
The Epidemiology of Mood Disorders

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INTRODUCTION

Research in epidemiology is critical to understanding mood disorders for several reasons. First, on a societal level, health care planning can be assisted by assessing the magnitude of the burden of disease in the population. Mood disorders are among the major health problems world wide for two reasons: they are highly prevalent in the general population, and they cause significant loss of quality of life and social functioning in the affected individual. Further, mood disorders contribute to a poorer outcome of comorbid mental as well as somatic conditions. On the basis of epidemiological data and health economic measures based on clinical severity ratings it has been projected that major depression will be responsible for the largest burden of disease of any illness by the year 2020 (Murray and Lopez, 1996). With regard to health care planning, the assessment of the effectiveness of intervention programs in the community is important. Second, in addition to the mere reporting of prevalence or incidence rates in a circumscribed population (*descriptive epidemiology*), *analytical epidemiology* supplements clinical research in identifying vulnerabilities as well as factors that trigger the onset, and influence the course of the condition under study. This is particularly applicable to mental disorders. It is well known that subjects with mental disorders often do not seek psychiatric consultation (Goldberg and Huxley, 1980); therefore, cases that come under the observation of specialists cannot be considered fully representative of the characteristics of psychiatric disorders in the general population. Epidemiological community surveys consistently show that the number of cases referred to psychiatrists is relatively small and unlikely to be representative of psychiatric disorders as they occur in the

general population (Bijl et al., 2003). Psychiatric samples, therefore, could be biased not only quantitatively but also qualitatively (Galbaud du Fort et al., 1993). Thus, studies conducted with non-clinical samples are necessary in order to complete our knowledge of psychiatric pathology – in basic research on mechanisms as well as in refining diagnostic criteria and nosology.

This chapter will focus on the following topics: (1) methodological issues in the epidemiological investigation of mood disorders; (2) distribution of mood disorders in the general adult population (prevalence, comorbidity, onset, course) and (3) risk factors and correlates of mood disorders.

METHODOLOGICAL ISSUES

Historical Development: First, Second and Third Generation Studies

In a classic review Dohrenwend and Dohrenwend (1982) identified three generations of psychiatric community epidemiological surveys. In the first generation of studies, which dates back to the mid-1800s, community residents were not directly interviewed and the identification of cases of psychiatric disorders relied essentially on agency records and key informants, such as general practitioners and clergymen. The second generation of studies began after World War II and its major advancement is represented by the fact that randomly selected community residents were directly contacted; in these surveys subjects either filled out forms which yielded global ratings of psychopathology (but not a diagnosis) or were assessed by interviewers (generally clinicians) who determined the diagnoses (Streiner, 1998). When diagnoses were obtained, the lack of clear operationalized diagnostic criteria and of standardized and reliable assessment instruments resulted in a poor reliability and represented a major shortcoming of these studies. Diagnostic categories of affective pathology in particular were quite different from current ones. Due to a unitary view of psychopathology, milder forms of mood disorders were generally grouped together with anxiety and other disorders and labelled as ‘neuroses’, while the category of ‘affective psychosis’ included both depressive and bipolar severe mood disorders. Neugebauer et al. (1980) reviewed 3 North American and 13 European (mostly Scandinavian) second generation studies and reported period prevalence rates for affective psychosis ranging from 0.0% to 1.9%.

In spite of their limitations, the first and second generation studies were fundamental for the development of psychiatric epidemiology since they clarified that mental illness was a major public health problem and that most subjects suffering from psychiatric disorders did not seem to have adequate access to treatment (Tohen et al., 2000).

During the 1970s concerns about the low reliability of psychiatric diagnoses led to the development of explicit, operationalized sets of diagnostic criteria such as the St.

Louis criteria (Feighner et al., 1972), the Research Diagnostic Criteria (RDC; Spitzer et al., 1978), the third edition of the American Psychiatric Association's Diagnostic and Statistical Manual (DSM-III and the subsequent editions DSM-III-R and DSM-IV; American Psychiatric Association, 1980, 1987, 1994/2000), the ninth and tenth revisions of the World Health Organization's International Classification of Diseases (ICD-9 and ICD-10; World Health Organization, 1978, 1993). Concurrently, standardized diagnostic interviews were developed in order to reduce potential sources of disagreement between different assessors (Box 1).

Utilization of operationalized diagnostic criteria and standardized interviews in community samples reflect the major advance of the *third and current generation* of psychiatric epidemiological surveys. These developments allowed researchers to obtain reliable information about the prevalence rates of specific disorders and as a result the past 20 years have been a highly productive period for psychiatric

Box 1: Selected Assessment Instruments

Along with the development of diagnostic systems based on explicit criteria, standardized diagnostic interviews were developed and refined in order to reduce potential sources of disagreement between different assessors. There are basically two types of instruments (Brugha et al., 1999a): semi-structured interviews (for use by interviewers with clinical experience) and fully standardized interviews (for use by lay interviewers). Note: in some recent studies mandatory standardized assessment is accompanied by clinical severity ratings, preferably administered by clinically trained interviewers; thus, the dichotomy of these approaches is not absolute.

Prominent examples are:

(A) Semi-structured interviews

- Present State Examination (PSE; Wing et al., 1974)
- Schedule for Affective Disorders and Schizophrenia (SADS; Endicott and Spitzer, 1978)
- Schedules for Clinical Assessment in Neuropsychiatry (SCAN; Wing et al., 1990)
- Structured Clinical Interview for DSM-IV (SCID; First et al., 1997)

(B) Standardized interviews

- Diagnostic Interview Schedule (DIS; Robins et al., 1981)
- Composite International Diagnostic Interview (CIDI; Robins et al., 1988, and several modified/updated versions)
- Revised Clinical Interview Schedule (CIS-R; Lewis et al., 1992).

Another example for a widely used instrument is the Mini-International Neuropsychiatric Interview (Sheehan et al., 1998), a short structured diagnostic interview, developed jointly by psychiatrists and clinicians in the United States and France, for DSM-IV and ICD-10 psychiatric disorders. With an administration time of approximately 15 minutes, it was designed to meet the need for a short but accurate structured psychiatric interview for multicentre clinical trials and epidemiology studies and to be used as a first step in outcome tracking in nonresearch clinical settings.

epidemiology, with a large number of surveys conducted in several countries, although little evidence is still available from nations with low-income economies (de Girolamo and Bassi, 2003).

Assessment and Design Issues

Despite the remarkable advances of current semi-structured or standardized assessments, important methodological issues still remain unresolved. Most importantly, the validity of community diagnostic assessment remains controversial. This is a crucial issue since it has been repeatedly shown in community samples that even relatively small changes in diagnostic criteria and assessment methods may produce substantially different results (Brugha et al., 1999b; Regier et al., 1998; Narrow et al., 2002). Thus, it is important to investigate whether differences in prevalence rates between studies are attributable to real differences or to methodological factors (population/sampling, threshold definitions (see Box 2), modifications in the instrument, or use of clinically trained vs. lay interviewers).

