

**Part I**

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# UNIPOLAR DEPRESSION

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# THE CLASSIFICATION AND EPIDEMIOLOGY OF UNIPOLAR DEPRESSION

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## INTRODUCTION

In this chapter, I will deal with the difficult problem of classifying a disorder that looks more like the expression of a continuum than a useful category. The way affective symptoms are distributed in the general population calls into serious question the utility of a medical classification, and certainly makes procedures of case definition and case finding very difficult. Nevertheless, researchers do rely on these procedures to establish the epidemiology of the disorder, and in the second part of the chapter I will pull together recent findings on the prevalence and distribution of unipolar depression.

## CLASSIFICATION AND UNIPOLAR DEPRESSION

The idea of unipolar depression is primarily a medical one; that is, it involves a particular way of looking at psychological disturbance. This centres on the notion of a *syndrome* that is distinct from other psychiatric syndromes. Some of these can be relatively easily distinguished—for example, paranoid schizophrenia—while others are acknowledged to be related. The disorders that most resemble unipolar depression are other affective disorders, that is, conditions that are characterized centrally by mood disturbance. They cover a number of anxiety disorders, other depressive conditions, and bipolar mood disorder.

Bipolar disorder is identified by the presence of two sorts of episode in which the associated mood is either depressed or predominantly elated. It is distinct from unipolar disorder in a variety of ways (such as inheritance, course, and outcome), and the distinction is therefore almost certainly a useful one. However, depressive episodes in bipolar disorder cannot be distinguished symptomatically from those of unipolar depression. As perhaps half of all cases of bipolar disorder commence with a depressive episode, this means that unipolar depression is a tentative category—the disorder will be reclassified as bipolar in 5% of cases (Ramana & Bebbington, 1995).

Psychiatric disorders are classified in the hope that the classification can provide mutually exclusive categories to which cases can be allocated unambiguously (case identification). Categories of this type are the basis of the medical discipline of *epidemiology*, which is the study of the distribution of diseases (that is, medical classes) in the population. This has been a very powerful method for identifying candidate causal factors, and is thus of great interest to psychiatrists as well as to clinicians from other specialities.

Syndromes are the starting point of aetiological theories, and of other sorts of theory as well—theories of course and outcome, of treatment, and of pathology (Wing, 1978). There is no doubt that the medical approach to malfunction has been a very effective one, generating new knowledge quickly and efficiently by testing out theories of this type (Bebbington, 1998).

## **SYMPTOMS AND SYNDROMES**

The first stage in the establishment of syndromes is the conceptualization of individual symptoms. Symptoms in psychiatry are formulations of aspects of human experience that are held to indicate abnormality. Examples include abnormally depressed mood, impaired concentration, loss of sexual interest, and persistent wakefulness early in the morning. They sometime conflate what is abnormal for the individual and what is abnormal for the population, but they can generally be defined in terms that are reliable. Signs (which are unreliable and rarely discriminating in psychiatry, and thus tend to be discounted somewhat) are the observable concomitants of such experiences, such as observed depressed mood, or behaviour that could be interpreted as a response to hallucinations. Different symptoms (and signs) often coexist in people who are psychologically disturbed, and this encourages the idea that they go together to form recognizable syndromes. The formulation of syndromes is the first stage in the disease approach to medical phenomena, as syndromes can be subjected to investigations that test the various types of theories described above.

While syndromes are essentially lists of qualifying symptoms and signs, individuals may be classed as having a syndrome while exhibiting only some of the constituent symptoms. Moreover, within a syndrome, there may be theoretical and empirical reasons for regarding some symptoms as having special significance. Other symptoms may be relatively non-specific, occurring in several syndromes, but, even so, if they cluster in numbers with other symptoms, they may achieve a joint significance. This inequality between symptoms is seen in the syndrome of unipolar depression: depressed mood and anhedonia are usually taken as central, while other symptoms (such as fatigue or insomnia) have little significance on their own. This reflects serious problems with the raw material of human experience: it does not lend itself to the establishment of the desired mutually exclusive and jointly exhaustive categories.

In an ideal world, all the symptoms making up a syndrome would be discriminating, but this is far from true, and decisions about whether a given subject's symptom pattern can be classed as lying within a syndrome usually show an element of arbitrariness. The result is that two individuals may both be taken to suffer from unipolar depression despite exhibiting considerable symptomatic differences.

This is tied in with the idea of symptom severity: disorders may be regarded as severe either from the sheer number of symptoms, or because several symptoms are present in severe degree. In practice, disorders with large numbers of symptoms also tend to have a greater severity of individual symptoms.

