# Major Depressive Disorder

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A random sample of 3258 adult household residents of Edmonton, Alberta, Canada, were interviewed by trained lay interviewers, using the Diagnostic Interview Schedule (DIS), which generated DSM-III diagnosis data. This paper reports results for major depressive disorder (MDD). MDD was found to affect women more than men by a ratio of nearly 2 to 1. The lifetime prevalence rate for both sexes combined was 8.6%. The period prevalence rates for both sexes combined were 3.2% and 4.6%, for six month and one year, respectively. The presence of a recurrent Major Depressive Disorder was associated with an increased risk of substance abuse, panic disorder and dysthymia, whereas a single major depressive episode was not associated with increased comorbidity.

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## Introduction

The importance of epidemiologic research is well recognized. The information generated by epidemiologists can yield new ideas about etiology, pathogenesis, treatment, and prevention, while at the same time provide insights which may improve the delivery of medical care (1). However, in the field of psychiatry, epidemiologic research has been hampered by the lack of reliable research instruments (2), and by the failure of researchers to reach a consensus on a reliable, valid diagnostic classification system of psychiatric illness.

This report will deal with one such illness, major depressive disorder, and will review some of the historic developments which have led to its modern conceptualization as a distinct nosologic entity. The epidemiology of depression will be reviewed in terms of our current knowledge, and data from a study which makes use of recent developments in epidemiologic research and diagnosis will be presented.

### Historical Overview

Aretaeus the Cappadocian (ca. 150) made reference to a lovesick shepherd's "severe dejection" and felt that it differed fundamentally from true "melancholia", despite acknowledging that "it would appear as such to the average person" (3). This early observation, that not all depressions are alike, set in motion a great debate that is as yet unresolved. Certainly the last two centuries have produced a bewildering array of classifications of depression. Kendell, somewhat ironically, published a classification of classifications (4) in a discussion as to why there are so many competing classifications and unresolved controversies, despite extensive research. As he indicates, part of the reason is that the classification of depression has provided an arena for several disputes about the nature and classification of mental illness as a whole, involving unresolved philosophical differences that stretch back to Plato and Hippocrates.

Yet, as Akiskal (5) notes, "classification has the general purpose of promoting understanding ..., and making a diagnosis is a form of classification". Despite the composer Berlioz's rather unkind comment, " ... after their studies are complete, the rhetorician writes a tragedy, while a psychiatrist writes a classification" (6), the debate regarding diagnostic classification continues to the present day.

A brief historical overview is necessary to place into context the current concept of major depressive disorder. Moebius in the late nineteenth century (3), introduced the dichotomous distinction between endogenous versus exogenous etiologies as the basis for classifying psychiatric disorders, where "endogenous" came to imply "hypothetical, intangible, elusive predispositions, constitutional or hereditary forces which could be conjectured but not demonstrated", and "exogenous" came to imply identifiable, and often measurable causes (7). German-speaking psychiatrists, making use of the elegant descriptions of psychiatric signs and symptoms of Esquirol (3) and the French school of the early nineteenth century, had created numerous syndromic categories. However, it was Kraepelin (8) who, dissatisfied with the considerable symptomatic overlap among the various syndromes, developed his prognostic principle which led to the now familiar division of functional psychoses into dementia praecox and manic depressive illness. All major disorders of mood were subsumed under the rubric of manic depressive illness, though Kraepelin himself believed that this

was a heterogeneous category that would eventually be subclassified. Manic depressive illness was believed by Kraepelin to be a severe, episodic, recurrent illness with good prognosis, as opposed to the irreversible deterioration of mental life in dementia praecox. This broad classification was a heuristic solution to the chaos that preceded it, but as Akiskal states, "one cannot make a diagnosis out of prognosis" (9); prognosis is now known to represent a complex interplay between the organism and the environment. This century has produced numerous efforts to reorder the Kraepelinian schemata.