In mood disorders, valid assessment is difficult for various reasons (see Box 3). The standardized approach of the assessment (e.g. M-CIDI; Wittchen et al., 1998) offers good reliability and validity, in particular in its current versions, for depressive disorders but to a lesser degree in bipolar disorders (Kessler et al., 1998, 2003; Wittchen, 1994). Considering the difficulties in assessing the whole spectrum of mood disorders the use of clinicians as interviewers might be of special importance, as well as in certain other domains (e.g. psychosis, mental disorder due to general

Box 2: Subthreshold Mood Disorders

Various studies suggest that a large proportion of subjects with clinically significant depression in the community fail to meet current diagnostic criteria for either major depressive disorder or dysthymia (Angst and Merikangas, 1997). For instance, in the NCS the lifetime prevalence of DSM-III-R 'minor depression' was 10.0% and its correlates were substantially similar to major depression (Kessler et al., 1997), while in a recent Italian survey the lifetime prevalence of DSM-IV 'depression not otherwise specified' was 7.8% (Faravelli et al., 2004b).

Recurrent brief depression is perhaps the most extensively studied subthreshold mood disorder since its first operationalized definition on the basis of epidemiological observations from the Zurich study (Angst and Dobler-Mikola, 1985). In a recent review of four community studies the lifetime prevalence of recurrent brief depression ranged between 2.6% and 21.3%; the disorder also seems associated with significant clinical impairment (Pezawas et al., 2003).

Data from the Zurich study also suggest the broadening of the boundaries of bipolarity; in this survey about 11% of community residents could be included in the expanded spectrum of bipolar disorders and 13% presented attenuate expressions of bipolarity intermediate between bipolar disorder and normality (Angst et al., 2003a,b); however, these findings, being derived from a single small-size study, need replication.

Box 3: Challenges in the Assessment of Mood Disorders in Epidemiological Studies

In mood disorders, valid assessment is difficult for various reasons:

- Even chronic and recurrent mood disorders show an episodic and fluctuating course. This results in difficulties in assessing exact time frames where enough symptoms are present concurrently with sufficient severity to justify the diagnosis. Example: Results will differ if the 12-month time frame is completely assessed before further lifetime psychopathology (for the disorders where no 12-month symptoms were present) vs. lifetime episodes are inquired about first, followed by a recency question (When was the last time it happened?) and prescribing a 12-month diagnosis according to the answer to this recency question. The first interview version produces better 12-month prevalence estimates.
- With regard to the unstable course it may be reasonable also to take subthreshold conditions into account (e.g., to identify prodromal states, partial remissions, or a new diagnosis in its own right, see Box 2), describing further potential complications.
- Mood disorders require lifetime assessment especially with regard to (differential) diagnosis of bipolar disorders. Distinguishing normal mood swings and nonpathological exalted mood states from (hypo-) manic symptoms requires additional procedures to achieve reliability as well as clinical relevance of the diagnosis; the use of clinically trained interviewers may be necessary.

medical factor, somatoform disorders). This also refers to the validity of study designs (e.g. one cross-sectional interview in household vs. sequential assessment by the subject's primary care physicians; Faravelli et al., 2004a).

The debate about a 'gold standard' of the epidemiological assessment – semi-structured vs. standardized interviews (Brugha et al., 1999a) – may continue until the theoretical advantage of a clinical approach provides more promising psychometric properties than standardized interviews do. In some areas such as disclosure vs. bias due to social acceptability standardized methods can even achieve better results than a method that resembles clinical practice (Turner et al., 1998). Following Wittchen et al.'s (1999a) arguments, the use of semi-structured clinical interviews as the central approach to carrying out epidemiological surveys might be likely to create more problems than it solves. In any case, the results of CIDI and SCID diagnoses seem to converge, presumably due to the development of improving accuracy within the latest CIDI versions. Also Faravelli et al. (2004b) conclude that their results of a naturalistic study are comparable to previous studies: in spite of the broad methodological differences, the similarities seem much greater than the differences.

Among other current methodological developments in the assessment of mood and other mental disorders as well as in the design of epidemiological studies, are: the inclusion of severity measures and more comprehensive analyses of disability and help-seeking, enhanced probing and rating procedures, inclusion of variables suited for health economic analyses, and the increasing availability of longitudinal

data, allowing more sophisticated analyses with regard to causes and courses of mental disorders.

THE DISTRIBUTION OF MOOD DISORDERS IN THE COMMUNITY: PREVALENCE, COMORBIDITY, AND THEIR CORRELATES

Lifetime and Current Prevalence Rates in the General Population

Major Depression and Dysthymia

Prevalence rates of Major Depression and Dysthymia in selected third generation epidemiological surveys are presented in Table 1.1. Note that in the total rates shown, male and female values are averaged: prevalence rates have been consistently found 1.5–2.5 times higher in women than in men; for example, in the German study (Jacobi et al., 2004) the prevalence of any depressive 12-month-diagnosis in women is 14% vs. 7.5% in men. Prevalence rates for major depression and dysthymia in these surveys vary widely across countries (for references see Table 1.1) and, in particular, very low rates of major depression have been reported in studies conducted in Eastern Asian nations. Sociodemographic differences (e.g. discrepancies in the distribution of marital status) or cross-cultural variations (e.g. different social acceptability of the expression of emotions) could explain the discrepancies between the results. Also variability of instruments and design used in these studies can account for differences. For example, the clinicians in the Sesto Fiorentino Study diagnosed ‘depressive disorder NOS’ significantly more frequently than is reported in studies based on a different methodology; this might explain lower rates of major depression (9.5% vs. 13–17% lifetime prevalence in other recent studies).

Roughly 20–40% of unipolar depressive cases are assigned dysthymia as a diagnosis (3–6% lifetime prevalence over most studies). Studies are generally concordant in pointing out that major depression and dysthymia frequently coexist, a disorder sometimes referred to as ‘double depression’. The lifetime prevalence of double depression has been reported to range between 1.5% and 2.5% (Bland, 1997).

Data from most cross-sectional community surveys suggest that the prevalence of major depression is increasing in successive generations born after World War II (Cross-National Collaborative Group, 1992; Kessler et al., 1996, 2003). However, studies relying on single retrospective interviews may be biased by methodological factors such as recall bias increasing with age (Bland, 1997; Paykel, 2000). Long-term longitudinal follow-up surveys are a much more reliable source of information about this topic; however, available evidence from such studies is limited and inconsistent (Hagrell et al., 1982; Lehtinen et al., 1991; Murphy et al., 2000a,b)

and therefore this issue remains open to debate. Selected findings about the prevalence in primary care are presented in Box 4.

