Cost-Effectiveness of a Disease Management Program for Major Depression in Elderly Primary Care Patients

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BACKGROUND: Major depression is common in older adults and is associated with increased health care costs. Depression often remains unrecognized in older adults, especially in primary care.

OBJECTIVE: To evaluate the cost-effectiveness of a disease management program for major depression in elderly primary care patients compared with usual care.

DESIGN: Economic evaluation alongside a cluster randomized-controlled trial.

PARTICIPANTS: Consecutive patients of 55 years and older were screened for depression using the Geriatric Depression Scale and the PRIME-MD was used for diagnosis.

INTERVENTIONS: General practitioners in the intervention group received training on how to implement the disease management program consisting of screening, patient education, drug therapy with paroxetine, and supportive contacts. General practitioners in the usual care group were blind to the screening results. Treatment in this group was not restricted in any way.

MEASUREMENTS: Severity of depression, recovery from depression, and quality of life. Resource use measured over a 12-month period using interviews and valued using standard costs.

RESULTS: Differences in clinical outcomes between the intervention and usual care group were small and statistically insignificant. Total costs were $2,123 in the intervention and $2,259 in the usual care group (mean difference −$136, 95% confidence interval: −$1,194; $1,110). Cost-effectiveness planes indicated that there were no statistically significant differences in cost-effectiveness between the 2 groups.

CONCLUSIONS: This disease management program for major depression in elderly primary care patients had no statistically significant relationship with clinical outcomes, costs, and cost-effectiveness. Therefore, based on these results, continuing usual care is recommended.

KEY WORDS: depression; disease management program; elderly; primary care.
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The 1-month prevalence of major depression in elderly people ranges from 2.0% in the community to 8.7% in primary care.[1,2] Major depression in the elderly is associated with increased physical disability, impaired well-being, and increased health service use and health care costs.[3–7] Treatment with antidepressants and psychotherapy has proven to be efficacious in older adults with major depression.[8] Nevertheless, major depression often remains unrecognized and undertreated in elderly people, especially in primary care.[9,10] Recognition and treatment is complicated by comorbid physical and psychiatric illnesses, life-stress, and social and financial problems.[9,10] Furthermore, symptoms of depression may be attributed to aging by both the physician and the patient.[11]

Screening for depression in primary care may improve outcomes, particularly when screening is followed by adequate treatment.[12] A recent review concluded that disease management programs can improve quality of care and outcomes for patients with depression and that research is needed to assess the cost-effectiveness of such programs.[13]

In this study, we evaluated the cost-effectiveness of a disease management program consisting of screening, diagnosis, and treatment of major depression in elderly primary care patients in comparison with usual care.

METHODS

Design and Setting

A cluster randomized-controlled trial was performed in 34 general practices in the Netherlands. Randomization took place at practice level. The Medical Ethical Committee of the VU University Medical Center in Amsterdam approved the study protocol. The design of the study has been described extensively.[14]

Patient Selection

In the participating general practices, all consecutive patients 55 years and older visiting their general practitioner (GP), were requested by the practice assistant to complete the Geriatric Depression Scale (GDS-15).[15] In the intervention group, patients with a GDS-15 score of 5 or higher were further evaluated by their GP using the mood module of the PRIMary care Evaluation of Mental Disorders (PRIME-MD).[16] In the usual

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care group, the PRIME-MD was administered by a research assistant in order to keep the GP blind to the screening results. Patients who were diagnosed with major depression according to the PRIME-MD were eligible for the study. Exclusion criteria were as follows: current use of antidepressants, current psychosis, bipolar disorder, or alcohol or drugs abuse, severe social dysfunction, inability to communicate in Dutch, and impaired cognitive functioning. General practitioners of intervention patients had to agree with the diagnosis of major depression and to be willing to prescribe an antidepressant. Written informed consent was obtained from the patients both after screening and after the diagnostic interview.

Usual Care Treatment

General practitioners in the usual care group remained blind to the results of the screening process and did not receive any training. Treatment of depression in the usual care group depended on whether the GP recognized the patient as being depressed and was not restricted in any way. Dutch GPs are encouraged to work according to the depression guideline issued by the Dutch college of GPs, which recommends that treatment of depression primarily consists of education and coaching. Antidepressant treatment and/or referral for psychotherapy can be added, depending on the duration and severity of the depressive symptoms, the limitations in daily functioning, and the patient's preference.[17] General practitioners are free to deviate from these guidelines and to organize care according to their own views.

