Predicting the Short-Term Outcome of First Episodes and Recurrences of Clinical Depression: A Prospective Study of Life Events, Difficulties, and Social Support Networks

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Background: The study employed interview-based, investigator-rated measures of symptoms and psychosocial adversity in a panel survey to predict clinical course of depression.

Method: 130 men and women attending psychiatric hospitals for episodes of depressive disorders were interviewed with the Present State Examination and Life Events and Difficulties Schedule. After a mean 4-month interval, 119 were successfully reassessed to test the hypothesis that recovery from clinical depression is related to rates of life event stress and difficulties (termed *psychosocial adversity*) in the 6 to 12 months preceding initial evaluation.

Results: The severity ($p < .01$) and the duration ($p < .01$) of the episode of depression up until the initial evaluation emerged as the only significant background predictors of episode severity at later follow-up. High levels of adversity were significantly ($p < .05$) related to a poor clinical course, due to failure to recover from first-onset and from second episodes. Recovery from all but first episodes was predicted by higher levels of social support rated at initial attendance. There was no evidence for the buffering of the harmful effects of adversity by larger, more connected social support networks.

Conclusion: Both life event stress and support network characteristics are associated with the short-term outcome of depressive episodes. The findings for social support in particular confirm growing evidence of the importance of distinguishing between early and later relapsing episodes in causal investigations of depression. They reveal a progressive vulnerability to deficits in social circumstances with advancing course of disorder.

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Interest in the influence of social circumstances on the course and outcome of depressive disorder has been considerable. Two methodological problems with such research have proved less amenable than others to rectification: biased recall of retrospectively gathered data and the influence individuals have on their own risk of exposure to life event stress and to unsupportive social networks. According to Helzer,[1] "It is doubtful that the etiological role of life events in depression can be adequately studied using a retrospective design, a design that nearly all investigators still use." Therefore, two methodological solutions may be suggested. First, as in this work, prospective observational or panel surveys have been conducted in which data on life event stress and social support and symptom severity are compared with subsequently gathered data on symptom severity. Second, it might be possible to test the effect on later health status of experimentally reducing exposure to life event stress or to test the effects of stress-buffering interventions, for example, by marshalling additional social support or by enhancing problem solving and coping.[2] Both study designs, whether based on naturalistic observation or involving intervention under controlled conditions, have their own disadvantages. Thus, both approaches to investigating the influence of social factors should be attempted.

The past decade has seen a number of observational studies in which measures of life event stress and of psychiatric disorder (mental health status) have been administered on two or more occasions in general population and clinical samples.[3–6] Most have assessed psychiatric status and the history of life events at the same time; this

means that when the life event history relates to a time before the mental state, the history is still open to distortion by the mental state.[1,7] However, this distortion may be avoided if the event history is related to the mental state at the *next* assessment.

The determinants of outcome of episodes of depression may overlap with those of its onset, but are unlikely to be identical. Examples of potential influences on outcome are the buffering or ameliorating effect of social support[8] and the exacerbating effect of a delay in seeking treatment.[9]

There is a growing acknowledgment of the importance of distinguishing between first episodes and recurrences.[10,11] Kessler and Magee[10] found differences in predictors of outcome of major depression according to whether respondents had experienced prior episodes. It has also been suggested that life events may be more strongly associated with first, rather than subsequent, episodes of affective disorder.[11–13]

Little guidance is available to investigators on the time period to be adopted in a panel design in a prospective study of outcome. The risk period for the onset of depression following a threatening life event is generally thought to be 2 or 3 months and is almost certainly no more than 6 months.[14,15] But it is not clear how long a life event may operate to maintain a depressive state once it has developed. Depressive episodes treated by specialized services often last longer than 6 months. Therefore, it is possible that the duration of these longer episodes may not be positively associated with antecedent life events. However, the longer the interval between successive assessments, the more ambiguous is the relationship between life event stress rated earlier and current mental state. In the same way, little guidance is available concerning possible time relationships between social support and clinical outcome. Taking these and practical considerations into account, we decided to opt for a relatively short follow-up interval. Our aim was to test the hypothesis that episodes of depression involving life event stress improve to a greater extent in 3 to 6 months than do depressive episodes not associated with adverse events.