## COMPETING CLASSIFICATIONS

The indistinctness of psychiatric syndromes and of the rules for deciding whether individual disorders meet symptomatic criteria has major implications for attempts to operationalize psychiatric classifications. There are currently two systems that have wide acceptance, the *Diagnostic and Statistical Manual* (DSM) of the American Psychiatric Association (APA) and the World Health Organization (WHO)'s *International Classification of Disease* (ICD). In the early days, revision of classificatory schemata relied almost wholly on clinical reflection. However, since the classifications are set up primarily for scientific purposes, they should properly be modified in the light of empirical research that permits definitive statements about their utility. The standardized and operationalized classifications that are now in existence offer an opportunity for using research in this way.

Unfortunately, much of the pressure for change has continued to originate from clinical and political demands. Revisions have sometimes had the appearance of tinkering in order to capture some imagined essence of the disorders included (Birley, 1990). What looks like fine-tuning can nevertheless make considerable differences to whether individual cases meet criteria or not, and thus disproportionately affects the putative frequency of disorders. We should jettison classifications only on grounds of inadequate scientific utility and as seldom as possible, since too rapid revision defeats the objective of comparison. Like all such classifications, DSM and ICD are created by committees. The natural tendency to horse-trading between experts selected precisely because they are powerful and opinionated leads to an over-elaborate structure, an excess of allowable classes and subclasses, and complicated defining criteria. Thus, in DSM-IV-R (APA, 1994), there are potentially 14 categories to which depressed mood can be allocated, and in ICD-10 (WHO, 1992) there are 22. Greater utility would probably accrue from limiting the primary categories to three (bipolar disorder, unipolar depressive psychosis, and unipolar non-psychotic depression), and epidemiological research often uses these categories in any case. In Table 1.1, I have provided a comparison of the definitions of depressive disorder under DSM-IV (APA, 1994) and ICD-10 (WHO, 1992), slightly simplified. Over the years, there has been considerable convergence between the systems. However, the differences remain important. The categories are too close together for empirical studies to establish their relative validity, but far enough apart to cause discrepancies in identification. Relatively severe cases are likely to be classified as depressive disorder under both systems. However, milder disorders may be cases under one system, and not the other. This becomes important in epidemiological studies of depressive disorder in the general population because such studies usually report their results under one system or the other, and the degree of comparability is hard to quantify. Thus, the use of different classificatory systems is one barrier to comparison between studies: there are others.

It is of interest to see the effect of applying algorithms for the diagnostic categories defined by different systems to a common set of symptom data. The Schedules for Clinical Assessment in Neuropsychiatry (SCAN) (WHO, 1992) allows diagnosis under both DSM and ICD. In Table 1.2, I have illustrated the effect of applying ICD-10 and DSM-IV criteria to the data from the Derry Survey (McConnell et al., 2002) on the identification of cases of depressive episode (ICD) and depressive disorder (DSM). Of the 18 participants diagnosed as having a depressive condition by one classification, two-thirds were diagnosed by both. Five cases of depressive episode were not diagnosed as DSM depressive disorder, whereas only one case of depressive disorder was not diagnosed as ICD depressive episode. In contrast, DSM recognized many more cases of anxiety disorder. Fifteen of the cases

**Table 1.1** Criteria for depressive episode

DSM-III-R/DSM-IV	ICD-10
<b>Symptoms present nearly every day in same 2-week period</b>	<b>Episode must have lasted at least 2 weeks with symptoms nearly every day</b>
<b>Change from normal functioning</b>	<b>Change from normal functioning</b>
<b>Key symptoms (n = 2)</b> Depressed mood Anhedonia	<b>Key symptoms (n = 3)</b> Depressed mood Anhedonia Fatigue/loss of energy
<b>Ancillary symptoms (n = 7)</b> Fatigue/loss of energy Weight/appetite loss/gain Insomnia/hypersomnia Observed agitation/retardation Low self-esteem/guilt Impaired thinking/concentration Suicidal thoughts	<b>Ancillary symptoms (n = 7)</b> Weight and appetite change Sleep disturbance Subjective or objective Agitation/retardation Low self-esteem/confidence Self reproach/guilt Impaired thinking/concentration Suicidal thoughts
<b>Criteria:</b> one key, five symptoms in total <b>Plus</b> Significant distress <b>Or</b> Social impairment	<b>Criteria:</b> Mild episode: two key, four symptoms in total Moderate: two key, six symptoms in total Severe: three key, eight symptoms in total
<b>Exclusions</b> Not mixed episode Not substance related Not organic Not bereavement Not psychotic	<b>Exclusions</b> No history (ever) of manic symptoms Not substance related Not organic

