British Journal of Psychiatry (1994), **164**, 342–348

Heterogeneity of Depression
Classification of Depressive Subtypes by Longitudinal Course

KATHLEEN RIES MERIKANGAS, WERNER WICKI and JULES ANGST

This paper describes the application of prospective longitudinal data from an epidemiological sample of young adults to define subtypes of major depression. Depression was classified on a spectrum from subthreshold manifestation of symptoms and duration at one end, to cases with recurrent episodes of depression meeting duration criteria for major depressive episodes at the other. There was a direct relationship between the severity of depression over the longitudinal course and both duration and recurrence of depressive episodes. The subgroup of depression with recurrence of both brief and longer duration episodes could be discriminated on most of the indicators of validity including symptoms, impairment, family history, and suicide attempts. In light of the young age of this cohort, the strong history of suicide attempts and other complications of depression among the subjects with recurrent depression was striking. These findings underscore the importance of employing course as a classification criterion of depression, and the inclusion of subthreshold episodes of depression in the characterisation of course.

The importance of systematic consideration of the course of psychiatric disorders was first proposed by Kahlbaum in 1874 and later implemented by Kraepelin (1899). Understanding of the course of a particular disorder may be applied to facilitate predictions about the outcome of subjects with the condition, to validate the diagnostic category, and to classify subtypes of the disorder. This paper applies data on patterns of course in an epidemiological cohort study of young adults to identify subtypes of affective disorders.

Background: course

The course of depression among psychiatric in-patients and out-patients has been the focus of numerous studies (Zis & Goodwin, 1979; Bland & Orn, 1982; Coryell & Winokur, 1982; Fukuda *et al*, 1983; Angst, 1988). In a comprehensive review of the course and outcome of depression in follow-up studies of clinical samples, Angst (1988) found that approximately 10–20% of unipolar depressives exhibited a chronic, unremitting course; 40–50% showed complete recovery from depression over 1–40 years; and the remainder suffered from intermittent depressive episodes over time.

Studies of the course of affective disorders in epidemiological samples have provided information on the prediction of long-term outcome and disability and the estimation of treatment needs. Epidemiological data on course resemble those obtained from clinical samples. In his review of prospective studies of depression in epidemiological samples, Angst (1990), concluded that approximately 50% of all depressives in the community experience only one episode, 20% exhibit recurrent course, and 30% become chronically depressed. Wide variation in methods, however, precluded aggregation of the findings into a conclusive summary of the risk of recurrence of depressive episodes in the community. In his own epidemiological study, Angst (1990) found a substantially lower rate of single-episode depression than that reported above, with only 25% of the subjects with major depression in the community experiencing a single episode over time.

The third application of information on the course of depression is the classification of depressive subtypes. When course is used as a classification criterion, different patterns of course are used to define subtypes of depression (Angst, 1993*a*). Despite widespread recognition of the variation in the course of different subgroups of depressives, however, course has only rarely been employed as a criterion to classify subtypes of major depression in the major diagnostic systems.

During the past decade, there has been considerable progress in the development of diagnostic criteria for depression. Nearly all systems require a specified number of symptoms for a particular duration, and some also require evidence of impairment or significant distress. The symptom and duration criteria in multiple diagnostic systems were reviewed by Winter *et al* (1991). Duration of depressive symptoms is a criterion for the diagnosis of major depression in all diagnostic systems. Duration criteria for major depression range

from a minimum of two weeks in the DSM-III and DSM-III-R to a minimum of four weeks in the St Louis Diagnostic System (Feighner *et al*, 1972). More recently, Angst has defined a syndrome called recurrent brief depression (RBD) which requires episodes of less than two weeks, but with recurrence over 12 months, and impairment in major role functioning (Angst & Dobler-Mikola, 1985).

In contrast, course has rarely been employed in the classification of depression. Two major components in the characterisation of course are chronicity, defined according to the duration of episodes without remission, and recurrence, defined by the number of episodes interspersed with periods of remission. Chronic depression, which is usually defined as non-recovery over more than two years since the last observation, can develop at any point during the course of depression. Chronicity may be examined by comparing the proportions of persons with single episodes of depression with those of subjects who manifest recurrent episodes of depression or fail to exhibit remissions over time.

