British Journal of Psychiatry (1988), **153**, 741–751

The Long-Term Outcome of Maudsley Depressives

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Eighty-nine consecutive admissions with primary depressive illness were prospectively ascertained and diagnosed in 1965–66 by R. E. Kendell, who also allocated each a position on a neurotic–psychotic continuum on the basis of previous discriminant function analysis. In 1983–84, 94% of the survivors were personally interviewed by a psychiatrist blind to index admission data. Operational outcome criteria were employed and longitudinal data were established for 98% of the series. Mortality risk was doubled overall, and increased sevenfold for women under 40 years at index admission. Less than one-fifth of the survivors had remained well, and over one-third of the series suffered unnatural death or severe chronic distress and handicap. Patients whose index episode marked their first psychiatric contact had a 50% chance of readmission within their lifetime, but those with previous admissions had a 50% chance of readmission within three years. Readmissions occurred even after 12 years of being symptom-free, and conversely patients recovered after as long as 15 years of illness. There was a high incidence of other disorders (schizoaffective disorder, alcoholism, schizophrenia), and only four patients showed pure recurrent unipolar histories. Patients at the psychotic end of the continuum were more likely to be readmitted and to have very poor outcomes.

What can a patient in hospital with depression expect from the future? What is the chance of complete recovery without further disabling episodes? What are the probabilities of further episodes requiring admission? What is the likelihood of death from unnatural causes? These questions are often of pressing concern to patients and their relatives. In answering them, clinicians weigh the features of each particular case against a background of general expectations drawn from their own experience and the psychiatric literature. Unfortunately, uncertainty and vagueness prevail in the literature, reflecting the paucity of soundly based long-term follow-up studies.

Most of the long-term follow-up studies of depressives admitted to hospital were carried out before modern treatments were available (e.g. Rennie, 1942; Lundquist, 1945), and none, even of the more recent studies, has escaped serious criticisms (Robins & Guze, 1972; Zis & Goodwin, 1979; Bebbington, 1982). Few have related prospectively rated patient variables to long-term outcome. Ascertainment of patients has usually been retrospective, and diagnosis has often been from case-notes of variable quality (e.g. Winokur & Morrison, 1973). In many studies, significant numbers of patients have been lost to follow-up (e.g. Shobe & Brion, 1971), and outcome assessment has often been made by clinicians who were not blind to the index admission data.

Understandably, most textbooks (e.g. Kaplan & Sadock, 1985) fall back on Kraepelin's postulate that manic–depressive insanity is a remitting illness, thereby striking a note of relative optimism. There are a number of reasons why such optimism holds sway. First, numerous controlled trials have shown the effectiveness of antidepressants and other therapeutic measures. Just as antipsychotics have improved the outlook for schizophrenia, it seems reasonable to assume that antidepressants and lithium have similarly modified affective disorder, so that it retains its place as the more benign of the two major functional psychoses.

However, very few therapeutic trials extend beyond two years, so that if later relapse and chronicity were a common feature of depressive illness, it would seldom be documented. Long-term follow-up studies under modern conditions are extremely rare, and those which have followed cohorts of depressives for longer than five years (e.g. Shobe & Brion, 1971; Nystrom, 1979) have usually selected patients from among the less severely ill, often out-patients.

The Meyerian approach to psychiatry, viewing depression as part of a continuum of normal experience, also focuses attention on less severe cases, as does the study of the relationship between depressive mood and adverse life events. Paradoxically, the definition of bipolar disorder as a separate diagnostic category, with a demonstrably poorer prognosis, has also led to raised expectations for those patients who present with unipolar histories.

But ominous findings have surfaced in the USA. For example, Weissman & Klerman (1977) drew

attention to the risk of chronicity in a cohort of major depressives examined one year after the end of a trial of maintenance therapy. More recently Keller *et al* (1984, 1986), reporting on an NIMH collaborative study of depression, demonstrated a 21% risk of chronicity at two years, and a 22% risk of further one-year chronicity among those who recovered but subsequently relapsed. They commented that the cumulative risk of unremitting depression may be as high as 30%.

In this context we report an 18-year follow-up of a consecutive series of depressed in-patients. The follow-up has been comprehensive, and conducted by a psychiatrist who was blind to the index admission data. Many of the findings are presented using actuarial techniques. We have also examined the predictive power of whether the index episode had a neurotic or psychotic character. We have been able to do this because R. E. Kendell prospectively ascertained and diagnosed the series, and rated the position of each patient on a neurotic–psychotic continuum. We believe that the results go some way towards providing an account of the contemporary natural history of patients admitted to hospital with depression.

Method

The series

The 89 patients selected for the study comprised a consecutive series admitted to the Maudsley Hospital with primary depressive illnesses in 1965–66. All were examined personally by R. E. Kendell shortly after admission, and participated both in his research into the classification of depressive illness (1968), and also in research into changes in personality measures during depression (Kendell & Discipio, 1968, 1970).

There were 27 men and 62 women. Their age distribution in 1965–66 is shown in Table I. For 54 of the patients this was their first psychiatric admission, while 35 had been previously admitted. Table I also shows social class distribution and area of residence. Kendell clinically diagnosed 48 (54%) as neurotic and 41 (46%) as psychotic. Diagnoses were made according to ICD criteria, so that psychotic did not necessarily imply the presence of hallucinations or delusions. All patients satisfied Research Diagnostic Criteria (RDC) for major depressive disorder (Spitzer *et al*, 1978).