Bipolar Disorders

Prevalence rates of bipolar disorders in selected third generation epidemiological surveys are presented in Table 1.2; here, rates in women and men are roughly the same (lifetime 1–2% in most studies). The differences between lifetime and current (12-month) rates are smaller than in unipolar depressions; this could indirectly indicate a higher chronicity. It has to be mentioned that in this overview bipolar I and bipolar II disorders are lumped together, but most by far of the epidemiological studies on bipolar illness have examined bipolar I disorder.

Younger and Older Age

This chapter focuses on the epidemiology of mood disorders in adults but some basic information for children and adolescents is given in Box 5. The results for depressive symptoms among the elderly population are quite variable across studies. These results are summarized in Table 1.3. By contrast with depressive symptoms, rates of major depression seem to be much lower. When the Diagnostic Interview Schedule (DIS) (Robins et al., 1981) is used, the 6-month prevalence of major depression in the community ranged from 1.7% (Weissman et al., 1985) to 4.85% (Potter et al., 1995). Other methods have been used in order to assess depressive disorders in the elderly (Uhlenhuth et al., 1983; Ben-Arie et al., 1987; Carpinello et al., 1989; Forsell et al., 1995; Steffens et al., 2000). The prevalence rates found in these studies vary from 5.1% (Uhlenhuth et al., 1983) to 15.8% (Steffens et al., 2000).

Box 4: Depression in primary care

In addition to representative community studies it should be noted that the prevalence of depressive disorders has also been examined in primary care all over the world (e.g. WHO studies; Üstün and Sartorius, 1995). Point prevalence estimates of major depression have varied widely across 15 centres (Simon et al., 2002); from a low of 1.6% in Japan to a high of 26.3% in Chile. In Germany, recent studies in primary care with large samples ($N > 20\,000$) report point prevalence estimates of over 10% for depressive disorders (Jacobi et al., 2002a; Wittchen and Pittrow, 2002).

Although primary care physicians show better recognition rates than in former WHO studies, there is still much room for improvement. Case recognition (any mental disorder among the patients diagnosed by the physicians as depressive) is better than diagnostic recognition (correct depressive diagnosis) – but often primary care physicians tend to over-diagnose depression (compared to standardized study assessment; Höfler and Wittchen, 2000).

TABLE 1.1 Third generation prevalence studies of major depression and dysthymia

	Major depression			Dysthymia		
	Lifetime	6-12-month	1-month	Lifetime	6-12-month	1-month
<i>Semi-structured interviews</i>						
Weissman and Myers, 1978						
Faravelli et al., 1990	18.0	—	3.7 ^a	—	—	—
Angst, 1996	—	6.3	2.8 ^a	—	3.0	1.0 ^a
Almeida-Filho et al., 1997	16.1	7.3	1.5	—	—	—
	1.9-10.2 ^b	—	—	—	—	—
	interview/DSM-III					
Faravelli et al., 2004a,b	9.5	3.4	2.7 ^a	1.5	0.9	0.8 ^a
Henderson et al., 1979, 1981	—	—	4.8 ^b	—	—	—
Bebbington et al., 1981	—	—	7.0 ^b	—	—	—
Mavreas et al., 1986	—	—	7.4 ^b	—	—	—
Hodiamont et al., 1987	—	—	5.4 ^b	—	—	—
Vázquez-Barquero et al., 1987	—	—	6.2 ^b	—	—	—
Lehtinen et al., 1990	—	—	4.6 ^b	—	—	—
Roca et al., 1999	—	—	1.6	—	—	3.1
Ayuso-Mateos et al., 2001	—	—	4.1-4.7	—	—	0.3-1.1
	—	—	6.2-8.9	—	—	0.5-2.9
	—	—	7.0-8.4	—	—	0.9-1.5
	—	—	1.8	—	—	0.5
	—	—	4.8-15.0	—	—	0.2-0.3
	—	—	—	—	—	—
	5.8	3.0	2.2	3.3	—	—
<i>Fully structured interviews</i>						
Regier et al., 1988; Weissman et al., 1991						
Canino et al., 1987	4.6	3.0	—	4.7	—	—
Bland et al., 1988a,b	8.6	3.2	2.3	3.7	—	—
Wells et al., 1989; Oakley-Browne et al., 1989	12.6	5.3	—	6.4	—	—

(continued)

Hwu et al., 1989	Taiwan (3 samples)	DIS/DSM-III	0.9-1.7	0.6-1.1	-	0.9-1.5	-
Lee et al., 1990a,b	Korea (2 samples)	DIS/DSM-III	3.3-3.5	-	-	1.9-2.4	-
Wittchen et al., 1992	Former West Germany	DIS/DSM-III	9.0	3.0	-	3.9	-
Chen et al., 1993	Hong Kong	DIS/DSM-III	1.3 (M)-2.4 (F)	-	-	1.0 (M)-2.8 (F)	-
Szadoczky et al., 1998	Hungary	DIS/DSM-IIIIR	15.1	7.1	2.6	4.5	-
Kessler et al., 1994b; Blazer et al., 1994	USA (NCS)	CIDI/DSM-IIIIR	17.1	10.3	4.9	6.4	2.5
Offord et al., 1996	Ontario, Canada	CIDI/DSM-IIIIR	-	4.1	-	-	0.8
Bijl et al., 1998	The Netherlands	CIDI/DSM-IIIIR	15.4	5.8	2.7	6.3	2.3
Wang et al., 2000	USA (MIDUS)	CIDI/DSM-IIIIR	-	14.1	-	-	-
Kringlen et al., 2001	Oslo (Norway)	CIDI/DSM-IIIIR	17.8	7.3	-	10.0	3.8
Sandanger et al., 1999	Norway (2 samples)	CIDI/ICD-10	-	-	2.6 ^{de}	-	-
About-Saleh et al., 2001	Al Ain, United Arab Emirates	CIDI/ICD-10	3.4	-	-	-	-
Andrade et al., 2002	Sgo Paulo, Brazil	CIDI/ICD-10	16.8	7.1	4.5	4.3	1.4
Andrews et al., 2001	Australia	CIDI/DSM-IV	-	6.3	3.2	-	1.1
Kessler et al., 2003	USA (NCS-R)	CIDI/DSM-IV	16.2	6.6	-	-	-
Jenkins et al., 1997	Great Britain	CIS-R/ICD-10	-	-	2.3 ^a	-	-
Araya et al., 2001	Santiago, Chile	CIS-R/ICD-10	-	-	5.5 ^a	-	-
Jacobi et al., 2004	Germany	M-CIDI/DSM-IV	14.8	8.3	3.4	4.5	3.6
The ESEMeD-MHEDEA 2000 Investigators, 2004	Belgium, France, Germany, Italy, the Netherlands, Spain	WMH-CIDI/DSM-IV	12.8	3.9	-	4.1	1.1