Course and classification of depression

As reviewed by Angst (1988), both chronicity and recurrence have been frequently employed in the classification of course. Most diagnostic systems, however, have rarely specified operational criteria for both recurrence and duration of depressive episodes. RBD, described above, is based on symptomatic criteria and recurrence. The subtype of RBD was validated in a seven-year follow-up of this cohort of young adults (Angst & Wicki, 1991).

In this paper, depression is classified according to recurrence and duration of depressive episodes in a prospective 10-year, longitudinal cohort study of 20-year-olds in Zurich, Switzerland (Angst *et al*, 1984). We investigate the validity of the classification by assessing the symptoms, impairment, family history, and suicide attempts.

Method

The sample for the study is a cohort of 591 young adults who have participated in a longitudinal epidemiological study in Zurich, Switzerland from 1978–1988 (Angst *et al*, 1984). The sample was selected from 4547 males and females who were randomly chosen from all 19 and 20-year-olds from the canton of Zurich in 1978, based upon their scores on the Symptom Checklist-90, Revised (SCL-90-R; Derogatis, 1977). In order to maximise the number of potential cases, two-thirds of the sample were selected from high scorers (that is, above the 85th percentile) and a third were randomly selected from those who scored below the 85th percentile on the SCL-90.

There were four waves of interviews: 1979, 1981, 1986, and 1988. The original sample in 1979 included 591 subjects. These subjects were reinterviewed on three additional occasions: 1981, 1986, and 1988. Additionally, all of the subjects were contacted by mail in 1980. The samples in each of these years were recruited from the 1979 cohort, so that varying proportions of the initial cohort participated in each additional wave of interviews. The numbers of subjects at each of the subsequent interviews were 456 in 1981, 457 in 1986, and 424 in 1988. The drop-out rate after the fourth interview wave, 11 years after the first interview, was 30%. A total of 356 subjects completed all four interviews, and 89% were interviewed at least twice.

The sample for this study consists of the 591 subjects who were interviewed at least once during the 10 years of the study. Subjects were classified into the following five groups according to the duration and recurrence of depressive symptoms over four interviews during the 11 years of follow-up: controls with no depression ($n = 338$); single episode of major depression ($n = 33$); recurrent episodes of major depression ($n = 61$); recurrent brief depression only ($n = 103$); and major depression plus recurrent brief depression ($n = 53$). The 22 cases of dysthymia who also met criteria for major depressive disorder (MDD) or RBD were subsumed under the appropriate categories of depressive subtypes, and three subjects with pure dysthymia over the 10 years were excluded from the analyses herein. Thus, the total number of subjects in the analyses below is 588. (Evidence of the poor reliability and low rates of dysthymia as a discrete subtype of depression was discussed by Angst & Wicki (1991).)

Diagnostic assessment and criteria

The diagnostic instrument employed in this study was the SPIKE, a semi-structured instrument which was developed for epidemiological studies (Angst *et al*, 1984). The SPIKE was designed for administration by trained psychiatric residents and clinical psychologists. Information is collected on childhood characteristics, treatment history, psychiatric and somatic syndromes, and on use and abuse of various substances. Symptoms, duration and frequency, subjective degree of suffering, treatment, social consequences, previous history, and family history are assessed for each syndrome. The instrument is not based on a particular diagnostic system. Therefore, diagnostic algorithms from multiple systems can be applied to the data for each syndrome.

The diagnoses from the 1986 and 1988 interviews were made according to the DSM-III or DSM-III-R criteria for most of the major diagnostic categories including major depression, dysthymia, general anxiety, panic disorder, agoraphobia, mania or hypomania, simple and social phobia, alcohol abuse, and substance abuse. The criteria for the diagnosis of RBD are identical to the diagnostic criteria for major depression concerning mood and number of symptoms. As in the Research Diagnostic Criteria (Spitzer *et al*, 1978), the definition of RBD also requires occupational impairment. The requirement for the length of depressive episodes has been reduced to less than two

weeks, however, but such episodes must recur monthly over a one-year period. These cut-off points were chosen because the distribution of subjects with depressed mood who simultaneously met symptomatic and occupational impairment criteria clustered at a frequency of at least one per month. A very small additional number of subjects met the symptom and impairment criteria, but had only a few episodes per year. Despite the threshold for duration of less than two weeks, the duration of depressive episodes was less than one week among all of the subjects with RBD, and was only one to three days in 90% of this group (Angst, 1993*b*).