Kendell also systematically recorded the presence or absence of 41 diagnostic items concerning personal and family history, phenomenology, and possible precipitants. On this basis, using loadings derived from previous discriminant function analysis of 696 patients, he accorded each patient a score on a neurotic–psychotic continuum (Kendell, 1968).

Diagnostic index score

The distribution of scores is shown in Table I. Kendell found that the diagnostic index (DI) score correlated well with the Newcastle Diagnostic Index (Carney *et al*, 1965), high scores indicating endogenous depression. It also correlated with clinical diagnosis according to the International Classification of Diseases (ICD-7), high scores indicating manic–depressive psychosis, low scores indicating depressive neurosis. There was a linear relationship between higher DI scores, better response to ECT, and also better short-term outcome. Kendell (1976) argued that this index represented a continuous dimension, at the upper end of which lay pure type A depressive illnesses with biological/psychotic/endogenous character.

Follow-up

Eighteen years after Kendell's interviews, the series was followed up by a research psychiatrist (ASL). Subjects were traced through the NHS Central Register, and a questionnaire was sent to their current medical practitioners inquiring into progress, current health and present circumstances, and seeking permission to contact the patient. A letter was then sent to the subject, requesting co-operation with a research interview.

Interviews lasted 1½–5 hours and included (a) the SADS–L (Endicott & Spitzer, 1978), which gave a longitudinal picture of psychiatric morbidity between 1965 and 1983, with episodes diagnosed according to the RDC (Spitzer *et al*,

TABLE I
Age, social class, diagnostic index score, and geographical description of the sample

	Number
Age at index	
16–25	12
26–35	26
36–45	19
46–55	24
56–65	6
66–75	2
DI score	
−14 to −5	15
−4 to 5	32
6 to 15	23
16 to 25	14
26 to 35	5
Social class	
I	1
II	21
III	46
IV	14
V	7
Area of residence	
Camberwell District	16
Adjoining postal districts	35
Greater London and Home Counties	30
Other parts of Britain	8

https://doi.org/10.1192/bjp.153.6.741 Published online by Cambridge University Press

1978); (b) the Social Adjustment Scale (SAS) of Weissman & Paykel (1974); (c) the Social Stress and Support Interview (Jenkins *et al*, 1981); and (d) the Global Assessment Scale (GAS) of Endicott *et al* (1976). Subjects also completed the Wakefield Self-Assessment Depression Inventory (Snaith *et al*, 1971). An unstructured interview concerning events and quality of life since 1965 was also conducted. Information was collected about the pattern of illness, treatment received, amount of time disabled with regard to work, and the patient's own view of his or her illness.

Corroboration was obtained from record searches, including hospital in-/out-patient records; and replies to yearly questionnaires to general practitioners, patients or relatives sent out by the Maudsley Professorial Unit Follow-up. Information on hospital admissions throughout England and Wales was obtained from the records of the DHSS Mental Health Inquiry, and where information was scarce, relatives or current doctors were also interviewed.

Throughout the interviewing and data collection, ASL remained blind to the 1965–66 admission data, taking care in the follow-up to refer only to events after discharge in 1965–66.

Tracing and interviews

Eighty-eight (98%) of the series were traced either to their death or to their current residence. Twenty had died, and notifications were secured in every case, giving cause of death, and where appropriate the coroner's verdict. It was also possible in all 20 cases to establish progress between 1965–66 and death, by reference to psychiatric case-notes, yearly Professorial Unit Follow-up inquiries, relatives etc.

Of the survivors, 65 (94%) were interviewed. Sixty-four interviews were conducted by ASL either at the Maudsley or in places as diverse as luxury apartments in central London and a croft in Southern Ireland. One was conducted by a colleague, trained in the use of the instruments, in Australia. Fifty-eight of the interviews were comprehensive (84% of the survivors). All of the remainder were supplemented by interviews with spouses, current doctors or mental health workers.

In four cases either subjects refused interview or their doctor advised against approach. For three, adequate follow-up information was established from at least two other independent sources; in the fourth, information came from a telephone interview with the patient's general practitioner, who had known her for 16 years.

It was possible to examine records of all admissions reported by patients or documented in the Mental Health Inquiry, except in two cases. Corroborated data on course and outcome were determined for 96–98% of the series. Where information was uncertain, patients were excluded from relevant analyses, therefore numbers differ depending on the data considered. No analysis excluded more than four patients.

Definition of global outcome categories

While ASL was still blind to the index admission data, he determined outcome categories by

(a) plotting frequency distributions of outcome measures, such as duration of subsequent periods in hospital, and number of days lost from work with psychiatric symptoms
(b) choosing thresholds for each distribution which separated extreme subgroups (often containing a separate mode).

In this way it was possible to derive elements of operational criteria; e.g. (i) more than one-third of follow-up years affected by periods in hospital, (ii) less than one year of treatment with psychotropic medication.

The final categories were chosen to reflect clinical practice in grading outcome, while retaining the advantage of operational definitions enabling comparison with other series. The 'very good outcome' group were those patients whose lives showed almost total freedom from further psychiatric disorder, while patients in the 'very poor outcome' group all had lives severely damaged by psychiatric disability. Detailed criteria for the four categories are described in Table II.