THE PRESENT STUDY

The Camberwell Collaborative Depression Study[15] was designed to examine social and familial influences on the course of moderate and severe clinical depression. The study design made it possible to examine whether the relationship between social factors and clinical course was stronger in neurotic than in endogenous types of depression. In earlier analyses, we have shown that aspects of the social network predict the course of depressive disorders[8,16] and that levels of life event stress and social support are independent of one another over a short follow-up period.[17] We have also reported on the ineffective use[18] and under-use[19] of efficacious treatments. In the current report, therefore, we seek to establish the relationship between life event stress and subsequent clinical course and whether this relationship is conditional on social network support (which might buffer the effects of stressors), on whether the episode is a first onset or a recurrence, on age and gender, and on the type of depressive episode, as suggested by earlier work.[3,8,10–13,16] Significant conditional associations, or interactions, of this kind could lead to more selected targeting of treatments and interventions for the most affected subgroups.

Specifically, we hypothesized that life event stress in the period preceding an initial assessment interview, within 6 months of episode onset, would be inversely related to severity of depression assessed independently approximately 4 months later. Methods of clinical assessment and research diagnostic classification were used in line with previous studies of social risk factors by the same investigators[20,21]; these were designed to operationalize clinical guidelines approximately equivalent to those in the International Classification of Diseases (ICD)[22] then in official use.

METHOD

Design

A general description of the study and its design is provided by Bebbington and colleagues[15]; more details can be obtained from the authors. The design chosen was an observational, cohort (panel) survey of patients presenting with episodes of depression. The study was carried out in Camberwell, predominantly a densely populated, working class area of South London, characterized by high rates of male unemployment, single-parent families, and a substantial ethnic minority population comprising mainly people of African-Caribbean and African origins.

Patients

The patients were consecutive series of men and of women from the Camberwell area presenting at the Maudsley Hospital outpatient and emergency clinics with episodes of depression. Sampling criteria are given in Table 1. Subjects had to be diagnosed as suffering from a depressive episode for no longer than 6 months at the point of recruitment. The design required approximately equal numbers of men and women. Altogether, 130 patients were assessed, and follow-up clinical data were obtained on 119.

Measures and Procedures

All initial or re-referrals to the outpatient and emergency clinic facilities of the Maudsley Hospital were scrutinized. With outpatients, this could be done to an extent in advance as there was usually a preceding referral

Table 1. Sampling Criteria*

Inclusion criteria
Clinical diagnosis of primary depression
Definite positive rating of depressed mood (Item 23 of PSE-9)
British- or Irish-born Camberwell resident
Age 18–64 y
No episode or contact with psychiatric services for 6 mo preceding onset of episode
Episode onset in last 6 mo
PSE ID-CATEGO Class D, R, N, or A
Exclusion criteria (based on ICD-9 guidelines)
Organic disorder
Drug misuse or significant alcohol misuse or dependency (MAST Alcohol Screening Questionnaire positive)
Significant personality disorder
Nonaffective psychosis or mania

*Abbreviations: ICD-9 = International Classification of Diseases, 9th edition; ID-CATEGO = research diagnostic algorithms and classification rules for the PSE (Classes D and R = endogenous depression, Classes N and A = neurotic depression). MAST = Michigan Alcoholism Screening Test; PSE-9 = Present State Examination, 9th edition.

letter that gave a rough indication of the problem. If there was a possibility that an outpatient was going to be suitable, further information was sought from the examining doctor, from the case notes completed at the first appointment, or from the patient himself.

Patients attending the emergency clinic had their details entered into a book after they were seen. The entry included a provisional diagnosis. The case notes of any person whose entered diagnosis raised the possibility that he or she might be depressed were perused. If necessary, the patient was then contacted, usually at home or by telephone, to verify eligibility. Informed consent for the first interview was sought from eligible patients who met the first five inclusion criteria (see Table 1). On the basis of this interview, the full criteria were applied, and those patients meeting them were invited to participate in the rest of the study.