**Table 1.2** DSM-III-R and ICD-10 classification based on the same symptom data. The Derry Survey (McConnell et al., 2002)

	No depressive diagnosis	Depressive disorder DSM
No depressive diagnosis	289 (94%)	1 (0.3%)
Depressive episode ICD-10	5 (1.6%)	12 (3.9%)
<b>Kappa =</b>	<b>0.79</b>	
	No anxiety diagnosis	Anxiety disorder DSM
No anxiety diagnosis	269 (87%)	15 (4.9%)
Anxiety disorder ICD	2 (0.7%)	21 (6.8%)
<b>Kappa =</b>	<b>0.68</b>	

defined by DSM were not classed as anxiety disorders by ICD, while only two classified by ICD were not so classed by DSM. Thus, the ICD criteria appear to be less stringent for depressive episode, while the reverse is true of anxiety. The results suggest that the difference between the two systems arises because of differing thresholds rather than because of wide differences in the symptom contents of the classes.

## THE LIMITS OF CLASSIFICATION

As classification aspires to ‘carve nature at the joints’, the empirical relationships between psychiatric symptoms create special difficulties of their own. In particular, symptoms are related non-reflexively: thus, some symptoms are common and others are rare, and, in general, they are hierarchically related, rather than being associated in a random manner. Rare symptoms often predict the presence of common symptoms, but common symptoms do not predict rare symptoms. Deeply (that is, ‘pathologically’) depressed mood is commonly associated with more prevalent symptoms, such as tension or worry, while, in most instances, tension and worry are *not* associated with depressed mood (Sturt, 1981). Likewise, depressive delusions are almost invariably associated with depressed mood, whereas most people with depressed mood do not have delusions of any kind. The consequence is that the presence of the rarer, more ‘powerful’ symptoms indicates a case with many other symptoms as well, and therefore a case that is more symptomatically severe. It is because of this set of empirical relationships between symptoms that psychiatric syndromes are themselves largely arranged hierarchically. Thus, schizophrenia is very often accompanied by affective symptoms, although these are not officially part of the syndrome. Likewise, psychotic depression is not distinguished from non-psychotic depression by having a completely different set of symptoms, but by having extra, discriminating, symptoms, such as depressive delusions and hallucinations.

## LEAKY CLASSES AND COMORBIDITY

The operational criteria set up to identify and distinguish so-called common mental disorders cut across the natural hierarchies existing between symptoms. The consequence is that many people who have one of these disorders also meet the criteria for one or more of the others. This *comorbidity* has generated much interest, and was even responsible for the name of one of the major US epidemiological surveys (the National Comorbidity Survey) (Kessler et al., 1994). Researchers, then, divide into two camps: those who think the comorbidity represents important relationships between well-validated disorders; and those who think it arises as an artefact of a classificatory system that is conceptually flawed and fails adequately to capture the nature of affective disturbance.

Thus, Kessler (2000) has defended the status of generalized anxiety disorder (GAD) as an independent condition, despite its high comorbidity, arguing that it does, for example, precede major depression, and also outlasts it. However, this would be expected if GAD represented a low threshold disorder that could transmute into a higher threshold disorder with the addition of a few symptoms. GAD and depression certainly share a common genetic diathesis (Mineka et al., 1998). The superimposition of major depression on a long-lasting minor depressive disturbance (dysthymia) has been called double depression (Keller et al., 1997). The comorbidity of anxiety and depression may arise because anxiety states can transform into depressive disorders with the addition of relatively few symptoms (Parker et al., 1997). Depression/anxiety is equally apparent in adolescents (Seligman & Ollendick, 1998), as is the link between dysthymia and major depression (Birmaher et al., 1996). The idea that there are several distinguishable affective disorders is, to some extent, self-perpetuating, as it prevents clinicians from seeking out the full range of symptoms that

are reflected in comorbidity. I imagine that it will turn out to be much more useful to see these comorbidities as an indication of common underlying processes leading to, but not necessarily reaching, a common destination.

