Chapter 9

Cost-effectiveness of a stepped care program to prevent anxiety and depression in homes for the elderly: a randomised controlled trial

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Abstract:

Background

Depression and anxiety are common in residents of elderly homes. Both disorders have negative effects on functioning, well being and healthcare utilization. Besides treatment, prevention can be an option to reduce the burden of mental disorders.

Objective

The objective of this study was to evaluate the cost-effectiveness of a stepped care programme to prevent the onset of depression and anxiety disorders in residents of elderly homes compared with usual care from a societal perspective.

Methods

Outcomes were incidence of depression and/or anxiety, severity of depressive and anxiety symptoms and quality-adjusted life years. Healthcare utilization was measured during interviews. Multiple imputation was used to impute missing cost and effect data. Uncertainty around cost-differences and incremental cost-effectiveness ratios was estimated using bootstrapping. Cost-effectiveness planes and acceptability curves were created.

Results

The incidence of depression and anxiety combined in the intervention group was not reduced in comparison with the usual care group. There was also no effect on the other outcomes. Mean total costs in the intervention group were €838 higher than in the usual care group, but this difference was not statistically significant (95% CI -593 to 2420). Cost-effectiveness planes showed that there was considerable uncertainty. Cost-effectiveness acceptability curves showed that the maximum probability of the intervention being cost-effective in comparison with usual care was 0.46 for reducing the incidence of depression and anxiety combined.

Conclusion

A stepped care programme to prevent depression and anxiety in elderly people living in elderly homes was not considered cost-effective in comparison with usual care.

Introduction

Compared with community-dwelling elderly people, elderly people living in long-term care facilities have an increased prevalence of psychiatric disorders with prevalence estimates of clinically relevant symptoms of depression and anxiety as high as 35% (1-3). Depression and anxiety disorders in the elderly often follow a chronic intermittent course (4;5). Both depression and anxiety disorders have a profoundly negative impact on the functioning and well-being of elderly people. These disorders are also associated with increased health care utilization and mortality rates and worsen the outcomes of many medical illnesses (6-9).

The burden of depressive and anxiety disorders can be reduced in two ways: treating existing cases and preventing new cases. Most research has focused on the treatment of these disorders. However, even under ideal circumstances (100% coverage and optimal treatment), the burden of depressive and anxiety disorders can be reduced by maximally 35% and 50%, respectively (10). Thus, prevention may also play an important role in reducing the burden of depressive and anxiety disorders in elderly people.

Several prevention strategies are possible. Universal prevention is directed towards the whole population, selective prevention targets that portion of the population with known risk factors, and indicated prevention people who have already developed some signs or symptoms of the disorder but at an early or subsyndromale stage (11). Smit et al showed that the incidence of new cases of depression can be reduced by 40% if the occurrence of full-blown depressive disorder is prevented in all elderly people with depressive symptoms (12). Therefore, indicated prevention seems like a viable option to reduce the burden of depressive and anxiety disorders in elderly people. Van 't Veer-Tazelaar et al showed that a stepped care prevention programme reduced the incidence of depressive and anxiety disorders by 50% at affordable costs and that these effects were sustained over 24 months (13-15). Dozeman et al evaluated a similar stepped care programme to prevent depressive and anxiety disorders in residents of homes for the elderly with above average levels of symptoms of depression or anxiety, but not yet meeting the diagnostic criteria for a disorder. They already showed that this intervention was effective in preventing depressive disorders in this frail elderly population with multiple risk factors (16). However, implementing such a programme requires scarce resources that otherwise could be employed elsewhere. Therefore, the aim of the study was to evaluate the cost-effectiveness of this stepped care prevention programme in comparison with usual care from a societal perspective.

Methods

Design

The economic evaluation was performed alongside a pragmatic randomised controlled trial evaluating a stepped care prevention programme in comparison with usual care from a societal perspective. The follow-up of the study was 10 months. Fourteen residential homes in Amsterdam and surroundings participated in the trial. Randomisation of participants, stratified for residential home, took place after the baseline measurements in blocks of four with an equal allocation ratio and was carried out by an independent statistician using random number tables. Details of the study design have been described in detail elsewhere (17). The Medical Ethics Committee of the VU University Medical Center approved the study protocol.