Intervention Treatment

General practitioners in the intervention group attended a 4-hour training session that focused on the screening for, and diagnosis and treatment of late-life depression. The treatment offered by the GPs consisted of education and information, drug therapy (20 mg of paroxetine once daily), and supportive contacts and was based on the Dutch depression guideline.[17] Two treatment phases were distinguished: an acute treatment phase during which patients were seen every 2 weeks by their GP for a period of 2 months, and a continuation phase during which patients were seen monthly for a period of 4 months.

Clinical Outcome Measures

Trained interviewers, who were unaware of the allocation status of the participating GPs, measured outcomes and resource use during interviews at the patients' home. Recovery from depression was defined as absence of a PRIME-MD diagnosis of major depression at 12 months. The Montgomery Asberg Depression Rating Scale (MADRS) was used to assess changes in severity of depressive symptoms during the 12 months of the study.[18] Quality of life was measured using the EuroQol (EQ-5D).[19] Quality Adjusted Life Years (QALYs) were calculated by multiplying the utility based on EuroQol scores with the amount of time a patient spent in a particular health state.[20] Transitions between health states were linearly interpolated. All clinical outcome measures were measured shortly after the screening (T0) and at 2 (T1), 6 (T2), and 12 (T3) months of follow-up, with the exception of the PRIME-MD, which was not measured at 2 months of follow-up. Because the first interview was conducted shortly after the screening, treatment in the intervention group had already started at T0.

Cost Measures

Costs were measured at T0, T2, and T3 from a health care perspective using interviews. Patients were asked whether they had visited a specific health care provider in the past 6 months and if so, how many times. Because the interviews were conducted at the patients' home, it was possible for patients to get a diary to check their health care utilization. All direct health care and nonhealth care costs were considered, because it is very hard to discern which costs are depression-related and which are not. Of medication costs, only costs of psychotropic medication were included in the analyses. Intervention costs consisted of the total costs of the training sessions for the GPs and were equally allocated to the included intervention patients. Indirect costs of production losses were not measured, because it was assumed that a substantial proportion of the included patients had already retired. If available, Dutch guideline prices were used to value resource use.[21,22] The cost categories and prices used are listed in the (online Appendix). Medication costs were valued using prices of the Royal Dutch Society for Pharmacy.[23] Costs of complementary medicine visits were based on patients' estimates. All costs were adjusted to the year 2002 using consumer price indices. Discounting was unnecessary, because neither costs nor benefits were recorded beyond 12 months.

Statistical and Economic Analyses

We estimated that 68 patients in each group would be needed (2-sided $\alpha=0.05$, $\beta=0.20$) to detect moderate clinical effects (Cohen's $d=0.50$). Moderate clinical effects were considered to be clinically relevant and convincing for GPs.[14] All analyses were intention-to-treat and limited to patients completing all follow-up assessments. Differences between both groups in improvement in severity of depression and QALYs gained at 12 months were tested using t tests and differences in recovery using χ^2 tests.

To compare costs between the 2 groups, confidence intervals (CIs) for the mean differences in costs were calculated using bias-corrected and accelerated bootstrapping with 2,000 replications.[24] For the cost-effectiveness analyses, the difference in total costs between the treatment groups was compared with the difference in improvement in the MADRS score, the difference in recovery rate based on the PRIME-MD, and for the cost-utility analysis with the difference in QALYs. Uncertainty around the cost-effectiveness and cost-utility ratios was calculated using the bias-corrected percentile bootstrapping method (5,000 replications).[25] The bootstrapped cost-effect pairs were plotted on a cost-effectiveness plane.

RESULTS

Of the 34 participating general practices, 18 were allocated to the intervention group and 16 to the usual care group. There were no significant differences between GPs in the intervention and usual care group with regard to age, gender, and experience of GPs, and type and size of practice (data not shown).

