinkel.nl>, <http://www.hulpplus.nl>, and <http://www.medireva.nl>; and 6, as reported by the patient or caregiver.

<sup>b</sup> A indicates hospital information system; B, electronic patient file, CMHT; C, registries of local pharmacies; D, informal care questionnaire; and E, cost diaries. See the "Methods" section for more information.

<sup>c</sup> The interventions and medications are highly varied; a full listing is available on request.

<sup>d</sup> Sensitivity analyses were performed on admission to a nursing home (range, €106.00 to €318.00), nursing home care (€20.79 to €62.37), and informal care (€8.54 to €32.67).

<sup>e</sup> Incontinence materials, bandages, adhesive dressings, cleansing tissues, and plastic gloves.

<sup>f</sup> Mobility aids (wheelchair, tri-walker, walking frame, and walking cane), hearing aids, bathroom aids (bath elevator, grab rail, and shower seat), stair lift, wheelchair pillow, therapeutic foot gear, special undergarments, bed elevator, toilet elevator, glasses, special bed, stair gate, girdle, alarm, medication box, special clock, and therapeutic stockings.

<sup>g</sup> The mean distance to the general practitioner or health care professional was 1.8 km; the mean distance to the hospital was 7.0 km (from Oostenbrink et al<sup>12</sup>).

to health care professionals such as physical therapists, and visits to alternative health care professionals. Furthermore, proxies were asked to list resources or aids that had been bought. Finally, out-of-pocket costs for the patients were reported, which

were largely for meals brought to the patients' homes. The proxies were asked to fill in these diaries prospectively on 5 occasions during the study (baseline and 3, 6, 9, and 12 months) for 4 successive weeks.

**Table 2. Baseline Demographic Characteristics of the Total Study Population and the CEA Subset**

Characteristic	Total		CEA	
	DOC-PG (n=137)	Usual Care (n=93)	DOC-PG (n=131)	Usual Care (n=88)
Patient sex, No. (%) F	89 (65.0)	59 (63.4)	85 (64.9)	58 (65.9)
Patient age, y				
Mean (SD)	78.3 (6.5)	77.3 (6.8)	78.3 (6.6)	77.5 (6.9)
Range	55-93	60-94	55-93	60-94
Relationship of proxy, No. (%) <sup>a</sup>				
Spouse	51 (37.2)	37 (39.8)	46 (35.1)	34 (38.6)
Child or child's spouse	73 (53.3)	46 (49.5)	72 (55.0)	45 (51.1)
Other	13 (9.5)	10 (10.8)	13 (9.9)	9 (10.2)
Sex of proxy, No. (%) F	90 (65.7)	62 (66.7)	87 (66.4)	58 (65.9)
Age of proxy, y				
Mean (SD)	60.4 (13.5)	59.8 (13.9)	59.9 (13.4)	59.4 (14.6)
Range	30-84	34-91	30-84	34-91
Dementia, No. (%)				
Alzheimer disease	66 (48.2)	31 (33.3)	62 (47.3)	31 (35.2)
Vascular dementia	12 (8.8)	14 (15.1)	12 (9.2)	13 (14.8)
Mixed dementia	15 (10.9)	6 (6.5)	15 (11.5)	5 (5.7)
Other dementia	4 (2.9)	15 (16.1)	4 (3.1)	15 (17.0)
No dementia, No. (%)	40 (29.2)	27 (29.0)	38 (29.0)	24 (27.3)
Cognitive impairment/MCI	24 (17.5)	15 (16.1)	22 (16.8)	12 (13.6)
Other cognitive impairment	16 (11.7)	12 (12.9)	16 (12.2)	12 (13.6)
MMSE score, mean (SD)	20.4 (5.6)	20.1 (6.0)	20.5 (5.5) <sup>b</sup>	19.9 (6.1) <sup>c</sup>
NPI score, mean (SD)	23.8 (16.3)	23.4 (17.1)	23.4 (15.6) <sup>b</sup>	22.6 (16.5) <sup>c</sup>

Abbreviations: CEA, cost-effectiveness analysis; DOC-PG, Diagnostic Observation Centre for PsychoGeriatric Patients; MCI, mild cognitive impairment; MMSE, Mini-Mental State Examination; NPI, Neuropsychiatric Inventory.

<sup>a</sup>Because of rounding, percentages may not sum to 100.

<sup>b</sup>N=115.

<sup>c</sup>N=77.

## STATISTICAL ANALYSES

Incomplete data on the questionnaires (EQ-5D, MMSE, NPI, cost diary, and informal care survey) were imputed by means of a regression model (SPSS version 12.0.1; SPSS Inc, Chicago, Illinois). Complete missing data or data missing covariates were imputed by means of Rubin's multiple imputation procedure<sup>30</sup> (Stata version 8.2; StataCorp, College Station, Texas). This method generates 10 different data sets for imputed data. All analyses were performed with each of these 10 data sets, and these results were pooled. The complete missing data of patients were imputed when a participant had completed the EQ-5D, MMSE, and NPI at baseline and at least 1 other occasion. Patients who had completed the questionnaires on fewer than 2 occasions or patients with a missing baseline measurement were considered study dropouts. With a logistic regression analysis, the probability of being a study dropout was assessed and sampling weights (pweights) were calculated ( $1/[1 - \text{predicted probability}]$ ). This allowed for differential weighting of patients (according to their sex and severity of the dementia, which were the variables significantly associated with the probability of being a study dropout) during the analysis and description of the data by indirectly including the data of these dropouts.<sup>31</sup>

To represent the uncertainty in the costs and effects (Stata and Microsoft Excel [Microsoft Corp, Redmond, Washington]), we undertook nonparametric bootstrapping on the incremental costs and effectiveness with 1000 replications.<sup>32</sup> The bootstrap simulations were performed with a pweight correction. These pweights were multiplied by 100, and each patient was added *N* times in the data file according to this pweight.

The incremental costs and effects can be represented visually by using the incremental cost-effectiveness plane.<sup>33</sup> The horizontal axis divides the plane according to incremental effects, whereas

the vertical axis divides the plane according to incremental costs. This results in 4 quadrants: (1) in the southeast quadrant, DOC-PG is less costly and more effective than usual care: DOC-PG is dominant; (2) in the northwest quadrant, DOC-PG is more costly and less effective than usual care: DOC-PG is inferior; (3) in the southwest quadrant, DOC-PG is less costly and less effective than usual care: the cost-effectiveness depends on the minimum amount of money society is willing to accept for loss of effectiveness; and (4) in the northeast quadrant, DOC-PG is more costly and more effective than usual care: the cost-effectiveness depends on the maximum amount of money society is willing to pay for a gain in effectiveness. The probability that a treatment is cost-effective varies according to the ceiling ratio, which is society's willingness to pay for health gain or accept for health loss. This probability can be shown in a cost-effectiveness acceptability curve, which is based on the nonparametric bootstrapping.<sup>34</sup> One-way sensitivity analyses were performed to study the robustness of the main cost-effectiveness results related to deterministic variables in the calculations. The cost prices of the resources with the largest cost differences between both groups were varied (-50%, +50%). Furthermore, the "proxy good method" was applied as an alternative for valuing informal care, whereby housekeeping activities were valued against the wage rate of a housekeeper and personal care was valued against the wage rate of a nurse.<sup>28</sup>

