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Life events, difficulties and onset of depressive episodes in later life

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ABSTRACT

Background. The importance of stressful life events and long-term difficulties in the onset of episodes of unipolar depression is well established for young and middle-aged persons, but less so for older people.

Method. A prospective case–control study was nested in a large community survey of older people. We recruited 83 onset cases during a 2-year period starting $2\frac{1}{2}$ years after the survey, via screening ($N = 59$) and GP monitoring ($N = 24$), and 83 controls, a random sample from the same survey population. We assessed depression with the PSE-10 and life stress exposure with the LEDS.

Results. Risk of onset was increased 22-fold by severe events and three-fold by ongoing difficulties of at least moderate severity. Severe events accounted for 21% of all episodes but ongoing difficulties for 45%. The association of onset with life stress, often health-related such as death, major disability and hospitalization of subject or someone close, was most pronounced in the cases identified by screening. While a clear risk threshold for events was found between threat 2 and 3 (on a scale of 1–4), the risk associated with difficulties increased more gradually with severity of difficulty. Compared with controls, severe events involved a larger risk for cases without a prior history of depression (OR = 39·48) than for cases with (OR = 8·86). The opposite was found for mild events (OR = 2·94 in recurrent episodes; OR = 1·09 in first episodes). The impact of ongoing difficulties was independent of severity of episode and history of depression.

Conclusion. Although the nature of life stress in later life, in particular health-related disability and loss of (close) social contacts, is rather different from that in younger persons, it is a potent risk factor for onset of a depressive episode in old age. Severe events show the largest relative risk, but ongoing difficulties account for most episodes. The association of severe events with onset tends to be stronger in first than in recurrent episodes. Mild events can trigger a recurrent episode but not a first one.

INTRODUCTION

The significance of stressful life events and long-term difficulties in the aetiology of unipolar depression is well established for young and middle-aged persons, in particular women (Cooke, 1987; Brown & Harris, 1989; Jenaway & Paykel, 1997). The common denominator of the depressogenic life stress in these age groups involves loss, humiliation (e.g. being devaluated; loss of status; social putdown) and/or entrapment (e.g. caught up in poor marriage or job) (Brown *et al.* 1995).

Less is known about the role of life stress in the aetiology of depressive episodes in older people (Orrel & Davies, 1994). Murphy (1982), using the investigator-based Present State Examination (PSE) and Life Event and Difficulty Schedule (LEDS), found a strong association between life stress and onset of depression in the

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elderly, suggesting a similar link between life stress and depression in later life as seen in younger age groups. Life stress often involved health-related difficulties and loss of (close) social contacts. Studies following Murphy's pioneering work have generally confirmed her observation (Linn *et al.* 1980; Patrick & Moore, 1986; Lam *et al.* 1987; Evans & Katona, 1993; Beekman *et al.* 1995; Prince *et al.* 1997*a*). The interpretation of these studies, however, is not entirely straightforward. All have one or more of the following limitations: (*i*) selection bias due to the use of patient samples; (*ii*) information bias since well-established investigator-based assessment procedures for life stress and psychopathology were not used and/or occurrence of events and onset of depression not dated; or (*iii*) limited generalizibility because episodes were not stratified by severity and history of depression. Detailed knowledge of the contribution of life stress to the onset of depressive episodes in later life is important, because the prevalence of (mild) depression in the elderly is considerable (Koenig & Blazer, 1996; Beekman *et al.* 1999) and the elderly are an expanding age group, relatively as well as in absolute numbers.

The present, community-based case–control study seeks to document the relevance of life stress for the onset of depressive episodes in older people. Our aim is fourfold. First, to test the hypothesis that an excess of life stress occurs in the months preceding onset in cases compared with controls and to estimate the proportion of episodes that can be attributed to this excess. Secondly, to test the hypothesis that risk continuously increases with severity of life stress. Thirdly, to test the hypothesis that risk depends on severity of episode and history of depression but is independent of method of recruitment (cases identified by screening *versus* cases identified by general practitioners). Severe events will be more strongly associated with onset in first than in recurrent episodes, and in minor than in major episodes. Mild events will only be associated with onset in recurrent episodes, assuming that a history of depression indicates more vulnerability. Finally, we attempt to identify the nature of depressogenic life stress in later life. We expect that the majority of stressful events and difficulties will involve loss of physical abilities and loss of social contacts due to illness and death, not interpersonal stress and humiliation.