Between June 2000 and October 2002, of 3,937 patients screened for depressive symptoms with the GDS-15, 579 screened positive and were evaluated further using the PRIME-MD, resulting in 178 patients with major depression according to the PRIME-MD. Of the detected patients, 145

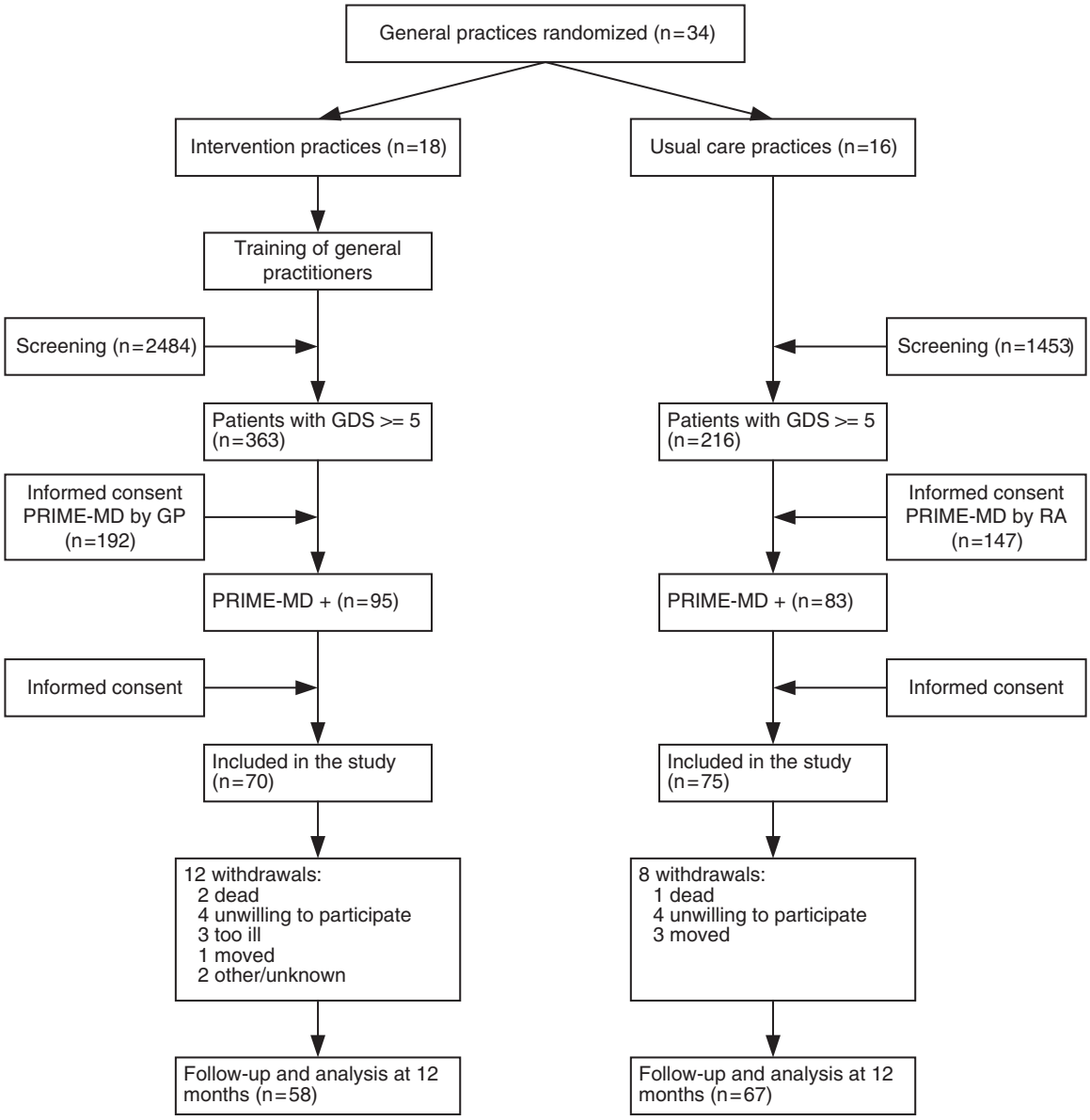

FIGURE 1. Flow of participants through the trial; GDS, Geriatric Depression Scale, PRIME-MD, PRIMary care Evaluation of Mental Disorders.