TABLE II
Operational criteria of outcome

Very good outcome
At least three of the following during the follow-up period:
- Less than four episodes of major depression[1]
- No time lost from work with psychiatric disability
- No other psychiatric disorder
- Less than one year of psychotropic medication

Moderate outcome, not readmitted
Not readmitted during the follow-up period
Not satisfying criteria for very good outcome

Moderate outcome, readmitted
At least one readmission during the follow-up period
Not satisfying criteria for very poor outcome

Very poor outcome
Unnatural death, *or*
Emergence of chronic[1] or subchronic[1] schizoaffective disorder[1] or schizophrenia[1] *or*
Incapacitated[1] throughout follow-up *or*
More than two-thirds of follow-up years affected by admission to hospital, *or*
Three or more of the following:
- Leucotomy with residual chronic disability
- More than 70% of follow-up incapacitated[1]
- More episodes of major depression than years of follow-up
- More than one-third of follow-up years affected by admission to hospital
- Episodes of major depression[1] lasting longer than two years

1. RDC definitions

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Data analysis

Discharge. Using survival analysis (Hill, 1966), a curve was plotted describing the cumulative probability of being discharged at monthly intervals following Kendell's interview.

Pattern of illness. Patients were asked to describe the course of their illnesses and to chart their pattern over the 18 years, relating severity to time. This was combined with the objective data, and a best estimate made by two independent raters of the illness course. The categories employed tapped three dimensions of symptoms: severity (well, mild, severe); frequency (occasional, frequent, chronic); and overall pattern (improving, deteriorating). In 82% of cases there was complete agreement on classification; the remainder were discussed to achieve consensus. Patients who had died were similarly rated on the basis of available history.

Readmissions. Cumulative risks of first readmission were calculated for each of the first 16 years after Kendell's interview. This was done for various subgroups, e.g. male, female, neurotic, psychotic. Again, survival analysis was used following the recommendation of Weissman (1977); it had the advantage of allowing for long index admissions, deaths, and incomplete information, and made maximal use of readmission information. From the survival curves, the following probabilities were determined: R_{16} = the risk of being readmitted at least once within 16 years, R_{Life} = the estimated lifetime risk of at least one readmission, and $T_{½}$ = the median survival time, i.e. the time to which the risk of readmission reached ½.

Mortality. Cumulative mortality risks were calculated for each of the first 15 years of follow-up, again using survival analysis. Observed risks were compared with expected risks, derived by constructing life tables year by year for each patient using the age/sex/year-specific rates supplied by the Office of Population Censuses and Surveys (OPCS). Statistical comparisons between observed and expected risks were made using chi-square estimations of the standardised mortality ratio. Early death was defined as any death occurring before age 50.

Predictive power of the neurotic/psychotic distinction. Categorical data, including deaths, occurrence of at least one readmission, and global outcome, were tested for association with index diagnoses of neurotic and psychotic depression using chi-square statistics for 2×2 contingency tables. The index DI continuum was then divided into four segments: $DI \leqslant 0$; $0 < DI \leqslant 10$; $10 < DI \leqslant 20$; and $20 < DI$. Associations between the continuum and categorical outcome were examined by using chi-square tests for trend in 4×2 contingency tables.

Results

Discharge and recovery

Figure 1 shows the cumulative probability of discharge for the months following Kendell's interview. Eighty per cent of patients were discharged from the index admission within four months, 6% remained in hospital longer than one year, and all were discharged within 2½ years. The curve reflects a linear increase in cumulative probability of 20% per month for the first four months (suggesting a fixed rate of discharge with regard to time), followed by a much slower exponential (time-independent) increase thereafter. Discharge did not always imply recovery. On the basis of the best estimates of pattern, at least ten patients (15% of survivors) never recovered and remained severely incapacitated throughout the 18 years of follow-up. Conversely, one patient recovered after 15 years of continuing symptoms.

Mortality

Mortality risks for the series are shown in Fig. 2. The observed mortality was almost twice that expected, and this excess was significant at the 1% level. The greatest excess

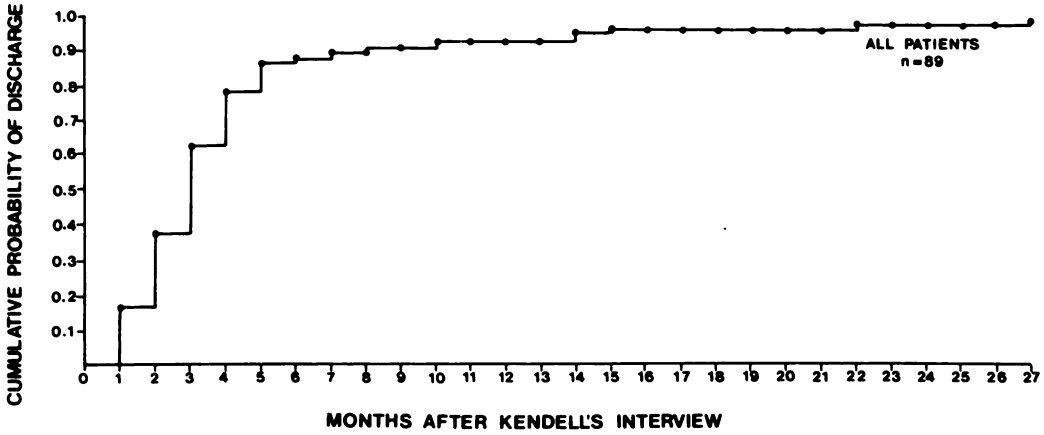

FIG. 1. Cumulative probability of discharge from the index admission: all patients.