METHOD

Study design

The present study used a case–control comparison. We compared 83 cases (i.e. persons with a recent onset of depression according to the below-described criteria) recruited from April 1996 through April 1998, with 83 controls. All cases and controls were recruited from the participants in the NESTOR community survey among persons aged 57 years or more, carried out in 1993 to study correlates of quality of life in the elderly (for details, see Kempen *et al.* 1996; Ormel *et al.* 1997*a*, 1998). Of the 5279 persons who participated in the survey in 1993, 457 did not give informed consent for further contact, leaving 4822 persons. For the present study on depression, we identified cases during a 24-month period from April 1996. Controls were selected throughout the last 12 months of this period. During the enrolment period on average 3700 of the eligible 4822 persons were available for screening. Non-availability was due to death since 1993, severe physical or mental impairments, or participation in another study (e.g. on falls, myocardial infarction and cancer). The selection procedure is described in more detail below. Cases and controls were interviewed in their homes by female interviewers, aged 35 to 50, who were extensively trained by experienced staff members and maintained their skills in bi-weekly booster sessions. Cases were interviewed twice (within a few weeks), first with the PSE-10 and then with the LEDS. The control group, whose main purpose was to furnish data on the 'natural' exposure to life stress in later life, received the LEDS but not the PSE.

Selection of cases and controls

Cases were selected in three stages. The first stage involved two complementary approaches: the records of general practitioners (GPs) and a screening questionnaire. During the 24-month recruitment period, a research physician checked the medical records of all survey participants monthly and identified 83 'GP-positives' whom the GP had diagnosed as having depressive

illness (ICPC codes P03 and P76; Lamberts & Wood, 1987). In addition, because older people often do not present as depressed or are not diagnosed as such by GPs, we also screened twice for a recent onset of depression using the Geriatric Depression Scale (GDS-15) (Yesavage *et al*. 1982; Lesher & Berryhill, 1994) with a 1-month time frame. In total 7566 GDS questionnaires were sent out of which 85·4% were returned fully completed. The 269 persons with a GDS-15 score of six or more and a probable depression core symptom were considered 'screen-positive'.

The second stage was a brief telephone interview of the 347 GP-positive and/or screen-positive persons from which we identified 202 persons who had at least one depression core symptom that had emerged in the previous 9 months (84 did not; 61 refused). The third stage comprised the clinical interview. Of the 202 eligible persons, 19 (10·1%) were excluded because of incomplete or unreliable data, 18 (9·6%) did not meet the diagnostic criteria for (minor) depression, 49 (26·1%) did not meet the recency of onset criterion, 14 (7%) refused the clinical interview, and 19 (10·1%) were unprepared or unable to complete the life stress interview, leaving 83 cases with complete data (59 'screening cases' and 24 'GP cases').

Controls were selected at random from the available 3700 survey participants. Hence, the controls are not necessarily free of depressive symptoms. Of 102 controls approached, 83 (81·4%) participated.

Instruments and measures

Depression

Diagnostic assessment was based on the tenth version of the Present State Examination (PSE-10) (Wing *et al*. 1998) module from the Schedules for Clinical Assessment in Neuropsychiatry (SCAN) (WHO, 1992). Respondents were asked to indicate the 4-week period during the last 3 months preceding the interview at which they felt worst, and that period was assessed by the PSE-10. Controls were not interviewed with the PSE. We distinguished two categories of depressive episode: major episode, if the criteria for a DSM-IV (APA, 1994) major depressive episode were met ($N = 25$, 30·1% of cases) and *minor* episode ($N = 58$; 69·9%). The last category was defined as at least three symptoms (including depressed mood or loss of interest/pleasure) of subclinical severity or two symptoms of clinical severity, and no major depression. Subclinical severity means that the symptom was present, but to a degree insufficient for diagnostic classification according to the PSE-DSM-IV criteria. Depressive symptoms were scored only if they did not meet criteria for a mixed episode, were not attributable to direct physical effects of substance use or somatic illness, or bereavement.

Following the PSE, information on the history of depression was gathered with an interview specially developed for this purpose. First episode, means that there (probably) has never been a (minor) depressive episode before. Recurrent episode, means that there has been at least one previous episode that would have met the criteria for at least a minor depressive episode. Onset, refers to the transition from not meeting research criteria for at least minor depression to meeting criteria for a minor or major depressive episode. Since it is difficult to date onset, particularly if insidious, a calendar including neutral markers like national and local events, holidays, birthdays of close relatives was used to anchor them. We determined the week of transition by extensive probing, including information from significant others.