## RESULTS

### PARTICIPANTS

**Table 2** summarizes sample characteristics. Of the 230 patients, 148 (64.3%) were female. Of the proxies, 152

**Table 3. Problems Reported, Utility Scores and QALYs, and Scores on the MMSE and NPI**

	Baseline		6 mo		12 mo	
	DOC-PG (n=131)	Usual Care (n=88)	DOC-PG (n=120)	Usual Care (n=83)	DOC-PG (n=115)	Usual Care (n=77)
Problem, No. (%)						
Mobility						
Some	87 (66.4)	64 (72.7)	62 (51.7)	54 (65.1)	72 (62.6)	49 (63.6)
Severe	0	0	8 (6.7)	6 (7.2)	2 (1.7)	1 (1.3)
Self-care						
Some	50 (38.2)	41 (46.6)	42 (35.0)	30 (36.1)	40 (34.8)	29 (37.7)
Severe	19 (14.5)	10 (11.4)	21 (17.5)	23 (27.7)	32 (27.8)	26 (33.8)
Usual activities						
Some	66 (50.4)	40 (45.5)	53 (44.2)	36 (43.4)	47 (40.9)	22 (28.6)
Severe	29 (22.1)	22 (25.0)	33 (27.5)	28 (33.7)	39 (33.9)	39 (50.6)
Pain/discomfort						
Some	56 (42.7)	39 (44.3)	45 (37.5)	39 (47.0)	44 (38.3)	32 (41.6)
Severe	13 (9.9)	6 (6.8)	6 (5.0)	5 (6.0)	9 (7.8)	5 (6.5)
Anxiety/depression						
Some	60 (45.8)	43 (48.9)	49 (40.8)	36 (43.4)	32 (27.8)	32 (41.6)
Severe	15 (11.5)	6 (6.8)	3 (2.5)	8 (9.6)	12 (10.4)	8 (10.4)
Utility scores and QALYs, mean (95% CI) <sup>a</sup>	(n=131)	(n=88)	(n=131)	(n=88)	(n=131)	(n=88)
Utility scores	0.52 (0.50-0.54)	0.53 (0.51-0.55)	0.53 (0.51-0.55)	0.46 (0.44-0.49)	0.43 (0.41-0.45)	0.37 (0.35-0.40)
QALYs	0.50 (0.49-0.52)	0.45 (0.43-0.47)	NA	NA	NA	NA
Test scores, mean (SD)	(n=115)	(n=77)	(n=115)	(n=77)	(n=115)	(n=77)
MMSE	20.5 (6.0)	19.8 (6.6)	18.8 (7.8)	19.2 (7.5)	18.0 (7.7)	17.4 (8.8)
NPI	23.4 (15.6)	22.6 (16.5)	24.3 (18.5)	27.3 (20.8)	28.4 (20.8)	29.0 (21.0)

Abbreviations: CI, confidence interval; DOC-PG, Diagnostic Observation Centre for PsychoGeriatric Patients; MMSE, Mini-Mental State Examination; NA, not applicable; NPI, Neuropsychiatric Inventory; QALY, quality-adjusted life-year.

<sup>a</sup>Utility scores and QALYs are given with sampling weight (pweight) correction and include data from patients who died during the course of the study.

(66.1%) were female and most often a child, spouse of a child, or spouse of the patient (207 [90.0%]). In most cases, dementia (present in 163 [70.9%] of the patients) was associated with Alzheimer disease (97 [42.2%]). Six patients (4.4%) in the intervention group and 5 patients (5.4%) in the usual care group withdrew from the study after the baseline measurement, and these were considered study dropouts.

The remaining 219 patients were included in the main cost-effectiveness analysis. Of the 219 patients, 16 (12.2%) in the intervention group and 11 (12.5%) in the usual care group died during the course of the study. These 27 patients could not be included in the secondary cost-effectiveness analyses, leaving 192 patients. The 219 patients whose data were analyzed in the main cost-effectiveness analysis and the 192 patients whose data were analyzed in the secondary analyses were comparable to the total study population on all outcome measures at baseline ( $P > .05$ ).

### EFFECTIVENESS

**Table 3** summarizes the percentage of patients reporting problems on the EQ-5D, their utility scores and QALYs, and the scores on the MMSE and NPI with pweight correction at the 3 measurements. After 1 year, the most severe problems were encountered by the participants in both groups regarding self-care and usual activities. A larger proportion of patients in the usual care group experienced severe problems on these domains. This was also reflected in the higher mean utility scores for the intervention group (0.43 vs 0.37). Furthermore, patients in the usual care group showed a greater de-

cline in utility score (0.16) after 1 year when compared with patients in the DOC-PG group (0.09). The average incremental effect (QALY) was 0.05 (0.50 vs 0.45). The utility scores at the 6- and 12-month follow-up measurement, as well as the QALYs, differed significantly between the groups ( $P < .001$ ). Nonsignificant differences between the groups were found in terms of cognition and behavioral problems. Both groups showed deterioration on the MMSE and the NPI during the course of 1 year. A difference of 0.07 between the 2 groups (more deterioration for the DOC-PG group) was found on the change score of the MMSE after 1 year ( $P = .78$ ), and a difference of 1.48 between the 2 groups (less deterioration for the DOC-PG group) was found on the change score of the NPI after 1 year ( $P = .61$ ).

### COSTS

The use of health care resources is summarized in **Table 4**. We calculated pweight-corrected costs for all patients (Table 4). Because cost diaries were poorly completed (60%), we had to impute GP costs, costs of other professionals, and patients' expenses in more cases than the other cost categories. The total mean costs for the main analysis ( $n = 219$ ) during a 1-year period amounted to €38 396 in the DOC-PG group and €38 331 in the usual care group. Admissions and informal care constituted the largest portions (25% and 17%, respectively) in both groups. In addition, 16% of the costs were spent on contacts with various health care professionals and on home care, 9% on out-of-pocket costs, 7% on day care, 4% on medication, and the remainder on durables, consumables, and traveling expenses. The largest cost differences between groups

**Table 4. Usage of Health Care Resources During 12 Months of Follow-up, Mean Costs per Patient, Mean Effects, and ICERs With Sampling Weight (Pweight) Correction**

