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Residual symptoms after partial remission: an important outcome in depression

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SYNOPSIS This paper draws attention to an important adverse outcome in depression, the occurrence of residual symptoms after partial remission. Among patients with definite major depression followed every 3 months to remission and thereafter, residual symptoms reaching 8 or more on the Hamilton Depression Scale 17-item total were present in 32% (19) of the 60 who remitted below major depression by 15 months. The pattern was of mild but typical depressive symptoms. Residual symptoms were more common in subjects with more severe initial illness, but were not related to any other predictors, including longer prior illness, dysthymia, or lower dose of drug treatment during the illness episode. There were weak associations with personality that might have been consequences of symptom presence. Residual symptoms were very strong predictors of subsequent early relapse, which occurred in 76% (13/17) of those with residual symptoms and 25% (10/40) of those without.

INTRODUCTION

In recent years it has become apparent that, although most patients experiencing an episode of depression undergo some improvement in the next few months (Keller *et al.* 1982), the longer term outcome is still problematical. Failures to achieve a good outcome may take a number of forms. Those usually described have been: (*i*) delay or absent remission (chronicity); (*ii*) relapse (early return of symptoms that may be regarded as return of the index episode); and (*iii*) recurrence (later occurrence of symptoms that follows recovery and might be regarded as a new episode) (Prien, 1992). Definitions for recovery, relapse and recurrence have been proposed by Frank *et al.* (1991). Chronicity has usually been defined in recent follow-up studies as failure to achieve remission over 2 years (Scott, 1988; Coryell *et al.* 1990).

In a companion paper (Ramana *et al.* 1995) we describe the course of a longitudinally studied cohort of depressives, with respect to remission and relapse and their predictors. The purpose of this paper is to draw attention to another adverse outcome, partial remission with residual symptoms, which has key prognostic significance. Although the latter finding is apparent in previous published reports, residual symptomatology has received relatively little explicit study.

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METHOD

A separate paper (Ramana *et al.* 1995), gives full details of methods, which will be summarized briefly here.

Subjects

Subjects were psychiatric in-patients or out-patients aged 18–65 satisfying the Research Diagnostic Criteria (Spitzer *et al.* 1978) for definite primary unipolar major depression. Subjects were identified at presentation at a treatment facility and were consecutive patients except where staffing did not permit screening of settings at certain times. Out-patients were under-represented, and the sample predominantly comprised in-patients.

Follow-up design

After detailed initial assessment the patients were followed longitudinally. A full interview was undertaken every 3 months, and patients

were in addition, asked to return a Beck Depression Inventory (Beck *et al.* 1961) in the intervening 2 months. The purpose of this was to identify indications of change towards remission and relapse, which might bring forward the timing of the next interview. Patients were followed systematically to the point of remission (defined as 2 consecutive months, retrospectively rated, below the inclusion criterion of definite major depression), or until 15 months without remission had elapsed. Patients who remitted were then followed up systematically in the same way, with 3-monthly interview and Beck Depression Inventories in the intervening months, for a further 12–15 months (curtailed in some patients, to permit timely conclusion). The purpose of the second phase was to identify relapse, defined as a return to satisfy RDC definite major depression for at least 1 month, rated retrospectively.

Assessments

Patients were interviewed initially by a research psychiatrist or research psychologist and a comprehensive set of background and clinical data obtained. Instruments included: (1) background information, obtained on a semi-structured interview covering sociodemographic data, previous and recent psychiatric history, and personal history variables; and (2) mental state, assessed on a combined interview used in previous studies (Sireling *et al.* 1985; Paykel *et al.* 1988), including the Clinical Interview for Depression (CID) (Paykel, 1985), and the Hamilton Depression Rating Scale (Hamilton, 1967). Additional information was obtained to enable completion of the Research Diagnostic Criteria, together with classification on DSM-III-R (American Psychiatric Association, 1987) and ICD-10 (World Health Organization, 1992).

