

# Stepped-Care Prevention of Anxiety and Depression in Late Life

## *A Randomized Controlled Trial*

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**Context:** Given the public health significance of late-life depression and anxiety, and the limited capacity of treatment, there is an urgent need to develop effective strategies to prevent these disorders.

**Objective:** To determine the effectiveness of an indicated stepped-care prevention program for depression and anxiety disorders in the elderly.

**Design:** Randomized controlled trial with recruitment between October 1, 2004, and October 1, 2005.

**Setting:** Thirty-three primary care practices in the north-western part of the Netherlands.

**Participants:** A total of 170 consenting individuals, 75 years and older, with subthreshold symptom levels of depression or anxiety who did not meet the full diagnostic criteria for the disorders.

**Intervention:** Participants were randomly assigned to a preventive stepped-care program (n=86) or to usual care (n=84). Stepped-care participants sequentially received a watchful waiting approach, cognitive behavior

therapy-based bibliotherapy, cognitive behavior therapy-based problem-solving treatment, and referral to primary care for medication, if required.

**Main Outcome Measures:** The cumulative incidence of DSM-IV major depressive disorder or anxiety disorder after 12 months as measured using the Mini International Neuropsychiatric Interview.

**Results:** The intervention halved the 12-month incidence of depressive and anxiety disorders, from 0.24 (20 of 84) in the usual care group to 0.12 (10 of 86) in the stepped-care group (relative risk, 0.49; 95% confidence interval, 0.24 to 0.98).

**Conclusions:** Indicated stepped-care prevention of depression and anxiety in elderly individuals is effective in reducing the risk of onset of these disorders and is valuable as seen from the public health perspective.

**Trial Registration:** isrctn.org Identifier: ISRCTN26474556.

*Arch Gen Psychiatry.* 2009;66(3):297-304

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**D**EPRESSION AND ANXIETY are common causes of reduced quality of life and impaired functioning in late life.<sup>1-3</sup> Both disorders are associated with excess rates of mortality, and have considerable economic ramifications.<sup>4-7</sup> In this study, we focus on the prevention of depression and anxiety disorders because in late life these disorders have a high prevalence, co-occur frequently, and have a significant effect on well-being and functioning.<sup>4,8-14</sup> Although important advances have been made in the treatment of anxiety and depression in elderly patients,<sup>15</sup> there is still cause for concern. Even in more affluent countries, no health service could possibly provide adequate treatment for all, and

even if such a scenario would be conceivable, formidable obstacles in case recognition, diagnosis, and provision of treatment would limit the effectiveness of the interventions at the population level.<sup>16-18</sup> A final concern is that current treatments are not as effective as we would like them to be.<sup>19,20</sup> Therefore, although treatment has improved, there is a dire need for alternative strategies, such as effective prevention programs, to alleviate the burden of disease associated with late-life anxiety and depression.

Mrazek and Haggerty<sup>21</sup> suggest 3 types of interventions to prevent mental disorders: first, "universal preventive interventions" targeted to the general population (eg, mass media campaigns); second, "selective preventive interventions" tar-

geted to population segments with increased risk of developing a mental disorder because they have been exposed to risk factors (eg, support groups for widows); and finally, "indicated preventive interventions" targeted to people with some symptoms that possibly foreshadow the onset of a mental disorder but who do not meet the *DSM-IV* diagnostic criteria. Indicated prevention aims to reduce the occurrence of new cases or to delay the onset of the disorder. In addition, indicated prevention may reduce symptom severity and the time spent in the subthreshold condition. Of the 3 types of preventive interventions, indicated prevention most closely resembles conventional treatment and has the best chance of detecting groups of individuals with subthreshold disorders, whose condition harbors a high risk of developing major anxiety or depression disorder.<sup>22-27</sup> Indicated prevention studies in subclinically depressed populations have shown a reduction in the incidence of depression by 25%.<sup>28</sup>

Taking into account the seriousness of depression and anxiety in late life and the possibilities of a preventive approach, the next step was to conduct an evaluation of an indicated prevention program designed to reduce the incidence of anxiety and depressive disorders in elderly people. The intervention applied in the present study was a stepped-care program.<sup>29,30</sup> The aim of stepped-care models is to maximize the effectiveness of an intervention while making the best use of available resources. Although stepped care seems to be a logical approach from clinical and economic perspectives, few studies have investigated the effects of stepped-care programs, none of which focused on preventive interventions. We hypothesize that a stepped-care program designed to reduce the incidence of major depressive and anxiety disorders, offered to elderly people with subthreshold depressive or anxiety symptoms, would be more effective than the usual care provided.

## METHODS

### DESIGN

We conducted a pragmatic randomized clinical trial in 2 parallel groups. The intervention was intended to be flexible, to be closely linked with real-life situations, and to easily fit in with routine clinical care. Participants were allowed to accept or reject parts of the treatment. Randomization took place after the baseline measurements, and participants were randomized with equal probability to either usual care or the preventive intervention in blocks of 4 by an independent statistician using random-number tables. The main clinical outcome was the cumulative 12-month incidence of anxiety (panic disorder, agoraphobia, social phobia, and generalized anxiety) and depressive disorder meeting the *DSM-IV* diagnostic criteria and measured using the Mini International Neuropsychiatric Interview (MINI) at 6 and 12 months. In this project we used Mini Manager 2.0 (created by Edwin de Beurs, Netherlands Institute of Forensic Psychiatry and Psychology), a computer-assisted version of the Dutch MINI (5.0). The interviewers who measured the primary outcome were kept unaware of the randomization status of the participants. The trial was powered to detect a difference of 25% in the cumulative incidence rates of MINI/*DSM-IV* anxiety and depressive disorders between the conditions across 1 year. These differences were expected to

be 35% in the usual care group and 10% in the intervention group on the basis of longitudinal studies.<sup>31,32</sup> We calculated that 65 participants per group would be needed, assuming a 2-sided test at  $\alpha = .05$  and a power of  $(1 - \beta) = 0.90$ .