	No. (%) of Patients		Mean Visits per Patient (95% CI)		Mean Costs per Patient, € (95% CI)		Incremental Costs, €/Effects
	DOC-PG (n=131)	Usual Care (n=88)	DOC-PG (n=131)	Usual Care (n=88)	DOC-PG (n=131)	Usual Care (n=88)	
<b>Costs<sup>a</sup></b>							
Intervention (A, B)	131 (100.0)	88 (100.0)	NA	NA	857 (854 to 860)	492 (473 to 511)	365
Hospital (A)	100 (76.3)	66 (75.0)	NA	NA	3457 (3125 to 3787)	2033 (1750 to 2316)	1424
CMHT (B)	93 (71.0)	55 (62.5)	8.7 (8.0 to 9.4)	7.8 (7.1 to 8.5)	1112 (1018 to 1204)	1001 (917 to 1084)	111
Medication (C, E)	127 (96.9)	88 (100.0)	NA	NA	1457 (1375 to 1539)	1586 (1483 to 1688)	-129
Admission (D)							
Nursing home	18 (13.7)	15 (17.0)	23.8 (19.9 to 27.6)	34.8 (29.1 to 40.4)	5039 (4224 to 5853)	7370 (6177 to 8563)	-2331
Home for elderly persons	20 (15.3)	14 (15.9)	41.4 (35.3 to 47.5)	35.3 (28.6 to 41.9)	3620 (3086 to 4153)	3084 (2504 to 3665)	536
Home care (D)							
Domestic help	71 (54.2)	51 (58.0)	90.8 (84.2 to 97.4)	91.5 (83.4 to 99.6)	2027 (1879 to 2174)	2043 (1862 to 2224)	-16
Nursing	66 (50.4)	46 (52.3)	106.2 (94.4 to 118.0)	88.5 (76.3 to 100.7)	4415 (3926 to 4904)	3677 (3170 to 4185)	738
Day care (D)							
In nursing home	18 (13.7)	16 (18.2)	10.3 (8.5 to 12.0)	13.0 (10.6 to 15.4)	1277 (1056 to 1498)	1616 (1318 to 1913)	-339
In home for elderly persons	34 (26.0)	30 (34.1)	31.2 (27.4 to 35.0)	24.7 (21.6 to 27.8)	1557 (1366 to 1747)	1232 (1075 to 1388)	325
In community center	2 (1.5)	8 (9.1)	0.4 (0.2 to 0.6)	4.7 (3.5 to 5.9)	2 (1 to 3)	24 (18 to 30)	-22
General practitioner (E)	117 (89.3)	78 (88.6)	22.6 (21.3 to 23.9)	25.9 (24.3 to 27.6)	491 (462 to 520)	543 (505 to 581)	-52
Other professionals (E)	88 (67.2)	62 (70)	51.6 (48.4 to 54.8)	53.5 (49.5 to 57.4)	1447 (1361 to 1533)	1470 (1364 to 1576)	-23
Informal care (D)	131 (100.0)	88 (100.0)	807.2 (739.2 to 875.1)	888.0 (792.2 to 983.7)	6311 (5793 to 6829)	6934 (6207 to 7661)	-623
Housekeeper (D)	83 (63.4)	66 (75.0)	83.4 (77.9 to 88.9)	92.3 (85.5 to 99.0)	631 (588 to 673)	696 (642 to 749)	-65
Durable goods (E)	60 (45.8)	40 (45.5)	NA	NA	453 (414 to 493)	531 (476 to 585)	-78
Consumable goods (E)	86 (65.6)	65 (73.9)	NA	NA	145 (137 to 153)	180 (169 to 191)	-35
Out-of-pocket patient (E)	89 (67.9)	66 (75.0)	NA	NA	1042 (988 to 1095)	1170 (1098 to 1241)	-128
Out-of-pocket caregiver (D)	119 (90.8)	77 (87.5)	NA	NA	2399 (2324 to 2475)	2027 (932 to 2123)	372
Traveling costs, GP and other professionals (E)	NA	NA	NA	NA	35 (32 to 37)	37 (34 to 39)	-2
Traveling costs hospital (A)	NA	NA	NA	NA	9 (8 to 10)	10 (9 to 11)	-1
Traveling costs day care (D)	NA	NA	NA	NA	598 (538 to 658)	558 (01 to 614)	40
Parking costs (A)	NA	NA	NA	NA	9 (8 to 10)	11 (10 to 12)	-2
Total costs (A-E)	NA	NA	NA	NA	38 396 (37053 to 39738)	38 331 (36428 to 40234)	65
Effects, QALY					0.503 (0.487 to 0.519)	0.452 (0.432 to 0.472)	0.05
ICER, €/QALY						1267	
In patients with MMSE and NPI scores					(n=115)	(n=77)	
Total costs (A-E)	NA	NA	NA	NA	41 084 (39 636 to 42 530)	41 107 (39 036 to 43 178)	-23
Effects (change in score)							
MMSE					-2.44 (-2.75 to -2.14)	-2.37 (-2.74 to -2.00)	0.07
NPI					4.94 (3.88 to 6.00)	6.42 (5.23 to 7.61)	-1.48
ICER							
MMSE							
NPI							
					-€333/Additional point deterioration		
						Dominance	

Abbreviations: CI, confidence interval; CMHT, community mental health team; DOC-PG, Diagnostic Observation Centre for PsychoGeriatric Patients; GP, general practitioner; ICER, incremental cost-effectiveness ratio; MMSE, Mini-Mental State Examination; NA, not applicable; NPI, Neuropsychiatric Inventory; QALY, quality-adjusted life-year.

<sup>a</sup>Source of volume information is given in parentheses: A, hospital information system; B, electronic patient file, CMHT; C, registries of local pharmacies; D, informal care questionnaire; and E, cost diaries. See the "Methods" section for more information.

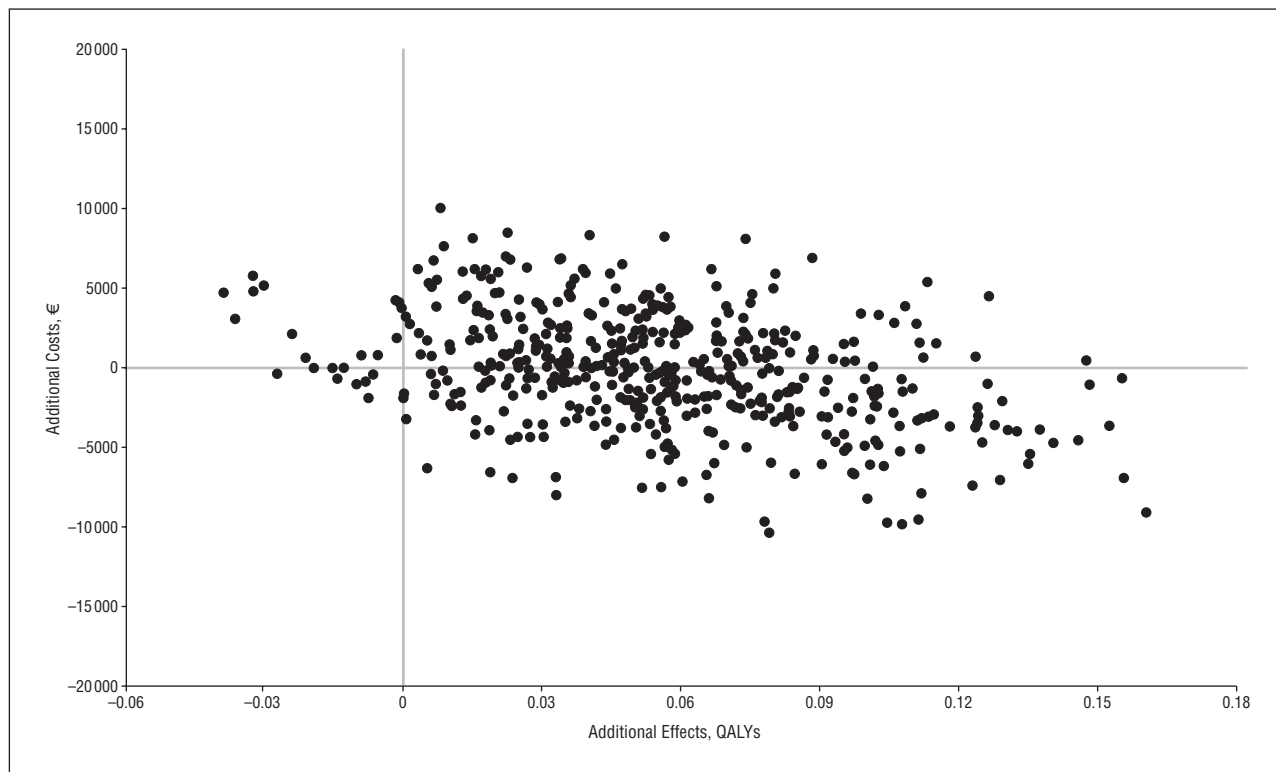
were for admissions to a nursing home, hospital costs, home care (nursing home), and informal care. Of these, the costs of admissions and informal care were lower for the DOC-PG group. The average incremental cost was €65. The total mean costs for the secondary analyses (n=192) amounted to €41 084 in the DOC-PG group and €41 107 in the usual care group. The average incremental cost was -€23 (in favor of the DOC-PG).