At 3-monthly intervals thereafter (brought forward if there was evidence of marked change on the Beck Depression Inventory), patients were reinterviewed to establish symptom status, using a shorter combined interview, comprising: (1) the shorter version of the Clinical Interview for Depression to measure severity, from which depression and anxiety total scores were obtained (Paykel, 1985); (2) the Hamilton Depression Rating Scale, from which the 17-item total was used (Hamilton, 1967); (3) the Raskin Three Area Total Score (range 3–15) (Raskin *et al.* 1970); (4) a seven-point global rating of severity of illness, which was also completed for the intervening months; and (5) the Beck Depression Inventory was completed in the intervening months. It was not intended to be used as an outcome measure, but as a trigger for earlier interview.

Personality was assessed within a few weeks of the recovery rating at interview with the patient by a psychiatrist using the Personality Assessment Schedule (Tyrer, 1988). Additional data were collected at initial interview and every 3 months on a number of psychosocial measures, to examine effects of social adversity. This is reported elsewhere (Paykel *et al.* 1996).

RESULTS

Sample and overall outcome

General findings regarding study flow, course of remission and relapse and their predictors are presented in a companion paper (Ramana *et al.* 1995). A total of 70 patients were included initially in the study. Six were lost to follow-up soon after the initial interview, leaving 64 subjects followed. Forty-eight were in-patients and 16 were out-patients. All but four of these 64 subjects had remitted by 15 months. Among the 60 patients followed beyond remission, three were lost to follow-up and the remaining 57 were followed up to relapse or completion.

For most subjects improvement occurred moderately rapidly. However, relapse was common, and 40% (23/57) relapsed to definite major depression over the subsequent follow-up period.

Residual symptoms

Residual symptoms at the time of remission were regarded as present when the Hamilton total score was 8 or more. Table 1 shows the distribution of Hamilton total scores at the remission rating. Residual symptoms were present at remission in 19/60 (32%) of the sample. They spanned a range from 8 to 18 on the Hamilton scale.

Individual symptoms

In order to explore the nature of residual symptoms, distributions of individual symptom ratings were examined for the 19 subjects with residual symptoms, and mean scores compared

Table 1. *Distribution of Hamilton Total Scores at remission rating*

Hamilton 17-item score	*N*	%
0–4	28	46·7
5–7	13	21·7
8–10	4	6·7
11–12	7	11·7
13–15	3	5·0
16–18	5	8·3
Total	60	100

in those with and without residual symptoms. Findings for the Hamilton scale are shown in Table 2. Item score ranges in this scale are partly 0–2 and partly 0–4. For this analysis they were grouped into three groups: none, mild (rating 1), moderate (rating 2 or more). The symptoms present were those typical of depression. At least 47% (9) of the subjects showed ratings at the level of moderate or greater on the items of depression, impairment of work and activities, psychic anxiety and genital symptoms. The remaining symptoms were present to at least a mild degree in 47% or more of subjects, the exceptions being a group of symptoms typical of severe depression, including some biological symptoms: late insomnia, retardation, agitation, hypochondriasis, weight loss and loss of insight. Mean scores on all individual symptoms differentiated significantly between subjects with, and without, residual symptoms, except for these items.

Table 3 shows findings for a parallel set of analyses carried out on the Clinical Interview for Depression (1–7 Scales; mild = 3, moderate = 4). Findings were similar. Depressed mood, guilt, hopelessness, impaired work and interests, psychic anxiety and anorexia were present to moderate degree in at least 37% (7) of the patients. The remaining symptoms were present to at least a mild degree in at least 47% (9) except for delayed insomnia, retardation, agitation, panic attacks, increased appetite and depressed appearance. Mean scores on all symptoms except the first four significantly differentiated those with, and without, residual symptoms. Particularly noteworthy was the lower score for increased appetite in those with residual symptoms.