The necessity for spreading the net widely and the stringency of the inclusion criteria (which rapidly became apparent) meant that over 2000 patients were canvassed at least briefly to obtain the final sample. However, because of the multistage screening procedure, only three patients were omitted on the basis of the first interview. The rarity of depressed males fulfilling our criteria made it necessary to add cases from socioeconomically similar areas surrounding Camberwell and to extend collection of male patients after we ceased collecting female patients.

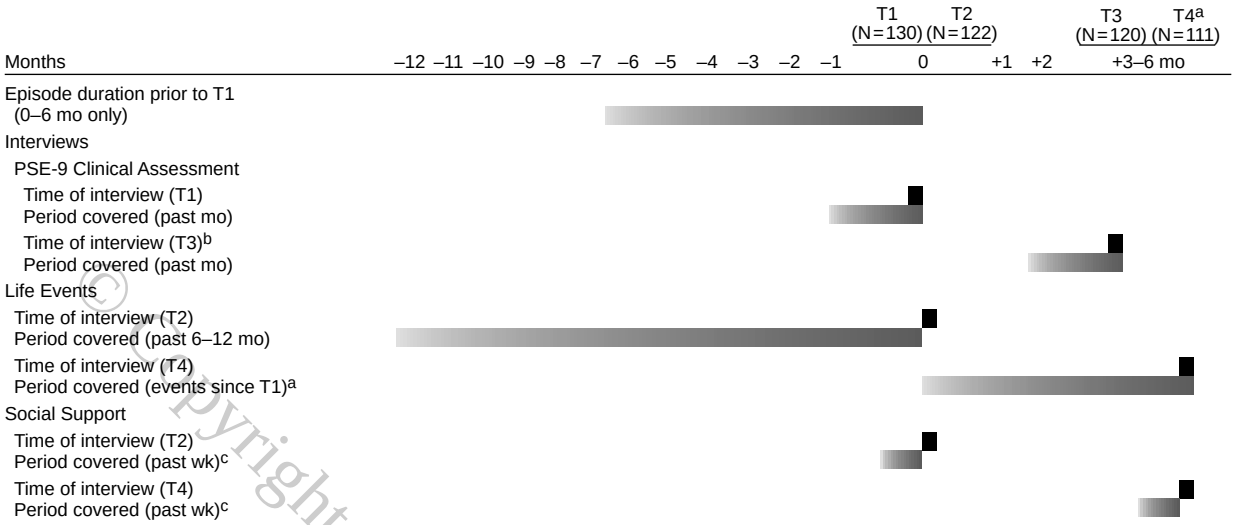
A period ranging from 3 to 6 months separated the four independent clinical and social assessments of potential subjects (numbered T1 to T4, see Figure 1). The first assessment was conducted by a research psychiatrist as soon as possible after patients had been seen at the Maudsley (T1). This first interview determined the subject's psychiatric state, clinical history, basic sociodemographic characteristics, and social class grading.[23] With the subject's consent, past medical records were sought to assess the clinical history further. This was followed within a week by a second interview (T2) with another member of the team concerning recent experience of life events and details of social supports. The interviewers at T2 were given details of the date of onset of the episode, but remained ignorant of its symptomatic pattern. Occasionally, it was impossible to be unaware, for instance, that a patient was seriously retarded, thus introducing the possibility of bias. However, such instances were rare.

After a mean interval of 4 months (range, 3 to 6), subjects were contacted again, and their current psychiatric state was established by the same psychiatrist at a third interview (T3). Details of interim treatment and disposal were obtained. A fourth interview (T4) at that time sought information about intervening adversity and current social contacts, but these data were employed in this report in secondary explanatory analyses only.