The family history for each syndrome was routinely obtained separately for fathers, mothers, and siblings, irrespective of the subjects' response to the symptom probes for each syndrome. Although specific diagnostic criteria were not systematically assessed for each of the relatives, the presence or absence of the general syndrome was assessed. Moreover, the treatment history, if any, for each syndrome was obtained for all first-degree relatives. For this analysis, family history was defined according to the proportion of probands with at least one parent or sibling with a history of depression or treatment for depression. The methodology of the study is presented in further detail by Angst *et al* (1984) and Angst (1988).

Statistical analysis

The statistical analyses conducted to test the significance of the differences for comparisons of the categorical variables were χ^2 corrected for continuity. The continuous variables were tested by analyses of variance using the general linear models procedure of the statistical analysis system (Reinhardt & Winston, 1985). Group mean differences were compared with the Duncan multiple range test, which reduces the chance of not rejecting the joint hypotheses relative to the group means (Duncan, 1975).

Results

Table 1 presents the raw and weighted rates of depressive subjects according to mutually exclusive categories of: no depression; major depression, single episode; major depression, greater than one episode; recurrent brief depression; and the combination of major depression and RBD. Approximately 40% of the sample had a depressive episode during the 10 years of the follow-up. A total of 20% of the subjects had either a history of both RBD and MDD or of multiple episodes of MDD. The overwhelming majority (87%) of the subjects with a history of depressive episodes exhibited recurrent episodes over the longitudinal course.

Investigation of the demographic characteristics of the sample by the longitudinal classification of depressive subtypes revealed a significant difference in the proportion of men and women with a history of each of the depressive subtypes. A greater proportion of women (51%) than men (33%) reported at least one depressive episode during the 10-year period. There was no sex difference, however, either in the proportion of subjects with recurrence of depression, among three subjects who experienced at least one episode of depression over time, or in the proportion who experienced a single episode of MDD.

Table 2 examines the longitudinal course of the depressive subtypes over the 11 years of follow-up of the cohort according to the age of onset, treatment history, chronicity of depression, and suicide attempts. Significant differences emerged between the groups on all of the indicators of severity. The age of onset was significantly earlier in all of the groups that were characterised by recurrence, with the combined group and the group with RBD alone having the earliest age of onset of depression (mean age 16 years). In contrast, those who had had single episodes of depression had had onset at a significantly later age (mean age 19.2 years) than any other group. For all of the groups, the mean age of onset occurred during the mid-to-late teen years, nearly 10 years earlier than the most recent interview.

As expected, the lifetime history of professional treatment and the number of years for treatment of depression were associated with both recurrence and duration of depression. Whereas only 10% of the subjects with no depression or only a single episode had been engaged in treatment for emotional or psychological problems, 60% of those with recurrent depression had sought professional treatment. Inpatient treatment and the number of years of treatment were also associated with recurrent episodes of depression.

The most striking finding that indicates the severity of recurrent depression is the lifetime history of suicide attempts. A third of those subjects with both MDD and RBD had made at least one suicide attempt, and 18% of the other groups with recurrent depression reported a history of suicide attempts. This is in sharp contrast to the rates of suicide attempts (3%) observed in a single episode of MDD.