### COST-EFFECTIVENESS

The mean ICER in the main bootstrap simulation was €1267/QALY. The incremental costs in the bootstrap simulation ranged from -€7435 (2.5th percentile) to €6750 (97.5th percentile). The incremental effectiveness ranged from -0.01 (2.5th percentile) to 0.13 (97.5th percentile). On the cost-effectiveness plane (**Figure 1**), most of the incremental cost-effectiveness pairs (94%) are situated in the east section, meaning that DOC-PG is more effective than usual care. The majority of these

incremental cost-effectiveness pairs (51%) are situated in the quadrant indicating dominance for the DOC-PG, whereas 43% are situated in the northeast quadrant. When the ceiling ratio is €45 000 (corresponding to the threshold put forth by the National Institute for Health and Clinical Excellence guidelines: ±£30 000<sup>35</sup>), the probability that the DOC-PG is cost-effective is 72% (**Figure 2**). When the ceiling ratio is €80 000 (the threshold determined by the Dutch Council for Public Health and Health Care<sup>36</sup>), this probability increases to 80%.

The mean ICER in the secondary bootstrap simulation on the MMSE was -€333 per additional point decrease on the MMSE (the DOC-PG was less costly but showed more deterioration than usual care). The incremental costs in the bootstrap simulation ranged from -€7758 (2.5th percentile) to €8162 (97.5th percentile). The incremental effectiveness ranged from -1.54 (2.5th percentile) to 1.40 (97.5th percentile). The incremental cost-effectiveness pairs in **Figure 3** are situated around the origin. Irrespective of the ceiling ratio, the probabil-



**Figure 1.** Scatterplot of the estimated incremental costs and incremental effects (quality-adjusted life-years [QALYs]) of the Diagnostic Observation Centre for PsychoGeriatric Patients intervention vs usual care obtained by bootstrap simulations.

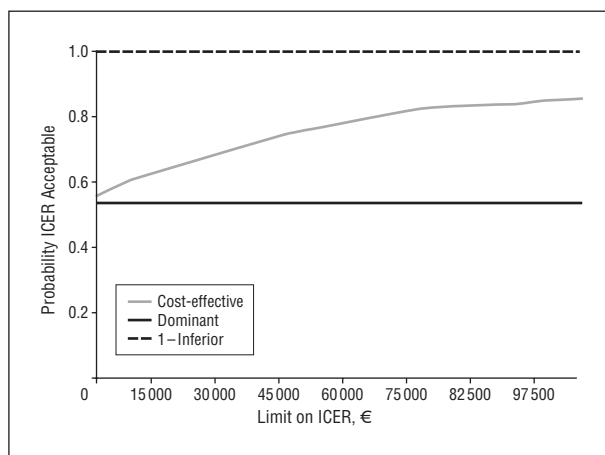
ity that the DOC-PG is cost-effective is about 50% (**Figure 4**), which indicates that results are indecisive.

The mean ICER of the secondary bootstrap simulation on the NPI showed dominance, ie, the DOC-PG was less costly and more effective (less deterioration than usual care). The incremental costs in the bootstrap simulation ranged from -€7955 (2.5th percentile) to €8405 (97.5th percentile). The incremental effectiveness ranged from -3.77 (2.5th percentile) to 6.31 (97.5th percentile). The scatterplot (**Figure 5**) shows that 69% of the pairs indicate that the DOC-PG is more effective than usual care. Most of these pairs (37%) are situated in the northeast quadrant, whereas 32% are situated in the quadrant indicating dominance. The cost-effectiveness acceptability curve (**Figure 6**) shows that the probability that the DOC-PG is cost-effective ranges from 47% at a ceiling ratio of €0 to 62% at a ceiling ratio of €1500 (with a maximum probability of 69% at a ceiling ratio of €7700; not shown).

The results of the 1-way sensitivity analyses on the main cost-effectiveness data show that results are robust and even demonstrate dominance of the DOC-PG in 3 of the 5 cases (**Table 5**).