Participants

Interviewers visited the residential homes and asked residents for permission to screen for depressive symptoms using the Center for Epidemiologic Studies Depression Scale (CES-D) (18). Respondents with a CES-D score of 8 or more (19), were invited for a follow-up interview consisting of a diagnostic (Mini International Neuropsychiatric Interview, MINI) and cognitive (Mini Mental State Examination, MMSE) assessment (20;21). Residents who met the criteria for a DSM-IV depressive or anxiety disorder, or with substantial cognitive impairment (MMSE score of 21 or less) were excluded. Residents who gave written informed consent and had sufficient command of the Dutch language were eligible for participation in the study.

Stepped care prevention programme

The intervention was designed in such a way that participants were first offered the least intensive intervention, and if necessary more intensive care was offered. The intervention started off with one month of watchful waiting and was then structured in cycles of 3 months. If the resident's level of symptoms had not improved by at least 5 points on the CES-D, the resident stepped up to the next level of care. The stepped care programme consisted of the following steps:

1) watchful waiting during one month;
2) activity-scheduling: a module from the self-help course "Coping with Depression"(22;23) with coaching by the staff in the residential homes;
3) life review and consultation with the general practitioner: mental health nurses provided this brief structured personal intervention (24;25), while participants were also advised to consult their general practitioner;
4) visit to the general practitioner for additional treatment: participants who had a CES-D score of 16 or more after the third follow-up interview were advised to consult their general practitioner about treatment with antidepressants or a referral to a mental health specialist.

Usual care
Residents in the usual care group had unrestricted access to any form of health care that was considered to be appropriate.

Clinical outcome measures
Clinical outcomes were measured at baseline and at 1, 4, 7 and 10 months of follow-up. The primary clinical outcome in this study was the incidence of major depressive disorder and anxiety disorders assessed using the MINI, a short structured interview to diagnose DSM-IV mental disorders (20).

Secondary outcomes included depressive and anxiety symptoms, and quality of life. Depressive and anxiety symptoms were measured using the CES-D which consists of 20 items with total scores ranging between 0 and 60.(18) The CES-D was originally designed to measure depressive symptoms, but has also been found to be useful to assess both depressive and anxiety symptoms in this setting (26).

Quality of life was measured using the EuroQol questionnaire(EQ-5D) (27). Utility scores were calculated using the Dutch tariff developed by Lamers et al. (28) QALYs were calculated by multiplying the utilities with the amount of time a patient spent in a particular health state. Transitions between health states were linearly interpolated.

Cost measures
Costs were measured from a societal perspective during interviews based on the Trimbos/iMTA questionnaire for Costs associated with Psychiatric illness (TiC-P). (29) Since all participants were living in a home for the elderly, lost productivity costs and costs for home care and informal care were not considered relevant and, thus, not included in this study. All direct costs were included, because it is difficult to indicate which costs are related to mental disorders and which are not. Costs were calculated by multiplying the units of resource use by their cost price according to the Dutch guidelines for health economic evaluations.(30) Medication costs were valued using prices of the Royal Dutch Society for Pharmacy plus the pharmacy dispensing costs of €5.30 (30;31). Table 1 lists the cost categories and prices used in the economic evaluation. All costs were adjusted to the year 2008 using consumer price indices if necessary (32). The year 2008 was chosen, because most cost data were collected during this year.
The intervention costs were calculated using a bottom-up approach. The average cost of screening the residents was estimated to be €10.17. This cost price includes 15 minutes of administration and interview time by the staff of the residential home (€7.08) and the time needed by the participants to complete the interview (€3.09). The first step of the intervention consisted of watchful waiting to which

Cost category	Unit	Unit cost (€, 2008)
General practitioner	Consultation	27.65
Regional mental health service	Contact	168.89
Psychologist	Contact	79.01
Physiotherapist	Treatment session	35.56
Social worker	Contact	64.20
Medical specialist at outpatient clinic	Consultation	71.11
Day treatment, elderly home	Half day	44.44
Day treatment, nursing home	Half day	117.53
Day treatment, hospital	Day	247.90
Hospital admission, academic hospital	Day	567.91
Hospital admission, general hospital	Day	429.63

