Natural history of depression in the oldest old

Population-based prospective study

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Background Despite its negative consequences, little is known about the natural history of depression in the oldest old.

Aims To study the incidence, course and predictors of depression in the general population of the oldest old.

Method The Leiden 85-plus Study is a prospective population-based study of 500 people from their 85th to their 89th birthdays. Depressive symptoms were annually assessed with the 15-item Geriatric Depression Scale, using a cut-off of 4 points.

Results During a mean follow-up of 3.9 years, the annual risk for the emergence of depression was 6.8%. Poor daily functioning and institutionalisation predicted depression. Among the 77 participants with depression at baseline (prevalence 15%) the annual remission rate was ony 14%. In more than half of the participants with a remission of depression, we observed a relapse of depression during follow-up. No predictors of remission could be identified.

Conclusions Among the oldest old, depression is frequent and highly persistent. More active case-finding and treatment would be potentially rewarding.

Declaration of interest None.

Depression ranks among the most significant health problems in older adults but is potentially treatable at all ages. The consequences of both major and minor depression in older adults are severe and include diminished quality of life, functional decline, marked disability, increased service utilisation and high mortality from comorbid medical conditions. To date, few studies have been published on the incidence of depression in the oldest old and none about its course (Meller *et al*, 1996; Haynie *et al*, 2001; Palsson *et al*, 2001). Given the rapidly increasing number of older adults in society, we studied the incidence and course of depression in the oldest old within the Leiden 85-plus Study.

METHOD

Study design

The Leiden 85-plus Study is a population-based prospective study of a large cohort of community-dwelling older adults in Leiden, The Netherlands. Between 1997 and 1999 all members of the 1912–1914 birth cohort living in Leiden were enrolled in the month of their 85th birthday. No *a priori* selection criteria with respect to health, cognitive functioning or living situation were applied.

Study setting and procedures

The community of Leiden, consisting of 120 000 inhabitants, is a mostly urban area in the western part of The Netherlands with a mixed socio-economic make-up. Demographic characteristics of the participants were representative of the general Dutch population of 85-year-old persons. Upon enrolment, information was given by mail; further contact was made by telephone or a home visit to ask for approval. Participants were then visited at their place of residence by medical staff and research nurses. During the baseline visits, structured face-to-face interviews were conducted, an electrocardiogram was recorded and blood samples were collected. Follow-up interviews were carried out for all eligible participants each year during the study period of 4 years. The medical ethics committee of the Leiden University Medical Centre approved the study.

Depression

Each year we administered the 15-item Geriatric Depression Scale (GDS–15), a questionnaire especially developed as a screening instrument for the presence of depressive symptoms in elderly populations (Sheik & Yesavage, 1986). Depression was considered present when the score on the GDS–15 was 5 points or more. This cut-off gives the best sensitivity and specificity for the presence of major depression in the general population (Sheik & Yesavage, 1986), in geriatric in-patients (Shah *et al*, 1996), in primary care settings (D'Ath *et al*, 1994; Lyness *et al*, 1997) and in medical in-patients (Pomeroy *et al*, 2001), and was found to have a good specificity (0.85) in a representative sample of community-dwelling oldest old for the presence of major depression (de Craen *et al*, 2003). Because the reliability and the validity of the GDS–15 are compromised in older adults with serious cognitive impairment, the GDS–15 was not administered to participants with a Mini-Mental State Examination (MMSE; Folstein *et al*, 1975) score of less than 19 points.

Incidence and course

The incidence of depression was studied by following the participants without depression at baseline, defined as having a GDS–15 score of 0–2 points at age 85 years, over a 4-year period. Incident depression was considered to be present when the GDS–15 increased to 5 points or more during the follow-up measurements.

The course of depression was studied by following the participants with depression at baseline, defined as a GDS–15 score of 5 points or more, for 4 years. Remission of depression was defined as returning to a GDS–15 score of 0–2 points at any measurement during follow-up.

Risk factors

Demographic variables

Gender, marital status, living arrangements, loss of a spouse, income and institutionalisation were recorded. The majority of participants had received only

https://doi.org/10.1192/bjp.188.1.65 Published online by Cambridge University Press

Table 1 The incidence of depression[1] during a 4-year follow-up of 334 participants without depression at baseline[2] from age 85 years

Follow-up year	Participants at start of year (*n*)	Reasons for attrition			GDS–15 completed	GDS–15 ⩾5 points
		Dead	Refusal	Severe cognitive impairment[3]		
1	334	19	24	14	277	8
2	269	14	5	9	241	21
3	220	17	2	8	193	22
4	171	14	8	8	141	5

GDS–15, 15-item Geriatric Depression Scale.
1. Incident depression was present when the score on the GDS–15 was ⩾5 points.
2. Depression was absent when the GDS–15 was 0–2 points.
3. Severe cognitive impairment was present when the Mini-Mental State Examination score was below 19 points.

