

Three-year prognosis of depression in the community-dwelling elderly

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Background Depression is the most common mental disorder in the community-dwelling elderly.

Aims To determine the three-year prognosis of depression in a cohort of 127 community-dwelling elderly subjects and identify factors relevant to outcome.

Method The subjects, diagnosed depressed at year 0 using the GMS–AGECAT package, were followed up three years later. A number of factors were investigated for an association with recovery from, or persistence of, depression.

Results At follow-up, 30.2% of the depressed subjects had died, 34.9% had persistent or relapsed case-level depression, 24.5% had other case- or sub-case-level mental illness and 10.4% had recovered completely. Physical ill-health, bereavement and positive family history of depression were associated with poor outcome, whereas treatment with antidepressant medication significantly improved prognosis.

Conclusions Late-life depression in community-dwelling subjects is a chronic condition. However, the positive response to antidepressant medication suggests that it should be vigorously treated.

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Factors reported to be associated with a poor prognosis in late-life depression include female gender, living alone, negative life-events, physical ill-health and poor social support. Late-life depression has also been suggested to be a prodromal feature of dementia (Burns, 1990; Jorm *et al*, 1991). The assumption of a poor prognosis for late-life depression has led to pessimism regarding its treatment, which is reflected in low treatment and referral rates in primary care (MacDonald, 1986; Banerjee *et al*, 1996).

In 1997 our group reported on the prevalence of mental disorders in the community-dwelling elderly in Dublin (Kirby *et al*, 1997). We identified 127 cases of depression, giving a prevalence rate of 10.3%. The aims of the present study are as follows: to report on the three-year outcome of the depressed cohort; to identify factors associated with the persistence or remission of depressive states; to examine the effect of treatment with antidepressant medication on outcome; and to test the hypothesis that depression in the elderly is a risk factor for the subsequent development of organic cognitive impairment.

METHOD

GMS–AGECAT

The Geriatric Mental State (GMS) (Copeland *et al*, 1976; Gurland *et al*, 1976) is a semi-structured interview designed for the detection of psychiatric disorders (functional and organic) in the elderly. The data obtained from the GMS provide a standardised psychiatric diagnosis when the computerised system AGECA (Automated Geriatric Examination for Computer Assisted Taxonomy) (Copeland *et al*, 1986) is applied.

Subjects are awarded a score representing the level of confidence in the diagnosis for each psychiatric syndrome. Subjects with diagnostic confidence levels of 1 and 2 are

classified as sub-cases (i.e. symptoms do not reach case criteria), and scores of 3 or above are classified as cases. These classifications approximate closely to the diagnoses of psychiatrists (Copeland *et al*, 1990). Depression is defined as either 'neurotic' (DN3–DN5), with symptoms characteristic of neurotic, reactive depression or dysthymic mood, or 'psychotic' (DP3–DP5), with symptoms characteristic of psychotic, endogenous depression or major affective disorder (Copeland *et al*, 1987). The GMS–AGECAT has been modified for use in the community (Copeland *et al*, 1987); and this version was used in the present study.

Sample selection and follow-up

The original 'year 0' (baseline) sample was selected by contacting all individuals aged 65 years and over on the practice lists of seven general practitioners (GPs) located within the catchment area of St James's Hospital, Dublin, Ireland, and inviting them to participate in the study. A total of 1232 elderly individuals consented to interview, of whom 127 (10.3%) were diagnosed with depression (Kirby *et al*, 1997).

In the first stage of the year 3 follow-up study, GPs involved in the prevalence study were contacted by letter or telephone and their consent to continued participation was reaffirmed. Deaths and changes of address in the depressed cohort were recorded.

Subjects were sent a letter which explained the purpose of the reassessment and stated a day on which the interviewers would call. A telephone contact number was provided in order to enable subjects to arrange an alternative interview time or have any queries answered regarding the survey. Subjects who did not answer the door to the interviewer were contacted again by letter. Failure to make contact after two visits was deemed a refusal.

