Effects of a stepped-care intervention programme among older subjects who screened positive for depressive symptoms in general practice: the PROMODE randomised controlled trial

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Effects of a stepped-care intervention programme among older subjects who screened positive for depressive symptoms in general practice: the PROMODE randomised controlled trial

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Abstract

Objectives: to determine (cost)-effectiveness of a stepped-care intervention programme among subjects ≥75 years who screened positive for depressive symptoms in general practice.
Design: the pragmatic cluster-randomised controlled trial with 12-month follow-up.
Setting: sixty-seven Dutch general practices.
Subjects: two hundred and thirty-nine subjects ≥75 years screened positive for untreated depressive symptoms (15-item Geriatric Depression Scale ≥5).
Methods: usual care (34 practices, 118 subjects) was compared with the stepped-care intervention (33 practices, 121 subjects) consisting of three steps: individual counselling; Coping with Depression course; and—if indicated—referral back to general practitioner to discuss further treatment. Measurements included severity of depressive symptoms [Montgomery-Åsberg Depression Rating Scale (MADRS)], quality of life, mortality and costs.
Results: at baseline subjects mostly were mildly/moderately depressed. At 6 months MADRS scores had improved more in the usual care than the intervention group (−2.9 versus −1.1 points, $P = 0.032$), but not at 12 months (−3.1 versus −4.6, $P = 0.084$). No significant differences were found within two separate age groups (75–79 years and ≥80 years). In intervention practices, 83% accepted referral to the stepped-care programme, and 19% accepted course participation. The control group appeared to have received more psychological care.
Conclusions: among older subjects who screened positive for depressive symptoms, an offered stepped-care intervention programme was not (cost)-effective compared with usual care, possibly due to a low uptake of the course offer.
Trial registration: www.controlled-trials.com/ISRCTN 71142851v.

Keywords: *cost-utility, screening, depressive symptoms, stepped-care intervention, oldest old, primary healthcare, elderly*

Introduction

Depressive symptoms at old age have a negative impact on well-being [1, 2], quality of life [3], daily functioning and mortality [4], and increase the risk of developing major depression [5]. At old age depressive symptoms are reported to be under-recognised and undertreated [6], although psychological interventions have shown positive effects on clinical outcomes [7, 8].

Therefore, screening older subjects for depressive symptoms, followed by effective treatment of screen-positive subjects, is advocated [6]. Two large randomised controlled trials (RCTs) in the USA evaluated the (cost)-effectiveness of care management programmes for depressed subjects ≥60 years, who were (partly) detected by screening, and showed reduced suicidal ideation [9], reduced depressive symptoms [10] and cost-effectiveness [11]. However, it is unknown whether screening for depressive symptoms followed by an intervention offer is beneficial and cost-effective for the oldest old. Therefore, the PROMODE study (Proactive Management of Depression in the Elderly) was initiated. PROMODE consisted of a screening study [12] and a subsequent pragmatic RCT offering either a stepped-care intervention or usual care.

The aim of the present study was to investigate the effects and costs of the stepped-care intervention offered to subjects ≥75 years who were screened positive for untreated depressive symptoms, compared with usual care. Subjects aged 75–79 years and ≥80 years were also examined separately, to reveal possible age-dependent differences in the effect of this programme.

Methods

Study procedures and population

From April 2007 until July 2008, in 67 general practices in the Leiden region (the Netherlands) all 11,635 registered subjects aged ≥75 years were invited for screening at home for depressive symptoms. Exclusion criteria were current treatment for depression, clinical diagnosis of dementia or a Mini-Mental State Examination (MMSE) score <19 points, loss of partner or child in the preceding 3 months, life expectancy ≤3 months and not speaking Dutch. Screening procedures have been described previously [12].

Screening yielded 264 screen-positive subjects according to a ≥5 points score on an interviewer-administered 15-item version of the Geriatric Depression Scale (GDS-15) [13]. Of those, 239 subjects gave written informed consent to participate in the randomised trial.