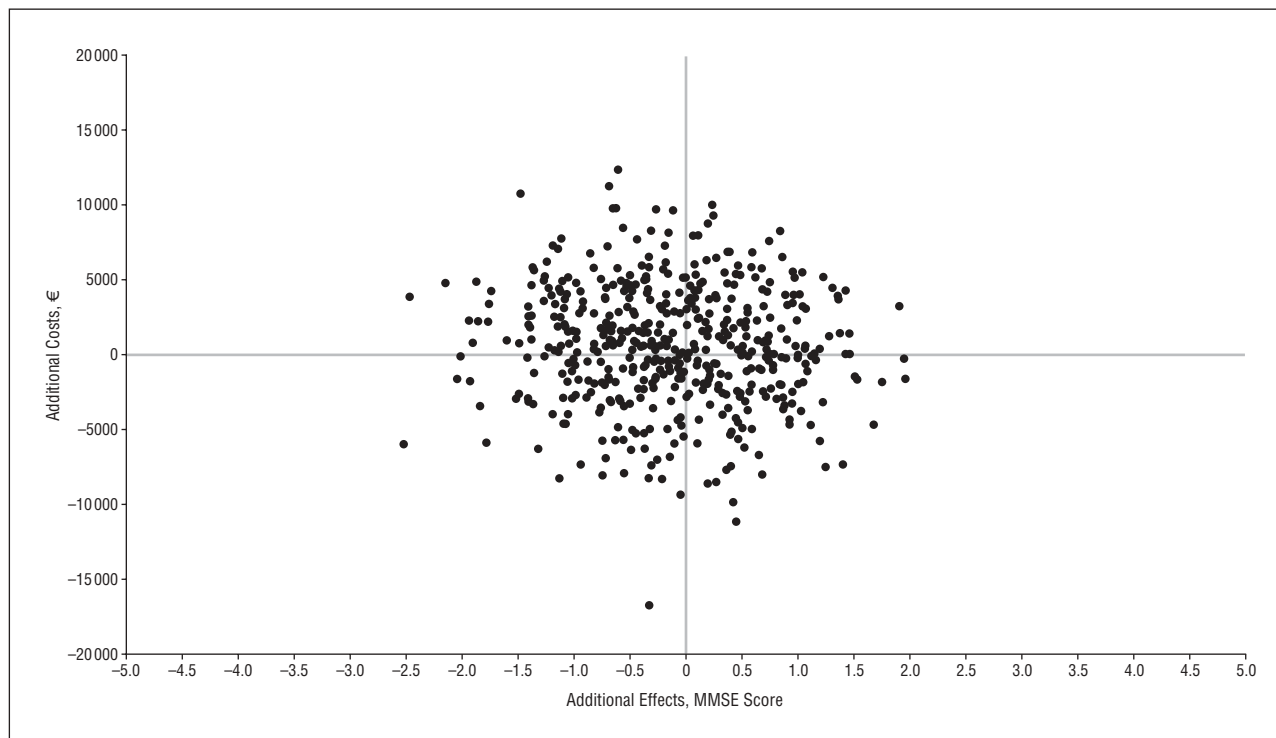
#### COMMENT

This article reports on a full economic evaluation of an integrated multidisciplinary facility for diagnosing dementia conducted alongside a randomized trial. The results of the main cost-effectiveness analysis show that, when compared with patients who received usual care, patients who visited the DOC-PG gained a mean of 0.05 QALY. The incremental cost per QALY amounted to

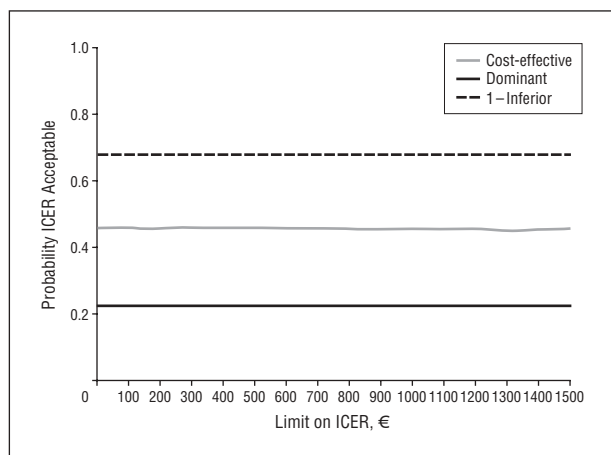


**Figure 2.** Cost-effectiveness (quality-adjusted life-years) acceptability curves showing the probability that the Diagnostic Observation Centre for PsychoGeriatric Patients intervention is cost-effective when compared with usual care over a range of values for the maximum acceptable ceiling ratio (limit on incremental cost-effectiveness ratio [ICER]).

€1267. The probability that the DOC-PG is cost-effective ranges from 63% when a conservative ceiling ratio of €20 000 is applied to 80% with a ceiling ratio of €80 000. The National Institute for Health and Clinical Excellence guidelines<sup>35</sup> state that the reimbursement of interventions costing less than £30 000 (approximately €45 000) are generally not questioned. This threshold has recently been set at €80 000 by the Dutch Council for Public Health and Health Care<sup>36</sup> for diseases with a high burden, such as Alzheimer disease. Clearly, our point estimate lies beneath this threshold and is surrounded by



**Figure 3.** Scatterplot of the estimated incremental costs and incremental effects (Mini-Mental State Examination [MMSE] score) of the Diagnostic Observation Centre for PsychoGeriatric Patients intervention vs usual care obtained by bootstrap simulations.



**Figure 4.** Cost-effectiveness (Mini-Mental State Examination) acceptability curves showing the probability that the Diagnostic Observation Centre for PsychoGeriatric Patients intervention is cost-effective when compared with usual care over a range of values for the maximum acceptable ceiling ratio (limit on incremental cost-effectiveness ratio [ICER]).

an acceptable amount of uncertainty. Therefore, using QALYs as the outcome measure, we consider an integrated approach to dementia as provided by the DOC-PG to be cost-effective.

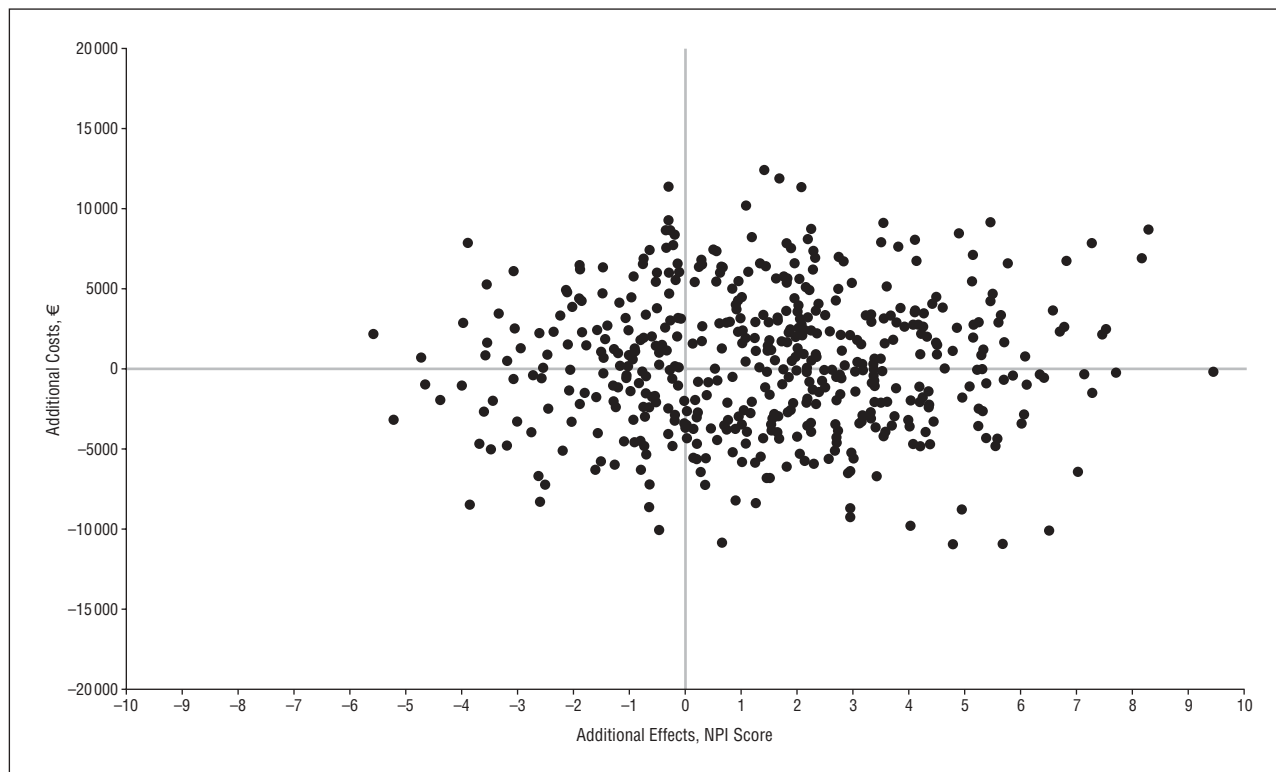
With respect to the secondary cost-effectiveness analyses, it is difficult to draw conclusions because it is not known what society is prepared to pay for a gain, or accept for a loss, in cognition and behavior. However, a reflection of society's willingness to pay for a 1-point decrease on the MMSE can be derived from a retrospective study by Wolstenholme et al<sup>20</sup> and a survey by Hux et al<sup>22</sup> regarding the costs of dementia care. These studies indi-