To test the impact of the intervention on Center for Epidemiologic Studies Depression Scale (CES-D) scores across time (3, 6, 9, and 12 months), we conducted a generalized estimating equation analysis for Gaussian-distributed data. The study protocol was approved by the Medical Ethics Committee of the VU University Medical Center.

### PARTICIPANTS

Eligible individuals for this project were identified from the study population of a large prevention project, the PIKO project (Preventive Intervention for Frail Elderly), and were recruited between October 1, 2004, and October 1, 2005. The PIKO project was based on the results of a self-rated health inventory completed by general-practice patients 75 years and older. The PIKO database provided data for 3 studies.<sup>33-35</sup> The health inventory included several questionnaires on which the recruitment of participants for the 3 studies was based. For this project, it entailed the self-report CES-D, a screening questionnaire for subthreshold depression and anxiety. Individuals in the PIKO database with a CES-D score of 16 or greater were approached regarding participation in the stepped-care prevention project. People 75 years and older with a relevant score on the CES-D screening questionnaire who did not meet the *DSM-IV* criteria for depressive or anxiety disorder according to the MINI during the past 12 months were included in the trial. Anxiety disorder entailed the following: panic disorder, agoraphobia, social phobia, or generalized anxiety disorder. Eligible individuals gave informed consent before inclusion. Elderly individuals with serious cognitive decline according to the self-rated IQCODE (Informant Questionnaire on Cognitive Decline in the Elderly) were excluded.<sup>34</sup>

The aforementioned PIKO self-rated health inventory, including the CES-D, was sent to 5207 elderly individuals. These individuals were registered in 33 primary care practices in the northwestern region of the Netherlands. The total number of people 75 years and older who consented to being screened was 5207. Of these, 2850 (54.7%) completed the CES-D, resulting in 886 screen positives with CES-D scores of 16 or greater.<sup>36</sup> Subsequently, 325 elderly individuals were randomly approached for participation in the stepped-care anxiety and depression prevention trial. Reckoning with 50% attrition, we would still have enough participants per group to detect a difference of 25% in the cumulative incidence rates of MINI/*DSM-IV* anxiety and depressive disorders between the conditions across 1 year. Of the 325 approached elderly individuals, 170 (52.3%) met the inclusion criteria and were randomized. Of the remaining 155 individuals, 105 (67.7%) did not meet the inclusion criteria and 50 (32.3%) withdrew their consent before randomization (**Figure**).

### INTERVENTION

It is consistently described that subclinical manifestations of depressive and anxiety disorders are the best predictors of the onset of full-blown disorders.<sup>22-24,37</sup> It is also understood that the subclinical manifestations are amenable, particularly through preventive cognitive behavior therapy-based bibliotherapy and problem-solving treatment (PST), as is evidenced by a meta-analysis of randomized prevention trials.<sup>28</sup> Both treatment types help individuals acknowledge their symptoms and encourage them to switch to more active self-management strategies. This makes bibliotherapy and PST promising candidates for pre-

vention; for this reason, we chose them for steps 2 and 3, respectively.

The stepped-care program consisted of the following 4 steps lasting 3 months each (**Table 1**):

**Step 1: Watchful waiting.** Participants with a minimum CES-D score of 16 were invited to complete a second CES-D questionnaire after 3 months. These first 3 months constituted a period of watchful waiting, which is appropriate because it is known that depressive symptoms disappear spontaneously in many cases. However, if the second measurement revealed a score at or above the cutoff point, the participant underwent a diagnostic MINI. If no depressive or anxiety disorder could be established (ie, a negative MINI result), then it was concluded that the participant had only subthreshold levels of depression or anxiety. Participants who met these criteria were randomized.