The Medical Ethical Committee of the Leiden University Medical Center approved the study.

Intervention and usual care

General practitioners (GPs) in intervention practices were instructed to inform screen-positive subjects about screening result and to motivate them for referral to the community mental health centre. The subsequent stepped-care intervention consisted of: step 1—individual counselling concerning treatment needs and motivation of the subjects during one or two home visits by a community psychiatric nurse; step 2—coping with Depression course by trained mental health professionals; if indicated (irrespective of course participation), step 3—referral back to GP to discuss further treatment.

The 'Coping with Depression' course, based on cognitive behavioural therapy, is effective in treating older subjects with depressive symptoms [14]. It consists of 10 weekly group meetings, with 2 course instructors and about 6–10 participants. If subjects were willing to accept the course offer, but had problems with attending group sessions, the course was offered on an individual basis at their home.

To ensure usual care, GPs in control practices were not informed about screen-positive subjects in their practice before the end of the study. Only in case of severe depressive symptoms [Montgomery-Åsberg Depression Rating Scale (MADRS)] score >30 points, see section 'Measurements') and/or suicidal ideation was the GP contacted by the researcher. Patients in the control practices were not individually informed about being screen-positive and treatment allocation.

Randomisation and blinding

A cluster randomised design, with the general practice as unit of randomisation, was chosen to prevent contamination [15]. After completion of screening and baseline assessment, block randomisation was performed using opaque envelopes. Research nurses were not informed about practice allocation.

Measurements

The GDS-15 was used as a screening tool for depression. To measure cognitive functioning the MMSE was used [16]. Subjects with an MMSE score <19 points were excluded because of reduced reliability and validity to fill out the other questionnaires.

The primary outcome measure was change in severity of depressive symptoms between study groups after 6 months as assessed with the MADRS [17]. The MADRS scale consists of 10 items representing the depression core symptoms. For each item, scores range from 0 to 6 points, with higher scores indicating more serious depression. Training of nurses occurred on a regular basis, with special attention paid to administering and scoring the MADRS in a uniform way. Therefore, the MADRS part of the interviews was videotaped; all MADRS scales were scored by both the interviewer and another research nurse and consensus scores were used in the analyses.

Secondary outcome measures were change in the MADRS score between study groups after 12 months; percentage responders to treatment (intervention or usual care) defined as ≥50% decrease in the MADRS score

compared with baseline at 6 and 12 months; quality of life, mortality and costs. For further measurements see Supplementary data, available in *Age and Ageing* online, Appendices 1 and 3.

Follow-up

At 6 and 12 months after baseline measurements, subjects were visited at home to assess the GDS-15, MADRS, SF-36, chronic pain and MMSE (only at 12 months).

Sample size calculation

It was assumed that each cluster would provide 3 screen-positive subjects, on an average 1.5 subjects per age group. We planned to include 33 clusters per study arm to detect a clinically relevant difference in the MADRS score of at least 6 points in each age group (assumptions: SD = 10 points; power 80%; $\alpha = 0.05$; intracluster correlation coefficient (ICC) = 0.2). The (unknown) ICC was chosen conservatively to ascertain sufficient power [18].

Statistical analysis

Analyses were performed for all subjects and for both age groups separately. MADRS score changes after 6 and 12 months were analysed according to an intention-to-treat basis.

First, we analysed outcomes on the subject level. Sensitivity analyses were performed by substituting missing MADRS score data at 6 and 12 months following three methods: (i) last-observation-carried-forward (LOCF), (ii) highest MADRS scores in our study (30 points at 6 months and 29 points at 12 months) and (iii) lowest MADRS score in our study (0 points at 6 and 12 months).

Second, MADRS data were analysed using linear mixed models (LMM) to account for clustering at the practice level, with adjustment for MADRS scores at baseline, age and gender. Finally, measurements at 12 months were also included in the model to analyse the long-term effect.