Table 1
Mutually exclusive categorisation of subtypes of depression by sex over 10-year course ($n = 588$)

	No depression ($n = 338$)	MDD, single episode ($n = 33$)	MDD, >1 episode ($n = 61$)	Recurrent brief depression ($n = 103$)	MDD + RBD ($n = 53$)	
Male	193 (57.1)	15 (45.5)	20 (32.8)	45 (43.7)	17 (32.1)	
Female	145 (42.9)	18 (54.6)	41 (67.2)	58 (56.3)	36 (67.9)	**
Total	338 (57.2)	33 (5.6)	61 (10.3)	103 (17.4)	53 (9.0)	
Weighted rates	N/A	7.3	7.3	12.5	6.6	

Data are mean (s.d.).
RBD = Recurrent brief depression; MDD = Major depressive disorder; N/A = not applicable.
**$P < 0.01$.

https://doi.org/10.1192/bjp.164.3.342 Published online by Cambridge University Press

Table 2
Longitudinal course of depressive subtypes over 11 years ($n = 588$)

	No depression	MDD single episode	MDD >1 episode	Recurrent brief depression	MDD + RBD	
Age of onset of depression (years)	N/A	19.2	17.6	16.2	16.4	**
Duration of treatment (years)	0.1	0.03	1.3	0.9	1.8	***
Lifetime history of treatment (%)	11.1	9.1	60.7	50.5	64.2	***
History of in-patient treatment (%)	0.3	0	8.2	2.9	7.6	***
Duration of depression (years)	2.5	3.9	6.6	6.4	7.5	***
Suicide attempts (%)	3.6	3.0	19.7	14.6	32.1	**

***$P < 0.001$; **$P < 0.01$.

We also investigated whether the greater severity and chronicity of the recurrent depressives was associated longitudinally with an increased frequency of other psychiatric disorders (Table 3).

Although the other conditions were significantly associated with the longitudinal categorisation of depression, no consistent pattern was apparent among specific depressive subtypes: recurrent depression, either brief or long duration, was associated with panic disorder; major depressive disorder, either recurrent or non-recurrent, was associated with agoraphobia, generalised anxiety disorder, and hypomania; and all of the categories of depression were associated with social phobia, when compared with the controls who had no depression.

The family history of depression among the parents and siblings of the subjects according to the longitudinal depressive subtypes is shown in Table 4. The family history of depression, but not of treatment, differed significantly by the groups of depressives. Patients with recurrent depression exhibited remarkably elevated rates of depression in both their parents and siblings, with a positive history of depression in the parents of over half the patients with recurrent depression, and in between 20 and 33% of their siblings. These rates are particularly high if one considers

Table 3
Unweighted rates/100 of associated psychiatric disorders by longitudinal depressive subtypes ($n = 588$)

	No depression ($n = 388$)	MDD single episode ($n = 33$)	MDD >1 episode ($n = 61$)	Recurrent brief depression ($n = 103$)	MDD + RBD ($n = 53$)	
Generalised anxiety	2.9	10.3	7.6	3.3	16.3	*
DSM-III panic	1.5	6.1	11.5	15.5	15.1	***
All panic	5.9	6.1	24.6	38.8	32.6	**
Panic + generalised anxiety	7.7	15.2	29.5	40.8	41.5	**
Agoraphobia	2.1	9.1	6.6	0.0	6.1	*
Social phobia	2.5	6.9	15.1	10.0	6.1	*
Simple phobia	10.9	27.6	24.5	16.7	12.2	*
All phobias	13.5	31.0	32.2	21.1	18.4	**
Hypomania	9.0	15.2	15.3	8.3	28.3	***

***$P < 0.001$; **$P < 0.01$; *$P < 0.05$.

Table 4
Proportion of subjects with a family history of depression by longitudinal classification of depressive subtypes

	No depression	MDD single epidoe	MDD >1 episode	Recurrent brief depression	MDD + RBD	
Parents						
History of depression	26.9	34.5	50.0	55.5	65.3	***
Treatment	7.3	10.3	17.3	16.7	14.3	†
Siblings						
History of depression	14.1	10.3	19.2	32.2	32.7	***
Treatment	5.6	3.5	5.8	8.9	12.2	NS
Parents or siblings						
History of depression	36.8	41.4	53.9	66.7	77.6	***
Treatment	12.8	13.8	23.1	21.1	24.5	NS

***$P < 0.001$; †$P < 0.10$; NS = not significant.

https://doi.org/10.1192/bjp.164.3.342 Published online by Cambridge University Press

that the current age of this cohort is between 29 and 30 years. Although the treatment rates were not significantly different in the relatives of the depressive groups, the subjects with recurrent depression still reported nearly double the rates of positive family history of treatment for depression than the controls, or patients with the single episodes of depression.