Stressful life events and (long-term) difficulties

We used the Life Events and Difficulties Schedule (LEDS) (Brown & Harris, 1978, 1989) to elicit and rate life events and difficulties in the 12 months preceding the interview. The LEDS is an investigator-based, semi-structured interview with excellent measurement properties, also in the elderly (Wilkinson *et al*. 1986; Orrel & Davies, 1994). LEDS interviews were rated by the interviewer and the research assistant who supervised the LEDS interviews. In case of discrepancies a consensus rating was achieved.

Although the LEDS covered the preceding 12 months, only events and difficulties occurring in a 3-month time window were compared. For cases, this was the 3 months preceding the onset of the depressive episode. For controls, it was the 3-month period starting 7·7 months prior to the LEDS interview and, hence, ending 4·7

months before the interview. This time window for the controls was chosen because the mean number of months between onset of the depressive episode in the cases and the LEDS was 4·7 months. This will reduce recall and reporting differences between cases and controls in as far as these are associated with the length of time between interview and life stress occurrence. The length of the reference period was chosen because analyses showed that the difference in occurrence rate of events between controls and cases began to emerge approximately 3–4 months prior to onset of the depressive episode (see Results section).

A stressful life event, is an event with a rating of 1–4 on Brown & Harris' 4-point contextual long-term threat scale that was (probably) not caused by (insidious) depressive symptoms (1 = mild; 2 = moderately severe; 3 = severe; 4 = very severe).

An ongoing difficulty, is a difficulty with a rating of 1–6 (mild to very severe) on Brown & Harris' contextual threat rating scale that was (probably) not due to (insidious) depressive symptoms, was present for at least 4 weeks during the reference period, and still present at the time of onset. We refer to the start of a difficulty in the LEDS reference period as a 'start of difficulty', and to the increase of the severity of a difficulty during this reference period as an 'increase severity difficulty'. Some 'increase severity difficulties' and 'start of difficulties' also met the criteria for an 'ongoing difficulty', and three 'start of difficulties' met criteria for an 'increase severity difficulty' (1 in the case group and 2 in the controls). Some life events were also rated as the start of a difficulty.

Statistical analysis

To examine selectivity of refusal we compared, at each stage of the recruitment process, those who refused participation with those who did not. Logistic regression analysis with STATA, with depression onset (cases *versus* controls) as the outcome variable, was used to examine the association between life stress and onset. The strength of the association was expressed in odds ratios (ORs) and a P value $< 0{\cdot}05$ (two-tailed) was considered statistically significant. To estimate the association of each severity level of events and difficulties with onset (Table 2), we performed logistic regression analyses in which each severity level was contrasted separately with the reference category. We also calculated the population attributable fraction (PAF = $[(OR-1)P1]/OR$, where P1 is the proportion of cases that is exposed (Rothman, 1986, p. 39)). For outcomes with a prevalence of about 3–10% in the population at large, the OR can be regarded as a reasonable estimate of the relative risk. Because there were more women in the group of cases than in the control group, analyses were adjusted for gender differences.

RESULTS

Non-response bias

We examined selectivity of refusal at three stages: the mail screening questionnaire, the telephone interview, and the face-to-face interviews (PSE and LEDS). The comparison involved the following variables measured in the 1993 survey: gender, age, marital status, educational level, cognitive and physical function, and depressive symptoms (tables available upon request). Regarding the mail screening questionnaire, responders were younger, more often living with a partner, less often widowed, had more often achieved secondary education, better cognitive and physical functioning, and less depressive symptoms than those not available for screening and those who did not return a two screening questionnaire. Regarding non-response at the telephone interview, responders were younger, had better cognitive functioning, but more depressive symptoms. Regarding refusal of the PSE and/or LEDS, we found no significant differences between responders and those who refused or broke off the interview.

Occurrence rates across time: establishing the 3-month LEDS reference period

Fig. 1 shows the monthly occurrence rate of events per 100 cases and controls. For cases the rate concerns the 6 months prior and the three months after onset. LEDS data for this period of nine months were available for 46 cases. For controls the rate concerns the period of 7·3 months before the 'equivalent of onset' (see Method section) and the period of 4·7 months thereafter. Occurrence rates of cases and control begin to diverge 3–4 months before onset. This is particularly salient for severe events. After onset the rates in cases drop again. For controls