(81%) gave informed consent. Sixteen otherwise eligible intervention patients were not included, because their GP disagreed with the depression diagnosis or refused to prescribe antidepressants. Complete follow-up was available for 125 (86%) patients (Fig. 1). Patients who were lost to follow-up were older and more severely depressed than patients with complete follow-up.

Except for marital status, there were no significant differences at T0 in patient characteristics between the intervention and the usual care group (Table 1), nor did these patient characteristics differ between general practices (data not shown).

Table 1. Characteristics of Patients Allocated to the Intervention or Usual Care Group

	Intervention (*n*=58)	Usual Care (*n*=67)
Mean (SD) age in years	66.4 (8.6)	64.7 (7.5)
Female	38 (66)	36 (54)
Married/living together	34 (59)	52 (78)
Previous depression	49 (85)	55 (82)
Mean (SD) MADRS score	19.3 (8.7)	18.7 (7.7)

Values are numbers (percentages) of patients unless stated otherwise.
MADRS, Montgomery Asberg depression rating scale.

Clinical Effectiveness

Twenty-five (43%) and 32 (48%) of the patients in the intervention and usual care group, respectively, had recovered based on the PRIME-MD after 12 months. This difference in recovery rate was not statistically significant. The differences in improvement in severity of depressive symptoms and QALYs gained between the 2 treatment groups were small and not statistically significant (Table 2).

Table 2. Clinical Outcomes After 12 Months

Outcome measure	Intervention (n=58)	Usual Care (n=67)	Intervention Versus Usual Care*	P Value
% (No.) Recovered (PRIME-MD)	43.1 (25)	47.8 (32)	−4.7 (−22.5; 13.1)	.60
Mean (SD) improvement in MADRS score	−7.8 (9.0)	−7.2 (9.0)	−0.6 (−3.8; 2.6)	.70
Mean (SD) QALYs gained (EQ-5D)	0.65 (0.19)	0.70 (0.21)	−0.04 (−0.11; 0.03)	.20

*Difference (95% confidence interval).
PRIME-MD, PRIMary care Evaluation of Mental Disorders, MADRS=Montgomery Asberg Depression Rating Scale, EQ-5D, EuroQol.

Health Care Utilization

Table 3 presents the utilization of health care resources in the 2 groups over 12 months. During the study period, 95% and 94% of the intervention and usual care patients, respectively, had at least 1 contact with their GP. Forty-six (79%) intervention and only 8 (12%) usual care patients received some form of mental health care (antidepressant medication or referral) during the follow-up period. At all 3 measurements, intervention patients were more likely to use an antidepressant. Twenty-eight (48%) intervention patients received antidepressant treatment for at least 6 months as recommended by the Dutch depression guidelines.[17]

Table 3. Mean (Standard Deviation) Health Care Utilization of Patients Allocated to the Intervention or Control Group During 12 Months

Type of utilization	Intervention (n=58)	Usual Care (n=67)
Direct health care		
Primary care		
General practitioner (no. visits)	7.8 (5.5)	6.3 (5.5)
Dentist (no. visits)	1.3 (1.8)	0.8 (1.1)
Dietitian (no. visits)	0.3 (1.4)	0.6 (1.8)
Physical therapist (no. visits)	4.8 (14.3)	11.0 (20.6)
Social worker (no. visits)	0.2 (0.8)	0.0 (0.3)
Secondary care		
Psychiatrist (no. visits)	0.0 (0.3)	0.4 (2.9)
Medical specialist (no. visits)	2.9 (3.1)	3.5 (5.1)
Hospital admission (no. d)	1.3 (3.1)	1.2 (3.1)
Hospital admission (no. d on ICU)	0 (0)	0.1 (0.3)
Psychiatric hospital admission (no. d)	0 (0)	0 (0)
Regional institute for mental welfare (no. visits)	0.1 (0.4)	0.3 (1.4)
Psychogeriatric services (no. visits)	0 (0)	0.1 (0.6)
Rehabilitation center (no. h)	0 (0)	2.7 (19.3)
Nursing home —temporary admission (no. d)	1.3 (9.8)	0 (0)
Nursing home—outpatients' treatment (no. d)	0.4 (3.4)	0 (0)
Home for the elderly—temporary admission (no. d)	0.5 (3.7)	0.2 (1.7)
Home for the elderly—outpatients' care (no. daily periods)	0.9 (6.8)	0 (0)
Supportive care		
District nurse (no. h)	0.9 (4.1)	1.0 (3.4)
Home care (no. h)	9.4 (32.9)	14.0 (38.2)
Home help (no. h)	16.1 (45.6)	10.5 (35.7)
Home for the elderly—meal supply (no. meals)	3.1 (23.9)	0 (0)
Meal supply at home (no. meals)	1.3 (10.2)	3.9 (31.8)
Direct nonhealth care		
Primary care		
Alternative therapist (no. visits)	0.2 (1.2)	1.8 (8.5)
Memory training (no. contacts)	0 (0)	0.0 (0.1)