Clinical Assessment

The psychiatric status of our subjects was established at both T1 and T3 through the Present State Examination (PSE-9) and the associated classification algorithm (ID-CATEGO)[24,25] and through the Michigan Alcoholism Screening Test.[8] The PSE is a semistructured, highly flexible, clinically based assessment interview covering the key psychotic and neurotic symptoms required for the major functional psychiatric disorders in ICD-8.[22] Formal training and a background of clinical experience are required to administer the interview. Symptoms are rated present by the examiner only when the patient's description matches the predefined Glossary definition of each symptom; it is the investigator and not the respondent who decides whether the patient has the symptom.[21] Where available, written evaluations from past treated episodes were also assessed, and ratings of clearly described symptoms were recorded on a Syndrome Checklist (SCL).[24,25] ID-CATEGO is a separate set of research diagnostic algorithms and classification rules for PSE and SCL ratings, which may be used after an interview or medical record assessment has been completed and rated. ID-CATEGO is used to allocate each patient to a single category that is, within limitations, approximately equivalent to an ICD-8 class.[22] In addition to applying the ID-CATEGO classification rules[24,25] to the PSE and SCL data sets, the ICD-10 rules for depressive episode and the DSM-III-R rules for major depressive episode were also applied to the PSE interview assessments, as described elsewhere.[26] The eight-level dependent variable (ID: Index of Definition) in this study was derived by means of the ID-CATEGO rules. ID level 1 is defined by the absence of PSE symptoms; level 5 represents the "threshold" category; levels 6, 7, and 8 indicate an increasing degree of confidence that the symptoms present can be classified into one of the conventional categories using the ID-CATEGO rules as embodied in the computer

Figure 1. Timing and Time Coverage of Assessments of Cohort



[a]T4 data used in secondary analyses only in this report.
[b]PSE-9 at T3 to assess presence of symptoms and disorder, but subsequent time course and timing of recovery not recorded or estimated.
[c]Refer to the text for further details of the period covered by the social support interviews.

program CATEGO4: i.e., "endogenous" depression (CATEGO Classes D and R) and "neurotic" depression (Classes N and A). The actual date of onset of their episode of depression was carefully established at interview. There is extensive evidence for the reliability of the PSE in clinical and general population surveys.[27] The PSE was carried out by research clinicians of 5 to 15 years' experience as psychiatrists. Regular meetings were held during field work to discuss difficulties with ratings and to review CATEGO4 output. To minimize measurement error arising from divergence between raters, each examiner was responsible for both the initial (T1) and follow-up PSE assessment (T3) of each patient.

Recent Adversity (Stressful Life Events)

Social circumstances were assessed within a week of each clinical interview at T2 and T4 by interviewers other than those who administered the PSE.[15] The occurrence of life events or difficulties during the period beginning 6 months before the onset of their episode of depression and up to the time of the T1 interview was established using the reliable semistructured Life Events and Difficulties Schedule (LEDS).[14,18,29] Interview data on possible adverse life events and difficulties were later presented to a panel of trained raters blind to the identity of subjects, the type or severity of their episodes of depression, and their actual responses to the event or difficulty. The panel then made ratings of life events and difficulties, taking account of the context in which they occurred. For example, a higher level of threat would be rated in a mother whose child developed persistent, unexplained anemia and malaise if she had previously suffered the death of an older child through a hematologic malignancy. Training was provided by developers of the LEDS, and reliability has since been corroborated in hospital cases.[29] Events and difficulties were also rated in terms of the degree to which they appeared independent of the subject's symptomatic behavior: logically independent, possibly independent, and dependent. Event rates for the period between T1 and T3, the follow-up interview, were also established for the purposes of secondary, explanatory analyses because reports of these events could have been contaminated by the clinical state at outcome.

Event rates were calculated for each subject according to the method described by Surtees and Duffy.[30] For each type of event considered, the number (N) of such events that occurred per 6 months per 100 subjects was calculated. This continuous or rate measure (R) took account of the variable period of time (T) in weeks covered by the LEDS[14] interview (26 to 52 weeks up to T1; Figure 1) using the formula $R = N/(T + 26)$. Surtees and Duffy[30] have shown the rate measure to have greater predictive validity than the conventional binary method.

