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The relationship between depression and mortality in elderly subjects with less severe dementia

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ABSTRACT

Background. Little is known about the effects of depression on the mortality rates of elderly subjects with dementia.

Methods. Logistic regression analysis, adjusting for possible confounders, was used to study the associations between GMS-AGECAT derived syndrome and symptom measures and 12-month mortality rates in a cohort of 73 elderly subjects who met the DSM-III-R criteria of dementia with a median MMSE score of 19.

Results. Twenty-three subjects (32%) died within the 12 month follow-up period. A baseline diagnosis of syndromal or subsyndromal depression was associated with increased mortality. At the symptom level mortality was predicted by higher scores on the factor 'mood symptoms'. The effects of interactions between depression measures and severity of dementia were not significant.

Conclusions. Short-term mortality in elderly subjects with less severe dementia is predicted by the presence of (sub) syndromal depression and by mood symptoms. The effects of depression and severity of dementia on the mortality rates seem to be largely independent.

INTRODUCTION

Depression is associated with excess mortality in elderly subjects (Davidson *et al.* 1988; Jorm *et al.* 1991; Henderson *et al.* 1997). Although it is known that depression frequently co-occurs with dementia (Wragg & Jeste 1989; Burns 1991; Janzing *et al.* 1993) the relationship between mortality and depression in subjects with dementia has attracted little attention.

In a sample consisting of patients with Alzheimer's disease, Burns *et al.* (1991) found increased mortality rates associated with co-morbid depression. Only a diagnosis of 'observed depression' could be made in their subjects because of the severity of dementia. Up to now it is unknown whether these results can be generalized to subjects with less severe dementia. In addition, the effects of depression measures, in which anamnestic information is included, have not been investigated.

In the present study the associations between various measures of depression and 1 year mortality were examined in subjects with milder dementia. The following questions were addressed:

1 To what extent are depressive syndromes and symptoms associated with mortality?

2 Are the effects of depression on mortality influenced by the severity of dementia?

METHOD

Subjects

The study took place in six homes for the elderly in the region of Nijmegen, the Netherlands. Informed consent was obtained from the subjects themselves or in the case of severe cognitive impairment from close relatives.

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Table 1. *Baseline characteristics of 73 elderly subjects with dementia*

Characteristic	
Age (years)	
Median	87
(P25, P75)	(82, 90)
Sex	
Male	$N = 9$ (12%)
Female	$N = 64$ (88%)
Marital status	
Married	$N = 3$ (4%)
Unmarried	$N = 70$ (96%)
Education (years)	
Median	6
(P25, P75)	(6, 8)
MMSE score	
Median	19
(P25, P75)	(15, 21)
Diagnosed diseases	
Median	2
(P25, P75)	(1, 3)
AGECAT depression	
Case	$N = 11$ (15%)
Subcase	$N = 21$ (29%)
No depression	$N = 41$ (56%)
Depressive symptoms	
Median	6
(P25, P75)	(3, 11)
Mood symptoms	
Median	2
(P25, P75)	(0, 4)
Motivation symptoms	
Median	1
(P25, P75)	(0, 3)

Subjects were residents who showed evidence of cognitive impairment in the screening phase of the study (Mini-Mental State Examination (MMSE) score $\leqslant 24$ and Short Blessed Test (SBT) score > 6 (Folstein *et al*. 1975; Katzman *et al*. 1983). In addition, they fulfilled the DSM-III-R criteria for dementia (American Psychiatric Association, 1987) based on information gathered with the Clinical Assessment Battery (CAB) of the Consortium to Establish a Registrary for Alzheimer's Disease (CERAD) (Morris *et al*. 1989). The type of dementia was not specified. Heteroanamnestic information was obtained from both staff members of the homes and relatives of the subjects. The baseline total MMSE score was used as the measure of dementia severity (Weissman *et al*. 1985).