Predictors of residual symptoms

Initial characteristics predictive of residual symptoms at remission were examined by dividing the sample into subjects with, and without, residual symptoms and comparing the

Table 2. *Individual symptoms on the Hamilton Scale*

Symptom	Distribution in patients with residual depression (*N* = 19)			Mean scores	
	None (0) *N* (%)	Mild (1) *N* (%)	Moderate or more (2 or 2–4) *N* (%)	No residual depression (*N* = 41)	Residual depression (*N* = 19)
Depressed mood	3 (16)	7 (37)	9 (47)	1·00	1·42***
Guilt	6 (32)	9 (47)	4 (21)	0·32	0·89***
Suicide	9 (47)	5 (26)	5 (26)	0·07	0·84**
Early insomnia†	10 (53)	2 (10)	7 (37)	0·22	0·84*
Middle insomnia†	9 (47)	8 (42)	2 (11)	0·17	0·63*
Late insomnia†	16 (84)	1 (5)	2 (11)	0·15	0·26
Work and interests	3 (16)	5 (26)	11 (58)	0·44	1·58***
Retardation	16 (84)	3 (16)	0 (0)	0·05	0·16
Agitation	18 (95)	1 (5)	0 (0)	0·00	0·05
Psychic anxiety	4 (21)	6 (32)	9 (47)	0·24	1·26***
Somatic anxiety	4 (21)	11 (58)	4 (21)	0·17	1·00***
GI symptoms†	11 (58)	6 (32)	2 (11)	0·02	0·53**
General somatic symptoms†	1 (5)	13 (68)	5 (26)	0·61	1·21***
Genital symptoms†	4 (21)	5 (26)	10 (53)	0·59	1·32***
Hypochondriasis†	16 (84)	1 (5)	2 (11)	0·05	0·26
Weight loss†	14 (74)	2 (10)	3 (16)	0·10	0·42
Insight†	19 (100)	0 (0)	0 (0)	0·00	0·00

* Significant difference at $P < 0·05$ by *t* test; ** $P < 0·01$; *** $P < 0·001$.
† 0–2 scale, remainder 0–4.

Table 3. *Individual symptoms on Clinical Interview for Depression*

Symptom	Distribution in patients with residual depression ($N = 19$)			Mean scores	
	None (1–2) N (%)	Mild (3) N (%)	Moderate (4–7) N (%)	No residual depression ($N = 41$)	Residual depression ($N = 19$)
Depressed mood	3 (16)	9 (47)	7 (37)	1·88	3·42***
Guilt	7 (37)	5 (26)	7 (37)	1·70	2·95***
Hopelessness	4 (21)	6 (32)	9 (47)	1·78	3·32***
Suicidal tendencies	11 (58)	5 (26)	3 (16)	1·12	2·21**
Work and interests	5 (26)	6 (32)	8 (42)	1·68	3·26***
Psychic anxiety	5 (26)	6 (32)	8 (42)	1·56	3·11***
Panic attacks	17 (89)	0 (0)	2 (11)	1·11	1·32
Phobic anxiety	9 (47)	8 (42)	2 (11)	1·34	2·37**
Somatic anxiety	10 (53)	7 (37)	2 (11)	1·27	2·42***
Anorexia	12 (63)	0 (0)	7 (37)	1·10	2·32**
Increased appetite	18 (95)	1 (5)	0 (0)	1·59	1·11*
Initial insomnia	11 (58)	3 (16)	5 (26)	1·44	2·32*
Delayed insomnia	17 (89)	2 (11)	0 (0)	1·22	1·26
Retardation	17 (89)	2 (11)	0 (0)	1·05	1·32
Agitation†	18 (95)	1 (5)	0 (0)	1·00	1·11
Depressed appearance at interview	15 (79)	3 (16)	1 (5)	1·10	1·84**

* Significant difference at $P < 0·05$ by t test; ** $P < 0·01$; *** $P < 0·001$.
† 1–4 scale.