The GMS–AGECAT (community version) was administered by a trained interviewer (research nurse) who had also conducted the baseline interviews. Subjects with comorbid case-level diagnoses of organic disorder and depression at baseline were excluded from follow-up. In all cases the AGECA diagnosis was validated by a psychiatrist using DSM–IV criteria (American Psychiatric Association, 1994). The outcome measures described are death, persistent or relapsed case-level depression, current case-level organic disorder, currently 'well', and other

Table 1 Three-year outcome of diagnostic cases of depressive disorder

Year 0 AGE-CAT diagnosis	Year 3 AGE-CAT diagnosis (n (%))						
	Dead	DP3–DP4	DN3–DN4	Organic cases	Other cases	Well	Sub-cases
DP3–DP4 (n=8)	2 (25)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	6 (75)
DN3–DN4 (n=119)	30 (30.6)	7 (7.6)	30 (30.6)	2 (2.0)	3 (3.1)	11 (11.2)	15 (15.3)
Total cases (n=127)	32 (30.2)	7 (6.6)	30 (28.3)	2 (1.9)	3 (2.8)	11 (10.4)	21 (19.8)

At year 3 follow-up, 21 of the original 127 depression cases refused interview or were untraceable; 106 were re-interviewed or dead. DN, neurotic depression; DP, psychotic depression.

psychiatric diagnoses at year 3, at both case and sub-case level.

Instruments

Basic socio-demographic data were collected by using the minimum data set devised for the Ageing in Liverpool: Health Aspects (ALPHA) study (details available from the first author upon request). Social network type was identified on the basis of the answers to eight questions in the minimum data set mentioned above (Wenger, 1997). A modified version of the List of Threatening Events (LTE; Brugha *et al*, 1985) was used to identify serious life events in the preceding two years. The version used here covers six serious events.

Patient-reported chronic medical conditions were recorded on the basis of a checklist devised for the Medical Outcomes Study (Wells *et al*, 1989). Disability was measured by using a five-point scale modified from the Older Americans Resources and Services (OARS) programme (Fillenbaum, 1985). An observer- and self-rated global illness severity scale, also from the OARS, was used. Details of medication usage were recorded, as was personal and family history of psychiatric illness, specifically depression.

Statistical analyses

Using data from the follow-up interviews, a backwards stepwise multivariate logistic regression analysis was performed on the persistent/relapsed depressed group and the recovered group. The dependent variable was a diagnosis of depression or recovery at the follow-up interview. The factors investigated for an association with recovery were: age, gender, physical health status, functional impairment, treatment with antidepressant medication, bereavement, social network, and family history (first-degree relative) of depression. All factors were entered initially, then the least significant variables were removed, one at

a time, until only significant factors ($P < 0.05$) remained. All analyses were performed with Datadesk 5.0 software (Data Description Inc, Ithaca, NY).

RESULTS

Nineteen subjects (14.9%) declined to participate in the follow-up interviews, two subjects (1.6%) had moved and were untraceable. Follow-up information was therefore available on 106 initially depressed subjects. Table 1 shows the outcome of diagnostic cases of depression after three years.

Of the total number of depression cases, 30.2% were dead, 34.9% had persistent or relapsed case-level depression, 1.9% had developed organic caseness, 2.8% had developed anxiety neurosis, 19.8% had sub-case-level mental illness (8.5% sub-case depression and 11.3% other sub-case syndromes), while only 10.4% had recovered

completely (i.e. were free from case- or sub-case-level mental illness). Table 2 shows the gender breakdown of subjects at follow-up. The mean age of subjects at follow-up was 75.2 years (range 68–91, s.d.=6.75).

In the recovered group (i.e. those with case-level depression at baseline who were 'well' or had sub-case-level depression or neurosis at follow-up), 62.5% either were on antidepressant medication currently or had received a course of it in the intervening three years, with 15% of treated individuals receiving sub-therapeutic dosages (defined, for this age-group, as less than 75 mg/day amitriptyline equivalent). Twenty-two per cent were taking or had been prescribed benzodiazepines, two of whom had comorbid anxiety symptoms.