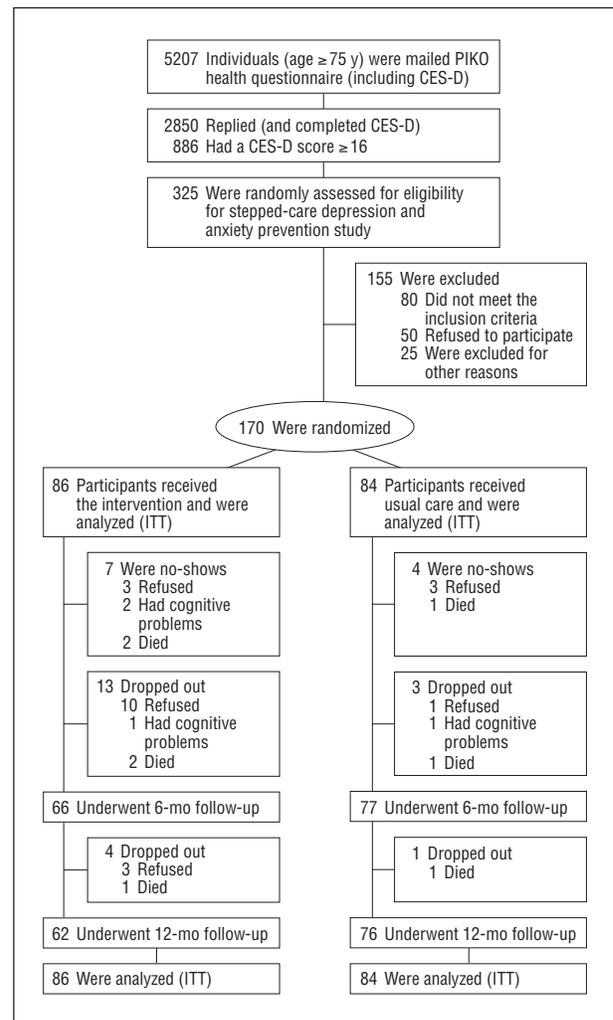
The interventions in the following steps were offered to participants with continuous depressive and anxiety symptoms (CES-D score of  $\geq 16$ ) as measured at every start of the following 3 months.

**Step 2: Cognitive behavior therapy–based bibliotherapy.** Participants received a telephone call in which the intervention was explained. After the call, participants were visited by a specially trained home care nurse who delivered a brochure that contained information about mild depression and anxiety and simple advice on how to cope with anxiety and depressive symptoms. During a subsequent visit, a self-help course (Coping With Depression) was offered to participants.<sup>38–40</sup> For this study, the Coping With Depression course was extended to a Coping With Depression and Anxiety version and was adapted for individual use by people 75 years and older. The Coping With Depression and Anxiety course helps people improve social skills, address depressogenic or anxiogenic thinking, and increase pleasant activities and relaxation to cope with problems assumed to be related to one's depression or anxiety. Participants worked through the course at their convenience. The nurse made visits (mean [SD], 3 [1]) or telephone calls (mean [SD], 2 [0.5]) to encourage participants to continue with the course. After 3 months, an evaluation form was completed by the nurse.

**Step 3: Brief cognitive behavior therapy–based PST.** In this step, participants were offered PST, which is a brief cognitive behavioral intervention that focuses on practical skill building. It consists of 7 sessions during which the stages of problem solving are explained and then applied to problems that are encountered in daily life. The goal of PST is to help patients regain control of their lives.<sup>41,42</sup> Again, participants first received information about the intervention via telephone. If the participant agreed, a specially trained community psychiatric nurse made the first appointment for a visit. All the nurses were familiar with the PST protocol, were trained during a 2-day PST workshop, and had to attend monthly supervision meetings. Treatment integrity in this phase was monitored through tape recordings of the sessions. The task of these nurses was to help participants acquire problem-solving skills. At the end of the intervention, an evaluation form was completed by the nurse.

**Step 4: Referral to primary care.** Participants with continuously elevated CES-D scores received written advice to discuss suitable medications (ie, antidepressant or anti-anxiety medications) with their primary care physician.

To summarize, the flow of participants in the intervention group through the stepped-care program depended on having their symptoms measured using the CES-D every 3 months for 1 year. Participants who still had elevated symptom levels after the conclusion of an intervention were offered participation in the next step. A score below the cutoff point resulted in a period of watchful waiting until an elevated CES-D score indicated the need for the following step of the intervention. People



**Figure.** Flowchart of participants in the trial. CES-D indicates Center for Epidemiologic Studies Depression Scale; ITT, intention to treat; PIKO, Preventive Intervention for Frail Elderly.

who met the MINI diagnostic criteria for the disorders at baseline or at 6 or 12 months, which was considered the main clinical outcome, were referred to their primary care physician.

## USUAL CARE

Participants in the usual care group had unrestricted access to usual care for their depression or anxiety concerns. Their health care uptake (including their use of prescription medications) was recorded.

## MEASURES

The MINI was administered by trained interviewers at baseline and at 6 and 12 months. The MINI<sup>43,44</sup> is a brief structured diagnostic interview developed by psychiatrists and physicians in the United States and Europe for *DSM-IV* and *ICD-10* psychiatric disorders. With an administration time of approximately 20 minutes, the MINI has become the structured interview of choice for psychiatric evaluation in many clinical trials and epidemiologic studies.

The CES-D<sup>45–48</sup> was used to screen for subthreshold depression and anxiety at baseline and after 3, 6, 9, and 12 months. It consists of 20 items and has a total score ranging from 0 to 60. Minimum scores of 16 indicate clinically significant levels of de-

**Table 1. Clinical Pathway of the Stepped-Care Program**

	Step 1	Step 2	Step 3	Step 4
CES-D score $\geq 16$	Watchful waiting	Bibliotherapy	PST	Medication
CES-D score $< 16$	Watchful waiting	Watchful waiting	Watchful waiting	Watchful waiting

Abbreviations: CES-D, Center for Epidemiologic Studies Depression Scale; PST, problem-solving treatment.