two groups on initial characteristics, testing continuous variables by t test and categorical variables by chi-square with Yates' correction where appropriate. The predictors examined are listed in Ramana *et al.* (1995). They included sociodemographic variables (5 variables), family and personal history (6), past and present illness history (5), diagnosis and classification (5) and illness severity (3). Only two significant predictors were found at the 5% level. Patients with residual symptoms had higher initial scores on the Clinical Interview for Depression anxiety total (mean = 13·71) than those without (mean = 11·13, $t = 2·08$, $P < 0·05$). Similarly, they showed higher initial mean scores on the Hamilton scale 17-item total score (22·24) than those without (19·55, $t = 2·03$, $P < 0·05$). The rated initial symptom levels in both groups were probably underestimates, since it was not always possible to rate the patients until a few days after admission. There was also a trend at the 10% level for residual symptoms to be more common where the illness satisfied ICD-10 criteria for a severe, rather than moderate episode, confirming a consistent but weak relationship to initial severity. Residual symptoms were not predicted by a longer illness prior to presentation or more previous episodes or, in an additional analysis, by a longer time to remission.

Personality

A potentially important factor in residual symptoms was the presence of disturbance before illness, whether viewed as personality-related or as reflecting lower level illness, as in dysthymia. A number of variables measured this possibility. These included judgements of previous personality abnormality and diagnosis of dysthymia on DSM-III-R criteria made at initial interview. None of these variables was associated with residual symptoms. Only 11% (2/19) of those with residual symptoms satisfied DSM-III-R criteria for dysthymia as opposed to 17% (7/41) of those without residual symptoms.

Findings on personality as assessed by the Tyrer Personality Assessment Schedule at remission are shown in Table 4. Personality assessments were obtained for 13 subjects with residual symptoms and 35 without. Findings are shown for overall presence or absence of personality disorder or difficulty as defined in the schedule, and for mean scores on the key personality traits (schizoid, sociopathic, passive–dependent, anankastic). There was a weak general trend for more personality abnormality in those patients with residual symptoms. This reached significance only for the passive–dependent trait score. Specific personality disorders occurred too infrequently to be examined

Table 4. *Personality Assessment Schedule*

	No residual depression ($N = 35$)		Residual depression ($N = 13$)	
	N	%	*N*	%
Any PAS personality disorder	11	31·4	7	53·8
Any PAS personality difficulty	17	48·6	8	61·5
Grouped personality traits		Mean		Mean
Schizoid		1·13		1·46
Sociopathic		1·04		1·23
Passive–dependent*		0·83		1·46
Anankastic		1·36		1·36

* $P < 0·05$ by t test.

Table 5. *Drug treatment and care status*

	No residual depression ($N = 41$) *N* (%)	Residual depression* ($N = 19$) *N* (%)
Drug treatment adequate†	20 (49)	14 (74)
Drug treatment high‡	7 (17)	4 (21)
Care status§		
In-patient	0 (0)	1 (5)
Day-patient	3 (7)	4 (21)
Out-patient	27 (66)	14 (74)
Seeing other worker	10 (24)	5 (26)
Seeing GP	25 (61)	13 (68)

* No significant differences.

† Adequate drug treatment = at least imipramine 150 mg daily, or phenelzine 45 mg, fluoxetine 20 mg, lithium 800 mg, or dose equivalent within drug class.

‡ High drug treatment or at least imipramine 200 mg daily, phenelzine 75 mg daily, fluoxetine 40 mg daily, or equivalent.

§ Care at time of assessment; mutually exclusive only for in-patient/day-patient/out-patient.

individually for presence or absence. Mean scores on the 13 personality types in the schedule were examined in the two groups. There were significant differences on two of these, with higher scores in those with residual symptoms on avoidant (mean scores 1·90 and 1·10, $t = 2·10$, $P < 0·05$) and passive dependent personalities (mean scores 1·46 and 0·83, $t = 2·3$, $P < 0·05$). It was difficult to interpret these findings since presence of mild depressive symptoms after remission might particularly have influenced these personality traits.