Social Relationships

The range and connectedness of social networks and levels of social support were assessed by the Interview Measure of Social Relationships (IMSR).[31] Subjects were asked to nominate other adults whom they considered close relatives or good friends. The structure of the network was assessed by asking subjects to say, for each member of the primary group, which other members he or she knew well and had at least monthly contact with. This is indicated by the term *network connectedness*. Within the same study population, interrater reliability and temporal stability for the IMSR are satisfactory.[17,31]

Analyses and Statistical Methods

Primary analyses were carried out to investigate associations between events before T1 and social networks at T2 and the PSE-ID level representing clinical state at T3 independently, in the whole sample. Associations were first examined with nonparametric correlation coefficients (Kendal's tau) and plotted graphically to ascertain nonlinear trends. Degrees of freedom are quoted for specified tests. Multiple regression analyses were then carried out. Because sampling procedures differed in the two sexes, gender was included before adversity and other predictor variables in multiple regression analyses. Assuming a two-sided significance level of .05 and 80% power, we calculated that the study size was capable of detecting main effect correlations of at least .15; the power to detect interactions would be far more limited. Such interactions are known to have a low probability of replication in independent samples. The most parsimonious model fit was sought by testing higher order interactions and main effects and then removing those that were not significant predictors. Multiple linear logistic regression analysis was also used to fit ordinally scaled forms of the dependent variable by the method of maximum likelihood.[32] Survival analysis could not be used because we lacked precise data on the timing of recoveries between T1 and T3.

RESULTS

It was not possible to determine if 5 of the patients who seemed to meet study criteria were indeed eligible, as we failed in all attempts to contact them. In addition, 9 of those who met study criteria refused to participate. There were 130 successful first (T1) interviews. The T2 and T3 interviews were conducted on 122 and on 120 respondents, respectively. One of the 120 patients completing the T3 interview did not complete the T2 interview covering stressful life events and social support; thus, 119 patients were included in the following outcome analyses. Although this represents an above average follow-up rate, the representativeness of those reinterviewed was checked. When follow-up responders and nonresponders were compared, there was a small but statistically nonsignificant trend for more follow-up interview failures in female subjects.

The sociodemographic and clinical characteristics of these 130 patients have already been described elsewhere.[8,15] There were 33 men and 34 women with endogenous depression (CATEGO Classes D and R) and 21 men and 42 women with neurotic depression (Classes N and A). At the first interview, 99 (76%) of 130 were definite cases, and 30 were threshold cases according to the ID. Of the 130 patients on whom a PSE-9 was completed, 114 had sufficient symptoms to fulfill the DSM-III-R criteria for major depressive episode[33]; 116 patients had sufficient PSE-9 symptoms to fulfill ICD-10 Diagnostic Criteria for Research[34] (DCR) for depressive episode, of whom 92 were moderate and 28 were severe cases. Eighty-six of the series had recurrent depressions, and 1 patient, who was not successfully followed up at T3, had previous manic and depressive episodes rated on the SCL. At the third interview (T3), 76 (63%) of those reassessed with the PSE had improved by at least two ID levels; 35 patients still fulfilled DSM-III-R major depression criteria, 43 still fulfilled ICD-10 depressive episode criteria, and 3 patients had developed manic episodes (PSE-9 CATEGO class M).

Independent events with a rating of 1 or 2 on long-term threat occurring in the period of 6 to 12 months before the initial interview gave a mean rate in men of 58.0 events per 100 men per 6 months, and in women of 90.3 per 100 women per 6 months. Correlation coefficients (Kendal) were calculated between the T2 LEDS event rates and the T3 PSE-ID index of clinical severity. For independent events, the correlation was $r = .13$, $df = 1,118$; $p = .06$ for all 119 probands; and for the nonbipolar probands, it was .15, $p = .04$; for both independent and possibly independent events, the correlation was $r = .11$, $df = 1,118$; $p = .10$ for all probands; and for the nonbipolar probands, it was .14, $p = .05$. The same analyses were carried out using LEDS ongoing long-term difficulties (up to T1) instead of events, and no correlations with the T3 PSE-ID index of clinical severity emerged. Similarly, event and difficulty rates during the interval between T1 and T3 were not related to outcome.