**Table 2. Baseline Characteristics of the Participants**

Characteristic	Intervention Group (n = 86)	Usual-Care Group (n = 84)	Total (N = 170)
Female sex, No. (%)	60 (69.8)	65 (77.4)	125 (73.5)
Age, mean (SD), y	81.8 (3.8)	81.1 (3.5)	81.4 (3.7)
Married or living with partner, No. (%)	26 (30.2)	24 (28.6)	50 (29.4)
Education beyond high school, No. (%)	24 (27.9)	22 (26.2)	46 (27.1)
Rural residence (<10 000 inhabitants), No. (%)	36 (41.9)	39 (46.4)	75 (44.1)
Chronic diseases ( $>2$ ), No. (%)	36 (41.9)	45 (53.6)	81 (47.7)
CES-D score, mean (SD)	21.2 (5.0)	22.1 (5.2)	21.6 (5.1)

Abbreviation: CES-D, Center for Epidemiologic Studies Depression Scale.

pressive symptoms. The CES-D has been found to be a satisfactory instrument with which to screen for anxiety disorders.<sup>47</sup>

## STATISTICAL ANALYSIS

The analyses were performed in agreement with the intention-to-treat principle, that is, all participants were analyzed in the group to which they were randomized. The analyses were performed using a software program (Stata version 8.2; StataCorp LP, College Station, Texas), in several steps. First, we present descriptive statistics of the baseline characteristics of the intervention group, the usual care group, and total participants (**Table 2**).

Second, the intention-to-treat approach requires that analyses of outcome data are based on all randomized participants, and, therefore, missing observations need to be replaced by their most likely values while also taking into account the mechanism that generated the missing values. To that end, predictors of outcome and missingness were identified. Predictors of outcome help obtain the most precise values of the outcome variable, and predictors of missingness help correct for the bias that may be caused by differential loss to follow-up, as far as differential dropout is related to available predictors. The statistically significant predictors were duly used in a regression imputation (as implemented in Stata) to obtain the required predicted values. By way of sensitivity analysis, we also used 2 other imputation strategies. First, we repeated the main analysis, basing it on multiple imputation. To that purpose, missing end points were not replaced by a single estimate but by 10 new estimates. For this we used the Stata hotdeck procedure stratified for baseline CES-D score (dichotomized at 20) and age (dichotomized at 81 years) because these variables were predictors of outcome and loss to follow-up, respectively. Compared with regression imputation, this approach produces more conservative outcomes that strengthen the null hypothesis of no effect. Finally, we applied a worst-case scenario and replaced missing scores with scores indicating that a depressive or anxi-

ety disorder had occurred. This was the most conservative way to handle missing end points.

Third, to test the hypothesis that the intervention would be more successful than usual care in reducing the risk of depression and anxiety disorders, we performed a logistic regression analysis of the outcome (1 = disordered and 0 = disorder free) on the treatment indicator (0 = usual care and 1 = intervention) to obtain the odds ratio (OR) that describes the reduction in the risk of a MINI/DSM-IV depressive or anxiety disorder in the intervention group relative to the control group. The superiority of the intervention would be supported if the OR fell below 1 (indicating risk reduction) and would be significant at  $P < .05$ , 2-tailed. This analysis was conducted 3 times for each of the different imputation strategies. To gauge the robustness of the findings, we also performed a Poisson regression analysis to obtain the person-time-based incidence rate ratio and repeated the test of the hypothesis under this model specification.

Fourth, following the pertinent CONSORT (Consolidated Standards of Reporting Trials) guideline, we obtained the number needed to treat as the inverse of the risk difference. The risk difference was obtained by regressing the outcome on the treatment indicator variable in a linear probability model. The latter was specified as a generalized linear model for a binary outcome, with identity as the link function.

To test the impact of the intervention on CES-D scores across time, we evaluated the group  $\times$  time interactions for each of the time points (3, 6, 9, and 12 months) on the CES-D scores under a generalized estimating equation model.

## RESULTS

### PARTICIPANT FLOW

People with a CES-D score of 16 or greater who did not meet the diagnostic criteria for MINI/DSM-IV depressive or anxiety disorder were invited to participate in the stepped-care prevention program (n = 325). Of these, 170 met all the inclusion criteria and gave informed consent. They were randomized to the intervention (n = 86) or the usual care (n = 84) condition (Figure).

### BASELINE CHARACTERISTICS

The participants were mainly women (73.5%) and had a mean (SD) age of 81.4 (3.7) years (Table 2). About 30% of the participants were married or living with a partner, and 72.9% had an educational level that was lower than or equivalent to the completion of high school. Almost 50% had more than 2 chronic physical diseases (such as ischemic heart disease and arthritis). At baseline, the mean (SD) CES-D score was 21.6 (5.1). There were no significant differences in sociodemographic or clinical characteristics between the intervention and usual care groups.

Regarding previous episodes of anxiety or depressive disorders, 24 participants (14.1%) reported a disorder that

**Table 3. Uptake of Interventions of the Stepped-Care Program by Quarter**

Characteristic	Participants, No. (%)			
	0-3 mo (n = 79)	4-6 mo (n = 66)	7-9 mo (n = 64)	10-12 mo (n = 62)
Bibliotherapy	79 (100)			
Problem-solving treatment		23 (34.8)	14 (21.9)	6 (9.7)
Referral to primary care physician			12 (18.8)	13 (21.0)

had remitted more than a year preceding randomization. These 24 participants were distributed evenly across the conditions: 11 in the intervention condition and 13 in the usual care condition.

### ANALYSIS OF DROPOUT

We systematically assessed whether dropout was associated with any characteristics of the participants as measured at baseline. We found that dropout was not associated with baseline depression score (CES-D), age, sex, educational level, living in a supported environment, the presence of a somatic illness, or living alone. However, dropout was associated with randomization status, in particular with being a participant in the intervention group ( $\chi^2=9.398, P=.002$ ) (Figure).