ECA: Epidemiologic Catchment Area Study; NCS: National Comorbidity Survey; MIDUS: Midlife Development in the United States survey; SADS: Schedule for Affective Disorders and Schizophrenia (Endicott and Spitzer, 1978); SPIKE: Structured Psychopathological Interview and Rating of the Social Consequences for Epidemiology (Angst et al., 1984); FPI: Florence Psychiatric Interview (Faravelli et al., 2001); PSE: Present State Examination (Wing et al., 1974); SCAN: Schedules for Clinical Assessment in Neuropsychiatry (Wing et al., 1990); DIS: Diagnostic Interview Schedule (Robins et al., 1981); CIDI: Composite International Diagnostic Interview (Robins et al., 1988); CIS-R: Revised Clinical Interview Schedule (Lewis et al., 1992).

^a1-2-week prevalence.

^bPSE/CATEGO/ICD-9 depressive disorders.

^cMajor depressive episode and dysthymia.

Among the specific difficulties in this area are: great variability according to age group (>55 vs. >65 vs. >70 vs. >80 in different studies), problems with diagnostic instruments developed for younger adults (Knäuper and Wittchen, 1994), interference/symptom overlap with comorbid somatic conditions, and the need for modified (but not yet established) diagnostic criteria for the elderly.

But independently of the assessment method used, prevalence rates of depressive symptoms and major depression are lower in elderly people in the community than in younger people. These results may be explained by a selective mortality bias, a recall bias of psychiatric symptoms, a more frequent denial of psychiatric symptoms by elderly, more prominence of physical symptoms of depression in aged people or a possible cohort effect.

Comorbidity, Onset, and Course

Comorbidity

Community studies are generally concordant in pointing out that major depression is a highly comorbid disorder. Figure 1.1 presents comorbidity data from a German study (Jacobi et al., 2002b, 2004) with percentages and odds ratios for anxiety, somatoform and substance disorders when a major depression or dysthymia is

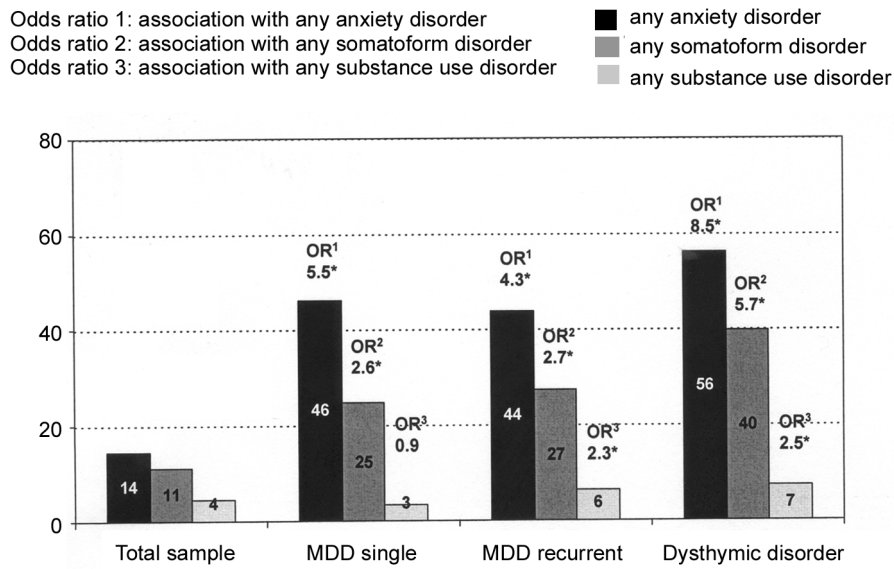


Figure 1.1 Comorbidity of 12-month depressive disorders: proportions and associations with anxiety, somatoform and substance use disorders in respondents with any disorder, MDD single, MDD recurrent and dysthymic disorder (GHS-MHS; N=4181)

TABLE 1.2 Third generation prevalence studies of bipolar disorder

			Lifetime	6/12 month	1 month
<i>Semi-structured interviews</i>					
Weissman and Myers, 1978	New Haven, USA	SADS/RDC	1.2	—	0.0 ^a
Faravelli et al., 1990	Florence, Italy	SADS/DSM-III	—	1.5	0.5 ^a
Almeida-Filho et al., 1997	Brazil (3 samples)	Semistructured interview/ DSM-III	0.3–1.1	—	—
<i>Angst and Gamma, 2002</i>					
Faravelli et al., 2004a,b	Zurich, Switzerland	SPIKE/DSM-IV	2.3	—	—
Henderson et al., 1979, 1981	Florence, Italy	FPI/DSM-IV	0.8	0.3 ^a	0.3 ^a
Bebbington et al., 1981	Canberra, Australia	PSE/ICD-9	—	—	0.2
Hodiamont et al., 1987	Camberwell, UK	PSE/ICD-9	—	—	0.8
Vázquez-Barquero et al., 1987	Nijmegen, the Netherlands	PSE/ICD-9	—	—	0.1
Lehtinen et al., 1990	Santander, Spain	PSE/ICD-9	—	—	0.1
Roca et al., 1999	Finland (2 samples)	PSE/ICD-9	—	—	0.4
	Formentera, Spain	SCAN/ICD-10	—	—	0.9
<i>Fully structured interviews</i>					
Regier et al., 1988; Weissman et al., 1991	USA (ECA; 5 samples)	DIS/DSM-III	0.8	0.5	0.4
Cannino et al., 1987	Puerto Rico	DIS/DSM-III	0.5	0.3	—
Bland et al., 1988a,b	Edmonton, Canada	DIS/DSM-III	0.6	0.1	0.1
Wells et al., 1989	Christchurch, New Zealand	DIS/DSM-III	0.7	—	—
Hwu et al., 1989	Taiwan (3 samples)	DIS/DSM-III	0.1–0.2	0.1	—
Lee et al., 1990a,b	Korea (2 samples)	DIS/DSM-III	0.4	—	—
Wittchen et al., 1992	Former West Germany	DIS/DSM-III	0.2	0.2	—
Chen et al., 1993	Hong Kong	DIS/DSM-III	0.1 (M)–0.2 (F)	—	—
Szadoczky et al., 1998	Hungary	DIS/DSM-IIIIR	1.5	0.9	0.5
Kessler et al., 1994	USA (NCS)	CIDI/DSM-IIIIR	1.6	1.3	—
Offord et al., 1996	Ontario, Canada	CIDI/DSM-IIIIR	—	0.6	—
Bijl et al., 1998	The Netherlands	CIDI/DSM-IIIIR	1.6	0.9	—
Kringlen et al., 2001	Oslo (Norway)	CIDI/DSM-IIIIR	1.8	1.1	0.6
Abou-Saleh et al., 2001	Al Ain, United Arab Emirates	CIDI/ICD-10	0.3	—	—
Andrade et al., 2002	Sgo Paulo, Brazil	CIDI/ICD-10	1.0	0.5	0.4
Jacobi et al., 2004	Germany	M-CIDI/DSM-IV	1.0	0.8	0.6