Table 1. Cost categories included and cost prices used.

no costs were attached. The second step of the intervention consisted of activity scheduling. Costs that were included in the cost price calculation for this step were the printing costs of the booklet participants received (€11.77), the costs of coaching and administration time invested by the residential home staff (€28.32 per hour), the time costs of the residents (€12.35 per hour), and the costs associated with training the residential home staff (€13.18 per resident). The third intervention step involved life review consisting of 4 sessions with a duration of 1 hour. Costs of this step included the time spent by the mental health nurses on the life review sessions (€209.01), travel time costs for the mental health nurses (€107.49), participant time costs (€49.40), and training and supervision costs (€22.85). Costs of the fourth intervention step, the advice to visit the general practitioner, were considered to be included in the interviews during which healthcare utilization was measured.

Statistical analysis

The statistical analyses were performed according to the intention-to-treat principle. Multiple Imputation (MI) as implemented in SPSS-17 was used to impute missing cost and effect data. Variables that were found to be related to missing follow-up data, were included in the MI model. By MI 20 imputed data sets were created, each of which was analyzed separately. The results of the 20 analyses were pooled using Rubin's rules (33).

Costs generally have a highly skewed distribution. Therefore, bootstrapping with 5000 replications was used to estimate "approximate bootstrap confidence" (ABC) intervals around cost differences (34;35).

Incremental cost-effectiveness ratios (ICERs) were calculated by dividing the difference in total costs between the intervention and usual care group by the difference in clinical effects. Non-parametric bootstrapping was also used to estimate the uncertainty surrounding the incremental cost-effectiveness and cost-utility ratios (5000 replications). The bootstrapped cost-effect pairs were plotted on a cost-effectiveness plane (CE plane) and used to estimate cost-effectiveness acceptability curves (CEA curves). In a CE plane, incremental costs between the intervention and usual care are plotted on the y axis and incremental effects on the x axis resulting in four quadrants. The northeast quadrant indicates that the intervention is more expensive and more effective than usual care. In the southeast quadrant the intervention dominates usual care, i.e. is less expensive and more effective than usual care. In the southwest quadrant the intervention is less expensive and less effective than usual care. Finally, in the northwest quadrant the intervention is dominated by usual care (more expensive and less effective). Most newly developed interventions are more expensive and more effective than usual care, which implies that a trade-off needs to be made whether the additional benefits justify the additional costs. This decision depends on the societal willingness to pay (WTP) for an additional unit of effect. However, this WTP is generally not known. CEA curves show the probability that the intervention is cost-effective in comparison with the control treatment for a range of WTP values (36).

Results

Of the 1784 residents invited for the screening interview, 754 (51%) participated. Of these, 459 (61%) scored 8 points or more on the CES-D. Informed consent was given by 270 (59%) participants, but another 85 participants were excluded because they were suffering from a mental disorder, cognitive impairment, or both. Thus, in total 185 participants were included in the trial (93 intervention and 92 usual care participants). Thirty-five (38%) intervention participants dropped out and 20 (22%) usual care participants. Complete follow-up on the questionnaires was available for 96 (52%) participants for clinical effects and for 91 (49%) participants for costs.

Almost 75% of the participants were female and the mean age was 84 years (Table 2). A minority of the participants was married or living together with a partner (17%). Around 40% of the participants had 3 or more chronic conditions. There were no significant differences in baseline characteristics between the intervention and usual care group.

Participants with complete data were more likely to be randomized to the usual care group, less depressed, more lonely, less cognitively impaired, and had more