In the relapsed/persistently depressed group (i.e. those with case-level depression at both year 0 and year 3), 38% were currently being treated with antidepressants, or had been so treated in the three-year period, with 29% of treated individuals

Table 2 Three-year follow-up diagnosis by gender

Year 3 diagnosis	Males (n(%))	Females (n(%))	Total (n(%))
Cases			
Depression			
Psychotic	1 (0.9)	6 (5.7)	7 (6.6)
Neurotic	15 (14.2)	15 (14.2)	30 (28.3)
Total	16 (15.1)	21 (19.9)	37 (34.9)
Anxiety neurosis	0 (0)	3 (2.8)	3 (2.8)
Organic	0 (0)	2 (1.9)	2 (1.9)
All cases	16 (15.1)	26 (24.5)	42 (39.6)
Sub-cases			
Depression	5 (4.7)	5 (4.7)	10 (9.4)
Anxiety neurosis	3 (2.8)	6 (5.7)	9 (8.5)
Phobic neurosis	0 (0)	1 (0.9)	1 (0.9)
Obsessional neurosis	0 (0)	1 (0.9)	1 (0.9)
All sub-cases	8 (7.5)	13 (12.3)	21 (19.8)
Well	2 (1.9)	9 (8.5)	11 (10.4)
Dead	23 (21.7)	9 (8.5)	32 (30.2)
All subjects	49 (46.2)	57 (53.8)	106 (100)

Table 3 Use of antidepressant and benzodiazepine medication in the relapsed/persistent v. recovered groups

Medication	Relapsed/ persistent (n=37)	Recovered (n=32)
Antidepressants		
Current	11	8
Previous	3	12
Total	14 (38%)	20 (62.5%)
Benzodiazepines		
Current	20	5
Previous	2	2
Total	22 (59%)	7 (22%)

receiving sub-therapeutic dosages, while 59% were taking or had been prescribed benzodiazepines, all of whom had comorbid anxiety symptoms, which reached case level in five subjects (Table 3).

Four of the eight subjects with an initial diagnosis of psychotic depression received antidepressant treatment, compared with 30 of the 119 (25%) subjects with neurotic depression – a non-significant difference ($P=0.12$). The main types of antidepressants prescribed were selective serotonin reuptake inhibitors and tricyclic antidepressants.

Of the eight risk factors studied, four were significantly associated with prognosis following multivariate analysis (Table 4). The persistently depressed/relapsed group had significantly more chronic medical conditions than the recovered group ($P=0.0001$). Bereavements in the two years prior to the follow-up interview were significantly more common in the persistent/relapsed group than in the recovered group ($P<0.01$). The recovered group were

significantly more likely to have received treatment with antidepressant medication ($P<0.05$). A family history of depression was significantly more common in the persistent/relapsed group than in the recovered group ($P<0.001$).

The persistent/relapsed group was more functionally impaired than the recovered group, but this difference did not reach significance ($P=0.06$). No significant difference was demonstrated between groups for age, gender or social network type.

DISCUSSION

Post (1972) defined the outcomes of depression as one of the following: complete recovery with no relapse; relapse with subsequent recovery; residual symptoms but no longer meeting criteria for caseness; persistent depression at case-level severity. Our three-year follow-up data can only distinguish between those currently depressed at case-level and those currently recovered, so our currently depressed group combines both persistent and relapsed cases, and our currently recovered group includes both fully recovered cases and those who have relapsed and subsequently recovered.

Outcome

The outcome for depression cases is poor, with 70% of cases either dead or suffering from case-level mental illness at three years. Of those still alive after three years, one half were still suffering from case-level depressive disorder. Indeed, this may well be an underestimate, as it is likely that there are even higher depression rates in those who decline follow-up interviews (Kessler *et al*, 1994). Although there was substantial attrition due to mortality in the cohort

(30%), loss of subjects owing to refusal or untraceability (16%) compares satisfactorily with the figure of 13% reported by Copeland *et al* (1992), who reported follow-up data on a similarly sized cohort of subjects with depression over a comparable time period in the community.

The mortality rate for elderly people with depression is reported to be greater than that expected in the general population (Murphy, 1983). Our mortality rate of 30% at three years is similar to that reported by other authors over a similar time period (21.7% reported by Henderson *et al* (1997), 23.4% by Copeland *et al* (1992) and 38.2% by Forsell *et al* (1994)). It appears that the excess mortality may not be directly due to depression itself, but to the excess of physical ill-health in individuals with depression (Prince *et al*, 1998). The relationship between depression and mortality remains ambiguous and warrants further investigation.