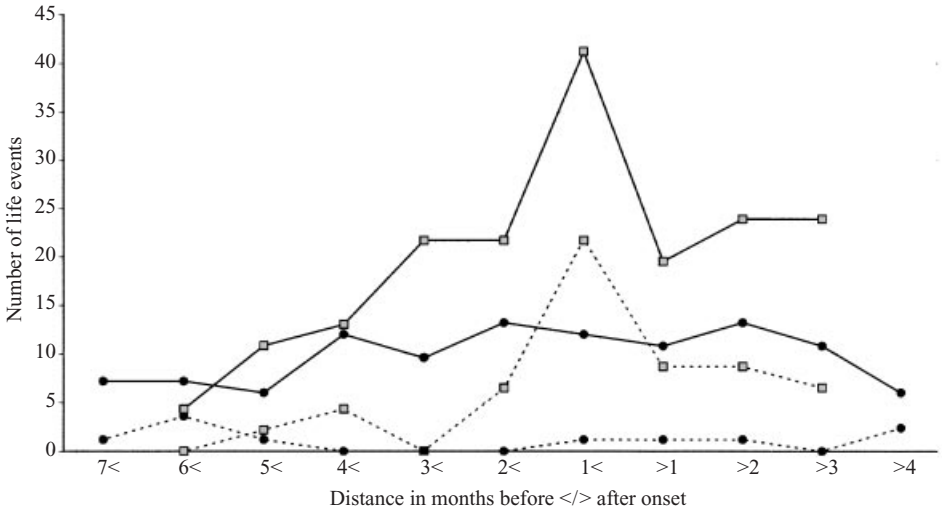

FIG. 1. Frequency of stressful life events in the 6 months prior to and 3 months after onset for cases ($N = 46$) and comparable periods for controls ($N = 83$); standardized per 100 persons. (—□—, Life events cases; - - □ - -, severe life events cases; —●—, life events controls; - - ● - -, severe life events controls.)

the rates are rather constant over the entire period, suggesting minimal recall bias. Cases reported the highest level of events for the 30 days preceding onset. The ultimate LEDS reference period was set at 3 months preceding onset.

Characteristics of subgroups of cases and controls

Table 1 reports sociodemographic and clinical characteristics of the 24 GP cases, the 59 cases recruited via screening, the 83 controls, and the 1993 survey sample. With regard to the sociodemographic characteristics only differences in age were found. GP cases were younger than both screening cases and controls. For the total case group no age difference with controls was found. With regard to the clinical characteristics, differences in mean GDS-score were found between all three subgroups. We found no significant differences in diagnostic mix and history of depression between GP and screening cases. Also minor and major episodes did not differ significantly as regards recurrence rate (48%, 52%), mean number of previous depressive episodes (1·2, 1·9) and age at onset of first episode (59 and 57 years). The mean GDS-score shows that the controls were not entirely without depressive symptoms, which was to be expected since they were selected at random from the community survey sample.

Table 2 shows, for the same subgroups as in Table 1, life stress exposure in terms of each level of severity for: events; start of a difficulty; increase of severity of an existing difficulty; and, ongoing difficulty. Some severity levels were collapsed because of prevalence considerations. Cases experienced more life stress than controls. While we did not find statistically significant differences between GP cases and cases identified through screening, the differences in exposure to life stress between GP cases and controls had the tendency to be less pronounced than those between screening cases and controls.

Do risks gradually increase with severity of life stress?

Table 2 also shows, for GP and screening cases together, the risk (OR) associated with various levels of event and difficulty severity (last two columns). Results clearly suggest that mild events (severity 1 or 2) and difficulties (1 or 2) are not associated with increased risk of onset. Severe events ($\geqslant 3$), start of severe difficulties ($\geqslant 3$ at the beginning), increase in severity of an existing difficulty with two or more points, and moderate (3) and severe ($\geqslant 4$) ongoing difficulties increased risk. While there was a large increase in risk for events between severity level 2 and level 3, the risk associated with ongoing difficulties increased more gradually with severity of difficulty.