ECA: Epidemiologic Catchment Area Study; NCS: National Comorbidity Survey; SADS: Schedule for Affective Disorders and Schizophrenia (Endicott and Spitzer, 1978); SPIKE: Structured Psychopathological Interview and Rating of the Social Consequences for Epidemiology (Angst et al., 1984); FPI: Florence Psychiatric Interview (Faravelli et al., 2001); PSE: Present State Examination (Wing et al., 1974); SCAN: Schedules for Clinical Assessment in Neuropsychiatry (Wing et al., 1990); DIS: Diagnostic Interview Schedule (Robins et al., 1981); CIDI: Composite International Diagnostic Interview (Robins et al., 1988).

^a1-week prevalence.

Box 5: Mood Disorders in Children and Adolescents

Empirical studies have documented that the phenomenology of depression is quite similar between adolescents and adults (Roberts et al., 1995; Ryan et al., 1987) even if differences exist in the expression of mood disorders between adults and children and adolescents. One of those differences is irritability, which is a symptom of depression in children and adolescents but not in adults.

Assessment of depression in children and adolescents encounters several methodological difficulties:

- Dimensional or diagnostic instruments assessing depression specifically in delimited age groups do not exist yet. So, clinicians and researchers use the same instrument to assess mood disorders in children and adolescents regardless of the fact that the reliability and validity of these instruments change with the age of the patient.
- When a diagnostic interview is used, the multiplicity of informants (parents, teachers or the patient) and the uncertainty as to how combine these data to yield a diagnosis constitute a methodological problem.
- Another difficulty with diagnostic interviews is the lack of explicit criteria assessing the impairment or the distress due to the mental disorder in children. In DSM-IV, this criterion is made more explicit.
- Dimensional self-report checklists assessing mood disorders in children and adolescents are numerous but there is a lack of specificity with most high-scoring youngsters failing to meet diagnostic criteria for depression.

Major Depression

In the community, the point prevalence of major depression ranges between 1% (McGee and Williams, 1988) to 6% (Kessler and Walters, 1998). Canino et al. (2004) assessed the prevalence of mental disorders in 1897 children and adolescents aged 4 to 17 years. The 12-month prevalence of major depression according to DSM-IV criteria was 3% in this population. The rates of lifetime prevalence of major depression in children and adolescents are higher, ranging from 4% (Whitaker et al., 1990) to 25% (Lewinsohn et al., 1998), which is comparable to the lifetime rate of major depression in adults. The gender ratio of major depression is 1:1 in children and increases to 2:1 female-to-male ratio in adolescents (Kessler et al., 1994b).

Bipolar Disorders

Between 20% and 40% of adolescents with major depressive disorder develop Bipolar I disorder within a period of 5 years after the beginning of the mood disorder (Rao et al., 1995; Geller et al., 1994; Strober et al., 1993). Risk factors of bipolar disorder in adolescents with depressive disorder include early-onset depression, mood disorder with psychotic features, family history of bipolar disorder and pharmacologically induced hypomania (Akiskal et al., 1995; Geller et al., 1994). It is important to recognize the existence of bipolar disorders in adolescents because this mood disorder may be misdiagnosed as conduct disorder or a personality disorder. Studies assessing the prevalence of bipolar disorder in children and adolescents are rare and reported estimates range from 0.0% to 1.0% (Kessler and Walters, 1998; Costello et al., 1996).

TABLE 1.3 Prevalence of depressive symptoms in the elderly

Site	Author	N	Age	Methods of assessment	Prevalence (%)
<i>US community studies</i>					
Durham County	Blazer and Williams, 1980	997	≥65	OARS, Depression Scale	14.7
Los Angeles County	Frerichs et al., 1981	126	≥65	CES-D ≥16	16.7
Kentucky	Murrell et al., 1983	2517	≥55	CES-D ≥20	F: 18.2, M: 13.7
Washington	Goldberg et al., 1985	1144	65–75	CES-D ≥16	9.5
New Haven	Berkman et al., 1986	2806	≥65	CES-D ≥16	F: 19.2, M: 11.3
New York	Copeland et al., 1987	445	≥65	GMS-AGECAT	16.2
New York	Kennedy et al., 1989	2317	≥65	CES-D ≥16	F: 19.9, M: 11.1
Duke-EPESE	Blazer et al., 1991	3998	65–74	Revised CES-D	8.1
			75–84		10.3
			≥85		12.3
New York City	Potter et al., 1995	1140	≥65	CES-D ≥16	11.4
Tennessee	Okwumabua et al., 1997	110	≥60	CES-D ≥16	19.8
<i>European community studies</i>					
Liverpool	Copeland et al., 1987	1070	≥65	GMS-AGECAT	11.5
London	Lindesay et al., 1989	890	≥65	CARE Depression Scale	13.5
North London	Livingston et al., 1990	811	≥65	Short CARE	15.9
France	Dufouil et al., 1995	2797	≥65	M: CES-D ≥17, F: CES-D ≥23	15.9
					15.9
London	Prince et al., 1997	654	≥65	Short CARE	17
Dublin	Kirby et al., 1997	1232	≥65	GMS-AGECAT	10.3

CES-D: Center for Epidemiologic Studies Depression Rating Scale. GMS-AGECAT: Automated Geriatric Examination for Computer Assisted Taxonomy Package. CARE: Comprehensive Assessment and Referral Evaluation.

present vs. the base rates of the disorders in the total sample. There are markedly elevated rates, reaching up to 56% anxiety disorders in dysthymia (vs. 14% in the general population); overall, roughly 60% of major depressions and 80% of dysthymia were accompanied by at least one additional diagnosis.