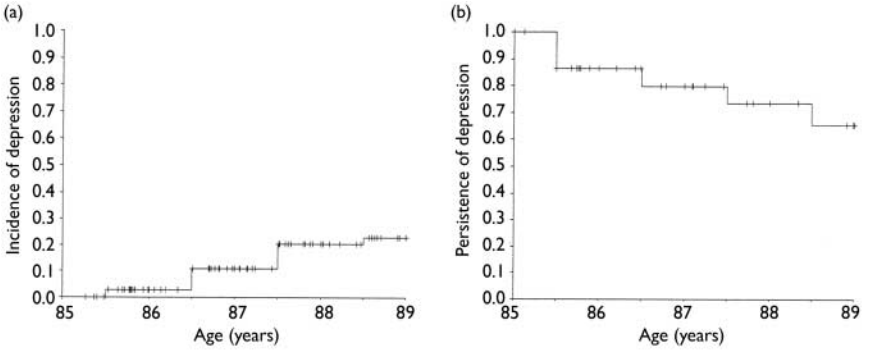

Fig. 1 (a) The cumulative incidence of depression in 334 participants without depression at baseline, defined as a score on the 15-item Geriatric Depression Scale (GDS–15) between 0 and 2 points, from age 85 to 89 years. Incident depression was defined as a GDS–15 score ⩾5 points during any of the follow-up measurements. (b) The cumulative persistence of depression in 77 participants with depression at baseline, from 85 to 89 years. Remission was defined as a GDS–15 score of 0–2 points at any of the follow-up measurements.

compulsory primary school education; a minority had additional education. Therefore the level of education was dichotomised at 6 years. As low income is a putative risk factor (Cole & Dendukuri, 2003) the income was dichotomised across state pension only and state pension plus additional income.

Disability in daily functioning

The Groningen Activity Restriction Scale (GARS; Kempen *et al*, 1996) was applied to measure disability in daily functioning. Poor daily functioning was defined as a GARS score above 23 points (33rd percentile). Furthermore, the self-rated presence of loneliness was assessed.

Health-related correlates

Information on the use of medication was obtained from the pharmacists' registers. Data on physical diseases were obtained via a structured questionnaire and based on general practitioners' diagnoses, blood samples and the results of the electrocardiogram. These included cardiovascular disease (stroke, myocardial infarction or ischaemia, arterial surgery, intermittent claudication), malignancy, Parkinson's disease, diabetes mellitus, chronic obstructive pulmonary disease, and arthritic disease at baseline or in the past. Diabetes was considered present in the case of a positive medical history, or current use of antidiabetic medication, or a non-fasting glucose concentration of 11.1 mmol/l or higher.

Statistical analysis

First, to make optimal use of the repetitive measurements and to correct for attrition due to mortality and cognitive decline, the cumulative incidence and the cumulative remission rate of depression with the corresponding 95% CI were calculated from life tables. The assumption was made that depression developed or remitted midway during the follow-up period in which the participant passed the GDS–15 cut-off point. Second, relative risks (and 95% CI) of risk factors for the incidence and the remission of depression were calculated in a Cox proportional hazards model, with the assumption that depression developed or remitted midway during the follow-up period in which the participant passed the GDS–15 cut-off point.

RESULTS

Baseline assessments

During the study period 705 inhabitants of Leiden reached 85 years of age and were eligible to participate. Fourteen died before they could be enrolled and 92 refused to participate. At baseline the response rate was 87%, resulting in a sample of 599 participants. There were no significant differences for various socio-demographic characteristics and the presence of depressive symptoms between the 599 participants and the source population (Bootsma-van der Wiel *et al*, 2002). Of the 599, 500 had MMSE scores of 19 points or more and were included in the present analysis. Of the 500 participants at baseline, 334 (67%) had no significant symptoms of depression, as evidenced by GDS scores of 0–2 points.