Table 1. *Sociodemographic, cognitive and clinical characteristics*

	GP cases ($N = 24$)	Screening cases ($N = 59$)	Controls ($N = 83$)	Survey sample 1993 ($N = 5279$)
Gender				
Female, %	66·7	71·2	55·4	56·2
Age[a], %				
55–64	37·5**	18·6**	27·7	34·8
65–74	54·2**	44·1**	41·0	39·4
75–84	8·3**	33·9**	28·9	22·0
⩾ 85	0**	3·4**	2·4	3·8
Mean age, year	67·2**	72·2**[GP]	71·3**[GP]	69·6
Marital status[a], %				
Living with partner	70·9	57·6	71·1	67·2
Widowed	12·5	30·5	20·5	24·0
Educational level[b]				
At least 'Secondary', %	37·5	40·7	45·8	36·8
Mean rank (K–W)	77·9	79·6	87·9	
Cognitive functioning[c]				
MMSE-12, mean	10·9	11·1	11·1	10·9
Depressive symptoms				
GDS-15, mean	3·9**	5·5**	1·2**	NA
Diagnosis, %				
Symptomatic episode	16·7	27·1	NA	NA
DSM minor episode	41·7	47·5	NA	NA
DSM major episode	41·7	25·4	NA	NA
History of depression				
Previous episodes[d]	1·50	1·38	NA	NA
Age onset first episode[e], year	52·7	60·9	NA	NA
Recurrent episode[f], %	58·3	45·8	NA	NA
Onset first episode < 50 year, %	33·3	22·0	NA	NA

** $P < 0{\cdot}005$ pairwise tests (GP *v.* Screening; GP *v.* Controls; and Screening *v.* Controls; survey sample not included in tests; **GP = only significant difference with GP cases); chi-square (Gender; Civil status; Diagnostic categories; Recurrent; Onset first episode < 50 year), Mann–Whitney *U* test (Age categories; Education – see[b]; Diagnostic categories), otherwise *t* test; GDS-15 Screening *versus* GP cases actually $P = 0{\cdot}04$.

[a] Cases and controls: age and marital status just before the (3-month) LEDS reference period; percentage widowed at clinical interview: 20·8% of GP cases and 37·3% of Screening cases.

[b] Based on a six-point scale ('Secondary' is category four); data collected in 1993.

[c] Cases and controls: data collected at (first) interview in 1996–1998.

[d] Three screening cases could not give (an estimate of) number of previous episodes; mean number of previous episodes for recurrent cases only, 2·57 (GP) and 2·96 (Screening).

[e] Five screening cases were unable to give (an estimate of) their age at onset first episode; mean age at onset first episode for recurrent cases only, 42·4 year (GP) and 43·7 year (Screening).

[f] Two screening cases (one minor and one major) did not remember whether they had a prior episode or not.

K–W, Kruskal–Wallis; NA, not applicable.

Do risks depend on recruitment method, severity of episode and history of depression?

We selected three stress indices to examine whether the association of life stress and onset was independent of recruitment method, severity of episode, and history of depression: event ⩾ 3; ongoing difficulty ⩾ 3, and 'any life stress ⩾ 3'.

Table 3 presents the association of the event ⩾ 3 index with onset, stratified by recruitment method (GP cases *versus* screening cases), for minor and major episodes (rows 1–4), and recurrent and first episodes (rows 5–8) separately. The results suggest a more important role of severe events (⩾ 3) in first than in recurrent episodes. This applies to both GP cases and cases identified through screening, albeit the difference is only statistically significant for the total group. The strength of the association of severe events with onset was independent of severity of episode.

The associations of ongoing difficulties ⩾ 3 and 'any life stress ⩾ 3' with onset were independent of recruitment method (GP *versus* screening cases), severity of episode, and history of depression. The ORs for the subgroup GP cases (*versus* controls) ranged from 1·44 to 3·36, none of which were significant; the ORs for the

Table 2. *Three-month exposure to life stress, c.q. four life stress measures, for two case-groups according to recruitment method and controls; and results from logistic regression analyses, in which each severity level was contrasted separately with the reference category, all cases* versus *controls*

	GP cases ($N = 24$)	Screening cases ($N = 59$)	All cases ($N = 83$)	Controls ($N = 83$)	Odds ratio[a]	95% CI
Event, %						
No events[b]	62·5	40·7**	47·0**	74·7		
Threat 1	4·2	11·9**	9·6**	7·2	2·12	0·68–6·57
Threat 2	16·7	23·7**	21·7**	16·9	2·04	0·91–4·57
Threat 3 or 4	16·7	23·7**	21·7**	1·2	28·62	3·67–> 100
Start of difficulty, %						
No start of difficulties[b]	83·3	74·6**	77·1*	91·6		
Threat 1 or 2	4·2	8·5**	7·2*	7·2	1·19	0·37–3·86
Threat 3, 4 or 5	12·5	16·9**	15·7*	1·2	15·44	1·97–> 100
Increase severity difficulty, %						
No severity increases[b]	79·2	72·9*	74·7*	90·4		
Severity increase $\geqslant 1$	8·3	18·6*	15·7*	8·4	2·25	0·84–5·98
Severity increase $\geqslant 2$, $\geqslant 3$ or $\geqslant 4$	12·5	8·5*	9·6*	1·2	9·68	1·18–79·50
Ongoing difficulty, %						
No ongoing difficulties[b]	16·7	8·5**	10·8**	21·7		
Severity 1 or 2	25·0	20·3**	21·7**	37·3	1·16	0·43–3·12
Severity 3	29·2	40·7**	37·3**	27·7	2·70	1·03–7·08
Severity 4 or 5	29·2	30·5**	30·1**	13·3	4·55	1·56–13·24