The strong association with anxiety has been consistently reported before (Weissman et al., 1996; Kessler et al., 1996; Angst, 1996). Regarding specific anxiety disorders, an examination of the findings of six epidemiological surveys (Merikangas et al., 1996) showed that panic disorder had a much stronger association with major depression than phobias. Of the phobic disorders, social phobia had a stronger association with major depression than either agoraphobia or simple phobia; a significant association with both generalized anxiety disorder and obsessive-compulsive disorder has also been reported. Generally anxiety disorders (possibly with the exception of panic disorder) appear temporally primary to major

depression in the majority of subjects in both cross-sectional and prospective longitudinal studies (Merikangas et al., 1996; Wittchen et al., 2000; Kessler et al., 2003).

In most studies substance use disorders are also associated with major depression, although findings are less consistent than those regarding anxiety disorders, and the association appears weaker.

Finally, data from the recent US National Comorbidity Survey Replication (Kessler et al., 2003) also suggest that about one-third of the subjects with major depression may have a lifetime comorbid impulse control disorder, although comorbid impulse control disorder is often thought to be more strongly related to bipolar than to unipolar depression (McElroy et al., 1996); according to the authors this could reflect broader factors of the existence of what has recently been called 'soft bipolar spectrum' in which comorbid impulse control disorder among patients with major depression represents a marker of bipolar susceptibility (Perugi et al., 1998).

Dysthymia also shows a high co-occurrence rate with anxiety disorders; of the specific anxiety disorders, dysthymia seems more strongly comorbid with generalized anxiety disorder and panic disorder and less strongly comorbid with phobias and obsessive-compulsive disorder.

A comorbid anxiety disorder is diagnosed in 40% to 90% of subjects with bipolar disorder in community samples (Kessler et al., 1997; Szadoczky et al., 1998); the stronger associations appear to be with panic disorder, obsessive-compulsive disorder and generalized anxiety disorder, while the comorbidity with phobias seem weaker. It has also been suggested that subjects with bipolar II disorder may have a particularly high comorbidity rate with anxiety disorders when compared to subjects with bipolar I disorder (Rihmer et al., 2001).

Co-occurrence of bipolar and addictive disorders is also particularly frequent. A comorbid lifetime alcohol/substance use disorder is present in 20% to 70% of bipolar subjects (Regier et al., 1990; Fogarty et al., 1994; Kessler et al., 1997; Fara-velli et al., 2004b); in the ECA study the prevalence of alcoholism in bipolar disorder was three times higher than in major depression (Helzer and Pryzbeck, 1988).

Age of Onset

In the majority of studies, the mean age of onset is in the mid to late 20s for major depression while for bipolar disorder it ranges between the mid-teens and the mid-20s. More differentiated than the comparison of means is the comparison of the whole cumulative age of onset distributions (i.e. curves that show what proportion of all lifetime cases report the onset before a given age). These are presented in Figure 1.2 for several types of mood disorders. The differences between bipolar disorders, major depression and dysthymia are obvious: bipolar disorders begin very early (50% of the subjects with a lifetime diagnosis report an onset before 18 years), whereas the median age of onset in major depression is 30 years and in

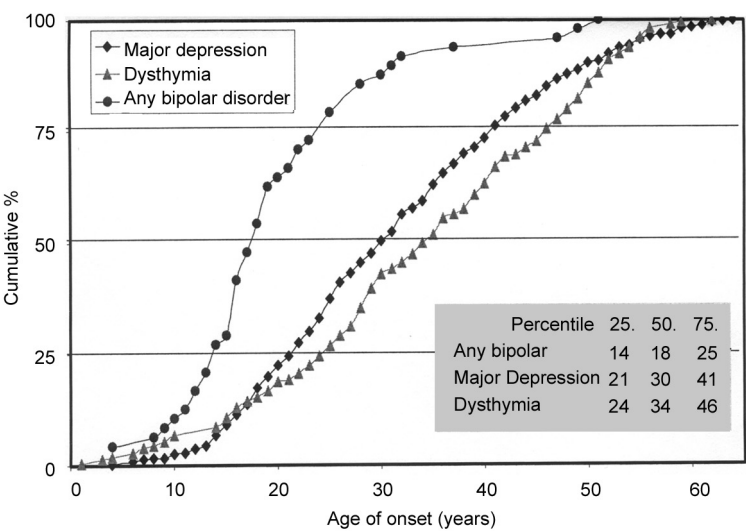


Figure 1.2 Age of onset distributions (source: GHS-MHS; Jacobi et al., 2004)

dysthymia 34 years. Only 25% develop a bipolar disorder after age of 25, whereas the 75th percentile in major depression is 41 and 46 years in dysthymia.

There are no marked effects on type of major depression (single vs. recurrent), type of bipolar disorder (bipolar I vs. bipolar II), when considering gender either. But age effects are very significant: younger cohorts consistently report an earlier onset. Age-related differential recall, differential willingness to disclose, or other methodologic factors could play important parts in this pattern, although a genuine increase in the prevalence in recent cohorts may have occurred (Kessler et al., 2003).

Course of Major Depression and Bipolar Disorders

As evidence to date suggests, the course of depression is likely to differ considerably depending on several factors, often considered subtype qualifiers, such as age of onset (early vs. late), subclinical vs. clinical criteria, vegetative vs. non-vegetative. The commensurate treatment implications of information about course are considerable. For instance, a seemingly increasingly important and timely, but difficult to study, emerging area appears to be the relationship between treatment use (both antidepressant and psychotherapy, as well as other treatments) and the course of major depression in the community. In addition, information gained from clinical follow-up studies showing that the majority of severe depression cases are recurrent have led to a re-focusing of much depression treatment to a prevention of recurrence, rather than being purely directed toward offset of current episode.

Yet, to date there is relatively little available epidemiologic information on the course of major depression in the community. Specifically, there are only a few prospective, long-term, community-based studies with multiple follow-ups of depression, which are needed in order to understand the natural course of the disorder. While bipolar disorder is thought to be a very chronic condition (Coryell and Winokur, 1992), most available information comes from clinical samples not representative of the course of bipolar disorder and bipolar spectrum disorder in the community. Little epidemiologic evidence is available on the course of bipolar disorder, largely due to the methodological challenges mentioned above, as well as some additional obstacles to accurate and reliable measurement needed to describe course. Additional challenges to measuring the course of bipolar disorder in the community include prospective measurement of onset, episodes and remission, as well as periods when subclinical symptoms may be present. Since there have been few prospective studies of bipolar disorder in the community, reliance on retrospective recall of first onset and past episodes has been much more common than in research on depression or other mental disorders.

Correlates and Risk Factors

Epidemiologic research is the key to the identification of risk factors for mental disorders. Cross-sectional epidemiologic studies can be used to describe associations or even *correlates* of major depression. Such associations between the investigated factors and major depression reflect that they are symptoms, maintaining factors or the consequences of having a major depression. The identification of *true risk factors* is not possible in cross-sectional studies due to reliance on retrospective recall with some exceptions for fixed factors such as race and gender. In most cases, longitudinal data are needed in order to identify potential risk factors and examine them prospectively. Given that most findings concerning major depression are based on cross-sectional epidemiologic data, according to Kraemer et al. (1997) we prefer to use the term 'correlate' rather than 'risk factor'.