Maintenance rate for depression was 50%. Four community studies with similar follow-up periods have reported maintenance rates between 20% and 85% (Ben-Arie *et al*, 1990; Copeland *et al*, 1992; Forsell *et al*, 1994; Henderson *et al*, 1997).

As studies use different diagnostic criteria for diagnosing depression, direct comparisons are difficult. Despite the relatively favourable outcome (20% maintenance rate) reported by Henderson *et al* (1997), our study and the other studies cited above suggest that depression afflicting elderly persons in the community is indeed a chronic condition.

In our analysis we have attempted to account for as many factors as possible which could potentially have an effect on prognosis; cases of comorbid depression and cognitive impairment were excluded from the follow-up group, and information was gathered regarding disability, physical illness, life events, social factors, drug treatments for depression and personal and family history of psychiatric disorder, specifically depression.

Medication usage

The rates of drug treatment for depression have been described in three previous longitudinal community studies (Ben-Arie *et al*, 1990; Copeland *et al*, 1992; Forsell *et al*, 1994). Rates of treatment with antidepressant medication vary from 4% at the time of the baseline interview (Copeland *et al*, 1992) to zero at three-year follow-up (Ben-Arie *et al*, 1990; Forsell *et al*, 1994),

Table 4 Multivariate logistic regression analysis of putative risk factors for the persistence of depression after three years

Risk factor	d.f.	F	P
Age	1	0.64	0.42
Gender	1	0.65	0.053
Bereavement	1	10.8	<0.01*
Social network	1	2.4	0.126
Number of chronic medical conditions	1	16.6	0.0001*
Functional level (ADL score)	1	3.6	0.062
Antidepressant medication	1	6.0	<0.05*
Family history of depression	1	13.0	<0.001*

*Statistically significant.

ADL, activities of daily living scale.

with only 17% receiving antidepressants at some time during the follow-up period (Forsell *et al*, 1994).

Our higher figure of 40% of depressed individuals receiving antidepressants currently or during the three-year follow-up period is encouraging. It is probably best explained by our policy of contacting GPs at baseline with a recommendation for treatment following the detection of cases of depression warranting intervention.

Antidepressant medication significantly increased the likelihood of recovery over three years, contradicting the view that milder depressive syndromes in the community-dwelling elderly are not amenable to treatment. It must be pointed out, however, that this was not a randomised controlled trial – information on medication usage over the three-year period was collected retrospectively from subjects and their GPs, and so the relationship between antidepressant therapy and outcome should be interpreted with some caution.

Our finding that twice as many individuals in the persistent/relapsed group received sub-therapeutic doses of antidepressant medication as did treated individuals in the recovered group suggests that inadequate treatment regimes may be at least partly responsible for treatment failures. Subjects with psychotic depression were twice as likely as those with neurotic depression to be treated with antidepressants (50% *v.* 25%). Although this difference was not statistically significant because of the small number of cases of psychotic depression, it suggests that the more serious forms of depression are more likely to be recognised and treated in the primary care setting.

In the persistent/relapsed group, subjects were 1.5 times more likely to be prescribed a benzodiazepine than an antidepressant (59% *v.* 38%), particularly in the presence of comorbid anxiety symptoms. This finding highlights the difficulty faced by primary care physicians in distinguishing between depression and anxiety as a primary diagnosis when symptoms of both are present.

Two previous prospective interventionist studies have reported positive outcomes for the treatment of depression in the elderly living at home, using a variety of treatment techniques (Blanchard *et al*, 1995; Banerjee *et al*, 1996), although neither study demonstrated a significant effect for antidepressant medication. Our

study appears to show a significantly better prognosis for those treated with antidepressant medication relative to the untreated group – the first demonstration, to our knowledge, of such an effect in a community-based population. Treatment in all cases was initiated by the GP (either independently or at our suggestion) and not, as in previous studies, by a psychogeriatric team (Banerjee *et al*, 1996) or nurse practitioner (Blanchard *et al*, 1995): specialist intervention in those studies may have been at least partly responsible for the positive treatment effects demonstrated. We argue that there is a definite role for antidepressant medication, at adequate doses, in the treatment of late-life depression in the primary care setting.