To check whether subgroups benefited from the intervention on the longer term, stratified analyses were performed using LMM with the outcome. MADRS score changes at 12 months dependent on the presence of DSM-IV depressive disorder, perceived loneliness, chronic diseases, treatment per protocol and baseline MADRS score >10 points.

Hazard ratios (HRs) for death were estimated using a Cox proportional hazards model. Statistical analyses were carried out using SPSS 16.0 for Windows.

Results

Study population

After baseline measurements, 33 practices with 121 subjects were randomly allocated to the intervention arm and 34 practices with 118 subjects to the control arm (Figure 1). The researcher contacted the GP for three subjects in control practices and for two subjects in intervention practices because of an MADRS score >30 points and/or suicidal ideation. In the intervention group 7 subjects died, 10 subjects refused follow-up visits at 6 and/or 12 months and 3 subjects were unable to reliably answer the questions at 12 months. In the control group, 17 subjects died (including one subject who committed suicide, with an MADRS score <30 points and no suicidal ideation at baseline), 6 subjects refused follow-up visits at 6 and/or 12 months and 2 subjects had become incompetent at 12 months. As a result, 210 subjects could be analysed at 6 months (107 intervention and 103 control subjects), and 194 subjects at 12 months (101 intervention and 93 control subjects).

Table 1 presents the demographic and clinical characteristics at baseline. Baseline characteristics between groups were similar. Median MADRS scores indicated that subjects mostly were mildly/moderately depressed.

Intervention uptake

In the intervention practices, 101 of all 121 screen-positive subjects (83%) accepted referral to the community mental health centre to start with the stepped-care intervention. Course participation was accepted by 23 (19%) subjects. Most of them (70%) finished the course. Additionally, two subjects followed the course on an individual basis and 21 participated in a group course. Five other subjects (4%) started another type of treatment.

Severity of depressive symptoms during follow-up

In the intervention group, median GDS scores remained stable at 6 points during follow-up; in the control group, scores decreased from 7 to 5. During follow-up, there was an overall decrease in MADRS scores, meaning an improvement in severity of depressive symptoms. After 6 months, this decrease was significantly stronger in the control group than in the intervention group, but not after 12 months (Table 2). Sensitivity analyses, after substitution of missing data by LOCF or by the highest or lowest MADRS scores in our study population, did not substantially change these results (data not shown).

Taking clustering of subjects into account, and controlling for the baseline MADRS score, age and gender, the decrease in the MADRS score after 6 months was 1.4 points less in the intervention group than in the control group ($P = 0.056$, ICC = 0). Including measurements at 12 months, MADRS scores in the intervention group tended to be higher at all measurement moments ($P = 0.088$, ICC = 0.045). In none of the analysed subgroups was a positive intervention effect observed (data not shown).