Sociodemographic Variables: Gender, Marital and Socioeconomic Status

Specific demographic characteristics are differentially associated with the prevalence and risk of depression onset among adults in the community. Among the most striking is female gender. So, we will review first the associations between depression and gender.

The importance of gender differences in mental health is usually illustrated in significantly different prevalences and incidence rates of major depression, whereas the explanations for these findings remains poorly studied. Despite the wide variations in lifetime prevalence estimates of major depression across countries and

studies, the roughly 2:1 sex ratio is consistent cross-culturally (Weissman et al., 1993; Kessler et al., 1994a; Meltzer et al., 1995; Bebbington, 1998; Gater et al., 1998; Jacobi et al., 2004). Conversely, most studies have found no gender difference in the prevalence of bipolar disorder (Tohen and Goodwin, 1995; Weissman et al., 1996).

In general, *biological*, *psychosocial* and *artefact* explanations have been proposed to explain the predominance of depressive disorders in women (for an extensive overview see Wilhelm and Parker, 1994; Bebbington, 1998; Piccinelli and Wilkinson, 2000; Kessler, 2003).

Artefact explanations assume that much of the observed differences in prevalence rates may be produced by gender-related bias or even artefacts such as differences in help-seeking behaviour and symptom-reporting patterns (Kessler et al., 1981; Nolen-Hoeksema, 1990; Loewenthal et al., 1995; Kessler, 1998), quality and quantity of symptoms (symptom profile; Young et al., 1990; Silverstein, 1999), recall bias (Ernst and Angst, 1992; Wilhelm and Parker, 1994), definitions of cases in epidemiological studies (threshold for caseness; Angst and Dobler-Mikola, 1985; Wilhelm and Parker, 1994; Piccinelli and Wilkinson, 2000), or even gender-biased case-finding measurements (Salokangas et al., 2002). It has been suggested that these artefactual factors may contribute to the female preponderance in depressive disorders to some extent, yet gender differences still seem to be genuine and can be shown even after these are accounted for (Nazroo et al., 1998; Piccinelli and Wilkinson, 2000).

Biological theories have proposed differences in brain structure and functioning between men and women, including neurotransmitter, neuroendocrine and circadian rhythms, as well as genetic factors and reproductive functioning (Joffe and Cohen, 1998; Kornstein, 1997; Paykel, 1991; Pajer, 1995; Leibenluft, 1999). Although attractive, explanations in biological terms face a number of difficulties. If higher rates in mental disorders, particularly in depressive disorders in women, are due to a universal biological vulnerability, the sex ratio ought to be unaffected by, for example, sociodemographic attributes. There is no convincing evidence for this, however (e.g. Bebbington, 1998). Therefore, biological explanations alone are not sufficient. This inevitably moves the focus of interest to psychosocial hypotheses for gender differences in depressive disorders.

From a *psychosocial* perspective, several possible explanations for gender differences have been suggested (Pajer, 1995; Kornstein, 1997; Bebbington, 1998; Piccinelli and Wilkinson, 2000), for example that women, in general, have a lower socioeconomic status. Surveys since the 1970–1980s have indicated a higher prevalence of mental disorders in the lower social classes, though perhaps only for women (Weissman and Myers, 1978; Kessler et al., 1994a). Higher rates of mood disorders for women may also reflect issues related to the fact that they may be subject to more significant, or more upsetting stressful life events or chronic difficulties (Brown and Moran, 1997; Bebbington, 1996; Nazroo et al., 1997, 1998), low social support (Brown and Andrews, 1986; Fuhrer et al., 1992), victimization and adverse experiences in childhood (e.g. sexual or physical abuse or parental separation/

divorce with resulting lack of child care in early years; Cutler and Nolen-Hoeksema, 1991; Rodgers, 1994; Bebbington, 1998), and maladaptive coping styles (Hobfoll et al., 1994; Nolen-Hoeksema et al., 1994). Other issues suggested to contribute to a higher risk of depressive disorders among women have been social roles, such as marital and employment status (unequal adult gender role stresses; Vazquez-Barquero et al., 1992; Cramer, 1993; Kessler et al., 1993; Loewenthal et al., 1995). Yet, in the light of contradictory findings, the reason for these differences remains unclear.

Overall, the emotional advantages or disadvantages of certain sociodemographic variables (marital status, employment status, number of children, parenthood and social class) apply *equally* to men and women (Klose and Jacobi, 2004). We cannot explain the female preponderance in most mental disorders by detecting specific unfavourable patterns of sociodemographic correlates, suggesting that determinants of gender differences in common mental disorders are still far from being understood.

Regarding marital status, the literature suggests that in general currently married persons had lower rates of both depressive and bipolar disorders than those who had never married or were currently separated, divorced or widowed (Kessler et al., 2003; Tohen and Goodwin, 1995; Weissman et al., 1996). Several studies have investigated the relationship between various measures of socioeconomic status and mood disorders but evidence is quite mixed, thus not allowing definitive conclusions (Kohn et al., 1998).

Familial Transmission

Family studies have shown that risk of depression onset and severity is associated with family history of depression (Bridge et al., 1997; Kendler et al., 1997; Klein et al., 2001; Warner et al., 1999; Wickramaratne et al., 2000). Yet, the majority of these data are drawn from clinical or other highly selected samples, and therefore it is not known whether findings are generalizable to the population. In one of very few community-based studies examining familial risk of depression, Lieb et al. (2002) showed that parental history of depression was associated with a significantly increased risk among offspring. Additionally, parental depression was associated with earlier onset and higher levels of morbidity (severity, impairment, recurrence). This study also showed that having two parents with depression was associated with higher risk than only one, though there did not appear to be any difference conferred by paternal or maternal risk. Of interest, this study also showed that parental depression was associated with increased risk of substance use disorders and anxiety disorders in offspring. Kendler et al. (1996) have also shown that familial history is associated with increased risk of depression, and that stressful life events are associated with an even higher risk of depression onset among those with familial or genetic vulnerability to depression. In particular, findings suggest that the increase in risk is pronounced during the first month following the event,

and then is no longer evident. Another interesting question is whether major depression and anxiety disorders are transmitted independently within families. Some studies suggest that there is an independent transmission and that the comorbidity between depression and anxiety is caused by non-familial aetiological factors (e.g. Klein et al., 2003; Weissman et al., 1993).