Prognostic factors

In keeping with the findings of our study, many community surveys have highlighted the important role of physical ill-health in the genesis and persistence of depression in the elderly (Henderson *et al*, 1997; Prince *et al*, 1998). This finding is in agreement with a large body of evidence from hospital-based research supporting such an association (Post, 1972; Murphy, 1983).

A smaller number of community studies have examined the role of life events as a predictor of depression prognosis in the elderly. In keeping with the findings of our study, Green *et al* (1994) reported that bereavement was significantly more likely in the relapsed/persistently depressed group than in the recovered group at three years. Harlow *et al*'s (1991) sample of bereaved widows also showed a consistent association between poor health and higher levels of depressive symptoms after bereavement.

The role of social support as a prognostic factor for depression is still widely debated. We used an operationalised procedure for the identification of social network type, which was based on the number and frequency of contacts with family, friends and neighbours and participation in clubs and groups. This provides a more objective measure of social support, relatively free from the bias of a subjective report of satisfaction or dissatisfaction with one's social network. The fact that we did not find a relationship between social network and prognosis may be explained by the fact that our subjects were drawn from an inner-city community with largely integrated social networks characterised by

considerable support from family and friends. Hence, the low prevalence of high-risk social networks for depression (e.g. local self-contained, family-dependent and private restricted social networks) in our sample population may explain our failure to detect a difference in network type between the recovered and depressed groups.

Henderson *et al* (1997), also using standardised scales for assessing social support in a large community sample, reported that lower social support was predictive of higher depression scores on follow-up 3–4 years later, but between-group comparisons at 3–4 years in the depressed and recovered groups were not specifically made. Green *et al* (1994) also failed to find a difference in frequency of contact with siblings, children, relatives and others between relapsed and recovered depression sufferers at three years.

The relevance of family history of depression to prognosis has been addressed infrequently in community surveys of older individuals. The Dutch study of van Ojen *et al* (1995) reported an association between family history of mental problems and the various subtypes of late-life depression. We chose to examine family history rather than personal history of depression, as many of the individuals diagnosed with depression at baseline failed to report a history of depression when re-interviewed at follow-up.

Our finding of a significant association between a positive family history of depression and persistence of symptoms at follow-up suggests that both intrinsic factors (genetic predisposition) and extrinsic factors (physical ill-health, bereavement etc.) independently contribute to the prognosis of late-life depression.

The effect of a positive family history of depression may be explained in part by the age of onset of the first depressive illness. Of those with a positive family history and persistent or relapsed depression, eight out of 16 (50%) had early-onset depression (first episode when aged less than 40 years) compared with one out of five (20%) in the recovered group. Early age of onset has previously been reported to be associated with a poorer prognosis than later-onset cases (Brodsky *et al*, 1993).

Is depression a risk-factor for dementia?

Only two subjects (1.9%) with depression at baseline had developed dementia three years

later. This result does not support the findings, largely in referred series, that depression is a risk factor for the subsequent development of dementia (Burns, 1990; Jorm *et al*, 1991). Our negative finding is in agreement with the community studies of Copeland *et al* (1992) and Henderson *et al* (1997).

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CLINICAL IMPLICATIONS

- Depression in community-dwelling elderly people appears to be a chronic condition.
- Physical ill-health, bereavement and a family history of depression contribute independently to a poor prognosis.
- Treatment with antidepressant medication may significantly improve prognosis, although the observed relationship is an indirect one.

LIMITATIONS

- The predictive prognostic value of risk factors measured at baseline was not assessed.
- The AGE-CAT interviewer at three-year follow-up was aware of the baseline diagnosis.
- Changes in caseness between baseline and follow-up should be interpreted cautiously because of the long interval between interviews; specifically, the diagnosis of depression at follow-up did not distinguish between those who had relapsed and those who were continuously depressed.

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