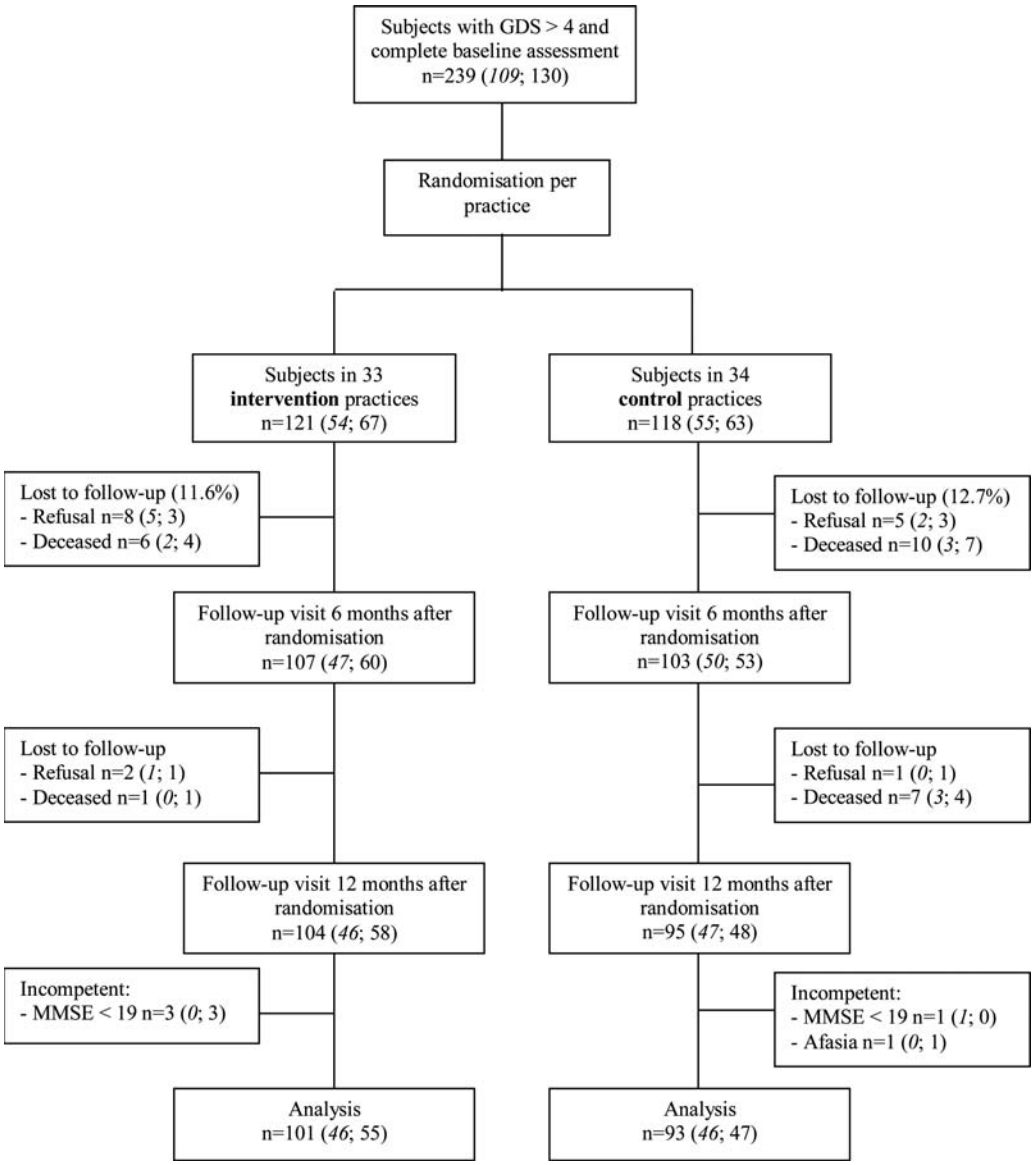

Figure 1. Flow chart of the PROMODE intervention study giving numbers of study subjects per age group between brackets (75–79 years in italics; 80 years and over not italicised).

Mortality

A total of 24 subjects died during follow-up, 7 (5.8%) in the intervention group and 17 (14.4%) in the control group (HR: 2.7; 95% CI: 1.1–6.5, adjusted for age and gender). After further adjustment for the baseline MADRS score and co-morbidity (CIRS-total score), the HR was 2.3 (95% CI: 0.94–5.6).

Age-stratified results

Between subjects aged 75–79 years and ≥80 years no differences were found in course participation and finishing the course. In both age groups, the intervention showed no positive effects on any of the MADRS outcomes or mortality (Supplementary data are available in *Age and Ageing* online, Appendix 2).

Economic evaluation

Costs of the stepped-care intervention were estimated at €333 per referral to the stepped-care programme ($n = 101$). No significant differences were found in other costs or quality of life (Supplementary data are available in *Age and Ageing online*, Appendix 3).

Discussion

The present study shows no beneficial effect regarding severity of depressive symptoms of a stepped-care intervention programme among subjects aged ≥75 years who screened positive for untreated depressive symptoms, which mostly were mild to moderate, in general practice. Without beneficial effect, also the cost-effectiveness of the programme is unfavourable.