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in mortality was among the youngest half of the women (i.e. those under 40 at index admission), in whom there was an almost sevenfold increase.

Table III documents the nine patients (10%) who died of unnatural causes, four of whom were judged by the coroner's court to have committed suicide. In addition to these, there were five other early deaths. These included, for example, (a) female died aged 41, in the eighth year of follow-up, from disseminated malignant melanoma (cumulative risk = 0.011), and (b) female died aged 41 in the twelfth year of follow-up, from cerebral involvement of systemic lupus erythematosus (cumulative risk = 0.013). In all, the deaths of 14 patients (16% of the series) were either unnatural or early or both. There was a non-significant trend towards excess deaths from cancer and autoimmune disease among women, comparing the series with OPCS cause-specific death rates, but this emerged only after a latent period of seven years of follow-up.

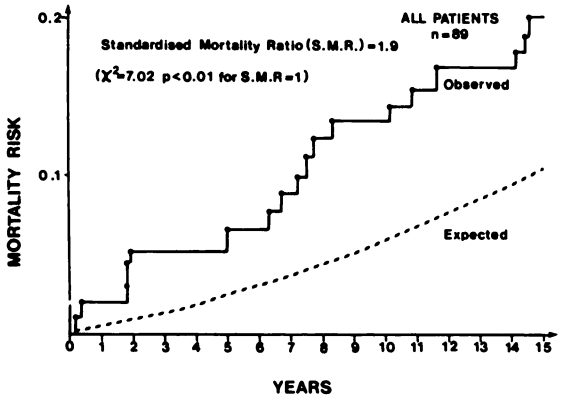

FIG. 2. Cumulative mortality risk (observed and expected): all patients.

TABLE III
Details of the nine unnatural deaths

Survival (years)	*Sex*	*Age at death*	*Coroner's verdict and cause of death*
0.1	F	29	Open verdict: barbiturate poisoning
0.4	M	38	Open verdict: barbiturate poisoning
1.8	M	42	Accidental death: postural asphyxia
1.9	M	59	Suicide: self-poisoning
5.0	F	40	Suicide: self-poisoning
6.1	M	60	Accidental death: fell from a building
8.1	F	28	Accidental death: fell from public transport
14.2	F	34	Suicide: hanging
17.5	F	51	Suicide: hanging

Relapse and readmission

On the basis of the 65 interviewed patients, we estimate that 95% of survivors had relapsed to the point of experiencing a recurrence of major depression, and 50% had relapsed into an episode of incapacitating depression (RDC definitions). In the first 16 years of follow-up 62% had been readmitted at least once, and 25% at least four times. One patient had 14 admissions in 16 years. The great majority of readmissions were for periods of less than six months, but one patient had been in hospital continuously for over six years.

Figure 3 shows the cumulative risk of being re-admitted for the first time for the series as a whole. The risk of readmission within 16 years (R_{16}) was 0.59 and the median survival time ($T_{½}$ = time to which the risk of first admission was one-half) was 7.5 years. Extrapolating the curve, the lifetime risk (R_{Life}) was 0.65. Neither age nor sex showed a clear effect on readmission probabilities.

Figure 4 shows that the risk was greater for patients who had been admitted previously ($R_{16} = 0.75$) as against patients who had never been admitted before ($R_{16} = 0.51$). Previously admitted patients were half as likely to remain out of hospital as those with no previous admissions. Similarly, the median survival time outside hospital ($T_{½}$) was much shorter for those previously admitted (3.0 years compared to 14.5 years for first admissions).

Once a patient had been readmitted, then the risks of further admissions were similar to those of the group with a history of previous admissions at the index. For example, while a patient admitted for the first time in 1965/1966 had only a 50% chance of being readmitted within the next 14.5 years; if this readmission did occur then there was a 50% risk of another admission occurring within the following three years.

Best estimates of pattern

Although almost all patients relapsed to the point of satisfying criteria for RDC major depression, 18% saw themselves as essentially well with only occasional mild

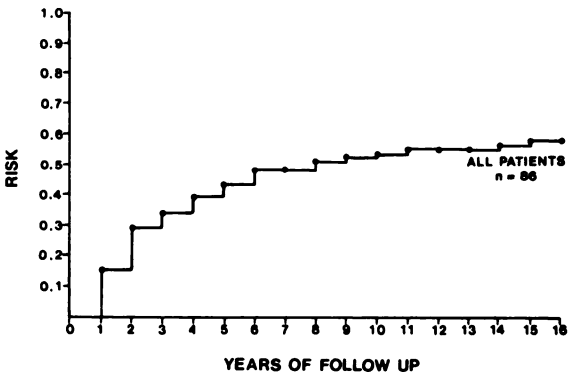

FIG. 3. Cumulative risk of first readmission: all patients.

