university of groningen

University Medical Center Groningen

University of Groningen

Depressive symptoms in elderly patients after a somatic illness event - Prevalence, persistence, and risk factors

de Jonge, P.; Kempen, G.I.J.M.; Sanderman, R.; Ranchor, A.V.; van Jaarsveld, C.H.M.; van Sonderen, E.; Scaf-Klomp, W.; Weening, A.; Slaets, J.P.J.; Ormel, J.

Published in:
Psychosomatics

IMPORTANT NOTE: You are advised to consult the publisher's version (publisher's PDF) if you wish to cite from it. Please check the document version below.

Document Version
Publisher's PDF, also known as Version of record

Publication date:
2006

Link to publication in University of Groningen/UMCG research database

Citation for published version (APA):
de Jonge, P., Kempen, G. I. J. M., Sanderman, R., Ranchor, A. V., van Jaarsveld, C. H. M., van Sonderen, E., Scaf-Klomp, W., Weening, A., Slaets, J. P. J., & Ormel, J. (2006). Depressive symptoms in elderly patients after a somatic illness event - Prevalence, persistence, and risk factors. *Psychosomatics*, *47*(1), 33-42.

Copyright
Other than for strictly personal use, it is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), unless the work is under an open content license (like Creative Commons).

The publication may also be distributed here under the terms of Article 25fa of the Dutch Copyright Act, indicated by the “Taverne” license. More information can be found on the University of Groningen website: https://www.rug.nl/library/open-access/self-archiving-pure/taverne-amendment.

Take-down policy
If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

Downloaded from the University of Groningen/UMCG research database (Pure): http://www.rug.nl/research/portal. For technical reasons the number of authors shown on this cover page is limited to 10 maximum.

Depressive Symptoms in Elderly Patients After a Somatic Illness Event

Prevalence, Persistence, and Risk Factors

PETER DE JONGE, PH.D., GERTRUDIS I.J.M. KEMPEN, PH.D.
ROBBERT SANDERMAN, PH.D., ADELITA V. RANCHOR, PH.D.
CORNELIA H.M. VAN JAARSVELD, PH.D., ERIC VAN SONDEREN, PH.D.
WINNIE SCAF-KLOMP, PH.D., ANNEMARIE WEENING, M.D.
JORIS P.J. SLAETS, M.D., PH.D., JOHAN ORMEL, PH.D.

Elderly patients with somatic illness are at increased risk of depression. The authors studied the prevalence and persistence of depressive symptoms during the first year after the events of myocardial infarction, congestive heart failure, fall-related injury, and the diagnosis of cancer and their putative pre-event risk factors. The GLAS study contains data from 614 patients who experienced post-baseline myocardial infarction, cancer, heart failure, or fall-related injury of the extremities within 5 years after the baseline assessment. Follow-up was conducted 8 weeks, 6 months, and 1 year after the somatic event. The authors studied the relative importance of 21 baseline risk factors for experiencing significant depressive symptoms during follow-up and the persistence of depression. Depressive symptoms were prevalent in 38.3% of the subjects during the post-event year; in about 19.1%, symptoms were mild. For a majority of patients (67.5%), symptoms persisted until the next assessment. Significant pre-event risk factors were depressive symptoms at baseline, age, smoking, poor general health, poor well-being, and neuroticism. Within the depressed group, only neuroticism was related to the persistence of symptoms. Neuroticism increases the risk of experiencing post-event depressive symptoms and is related to their persistence, which suggests the existence of a depression-prone personality.

(Psychosomatics 2006; 47:33–42)

Depression is a burdensome disorder with an increased prevalence in somatic illness (e.g., myocardial infarction,[1] diabetes mellitus,[2] congestive heart failure,[3] cancer,[4] stroke,[5,6] hip fracture,[7] and other fall-related injuries.[8] Since the proportion of elderly persons and, subsequently, their somatic illnesses, are on the rise, depression is expected to be among the biggest threats to health in the coming 25 years.[9] Depression is related to poor quality of life (QoL),[10–13] poor recovery after a somatic event,[1,13,14] and increased (non-suicide) mortality.[15–17] Attention, therefore, needs to be directed to interventions that may reduce depression and to clarification of the etiology of depression, especially in those who are at risk.

Received September 21, 2004; revised January 25, 2005; accepted February 21, 2005. From the Dept. of Psychiatry, Univ. of Groningen; Health Care Studies, Medical Sociology, Maastricht University; Northern Centre for Healthcare Research, Dept. of Public Health and Health Psychology, Univ. of Groningen; the Dept. of Internal Medicine, Academic Medical Center, Groningen. Address correspondence and reprint requests to Dr. de Jonge, Dept. of Psychiatry, Univ. of Groningen, P.O. Box 30.001, 9700 RB, Groningen, The Netherlands. e-mail: p.de.jonge@med.rug.nl
Copyright © 2006 The Academy of Psychosomatic Medicine

Depression tends to become chronic, and relapses often occur.[11,18–20] Moreover, the hypothetical underlying mechanisms explaining the relationship between depression and somatic illness (e.g., the HPA-axis, platelet reactivity, inflammatory processes, inadequate health behavior) all depend on the chronicity of symptoms.[21–23] In support of this, it was found that in elderly persons living in the community, only chronic and chronic-intermittent depression predicted mortality at 3-year follow up.[11] A single depressive episode, in this light, may be seen as a common reaction to an extremely stressful experience, whereas repeated episodes of depression or chronic symptoms may be related to more stable personality traits, such as neuroticism,[24,25] which would make subjects more vulnerable to future episodes. In fact, neuroticism may be regarded as a "depression-trait," whereas actual depressive symptoms may be seen as a "depression-state." Personality seems to be of particular interest in elderly people, since Oldehinkel et al.[25] found that neuroticism may mediate the effect of disability on the development of late-life depression.