Table 1. Baseline characteristics of the study subjects

	Intervention group ($n = 121$)	Control group ($n = 118$)
Sociodemographic characteristics		
Age in years	80 (77–84)	80 (77–84)
Female sex	85 (70)	88 (75)
Income social security only	17 (14)	23 (20)
Living alone	76 (63)	78 (66)
Living independently	86 (71)	85 (72)
Clinical characteristics		
Perceived loneliness present	81 (67)	83 (70)
Alcohol intake >14 drinks/week	10 (8)	13 (11)
Chronic pain present	81 (67)	80 (68)
Somatic co-morbidity (CIRS-TSC)	13 (9–16)	13 (10–17)
SF-36 Physical component score	45 (38–52)	44 (38–53)
SF-36 Mental component score	46 (40–52)	46 (40–51)
Neuropsychiatric characteristics		
MADRS score	12 (8–18)	14 (11–17)
GDS-15 score	6 (5–8)	7 (6–9)
DSM-IV diagnosis present	52 (43)	53 (45)
Major depression present	17 (14)	19 (16)
Minor depression present	16 (13)	12 (10)
Dysthymia present	19 (16)	22 (19)
HADS-A score	5 (3–6)	5 (3–8)
MMSE score	28 (26–29)	28 (26–29)

Data are presented as numbers and percentages or medians and inter-quartile ranges.

CIRS-TSC, cumulative illness rating scale total score; MADRS, Montgomery-Åsberg Depression Rating Scale; GDS-15, Geriatric Depression Scale 15-items version; DSM-IV, Diagnostic and Statistical Manual of Mental Disorders (4th edition); HADS-A, Hospital Anxiety Depression Scale, anxiety-subscale; MMSE, Mini-Mental State Examination; SF-36, Short-Form 36 items.

Table 2. MADRS outcomes at 6 months and 12 months in the intervention and control group

	Intervention ($n = 121$)	Control ($n = 118$)	*P*-value
MADRS scores at 6 months			
Subjects, *n*	107	103	
MADRS score, median (IQR)	12 (7–16)	11 (6–15)	0.22
MADRS responders, *n* (%)	17 (16)	23 (22)	0.24
MADRS change compared with baseline, mean (SEM)	−1.1 (0.61)	−2.9 (0.58)	0.032
MADRS scores at 12 months			
Subjects, *n*	101	93	
MADRS score, median (IQR)	10 (6–14)	10 (5–13)	0.45
MADRS responders, *n* (%)	21 (21)	31 (33)	0.049
MADRS change compared with baseline, mean (SEM)	−3.1 (0.61)	−4.6 (0.64)	0.084

MADRS, Montgomery-Åsberg Depression Rating Scale; IQR, inter-quartile range; SEM, standard error of the mean; Responder, subject with MADRS score decrease ≥50% compared with baseline.

Continuous data are compared with the Mann–Whitney *U* test, categorical data with the Chi-square test, and changes of means with independent samples *t*-test.

These negative findings are in contrast with the mainly positive reviews reporting that screening or case finding with subsequent enhanced care is effective in decreasing symptoms of depression [19–21], albeit sometimes marginally [22]. However, compared with the present study, most studies included in these reviews targeted their intervention at populations with more (serious) depressive symptoms and/or were performed in younger populations (mostly over 55 or over 60 years). Furthermore, studied interventions are heterogeneous and 'usual care' may have relevant cross-cultural differences. In the Dutch healthcare system, GPs are the primary caregivers for all community-living subjects and often have a longstanding and close relationship with their registered (older) patients. This enables a continuity of care that probably resembles the idea of a 'personal care manager', a seemingly important factor in successful interventions such as IMPACT [9]. Our aim was to enhance primary care in the intervention arm. However, we suspect the marginal role of the GP gave a breach in continuity of care that was not beneficial. In a recent Dutch trial stepped-care significantly reduced the risk of developing a major depressive or anxiety disorder. Although comparable with our study regarding healthcare setting and the age group, they included persons with persistent depressive symptoms and added problem-solving treatment to their intervention [8]. Our negative results are in line with a recent meta-analysis that concluded that psychological treatment for depressive symptoms is effective in primary care, but only when patients were referred by their GP for treatment and not when they were detected by screening [23].