Discussion

This paper describes the application of prospective longitudinal data from an epidemiological sample of young adults to classify subtypes of depression. Subjects with depression were classified according to both duration and episodicity of depressive episodes on a continuum from those with only single episodes of major depression, recurrent episodes of depression of brief duration, and recurrent episodes of both major depression and also brief periods of depression. There was a direct relationship between severity of depression over the longitudinal course according to symptomatology, impairment, consequences of depression, family history, and suicide attempts.

The findings of the present study underscore the importance of employing course as a classification criterion of depression. Although course has been used to discriminate the long-term outcome of inpatient samples, it has generally been distinguished broadly into chronic v. non-chronic or, less frequently, as single episode v. recurrence (Cassano *et al*, 1989). The simultaneous classification, of course, according to both recurrence and duration has not been previously employed in prospective epidemiological studies. The data reported here suggest that the ICD-10 and DSM-III-R distinction between recurrent v. single episodes of major depression is both valid and meaningful.

One of the most important findings of the present study is the distinction between subjects who experience only a single episode of depression and those who continue to manifest depression over time. A total of 22% of those who had a depressive episode experienced only a single episode of depression. This rate confirms the findings of Cassano *et al* (1989), who reported that 23% of a clinical sample of inpatients and out-patients experienced only a single episode of depression over an 18-month follow-up period. The low proportion reported here of patients who had had a single episode of depression was also similar to that observed in the epidemiological survey with a seven-year follow-up by Wittchen and von Zerssen (1987), who reported that 28% of the persons with major depression experienced only one episode over time. Several other epidemiological studies, however, reported substantially greater proportions of single episode depression than those cited above (Murphy *et al*, 1974; Surtees *et al*, 1986; Fichter *et al*, 1988; Rorsman *et al*, 1990; Sargeant *et al*, 1990).

Similar to the findings of Cassano *et al* (1989), those with single episode depression could be discriminated from both the controls and those with recurrent depression on all of the indicators of severity investigated in the present study. Indeed, in many respects, they were more similar to the controls than they were to those with other subtypes of depression.

Subjects with recurrent depression selected from the community exhibited a remarkable similarity to those described in published reports on the course of depression (Akiskal *et al*, 1989; Cassano *et al*, 1989; Angst, 1993*a*). Although cases identified in epidemiological samples would be expected to constitute a milder form of depression than that in clinical samples, the group of patients with both recurrent major depression and RBD in the study fell at the opposite end of the spectrum of severity of depression than the single episode depression on nearly all of the components of depression and associated factors. They exhibited greater severity in terms of the number and frequency of symptoms of depression, suicide attempts, greater distress from depression, earlier age of onset, higher proportion with a positive family history for depression, greater impairment in work and social activities, a higher divorce rate, and more chronic expression of symptoms of depression over time. The exceedingly high rate of suicide attempts is even more disturbing if one considers the age of this cohort of young adults, who, according to earlier estimates of the mean age of onset of depression, had only entered the period of risk for major depression.

Despite the distinctions between the groups of subjects based on recurrence and duration of episodes, there is no evidence that these groups constitute distinct nosological subtypes of depression. We have not demonstrated distinct aetiology for any of the groups assessed herein. Rather, it is likely that each of the subgroups manifest the same condition but at different levels of severity.

The difference in the sex ratio for recurrence and duration of episodes may have important implications for possible mechanisms for sex differences in depression. Whereas the sex ratio for those with single episode major depression was approximately equal, nearly twice as many women as men had recurrent major depression or RBD. Once a depressive disorder occurred, women were more likely than men to experience recurrent episodes. This suggests that early intervention may be more important in women

in order to avoid recurrence of depression and its associated consequences.