cate a range between €213 (£56 for a 4-month period) and €868 (\$1343), respectively. However, irrespective of the ceiling ratio, the probability that the DOC-PG is cost-effective based on the MMSE remains about 50%. Regarding the NPI, results from the observational cost study by Murman et al<sup>21</sup> showed that a 1-point increase on the NPI would result in a cost increase between €163 (\$247) and €270 (\$409). Taking €270 for a 1-point increase on the NPI as an estimate for the ceiling ratio, the probability that the DOC-PG is cost-effective would also be about 50%. Therefore, our secondary analyses based on 2 clinical outcomes provide no further evidence for the cost-effectiveness of the DOC-PG compared with usual care.

In our main study, the mean total costs per year per patient amounted to €38 396 for the DOC-PG group and €38 331 for the usual care group. In the DOC-PG group, more money was spent on the hospital costs. Although no cases of reversible dementia were detected, a more complete diagnostic assessment will likely contribute to the differentiation of the dementia syndrome into etiologic subtypes and the detection of excess disability by comorbid somatic or psychiatric disorders. This approach enables more specific treatment options, such as cholinesterase inhibitors or management of vascular risk factors.<sup>37</sup> Alternatively, it may make the unmet needs of patients and/or caregivers more apparent, which then would lead to more interventions and thus to more costs. It is important that these coexistent medical problems in patients with dementia be carefully managed because treatment of these problems can increase a patient's well-being.<sup>6</sup>

The largest difference in costs between the DOC-PG and usual care, in favor of the DOC-PG, relates to admissions to a nursing home. Patients from the DOC-PG

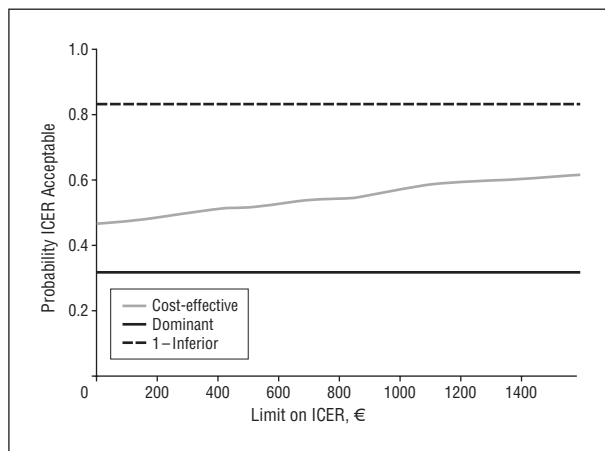




**Figure 5.** Scatterplot of the estimated incremental costs and incremental effects (Neuropsychiatric Inventory [NPI] score) of the Diagnostic Observation Centre for PsychoGeriatric Patients intervention vs usual care obtained by bootstrap simulations.

group stayed at home longer than did patients in the usual care group (who resided in a nursing home for a longer period than did patients in the intervention group [ $P=.01$ ]), which obviously results in a large cost difference. It remains unclear whether this difference in costs diminishes with time. Another notable difference in costs between the DOC-PG group and the usual care group is related to informal care. Informal care costs were considerably higher in the latter group. This is possibly because the DOC-PG team advised the more extensive involvement of professional care, such as home care.<sup>8</sup> These services, which are more expensive than informal care, were indeed used more extensively in the intervention group. An integrated approach may therefore affect the process (ie, accessibility and swiftness) of service delivery. Informal care is rarely included in economic evaluation studies because the collection of these data is often complex.<sup>38,39</sup> The measurement and valuation of informal care is still a matter of debate, and the costs are highly dependent on the valuation method used. In this study, we valued the time caregivers spent on informal care by using the hourly wage for housekeeping services.<sup>12</sup> This rather conservative approach probably resulted in an underestimation of the costs of informal care. Other methods for valuing informal care<sup>28</sup> would, in turn, result in a more attractive ICER for the DOC-PG.

Although the results showed a gain in QALYs for the DOC-PG group when compared with the usual care group, the mean HRQoL for both groups deteriorated during the year. Cognitive functioning, behavioral problems, ability to perform activities of daily living, and emotional functioning also worsened after a year,<sup>7</sup> which is



**Figure 6.** Cost-effectiveness (Neuropsychiatric Inventory) acceptability curves showing the probability that the Diagnostic Observation Centre for PsychoGeriatric Patients intervention is cost-effective when compared with usual care over a range of values for the maximum acceptable ceiling ratio (limit on incremental cost-effectiveness ratio [ICER]).

not surprising given that most patients had dementia. However, merely the deterioration in HRQoL was significantly different between the 2 groups, in favor of the DOC-PG. Additional analyses showed that the different rating of patients' HRQoL by their proxies could not be related to differences in caregivers' burden or caregivers' quality of life (data to be published separately). The difference in HRQoL mainly pertained to self-care and usual activities. Because both nursing home costs and informal care costs were notably lower in the DOC-PG group (which seems to be related to both domains), it

**Table 5. Results of Sampling-Weighted (Pweighted) Sensitivity Analyses, With and Without Regression Correction**

	Cost, €	Mean Total Costs per Patient, €		ICER, €/QALY
		DOC-PG (n=131)	Usual Care (n=88)	
Admission				
Nursing -50%	106.00	2847	3950	25 420
Nursing +50%	318.00	8443	11 851	Dominance
Home care <sup>a</sup>				
Nursing -50%	20.79	2448	2016	Dominance
Nursing +50%	62.37	7346	6048	11 698
Informal care (proxy good method) <sup>a</sup>				
HDL	8.54	3366	3181	
ADL	32.67	2821	4083	
IADL	32.67	16 858	20 023	
<b>Total</b>		<b>23 045</b>	<b>27 287</b>	Dominance

Abbreviations: ADL, activities of daily living; DOC-PG, Diagnostic Observation Centre for PsychoGeriatric Patients; HDL, household activities of daily living; IADL, instrumental activities of daily living; ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life-year.

<sup>a</sup>Volume information from informal care questionnaire.

can be argued that the difference in HRQoL is explained by a more efficient use of resources and not by a differential effect on clinical outcomes, such as cognition or neuropsychiatric symptoms.

The costs of dementia care in this study (±€40 000 per year) are comparable to those in other studies using similar cost categories (US \$31 000-\$46 700 per year).<sup>2</sup> To our knowledge, no studies have estimated the costs and/or cost-effectiveness of an integrated approach to diagnosing dementia, nor have they estimated the costs of other diagnostic services.<sup>5,6</sup> Few studies exist on the costs and cost-effectiveness of psychosocial therapies and scanning and imaging in diagnosing dementia.<sup>2,40-42</sup> A number of pharmaco-economic studies have focused on dementia.<sup>4,43</sup> However, there are international differences in the organization of health care, and it is therefore difficult to draw comparisons between the different studies.