### OUTCOMES

In the intervention group, 10 of 86 participants (11.6%) developed a major disorder, which compares favorably with the control group, in which 20 of 84 participants (23.8%) developed a major disorder, resulting in a relative risk of 0.49 (95% confidence interval [CI], 0.24 to 0.98). The intervention reduced the odds of developing a depressive or anxiety disorder by 57.9% (OR, 0.42%; 95% CI, 0.18% to 0.96%), concerning the first-ever onset of these disorders in most participants. The null hypothesis of no effect had to be rejected (SE=0.18;  $z=-2.05; P=.04$ ), thus lending support to the alternative hypothesis that the intervention is superior to usual care.

To gauge the robustness of the outcome, we repeated the first analysis, basing it this time on multiple imputation. This resulted in an OR of 0.34 (95% CI, 0.20 to 0.61), which was significant (SE=0.252;  $t=4.227; P<.001$ ), thus replicating the previous results. And finally, the worst-case analysis provided an OR of 1.19 (95% CI, 0.63 to 2.23), no longer significant (SE=0.38;  $z=-0.53; P=.60$ ).

The first analysis was replicated, using Poisson regression analysis: for this analysis, we obtained the person-time-based incidence rate ratio of 0.47, again confirming that the risk of disease onset is more than halved by the intervention. The incidence rate ratio had a 95% CI of 0.22 to approximately 1.00 (rounded) and was significant (SE=0.181;  $z=-1.97; P=.049$ ).

We obtained the number needed to treat as the inverse of the risk difference. The risk difference was 0.12 in favor of the intervention (95% CI, -0.236 to -0.007; SE=0.058;  $t=-2.10; P=.04$ ), which lent support to the alternative hypothesis. Its inverse, the number needed to treat, was  $1/0.122=8.2$ , which indicated that the onset of major de-

pression or anxiety disorder was prevented in 1 of every 8 people who received the intervention rather than usual care.

The generalized estimating equation model showed the following coefficients for the group  $\times$  time interactions for each of the time points on the CES-D scores: 8.2, 11.1, 12.1, and 12.2, indicative of substantial clinical superiority of the intervention compared with care as usual. The interaction terms were significant: for 3 months at  $P=.008$  and for all other time points at  $P<.001$ . This was replicated under the random-effects model, which produced nearly identical results.

After 1 year, the intervention group showed 4 depressive disorders, 3 anxiety disorders, and 2 co-occurrences of depression and anxiety. In the usual-care group, we found 10 depressive disorders, 5 anxiety disorders, and 5 co-occurrences. The distribution was compared across the 2 groups and was not significant ( $\chi^2=0.2158; P=.90$ ).

### USUAL CARE

During the first year of the study, we found that 23 participants in the usual-care group received antidepressant or anxiolytic-sedative medications vs 28 in the intervention group (which was not significant [ $P=.28$ ]). Regarding counseling or other types of psychoeducational or psychosocial interventions, 2 participants in the usual-care group mentioned that they had read information about depression or anxiety.

### ACCEPTABILITY

To obtain an impression of the acceptability of the intervention, we investigated “no shows,” “dropouts” (Figure), and the intervention uptake.

At the start of the study, 7 of the 86 intervention group participants and 4 of the 84 usual-care group participants chose not to participate. These 7 intervention and 4 usual-care individuals were referred to as *no shows* (Figure). A 2-tailed Fisher exact test suggested the absence of any significant effect ( $P=.54$ ). We then investigated the dropout rate across the conditions in those who did participate. We had 79 remaining intervention participants and 80 in the usual-care group. During the first 6 months, the dropout category showed 13 intervention participants (10 refusals) and 3 usual-care participants. The second 6-month period showed 4 and 1 dropouts, respectively. Dropout occurred at a significantly higher rate in the intervention group ( $P=.009$ , 2-tailed Fisher exact test) (Figure). A certain amount of dropout was due to mortality. In the intervention group,

3 of 79 active participants died, and, in the usual-care group, 2 of 80 active participants died. Mortality was not related to either condition ( $P = .99$ , 2-tailed Fisher exact test).

Data on the uptake of the interventions of the stepped-care prevention program are given in **Table 3**. No participants refused bibliotherapy, 9 refused PST, and none refused the written advice to discuss suitable medications with their primary care physician. As Table 3 shows, the stepped-care strategy was considerably successful. We will return to the acceptability of the intervention in the "Comment" section.

## COMMENT

### MAIN FINDINGS

The aim of this study was to test the hypothesis that an indicated stepped-care intervention to prevent depressive and anxiety disorders in people 75 years and older is more effective than usual care alone. These data suggest that the intervention halved the 1-year cumulative incidence rate of the disorders, and the null hypothesis of equal effectiveness had to be rejected in favor of the alternative hypothesis that the intervention is more effective than usual care in reducing the risk of major depression and anxiety.