Incidence of depression

During follow-up, the mean total GDS–15 score increased significantly from 0.96 (s.d.=0.80) points at baseline to 2.3 (s.d.=2.7) at age 89 years (paired *t*-test, $P<0.001$). Table 1 shows the incidence of depression, defined as a GDS–15 score of 5 points or more, in the 334 participants without depression at baseline. During a follow-up of 827 person-years at risk, depression occurred in 56 participants (incidence rate 68 per 1000 person-years, 95% CI 50–85), amounting to an annual risk of 6.8%. Figure 1 illustrates the cumulative incidence of depression from age 85 to age 89 years.

Risk factors for the incidence of depression

Table 2 shows the impact of various risk factors for the emergence of depression.

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Table 2 The risk of depression during follow-up in 334 participants without depression at baseline in relation to socio-demographic characteristics, daily functioning and health characteristics

Characteristic	*n* (%)	Relative risk (95% CI)[1]	*P*
Female gender	209 (63)	1.1 (0.6–1.9)	NS
Low educational level	195 (58)	1.0 (0.6–1.7)	NS
Low income	53 (16)	1.6 (0.8–3.1)	NS
Not married[2]	204 (61)	0.8 (0.4–1.5)	NS
Living alone[2]	194 (58)	1.1 (0.7–2.0)	NS
Loss of a spouse[2,5]	56 (17)	0.9 (0.5–1.7)	NS
Presence of loneliness[2]	29 (9)	1.3 (0.5–3.3)	NS
Institutionalisation[2]	23 (7)	3.4 (1.5–7.5)	0.003
Poor daily functioning[2,3]	173 (52)	2.2 (1.3–3.8)	0.006
Presence of chronic diseases[2,4]	249 (75)	1.1 (0.6–2.1)	NS
MMSE score 19–23 points[2]	41 (12)	0.3 (0.04–2.1)	NS
Use of analgesics[2]	81 (24)	1.2 (0.7–2.2)	NS
Use of benzodiazepines[2]	56 (17)	1.1 (0.5–2.2)	NS
GDS–15 score at baseline (per point)[2]	–	1.9 (1.3–2.6)	<0.001

GDS–15, 15-item Geriatric Depression Scale; MMSE, Mini-Mental State Examination.
1. Relative risks were estimated with Cox's proportional hazard models.
2. Adjusted for gender, educational level and income.
3. Poor daily functioning defined as a Groningen Activity Restriction Scale score of 24–72 points.
4. Chronic diseases included cardiovascular disease, diabetes mellitus, chronic obstructive pulmonary disease, arthritis, Parkinson's disease and malignancy.
5. Loss of a spouse was introduced in the model as a time-dependent covariate.

Neither demographic characteristics nor any of the health-related characteristics contributed to the incidence of depression. Institutionalisation and poor daily functioning were associated with an increased risk of the development of depresssion. The GDS–15 score at baseline was associated with an almost twofold increased risk per point increase. After adjustment for the GDS–15 score at baseline, the increased risks of depression due to institutionalisation (relative risk=2.8, 95% CI 1.3–6.4) and poor daily functioning (relative risk=1.9, 95% CI 1.1–3.4) were sustained.

Remission of depression

Of the 500 participants at baseline, 77 had GDS scores of 5 points or more, indicating depression (prevalence 15%, 95% CI 12–18%). During the 4-year follow-up we observed a remission in 16 participants, with an annual remission probability of 14% (Fig. 1b). Remission was sustained in 7 of the 16 participants, whereas in 9 participants there was a relapse during follow-up. None of the factors described in Table 2 significantly predicted remission (data not shown).

DISCUSSION

In the present study, we have annually assessed the presence of depression in a large representative sample of community-dwelling oldest old persons. We show that the oldest old are at high risk of developing depression and that, when present, depression is highly persistent. Predictors of depression in the oldest old were institutionalisation and poor daily functioning, but no predictors were identified for remission.

Other studies

In one of the few longitudinal studies of depression in the old-old (79–85 years), Palsson *et al* (2001) reported an incidence of depression according to DSM–III–R criteria (American Psychiatric Association, 1987) of 44 per 1000 person-years, associated with female gender. The lower incidence compared with our estimate of 70 per 1000 person-years is possibly due to the younger age of their participants. An age-associated increase in the incidence of depression is further strengthened by the findings of Meller *et al* (1996), who described a very high incidence of 140 per 1000 person-years in a population of octo- and nonagenarians (85–103 years). Changes in living situation and dementia were the main risk factors in their study, but these did not reach statistical significance. As changes in living situation in this age-group usually mean moving to institutionalised living, this seems to be in line with the finding of institutionalisation as a predictor of depression. The lower incidence of depression reported by Haynie *et al* (2001) from the OCTO-Twin study may be explained by their selection of very healthy persons at entry.