Significant difference with controls, pairwise Mann–Whitney *U* tests (over all categories): * $P < 0{\cdot}05$; ** $P < 0{\cdot}005$.

[a] Estimates the risk associated with each level of severity of event/difficulty.

[b] Reference category for each logistic regression analysis was the subgroup without: event; start of difficulty; increase in severity of difficulty; and, ongoing difficulty respectively.

Table 3. *Univariate effects of one major stress indice* (*Event* $\geqslant 3$) *for case-subgroups according to recruitment method, severity of episode and history of depression; case subgroups* versus *controls* (N = 83)

	Minor episode			Major episode			Difference	
Event $\geqslant 3$	*N*	OR	95% CI	*N*	OR	95% CI	χ^2	*P*
GP cases	14	6·30	0·37–> 100	10	35·10	3·22–> 100	1·90	0·17
Screening cases	44	27·30	3·39–> 100	15	20·50	1·97–> 100	0·15	0·69
Difference		$\chi^2 = 1{\cdot}79$ ($P = 0{\cdot}18$)			$\chi^2 = 0{\cdot}33$ ($P = 0{\cdot}57$)			
All cases	58	21·39	2·69–> 100	25	25·89	2·94–> 100	0·11	0·74
	Recurrent episode[a]			First episode[a]			Difference	
	N	OR	95% CI	*N*	OR	95% CI	χ^2	*P*
GP cases	14	6·31	1·02–> 100	10	35·14	3·22–> 100	1·90	0·17
Screening cases	27	10·25	0·37–> 100	30	41·00	4·96–> 100	3·66	0·06
Difference		$\chi^2 = 0{\cdot}16$ ($P = 0{\cdot}69$)			$\chi^2 = 0{\cdot}04$ ($P = 0{\cdot}85$)			
All cases	41	8·86	0·96–82·07	40	39·48	4·93–> 100	5·71	0·02

[a] One patient with minor depression and one with major depression did not know whether they had a prior episode or not.

screening cases ranged from 3·36 to 5·49 and were all significant, as were the ORs for the total group (full table available on request).

Nature of life stress in later life

We examined the 12-month incidence rate of specific events and difficulties in control subjects (a random sample from the population of older people) and the ratio of the percentage cases to controls who experienced the event or difficulty in the 3-month reference period, for all events and difficulties, and for those concerning the subject or a close relationship only (table available on request). Fifty-three per cent of all 12-month events and 75% of the difficulties of the controls were health-related. The ratio

coefficients showed that most types of events and difficulties occurred more often in cases than in controls, in particular events involving the subject or a close relationship. Two-thirds of the health-related events in cases compared to a quarter of these events in the 3-month period for controls, concerned the subject or a close relationship. If limited to relatively common events, the largest ratios were found for in-patient surgery and physical health events leading to a hospital admission involving the subject or a close relationship, and bereavement. Cases experienced these events 4–6 times more often than controls. All 23 deaths occurring in the control group during the full 12-month LEDS concerned persons who were not very close to the subject, whereas 6 out of the 13 deaths occurring in the 3-month pre-onset period concerned a person close to the subject. The difficulties confirmed the pattern observed for events, although the differences in occurrence rate were generally smaller. Illness and treatment related difficulties concerning the subject or a close relationship and non-marital relationship difficulties occurred about 1·5 times more often in cases than in controls.

Do events and difficulties have unique contributions?