Several potential risk factors for depression have been reported in the literature, such as age,[26] sex,[27] smoking,[28] functional and health status,[29,30] personality characteristics,[25] and social functioning and support.[31] The differential role of these risk factors remains largely unknown because the risk factors were rarely studied simultaneously. Because of their considerable interrelations and/or operational overlap, their relative importance thus remains unclear. To study this, a model including as many relevant (i.e., statistically significant) risk factors as possible should be constructed, together explaining a maximum amount of variance. Risk factors for the persistence of depression are much less studied.[32,33]

We set out to study the prevalence and persistence of depressive symptoms and their risk factors in a sample that was at risk: community-dwelling elderly subjects in the year after a major somatic event (myocardial infarction, congestive heart failure, cancer, or fall-related injury). Subjects underwent an extensive baseline assessment, including many of the well-known risk factors, and depressive symptoms were repeatedly assessed after the event, so that risk factors both for the prevalence and persistence of depressive symptoms could be studied. Depression was measured by use of a self-report rating scale, since depressive syndromes that do not fulfill rigorous diagnostic criteria are highly prevalent in elderly persons, and even mild symptoms of depression in this patient group are already consequential.[34–38] In order to clarify the way that depression may develop in somatic illness, we investigated which risk factors for depression in the elderly general population would hold true in the context of a somatic illness event.

METHODS

Procedures

We used data from the Groningen Longitudinal Ageing Study (GLAS), a population-based prospective cohort study of older persons.[39,40] The original study population consisted of 8,723 persons age 57 and older on January 1st, 1993, who were registered as patients with 27 general practitioners (GPs). A total of 3,214 refused to participate in the study; 152 had died or left the practice before contact, and 78 were excluded because of severe cognitive impairment, leaving a baseline sample of 5,279 subjects. During the baseline wave in 1993 until January 1st, 1998, the GPs provided the names of all patients who experienced a post-baseline episode or diagnosis of acute myocardial infarction (AMI), congestive heart failure (CHF), cancer, or fall-related injury of the extremities. The (suspected) occurrence of cancer was reported by the GPs and checked with the medical specialists and registration of the Comprehensive Cancer Centre North, in the Netherlands. Subjects with less serious forms of cancer, such as basal cell carcinoma, were excluded. The most frequent diagnoses within the group of subjects with cancer were breast cancer, cancer of the intestines, lung cancer, and prostate cancer. The other conditions were diagnosed according to the criteria of the International Classification of Primary Care (ICPC).[41] To fulfill the diagnosis of injury of the extremities that needed medical treatment, subjects had to fulfill one of the ICPC codes L72-L80 (hip fractures; fractures of wrist or forearm; ankle or lower leg; and hand or foot; and ankle sprains, knee sprains, or other sprains and dislocations) except for code L79, comprising only minor injuries at different places (bruises, abrasions). AMI (code K75) was diagnosed if two of the following findings were present: 1) chest pain characteristic of myocardial ischemia and lasting more than 15 minutes; 2) abnormal ST–T changes or Q-waves on an ECG; or 3) elevation of blood cardiac enzymes. CHF (code K77) was diagnosed if three of the following five clinical manifestations were present: 1) dependent edema; 2) raised jugular venous pressure or hepatomegaly in the absence of liver disease; 3) signs of pulmonary congestion or pleural effusion; 4) enlarged heart; and 5) dyspnea in the absence of pulmonary disease. Of patients that experienced more than one of the episodes or diagnoses during the follow-up period, the first illness

event was chosen. Follow-up consisted of three assessments, consisting of semistructured interviews and self-report questionnaires, administered at approximately 8 weeks, 6 months, and 12 months after the date of the somatic event, conducted at the respondents' homes.

Assessments

Depressive symptoms were assessed with the Hospital Anxiety and Depression Scale (HADS).[42,43] The HADS does not contain items referring to physical symptoms such as sleeping problems and weight loss, and it is therefore suitable for use in subjects with somatic illnesses. The Depression subscale consists of 7 items (5 positive, 2 negative) to be rated by the subject on a 4-point scale (0–3), with a score range of 0 (no symptoms) to 21 (maximum number of symptoms; $\alpha = 0.71$). A score of 0–7 indicates a normal score; 8–10 indicates mild symptoms; 11–14, moderate; and 15–21, severe symptoms of depression.[42,43] We constructed a binary variable reflecting whether the subject had at least mild depressive symptoms (HADS$>$7) at any of the three follow-up assessments, and a variable reflecting the severity of depressive symptoms by the maximum HADS score during follow-up. When significant depressive symptoms were present at 8 weeks or 6 months and were still present at least at one of the later follow-up assessments, they were considered persistent.

Risk Factors

We studied the effects of 21 baseline risk factors, divided into nine categories:

1. Sociodemographic characteristics: Sex, age, having a partner, educational level, height, and weight were assessed in the baseline interview with the patient. Level of education was derived from the International Standard Classification of Education by UNESCO, consisting of six categories, ranging from kindergarten to higher education. "No partner" was defined as being widowed, divorced, or single.

2. Health behavior: The Quetelet Index was calculated by dividing weight by height $\times$ height. It was then recoded as Healthy (QI: 20–25), Fairly Healthy (QI: 26–30 or$<$20), and Unhealthy (QI$>$30). Smoking was scored in an interview with the patient and recoded into three groups: never smoked or stopped $>$10 years ago, stopped $\leq$10 years ago, and smoking.

3. Somatic comorbidity: We scored the number of self-reported chronic illnesses for which, in the 12 months preceding baseline measurement, medical treatment was requested. The number of baseline chronic medical conditions was assessed by counting the presence of any of the following 19 diagnoses: asthma/chronic bronchitis, pulmonary emphysema, heart disease, hypertension, migraine/chronic headache, (consequences of) stroke, leg ulcer, stomach ulcer, rheumatoid arthritis, (other) back problems/joint conditions, diabetes mellitus, liver disorder or gallstones, prostate disease, kidney disease, thyroid gland disorder, serious dermatological disorders like psoriasis and eczema, cancer, multiple sclerosis, and Parkinson's disease or epilepsy.[44]

4. Physical functioning: We used the scales of the Groningen Activity Restriction Scale (GARS),[45] the Medical Outcomes Study Short Form-20 (MOS SF-20),[46] and the Symptoms Check List–90 (SCL–90).[47] The Physical Functioning scale of the MOS SF-20 measures global physical limitations; it consists of 6 items (two categories each; $\alpha = 0.79$) and ranges from 0 to 100. Higher scores indicate better physical functioning. The GARS consists of 18 items reflecting self-reported problems with aspects of self-care and household-related work. Scores range from 18 (no physical dysfunctioning) to 72 (maximum level of physical dysfunctioning; $\alpha = 0.93$). The SCL–90 Somatic Complaints subscale consists of 12 variables, with 5 answering categories each. The score reflects self-reported complaints and physical limitations during the last 7 days.