## DEPRESSION AND THE THRESHOLD PROBLEM

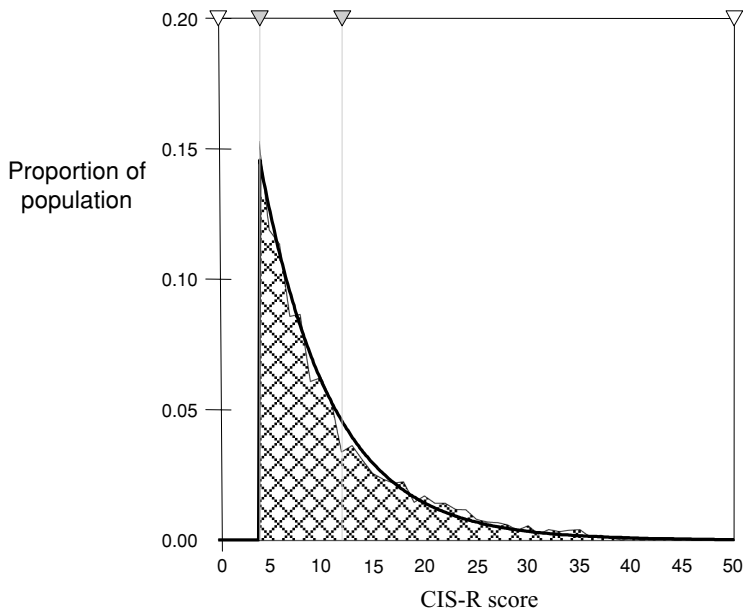
Another important empirical aspect of affective disorders is the distribution of symptoms in the general population. Many people have a few symptoms, while few people have many. This means that decisions have to be made about the threshold below which no disorder should be identified. People who have few symptoms may still be above this threshold if some of their symptoms are particularly discriminating, but, in general, the threshold is defined by the number of symptoms. There is always a tendency in medicine to move the threshold down, particularly as a sizeable proportion of the people with mental symptoms who are seen by primary-care physicians fall below the thresholds of DSM-IV or ICD-10. However, others in the medical profession have serious reservations about what they regard as medical imperialism, the medicalization of normal human experience (Double, 2002).

In response to the threshold problem, there has been a burgeoning literature recently relating to subthreshold, subclinical, minor, and brief recurrent affective disorder (Schotte & Cooper, 1999). The tendency to extend the threshold downwards is apparent in the establishment of the category of *dysthymia*, referred to above, a depressive condition characterized only by its mildness (that is, a *lack* of symptoms) and its chronicity. The category has, nevertheless, become a study in its own right: it has clear links with major depression, presumably because it is relatively easy for someone who already has some depressive symptoms to acquire some more and meet criteria for the more severe disorder. It is also associated with psychosocial distress, both recent and distant. Some authors have gone so far as to suggest that it reflects abnormalities of neuroendocrine and neurotransmitter function (Griffiths et al., 2000).

The imposition of a threshold on an apparent continuum lacks some of its arbitrariness if it is possible to demonstrate a naturally occurring ‘step-change’ in the distribution. Thus, while the distribution of IQ is largely continuous, there is a clear excess of subjects at the bottom of the continuum who are characterized by a distinct and identifiable pathology (Penrose, 1963). Many have argued that no such distinction exists in affective symptoms (Goldberg, 2000; Tyrer, 1985). While it might be possible to create a threshold that represented a step-change in social disability (Hurry et al., 1983), the evidence does, overall, suggest that affective symptoms are distributed more like blood pressure than IQ. Melzer and his colleagues (2002) have recently used symptom data from the British National Survey of Psychiatric Morbidity to test the smoothness of the distribution. A single exponential curve provided the best fit for the whole population, but there were floor effects that produced deviations at symptom counts of 0–3. Truncation of the data to take account of this provided an excellent fit (Figure 1.1). This was not affected by selecting for analysis subgroups characterized by especially high or low prevalence.

It can be concluded from this discussion that the epidemiological literature on depressive disorder is likely to be a mess. We have disorders that are identified as classes imposed on what is empirically a continuum. This is made worse by the fact that the classificatory schemes are changed at regular intervals. Moreover, two major schemes exist side-by-side. Added to this is the issue of how the symptoms of common mental disorders can be elicited,





**Figure 1.1** Proportion of population by truncated range of CIS-R scores, and fitted exponential curve. Reproduced from Melzer, D. et al. (2002). Common mental disorder symptom counts in populations: Are there distinct case groups above epidemiological cut-offs? *Psychological Medicine*, 32, 1195–1201. Reproduced by permission of Cambridge University Press

identified, and used, in order to decide whether, together, they can be said to constitute a case.