These findings must also be considered in terms of the limitations of the study. The high attrition rate of nearly 30% over the 10-year period of the study was of serious concern. Investigation of the characteristics of those who dropped out, however, suggested that there were no serious biases in terms of either caseness or scores on the SCL-90-R at the initial interview at age 20. Moreover, diagnoses were not made for the intervals between the four interviews over the 10-year period of the study. Therefore, bias could still characterise those findings that rest upon the subjects' recall, such as age at onset, symptoms during the intervals between interviews, and occurrence of symptoms during the past year. Another limitation of the interpretation of the findings is the relatively youthful age of the cohort, which precludes inferences about future course and chronicity of depression. Thus, the results cannot be generalised to older patients.

The importance of consideration of factors associated with both retrospective and prospective course in establishing subtypes of depression is the major implication of this work. This study demonstrates the importance of consideration of both recurrence and duration of depression in classification systems, because subjects who manifested both recurrent major depression and brief depressive episodes had a significantly more severe course than those with recurrent major episodes only. Identification of characteristics associated with the subtypes of depression will improve prediction of the subsequent course. Such information will ultimately contribute to prophylaxis of depression, increased recognition of its early signs, and identification of those subjects at greatest risk for the consequences of depression.

Acknowledgements

This work was supported in part by Research Scientist Development Award MH00499, AA07080, and DA53478 from Alcohol, Drug Abuse and Mental Health Administration of the United States Public Health Service to Dr Merikangas; and Grant 3.873.0.88 from the Swiss National Science Foundation to Dr Angst.

References

AKISKAL, H. S., CASSANO, G. B., MUSETTI, L., *et al* (1989) Psychopathology, temperament, and past course in primary major depressions. I. Review of evidence for a bipolar spectrum. *Psychopathology*, **22**, 268–277.

ANGST, J. (1988) Clinical course of affective disorders. In *Depressive illness: Prediction of course and outcome* (eds T. Helgason & R. J. Daly), pp. 1–48. Berlin: Springer.

—— (1990) Natural history and epidemiology of depression: Results of community studies. In *Prediction and Treatment of Recurrent Depression* (eds J. Cobb & L. M. Goeting), pp. 1–11. Duphar Medical Relations.

—— (1993*a*) Course as classifier of depression. In *Recurrent Mood Disorders. New Perspectives in Therapy*, vol. 8 (ed. G. F. Placidi), pp. 67–78. Bangalore: Macmillan India.

—— (1993*b*) Recurrent brief depression. In *Research in Mood Disorders: an Update* (eds H. Hippius & C. Stephanis with F. Müller-Spahn), pp. 17–30. Berne: Hogrefe and Huber.

—— & DOBLER-MIKOLA, A. (1985) The Zurich study: A prospective epidemiological study of depressive, neurotic, and psychosomatic syndromes. IV. Recurrent and nonrecurrent brief depression. *European Archives of Psychiatry and Neurological Sciences*, **234**, 408–416.

——, —— & BINDER, J. (1984) The Zurich study: A prospective epidemiological study of depressive, neurotic, and psychosomatic syndromes. I. Problem methodology. *European Archives of Psychiatry and Neurological Sciences*, **234**, 13–40.

—— & WICKI, W. (1991) The Zurich Study. XI. Is dysthymia a separate form of depression? Results of the Zurich cohort study. *European Archives of Psychiatry and Neurological Sciences*, **240**, 349–354.

BLAND, R. C. & ORN, H. (1982) Course and outcome in affective disorders. *Canadian Journal of Psychiatry*, **27**, 573–578.

CASSANO, G. B., AKISKAL, H. S., MUSETTI, L., *et al* (1989) Psychopathology, temperament, and past course in primary major depressions. 2. Toward a redefinition of bipolarity with a new semi-structured interview for depression. *Psychopathology*, **22**, 278–288.

CORYELL, W. & WINOKUR, G. (1982) Course and outcome. In *Handbook of Affective Disorders* (ed. E. S. Paykel), pp. 93–106. Edinburgh: Churchill Livingstone.