5. Well-being: With Cantril's ladder,[48] respondents indicate their general well-being, ranging from 0 (worst possible life) to 10 (best possible life). The MOS SF-20 General Health Perception scale consists of 5 items (5 categories each), in which respondents indicate their general health. The score ranges from 0 to 100, and higher scores indicate better functioning.

6. Social functioning: Social support was measured by the Social Support List-I (SSL-I),[49] which measures social skills in three dimensions; affect, support with problems, and appreciation. Total scores range from 12 to 48 ($\alpha = 0.83$). Social network was measured by the living arrangements and total network of each patient: partner and living arrangements with those over the age of 18, children (including foster and stepchildren), neighbors over the age of 18, and other contacts over the age of 18. For all network members who do not live with the respondent, type of re-

lationship and frequency of contact were measured. The frequency of contacts varied between a score of 1 (less than once per year) to 9 (daily contact). The Social Functioning scale of the MOS SF-20 consists of a single item, with 6 answering categories, reflecting the level in which the subject experienced limitations in his or her social contacts because of health problems during the last 4 weeks. Total scores ranges from 0 to 100.

7. Emotional dysfunction: Depressive symptoms and symptoms of anxiety were assessed at baseline with the Dutch-validated version of the Hospital Anxiety and Depression Scale (HADS; see above).[42,43]

8. Personality: Neuroticism was assessed with the Neuroticism subscale of the Revised Eysenck Personality Questionnaire (EPQ–R).[50] The scale consists of 12 items that can be answered Yes/No, and the score reflects the subject's tendency to emotional instability. Total scores range from 0 to 12 ($\alpha = 0.82$). Extroversion was assessed with the Extroversion subscale of the Revised Eysenck Personality Questionnaire (EPQ–R). The scale consists of 12 items that can be answered Yes/No, and the score reflects the tendency of the subject to impulsiveness and social interest. Total score ranges from 0 to 12 ($\alpha = 0.83$).

9. Psychological resources: Mastery, which reflects one of the subject's psychological coping resources, was measured by means of a 7-item scale developed by Pearlin et al.,[51] with scores ranging from 7 to 35 ($\alpha = 0.79$). The scale assesses the extent to which the person experiences personal control. Self-efficacy was measured by means of a 16-item test, with 5 answering categories each (Completely Agree, Agree, Neutral, Disagree, Disagree Completely), developed by Sherer et al.[52] and translated into Dutch by Bosscher et al.[53] The scale assesses the extent to which subjects have confidence in their own capabilities; score range from 16 to 80 ($\alpha = 0.84$).

Subjects

Of the original baseline sample, 1,124 subjects (21.3%) fulfilled the criteria of one of the four somatic events (207 diagnosed as AMI, 293 as CHF, 287 as injury of the extremities, and 337 as cancer). Of these subjects, 480 were excluded because of death, cognitive problems, or refusal, and 30 for other reasons, leaving 614 participants (Table 1). Details on the selection of patients in the specific samples can be found elsewhere (AMI and CHF sample,[54] injury sample,[55] cancer sample,[56]).

Data on depressive symptoms were available for 601 patients at 8-week follow-up, for 559 at 6-month follow-up, and 516 patients at 1-year follow-up, resulting in complete follow-up for 480 of the 644 participants (74.5%). Reasons for lost-to-follow-up status were the following: patient died ($N = 30$), patient too sick ($N = 21$), patient refused ($N = 25$), proxy refused/too sick ($N = 50$), other/unknown ($N = 38$). In order to prevent bias by excluding subjects with missing data, which is expected to be nonrandom, we used the multiple imputation technique to estimate missing data for all patients who dropped out except for those who died. Multiple-imputation technique is the most valid method to account for nonrandom attrition because it takes into account that missing data are often not random, but that estimations can be made on the basis of related variables.[57] Multiple estimations are generated, resulting in multiple data sets that are analyzed. The results of the data analyses are combined, taking into account the level of error generated by the estimation of the missing data. The computer program SOLAS 3.2 (© Statistical Solutions Ltd., 2001) was used for imputation and generated five imputations for each missing datapoint. We used the available baseline data to estimate baseline depression, and post-event depression was estimated by means of baseline data and the previous depression score. This resulted in data on 614 complete depression assessments, of which 601 had complete risk-factor assessments.

Statistical Analysis

For group comparisons on variables with an approximately normal distribution, we used *t*-tests, and, for categorical data, we used χ^2 tests. All multivariate data analyses were conducted on the five imputed data sets ($N = 614$). First, we explored which of the initial list of risk factors were independently predictive of the outcomes, in order to reduce the extensive list of risk factors. This was done by means of backward logistic-regression analysis (criterion for inclusion: $p<0.05$; criterion for exclusion: $p>0.20$). This resulted in a list of potential risk factors for the prevalence and for the persistence of depressive symptoms. The potential risk factors were then forced into the regression model. The significance of the risk factors was tested by means of combined statistics.[58] For any parameter (point-estimate), we calculated the mean of five imputed data sets. The variance of the parameters was estimated by combining the corresponding variance of each of the im-

puted data sets with the variability of the parameter estimates across the sets. This way, a broader estimate of the 95% confidence interval (CI) is constructed, which accounts for the uncertainty introduced by the estimation of the missing values.

On the basis of the method developed by Tosteson et al.,[59] for each individual predictor, sufficient power ($\beta = 0.80$) is reached when the effect on the outcome (depression: prevalent in about 40% of cases) per standard deviation (SD) increase in predictor has an odds ratio (OR) of at least 1.3–1.5 for prevalence of depressive symptoms (N = 600) and at least 1.6–1.9 for persistence of depressive symptoms (N = 200).