### STRENGTHS AND LIMITATIONS

This study has several strengths. The screening procedure identified a number of elderly individuals with depressive and anxiety symptoms who are usually not recognized by their primary care physicians as having problems. This finding is corroborated by evidence found by the US Preventive Services Task Force<sup>49</sup> in 2002 that screening improves identification of depressed patients in primary care settings. Another strong feature of this study is the fact that it was based on the empirically supported Improving Mood: Promoting Access to Collaborative Care Treatment (IMPACT) study.<sup>30</sup> Similar to the IMPACT study, the present intervention included information and options for engaging in brief psychotherapy sessions or pharmacotherapy treatments in the context of a stepped-care program. Unlike the IMPACT study, the present intervention was directed at elderly people ( $\geq 75$  years) and focused on depressive symptoms as opposed to diagnosed major depressive disorder, but then this program is "indicated prevention" and not treatment. A further strength of this intervention is that it also addressed anxiety, which is especially relevant in light of the high comorbidity between mood disorders and anxiety disorders.

A limitation of the study design is that it is impossible to assess the specific contributions of each of the various elements of the stepped-care program. In the analysis, the intervention had to be treated as a whole; a completely different study design would be required to deconstruct this package into its components. Another limitation concerns the differential dropout rates, which are of concern because they may indicate that the inter-

vention requires an extra effort from some participants, despite the apparent successful uptake of the intervention by others. The differential dropout rates may also have affected the results of the study. However, to overcome this problem, we performed intention-to-treat analysis based on 3 different imputation techniques, and in all instances we obtained nearly identical results, which underscores the robustness of the findings.

### PUBLIC HEALTH SIGNIFICANCE

Existing health care systems have difficulties addressing the demand for treatment of the vastly increasing number of elderly people in the population and can only avert a fraction of the total disease burden that is attributable to mental disorders.<sup>17,18</sup> In this context, it is important to prevent the onset of mental disorders. To our knowledge, this study is one of the first that supplies evidence that such an endeavor is effective: these results show that the risk of anxiety and depressive disorders can be halved when targeting a high-risk group of people with sub-threshold manifestations of the pertinent disorders. To halve the incidence rate of such crippling conditions is a feat in itself but, better still, the favorable results were achieved in a possibly economically affordable stepped-care program. After all, low-cost interventions were offered first, outcomes were monitored, and only if the interventions failed to maintain anxiety and depressive symptoms at acceptable levels were more intensive interventions offered. This makes the approach not only clinically effective but also potentially cost-effective.

Only long-term follow-up assessments will shed light on whether this intervention prevented or delayed mental illness. However, given the often chronic nature of anxiety and depressive disorders, the more realistic assumption is that we delayed onset in most participants rather than offering an enduring prophylaxis.<sup>50</sup> Although the latter is preferable, delay of onset is important in its own right given the disabling nature of these disorders. Every year lived without an avoidable depressive or anxiety disorder will result in considerably less suffering by patients and their families.<sup>28</sup>

We now need to gain better understanding about some remaining issues: the long-term effects of the intervention, the identification of target groups that would benefit most from the intervention, and the cost-effectiveness of the intervention.

**Submitted for Publication:** March 24, 2008; accepted August 5, 2008.

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**Financial Disclosure:** None reported.

**Funding/Support:** This work was supported by grant 2620.0003 from the Netherlands Health Research Council (ZonMw).

**Role of the Sponsor:** The sponsor provided financial support for the study only and had no role in the design or conduct of the study; the collection, management, analy-

sis, and interpretation of the study; or the preparation, review, or approval of the manuscript.

**Previous Presentation:** This study was presented in part at the British Society of Gerontology Conference; September 7, 2007; Sheffield, England.

**Additional Information:** The intervention entailed the Coping With Depression group course and the brief cognitive behavioral therapy. The Coping With Depression course was revised to cover the topic of anxiety and was adapted for individual use in a population 75 years and older. The intervention protocols were developed in collaboration with the Trimbos Institute (Institute of Mental Health and Addiction, the Netherlands) and a group led by Dr Laurence Mynors-Wallis (UK), respectively. In this project we used MiniManager 2.0 (created by Edwin de Beurs, Netherlands Institute of Forensic Psychiatry and Psychology), a computer-assisted version of the Dutch MINI (5.0).