Multiple regression analyses were undertaken in which the following predictor variables were added. These were the initial (T1) (mental) health status in the form of the PSE-ID level, number of weeks between depression onset and the PSE interview, number of previous episodes, type of disorder (CATEGO A or N versus R or D), together with age, social class, and antidepressant treatment. Only the initial PSE-ID level and the number of weeks between depression onset and the first PSE interview (T1) were associated (positively) with the later T3 PSE-ID level. This model accounted for 14% of the variance in the follow-up T3 PSE-ID level (Table 2). These two significant clinical predictors were therefore not excluded. The ineffectiveness of antidepressant treatment is detailed elsewhere.[18,19]

When the two background clinical predictors and gender were controlled, independent events preceding the T1 assessment were positively associated with clinical severity measured at T3 4 months later (Table 1), confirmed under logistic regression analysis.

Interaction terms were then added to the model. Only independent event rates were included in these analyses. Terms expressing interactions between adversity and age, gender, episode number, number of weeks between the T1 and T3 assessments, and the type of depression were entered. No significant interactions were found for age, gender, or the interval between T1 and T3. There was no evi-

Table 2. General Linear Models on Outcome of Present State Examination Index of Definition (PSE-9-CATEGO-ID): Clinical Model, Main Effects, and Interaction Terms

Predictor Model	F	df	Slope Estimate	Standard Error	p	%R^2	Change in R^2	Significant Improvement in Prediction p Value
Clinical and demographic								
Initial ID (severity) level at T1[a]	9.95	1,118	0.609	0.193	.002	7.8	…	…
+ time from episode onset to T1	9.08	2,117	0.062	0.022	.001	13.4	5.6	.007[b]
+ gender	0.72	3,116	–0.300	0.355	.001	14.0	0.6	NS[b]
+ Main effect of risk factors assessed at T2[a] interview								
Independent event rate 6 mo preceding and since episode began	6.04	4,114	12.540	5.100	.001	18.2	4.2	.02[c]
Network predictor assessed at contact with psychiatric service (T2 interview)	6.28	4,114	–0.018	0.007	.001	18.3	4.3	.02[c]
+ Interaction terms: conditional on number of past depressive episodes:								
Events × total number of episodes	0.11	6,112	–1.110	3.310	.001	18.4	0.2	NS[d]
Events × one or more recurrences	0.37	6,112	–6.840	11.280	.001	18.5	0.1	NS[d]
Network × total number of episodes	8.26	6,112	–0.012	0.004	.001	24.8	6.5	.003[d]
Network × one or more recurrences	8.09	6,112	–0.042	0.015	.001	23.9	5.6	.005[d]

[a]See Figure 1 for interview times: T1 and T2 were at initial contact with the psychiatric service and approximately 7 days apart.
[b]Improvement over immediately preceding model.
[c]Improvement over clinical model.
[d]Improvement over main effect model.

Table 3. General Linear Models on Outcome of PSE-9-CATEGO-ID Severity Level: Subset Analyses in First-Onset and Recurrence Cases, Clinical Model, and Main Effects

Sample Subset	Predictor	F	df	Slope Estimate	Standard Error	p	%R^2	Change in R^2	Significant Improvement in Prediction p Value
First onset cases	Clinical model[a]	1.61	3,35	[b]		NS	12.1	…	…
	Life events	3.41	4,34	18.8	10.2	NS	20.1	8.9	NS
	Network	0.63	4,34	0.011	0.014	NS	13.7	1.6	NS
First episode and first relapse	Clinical model[a]	4.48	3,80	[b]		0.006	14.4	…	…
	Life events	5.39	4,79	13.7	5.9	0.001	19.9	5.5	.02
	Network	1.85	4,79	–0.01	0.01	0.007	16.4	2.0	NS
All recurrences	Clinical model[a]	4.83	3,77	[b]		0.001	15.8	…	…
	Life events	2.89	4,75	10.3	6.1	NS	18.8	3.0	NS
	Network	15.6	4,75	–0.031	0.008	0.001	30.2	14.4	.001

[a]Clinical model (Table 2) = Initial severity + time since episode onset + gender.
[b]Details of specific parameters available on request.

dence of interaction between adversity and the PSE-CATEGO neurotic-endogenous classification (p = .33). The association between adversity and poor outcome was significant only in the neurotic depressives subgroup (p = .035), but not very different in the endogenous depressives (p = .134). Although the slope estimate and percentage variance explained in the follow-up PSE-ID appear greater in the neurotic subgroup, it is clear that the 95% confidence intervals for these estimates overlap considerably. The interaction term *adversity* by number of past episodes was not significant either (p = .08; and Table 2). Subset analyses were also carried out using groupings based on the number of past episodes of depression. When those with two or more past episodes of depression were examined, it was clear that prediction of outcome of depression was not related to adversity (Table 3). The predictive effect of adversity seen in the earlier main effect analyses seemed to be confined to those with no more than one past episode (F = 5.39; df = 4,79; p = .02).