As Akiskal also noted (9), the debate over classification followed different courses on either side of the Atlantic. In the United States, under the influence of the Freudian and Meyerian schools of thought, an "antinosologic bias" (10) developed. Post-Freudians became divorced from phenomonology, and often metapsychological constructs, largely theoretical and clinically untested, were introduced into diagnostic practice. The Meyerian approach, stressing individual life history and events, also undermined the process of formal diagnosis. The flourishing of antinosological approaches occurred at just the time when effective specific therapies, largely pharmacologic, were being developed (11). It was out of this philosophical wilderness that the St. Louis group (12, 13) developed their work on diagnostic criteria which, in collaboration with Spitzer and associates (14), resulted in the Research Diagnostic Criteria, the forerunner of DSM-III. The St. Louis group undertook extensive validation of their diagnoses, looking at clinical description, laboratory studies, delimitation from other disorders, as well as follow-up and family studies.

Meanwhile, in Britain, a debate raged over the fundamental issue of whether or not depression could be classified into "psychotic" and "neurotic" depressions, or, alternately, Type A and Type B symptom complexes, where the former denoted severe depression with guilt, retardation, severe insomnia, loss of weight, and diurnal variation of mood, and the latter a milder illness which is prone to fluctuate from day to day and lacking the characteristics of the severe form of depression (4). The Newcastle school (15) attempted to demonstrate that "endogenous" and neurotic depressions are distinct illnesses, while other researchers, notably Kendell and Gourlay (16), have sought to validate the observation of Lewis (17) which states that attempts to classify in terms of symptoms "are nothing more than attempts to distinguish between acute and chronic, mild and severe; and where two categories only are presented, the one - manic depressive - gives the characteristics of acute severe depression, the other of chronic mild depression".

In spite of Kendell's (16) strong arguments that depression is indeed a continuum, Andreasen (18) points out that "if this were the case, it would make no difference which end were sampled. The genetic mode of transmission or the neurochemical cause should be the same for both mild and severe forms. Yet to see depressions as etiologically homogeneous in this way runs counter to common sense".

Most useful in the "endogenous-neurotic" dichotomy is the endogenous half, which can be used to identify a subset of patients who differ in terms of response to treatment (19, 20), prognosis and outcome (21), and neurochemical and neuroendocrine studies (22, 23) from other patients. Though Zimmerman (24) points out that few controlled studies have been designed to examine the prognostic value of "melancholic/endogenous subtyping", melancholia as a subtype, which corresponds to Kendell's Type A, has been retained by DSM-III-R. The neurotic component on the other hand, has been shown to be unhelpful (25), and is likely an idea whose time has come and gone.

One attempt to subclassify depression which is now widely accepted on both sides of the Atlantic is the unipolar-bipolar distinction. First proposed by Leonhard, and subsequently supported by Perris, Angst and Winokur (26), the distinction is based on genetic and family studies (27, 28, 29, 30), response to treatment (31, 32), and course and prognosis (33).

Despite strong support for the unipolar-bipolar distinction, caution is necessary. There exist "transitional" forms of mood disturbance between unipolar and bipolar illness (34). Furthermore, persons having a first depressive episode may eventually prove to be unipolar (depressed) or have a subsequent manic episode and become bipolar, leading to some diagnostic confusion. However, on the basis of work done by Winokur and Morrison (35), Dunner et al. (36) suggest that patients be classed as unipolar after waiting 6 months following a single depression. Obviously some degree of misclassification can occur. Nonetheless, if the categories are recognized as fluid and open to change as new evidence emerges, they will continue to be useful.

Attempts have been made to subclassify unipolar disorders on the basis of family study data. In particular, Winokur (37, 38) has made divisions into pure depressive disorder (males with late onset, and a family history of depression only), depressive spectrum disorder (females with early onset and a family history of alcoholism and sociopathy in male relatives), and sporadic depressive disease. This

approach has demonstrated some promise but its validity has not been carefully explored.

One other classification scheme that has been shown to be useful is the distinction between recurrent and single episode depression. It is estimated that over 50% of people who have major depressive episode will eventually have another major depressive episode, thus meeting the criteria for major depression, recurrent. These people are at increased risk for developing a bipolar disorder and furthermore, Bland et al. (39) found that first degree relatives of probands with unipolar depression have significantly higher morbid risk for the development of a similar disorder when the proband has had recurrent rather than a single episode disease, indicating that the two populations may have differences with regards to genetic predisposition.

The many threads of this historical survey have been woven together into the DSM-III and DSM-III-R (41). The DSM-III is atheoretical with regards to etiology. Within each category of the disorder, attempts have been made to define diagnostic criteria in terms of descriptive psychopathology and manifest behaviour, with minimal inferences as to possible motivation or causation.