Treatment

In view of the possibility that residual symptoms might be a consequence of under-treatment, the presence or absence of residual symptoms was related to dose of drug treatment in standard dose equivalents (as in the companion paper, see Ramana *et al.* 1995) in the 3 months prior to the remission rating. Since presence of residual symptoms may indicate the need for high levels of treatment, an additional high drug treatment criterion was also defined (at least imipramine 200 mg daily, fluoxetine 40 mg daily, phenelzine 75 mg daily, or equivalent).

Findings are shown in Table 5. There were no significant relationships to drug treatment, and there were weak trends for patients with residual symptoms to have received higher rather than lower doses. Only a minority in either group received high doses. In addition 12 patients (19%) without residual symptoms and four (21%) with residual symptoms received ECT in the 3 months prior to remission (NS). There were no significant differences between subjects with, and without, residual symptoms in proportions receiving out-patient treatment, GP care, or follow-up care from community workers at recovery.

Residual symptoms and relapse

The relationship of residual symptoms to subsequent relapse was examined both by cross tabulation and in a life-table analysis, using the Kaplan–Meier method (Kaplan & Meier, 1958). Survival curves are shown in Fig. 1. There was a marked difference, with a very high relapse rate in those with residual symptoms. Overall, 76% (13/17) of these subjects relapsed over the follow-up, as opposed to 25% (10/40) of those without residual symptoms. The difference between the two survival curves was significant at $P < 0·001$. Relapses in both groups were all in the first 10 months, but were spread over this period.

Because it was possible that some subjects in the higher range of residual symptoms might merely have had a mild worsening to cross the major depression threshold, rather than a clear worsening from relative recovery, in an additional analysis the subjects with residual symptoms were divided into those with more severe residual symptoms (Hamilton total > 12, $N = 7$), and those with milder symptoms (Hamilton total 8–12, $N = 10$). Among the severe group 57% (4/7) relapsed; among the mild 90% (9/10) (NS). In the majority of relapses therefore, relapse did not represent a minor

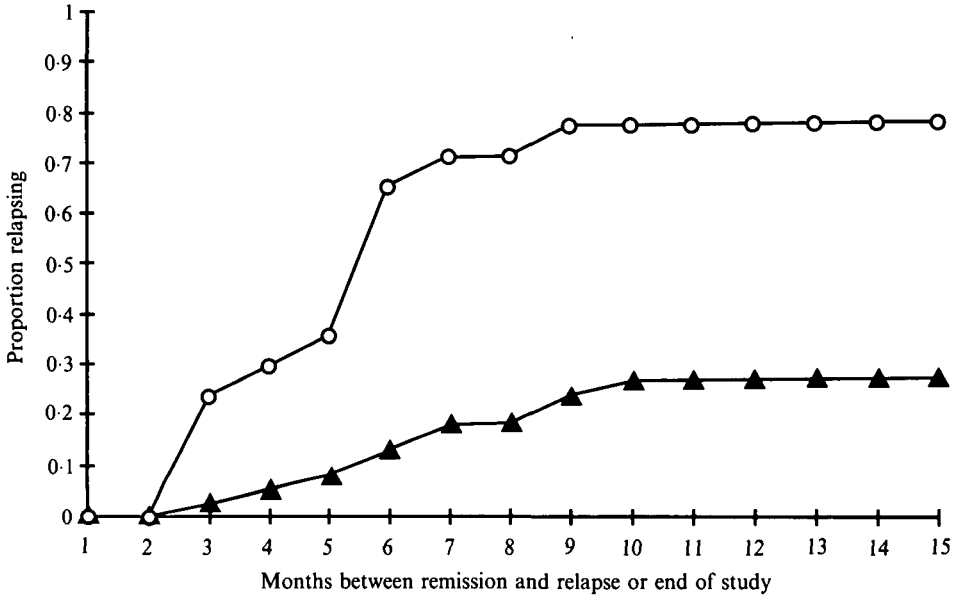

FIG. 1. Proportion of patients with (○) and without (▲) residual symptoms relapsing after remission. (Log rank statistic = 17·43, df = 1, $P < 0{\cdot}001$.)

fluctuation, but a clear worsening from mild residual symptoms.