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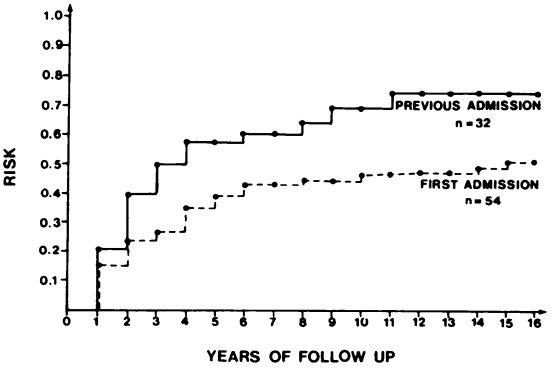

FIG. 4. Cumulative risk of first readmission: the effect of an admission prior to the index.

symptoms after recovery from the index episode. A further 7% had frequent or chronic mild symptoms. All the remainder experienced further severe symptoms; 19% of the total patients had infrequent severe episodes, and felt well between; 37% had either frequent severe episodes and felt well between, or less frequent severe episodes with mild chronic residual symptoms. Finally, 19% suffered frequent severe episodes with chronic residual symptoms or chronic severe distress and handicap.

Global outcome categories

Very good outcome (n = 11). Six male and five female survivors reported between zero and eight episodes of major depression (mean 1.8), none of which were incapacitating. No-one had attempted suicide. One had for several years satisfied RDC criteria for alcoholism, but then recovered. All were well at follow-up, except for one with minor depression. All showed good global functioning at follow-up (GAS > 65) and all scored positively on perceived social supports. Eight were married, all except one scoring highly on marital functioning (SASM ⩽ 2).

Moderate outcome, not readmitted (n = 14). Two male and twelve female survivors showed a pattern either of mild/moderate chronic fluctuating illness or of very slow recovery from the index episode. They reported episodes of major depression ranging between 1 and 30 (mean = 10). Six had episodes of incapacitating depression (RDC criteria). Three had made suicide attempts, none with serious intent. Five had episodes of phobic/anxiety symptoms. None showed bipolar illnesses. All but three had lost time from work because of symptoms, but only two had lost more than 20%. Only four were free from psychiatric disorder at follow-up, but all except two had GAS scores greater than 55. All except two scored positively on perceived social supports. Eleven were married, although only three showed good marital functioning (SASM ⩽ 2).

Moderate outcome, readmitted (n = 24). Seven male and seventeen female survivors showed a pattern of severe episodes, five having superimposed mild/moderate chronic impairment. Five developed bipolar disorder, one had episodes of schizoaffective disorder and two met criteria for chronic alcoholism. Twelve had made suicide attempts; nine had made attempts with serious medical threat. All had lost time from work owing to psychiatric symptoms; seven had lost more than 10%. Nine showed good global functioning (GAS > 65) at follow-up and eighteen scored positively on perceived social supports. Twelve were married, but only three showed good marital adjustment (SASM ⩽ 2).

Very poor outcome (n = 25). Sixteen survivors, three men and thirteen women, fell into this category. These were joined by the nine who died unnatural deaths. Of the survivors, all showed a pattern of chronic severe distress and handicap. Four had episodes of manic disorder, and two of these had also had schizoaffective episodes. Six others had schizoaffective episodes only. All except three had made suicide attempts (mean number = 4), all posing serious medical threat to life. All had lost more than 20% of the follow-up period from work; twelve had lost over 60%. None showed GAS scores > 65 and only two had GAS scores > 55. All showed very poor social and work functioning at follow-up (SAS scores ⩾ 5). All except three scored negatively on perceived social supports. Six were married, all showing poor marital functioning (SASM ⩾ 5). Seven had children; only one was functioning well as a parent. The survivors divided into (a) those divorced or single with multiple prolonged hospital admissions, and (b) those with unhappy marriages, few hospital admissions and a relative isolation from psychiatric services.

Change of diagnosis and other subsequent complications

Sixty-three per cent of the patients developed subsequent major complications. Change of diagnosis was common. In all, twelve patients had subsequent episodes of schizoaffective disorder, three developed chronic paranoid psychoses, and three were diagnosed at follow-up as schizophrenic with defect states. Ten cases became bipolar and seven developed alcoholism. Three cases developed bulimia nervosa and three (the same three) received leucotomies, leaving them with marked defect symptoms. Nine patients died unnaturally and a further nine developed malignant disease. One was diagnosed at follow-up as suffering from presenile dementia. (All diagnoses were made according to RDC where appropriate.)

Predictive power of the neurotic/psychotic distinction

Mortality. No significant differences were found in mortality between patients diagnosed by Kendell as neurotic and those diagnosed as psychotic, nor was there any clear relationship between the DI score and mortality. Neither unnatural death nor suicide showed any clear association with an initial diagnosis of neurosis or psychosis.

Readmission. Figure 5 shows the increased risk of readmission for those diagnosed psychotic. Psychotic patients had a 0.73 risk of readmission within 16 years

(R_{16}), as against 0.47 for neurotic patients: the latter were almost twice as likely to remain out of hospital. Psychotic patients had a 50% chance of being admitted within 3½ years and an over 80% chance of readmission within their lifetimes. More than half of the neurotic patients would never be readmitted.

When first-admission patients were considered separately, the excess risk for psychotic as against neurotic remained unchanged. Readmission risks and time to 50% risk of readmission for different subgroups are summarised in Table IV. Those with admissions prior to the index who were also diagnosed by Kendell as psychotic, were very likely to be readmitted, showing a 50% risk of readmission within two years, and an 84% risk of readmission by 16 years.