Costs

At 12 months, total direct costs were somewhat lower in the intervention group, but this difference was not statistically significant. Psychotropic medication costs in the intervention group were significantly higher than in the usual care group (Table 4). However, almost all point estimates of the differences in costs indicated small savings. Moreover, the higher GP and medication costs in the intervention group seem to be substituted by higher physiotherapy costs in the usual care group.

Total costs of visits to mental health care providers and psychotropic medication in the intervention group ($243) were higher than in the usual care group ($165), but this difference was not statistically significant (P=.22).

Cost-Effectiveness and Cost-Utility Analyses

Figure 2 shows the cost-effectiveness planes for the intervention group in comparison with the usual care group for recovery, improvement in severity of depression, and QALYs gained at 12 months. In all 3 cost-effectiveness planes, all cost-effect pairs are located near the origin of the plane, suggesting neither large nor significant differences in costs and effects. This shows that the intervention is not cost-effective in comparison with usual care.

DISCUSSION

We evaluated whether a disease management program for major depression in elderly primary care patients would be cost effective in comparison with usual care. Although antidepressant treatment rates were significantly higher in the intervention group, we found no statistically significant difference in total costs, effects, and cost-effectiveness between the 2 treatment groups.

Our findings are in line with 2 randomized trials that also found that disease management programs for elderly primary care patients with depression had no significant effect on depression severity.[26,27] In contrast, Katon et al.[28] found a significant effect, accompanied by a modest and insignificant increase in total health care costs. However, patients in that study had access to a depression care manager, which makes the intervention program much more intensive.

Several American observational studies reported much higher health care costs in depressed elderly patients than we do.[4,6,28–30] These studies used computerized databases to estimate costs, whereas our cost estimates were based on patient reports of resource use. Also, our study population was on average about 10 years younger than the study populations in the abovementioned studies.

There may be several explanations for the nonsignificant results of this study. First, despite the fact that all patients

Table 4. Mean (Standard Deviation) Total Costs in Dollars, Differences in Mean (95% Confidence Intervals)* Total Costs in Dollars, and *P* value† During Follow-up of 12 mo

	Intervention ($n=58$)	Usual Care ($n=67$)	Intervention Versus Usual Care	*P* Value
Primary care costs	336 (375)	494 (739)	– 157 (– 313;56)	.13
GP costs	170 (120)	137 (120)	33 (– 20;68)	.12
Physiotherapy costs	115 (340)	263 (490)	– 148 (– 276;19)	.05
Secondary care costs	885 (2,161)	1,021 (2,513)	– 136 (– 902;727)	.75
Outpatient costs	156 (165)	189 (274)	– 32 (– 107;46)	.42
Admission costs	664 (2,047)	466 (1317)	199 (– 418;729)	.79
Supportive care costs	575 (1,289)	663 (1,482)	– 88 (– 565;414)	.72
Medication costs	220 (162)	82 (333)	139 (4;407)	.003
Intervention costs	106	—	—	
Total direct costs	2,123 (2,661)	2,259 (3,922)	– 136 (– 1,194;1,110)	.82

**95% confidence intervals obtained by bias-corrected and accelerated bootstrapping.*
†P value obtained by applying the t *distribution on the* t *value that was obtained during bootstrapping.*
$1 = €0.80.
GP, general practitioner.