Characteristic	Intervention group (n=93)	Usual care group (n=92)	Total (n=185)
Female, n (%)	67 (72%)	68 (74%)	135 (73%)
Age, mean (SD)	84 (6.7)	84 (6.4)	84 (6.5)
MMSE score, mean (SD)	27.0 (2.1)	27.1 (2.0)	27.1 (2.1)
Married or living with a partner, n (%)	18 (19%)	13 (14%)	31 (17%)
Education, n(%)			
Low	39 (44%)	41 (45%)	80 (45%)
Middle	29 (33%)	33 (36%)	62 (35%)
High	20 (23%)	17 (19%)	37 (21%)
Number of chronic diseases, n (%)			
0	4 (4%)	5 (5%)	9 (5%)
1	13 (14%)	22 (24%)	35 (19%)
2	34 (37%)	29 (32%)	63 (34%)
3 or more	42 (45%)	36 (39%)	78 (42%)
CES-D score, mean (SD)	14.9 (5.7)	14.4 (5.3)	14.7 (5.5)
HADS score, mean (SD)	3.6 (2.8)	3.2 (2.6)	3.4 (2.7)
Loneliness score , mean (SD)	3.4 (0.87)	3.4 (0.80)	3.4 (0.83)
Major difficulties ADL, n (%)	43 (46%)	50 (54%)	95 (51%)
Utilitity score, mean (SD)	0.66 (0.26)	0.66 (0.24)	0.66 (0.25)

Table 2. Baseline demographic and clinical characteristics of the participants.

problems with their activities of daily life than participants without complete follow-up.

Clinical outcomes

The clinical outcomes were extensively described in the accompanying clinical paper (16), and are shortly summarized here. The multiply imputed clinical outcomes after 10 months are presented in Table 3. The incidence of any disorder was similar in both groups. The incidence of major depression was halved in the intervention group (0.09) in comparison with the usual care group (0.17). However, the incidence of anxiety was more than doubled in the intervention group. None of the differences in incidences were statistically significant. The intervention group

Outcome	Intervention group (n=93)	Usual care group (n=92)	Difference
Incidence of			
depression	0.09 (0.04)	0.17 (0.05)	-0.08 (-0.21 ; 0.04)
anxiety	0.13 (0.05)	0.05 (0.03)	0.08 (-0.03 ; 0.19)
depression and/or anxiety	0.20 (0.06)	0.19 (0.05)	0.01 (-0.14 ; 0.16)
Improvement CES-D	-3.2 (0.94)	-0.88 (0.79)	-2.3 (-4.8 ; 0.21)
QALYs	0.69 (0.02)	0.66 (0.02)	0.03 (-0.03 ; 0.09)

Table 3. Multiply imputed and pooled clinical outcomes after 1 year. Presented are means (SEs) and mean differences between the intervention and usual care group (95% CI).

Cost category	Intervention group (n=93)	Usual care group (n=92)	Difference
General practitioner	191 (15)	172 (15)	19 (-23 ; 61)
Other ambulant care	1287 (227)	833 (121)	454 (21 ; 1061)*
Outpatient clinic	355 (41)	301 (45)	54 (-70 ; 165)
Hospital admissions	856 (274)	1265 (418)	-409 (-1468 ; 481)
Medication	1387 (285)	874 (91)	513 (69 ; 1340)*
Intervention	209 (21)	0 (0)	209 (159 ; 260)*
Total	**4284 (595)**	**3446 (484)**	**838 (-593 ; 2420)**

* indicates a statistically significant difference between the intervention and control group

Table 4. Multiply imputed and pooled total costs after 1 year follow-up. Presented are means (SEs) and mean differences (95% CI) between the intervention and usual care group.

improved more on the CES-D than the usual care group, but not statistically significantly. The difference in QALYs was small and statistically insignificant.

Costs

Step 1 of the intervention (watchful waiting) was attended by all participants. Forty-five (48% of the intervention participants) participants received step 2 of the intervention (activity scheduling) and 31 (33%) participants step 3 (life review). Mean total intervention costs amounted to €209 per participant.