Our study has some major strengths. Firstly, we did not only focus on older persons with major depression and/or dysthymia, but we focused on subjects who screened positive for clinically relevant depressive symptoms, which represents the full spectrum of depression seen in general practice. This is especially important at old age, given the relatively high prevalence of subthreshold and minor depression, thereby enhancing the generalisability of our results in general practice. For the same reason, we chose a pragmatic study design, not strongly regulating the process of the intervention carried out by mental healthcare [24]. Secondly, our study was powered to investigate effects in two separate age groups, 75–79 years and ≥80 years. Mortality risk was higher in the control group than in the intervention group (if the age groups are combined) but not in the age-stratified groups, suggesting that our study may have been underpowered to draw definite conclusions per age group for mortality.

A possible limitation of the present study is that we chose a change in the MADRS score as our primary outcome measure. Although the MADRS is frequently used and validated to measure (changes in) severity of depressive symptoms among older subjects with moderate to severe depression, it may not be the optimal instrument to measure change in relatively mild depressive symptoms, and is not validated as such. Furthermore, our study could not be blinded and control subjects could have been triggered to seek help. This attention bias [25] may have played a role in our study, since the control group appeared to have received more psychological care than the intervention group. Also, the research nurses could not be completely

blinded for treatment allocation during follow-up visits, although they were not informed about this by the research team. To avoid a biased assessment and scoring of the MADRS, permanent training for the research nurses was provided and all videotaped MADRS interviews were independently scored. Finally, we were only partially informed about the third step of the intervention, in spite of our attempts to get complete and reliable information.

Our study shows a low uptake (19%) of the course offer among screen-positive older subjects, which probably is not surprising since these subjects did not (have the intention to) ask for help. In a qualitative exploration, we found that important reasons for declining the course offer were: not feeling depressed, or having negative thoughts about the course effect, about group participation or about being too old to change and learn new things [26]. Being screen-positive requires further exploration of subjective complaints and needs, as well as the motivation to accept help. Moreover, particularly in old age, it seems important that exploration of needs should not only focus on the depressive symptoms but also on other domains, such as functional limitations and chronic pain. Such an exploration will probably require a longitudinal approach with several stages and a broad scope with respect to possible intervention options. Furthermore, in the present study the GPs (who are a respected and trusted advisor for most elderly subjects) were allocated only a limited role, because we assumed that they could not invest the extra time required for the follow-up of screen-positive subjects. It is an important question whether an intervention programme would have been more successful if the GP had been more involved in exploring their patients' needs after screening.

In conclusion, among older subjects who screened positive for depressive symptoms in general practice the offer of a stepped-care intervention did not result in better clinical outcomes compared with usual care. Possibly, this was partly due to the low uptake of the main part of the intervention. Therefore, this combined screening/stepped-care intervention programme for depressive symptoms does not seem to be a useful strategy to deal with untreated depressive symptoms at old age. It seems worthwhile to explore whether a more individualised approach for screen-positive subjects would yield more effective results.

Key points

- The stepped-care intervention programme for screen-positive depressed subjects aged 75 years and over did not result in better clinical outcomes compared with usual care.
- Among screen-positive subjects the uptake of the main part of the intervention was only 19%.
- Economic evaluation of the stepped-care intervention programme also showed no favourable results.

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Conflicts of interests

None declared.

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Supplementary data

Supplementary data mentioned in the text is available to subscribers in *Age and Ageing* online.

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Tuberculosis in ageing: high rates, complex diagnosis and poor clinical outcomes

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