were diagnosed as having major depression according to the PRIME-MD, most patients detected by our screening method were only mildly to moderately depressed according to their MADRS scores at T0.[31,32] This may arise from the fact that screening in primary care typically leads to detection of mildly depressed patients.[33] Because patients with milder forms of major depression are not likely to be included in trials evaluating the efficacy of antidepressants, it is unclear whether antidepressants are efficacious in these patients.[34] Indeed, a recent review concluded that antidepressants have only moderate effects in older ambulatory patients with mild to moderate depression.[35]

Another partial explanation for the nonsignificant findings of this study may be the existence of a Hawthorne effect, although this seems inevitable in this type of research. The fact that GPs and patients knew they were participating in a study influences their behavior and perceptions and thereby may reduce any differences there might have been between the treatment groups. The fact that trained research assistants interviewed study patients at home may also have contributed to the Hawthorne effect. We tried to control for a Hawthorne effect by blinding usual care GPs to the screening results and the research assistants to the allocation status of the GPs. However, the Hawthorne effect may have been substantial, because, especially in the treatment of depression, attitudes, environment, time spent with patients, etc., will have an effect on the results. Related to the Hawthorne effect is that usual care patients frequently received GP care and physiotherapy for comorbid disorders. Treating comorbidity may improve outcomes of depression as well. This may also partly explain the relatively positive outcomes in usual care patients.

There are also 2 design aspects of our study that may have contributed to the nonsignificant findings of our study. First, we chose a pragmatic design, meaning that we tried to replicate everyday clinical practice as much as possible to enhance the generalizability of our findings. However, a disadvantage of a pragmatic design is that the contrast between the treatment groups may be diminished. Second, it was not possible to blind patients included in the usual care group. Although usual care patients were requested not to reveal to their GP that they were participating in this study, there is a risk that some patients informed their GP and subsequently received some kind of treatment for depression. However, as only a few usual care patients were prescribed antidepressants or referred to a mental health care provider, this problem seems to be small.

Initiation of mental health care treatment in both the intervention and the usual care group was associated with more severe depression at baseline. Thus, GPs use severity of depression as a criterion to initiate depression treatment, but this criterion alone seems insufficient to distinguish patients who will benefit from depression treatment from patients who will not benefit.

General practitioners of intervention patients had to agree with the depression diagnosis and had to be willing to prescribe antidepressants, which may have led to selection bias in the intervention group. In this case, it can be expected that intervention patients have more severe depression at baseline than usual care patients. Intervention patients were indeed somewhat more depressed than usual care patients at baseline, but the difference was small and not statistically significant. Therefore, we do not expect that this particular form of selection bias was very strong in our study.

The follow-up rate of 86% is very good for studies in elderly depressed populations. Patients who dropped out before the end of the study were older and more depressed than patients who completed all follow-up measurements. Moreover, although a sufficient number of patients was included in the study, the number of patients analyzed at 12 months was smaller than the required sample size to detect moderate clinical effects. However, the results of a missing value analysis using the Expectation Maximization algorithm[36] did not differ from the complete case analysis (data not shown). Therefore, we do not expect that inclusion of patients who dropped out before the end of the study would have altered our conclusions.

Our study was underpowered to detect relevant differences in costs, which is reflected in wide confidence intervals for cost differences. This is a common problem in "piggy back" economic evaluations. Because the distribution of cost data is typically heavily skewed, very large numbers of study patients are needed to detect relevant cost differences.[37] It is generally considered unethical to increase study sizes beyond the level needed to prove clinical effectiveness.