Usual care in our region consisted mainly of an active university memory clinic and a CMHT that have collaborated in the past on several projects. Thus, the contrast between the DOC-PG and care as usual may have been less than would have been the case in other regions.

Some limitations of this study need to be considered. A first weakness of this study relates to the poor completion of the cost diaries, which were used to calculate part of the cost volumes. These diaries appeared to be very time consuming and difficult to complete. Retrospective questionnaires would probably have resulted in a higher completion rate. Indeed, it may be more beneficial to use a cost questionnaire with structured closed questions for the assessment of health care utilization in economic evaluations alongside clinical trials.<sup>44</sup> Because it was not feasible to determine each patient's number of visits to the GP, number of visits to other health care professionals outside the hospital, and number of medical aids purchased, these costs were imputed in a larger sample than the rest of the costs. However, these costs constitute only a small proportion of the total costs (7%).

An additional potential limitation was our use of proxies to complete the questionnaires. The method of proxy rating was chosen because of the longitudinal nature of

the study, the complex health problems of the study population, and the progressive global deterioration of intellect and personality characteristics in members of the study population. It is generally acknowledged that, in the later stages of dementia, proxy measures are required because patients are often incapable of adequately evaluating their own health.<sup>45,46</sup> Nonetheless, it is possible that the scores on the instruments were biased because of a perceived caregiver burden.<sup>47</sup> This potential bias, however, applies to both groups. Another limitation concerns the blindness of the referring GPs (who were initially kept naive that randomization took place on the level of the GP practice), which could not be maintained fully until the end of the study. This probably resulted in a somewhat less favorable outcome for the DOC-PG.<sup>7</sup>

A final potential limitation concerns our follow-up period of 1 year. It can be argued that a longer duration of follow-up is important when examining treatment benefits for dementia, a disorder that results in a gradual progressive decline over several years.<sup>6</sup> Because of the lack of evidence, no extrapolation beyond our follow-up period could be performed.<sup>5</sup>

In conclusion, this full economic evaluation shows that an integrated approach to dementia by means of the DOC-PG is not demonstrably more expensive and has a high probability of being more effective in terms of QALYs. With the use of either cognition or behavioral problems as the outcome measure, results are inconclusive. However, the DOC-PG is not specifically aimed at reducing these symptoms of dementia but leads to a timely and more efficient allocation of services. Therefore, we contend that the DOC-PG is a cost-effective facility for the diagnosis and management of dementia. In light of our aging population, with increasing numbers of patients with dementia, appropriate multidisciplinary organizational models are necessary to ensure the quality of care while controlling the costs. Because there is a growing interest in organizational models designed to create connectivity, alignment, and collaboration within and between the cure and care sectors, the MEDICIE study provides the evidence to support this approach.

**Submitted for Publication:** January 16, 2008; final revision received August 22, 2008; accepted August 22, 2008.  
**Correspondence:** Frans R. J. Verhey, PhD, MD, Department of Psychiatry and Neuropsychology, University Hospital of Maastricht/Alzheimer Centre Limburg, PO Box 5800, 6202 AZ Maastricht, the Netherlands (f.verhey@np.unimaas.nl).

**Author Contributions:** Dr Verhey had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

**Financial Disclosure:** None reported.

**Funding/Support:** This study was funded by grant 945-02-055 from the Dutch Research Institute for Care and Medical Sciences (ZorgOnderzoek Nederland-Medische wetenschappen).

**Additional Contributions:** We thank the patients and their caregivers who participated in this study. Daniëlle Willems, MSc, collected and input most of the data, and Audrey Fiddelers, MSc, Heidi Lansdaal, MSc, Ilvy Mayen, MSc, and Andrea Wolf, MSc, collected and input the remainder of the cost data. The GPs and everyone working at the DOC-PG, the Maastricht Memory Clinic, and the Department of Old Age at the RIAGG Maastricht (CMHT), especially Niek Jaspers and Mike Verkaaik, provided valuable assistance in recruiting patients.