DEROGATIS, L. R. (1977) *SCL-90. Administration, Scoring and Procedures Manual-I for the R (Revised) Version and Other Instruments of the Psychopathology Rating Scales Series*. Johns Hopkins University, School of Medicine, Chicago, Illinois.

DUNCAN, D. B. (1975) t-Tests and intervals for comparisons suggested by the data. *Biometrics*, **31**, 339–359.

FEIGHNER, J. P., ROBINS, E., GUZE, S. B., *et al* (1972) Diagnostic criteria for use in psychiatric research. *Archives of General Psychiatry*, **26**, 57–63.

FICHTER, M. M., REHM, J., WITZKE, W., *et al* (1988) Der Verlauf affektiver und psychosomatischer Strörungen am Beispiel der oberbayerischen Felstudie: Ein lineares Kausalmodell verlaufsbeeinflussender Faktoren. In *Affektive Störungen. Diagnostische, Epidemiologische, Biologische und Therapeutische Aspekte* (eds D. von Zersson & H. G. Moller), pp. 84–98. Berlin: Springer.

FUKUDA, K., ETOH, T., IWADATE, T., *et al* (1983) The course and prognosis of manic-depressive psychosis: A quantitative analysis of episodes and intervals. *Tohoku Journal of Experimental Medicine*, **139**, 199–307.

KAHLBAUM, J. (1874) *Die Katatonie oder das Spannungsirresein. Eine Klinische Form Psychischer Krankheiten*. Berlin: Hirschwald.

KRAEPELIN, E. (1899) *Psychiatrie. Ein Lehrbuch fur Studierende und Aerzte* (6th edn). Leipzig: Barth.

MURPHY, G. E., WOODRUFF, R. A. & HERJANIC, M. (1974) Primary affective disorder. Selection efficiency of two sets of diagnostic criteria. *Archives of General Psychiatry*, **31**, 181–184.

REINHARDT, P. & WINSTON (1985) *SAS User's Guide: Statistics. Version 5*. SAS Institute, Cary, North Carolina.

RORSMAN, B., GRASBECK, A., HAGNELL, O., *et al* (1990) A prospective study of first-incidence depression. The Lundby study, 1957–72. *British Journal of Psychiatry*, **156**, 336–342.

SARGENT, J. K., BRUCE, M. L., FLORIO, L., *et al* (1990) Factors associated with one year outcome of major depression in the community. *Archives of General Psychiatry*, **47**, 519–526.

SPITZER, R. L., ENDICOTT, J. & ROBINS, E. (1978) Research diagnostic criteria. Rationale and reliability. *Archives of General Psychiatry*, **35**, 773–782.

SURTEES, P. G., SAHIDHARAN, S. P. & DEAN, C. (1986) Affective disorder amongst women in the general population: A longitudinal study. *British Journal of Psychiatry*, **148**, 176–186.

WINTER, P., PHILIPP, M., BULLER, R., *et al* (1991) Identification of minor affective disorders and implications for psychopharmacotherapy. *Journal of Affective Disorders*, **22**, 125–133.

WITTCHEN, H-U. & VON ZERSSEN, D. (1987) Verlaufe behandelter und unbelhandlter Depression und Angststrungen. *Eine Klinisch Psychiatrische und Epidemiologische Verlaufsuntersuchung*. Berlin: Springer.

ZIS, A. P. & GOODWIN, F. K. (1979) Major affective disorders as a recurrent illness. *Archives of General Psychiatry*, **36**, 835–839.

*Kathleen Ries Merikangas, PhD, *Associate Professor of Psychiatry and Epidemiology, Yale University School of Medicine, Departments of Psychiatry and Epidemiology, and Director, Genetic Epidemiology Research Unit, 40 Temple Street, Lower Level, New Haven, Connecticut 06510-3223*, USA; Werner Wicki, PhD, *Research Department, Psychiatric University Hospital, PO Box 68, 8029 Zurich, Switzerland (now at University of Basel, Switzerland)*; Jules Angst, MD, *Professor of Psychiatry and Head, Research Department, Psychiatric University Hospital, 8029 Zurich, Switzerland*

*Correspondence

(*First received March 1991, final revision January 1993, accepted February 1993*)