DISCUSSION

Methods and previous studies

This study has found residual symptoms on remission to be a common phenomenon in depression, occurring in 32% of patients who remitted. The pattern was one of mild typical depressive symptoms. Residual symptoms were not significantly associated with long prior illness, dysthymia, or most other predictive variables except for more severe initial illness. Residual symptoms at remission were strong predictors of subsequent early relapse, which occurred in 76% of those with residual symptoms and 25% of those without.

The findings inevitably depend on the remission criterion used. Phillip & Fickinger (1993) found that varying the number of DSM-III-R symptoms permitted from 4 (major depression requires 5) to 0 prolonged the time to remission. Our main criterion was derived by requiring depression below the level of major depression required for inclusion in the study; the level of 7 or less on the Hamilton scale required for absence of residual symptoms corresponds to a fairly low level of symptomatology. These two levels corresponded to suggested cut-off points for being fully symptomatic and asymptomatic in the paper by Frank *et al.* (1991). Patients below the threshold for major depression are commonly discharged from hospital, and all except one of our patients with residual symptoms were in the community at the time of rating. We required the remission to have been sustained at this level for 2 months, rather than the 2 weeks as in the definition of major depression, to exclude transient borderline improvements. The effect of requiring absence of residual symptoms for remission is presented in the companion paper (Ramana *et al.* 1995). The mean time to remission was lengthened, but not very markedly and it would have resulted in a failure to identify this important group of patients and their adverse later prognosis.

At its higher levels the amount of residual symptomatology present was clearly just below major depression and we might have been simply identifying a group of patients whose subsequent relapses reflected a minor worsening on already existent symptoms. However, this was not the case: relapses occurred mainly in those from the lower range of residual symptoms rather than the higher.

Residual symptoms as an outcome have received relatively little explicit study previously,

although they are clearly evident in the detail of studies, and a recent paper briefly reviewed some aspects (Fawcett, 1994). The absence is surprising, since clinical experience has long suggested that many patients treated initially as in-patients or out-patients improve only partly, leaving residual symptoms that persist and fluctuate in the community, causing considerable disability and family burden. Such patients appear to be common in out-patient clinics (Paykel & Griffiths, 1983).

Because many studies treat these patients either as non-remitted or as relapsed, their proportion has not been very well documented. Kupfer & Spiker (1981) found that among in-patients treated with amitriptyline, approximately one-third were complete responders, partial responders and non-responders, respectively. Berti Ceroni *et al.* (1984) reported partial remission in a 4-year follow-up, but only in a relatively small number of patients, probably because the study depended on retrospective case-note information. Weissman *et al.* (1978) reported a follow-up study of 4 years for a sample of female depressives who had responded to initial treatment with amitriptyline and had been included in a controlled trial of continuation antidepressant and psychotherapy. At 8 months 50% showed moderate or fluctuating symptoms, and 19% chronic symptoms, at 20 months the figures were 60% and 12%, at 48 months 46% and 30%. The group with moderate or fluctuating symptoms corresponded approximately to residual chronicity, but included some subjects who relapsed and then remitted. Keller *et al.* (1992) described 'subsyndromal' symptoms in about half of a sample of bipolar patients in a controlled trial of high or low dose maintenance lithium. In recent papers Ormel *et al.* (1993) noted the occurrence of residual symptoms in general practice patients with depression and anxiety and Brodaty *et al.* (1993) reported residual symptoms, not further defined, in 38% of elderly depressives at 1 year and 20% at 2–4 years.