RESULTS

Most of the subjects were age 60–80, with a slight overrepresentation of women (56%). About one-third had no chronic illness at baseline; one-third had one chronic illness; and one-third had multiple chronic illnesses. The most frequently occurring somatic event in our sample was fall-related injury (N = 198; 31.2%), and the least frequent was AMI (N = 94; 18.3%).

TABLE 1. Socio-Demographic Characteristics of the Sample (N = 614)

Characteristic	N (%)
Age, years	
57–60	53 (8.6)
61–64	107 (17.4)
65–69	113 (18.4)
70–74	141 (23.0)
75–79	118 (19.2)
80–84	58 (9.4)
85+	24 (3.9)
Marital status	
Married	361 (58.8)
Living together	24 (3.9)
Not living together	9 (1.5)
Widowed	176 (28.7)
Divorced	23 (3.7)
No partner	21 (3.4)
Number of chronic medical conditions	
0	171 (27.9)
1	202 (32.9)
2	140 (22.8)
3	56 (9.1)
4	29 (4.7)
5 or more	16 (2.7)
Somatic event after baseline	
Cancer	165 (26.9)
Fall-related injury	198 (31.2)
Congestive heart failure	157 (25.6)
Acute myocardial infarction	94 (18.3)

Depressive Symptoms

Compared with baseline, depressive symptoms were more prevalent after the somatic events (Table 2). Paired *t*-tests of the symptom score resulted in significant differences between baseline and the 6-month follow-up ($t_{[600]} = -3.0$; $p = 0.003$) and between baseline and 12-month follow-up ($t_{[558]} = -3.2$; $p = 0.003$); the difference between baseline depressive symptoms and 8-week follow-up was not significant ($t_{[600]} = -1.9$; $p = 0.053$). Similarly, the presence of significant depressive symptoms increased after the somatic events (from 20.2%, at baseline, to 22.8%, 23.2%, and 26.9% at the follow-up points). The chi-square test yielded a p value of 0.06 ($\chi^2 = 7.6$) for this increasing trend.

Of the 614 subjects, 235 subjects (38.3%) experienced significant depressive symptoms at least at one of follow-up assessments. For 112 subjects (19.1%), this represented mild symptoms, for 87 (14.2%), moderate symptoms, and, for 31 (5.0%), severe symptoms. Of the subjects who did not report significant depressive symptoms at baseline, 24.4% reported depressive symptoms at least at one of the follow-up assessments. Of the 200 patients with significant depressive symptoms within the first 6 months of follow-up, for a total of 135 subjects (67.5%), the symptoms persisted until the next follow-up assessment.

Risk Factors for the Prevalence of Depressive Symptoms During Follow-Up

Logistic-regression analysis resulted in the following 12 potential risk factors: age, smoking, Cantril's ladder, MOS SF-20 General Health perception, depressive symptoms, neuroticism, MOS SF-20 Physical Functioning, mastery, MOS SF-20 Social Functioning, extroversion, having no partner, and anxiety symptoms. Forcing these potential factors in one model resulted in nonsignificant ORs for MOS SF-20 Physical Functioning, Anxiety Symptoms, and Mastery. The final model (N = 601) thus consisted of nine variables (Table 3), of which six reached statistical significance in the combined-statistics approach.

Table 4 shows that, except for smoking and having no partner, all risk factors have a significant and monotonous association with the severity of depressive symptoms. In contrast to findings in the literature, age had a positive, rather than negative, relationship with severity of depressive symptoms.

Risk Factors for the Persistence of Depressive Symptoms

Logistic-regression analysis revealed the following nine potential risk factors: having no partner, number of chronic

TABLE 2. Depressive Symptoms at Baseline and During Follow-Up

	Baseline	8 Weeks Post-Event	6 Months Post-Event	12 Months Post-Event	Maximum During Follow-Up
Mean number of depressive symptoms (SD)	4.5 (3.7)	4.8 (3.9)	5.1 (4.1)	5.2 (4.2)	6.8 (4.2)
Severity of symptoms, %					
No	79.8	77.2	76.8	73.1	61.7
Mild	13.0	12.2	12.8	15.4	19.1
Moderate	5.9	8.9	7.7	8.4	14.2
Severe	1.3	1.7	2.7	3.0	5.0

Note: SD: standard deviation.

illnesses, MOS SF-20 Physical Functioning, Cantril's ladder, neuroticism, Quetelet index, SCL–90 Somatic Complaints, depression, MOS SF-20, and social functioning. Forcing the nine potential risk factors into one model resulted in nonsignificant ORs for no-partner, number of chronic illnesses, Quetelet index, SCL–90 Somatic Complaints, depressive symptoms, and MOS SF-20 social functioning. The final model (N = 200) thus consisted of three variables: MOS SF-20 physical functioning, Cantril's ladder, and neuroticism (Table 3), of which only neuroticism reached statistical significance in the combined-statistics approach.

Validation of Findings in Non-Imputed Data

With respect to the prevalence of depressive symptoms during follow-up, social functioning, extraversion, and having no partner were not independently related to the outcome variable. Both physical functioning and well-being were not independently related to the persistence of significant symptoms, whereas greater neuroticism was. Replication of these analyses in the non-imputed data set resulted in highly comparable parameter estimations, the exceptions being social functioning as a predictor for depression (OR: 0.99; 95% CI: 0.98–1.00; $p = 0.02$) and physical functioning as a predictor for persistence (OR: 0.98; 95%CI: 0.97–0.99; $p < 0.01$).