Events and difficulties are associated. An event can lead to a difficulty and people exposed to a difficulty more often experience an event than those without difficulties. By means of multivariate models we examined whether the life stress measures, dichotomized at different thresholds, had unique contributions to risk of onset. The first model assessed all four life stress categories with a severity of at least 1 (event $\geqslant 1$, OR = 2·95, $P = 0{\cdot}002$; start difficulty $\geqslant 1$, OR = 2·56, $P = 0{\cdot}06$; increase severity difficulty $\geqslant 1$, OR = 2·60, $P = 0{\cdot}04$; ongoing difficulty $\geqslant 1$, OR = 1·49, $P = 0{\cdot}40$). The second model used higher thresholds: event $\geqslant 3$ (OR = 15·77, $P = 0{\cdot}009$), start difficulty $\geqslant 3$ (OR = 6·88, $P = 0{\cdot}08$), increase severity difficulty $\geqslant 2$ (OR = 5·51, $P = 0{\cdot}12$), and ongoing difficulty $\geqslant 3$ (OR = 2·10, $P = 0{\cdot}04$). A third model, almost identical to the second one but with a one point higher threshold for ongoing difficulty, yielded only slightly higher ORs. These findings suggest partly unique contributions of events and moderately severe difficulties.

Population attributable fractions (PAFs)

We calculated the PAFs associated with a variety of life-stress measures. The PAF indicates the fraction of episodes that can be attributed to each category or combination of life stress. Unadjusted for each other, events $\geqslant 3$ accounted for 21% of the episodes, start of a difficulty $\geqslant 3$ for 15%, increase in severity of difficulty with $\geqslant 2$ points for 9%, and ongoing difficulties $\geqslant 3$ for 45%. Collectively (i.e. any of the above) these life stress measures accounted for 52% of all episodes, less that the sum of the individual, unadjusted contributions. Finally, any life stress (severity threshold $\geqslant 1$) accounted for 73% of episodes.

Mild life stress triggers recurrent episodes

We also examined the effect of mild events (severity 1 or 2) for first and recurrent episodes separately (stratified by method of recruitment as well as pooled). The association between onset and events with severity 1 or 2 tended to be stronger for recurrent than first onsets (pooled data, OR 2·94, 95% CI 1·30–6·66 *versus* OR 1·09; 95% CI 0·40–2·94; difference in ORs, $\chi^2 = 3{\cdot}29$, $P = 0{\cdot}07$). The difference in association was most pronounced in the cases identified by screening.

DISCUSSION

Our findings confirm earlier reports (Orrel & Davies, 1994), in particular the pioneering study by Murphy (1982), that life stress in later life is a potent risk factor for onset of a depressive episode. The association holds for both cases recruited through screening and through the GP, albeit it was weaker for the GP-diagnosed cases. As such this study expands findings on the role of life events and difficulties in the aetiology of depression in young and middle-aged people to the growing population of older people. Severe events increased risk 22-fold, and difficulties of at least moderate severity increased risk three-fold. Seventy-three per cent of all onsets could be attributed to life stress, which consisted, as Orrel & Davies (1994) already suggested, to a large extent of health-related events and difficulties, particularly death, physical disabilities, and hospitalization of someone close to subject, and to a lesser extent of

interpersonal stress. The role of life stress in depression in the elderly seems no less important than in non-elderly populations, given that estimates of the relative risk (RR) in younger populations generally range from 3–10 and the population attributable fraction (PAF) from 29–69% (e.g. Cooke, 1987; Brown & Harris, 1989; Jenaway & Paykel, 1997). Our study also expands the finding in younger samples (Brown *et al*. 1994; Frank *et al*. 1994) that the association of severe events with onset is stronger for first than for recurrent episodes. Major and minor episodes were equally strongly associated with severe events, although in the subgroup of GP cases severe events tended to play a more important role in major episodes. The impact of difficulties was independent of severity of episode and history of depression.

Limitations and strengths

Our study has several limitations. First, we used two recruitment methods. Persons whom we recruited via screening of the 1993 community survey sample ($N = 59$) were supplemented with persons from the same survey sample who had consulted their GP and were diagnosed as suffering form depression by the GP ($N = 24$). Hence, help-seeking factors may have introduced information bias. We think bias has been minimal however, since recruitment specific analyses showed that associations were in the same direction and did not significantly differ between the two recruitment groups.

Secondly, a quarter of the population surveyed in 1993 was not available during the two years of recruitment. Particularly non-response due to unwillingness, poor health and participation in another study (regarding e.g. cancer, myocardial infarction, fractures, bereavement) may have introduced selection bias. The analyses in which non-available persons and screening non-responders were compared with those who participated in the screening demonstrated poorer physical, cognitive, and mental health in 1993 in the first two groups. Consequently, we will have missed a number of onsets, also because the available survey participants were screened only twice during the 24-month recruitment period. However, if non-availability and refusal have caused selection bias, the bias will be conservative, as the missed onsets largely will have been reactive to poor health and bereavement.