Early Adversity

Several factors reflecting adversity in early childhood have been shown to increase the risk of depression onset, severity, and recurrence in longitudinal studies (Brown and Harris, 1993). Investigators have repeatedly documented associations between childhood physical and sexual abuse and neglect and increased risk of depression in adulthood (e.g. Brown and Harris, 1993; Kessler et al., 1997). In terms of life events and early adverse exposures, loss-related events appear particularly potent and somewhat specific to depression, compared with anxiety, as research has shown that a severe threatening event involving loss was most often involved in the onset of depression (Brown, 1993). Parental loss during childhood, by death or separation, is also associated with increased risk of depression in adulthood. Childhood abuse is associated with increased risk of a wide range of mental disorders during adulthood, while loss events appear strongly and somewhat specifically depressogenic.

Psychiatric Symptoms and Other Mental Disorders

Studies have consistently shown that previous mental disorders strongly increase the risk of first onset of major depression as well as increasing the likelihood of persistence, severity, and recurrence of the disorder (e.g. Hettema, 2003). Specifically, anxiety disorders have been shown to precede and predict the onset of major depression.

Research has shown that the link between prior symptoms and risk of major depression spans all developmental stages. Canals et al. (2002) looked at predictors of depression onset at age 18 and found that 80% with depression onset at 18 had symptoms of major depression between the ages of 11 and 14. These findings support a continuity of depression from adolescence to young adulthood with subclinical scores on the Children's Depression Inventory (CDI; del Barrio, 1993) as an early indicator of long-term risk. This study also found early symptoms of anxiety to be a predictor of depression at 18, but only among boys.

Stressful Life Events

Major stressful life events are a well-known risk factor for major depression (Paykel, 2001). Research suggests that there is no gender or age difference in susceptibility to

depression associated with stressful life events, but that women have a greater risk of depression related to distal losses (Maciejewski et al., 2001). Additionally, there are some data suggesting that different types of losses pose greater risks of depression between genders; for instance, familial conflict is associated with an increased risk of depression among females while financial strain is more strongly associated with depression among males. Brown and colleagues (Brown et al., 1995) have done extensive work on the aetiology of depression among women in the community. Their findings suggest that loss events are particularly depressogenic when combined with the experience of humiliation and entrapment. Such studies have also shown that loss is important in provoking depression and that positive events (i.e. fresh-start events) involving hope are particularly important in recovery from depression (Brown, 1993).

Other Factors

There are additional factors thought to be associated with risk of major depression. For instance, personality traits (e.g. neuroticism) (Kendler et al., 2003, 2004) and cognitive coping styles are associated with higher rates of depression.

ARE PREVALENCE ESTIMATES FOR MOOD DISORDERS TOO HIGH?

The high prevalence rates of mood disorders, especially in the recent CIDI surveys, has generated some scepticism about diagnostic validity (Parker, 1987; Frances, 1998; Bebbington, 2000; Henderson, 2000) and it has been proposed that a proportion of the syndromes identified in community surveys may represent transient homeostatic responses that are neither pathologic nor in need of treatment (Regier et al., 1998). Furthermore, it has been shown that cases identified in the community are not always consistently associated with social impairment (Bebbington, 1994; ten Have et al., 2002). For instance, Narrow et al. (2002) found that the application of a clinical significance criterion lowered the 1-year prevalence rates of mood disorders by 44% in the ECA study and by 32% in the NCS, while Henderson et al. (2001) showed that about 15% of subjects with a 1-month CIDI diagnosis of depressive disorder in an Australian sample reported no disability in daily life.

On the one hand, these findings suggest that the mere diagnosis cannot be equated with clinically relevant treatment need. In addition, it should be noted that no health care system in the world could ever provide (adequate) mental health care for roughly a third of the population. To estimate treatment need for public health reasons, prevalence rates must be supplemented by information on comorbidity, severity, treatment demand, social impact etc. But criticizing the absence of clinically significant disability or claiming irrelevance for clinical practice in a

relevant proportion of the diagnosed subjects in epidemiological studies needs to be separated from the question of whether 'mild' disorders should be eliminated from the DSM or other diagnostic systems. Kessler et al. (2003) show, for example, that longitudinal analyses using severity strata indeed produce differences in the risk of clinically significant outcomes – but differences between mild cases and noncases are consistently larger than differences between mild and moderate cases. Considerations should be given not only to current distress and impairment but also to the risk of progression from a mild to a more severe disorder. Thus, treatment of mild disorders may be cost-effective (prevention of later need of intensive treatment and long-term cost of illness). Also it should be acknowledged that mental disorders (like physical disorders) vary in severity, and the investigation of pathways and outcomes of psychopathology should not depend on arbitrary societal views of treatment need and the naturally limited health care resources.

SUGGESTED READINGS

Since the reference list is quite exhaustive, some selected recent publications that can be easily accessed via internet from universities and other institutions are recommended here for first suggested readings. More 'classic' references on diagnosis and nosology can be found in Chapter 3 of this book by Faravelli, Ravaldi and Truglia.

A comprehensive paper on the epidemiology of major depression in the *JAMA* reports, besides recent prevalence rates data on correlates, role impairment and treatment issues (from the second National Comorbidity Survey in the USA, NCS-R; Kessler et al., 2003). A short overview on the important issue of comorbidity is given by Wittchen (1996), and Merikangas et al. (1996) present an exemplary analysis on the comorbidity of mood disorders with anxiety disorders and substance use disorders. The discussion about clinical semi-structured versus standardized approaches is exemplarily included in an editorial section of *Psychological Medicine* (Brugha et al., 1999a vs. Wittchen et al., 1999a). Interesting information on self-report methodology is summarized by Kessler et al. (2000). A benchmark paper on risk factors is the one by Kraemer et al. (1997). As an example of a modern CIDI-study using clinically trained interviewers and investigating a relatively broad spectrum of disorders, the German Health Interview and Examination Survey and its Mental Health Supplement (Jacobi et al., 2004) is also mentioned here because this data set is available as a public use file and can be ordered from F.J., as well as the data from the prospective Early Developmental Stages of Psychopathology study (EDSP; exemplary publication on depression: Lieb et al., 2002).

Finally, at the end of the 1990s a cross-sectional study (The European Study of Epidemiology of Mental Disorders: the ESEMeD) has been carried out in six European countries (Belgium, France, Germany, Italy, the Netherlands and Spain) in order to evaluate the prevalence, the impact and the treatment patterns of mental disorders in Europe (Alonso et al., 2002). The results of this study

assessing more than 20 000 adults over 18 allow interesting cross-national comparisons in terms of mental health (The ESEMeD-MHEDEA 2000 Investigators, 2004; The WHO World Mental Health Survey Consortium, 2004). For a review of available European studies since 1990 see Wittchen & Jacobi (in press).

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