DI predicting readmission and global outcome. Both readmission and 18-year global outcome were significantly related to the neurotic-psychotic continuum scores recorded during index admissions. An initial DI score of greater than 10 (i.e the psychotic end of the spectrum) predicted a 90% chance of later readmission and a 50% chance of very poor global outcome. The cohort with DI scores below 10 (the neurotic end of the spectrum) contained all except one of those who fell into the very good outcome group 18 years later. Figure 6 shows the significant association between higher scores on the continuum (more psychotic) and increased likelihood of readmission (linear trend $\chi^2=9.51$, 1 d.f., $P<0.01$). Figure 7 demonstrates the significant association between higher scores (more psychotic) and increased likelihood of very poor outcome (linear trend $\chi^2=6.66$, 1 d.f., $P<0.01$).

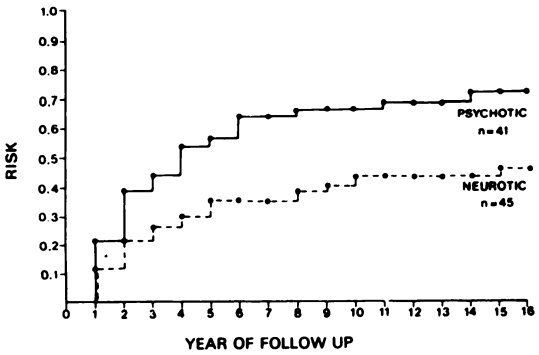

FIG. 5. Cumulative risk of first readmission: the effect of the neurotic/psychotic distinction.

TABLE IV
Risk of first readmission

Patient group	*16-year risk*	*Time in years to 50% risk*
All patients	0.60	7.5
Psychotic	0.73	3.5
Neurotic	0.47	20+
First admission	0.51	14.5
Previous admission	0.75	3.0
First admission, psychotic	0.65	5.0
First admission, neurotic	0.39	25+
Previous admission, psychotic	0.84	2.0

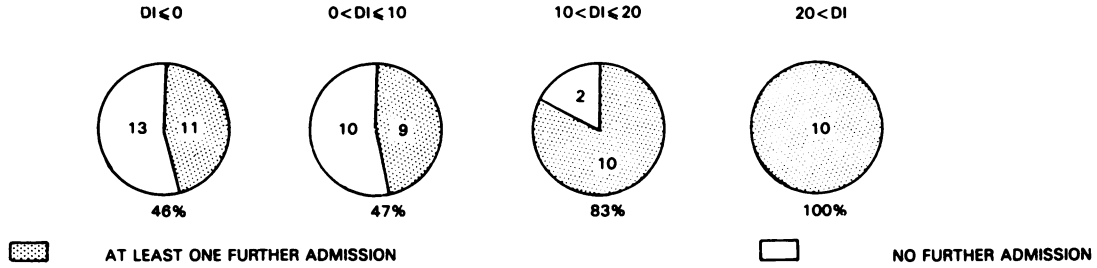

FIG. 6. Subsequent readmission: relationship to index DI scores. Proportions readmitted from within each of four intervals on the continuum, from most neurotic (46%) to most psychotic (100%). Linear trend, $\chi^2=9.51$, 1 d.f., $P<0.01$.

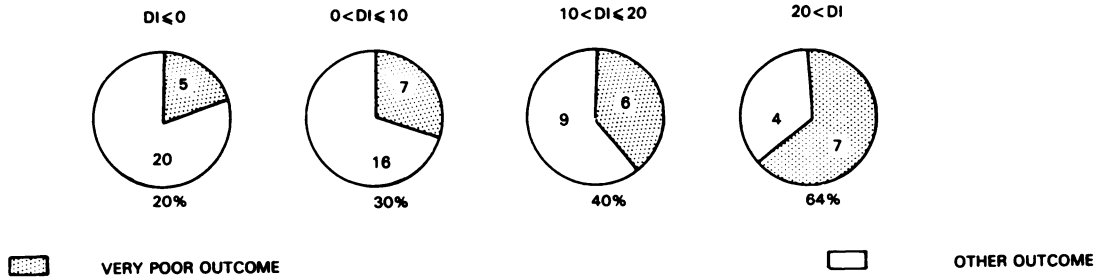

FIG. 7. Very poor outcome: relationship to index DI scores. Proportions with very poor outcome from within each of four intervals on the continuum, from most neurotic (20%) to most psychotic (64%). Linear trend $\chi^2=6.66$, 1 d.f., $P<0.01$.

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Discussion

Discharge

The two phases of the likelihood-of-discharge curve mirror the findings of Keller *et al* (1982), who analysed recovery from major depression using a similar technique of life table analysis. Eighty per cent of our patients were discharged in the first four months after entry into the series; but once this threshold had been passed, discharge became far less likely and the risk became independent of time.

Mortality

A twofold increase in mortality is in accord with the findings of Tsuang & Woolson (1977), who showed a similar increase in a retrospective 40-year follow-up of the Iowa 500 series. The sevenfold excess in women under 40 adds further support to the growing evidence, most recently reviewed by Black *et al* (1985), that the greatest excess mortality in depressive illnesses is among young women.