The nature of residual symptoms

No previous studies have examined the characteristics of residual symptoms or the patients who experience them. Our findings concern first the pattern of symptoms, and secondly the background on which they develop.

The analyses of the patterns of residual symptoms were limited to some extent by the comparatively small sample, with only 19 subjects showing residual symptoms. The pattern was one of typical, but mild, symptoms of depression. The common individual symptoms were depressed mood, guilt, hopelessness, impairment of work and activities, anorexia, early insomnia, together with anxiety. Most other depressive symptoms were also present. Mood disturbance, negative thought content and impaired function tended to be prominent.

The main absent symptoms were those that only accompany severe depression: particularly psychomotor changes and loss of insight. There was some tendency for biological symptoms to be absent. Weight loss, for which there was little evidence on the Hamilton scale, is difficult to rate on an ongoing basis. It is noteworthy that on the Clinical Interview for Depression the residual symptoms were not characterized by the atypical vegetative change of increased appetite. Psychic anxiety was not accompanied by panic attacks. There was also relatively little observable depressed appearance at interview, in spite of reported symptoms. This suggests the possibility that residual depression may be missed unless systematically enquired for.

When predictive and other associated variables were examined, the only convincing associations were with greater initial severity of illness. This set of associations was relatively weak, and only just achieved 5% significance, but it was consistent in several variables. It was also consistent with the findings of the companion paper (Ramana *et al.* 1995) of worse outcome with respect to delayed remission and more relapse. No other truly predictive variables were associated significantly with the development of residual symptoms.

One important group of features concerned low-grade symptoms and personality abnormality. The concept of dysthymia involves mild chronicity similar to residual symptoms. It evolved from earlier ideas of chronic depression as personality abnormality, but it regards persistent symptoms as indicating illness rather than characterological problems. A number of authors have drawn attention to the overlap between chronic depression and dysthymia (Akiskal *et al.* 1981; Hirschfeld *et al.* 1986; Scott, 1988). Rounsaville *et al.* (1980) found that

66% of a sample with RDC major depressive disorder also had a diagnosis of a chronic minor mood disorder, such as intermittent depressive disorder, cyclothymic personality or labile personality. The criteria in DSM-III-R for dysthymia, unlike DSM-III, exclude those cases where the symptoms immediately followed major depression. This may be artificial, particularly in relation to dysthymia with later, rather than earlier, onset (Klein *et al.* 1988).

In the present study DSM-III-R diagnosis of dysthymia did not predict residual symptoms. Only a small minority (below 20%) in either group satisfied the DSM-III-R criteria for dysthymia. More subjects fulfilled criteria for Tyrer PAS diagnoses and broader ratings of personality abnormality, and ratings tended to be higher in those with residual symptoms, reaching significance on passive–dependent grouped traits, avoidant and passive–dependent individual traits. The ratings of personality were only carried out after remission below major depression, in order to avoid major contamination by symptoms, but were not collected at initial rating so as to be true predictors, but were undertaken at the time of outcome. The minor differences found could have been attributable to presence of residual symptoms at the time of rating. This could have applied to a greater degree to the passive–dependent traits, which include such variables as anxiousness, resourcelessness and vulnerability. This finding is, therefore, inconclusive.

Another possible causative factor was undertreatment. Undertreatment with low dose antidepressants is common in general practice (Johnson, 1974). It may also occur in psychiatric practice (Kotin *et al.* 1973; Lehmann, 1974; Bridges, 1983; Schatzberg *et al.* 1983; Quitkin, 1985; Keller *et al.* 1986) and it has been found in resistant depressives.