The DSM-III and DSM-III-R diagnostic criteria, then, make an attempt to deal with the ancient observation that a depressed mood, of greater or lesser intensity, can be a phenomenon of normal everyday existence. The fundamental challenge is to define exactly when depression crosses the line from being a normal experience into a pathological state.

Though DSM-III-R attempts to reconcile the not inconsiderable problems of classification for researchers and clinicians alike, it is not without its critics. Nonetheless, it is a workable system that, most importantly, is not static but is prepared to evolve as new discoveries are made. J.W. Grove has written (about science) " ... it is a kind of storytelling, like the making of myths, but it differs from myth-making in important respects, notably in that its stories are constantly being rewritten in order to conform to the way the world is discovered to be" (40). If psychiatry is to be considered science, its classification systems must be prepared to change as new discoveries are made.

DSM-III-R defines mood disorders in terms of what Mellica (41) calls the symptom domains of somatic dysfunction and psychological distress. He describes a third domain, social disability, but notes that the precise interaction of these domains is still unexplored by epidemiologic research. The first two domains are clearly more easily measured.

When classifying depression as a "case", one assumes that the symptoms have become intense, pervasive, interfere with normal function, and persist over an inappropriately prolonged period of time. Of necessity, this period of time must be defined arbitrarily. In the case of DSM-III-R, the presence of diminished mood or loss of interest or pleasure in all activities for at least two weeks together with a cluster of other symptoms from the somatic and psychological domains, is necessary for a diagnosis of "major depression" to be made.

These core symptoms represent a distillation of the observations on depression made by clinicians from the beginning of recorded history. Kraepelin's description of what he called "melancholia simplex" neatly summarizes the nine diagnostic criteria of DSM-III-R in a precise, descriptive paragraph:

> "... the mood is dominated by a profound inward dejection, the patient is hopeless; he is indescribably unhappy, skeptical. Everything is disagreeable, he sees only the dark side of life; the world appears to him aimless, and he feels superfluous. Phobias may occur in simple melancholia, and the patient is tormented with guilt feelings. Energy is virtually absent, the patient has depressive concommitants such as decreased sexual interest, anorexia and weight loss, sleep disturbance with early morning awakening, and psychomotor retardation" (8).

### Epidemiological Issues

Predictably, the longstanding diagnostic confusion in the realm of mood disorders renders problematic any comparison between older and newer studies of its epidemiology. Dohrenwend (42) has called the older, pre-World War II studies, (which were characterized by the use of records and key informants to define "cases"), the first generation of epidemiology studies, while landmark studies from Stirling County (43), Baltimore (44), and Midtown Manhattan (45), which used the expanded psychiatric nomenclature developed after World War II, and were based for the most part on personal interviews, the "second generation". The studies from New Haven (46), and the more recent Epidemiological Catchment Area (ECA) studies (47) are part of the so-called "third generation", as these make use of a standardized diagnostic interviews, and use newer and more sophisticated techniques for sampling large community populations (48). The Edmonton study would also be considered a "third generation" epidemiologic study.

Issues that can be clarified by epidemiologic studies of this nature include period and lifetime prevalence rates, sex and age of onset differences and

comorbidity. Current knowledge of these issues will be briefly reviewed.

Studies prior to the ECA study were reviewed by Boyd and Weissmann (49), and demonstrated a lifetime prevalence of "non bipolar depression" ranging from 2.1% to 12.3% in males and from 4.7% to 25.8% in females. This contrasts with the findings of the ECA, which reports a mean lifetime prevalence rate of unipolar depression from the five sites studied, of 4.4% (50). The lower rate in the five ECA sites as compared with rates in previous studies was felt to be related in part to the criteria of major depression used, making use of exclusion criteria to separate bipolar depression from unipolar/major depressive illness.

The observation that women tend to suffer depression more frequently than men was exhaustively reviewed by Weissman and Klerman, who concluded that the sex difference was real and not an artifact of helpseeking behaviour (51). The ECA results supported this conclusion, reporting sex ratios in the one year prevalence rates of MDD ranging from 1.9 to 5.0, females to males.

The ECA data also demonstrates that the age of onset for MDD is considerably lower than once thought, the cross-site mean age of onset being 21.2 years (50).