Our results give no support to the view, mostly derived from out-patient studies, that modern treatment methods have virtually eliminated the risk of unnatural deaths in primary depressives (Martin *et al*, 1985). Two of the suicides in this series occurred in the last three years of the follow-up, and the overall picture was more consistent with the conclusion of Guze & Robins (1970), that at least 15% of such a series will eventually end their lives in unnatural deaths.

Relapse and readmission

Our finding that 95% of the series relapsed supports the claims of Angst *et al* (1973) that if cases of manic–depressive psychosis are followed closely enough and for long enough, virtually all relapse. Of those who did relapse, more than half experienced further depressions involving total loss of major functional roles, such as work or housekeeping. Many patients became more reluctant to seek psychiatric help as they experienced increasing numbers of episodes. This was reflected in the fact that over half of seriously disabled survivors had no contact with psychiatric services in the year prior to the follow-up interviews.

Between 20% and 33% of depressive relapses resulted in readmission. This is much lower than the 60% reported by Bratfos & Haug (1968), and reflects both a high identification rate for depressive relapses and also changes in readmission policies. For example, a number of patients were treated with out-patient ECT or crisis intervention. In the past, readmission data have been criticised as being more dependent on social circumstances than inherent psychopathology. However, in this series, readmission almost always marked an episode of severe socially disruptive or life-threatening psychopathology. With the exception of those married patients who turned away from psychiatric care and were looked after by their spouses, the percentage of follow-up time spent in hospital was the best single indicator of overall poor outcome.

Surprisingly, there were no differences in readmission rates between the sexes, neither was age a major factor. The increased likelihood of readmission in non-first-admission cases was as expected (e.g. Zis & Goodwin, 1979). Interestingly, the crucial factor proved to be neither first admission nor first episode, but first psychiatric contact. The better outcome among first-admission patients was due to there being more patients in this group where the index admission marked their first psychiatric contact, and these patients alone showed a lower probability of readmission. Patients never escaped entirely from the risk of readmission. First readmissions occurred after intervals as long as 12–15 years.

Subsequent illnesses and complications

The high rate (63%) and wide variety of other illnesses and complications is striking. At first sight this casts doubt on the ascertainment of a series of patients with pure depressive disorders. But is this an unusually high incidence of such developments?

Complicated outcomes in patients admitted to hospital for depression have been reported by many authors, though rarely have they been presented systematically to convey their cumulative impact. In a four-year follow-up, Brockington *et al* (1982) noted that of 55 patients originally receiving a diagnosis of RDC major depression, four were subsequently diagnosed as schizophrenic and nine had subsequent schizoaffective episodes. Copeland (1983) found that among 71 depressive in-patients, seven showed bipolar illnesses within a five-year period, and nine others suffered organic complications, including senile dementia, alcoholism and leucotomy. Kerr *et al* (1969) found a significantly increased number of depressive in-patients dying from malignancy within five years. Taking these findings together, one would expect about 60% of cases to be complicated in some such way, a figure similar to that which we found.

Bebbington (1982) has argued against the tendency to exclude complicated cases from outcome analysis. He points out that to do so gives a misleadingly optimistic picture of long-term prognosis. Our study

adds weight to the suggestion that such complications are better regarded as part of the wide variety of natural histories of patients who are admitted with depressive disorders. Pure cases may be the exception rather than the rule. In this series we searched for examples of pure unipolar histories with good asymptomatic recovery between episodes and no complications. We found only four.

Very good outcome

In a 12–18-year follow-up of 102 first-admission patients with affective disorder, Bland & Orn (1982) found that 41 experienced only a single index episode of depression. They argued that non-recurrent cases were a substantial and distinct subgroup. In our series the pattern was different. Patients with a very good outcome were hard to find, with only three reporting no further psychiatric disorder, and only six out of 51 first-admission cases meeting Bland & Orn's definition of single depressive episode cases. Nevertheless, there are distinctive features in our eleven very good outcome cases. All except two were diagnosed by Kendell as neurotic and none had DI scores greater than 15. At follow-up only three regarded themselves as having suffered from a mental illness at all; the remainder looked back on their depression as a reaction to circumstances or a crisis in development.

Very poor outcome

Our most striking finding is the high proportion of patients with a very poor global outcome ($n = 25$); a further five patients had died before the age of 50, and another had developed presenile dementia. Six more showed chronic disabling affective illnesses lasting 1–5 years before and during follow-up. The likelihood of being in one of these unfortunate groups was 42%.

This could be explained if the series was biased towards more serious cases. However, in the 1960s the Maudsley Hospital was criticised for a policy of only accepting patients for whom the prognosis was believed to be good. The distribution of patients in the series is skewed towards higher social class, which has been shown to be a good prognostic factor (Nystrom, 1979). We also examined outcome by location and found that good outcome was strongly associated with distance from the Maudsley Hospital. Eschewing the unpalatable notion that the Maudsley was exerting a malignant effect on long-term prognosis, this suggests that local referrals were diluted by better-outcome cases from more distant centres. All these factors indicate that, if anything, our series should be biased towards better outcome.

Poor outcome might also be due to the inclusion of readmission cases in the series (Zis & Goodwin, 1979). However, when only first admissions are considered, the poor outcome likelihood remains almost unchanged at 41%.