## REFERENCES

- Unützer J, Bruce ML; NIMH Affective Disorders Workgroup. The elderly. *Ment Health Serv Res.* 2002;4(4):245-247.
- de Beurs E, Beekman AT, van Balkom AJ, Deeg DJ, van Dyck R, van Tilburg W. Consequences of anxiety in older persons: its effect on disability, well-being and use of health services. *Psychol Med.* 1999;29(3):583-593.
- Lyness JM, Kim J, Tang W, Tu X, Conwell Y, King DA, Caine ED. The clinical significance of subsyndromal depression in older primary care patients. *Am J Geriatr Psychiatry.* 2007;15(3):214-223.
- Beekman AT, de Beurs E, van Balkom AJ, Deeg DJ, van Dyck R, van Tilburg W. Anxiety and depression in later life: co-occurrence and communality of risk factors. *Am J Psychiatry.* 2000;157(1):89-95.
- Reynolds CF III, Kupfer DJ. Depression and aging: a look to the future. *Psychiatr Serv.* 1999;50(9):1167-1172.
- Katon WJ, Schoenbaum M, Fan MY, Callahan CM, Williams J Jr, Hunkeler E, Harpole L, Zhou XH, Langston C, Unützer J. Cost-effectiveness of improving primary care treatment of late-life depression. *Arch Gen Psychiatry.* 2005;62(12):1313-1320.
- Smit F, Cuijpers P, Oostenbrink J, Batelaan N, de Graaf R, Beekman A. Costs of nine common mental disorders: implications for curative and preventive psychiatry. *J Ment Health Policy Econ.* 2006;9(4):193-200.
- Burns DD, Eidelson RJ. Why are depression and anxiety correlated? a test of the tripartite model. *J Consult Clin Psychol.* 1998;66(3):461-473.
- de Beurs E, Beekman A, Geerlings S, Deeg D, van Dyck R, van Tilburg W. On becoming depressed or anxious in late life: similar vulnerability factors but different effects of stressful life events. *Br J Psychiatry.* 2001;179:426-431.
- Leclercq Y. The burden of depression and anxiety in general medicine. *J Clin Psychiatry.* 2001;62(suppl 8):4-9.
- Lenze EJ, Mulsant BH, Shear MK, Schulberg HC, Dew MA, Begley AE, Pollock BG, Reynolds CF III. Comorbid anxiety disorders in depressed elderly patients. *Am J Psychiatry.* 2000;157(5):722-728.
- Schoevers RA, Deeg DJ, van Tilburg W, Beekman AT. Depression and generalized anxiety disorder: co-occurrence and longitudinal patterns in elderly patients. *Am J Geriatr Psychiatry.* 2005;13(1):31-39.
- Diefenbach GJ, Goethe J. Clinical interventions for late-life anxious depression. *Clin Interv Aging.* 2006;1(1):41-50.
- Bunevicius A, Peceliuniene J, Mickuviene N, Valius L, Bunevicius R. Screening for depression and anxiety disorders in primary care patients. *Depress Anxiety.* 2007;24(7):455-460.
- Pinquart M, Duberstein PR, Lyness JM. Treatments for later-life depressive conditions: a meta-analytic comparison of pharmacotherapy and psychotherapy. *Am J Psychiatry.* 2006;163(9):1493-1501.
- Docherty JP. Barriers to the diagnosis of depression in primary care. *J Clin Psychiatry.* 1997;58(suppl 1):5-10.
- Chisholm D, Sanderson K, Ayuso-Mateos JL, Saxena S. Reducing the global burden of depression: population-level analysis of intervention cost-effectiveness in 14 world regions. *Br J Psychiatry.* 2004;184:393-403.
- Andrews G, Issakidis C, Sanderson K, Corry J, Lapsley H. Utilising survey data to inform public policy: comparison of the cost-effectiveness of treatment of ten mental disorders. *Br J Psychiatry.* 2004;184:526-533.
- Wisniewski SR, Fava M, Trivedi MH, Thase ME, Warden D, Niederehe G, Friedman ES, Biggs MM, Sackeim HA, Shores-Wilson K, McGrath PJ, Lavori PW, Miyahara S, Rush AJ. Acceptability of second-step treatments to depressed outpatients: a STAR\*D report. *Am J Psychiatry.* 2007;164(5):753-760.
- Turner EH, Matthews AM, Linardatos E, Tell RA, Rosenthal R. Selective publication of antidepressant trials and its influence on apparent efficacy. *N Engl J Med.* 2008;358(3):252-260.
- Mrazek PJ, Haggerty RJ, eds; Committee on Prevention of Mental Disorders, Institute of Medicine. *Reducing Risks for Mental Disorders: Frontiers for Preventive Intervention Research.* Washington, DC: National Academies Press; 1994.
- Smit F, Ederveen A, Cuijpers P, Deeg D, Beekman A. Opportunities for cost-effective prevention of late-life depression: an epidemiological approach. *Arch Gen Psychiatry.* 2006;63(3):290-296.
- Smit F, Comijs H, Schoevers R, Cuijpers P, Deeg D, Beekman A. Target groups for the prevention of late-life anxiety. *Br J Psychiatry.* 2007;190:428-434.
- Schoevers RA, Smit F, Deeg DJ, Cuijpers P, Dekker J, van Tilburg W, Beekman AT. Prevention of late-life depression in primary care: do we know where to begin? *Am J Psychiatry.* 2006;163(9):1611-1621.
- Cuijpers P, Van Straten A, Smit F. Preventing the incidence of new cases of mental disorders: a meta-analytic review. *J Nerv Ment Dis.* 2005;193(2):119-125.
- Muñoz RF, Ying YW, Bernal G, Perez-Stable EJ, Sorensen JL, Hargreaves WA, Miranda J, Miller LS. Prevention of depression with primary care patients: a randomized controlled trial. *Am J Community Psychol.* 1995;23(2):199-222.
- Cole MG. Brief interventions to prevent depression in older subjects: a systematic review of feasibility and effectiveness. *Am J Geriatr Psychiatry.* 2008;16(6):435-443.
- Cuijpers P, Van Straten A, Smit F, Mihalopoulos C, Beekman A. Preventing the onset of depressive disorders: a meta-analytic review of psychological interventions. *Am J Psychiatry.* 2008;165(10):1272-1280.
- Haaga DA. Introduction to the special section on stepped care models in psychotherapy. *J Consult Clin Psychol.* 2000;68(4):547-548.
- Hunkeler EM, Katon W, Tang L, Williams JW Jr, Kroenke K, Lin EH, Harpole LH, Acrean P, Levine S, Grypma LM, Hargreaves WA, Unützer J. Long term outcomes from the IMPACT randomised trial for depressed elderly patients in primary care. *BMJ.* 2006;332(7536):259-263.
- Beekman AT, Penninx BW, Deeg DJ, Ormel J, Braam AW, van Tilburg W. Depression and physical health in later life: results from the Longitudinal Aging Study Amsterdam (LASA). *J Affect Disord.* 1997;46(3):219-231.
- Beekman AT, Bremmer MA, Deeg DJ, van Balkom AJ, Smit JH, de Beurs E, van Dyck R, van Tilburg W. Anxiety disorders in later life: a report from the Longitudinal Aging Study Amsterdam. *Int J Geriatr Psychiatry.* 1998;13(10):717-726.
- van Hout HP, Nijpels G, van Marwijk HW, Jansen AP, van't Veer PJ, Tybout W, Stalman WA. Design and pilot results of a single blind randomized controlled trial of systematic demand-led home visits by nurses to frail elderly persons in primary care [ISRCTN05358495]. *BMC Geriatr.* 2005;5:11.
- Jansen AP, van Hout HP, van Marwijk HW, Nijpels G, de Bruijne MC, Bosmans JE, Pot AM, Stalman WA. (Cost)-effectiveness of case-management by district nurses among primary informal caregivers of older adults with dementia symptoms and the older adults who receive informal care: design of a randomized controlled trial [ISRCTN83135728]. *BMC Public Health.* 2005;5:133.
- van't Veer-Tazelaar N, van Marwijk H, van Oppen P, Nijpels G, van Hout H, Cuijpers P, Stalman W, Beekman A. Prevention of anxiety and depression in the age group of 75 years and over: a randomized controlled trial testing the feasibility and effectiveness of a generic stepped care programme among elderly community residents at high risk of developing anxiety and depression versus usual care [ISRCTN26474556]. *BMC Public Health.* 2006;6:186.
- van't Veer-Tazelaar PJ, van Marwijk HW, Jansen AP, Rijmen F, Kostense PJ, van Oppen P, van Hout HP, Stalman WA, Beekman AT. Depression in old age (75+), the PIKO study. *J Affect Disord.* 2008;106(3):295-299.
- Smits F, Smits N, Schoevers R, Deeg D, Beekman A, Cuijpers P. An epidemiological approach to depression prevention in old age. *Am J Geriatr Psychiatry.* 2008;16(6):444-453.
- Lewinsohn PM, Antonuccio DO, Steinmetz JL, Teri L. *The Coping With Depression Course: A Psychoeducational Intervention for Unipolar Depression.* Eugene, OR: Castalia Publishing Co; 1984.
- Haringsma R, Engels GI, Cuijpers P, Spinhoven P. Effectiveness of the Coping With Depression (CWD) course for older adults provided by the community-based mental health care system in the Netherlands: a randomized controlled field trial. *Int Psychogeriatr.* 2006;18(2):307-325.