Outcome studies of MDD have essentially been based on studies of patients who sought treatment at university health centres. Of these patients, 80% to 90% recover within five years, while the remainder have chronic courses. A community-based survey has the advantage of identifying treated and untreated cases, but also tends to detect a higher proportion of less severe cases than found in practice (52). A predictor of recovery is the acuteness of onset and severity of MDD in patients without underlying dysthymia, while predictors of chronicity include protracted illness prior to seeking treatment and depressive illness secondary to another diagnosis (the so-called "secondary depression" of Robins and Guze) (53).

Although it is widely accepted that those with depression commonly suffer from a variety of nondepressive symptoms, only recently have these relationships been studied. Comorbidity is a term which implies that the concurrent presence of symptoms of affective and nonaffective symptoms may mean that two separate disorders are present. Keller notes the high rates of co-occurrence of alcoholism, eating disorders and anxiety disorders with major depression. The observation is made that although the association is well recognized, its nature is controversial and in need of further study (54).

## Methods

The design and field methods of the Edmonton survey of psychiatric disorders is reviewed in detail elsewhere (55). The results reported here are based on 3258 interviews conducted in Edmonton as part of a community survey assessing the prevalence of psychiatric disorders. This represents 71.6% of a total of 4,553 eligible addresses used for sample selection.

Subjects were selected utilizing a two-step procedure. First, households were randomly selected from a listing of residential addresses, and second, a single member of the household was selected using a respondent selection grid (56). The selected member had to be a usual occupant of the household and at least eighteen years of age.

Interviewers were selected and trained using the methods of Washington University, St. Louis. The data were checked for consistency and completeness prior to their double-entry into the computer. Further checks and edits were then done and a sample of questionnaires were triple-entered for further verification.

The main research instrument used was the Diagnostic Interview Schedule (DIS), a research instrument whose validity has been assessed (57). In this study diagnoses were made using the DIS computer program according to DSM-III criteria (without exclusion criteria).

In the sample studied, women were overrepresented (59% in the sample vs. 50% in the census) and the age agroup 18 - 24 was undersampled. In order to overcome these differences from the census population, the results were weighted for household size and poststratified by age and sex to the Edmonton census population (58). The SESUDAAN statistical program (59) was used to compute standard errors and test for differences between prevalence rates.

Table 1. Lifetime prevalence rates of major depressive disorder by age and sex (weighted data)

| Age | Number of unweighted cases, both sexes | Prevalence rate % (SE) | | |
|---|---|---|---|---|
| | | Both Sexes (N=3258) | Male (N=1330) | Female (N=1928) |
| 18-24 | 42 | 6.0 (1.0) | 3.3 (1.1) | 8.7 (1.6) |
| 25-34 | 134 | 11.5 (1.0) | 9.2 (1.4) | 14.1 (1.5) |
| 35-44 | 69 | 8.5 (1.1) | 3.3 (1.2) | 13.8 (1.8) |
| 45-54 | 52 | 12.0 (1.8) | 7.2 (2.2) | 17.0 (2.7) |
| 55-64 | 31 | 7.6 (1.5) | 8.4 (2.3) | 6.8 (1.9) |
| 65+ | 16 | 4.1 (1.1) | 1.8 (1.1) | 5.7 (1.6) |
| Total sample | 344 | 8.6 (0.5) | 5.9 (0.6) | 11.4 (0.8) |

N is the total unweighted sample.

Table 2. Six month prevalence rates of major depressive disorder by age and sex (weighted data)

| Age | Number of unweighted cases, both sexes | Prevalence rate % (SE) Both Sexes (N=3258) | Male (N=1330) | Female (N=1928) |
|---|---|---|---|---|
| 18-24 | 17 | 2.5 (0.7) | 1.1 (0.7) | 3.9 (1.2) |
| 25-34 | 52 | 4.5 (0.7) | 3.5 (0.8) | 5.8 (1.1) |
| 35-44 | 24 | 2.5 (0.6) | 1.3 (0.7) | 3.8 (0.9) |
| 45-54 | 14 | 3.2 (0.9) | 2.9 (1.2) | 3.4 (1.4) |
| 55-64 | 16 | 4.5 (1.2) | 6.1 (2.1) | 3.0 (1.3) |
| 65+ | 4 | 1.2 (0.6) | 0.9 (0.6) | 1.4 (1.0) |
| Total sample | 127 | 3.2 (0.3) | 2.5 (0.4) | 3.9 (0.5) |

N is the total unweighted sample.