The following exclusion criteria were applied (Morris *et al*. 1989): inability to be tested (severe deafness, severe visual handicap, severe aphasia, too demented) Parkinson's disease, choreatic disease, alcoholism, mental retardation, inclusion of the partner and missing data on depressive symptoms.

Physical illness

Using information from the general practitioners, a history of the following diagnoses was recorded: locomotor disease, cerebrovascular disease, diabetes mellitus, heart disease, hypertension, pulmonary disease, malignancies. Because no single diagnosis was significantly associated with 12-month mortality the total number of diagnoses was used as a measure of general health.

Measures of depression

The subjects underwent a full psychiatric assessment using the Geriatric Mental State (GMS community version) (Copeland *et al*. 1976). All measures of depression were derived from AGECAT, the computerized diagnostic package of the GMS-AGECAT system (Copeland *et al*. 1988). In AGECAT they are diagnosed independently from the organic syndromes (Copeland *et al*. 1992).

(*a*) *Depressive syndrome measure*

According to AGECAT, subjects were classified as 'not depressed', 'subcase of depression' or 'case of depression'.

(*b*) *Depressive symptoms*

The total number of positively rated AGECAT depression symptoms was computed (maximum score: 44).

(*c*) *Factors of depressive symptoms*

In an earlier phase of the study two factors with a sufficient Crohnbach's alpha ($> 0{\cdot}75$) and clinical face validity were obtained from an explorative principal component analysis on the AGECAT depressive symptoms of 91 subjects with dementia and 110 subjects without. These factors explained 22% of the total variance and were composed as follows: Factor 1 'motivation symptoms' (items: fatigue; subjective slowing in thinking; subjective slowing in movements; lack of energy; reduced activity; slowness or anergy does not lift with pleasant activities; sits around because of anergia; loss of interest; sudden recent loss of interest; and loss of interest

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because depressed); and Factor 2 'mood symptoms' (items: worried about almost everything; worries; depressed mood; wanting to cry; life not worth living; wishes to be dead; sleep disturbance; tremulous feelings; loneliness; and dissatisfaction).

The factors strongly resemble those found by Forsell *et al.* (1993). The totals of positively rated items per factor were used as the final factor scores (for both factors the maximum score was 10).

Statistical analysis

Logistic regression analysis was used to study the associations between the baseline measures of depression and 12-month mortality. For this analysis all the continuous variables were dichotomized at their medians. The threshold for significance was $P < 0{\cdot}05$ (two-sided).

RESULTS

At baseline 91 residents were eligible. From these subjects 16 (18%) refused follow-up. From two more subjects, who had been referred to nursing homes, no information was available at follow-up. The baseline demographic, cognitive and depressive characteristics of the dropouts were not significantly different from those of the other subjects.

Seventy-three subjects completed the study. AGECAT diagnosed 68 of them as organic cases (21 level O3, 44 level O4 and three level O5). From the remaining subjects three were organic subcases and two had no diagnosis at the organic cluster.

In Table 1 the baseline characteristics are presented. Apart from a high age, the sample is characterized by a large proportion of women. Most subjects live alone. The median MMSE score of 19 reflects mild dementia. A total of 23 (32%) subjects died within the 12-month follow-up period. AGECAT diagnosed 14% of the survivors and 17% of the non-survivors as depressive cases and 20% of the survivors and 48% of the non-survivors as depressive subcases.

Multivariate comparisons

Logistic regression models were used to study the effects of the baseline depression measures on the 12-month mortality. Potential confounders (age, sex, MMSE score and the number of diagnosed diseases) were included to adjust for their effects. The results are shown in Table 2. The effects of the potential confounders were insignificant in all models. Significant odds ratios were found for the presence of a case or subcase of depression (OR 4·31; 95% CI, 1·38–13·46) and mood symptoms (OR 3·94; 95% CI, 1·31–11·82).

The effects of the interactions between the depression measures and dementia severity (product depression measure * MMSE-score) were insignificant (data not shown).