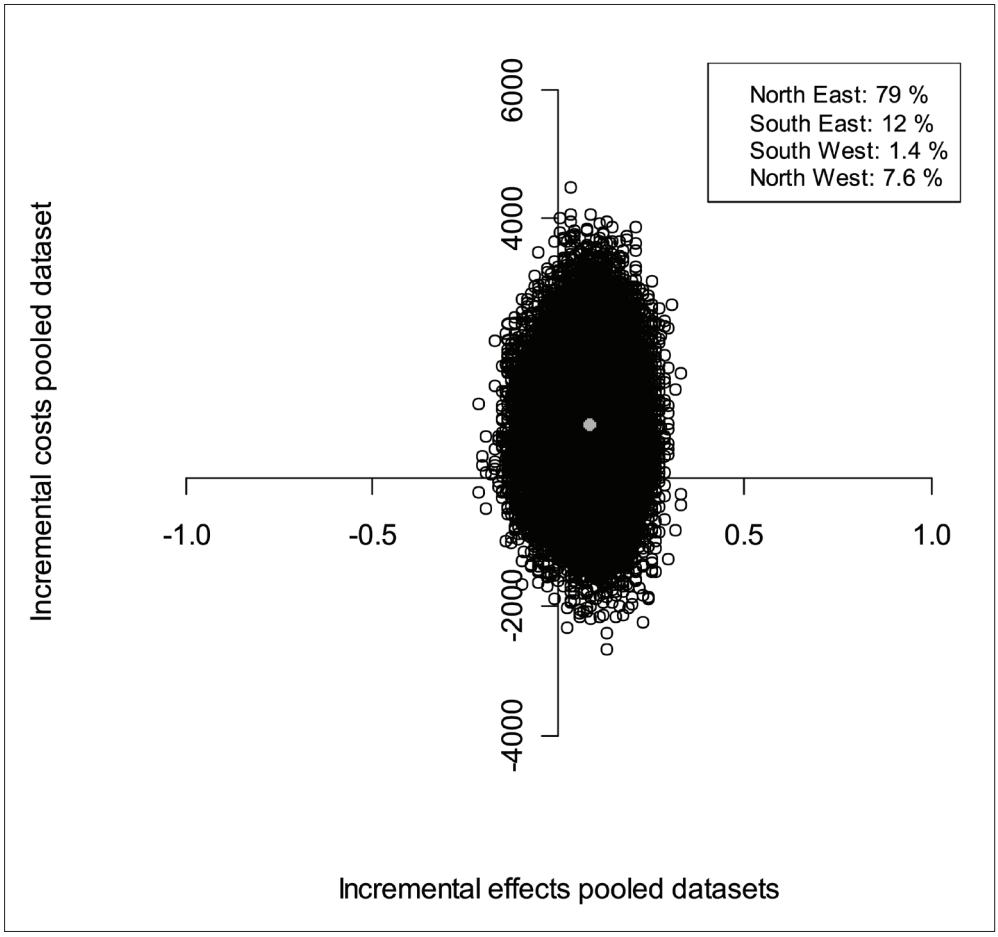

Figure 1. Cost-effectiveness plane for incidence of depression.

Table 4 presents mean total costs and differences in costs between the intervention and usual care group. Total costs in the intervention group were €838 higher than in the usual care group, but this difference was not statistically significant (95% CI -593 to 2420). Ambulatory care and medication costs in the intervention group were statistically significantly higher than in the usual care group, and hospital admission costs were substantially higher in the usual care group albeit not statistically significantly.

Cost-effectiveness and cost-utility

The results of the cost-effectiveness and cost-utility analyses are described in Table 5. Regarding the combined incidence of depression or anxiety, the conclusion is that the intervention was not cost-effective in comparison with usual care. The CE plane shows that 47% of the bootstrapped cost-effect pairs was situated in the