## CASE IDENTIFICATION IN RESEARCH

Case identification is the basis of epidemiology. The process of diagnosis involves allocating symptom patterns to a diagnostic class according to given rules. In recent years, these rules have been set out explicitly in the diagnostic criteria for research (DCRs) attached to specific classifications, such as DSM-III-R, DSM-IV, and ICD-10, so precisely that it is possible to incorporate them into computer algorithms such as CATEGO (Wing et al., 1990) and OPCRIT (McGuffin et al., 1991).

Once the presence of symptoms has been established, the information can be entered into one of these computer programs in order to provide a diagnostic classification. Human idiosyncrasy can be reduced to an absolute minimum in this process. However, researchers must still decide how carefully the underlying symptoms should be identified. The choices include unstructured clinical assessment, responses to questionnaires, and semi-structured research interviews.

The first option, unstructured clinical judgement, introduces variability into the process of case allocation, since researchers are relying merely on their devotion to a common educational tradition. This situation is even worse when the judgements of others (for

example, the treating physician) are used, as with the diagnostic information recorded in case registers or in national statistics.

In order to be practicable, questionnaires should seek simple responses to unelaborated questions. However, symptoms are traditionally recognized through an assessment of mental experiences that demand quite elaborate enquiry (Brugha et al., 1999). They are usually established by a process of clinical cross-examination. This process is rather complicated since it requires the questioner to frame further questions in a flexible way in the light of the answers given by the subject. While it might be possible to encapsulate this procedure in a standard questionnaire by using a branching algorithm, it would be exhaustive and exhausting—it might require paths comprising over a dozen questions just to establish the presence of pathologically depressed mood. In these circumstances, there are clearly practical limits to the process of standardization, and it is probably better to rely on the short cuts available from using the skills of trained clinicians. Since diagnosis is built around symptoms defined and elicited in this manner, redefinition in terms of answers to much more limited questions would involve changing the concept of diagnosis itself. No one has seriously suggested that the way psychiatric symptoms are conceptualized should be changed; therefore, if a questionnaire is used, phenomena may be recorded as present when subsequent clinical enquiry might reveal otherwise, and vice versa. Nevertheless, structured questionnaires do allow lay interviewers to be used, with considerable cost savings. The Diagnostic Interview Schedule (DIS) (Robins et al., 1981) and the Composite International Diagnostic Interview (CIDI) (Robins et al., 1988) are fully structured questionnaires that have been widely used, and have good reliability.

Semi-structured research interviews are costly in clinical time, and the way in which symptoms are established makes it impossible to standardize the procedure entirely (Robins, 1995). Because of the reliance on clinical judgement and the effect this has on the choice of follow-up questions, some variability will remain. This is the price paid for greater validity, that is, the closer approximation to the clinical consensus about the nature of given symptoms. The Schedules for Clinical Assessment in Neuropsychiatry (SCAN) (Wing et al., 1990) are based on a semi-structured interview, and are increasingly used in epidemiological research studies (e.g., Ayuso-Mateos et al., 2001; Bebbington et al., 1997; McConnell et al., 2002; Meltzer et al., 1995). SCAN has good interrater reliability despite its semi-structured format.

## QUESTIONNAIRES AND INTERVIEWS

If, as I have argued, there are doubts in principle about the validity of structured questionnaires, it is worth knowing how their performance compares with semi-standardized interviews. One head-to-head comparison has been made between SCAN and CIDI (Brugha et al., 2001). This permits two separate questions:

- (1) Does the questionnaire provide a similar frequency of disorder to that established by the semi-structured interview?
- (2) To what extent are the same cases identified by the two instruments?

Differences in frequencies would, at the very least, indicate some systematic biases separating the instruments. However, even if, for example, CIDI recognized more cases than SCAN, it could still be the case that CIDI picked up most or all of the cases identified

by SCAN. This would imply that the constraints of a rigid questionnaire tended to lower the threshold of case identification, as might be the case if the rigidity and the paucity of elaborative questions led to over-recognition of specific symptoms. If, however, in addition to over-recognition of cases, there were little overlap between the cases found by the two systems, this would indicate a more general failure of rigid questioning to establish symptoms properly.

Brugha and his colleagues (2001) conducted a two-phase study of the general population of Leicestershire, UK. In the second phase, 172 subjects selected for an increased probability of exhibiting cases of psychiatric disorder were interviewed with both CIDI and SCAN, in random order. The coefficients of concordance for the various ICD-10 diagnoses varied between poor and fair. The authors calculated that using CIDI would give prevalences about 50% greater than those obtained from SCAN. The index of agreement for any depressive episode was poor (0.14). As expected, the discrepancies arose particularly from cases around the threshold for recognition.