A third explanation could be that we have artificially inflated the poor outcome group by including patients who subsequently developed schizophrenia, schizoaffective disorder and bipolar disorder. When bipolar patients are excluded, the chances of poor outcome fall to 39%, and when those who developed schizoaffective or schizophrenic symptoms are removed, they fall further to 36%. However, it is just as sensible to exclude patients who recovered and remained well. Following this procedure, the chances of very poor outcome rise to 52%. It will be seen that manipulation of this kind, in either direction, can rapidly become absurd.

We believe that the findings do reflect the contemporary natural history of patients admitted to hospital with depression, and that the long-term outcome for between a quarter and a half of such patients is extremely poor. Figures of this order suggest that little has changed since the introduction of psychotropic drugs. They are in line with the most pessimistic of the early studies, which presented a chronicle of long-term morbidity and mortality (e.g. Poort, 1945), and add further substance to the warnings of Angst *et al* (1973) and Bebbington (1982) that we must not underestimate the serious prognostic import of an episode of severe depression requiring admission to hospital.

Bland & Orn (1982) found that, for patients with a recurrent illness, mean ratings for longitudinal psychiatric status were slightly worse for depressives than for those of their schizophrenic series. This also suggests that our gloomy findings may not be atypical.

Much psychiatric morbidity in depression remains hidden to both researchers and clinicians unless follow-up is very comprehensive. Over one-half of the 19 severely disabled survivors in our series were not in contact with psychiatric services at the time of follow-up. It is unclear whether the fact that many of the severely ill are hidden is a cause of the conventional psychiatric optimism that depressives recover, or an unfortunate result of it. When patients who are expected to recover do not, then their psychiatrists may find it hard to continue to see them, and the patients may in turn come to doubt the relevance of psychiatry to their problems.

Prediction of outcome

Readmission rates were higher for patients diagnosed psychotic at the index admission as against those diagnosed neurotic. This finding confirms and extends

the short-term (5–7 year) results of Kay *et al* (1969) and Copeland (1983), and provides further longitudinal validation of the distinction between neurotic and psychotic depression. The linear relationship between scores on the neurotic–psychotic continuum and subsequent readmission rates amplifies this. Figure 6 emphasises the ominous clinical significance of a high DI score. None of the ten patients who scored over 20 in 1965–66 escaped later readmission.

The relationship between high DI scores (more psychotic) in 1965–66 and very poor outcome is very surprising, given the previous literature. Traditionally, poor outcome in depression is associated with neurotic or non-endogenous subtypes, often being explained as the pathoplastic effect of a neurotic personality structure. Short-term studies (e.g. Weissman *et al*, 1978; Hirschfeld *et al*, 1986) have supported this, showing that neuroticism does predict poor outcome. Conversely, patients at the psychotic end of the neurotic–psychotic continuum have thus far been found to respond better to antidepressant treatments (Bielski & Friedel, 1976), and to show better overall outcome at 10 months (Paykel *et al*, 1974) and at 5–7 years (Kay *et al*, 1969). However, Copeland (1983) has reported that by five years some psychotic patients may begin to lose their advantage. This study indicates that by 18 years their overall outcomes are much worse.

Our positive finding is also surprising given the wide variety of life events, changing circumstances, and treatments and compliance that we noted in patients' histories between 1965 and 1983. It had seemed unlikely that any major effects of the cross-sectional analysis in 1965–66 would survive the welter of intervening variables. We had expected that our conclusion would be similar to that of Aubrey Lewis (1936), who, after searching for predictors of outcome in a careful prognostic study of 60 manic–depressive patients, decided that no clear signposts existed.

The finding of such a clear association therefore warrants careful review. We excluded all patients who were not first admissions in 1965–66, or who subsequently developed bipolar disorder, schizoaffective disorder or schizophrenia, but found that the linear relationship remained. We tightened and relaxed the criteria for poor outcome but this did not affect the relationship. We could find no individual items of the DI that were better predictors than the dimension as a whole. We intend to examine in much more detail the way in which high DI scores lead to poor outcome, but for the time being the impression is of a robust relationship which is of great clinical utility.

Conclusion

It appears that a widely held view needs major revision. Short-term follow-up studies have reported that although psychotic depressives are readmitted more frequently than neurotic depressives, their global outcomes are better and on the whole fairly good. These findings underpin the characterisation of neurotic depression as presenting chronic problems often requiring longer-term psychological treatments and social interventions, as against psychotic depression, where solutions tend to be seen more in terms of biological and short-term pragmatic therapies. This study suggests that, in the long term, it is the psychotic depressives who become more severely and chronically disabled, that very many of them do, and indeed that this disability can be predicted by the very same measure that predicts good response to antidepressants and ECT in the short term. Like the hare in Aesop's fable, psychotic depressives may race far ahead of the tortoise-like immediate progress of their neurotic counterparts, but in the long term they will, again as in Aesop's fable, fare much worse. Good immediate response to treatment may thus offer false hope. Fifty per cent of the 26 patients with DI scores greater than 10 in 1965–66 were eventually found to have very poor outcomes, despite apparently good immediate responses to physical treatments. There is a strong case for putting more emphasis on prophylactic and other treatment modalities for these high-risk patients.

Acknowledgements

This study could have been undertaken without the original pioneering work and subsequent encouragement of Professor R. E. Kendell. Betwyn Oppenheim and the late Pip Sturt gave valuable advice and assistance. We are also grateful to the patients for their co-operation, and to the Mental Health Foundation who provided financial support.

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