TABLE 3. Pre-Event Risk Factors for Depression (N = 601) and Its Persistence (N = 200)

Variable	OR (95% CI)	p
Prevalence of depression		
Age	1.29 (1.11–1.50)	**<0.01**
Smoking	1.49 (1.14–1.93)	**<0.01**
Cantril's Ladder of Well-Being	0.82 (0.70–0.97)	**0.02**
MOS SF-20 General Health	0.98 (0.97–0.99)	**0.03**
Depressive symptoms	1.21 (1.13–1.30)	**<0.01**
Neuroticism	1.10 (1.02–1.17)	**0.02**
MOS SF-20 Social Functioning	0.99 (0.98–1.00)	0.14
Extroversion	0.93 (0.87–1.00)	0.07
No partner	1.34 (0.85–2.11)	0.21
Persistence of depression		
Cantril's Ladder of Well-Being	0.78 (0.60–1.00)	0.09
MOS SF-20 Physical Functioning	0.99 (0.97–1.00)	0.09
Neuroticism	1.25 (1.12–1.40)	**<0.01**

Note: OR: odds ratio; CI: confidence interval; MOS: Medical Outcomes Study.

Effect of Neuroticism on Depressive Symptoms

To further assess the effects of neuroticism, we recoded the neuroticism score into Low Neuroticism (score: 0–1), Medium Neuroticism (score: 2–4), and High Neuroticism (5–12), in a way that the three emerging categories had approximately equal sizes. Compared with Low Neurotic subjects, subjects in the highest tertile had an almost-doubled chance of experiencing depressive symptoms (131/227 [58%] versus 54/210 [26%]; $\chi^2 = 50.9$; $p < 0.01$), and, of the subjects who reported significant symptoms, the chance that depression persisted also was much higher (92/112 [82%] versus 24/45 [53%]; $\chi^2 = 14.8$; $p < 0.01$). The association between baseline neuroticism and post-event prevalence and persistence of depressive symptoms is shown in Figure 1, revealing an almost "dose–response" association.

DISCUSSION

Depression is a major health problem, both because of its high prevalence and its adverse outcomes. In this study, we measured the prevalence, persistence, and risk factors of depressive symptoms in a sample of at-risk, elderly subjects experiencing a somatic illness event. A substantial minority of our sample (38.3%) experienced significant depressive symptoms during the 1-year follow-up period. About half of the cases concerned mild depressive symptoms, and excluding these from the depression cases would result in prevalence rates that are only slightly increased

compared with elderly subjects living in the community or younger somatic-illness patients. Compared with baseline depression, depressive symptoms were only somewhat increased during the 1-year follow-up period, and, especially, the group of subjects with moderate or severe depressive symptoms increased. The potential effect of the somatic event thus seemed to be limited and to be mediated by a series of other factors. Of the subjects reporting significant symptoms in the first half-year after the event, a majority (67.5%) experienced persistent symptoms that were still present at a later time within the 1-year follow-up. For the occurrence of significant depressive symptoms at any of the three follow-up assessments, age, smoking, self-reported well-being and general health, baseline depressive symptoms, and neuroticism were independent risk factors. Persistence of significant depressive symptoms was independently associated only with neuroticism. Although all risk factors reported in this study have been described before in the literature, they have not been studied in a sample of elderly patients after a somatic event, and not simultaneously. Since, in the present study, they were studied simultaneously, we can better assess the relative strength of the relations. We will now discuss the predictors we found.

Numerous epidemiological studies have shown that smoking is substantially associated with depression. With regard to the causality of this relationship, much remains unclear. Only recently, Dierker et al.[28] found some evidence for a shared etiology between dysthymia and heavy smoking, and, elsewhere, this finding has also been supported for major depression and heavy smoking. It is argued by Dierker et al. that certain personality traits may result in vulnerability for the development of depression and may be responsible for individual differences in nicotine response. Self-reported well-being and general health perception at baseline were also associated with the prevalence of post-event depression. The mutual relationship between self-reported disability, health status, well-being, and depression has been frequently described in the literature.[60] The present study provides support for an effect of well-being and health perception on the occurrence of depressive symptoms, independent of the level of depressive symptoms at baseline. In secondary analyses (not shown), we found that, especially, these self-report measures of well-being and health perception prevented an effect of self-reported disability, probably because disability fuels

FIGURE 1. Relationship Between Baseline Neuroticism Score and Risk of Post-Event Prevalence (N = 614) and Persistence (N = 200) of Depression

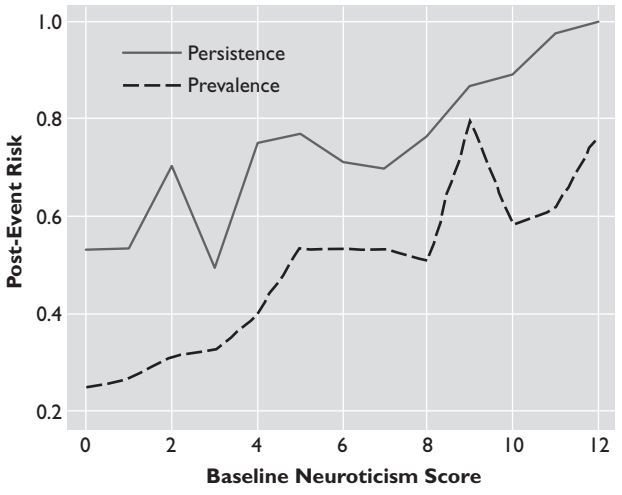

TABLE 4. Comparison of Subjects With Different Levels of Post-Event Depression Severity on Baseline Risk Factors for Depression

Risk Factor	No Depressive Symptoms (HADS<8) %	Mild Depressive Symptoms (HADS 8–10) %	Moderate Depressive Symptoms (HADS 11–14) %	Severe Depressive Symptoms (HADS 15–21) %	Analysis χ^2	Analysis p
Age ≥70 years	50.9	62.4	62.1	67.7	8.9	0.03
Current smoker	20.1	24.8	23.0	19.4	1.4	0.70
No partner	32.2	41.9	40.2	45.2	5.9	0.11
	Mean (SD)	**Mean (SD)**	**Mean (SD)**	**Mean (SD)**	**F**	**p**
Cantril's Ladder of Well-Being	7.8 (1.3)	6.6 (1.4)	6.7 (1.6)	5.9 (2.0)	45.9	<0.001
MOS SF-20 General Health	71.0 (21.8)	53.0 (22.9)	49.7 (25.1)	47.1 (29.0)	37.1	<0.001
Depressive symptoms	3.1 (2.7)	5.7 (3.2)	7.4 (3.8)	9.2 (4.9)	76.3	<0.001
Neuroticism	3.0 (2.8)	4.5 (3.3)	5.4 (3.3)	5.8 (3.7)	23.1	<0.001
MOS SF-20 Social Functioning	84.6 (23.3)	70.1 (28.3)	62.6 (29.2)	52.9 (38.8)	30.6	<0.001
Extroversion	7.2 (3.0)	5.9 (3.2)	5.6 (3.1)	5.2 (3.1)	11.5	<0.001