In this study residual symptoms did not appear to be associated with less treatment, either with drugs, or with respect to early discharge. The non-significant associations were in the opposite direction: patients with residual symptoms tended to receive higher drug doses and to be in higher levels of care. Findings for other aspects of outcome were similar (Ramana *et al.* 1995). It is always necessary to interpret treatment associations with caution in a naturalistic study rather than a controlled trial, since there is a possible two-way process: undertreatment may lead to a worse clinical state; a worse clinical state, whatever the cause, may lead to more treatment. Three-quarters of the patients with residual symptoms satisfied the criteria for adequate treatment, but only a minority received high drug doses or ECT. The direction of the differences does not suggest that undertreatment was a minor cause of residual symptoms, but it is possible that greater use of high dose medication would have produced better results. A controlled trial would be required to test this.

What can be concluded regarding the nature of residual symptoms? There are various possibilities. Residual symptoms might represent persistent illness, i.e. the original illness continuing in milder form. Alternatively, they might represent the phenomena preceding and underlying the depressive episode. Two possible aspects of the latter can substantially be discounted: subjects with residual symptoms were neither liable to be diagnosed dysthymics nor, except to a minor degree, to show more personality abnormality than those who remitted fully. A third possible underlying phenomenon is that the residual symptoms reflect a cognitive vulnerability of dysfunctional attitudes of the kind that has been postulated to underlie depression (Teasdale, 1988). However, the symptoms shown by the residual depressives (Tables 2 and 3), although inclusive of negative cognitions, were not all limited to these, but included equally depressive mood, anxiety, impaired function, work and interests, and initial insomnia. These appear too wide to be related easily to a single abnormality of low self-esteem.

It thus seems likely, given these findings and the lack of association of residual symptoms with anything else except subsequent relapse, that the explanation is the first of those given above, i.e. persistence of the original disorder. The most likely conclusion is the simplistic and somewhat circular one that residual symptoms are a manifestation of a disorder which, in spite of improvement, is still present – they are the evidence that the disorder continues.

Relapse

The most marked association of residual symptoms was with the very high rate of later relapse. As already noted these relapses were not simply minor fluctuations on the background symp-

toms: they mainly occurred in those with the lower levels of residual symptoms. Moreover, as is shown in Fig. 1, they were scattered evenly over the period of further follow-up, rather than clustering shortly after remission.

Residual symptoms have been found associated with higher relapse rates in a number of other studies, and this is the only aspect that has previously been well described. In a naturalistic follow-up study (Faravelli *et al.* 1986), relapsers in the year after remission showed significantly higher levels of symptoms on a clinical global impression at the time of remission than did non-relapsers. Differences on the Hamilton total were in the same direction, but were not significant. Residual symptoms predicted relapse during drug continuation in a study of the elderly (Georgotas *et al.* 1988) and in two drug discontinuation controlled trials (Mindham *et al.* 1973; Prien & Kupfer, 1986). In the first of these the protective effect of continuation medication was only apparent in those with residual symptoms of at least mild level; in the second trial relapse was also less common after a longer remission of 16 weeks. Residual symptoms were found to predict relapse across treatment conditions in two follow-up studies of controlled trials of cognitive therapy against drug treatment (Simons *et al.* 1986; Evans *et al.* 1992) and a follow-up of cognitive therapy treated patients from another trial (Thase *et al.* 1992). These findings are also in keeping with the consistent evidence that persistent dexamethasone non-suppression at recovery predicts early relapse (Paykel, 1994). It is not clear if DST non-suppression and residual symptoms are associated, but persistent non-suppression may also be a reflection that the disorder continues.

The most important implications of our findings concern future prognosis and treatment. It is mainly on the basis of the continuation drug trials cited above that a recommendation has been made that continuation treatment should not be withdrawn until the patient has experienced 4 months free of all symptoms (Prien, 1992). Although in the present naturalistic study treatment effects could not be evaluated directly, relapsers were not characterized by less continuation medication (Ramana *et al.* 1995). However, the present findings and the earlier literature highlight patients with partial remission, with residual symptoms as a group highly vulnerable to early relapse, on whom therapeutic efforts should be targeted. These may include both drug treatment and other approaches. We are currently carrying out a controlled trial of cognitive therapy in a new sample of residual depressives on antidepressant medication.

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