## Results

### Prevalence Rates

The unweighted number of lifetime cases of major depressive disorder (MDD) was 344, of which 17 were bipolar depressions, 85 single episode depressions, and 242 recurrent MDD. The lifetime prevalence of MDD (at least one episode of major depression in a lifetime) was 8.6% for both sexes combined, 5.9% for males and 11.4% for women (weighted data). The female to male ratio was 1.93 ($p<0.001$). Tables 1 and 2 present the lifetime and six month prevalence data by age and sex. The period prevalence, in all ages and both sexes (weighted) was 2.3% at one month, 3.2% at six months, and 4.6% at one year. The age group 55-64 had the highest six month prevalence rate in men (6.1%) while the age group 25-34 had the highest six month prevalence rate in women (5.8%).

### Morbidity risk

Morbidity risk estimates (i.e. the lifetime chance of having at least one depressive episode) were calculated using the method described by Newman et al. (60). Males had a 16.4% morbidity risk, while females had a 22.3% morbidity risk (female to male ratio of 1.4).

### Age of onset

The age of onset is based on lifetime recall of the first symptom in those who subsequently met the criteria for a particular diagnosis. The ages of onset for males and females were similar, with the mean age of onset in males 25.8 years and in females 23.4 years. Males showed a broader distribution of age of onset, with 95% of males having their onset by age 55, as opposed to 95% of females having their onset by age 43.

### One year recovery rate

This was defined as the proportion of those cases meeting lifetime criteria for the disorder but who had no symptoms in the year prior to the interview. The overall one year recovery rate was 46.4%. Alternatively, more than half of those who had ever had MDD had symptoms of the disorder in the year preceding the interview.

### Symptom Analysis

Table 3 compares the frequency of symptom groups occurring in cases of major depression to all other subjects in the sample. Those symptoms found most frequently in cases of MDD were sleep disturbance (90.3%) and trouble concentrating (82.7%).

### Comorbidity

Table 4 shows the lifetime prevalence of other psychiatric diagnoses in cases of major depression, compared with lifetime prevalence of the same psychiatric disorders in all other subjects. The prevalence ratio (PR) is defined to be the quotient of these prevalence rates. Sixty-one percent of lifetime MDD

Table 3. Lifetime prevalence of depressive symptoms in those who have and have not met criteria for major depressive disorder, both sexes combined (weighted data)

| Symptoms group | Lifetime prevalence % Major depressive disorder (N=344) | All others (N=2914) |
|---|---|---|
| Group 1 (loss of appetite, weight loss/gain) | 71.5 | 4.3 |
| Group 2 (sleep disturbance) | 90.3 | 5.9 |
| Group 3 (psychomotor retardation or restlessness) | 55.1 | 1.7 |
| Group 4 (decreased libido) | 45.7 | 1.5 |
| Group 5 (fatigue) | 67.4 | 3.2 |
| Group 6 (guilt) | 66.6 | 2.5 |
| Group 7 (decreased concentration, slow thought) | 82.7 | 3.9 |
| Group 8 (thoughts of death, suicidal thoughts) | 66.6 | 4.6 |

N equals the number of unweighted cases.

Table 4. Lifetime prevalence of other psychiatric disorders in those with and without a lifetime history of a major depressive disorder, both sexes combined (weighted date)

| Other psychiatric diagnoses | Lifetime prevalence % | | Prevalence ratio |
|---|---|---|---|
| | Major depressive disorder (N=344) | All others (N=2914) | |
| Any diagnosis listed below (except MMD) | 61.0 | 27.5 | 2.2 |
| Affective disorders | | | |
| Mania | 4.0 | 0.2 | 20.0 |
| Dysthymic disorder | 27.1 | 1.5 | 18.1 |
| Substance use disorders | | | |
| Alcohol abuse/dependence | 30.5 | 16.8 | 1.8 |
| Drug abuse/dependence | 14.9 | 6.1 | 2.4 |
| Schizophrenia/schizophreniform | | | |
| Schizophrenia | 3.6 | 0.3 | 12.0 |
| Schizophreniform disorder | 1.0 | – | – |
| Anxiety disorders | | | |
| Obsessive compulsive disorder | 10.2 | 2.3 | 4.4 |
| Panic disorder | 10.6 | 0.4 | 26.5 |
| Phobia | 20.6 | 7.8 | 2.6 |
| Somatization disorder | 0.6 | – | – |
| Anorexia nervosa | – | 0.1 | – |
| Antisocial personality disorder | 9.0 | 3.2 | 2.8 |