Note: HADS: Hospital Anxiety and Depression Scale; SD: standard deviation; MOS: Medical Outcomes Study.

depressive symptoms and perceptions of well-being and health, as well. In partial support of this, although bivariate correlations between disability and depressive symptoms were present, these correlations disappeared when well-being and health perception were entered into the model. The reason for the disappearing effect of disability may be due to the operational similarity between well-being and depressive symptoms. In line with several studies reported in a recent metaanalysis,[61] we found that the risk of post-event depressive symptoms increased with age. However, as mentioned elsewhere, this relationship may be due to other risk factors, such as physical health problems and their related disability and activity restriction.[25] In our sample of subjects experiencing a somatic illness event, age seemed to model the effect of physical dysfunction. First, age and MOS SF-20 Physical Functioning were highly correlated (–0.37). Second, the significant bivariate association between age and prevalence of depression disappeared when MOS SF-20 Physical Functioning was controlled for. In our model, presented in Table 3, MOS SF-20 Physical Functioning was excluded because it lost its significance because of overlap with MOS SF-20 General Health ($r = 0.50$) and MOS SF-20 ($r = 0.52$).

The findings in our study suggest that some elderly persons may already be vulnerable for depressive symptoms before the onset of a somatic-illness event. Neuroticism was associated with a higher risk of experiencing depressive symptoms, comparable with subgroup analyses of the GLAS study.[62] Interestingly, it also was the sole risk factor to be independently associated with the persistence of symptoms. The multivariate analyses showed that the effect of neuroticism was independent of the other risk factors. Remarkably, baseline neuroticism and baseline depressive symptoms emerged as independent risk factors despite their considerable intercorrelation ($r = 0.43$). The bivariate analyses showed the magnitude of the effect: highly neurotic subjects reported almost twice as many symptoms of depression in the year after the event, as compared with Low-Neurotic subjects; they had twice the chance of experiencing depressive symptoms during follow-up, and, if they did, the symptoms were persistent in a vast majority of subjects. In the literature,[24,63,64] neuroticism has been interpreted as a marker of "psychobiological vulnerability." According to the dynamic stress-vulnerability model,[65] vulnerability factors may influence risks of onset of depressive episodes by the generation of stressful life events (mediation) and amplification of their effects (modification). Since the subjects in the present study all experienced a somatic-illness event, the effect of neuroticism on the prevalence and persistence of depressive symptoms has to be interpreted as modification: stressful events in highly neurotic subjects led to an increased risk of a (persistently) depressive reaction. Interestingly, in recent years, much attention has been directed to the concept of frailty in elderly persons and the search for somatic indicators of frailty, such as IL-6.[66,67] Future studies are needed to investigate whether neuroticism may be seen as an indicator for frailty.

The findings should be considered in the light of the following strengths and weaknesses of the study: First, by including a large number of subjects at risk, we were able to obtain a sample of sufficient size. Second, because of the repeated follow-up assessment in the year after the somatic events, we were able to provide data on prevalence and persistence of depressive symptoms. Third, by using multiple-imputation techniques, we were able to conduct the data analysis in the presence of missing data, limiting a potential bias from selective dropout. The following limitations of the study should be also mentioned: Depressive symptoms were measured using a symptom rating scale, and not according to a diagnostic classification system. We did this because depressive syndromes not fulfilling diagnostic criteria are highly prevalent in elderly persons, and it has been shown that even minimal symptoms of depression result in disability and worse somatic prognosis. The disadvantage, however, is that we do not know to what extent our findings represent depressive disorders. A second limitation concerns the time difference between the baseline assessment and the post-event follow-up, which has varied between 0 and 5 years. In secondary analyses, however, we have found no effects of the time difference, nor of any alterations in the effects of the risk factors when the time difference was entered in the prediction models. A third potential limitation was that we studied prevalent, rather than incident, depression cases, which complicates the causal interpretation of our findings. However, the fact that neuroticism had an effect on post-event depressive symptoms that exceeded and was independent of pre-event symptoms clearly supports its etiological role. Fourth, we were not able to consider the role of pain in the relationship between the predictors and depressive symptoms, nor were we able to study to what extent our findings may have been affected by the treatment status of the depression.

The assessment of neuroticism is not standard practice in clinical care. Still, the present findings do stress that standard assessment of neuroticism might improve care for depression. First, neuroticism seems to be an excellent candidate measure for the assignment of preventive interven-

tions in subjects at risk of developing depression. Second, neuroticism may be used for the allocation of specific interventions to treat depression. For example, for depressed, highly neurotic subjects, therapy should be directed to long-term goals and relapse-prevention. More information of such aptitude/treatment interactions would be needed to support this claim. It is clear, though, that, in the coming years, more attention should be directed to adjusting treatment of depression to individual characteristics.[68]

This research is part of the Groningen Longitudinal Aging Study (GLAS). GLAS is conducted by the Northern Centre for Healthcare Research (NCH) and various departments of the University of Groningen in The Netherlands. The primary departments involved are Public Health & Health Psychology, Family Medicine, Psychiatry, Sociology (ICS), and Human Movement Sciences. GLAS and its substudies are financially supported by the Dutch government (through NESTOR), the University of Groningen, the Faculty of Medical Sciences, the Dutch Cancer Foundation (NKB/KWF), and the Netherlands Organisation for Scientific Research (NWO). The central office of GLAS is located at the NCH, P.O. Box 196, 9700 AD Groningen, The Netherlands (http://www.med.rug.nl/nch/).