## REFERENCES

1. Slobbe ICJ, Kommer GJ, Smit JM, Groen J, Meerding WJ, Polder JJ. *Cost of illness in the Netherlands* [in Dutch]. Bilthoven, the Netherlands: Rijksinstituut voor Volksgezondheid en Milieu, Centrum voor Volksgezondheid Toekomst Verkenningen; Centraal Bureau voor de Statistiek; Erasmus MC, afdeling Maatschappelijke Gezondheidszorg; 2006. Report No. 270751010.
2. Wimo A, Ljunggren G, Winblad B. Costs of dementia and dementia care: a review. *Int J Geriatr Psychiatry*. 1997;12(8):841-856.
3. Jönsson L. Economic evidence in dementia: a review. *Eur J Health Econ*. 2004;5(suppl 1):S30-S35.
4. Jönsson L. Pharmacoeconomics of cholinesterase inhibitors in the treatment of Alzheimer's disease. *Pharmacoeconomics*. 2003;21(14):1025-1037.
5. Wolfs CA, Dirksen CD, Severens JL, Verhey FR. The added value of a multidisciplinary approach in diagnosing dementia: a review. *Int J Geriatr Psychiatry*. 2006;21(3):223-232.
6. NICE. *Dementia: Supporting People With Dementia and Their Carers in Health and Social Care*. London, England: National Collaborating Centre for Mental Health; November 2006.
7. Wolfs CAG, Kessels A, Dirksen CD, Severens JL, Verhey FR. Integrated multidisciplinary diagnostic approach for dementia care: randomised controlled trial. *Br J Psychiatry*. 2008;192(4):300-305.
8. Wolfs CA, Verhey FR, Kessels A, Winkens RA, Severens JL, Dirksen CD. GP concordance with advice for treatment following a multidisciplinary psychogeriatric assessment. *Int J Geriatr Psychiatry*. 2007;22(3):233-240.
9. Verhey FR, Scheltens P, Olde Rikkert MG. The development of memory clinics in the Netherlands [in Dutch]. *Ned Tijdschr Geneesk*. 2007;151(10):578-580.
10. Gold MR, Siegel JE, Russell LB, Weinstein MC. *Cost-effectiveness in Health and Medicine*. New York, NY: Oxford University Press; 1996.
11. Drummond M, O'Brien B, Stoddart G, Torrance G. *Methods for the Economic Evaluation of Health Care Programmes*. 2nd ed. New York, NY: Oxford University Press; 1997.
12. Oostenbrink JB, Koopmanschap MA, Rutten FFH. *Handleiding voor kostenonderzoek: methoden en richtlijnrijzen voor economische evaluaties in de gezondheidszorg*. Amstelveen, the Netherlands: College voor zorgverzekeringen; 2004.
13. Brooks R. EuroQol: the current state of play. *Health Policy*. 1996;37(1):53-72.
14. Lamers LM, Stalmeier PF, McDonnell J, Krabbe PF, van Busschbach JJ. Kwaliteit van leven meten in economische evaluaties: het Nederlands EQ-5D-tarief. *Ned Tijdschr Geneesk*. 2005;149(28):1574-1578.
15. Lamers L, McDonnell J, Stalmeier P, Krabbe PFM, van Busschbach JJ. The Dutch tariff: results and arguments for an effective design for national EQ-5D valuation studies. *Health Econ*. 2006;15(10):1121-1132.
16. Jönsson L, Andreasen N, Kilander L, Soininen H, Waldemar G, Nygaard H, Winblad B, Jönhagen ME, Hallikainen M, Wimo A. Patient- and proxy-reported utility in Alzheimer disease using the EuroQoL. *Alzheimer Dis Assoc Disord*. 2006;20(1):49-55.
17. Wolfs CA, Dirksen CD, Kessels A, Willems DC, Verhey FR, Severens JL. Performance of the EQ-5D and the EQ-5D+C in elderly patients with cognitive impairments. *Health Qual Life Outcomes*. 2007;5(1):33.
18. Dolan P. Modeling valuations for EuroQol health states. *Med Care*. 1997;35(11):1095-1108.
19. Kind P. Guidelines for value sets in economic and on-economic studies using EQ-5D. In: Brooks R, Rabin R, Charro FD, eds. *The Measurement and Valuation of Health Status Using EQ-5D: A European Perspective*. Amsterdam, the Netherlands: Kluwer Academic Publishers; 2003:29-42.
20. Wolstenholme J, Fenn P, Gray A, Keene J, Jacoby R, Hope T. Estimating the relationship between disease progression and cost of care in dementia. *Br J Psychiatry*. 2002;181:36-42.
21. Murman DL, Chen Q, Powell MC, Kuo SB, Bradley CJ, Colenda CC. The incremental direct costs associated with behavioral symptoms in AD. *Neurology*. 2002;59(11):1721-1729.
22. Hux MJ, O'Brien BJ, Iskedjian M, Goeree R, Gagnon M, Gauthier S. Relation between severity of Alzheimer's disease and costs of caring. *CMAJ*. 1998;159(5):457-465.
23. Folstein MF, Folstein SE, McHugh PR. "Mini-mental state": a practical method for grading the cognitive state of patients for the clinician. *J Psychiatr Res*. 1975;12(3):189-198.
24. Kok RM, Verhey FRJ, Schmand B. Meetinstrumenten bij cognitieve stoornissen. *Tijdschr Psychiatr*. 2004;10:665-669.
25. Cummings JL. The Neuropsychiatric Inventory: assessing psychopathology in dementia patients. *Neurology*. 1997;48(5)(suppl 6):S10-S16.
26. Cummings JL, McPherson S. Neuropsychiatric assessment of Alzheimer's disease and related dementias. *Aging (Milano)*. 2001;13(3):240-246.
27. van den Berg B, Al M, Brouwer W, van Exel J, Koopmanschap M. Economic valuation of informal care: the conjoint measurement method applied to informal caregiving. *Soc Sci Med*. 2005;61(6):1342-1355.
28. van den Berg B, Brouwer W, van Exel J, Koopmanschap M, van den Bos GA, Rutten F. Economic valuation of informal care: lessons from the application of the opportunity costs and proxy good methods. *Soc Sci Med*. 2006;62(4):835-845.
29. Goossens ME, Rutten-van Molken MP, Vlaeyen JW, van der Linden SM. The cost diary: a method to measure direct and indirect costs in cost-effectiveness research. *J Clin Epidemiol*. 2000;53(7):688-695.
30. Rubin DB. *Multiple Imputation for Nonresponse in Surveys*. New York, NY: John Wiley & Sons; 1987.
31. Little RJA, Rubin DB. *Nonresponse in Sample Surveys. Statistical Analysis With Missing Data*. Toronto, ON: John Wiley & Sons Inc; 1987:50-72.
32. Briggs AH, Wonderling DE, Mooney CZ. Pulling cost-effectiveness analysis up by its bootstraps: a non-parametric approach to confidence interval estimation. *Health Econ*. 1997;6(4):327-340.
33. Black WC. The CE plane: a graphic representation of cost-effectiveness. *Med Decis Making*. 1990;10(3):212-214.
34. van Hout BA, Al M, Gordon G, Rutten FFH. Costs, effects and C/E-ratios alongside a clinical trial. *Health Econ*. 1994;3(5):309-319.
35. Raftery J. NICE: faster access to modern treatments? analysis of guidance on health technologies. *BMJ*. 2001;323(7324):1300-1303.
36. Raad voor de Volksgezondheid en Zorg. *Zinnige en duurzame zorg*. Zoetermeer, the Netherlands: Raad voor de Volksgezondheid en Zorg; 2006.
37. Olde Rikkert MG, van der Flier WM, de Leeuw FE, Verbeek M, Jansen RW, Verhey F, Scheltens P. Multiple diagnostic tests are needed to assess multiple causes of dementia [published correction appears in *Arch Neurol*. 2006;63(4):624]. *Arch Neurol*. 2006;63(1):144-146.
38. Evers SMAA, Ament AJAH, Blaauw G. Economic evaluation in stroke research: a systematic review. *Stroke*. 2000;31(5):1046-1053.
39. Evers SMAA, van Wijk AS, Ament AJAH. Economic evaluation of mental health care interventions: a review. *Health Econ*. 1997;6(2):161-177.
40. Knapp M, Thorgrimsen L, Patel A, Spector A, Hallam A, Woods B, Orrell M. Cognitive stimulation therapy for people with dementia: cost-effectiveness analysis. *Br J Psychiatry*. 2006;188:574-580.
41. McMahon PM, Araki SS, Neumann PJ, Harris GJ, Gazelle GS. Cost-effectiveness of functional imaging tests in the diagnosis of Alzheimer disease. *Radiology*. 2000;217(1):58-68.
42. McMahon PM, Araki SS, Sandberg EA, Neumann PJ, Gazelle GS. Cost-effectiveness of PET in the diagnosis of Alzheimer disease. *Radiology*. 2003;228(2):515-522.
43. Fillit H, Hill J. Economics of dementia and pharmacoeconomics of dementia therapy. *Am J Geriatr Pharmacother*. 2005;3(1):39-49.
44. van den Brink M, van den Hout WB, Stiggelbout AM, Putter H, van de Velde CJ, Kievit J. Self-reports of health-care utilization: diary or questionnaire? *Int J Technol Assess Health Care*. 2005;21(3):298-304.
45. Jönsson L, Andreasen N, Kilander L, Soininen H, Waldemar G, Nygaard H, Winblad B, Jönhagen ME, Hallikainen M, Wimo A. Patient- and proxy-reported utility in Alzheimer disease using the EuroQoL. *Alzheimer Dis Assoc Disord*. 2006;20(1):49-55.
46. Selai C. Using the EuroQol (EQ-5D) in dementia. In: Rabin R, Busschbach J, Charro F, Essink-Bot M, Bonsel G, eds. *Proceedings of the EuroQol Plenary Meeting, 2-3 October 1997*. Rotterdam, the Netherlands: Erasmus University; 1998:157-168.
47. Logsdon RG, Gibbons LE, McCurry SM, Teri L. Assessing quality of life in older adults with cognitive impairment. *Psychosom Med*. 2002;64(3):510-519.