N is total number of unweighted cases. Prevalence ratios were not calculated for schizophreniform, somatization, and anorexia because of insufficient numbers of cases.

cases met criteria for another DIS/DSM-III diagnosis, compared to 27.5% of all others in the sample, a prevalence ratio of 2.2.

Four percent of MDD (weighted) cases had at some time also experienced mania, thus meeting the criteria for bipolar affective disorder, representing twenty times the prevalence in the population not having had MDD. This is consistent with the observation in DSM-III-R that those people experiencing MDD are at increased risk for bipolar mood disorders.

Other frequent diagnoses in cases with major depression include dysthymia (27.1%), alcohol abuse/dependence (30.5%), drug abuse/dependence (14.9%), obsessive compulsive disorder (10.2%), phobia (20.6%) and panic disorder (10.6%). Anorexia nervosa was not found to co-occur in any of the cases with MDD; however the total number of cases of anorexia nervosa in the sample was very small (4 out of 3258).

The comorbidity of the subgroups of major depression - recurrent and single episode - is shown in Table 5. Of note is the fact that those with MDD single episode had a comorbidity profile not very dissimilar to that of all other subjects in the survey, their prevalence ratio for any other psychiatric diagnosis being only 1.1 (32.0/27.5). On the other hand, those diagnosed with MDD recurrent episodes, had 2.5 times the risk of all others and 2.2 times the risk of single episode MDD cases for having another DSM-III diagnosis. Codiagnosis of greatest frequency in this group includes dysthymic disorder (PR = 20.4) and panic disorder (PR = 10.3), while these patients were twice as likely to abuse alcohol and six times as likely to abuse drugs as all others in the survey.

### Physicians visits

The percentage of patients meeting criteria for major depression who had ever visited a physician for their symptoms of depression was 75.5%. However, the data do not indicate whether or not the patient was diagnosed or treated for the depression. The point should be stressed that in this study, the cases identified may or may not have been treated.

Table 5. Lifetime prevalence of other psychiatric disorders in those with a history of recurrent and single episode major depressive disorder, both sexes combined (weighted data)

| Other psychiatric diagnoses | Lifetime prevalence of major depressive disorder % | | Prevalence ratio |
|---|---|---|---|
| | Recurrent (N=242) | Single episode (N=85) | |
| Any diagnosis listed below | 69.8 | 32.0 | 2.2 |
| Substance use disorders | | | |
| Alcohol abuse/dependence | 35.7 | 14.8 | 2.4 |
| Drug abuse/dependence | 14.6 | 8.3 | 1.8 |
| Affective disorders | | | |
| Dysthymic disorder | 34.6 | 9.5 | 3.6 |
| Schizophrenia/schizophreniform | | | |
| Schizophrenia | 2.5 | 1.6 | 1.6 |
| Schizophreniform disorder | 0.6 | – | – |
| Anxiety disorders | | | |
| Obsessive compulsive disorder | 12.2 | 1.6 | 7.6 |
| Panic disorder | 11.0 | 6.9 | 1.6 |
| Phobia | 22.7 | 8.1 | 2.8 |
| Somatization disorder | 0.8 | – | – |
| Anorexia nervosa | – | – | – |
| Antisocial personality disorder | 10.5 | 3.8 | 2.8 |

N is total number of unweighted cases. Prevalence ratios were not calculated for schizophreniform, somatization, and anorexia because of insufficient number of cases.

## Discussion

The lifetime prevalence rate of MDD of 8.6% in this study is considerably higher than the mean rate reported in the ECA study of 4.4%. Case selection for this study used no exclusion criteria, and thus the sample includes both bipolar and unipolar depression, i.e., major depression has been, for this study, defined as an episode rather than a disorder. It should however be noted that in our study only 17 (5%) of the 344 subjects meeting criteria for major depressive episode had a manic episode also and are therefore bipolar. Removal of these cases still leaves a lifetime prevalence rate of over 8.0%. Weissman et al. (50) found that the use of the criterion of episode increases the ECA annual rate by nearly one percentage point. Both our data and the ECA findings on prevalence rates and sex ratios support the separation of bipolar disorder and MDD.