References

1. Frasure-Smith N, Lesperance F, Talajic M: Depression and 18 month prognosis after myocardial infarction. Circulation 1995; 91:999–1005
2. Anderson R, Clouse R, Freedland K, et al: The prevalence of comorbid depression in adults with diabetes. Diabetes Care 2001; 24:1069–1078
3. Freedland KE, Rich MW, Skala JA, et al: Prevalence of depression in hospitalized patients with congestive heart failure. Psychosom Med 2003; 65:119–128
4. Hammerlid E, Ahlner-Elmqvist M: A prospective multicentre study in Sweden and Norway of mental distress and psychiatric morbidity in head and neck cancer patients. Br J Cancer 1999; 80:766–774
5. Everson S: Depressive symptoms and increased risk of stroke mortality over a 29-year period. Arch Intern Med 1998; 158:1133–1139
6. Morris P: Association of depression with 10-year poststroke mortality. Am J Psychiatry 1993; 150:124–129
7. Holmes J, House A: Psychiatric illness predicts poor outcome after surgery for hip fracture. Psychol Med 2000; 30: 921–922
8. Scaf-Klomp W, Sanderman R, Ormel J, Kempen GIJM: Depression in older people after fall-related injuries: a prospective study. Age Ageing 2003; 32:88–94
9. Murray CJL, Lopez AD: Alternative projections of mortality and disability by cause, 1990–2020: Global Burden of Disease study. Lancet 1997; 349:1498–1504
10. Stuck AE, Walthert JM, Nikolaus T, et al: Risk factors for functional status decline in community-living elderly people: a systematic literature review. Soc Sci Med 1999; 48:445–469
11. Geerlings SW, Beekman ATF, Deeg DJH, et al: The longitudinal effect of depression on functional limitations and disability in older adults: an eight-wave, prospective, community-based study. Psychol Med 2001; 31:1361–1371
12. Penninx BWJM, Leveille S, Ferucci L, et al: Exploring the effect of depression on physical disability: longitudinal evidence from the Established Populations for Epidemiologic Studies of the Elderly. Am J Public Health 1999; 89:1346–1352
13. De Jonge P, Ormel J, Slaets JPJ, et al: Depressive symptoms in the elderly predict poor adjustment after somatic events. Am J Geriatr Psychiatry 2004; 12:57–64
14. De Groot M, Anderson R, Freedland KE, et al: Association of depression and diabetes complications: a metaanalysis. Psychosom Med 2001; 63:619–630
15. Lindesay J: Nonsuicidal mortality in late-life depression. J Geriatr Psychiatry 1989; 22:53–65
16. Schulz R, Drayer RA, Rollman BL: Depression as a risk factor for non-suicide mortality in the elderly. Biol Psychiatry 2002; 52:205–225
17. Cuijpers P, Smit F: Excess mortality in depression: a metaanalysis of community studies. J Affect Disord 2002; 72:227–236
18. Beekman AT, Geerlings SW, Deeg DJ, et al: The natural history of late-life depression: a six-year prospective study in the community. Arch Gen Psychiatry 2002; 59:605–611
19. Beekman AT, Deeg DJ, Geerlings SW, et al: Emergence and persistence of late-life depression: a three-year follow-up of The Longitudinal Aging Study, Amsterdam. J Affect Disord 2001; 65:131–138
20. Geerlings SW, Beekman AT, Deeg DJ, et al: Physical health and the onset and persistence of depression in older adults: an eight-wave prospective, community-based study. Psychol Med 2000; 30:369–380
21. Carney RM, Freedland KE, Miller GE, et al: Depression as a risk factor for cardiac mortality and morbidity: a review of potential mechanisms. J Psychosom Res 2002; 53:897–902
22. Tsigos C, Chrousos GP: Hypothalamic-pituitary-adrenal axis, neuroendocrine factors and stress. J Psychosom Res 2002; 53:865–871
23. Kiecolt-Glaser JK, Glaser R: Depression and immune function: central pathways to morbidity and mortality. J Psychosom Res 2002; 53:873–876
24. Ormel J, Oldehinkel AJ, Brilman EI: The interplay and etiological continuity of neuroticism, difficulties, and life events in the etiology of major and subsyndromal, first and recurrent depressive episodes in later life. Am J Psychiatry 2001; 158:885–890
25. Oldehinkel AJ, Bouhuys AL, Brilman EI, et al: Functional disability and neuroticism as predictors of late-life depression. Am J Geriatr Psychiatry 2001; 9:241–249
26. Mulsant B, Ganguli M: Epidemiology and diagnosis of depression in late life. J Clin Psychiatry 1999; 60:9–15
27. Hankin BL, Abramson LY: Development of gender differences in depression: description and possible explanations. Ann Med 1999; 31:372–379
28. Dierker LC, Avenevoli S, Stolar M, et al Smoking and depression: an examination of mechanisms of comorbidity. Am J Psychiatry 2002; 159:947–953
29. Prince MJ, Harwood RH, Blizaed RA, et al: Impairment, disability, and handicap as risk factors for depression in old age: The Gospel Oak Project, V. Psychol Med 1997 27:311–321