DISCUSSION

In the present study the effects of several measures of depression on mortality were investigated in a population of subjects with dementia. The considerable mortality and the high refusal rate of the sample reflect the high vulnerability of residents at homes for the elderly (Van Loveren-Huyben & Van der Bom, 1983). The mean dementia severity was substantially lower than that in the study of Burns *et al.* (1991) (present sample, mean MMSE score 17·8 (S.D. 4·5); Burns *et al.*, mean MMSE score 8·0 (S.D. 6·7)).

The main conclusions are: (1) the presence of a case or subcase of depression predicts short term mortality at the diagnostic level, at the symptom level the factor 'mood symptoms' is associated with 12 month mortality; and (2) there is no evidence that the effects of depression on mortality are influenced by the severity of dementia.

The combination of depressive subcaseness and depressive caseness was a better predictor of mortality in subjects with dementia than depressive caseness alone. In a community sample of subjects with and without dementia Jorm *et al.* (1991) drew a similar conclusion. Only after lowering the diagnostic threshold below case level they found a relationship between depression and mortality: not the diagnosis of DSM-III major depression but that of 'dysphoric mood' was associated with mortality.

In a number of studies (Macdonald *et al.* 1982; Ashby *et al.* 1991; Dewey *et al.* 1993; Skoog *et al.* 1996) symptoms indicating that life is not worth living have been found to be

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Table 2. *Summary of final models: odds ratio's for non-surviving*

Covariate	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Sex	1·95 (0·35, 10·80)	1·70 (0·28, 10·28)	1·90 (0·34, 10·60)	1·86 (0·32, 10·80)	1·97 (0·36, 10·91)
Age	0·76 (0·27, 2·16)	0·48 (0·15, 1·55)	0·66 (0·23, 1·95)	0·59 (0·19, 1·82)	0·78 (0·27, 2·25)
Number of diagnosed diseases	1·62 (0·51, 5·16)	1·30 (0·38, 4·39)	1·40 (0·43, 4·57)	1·19 (0·35, 4·06)	1·63 (0·51, 5·21)
MMSE	1·45 (0·51, 4·10)	1·27 (0·42, 3·82)	1·46 (0·52, 4·14)	1·48 (0·50, 4·35)	1·42 (0·50, 4·01)
Depression measure	1·27 (0·33, 4·90)	4·31 (1·38, 13·46)	1·86 (0·64, 5·37)	3·94 (1·31, 11·82)	0·91 (0·32, 2·59)
	Case	Case + Subcase	Depressive symptoms	Mood symptoms	Motivation symptoms

associated with mortality. The association between mortality and 'mood symptoms' (including the symptoms 'life not worth living' and 'wishes to be dead') in the present study seems to be in agreement. Although physical health appears to be a plausible confounder it was not identified as a mediator of the relationship between these depressive symptoms and mortality.

The absence of a significant relationship between the baseline severity of dementia and mortality contrasts with the results of earlier studies (Heyman *et al.* 1987, 1996; Knopman *et al.* 1988; Burns *et al.* 1991; Rosen & Zubenko, 1991). Probably the relatively small sample size and the short follow-up period in the present study account for this difference.

It is important to study the effects of interactions between depression measures and the severity of dementia because of the complex relationship between these variables. Forsell *et al.* (1993) showed that the symptomatology of depression changes with the severity of dementia. In addition, both depression and dementia have been shown to predict mortality (Davidson *et al.* 1988; Burns *et al.* 1991; Jorm *et al.* 1991; Henderson *et al.* 1997). The absence of significant interactions may indicate that the effects of depression and the severity of dementia on mortality are largely independent.

In the present study significant associations were found between measures of depression and short-term mortality in a population with milder dementia. These results are in agreement with those in subjects with severe dementia. However, it is difficult to draw general conclusions as the sample was restricted to residents of homes for the aged, who were characterized by a large proportion of females and a very high age.

The AGECAT analyses were performed at the AMSTEL project, Amsterdam, the Netherlands. The AGECAT computer program was installed and finally authorized by M. E. Dewey, Department of Psychiatry, University of Liverpool, UK.

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