The commonly accepted finding of increased lifetime prevalence in females compared with males was supported by our results, with a female with male ratio of 1.9 being reported. The morbidity risk of 16.4% in men and 22.3% in women is comparable to previously published data, with respect to the fact that the morbidity risk for major depression is large in the general population, and greater in women than men by a significant margin.

The age of onset (first symptom) data for MDD shows a wide range, with a small number of cases reporting onset before the age of 10, a high rate of onset in the late teens, with over 75% of cases having an onset prior to age 30. We found onsets fell away rapidly after the age of 30, with no peak appearing in the middle years as reported by Lewisohn et al. (61), and virtually all cases having first symptoms before age 50.

Our data reveal that by age 21, 50% of cases of MDD have experienced their first symptom. Although long-term prospective follow-up studies of large groups of depressed children have not been done, available evidence suggests that depression developing in adolescence often has a severe and chronic course. The finding that half of all of our cases experienced their first symptom by age 21 indicates that this area is in urgent need of further research, to determine if those at risk for developing MDD can be identified at an earlier age.

Our results show that the symptom groups are generally quite specific to the diagnosis of MDD, with cases of MDD reporting an average of 6.8 symptoms in an episode.

Over 75% of patients with MDD had visited a physician, which is consistent with results reported by Shapiro et al. (62) who found that 76% to 78% of patients in the ECA study areas had made mental or general health visits. These studies are comparable in that they identify both treated and untreated cases.

Over one-third of subjects with recurrent MDD had a second diagnosis of dysthymia, compared to less than 10% of subjects with MDD single episode. This represents, in the recurrent MDD group, a prevalence ratio of over 20 times compared to all others, while in the single episode group the prevalence ratio was only 2.6. The recurrent MDD group may contain a subset of dysthymics whose "subaffective disorder" as described by Akiskal (63), will break through into the so-called "double depression" (64), and may represent a group distinct from other recurrent MDD cases and from single episode MDD, which appears to manifest dysthymia only slightly more frequently than all others in the survey. More work is needed to further characterize this group. It also seems likely that the one third of those with recurrent depression who also have dysthymia represent an unfortunate group of people whose illness does not really remit.

We found that the recurrent MDD group carries twice the risk for alcohol and drug abuse/dependence over all others sampled. Whether the core depression leads to alcoholism, or vice versa, is a source of controversy. Tahka (65) argued that the depressed individual may try to medicate himself with alcohol, leading to abuse or addiction, while others (66) view the alcoholic lifestyle as being etiologic for the recurrence of depression. The group of MDD single episode showed no increased prevalence ratio for drug and alcohol abuse or addiction. It appears that alcoholism and depression are more likely to co-exist if the depression is recurrent rather than single episode though, again, the issue of causation is unresolved. However, the presence of recurrent depression should alert the clinician to search for substance abuse, and vice versa, as treatments may need to be targeted at each disorder if they co-occur.

Persons with MDD in this study also had an increased risk of panic disorder. The relationship between these two disorders is examined elsewhere (67), but our findings support the frequent observation that there is a strong association between anxiety states and depression. We showed that the prevalence ratio was much higher in recurrent MDD than in single episode MDD for panic disorder.

Our data shows that nearly 70% of people with recurrent MDD have had symptoms which meet the criteria for another core DIS/DSM-III disorder at some time during their lives. This represents 2.5 times the prevalence ratio compared to all others sampled. This contrasts with the finding that those with MDD single episode show the same prevalence

ratio of being diagnosed with a core DSM-III diagnosis as all others.

DSM-III uses exclusion criteria because of the assumption, confirmed by Boyd et al. (68), that "dominant" disorders sometimes present with symptoms of an "excluded" disorder. However Boyd et al. (68) also found that people with any DIS-generated disorder have significant odds of having almost any other DIS disorder. It is interesting that although recurrent MDD tends to co-occur with other DSM-III disorders, single episode MDD does not show this tendency. Although intuitively one suspects that a recurrent illness is more likely to render one susceptible to other illnesses, this finding requires further study.

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