30. Kennedy GJ: The dynamics of depression and disability. Am J Geriatr Psychiatry 2001; 9:99–101
31. Prince MJ, Harwood RH, Blizaed RA, et al: Social support deficits, loneliness, and life events as risk factors for depression in old age: The Gospel Oak Project, VI. Psychol Med 1997; 27:323–332
32. Prince MJ, Harwood RH, Thomas A, et al: A prospective, population-based cohort study of the effects of disablement and social milieu on the onset and maintenance of late-life depression: The Gospel Oak Project, VII. Psychol Med 1998; 28:337–350
33. Beekman AT, Deeg DJ, Smit JH, et al: Predicting the course of depression in the older population: results from a community-based study in The Netherlands. J Affect Disord 1995; 34:41–49
34. Wells KB, Stewart A, Hays RD, et al: The functioning and well-being of depressed patients: results from The Medical Outcomes Study. JAMA 1989; 262:914–919
35. Beekman ATF, Deeg DJH, Smit JH, et al: Consequences of major and minor depression in later life: a study of disability, well-being, and service utilization. Psychol Med 1997; 27:1397–1409
36. Judd LL, Schettler PJ, Akiskal HS: The prevalence, clinical relevance, and public health significance of subthreshold depressions. Psychiatr Clin North Am 2002; 25:685–698
37. Goldney RD, Fisher LJ, Dal Grande E, et al: Subsyndromal depression: prevalence, use of health services, and quality of life in an Australian population. Soc Psychiatry Psychiatr Epidemiol 2004; 39:293–298
38. Bush DE, Ziegelstein RC, Tayback M, et al: Even minimal symptoms of depression increase mortality risk after acute myocardial infarction. Am J Cardiol 2001; 88:337–341
39. Kempen GIJM, Jelicic M, Ormel J: Personality, chronic medical morbidity, and health-related quality of life among older persons. Health Psychol 1997; 16:539–546
40. Kempen GIJM, Ormel J, Brilman EI, et al: Adaptive responses among Dutch elderly: the impact of eight chronic medical conditions on health-related quality of life. Am J Public Health 1997; 87:38–44
41. Lamberts H, Wood M, Hofman-Okkes JM, (eds): The International Classification of Primary Care in the European Community. Oxford, England, Oxford Univ. Press, 1993
42. Zigmond AS, Snaith RP: The Hospital Anxiety and Depression Scale. Acta Psychiatr Scand 1983; 67:361–370
43. Spinhoven P, Ormel J, Sloekers PP, et al: A validation study of the Hospital Anxiety and Depression scale (HADS) in different groups of Dutch subjects. Psychol Med 1997; 27:363–370
44. Van de Berg J, van de Bos GA: Het (meten van het) voorkomen van chronische aandoeningen [The Assessment of Chronic Conditions], 1974–1987. Maandbericht Gezondheid (CBS) 1989; 89:4–21
45. Kempen GIJM, Miedema J, Ormel J, et al: The assessment of disability with the Groningen Activity Restriction Scale: conceptual framework and psychometric properties. Soc Sci Med 1996; 43:1601–1610
46. Stewart AL, Hays RD, Ware JE: The MOS Short-Form General Health Survey: reliability and validity in a patient population. Med Care 1988; 26:724–735
47. Derogatis LR, Rickels K, Rock AF: The SCL–90 and the MMPI: a step in the validation of a new self-report scale. Br J Psychiatry 1976; 128:280–289
48. Cantril H: The Pattern of Human Concern. New Brunswick, NJ, Rutgers Univ. Press, 1965
49. Kempen GIJM, Van Eijk LM: The psychometric properties of the SSL12-I, a short scale for measuring social support in the elderly. Soc Indicators Res 1995; 35:303–312
50. Eysenck SBG, Eysenck HJ, Barrett P: A revised version of the Psychoticism scale. Pers Indiv Diff 1985; 6:21–29
51. Pearlin LI, Schooler C: The structure of coping. J Health Soc Behav 1978; 19:2–21
52. Sherer M, Maddux JE, Mercandante B, et al: The Self-Efficacy Scale: construction and validation. Psychol Rep 1982; 51:663–671
53. Bosscher RJ, Laurijsen E, De Boer E: Competentie op latere leeftijd: een exploratieve studie. [Self-efficacy in late life: an exploratory study]. Bewegen en Hulpverlening 1992; 9:255–265
54. Van Jaarsveld CHM, Sanderman R, Miedema I, et al: Changes in health-related quality of life in older patients with acute myocardial infarction or congestive heart failure: a prospective study. J Am Geriatr Soc 2001; 49:1052–1058
55. Scaf-Klomp W, van Sonderen E, Sanderman R, et al: Recovery of physical function after limb injuries in independent older people living at home. Age Ageing 2001; 30:213–219
56. Ranchor AV, Sanderman R, Steptoe A, et al: Pre-morbid predictors of psychological adjustment to cancer. Qual Life Res 2002; 11:101–113
57. Twisk J, De Vente WJ: Attrition in longitudinal studies: how to deal with missing data. Clin Epidemiol 2002; 55:329–337
58. Rubin DB, Schenker N: Multiple imputation in healthcare databases: an overview and some applications. Stat Med 1991; 10:585–598
59. Tosteson T, Buzas JS, Demidenko E, et al: Power and sample size calculations for generalized regression models with covariate measurement error. Stat Med 2003; 22:1069–1082; published online: March 10, 2003
60. Ormel J, Rijsdijk FV, Sullivan M, et al: Temporal and reciprocal relationship between IADL/ADL disability and depressive symptoms in late life. J Gerontol Psychol Sci Soc Sci 2002; 57:338–347
61. Cole MG, Dendukuri N: Risk factors for depression among elderly community subjects: a systematic review and metaanalysis. Am J Psychiatry 2003; 160:1147–1156
62. Bosma H, Sanderman R, Scaf-Klomp W: Demographic, health-related, and psychosocial predictors of changes in late-middle-aged and older persons with fall-related injuries. Psychol Health 2004; 19:103–115
63. Duggan C, Sham P, Lee A, et al: Neuroticism: a vulnerability marker for depression: evidence from a family study. J Affect Disord 1995; 35:139–143
64. Fergusson DM, Horwood LJ: Vulnerability to life-events exposure. Psychol Med 1987; 17:739–749
65. Rijsdijk FV, Snieder H, Ormel J, et al: Genetic and environmental influences on psychological distress in the population: General Health Questionnaire analyses in UK twins. Psychol Med 2003; 33:793–801
66. Dentino AN, Pieper CF, Rao KMK, et al: Association of interleukin-6 and other biologic variables with depression in older people living in the community. J Am Geriatr Soc 1999; 47:6–11
67. Kiecolt-Glaser JK, Preacher KJ, MacCallum RC, et al: Chronic stress and age-related increases in the proinflammatory cytokone IL-6. Proc Natl Acad Sci U S A 2003; 100:9090–9095
68. Fisher D, Beutler LE, Williams OB: Making assessment relevant to treatment planning: The STS Clinician Rating Form: systematic treatment selection. J Clin Psychol 1999; 55:825–842