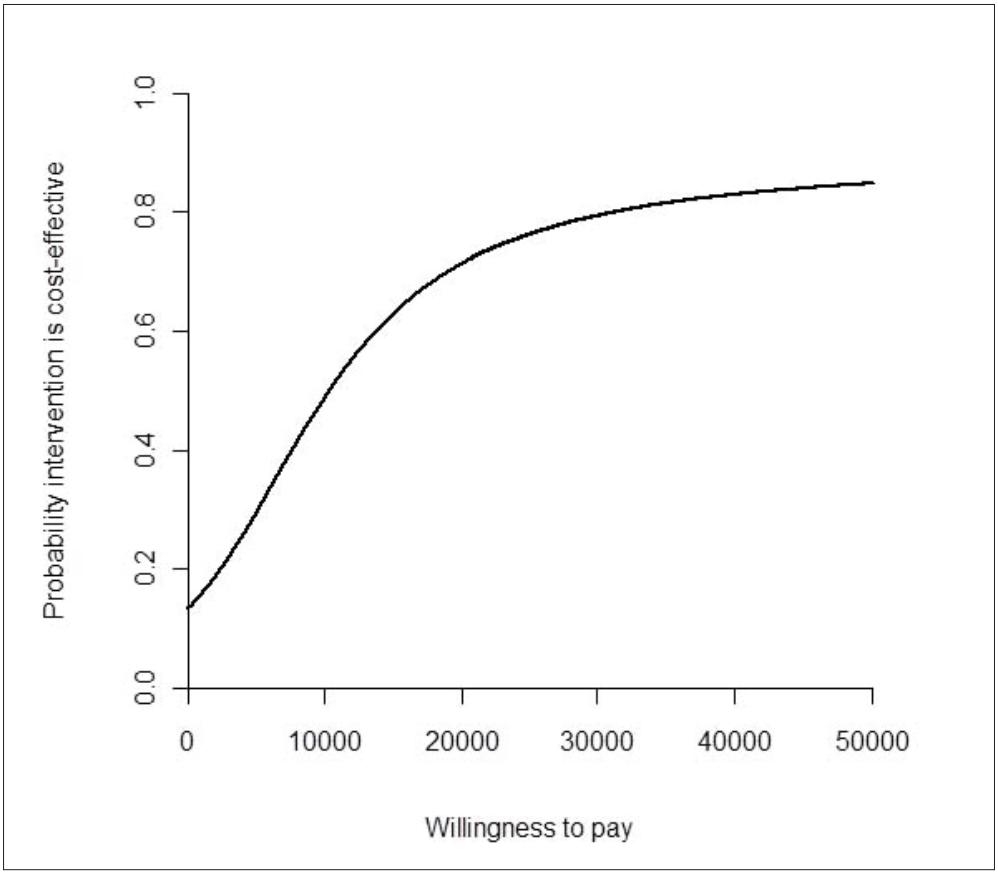

Figure 2. Willingess to pay (€ per prevented case of depression or anxiety).

northwest quadrant and 40% in the northeast quadrant (Figure 1), confirming that there were no statistically significant differences in effects and costs. The accompanying CEA curve shows that the probability that the intervention was cost-effective ranged from 0.13 if WTP is €0 to 0.46 if WTP is $+\infty$ (Figure 2).

The ICER for the incidence of depression was -10293, meaning that prevention of depression in 1 patient extra in the intervention group is associated with an extra cost of €10,293 in comparison with usual care (Table 5). Most bootstrapped cost-effect pairs (79%) were situated in the northeast quadrant of the CE plane, indicating that the intervention was more expensive and more effective than usual care. The accompanying CEA curve shows that for WTP rates of €0, €5000, €10,000 and €20,000 the probability that the intervention was cost-effective in comparison with usual care was 0.13, 0.28, 0.48 and 0.72, respectively.

The intervention was not considered cost-effective in comparison with usual care for preventing anxiety disorders, since the incidence of anxiety was increased

Outcome	Costs	Effects	ICER	Distribution on CE plane			
				NE	SE	SW	NW
Incidence depression	838 (-593 ; 2420)	-0.08 (-0.21 ; 0.04)	-10293	79%	12%	1%	8%
Incidence anxiety	838 (-593 ; 2420)	0.08 (-0.03 ; 0.19)	10328	6%	1%	12%	81%
Incidence depression or anxiety	838 (-593 ; 2420)	0.01 (-0.14 ; 0.16)	85521	40%	6%	7%	47%
Improvement CES-D	838 (-593 ; 2420)	-2.3 (-4.8 ; 0.21)	-364	84%	13%	0%	3%
QALYs	838 (-593 ; 2420)	0.03 (-0.03 ; 0.09)	26890	73%	12%	1%	14%

Table 5. Results of the multiply imputed cost-effectiveness analyses.

in the intervention group. The distribution of the bootstrapped cost-effect pairs on the CE plane confirms this with the majority of the pairs lying in the northwest quadrant (more expensive, less effective). The cost-effectiveness analysis of improvement in CES-D score indicated greater effectiveness of the intervention accompanied by non-significantly higher costs. The probability of the intervention being cost-effective in comparison with usual care was 0.95 or more for WTP values of €3500 or more. With regard to QALYs the intervention was not considered cost-effective in comparison with usual care (probability intervention was cost-effective according to the CEA curve ranged from 0.13 if WTP is €0 to 0.85 if WTP is $+\infty$).