Another limitation to the economic evaluation presented in this article is the manner in which cost data were collected. In interviews, patients were asked about their health care

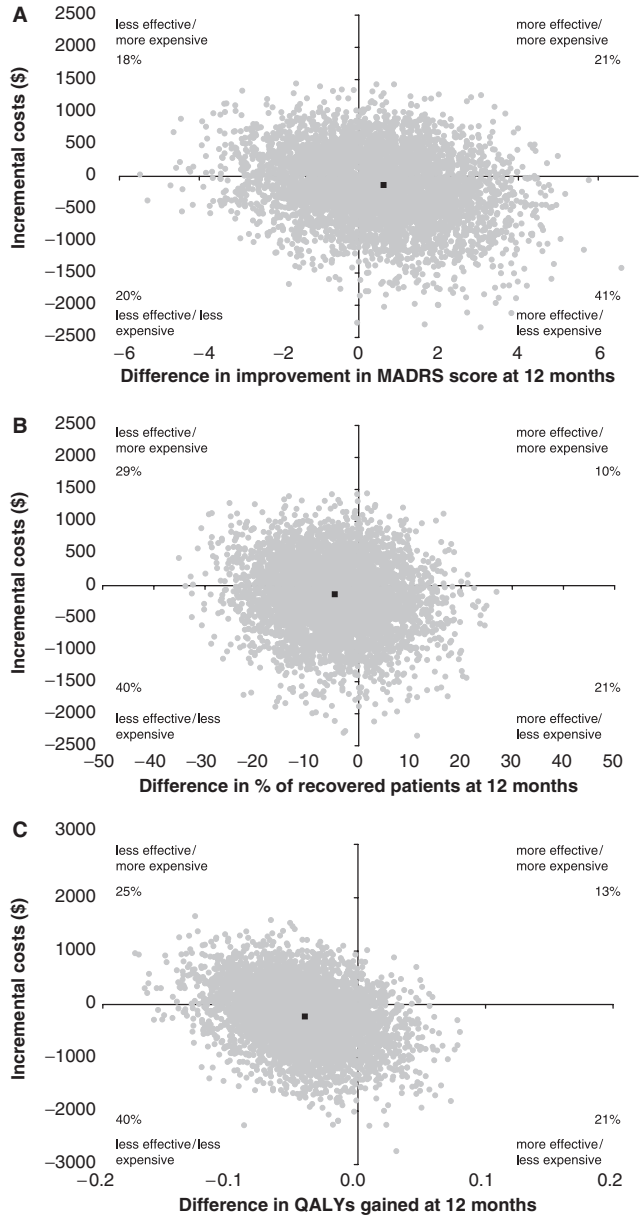

FIGURE 2. (A) Cost-effectiveness plane for the difference in improvement in Montgomery Asberg Depression Rating Scale score over 12 months (point estimate: −219; 95% confidence interval (CI): −17,054 to 1,065); (B) Cost-effectiveness plane for the difference in recovery rates based on the PRIMary care Evaluation of Mental Disorders after 12 months (point estimate: 29; 95% CI: −152 to 4,086); (C) Cost-effectiveness plane for the difference in Quality Adjusted Life-Years (QALYs) gained at 12 months (point estimate: 5,397; 95% CI: −28,108 to 450,977).

utilization over the past 6 months. Subjects in general, and elderly subjects in particular may not be able to recall health care utilization reliably over such a long period. This may have introduced recall bias. Most likely, our estimates are an underestimate of the true utilization rates for frequently occurring resources such as visits to the GP. For more seldom occurring resources such as hospitalizations, we expect our estimates to be reasonably adequate.

A final limitation is that costs of production losses and informal care giving were not measured. As the differences in clinical outcomes and direct costs were small, we consider it unlikely that inclusion of lost productivity costs would have altered the results of our study. Because our study population consisted of elderly subjects, it is probable that many subjects received informal care. Future studies should attempt to measure these costs.

In conclusion, this disease management program for major depression in elderly primary care patients was not cost-effective in comparison with usual care. There were no significant differences in depressive symptoms, quality of life, and costs between the intervention and usual care group at 12 months. Therefore, based on these results, we recommend continuing usual care by GPs, which mainly consists of "watchful waiting." In this situation, treatment for depression is initiated only when the GP diagnoses the patient as being depressed. We recommend that future research focuses on improvement of the detection of clinically important and treatable depression by GPs. Evidence is needed on indicators that help GPs in determining which patients may profit from depression treatment. Research is also needed on the (cost-) effectiveness of treatments for depression in elderly primary care patients, especially on the (cost-) effectiveness of treatments other than antidepressants, such as different forms of psychotherapy.

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Supplementary Material

The following supplementary material is available online for this article online at www.blackwellsynergy.com

Appendix: Costs applied in the economic evaluation.