We next considered the role of supportive social networks in predicting recovery. Since we had not previously examined the interaction effects of social support with age and the number of previous episodes of disorder,[8,16] these were considered; only the number of previous episodes interacted significantly with the IMSR social network variables. The most significant of these findings was with the number of frequent and strong social links between primary group members (*social network connectedness*). Both the main effect for this variable and its in-

teraction with the number of past episodes of depression predicted later clinical severity at high levels of statistical significance (Table 2), and this effect was greatest for recurrent episodes (Table 3). This was confirmed by logistic regression models. There was a highly significant *inverse* relationship between network connectedness (T2) and the subsequent PSE-ID level (T3) in patients with recurrent episodes (Table 3).

Adding network connectedness (social support) to the model containing life events improved prediction further: $F = 4.3$, $df = 5,113$; $p = .04$; total $\%R^2 = 21.2$. When the interaction between the support variable and the number of past episodes of depression was added, the explained variance in the outcome PSE-ID level rose from 21.2% to 26.5%. However, a three-way interaction term (life events × support × number of episodes of depression) was clearly not significant ($p = .5$).

In sum, the most parsimonious model consisted of the two clinical predictors (severity and duration at T1), the two main effects of life event stress and social support, and the number of past episodes of depression and its interaction with social support only. The statistical significance of this model was virtually unchanged when logistic regression was employed and when the patients who developed bipolar episodes were excluded. These analyses were repeated with the patients fulfilling major depression criteria: the loss of 14 patients had very little effect and made no change in the choice of the most parsimonious model. The interaction between support and the number of past episodes remained highly significant under both least squares and logistic regression modelling ($p = .002$). Similarly, the predictive power of life event stress as an independent main effect held up under all of these reanalyses.

DISCUSSION

We have shown that independent life events preceding an assessment during the first 6 months of an episode of depression significantly predicted clinical severity 3 to 6 months later. This ran counter to our hypothesis that adversity-related depression would have a better outcome. There is very little evidence for suggesting that failure to recover from neurotic as opposed to endogenous depressions is more strongly related to adversity. The strength of the association was independent of the actual interval between the initial (T1 and T2) and the follow-up (T3) assessment. These findings held even when background factors such as gender, age, social class, and the severity of the episode of depression were controlled.

Our study has methodological advantages. At its core was an epidemiologically based series, although we had to top up with some male patients from neighboring and outside areas. Losses at the initial referral and follow-up were low. Outcome and predictor variables were assessed independently of each other. Our methods of assessment were intensive and well established and were administered by well-trained interviewers. Adversity was rated by taking account of its context and its degree of independence from the illness process. Life events and social support were measured prospectively; the severity of psychiatric symptoms, which is by far the most important predictor variable in such observational studies, was also directly assessed at two time points. Previous studies have used retrospective assessments of adversity gathered at the same time as outcome data[4,35] or used self-completion or self-rated measures of adversity[4,36] or subsequent depression status.[37] Several studies reporting negative findings may in our view have opted for over-long periods of follow-up.[5,6,36] None has examined possible differences between first and later episodes, and some failed to control for initial psychiatric status in their models.

Inevitably, our study has a number of limitations and weaknesses. A deprived inner urban community may not reflect disorders within a national or whole population setting. Logistic regression analyses[32] were also carried out; these more stringent analyses produced essentially the same results. In addition to the PSE-CATEGO classification, we also applied the more recent ICD-10 and DSM-III-R rules. Analyses restricted to subjects fulfilling DSM-III-R major depression criteria produced virtually identical findings. Likewise, confining our analyses to a purely unipolar set of patients made very little difference to the results. The multiplicity of analyses inevitable in such studies may raise the type I error rate and emphasizes the need for replication, particularly when model building includes interaction terms. This limited sample size means that more complicated, interactional models, although interesting, cannot be as easily investigated. Type II error is just as likely to be a problem in a small study with limited statistical power, and we must therefore advise caution in drawing conclusions from it.