Discussion

This study shows that a stepped care prevention programme for people in elderly homes was unsuccessful in preventing depressive and anxiety disorders together compared with usual care. The incidence of depression in the intervention group was substantially lower than in the usual care group, but this difference was not statistically significant. Moreover, the incidence of anxiety was statistically non-significantly higher than in the usual care group. Costs in the intervention group were non-significantly higher than in the usual care group. Based on these findings, the stepped care intervention was not considered cost-effective in comparison with usual care.

There is a discrepancy between the findings of the clinical paper and this analysis with regard to incidence of depression. Although the difference between the intervention and usual care group is equal in both analyses (8%), despite the

different imputation methods used, this difference was statistically significant in the clinical analyses and non-significant in this cost-effectiveness analysis. This discrepancy is caused by the difference in analysis methods. In the clinical analyses, the results were adjusted for clustering and variables related to dropout, while unadjusted estimates are presented here.

The mean total costs of the stepped care prevention programme were €209 per resident. This compares favourably with the costs of the programme evaluated by Van 't Veer-Tazelaar et al (€532). This difference can be mainly explained by the fact that residents were coached by the residential home staff during the self-help intervention in this study instead of more expensive nurses as employed by Van 't Veer-Tazelaar et al. However, this may also be a (partial) explanation for the lack of effect of the programme evaluated in this study. Total societal costs in our study were considerably higher than in the study by Van 't Veer-Tazelaar et al. This is in line with our expectations, since this study included a residential population, while the study by Van 't Veer-Tazelaar et al included a community-dwelling population. To the best of our knowledge, no other papers have been published that present a cost-effectiveness analysis of an intervention to prevent depression and/or anxiety in an institutionalised population.

The most important limitation of this study is the dropout rate. The poor response is probably due to the overall poor functional status of the residents living in elderly homes (which is why they live in these homes). Dropout was related to allocation status, indicating potential bias due to selective loss of participants. We tried to overcome this limitation by applying multiple imputation to estimate missing values for participants with incomplete data. Multiple imputation is a technique that incorporates the uncertainty associated with estimating values for missing data. Research indicates that this imputation method provides more accurate estimates of missing data in economic evaluations than naïve methods, like (conditional) mean imputation and last observation carried forward (LOCF) (37;38). However, the selective dropout also indicates that implementation of the stepped care programme was difficult in this vulnerable population. The cost-effectiveness of the stepped care programme in comparison with usual care may be improved, if the acceptability and uptake of the programme can be increased. Another limitation is the statistical power of the study. The study was powered on clinical outcomes. However, during the analysis phase it turned out that the study was underpowered for both clinical and economic outcomes. Therefore, the results of the study should be interpreted cautiously.

Strengths of this study include the fact that this was a pragmatic study with few a priori exclusion criteria resembling usual circumstances as much as possible. This greatly enhances the generalisability of our results to other residential homes in The Netherlands. A second strength is that costs were measured from a soci-

etal perspective which enabled us to monitor whether there were important shifts in healthcare costs due to the intervention. Thirdly, a stepped care approach was implemented in this study. This approach ensures that only people in need of more intensive care receive this care. This is important, since resources are scarce and need to be reserved for people really needing them. Finally, a structured diagnostic interview was used to diagnose anxiety and depressive disorders, which enhances the credibility of the outcomes reported in this trial.

In conclusion, the stepped care prevention programme tested in this study was not cost-effective in comparison with usual care. The positive effect on depressive disorders is encouraging, but should be investigated further especially considering the negative effect on anxiety. Research should indicate which elements of the intervention are effective and how these elements can be offered in a cost-effective way to residents of elderly homes at risk for depression. However, it is also possible that the emphasis on mental functioning of the intervention investigated in this study may have scared off the participants. Perhaps integrated care interventions similar to the one evaluated by Boorsma et al with a wider scope and aiming to influence both mental and physical functioning,(39) are the way forward.

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