Course of depression in the oldest old

In contrast to previous studies on the incidence of depression, no data were available on its course in the oldest old. A strong tendency for chronic depression has been reported in the younger elderly (Beekman *et al*, 2002). Persistence of depression in the younger elderly could be extrapolated to the oldest old.

Possible limitations

An important limitation of our study is that depression was not formally diagnosed. The GDS–15 was originally developed as a screening instrument for depressive illness in older adults, not as a diagnostic procedure. However, given the nature and size of this study, further diagnostic procedures were not feasible. This lack of a second-stage standardised assessment of depression may have resulted in higher incidence and lower remission figures in our study. However, the GDS–15 was found to have a good specificity (0.85) in a representative sample of community-dwelling oldest old for the presence of major depression (de Craen *et al*, 2003). Moreover, it is becoming increasingly clear that significant depressive symptoms in older adults have as distinct deleterious effects as formally diagnosed depressive disorders (Gallo *et al*, 1997). It could also be questioned whether the GDS–15 is able to detect changes in depressive symptoms over time. Within the Leiden 85-plus Study, we demonstrated that the loss of a partner, which is a major negative life event and an important risk factor for the emergence of depression in older adults, was associated with a significant increase of more than two points on the GDS–15 (Vinkers *et al*, 2004*a*). Thus, the chosen GDS–15 criteria for the incidence and remission of depression should enable us to measure

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a relatively robust change in depressive symptoms over time.

Although the initial response rate in this study was very high, substantial attrition owing to mortality and cognitive decline is an intrinsic part of all prospective studies of depression in the oldest old. In an earlier analysis, we found an almost twofold increased mortality risk for oldest old participants of the Leiden 85-plus Study with depression; this was sustained when corrected for demographic and health-related factors (Stek *et al*, 2005). In the present study, refusal to participate was not related to depression at baseline (Bootsma-van der Wiel *et al*, 2002), but participants with incident depression might have refused more often at follow-up. Confounding by effects of specific treatment is probably very limited because, as reported before, the use of antidepressants was almost non-existent at baseline (Stek *et al*, 2004). We did not identify determinants that predicted remission, but as depression is associated with refusal and mortality, the numbers in our study might have been too small to detect these effects.

Role of cognitive functioning and early dementia

Depression and early dementia are closely linked. Earlier we showed that cognitive impairment at baseline predicted an accelerated increase of depressive symptoms in the oldest old, whereas depression at baseline was not related to increased cognitive decline (Vinkers *et al*, 2004*b*). Thus, cognitive impairment preceded depression but depression did not herald cognitive decline. Cognitive impairment or early-stage dementia might well play an important role in the high incidence of depression and its persistence in the oldest old, but the underlying mechanisms are still unresolved. Since participants who developed serious cognitive impairment (MMSE <19 points) were excluded from our study, incidence rates for depression may even have been underestimated.

Treatment of depression in the oldest old

Notwithstanding a lack of knowledge about the origins of depression in the oldest old, from a clinical perspective it is very important that depression occurs often in this age-group and has a poor prognosis. Poor daily functioning and institutionalisation are strong predictors of incident depression in the oldest old. In an earlier study of the oldest old (Stek *et al*, 2004), the recognition of depression by the general practitioner was poor and antidepressive treatment virtually non-existent. Taken together with the results of the present study, it is clear that more active case-finding is warranted, as treatment of depression in the oldest old is as potentially rewarding as in younger people.

CLINICAL IMPLICATIONS

- Depression occurs frequently and is highly persistent in the oldest old.
- Poor daily functioning and institutionalisation at baseline predicted depression.
- More active case-finding and treatment of depression in the oldest old would be potentially rewarding.

LIMITATIONS

- Depression was not formally diagnosed.
- Participants with severe cognitive impairment (Mini-Mental State Examination score of less than 19) were excluded from the analyses.
- Substantial attrition due to mortality and cognitive decline is an intrinsic part of all prospective studies of depression in the oldest old.

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(First received 18 May 2004, final revision 2 February 2005, accepted 16 March 2005)

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https://doi.org/10.1192/bjp.188.1.65 Published online by Cambridge University Press