40. Cuijpers P. A psycho-educational approach to the treatment of depression: a meta-analysis of Lewinsohn's "Coping with Depression" course. *Behavior Therapy*. 1998; 29:521-533.
41. Schreuders B, van Oppen P, van Marwijk HW, Smit JH, Stalman WA. Frequent attenders in general practice: problem solving treatment provided by nurses [ISRCTN51021015]. *BMC Fam Pract*. 2005;6:42.
42. Mynors-Wallis L, Davies I, Gray A, Barbour F, Gath D. A randomised controlled trial and cost analysis of problem-solving treatment for emotional disorders given by community nurses in primary care. *Br J Psychiatry*. 1997;170:113-119.
43. Sheehan DV, Lecrubier Y, Sheehan KH, Amorim P, Janavs J, Weiller E, Hergueta T, Baker R, Dunbar GC. The Mini-International Neuropsychiatric Interview (M.I.N.I.): the development and validation of a structured diagnostic psychiatric interview for *DSM-IV* and *ICD-10*. *J Clin Psychiatry*. 1998;59(suppl 20):22-33.
44. Pinninti NR, Madison H, Musser E, Rissmiller D. MINI International Neuropsychiatric Schedule: clinical utility and patient acceptance. *Eur Psychiatry*. 2003; 18(7):361-364.
45. Radloff LS. The CES-D Scale: a self-report depression scale for research in the general population. *J Appl Psychol Measur*. 1977;1(3):385-401.
46. Beekman AT, Deeg DJ, Van Limbeek J, Braam AW, De Vries MZ, van Tilburg W. Criterion validity of the Center for Epidemiologic Studies Depression scale (CES-D): results from a community-based sample of older subjects in The Netherlands. *Psychol Med*. 1997;27(1):231-235.
47. Breslau N. Depressive symptoms, major depression, and generalized anxiety: a comparison of self-reports on CES-D and results from diagnostic interviews. *Psychiatry Res*. 1985;15(3):219-229.
48. Radloff LS, Teri L. Use of the Center for Epidemiological Studies-Depression Scale with older adults. *Clinical Gerontologist*. 1986;1986(5):119-136.
49. Pignone MP, Gaynes BN, Rushton JL, Burchell CM, Orleans CT, Mulrow CD, Lohr KN. Screening for depression in adults: a summary of the evidence for the U.S. Preventive Services Task Force. *Ann Intern Med*. 2002;136(10):765-776.
50. Rovner BW, Casten RJ, Hegel MT, Leiby BE, Tasman WS. Preventing depression in age-related macular degeneration. *Arch Gen Psychiatry*. 2007;64(8):886-892.