The relation of adversity to later severity was independent of gender, age, and whether the type of depression is endogenous or neurotic in presentation. Similarly, the effects of life event stress prior to T1 on outcome was independent of the follow-up interview timing. Thus, the effect of adversity on outcome did not appear to decay over time. Incidentally, as reported elsewhere, there was a much higher rate of adversity, when the period before T1 was compared with the period before T3.[17] In secondary analyses, we also found that adversity in the period between T1 and T3 was not related to clinical outcome at T3, possibly because it was at a significantly low level during a time when many of the patients were in receipt of treatment. Why does adversity appear to exert an effect on the maintenance of depression over such a long period? This would be the case if the consequences of adversity persisted and still had to be coped with at a time of impaired functioning. We have no direct claim to support this idea.

The association between adversity and outcome did not interact significantly with the type of depression. This might be the consequence of small numbers once the case material was subdivided. However, our data suggest that any such interaction effect would be small and not of clinical significance. These findings may be of clinical value, since they provide an argument for focusing treatment on the management of the longer term psychological impact of negative stressful experiences irrespective of the type or the duration of the depressive episode.

We were unable to establish convincing evidence of significant interaction between adversity and relapse number. However, subset analyses did suggest that severe life events were more associated with nonrecovery in first and second episodes as compared to later episodes (Table 3). Our findings on adversity accord, to a limited degree, with Post's more recent conceptualization[11] of his earlier kindling hypothesis. He hypothesized that, in subsequent affective disorder episodes, sensitization to stressors and episode sensitization occur through encoding at the level of gene expression. In subsequent episodes, relatively minor events, not sufficiently threatening to be rated on the LEDS, might contribute to a poor outcome in patients.

We found no evidence for an interaction between support and adversity (even when we distinguished between first-onset and recurrent cases). Thus, our findings do not support the hypothesis that low social support makes depressed people vulnerable to life stress and thus less likely to recover quickly. The buffering hypothesis of social support was originally developed to explain why many individuals do not become ill after exposure to adversity. Far less consideration has been given to social predictors of recovery, and the same arguments need not apply. Indeed, our finding that the connectedness of support networks in the acute phase of relapse episodes leads to better clinical outcomes is also consistent with the idea that sensitivity to adverse social circumstances increases in recurrent cases.

Most attempts by other workers to show a relationship between illness and variables that are specifically concerned with network *structure* have resulted in negative findings.[38] We report here for the first time a relationship of network connectedness with course and short-term outcome. This variable is closely related to the structural concept known as *network density*[31]; it is also highly correlated with the size or range of the primary group. It implies that the members of the primary group include people who themselves have a large number of close relatives and friends and are thus likely to be more prosocial and positively supportive people. Help and support may flow more rapidly toward the index member because of the increased opportunity for intercommunication. The rating of this variable is also less likely to be open to subjective bias. Social connectedness was positively related to recovery in recurrent cases. Those nominated as close members of the network by patients undergoing later episodes were then more effective supporters. Could it be that some of those named as close during a first episode of depression proved less helpful, understanding, and reliable? Those chosen as close during later episodes might then exclude people who had previously failed to be reliable sources of support. Better outcomes would therefore be seen in patients with close networks that are larger and more prosocial, and these may possibly comprise persons who through earlier periods of illness have stood reliably by the patient. These questions, together with the study's main findings, should be considered in future research, using the same design but a larger sample with a broader representation of the general population.

In summary, adverse events and difficulties appear associated with the early course of depression as well as with onset. In contrast, *lack* of support, ordinarily construed as a less significant stressor, emerged as the most sensitive indicator of social adversity in the later, increasingly vulnerable stages in the natural history of depressive disorder.

CONCLUSION

The predictive power of social influences for the short-term course of depression appears to depend upon whether the disorder is an early or later episode. These findings have implications both for our understanding of depressive disorder and for its clinical management and call for attention in future research.

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