A third limitation concerns the fact that we cannot exclude information bias (both recall and observer) in the measurement of life stress. Exposure to life stress was elicited retrospectively, and, in cases, after onset. In addition, the LEDS and PSE were administered about two weeks apart by the same interviewer. We think that information bias will have remained within acceptable boundaries, for the following reasons: (*i*) the LEDS applies rigorous methodology to minimize information bias; (*ii*) we used an extensive calendar to help memory and dating; (*iii*) in the control group, occurrence rates were constant over time and did not fall off with recall time, suggesting that the LEDS performed well (while this does not exclude information bias in the cases, it supports the validity claim); (*iv*) events and difficulties that may have been caused by (insidious) psychopathology were excluded; (*v*) onset cases with a death of a loved one in the 2 months preceding the PSE-interview were excluded, unless the symptoms were clearly out of proportion; and, (*vi*) the nature of most life stress that we elicited (health-related disability and loss of close contacts due to illness and death) renders recall and observer bias less likely.

Controls were randomly selected from all available survey participants. Some may have been depressed during the 24-month recruitment period, or even at the time they took the LEDS. If this has been the case, it will have biased the results, but the bias will be conservative.

Major strengths of our study include the prospective case–control design nested in a large community-based study and the use of investigator-based semi-structured instruments for the measurement and dating of onset and life stress.

Risk threshold of life stress may be lower in later life

For events we found a definite threshold between severity rating 2 and 3. Difficulties also seem to have some threshold between rating 2 and 3, but the increase in risk was modest and more continuous with increasing severity. These results suggest that, for older people, a one point lower threshold than the one proposed by Brown & Harris for younger samples is probably a better choice. A lower threshold in older people may compensate for the low occurrence rate of very severe events (rating 4) and difficulties (5

and 6). This is consistent with Davies' (1994*a*, *b*) finding that, compared to younger subjects, the severity of events found in the elderly is relatively low.

Mild events can trigger recurrent episodes

Although mild events (severity 1 or 2) were not associated with onset of first episodes, they increased onset risk three-fold in the subgroup with a history of depression. This might point at a higher psychobiological vulnerability as a result of genetic factors, childhood experiences, and/or previous episodes (scarring) (Brown *et al.* 1994; Frank *et al.* 1994).

Nature of life stress in the elderly

Although life stress was more prevalent in onset cases than controls, there were hardly any differences in the nature of life stress. Health-related events and difficulties were by far the most common life stresses in both groups, followed by deaths of loved ones and problems in non-partner relationships. The largest differences between cases and controls were found for death of a (very) close tie and subject's or very close other's life threatening events. Our findings are in line with the high prevalence of health-related adversity in later life (Davies, 1994*a*; Bieliauskas, 1995; Prince *et al.* 1997*a*) and its association with depressive symptoms found in earlier studies (Beekman *et al.* 1997; Prince *et al.* 1997*b*, 1998). Women reported significantly more difficulties, in particular health-related, than men. Otherwise we found no clear gender differences in prevalence and nature of adversity.

Loss and the production of well-being

It is not surprising that loss of physical function and loss of contact with close ties is so depressogenic in the elderly. According to the Social Production Function theory physical capacities and close ties are important resources for achieving physical and social well-being (Ormel *et al.* 1997*b*; Steverink *et al.* 1998). Steverink *et al.* have argued that in later life the production of well being through the first-order instrumental goals of status, behavioural confirmation and 'stimulation' becomes more difficult, relative to the goals of affection and 'comfort'. It is precisely the latter two that are threatened by loss of contact with close ties and loss of physical function.

Clinical and public health implications

It is difficult to see how life stress in the elderly can be prevented. The majority consists of health-related events and difficulties, and thus seems largely outside subject's control. While it is unlikely that this kind of life stress is caused by psychosocial characteristics of the depressed individuals, these characteristics may influence appraisal of and coping with life stress, and hence its depressogenic potency. We have work on this in progress. Loss of physical function and social contacts should alert clinicians, nurses, and other providers of health and home care for the elderly. They may also 'warn' elderly people with a history of depression that mild events can trigger recurrence, and monitor them through the period of risk (Brugha *et al.* 1997). Because of the high prevalence of mild events, the benefit–cost ratio of such monitoring care may be low, however. Strategies to minimize the negative practical and emotional consequences of severe losses and to enhance environmental and psychosocial resources for substitution might be a better alternative. Such strategies may be cost-effective tools for the reduction and shortening of episodes of late life depression.

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