## **BOTTOM-UP AND TOP-DOWN CASE IDENTIFICATION**

The other way in which instruments differ is whether they are diagnosis-driven or symptom-driven. Instruments that are diagnosis-driven do not require to elicit the same set of symptoms in each case in order to establish the appropriate diagnostic category. All they have to do is to confirm that the required diagnostic criteria are met. DIS and CIDI are examples of such instruments. The advantage is that they can cut corners by not having to check out all symptoms once a diagnosis has been made: this is often the way clinicians work in their ordinary practice.

Symptom-driven instruments are exhaustive in their coverage of symptoms, and only then do they use the symptomatic information to check whether diagnostic criteria have been met (for example, SCAN and CIS-R). This has two advantages. The first is that, in theory, it should be possible to use the symptom information to serve a new algorithm if the diagnostic criteria were changed. This might be extremely arduous in practice, although attempts of this sort have been made (e.g., Murphy, 1994). The other advantage is of particular relevance to the study of the common affective disorders. Establishing whether or not a set range of symptoms is present allows an overall symptoms count to be made, and this is useful when it is appropriate to study the distributions of symptoms in the general population, as in the study by Melzer and his colleagues (2002) mentioned above.

## **THE FREQUENCY OF DEPRESSIVE DISORDER**

Frequency can be measured in a variety of ways: incidence; point, period, and lifetime prevalence; and morbid risk. Table 1.3 defines commonly used rates in epidemiology. General population surveys usually report period or lifetime prevalence rates, while investigations of clinical series often use first contact or admission as a proxy for incidence. In this chapter, I shall rely largely on studies of prevalence.

While community psychiatric surveys date back nearly a century, it is only in the past 25 years that they have used standardized methods of assessment that allow the comparison of research from different locations. I have reviewed studies based on the superseded

**Table 1.3** Epidemiological rates

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<b>Incidence rate:</b> the number of new cases in a given period as a proportion of a population at risk
<b>Point prevalence rate:</b> the number of cases identified at a point in time as a proportion of a total population
<b>Period prevalence rate:</b> the number of cases identified as in existence during a specified period as a proportion of a total population
<b>Lifetime prevalence rate:</b> a variant of period prevalence where the period for case identification comprises the entire lifetime of each subject at the point of ascertainment

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PSE-ID-CATEGO system (Wing et al., 1978) elsewhere (Bebbington, 1998). Those using the Diagnostic Interview Schedule (DIS) (Robins et al., 1985) developed for the US Epidemiological Catchment Area (ECA) surveys have been summarized by Weissman et al. (1996). Table 1.4 provides 1-year and lifetime prevalence rates according to this system from around the world.

Although Weissman and her colleagues (1996) argue that variation between locations is not great, the annual prevalences rates, in fact, range from 0.8% to 5.8%, and the lifetime prevalence from 1.5% to 16.4%.

The range of prevalences given in Table 1.4 is difficult to explain, as it does not correspond to the obvious cultural differences between the locations of the surveys. So, for instance, there are high rates in Europe compared with the USA, but the studies from Canada and New Zealand are also high. High rates in Beirut are perhaps understandable. The difficulties in the overall interpretation of these results suggest differences in the application of the interview.

Since these surveys, data have been published from a number of large-scale investigations based on national probability samples. These include the US National Comorbidity Survey (Kessler et al., 1993, 1994); two British National Surveys of Psychiatry Morbidity (Jenkins et al., 1997; Singleton et al., 2001), the Australian National Survey of Mental Health and Well-Being (Henderson et al., 2000), and the Finnish National Survey (Lindeman et al., 2000). They each involved interviews with several thousand subjects (see Table 1.5). All but the British surveys used variants of CIDI (the Composite International Diagnostic Interview)

**Table 1.4** Annual and lifetime prevalence of major depressive episode from studies using DIS

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Site	N	Annual	Lifetime
United States (ECA) (Robins & Regier, 1991)	18 571	3.0	5.2
Edmonton, Alberta (Bland et al., 1988)	3258	5.2	9.6
Puerto Rico (Canino et al., 1987)	1513	3.0	4.3
Paris (Lepine et al., 1989)	1746	4.5	16.4
West Germany <sup>1</sup> (Wittchen et al., 1992)	481	5.0	9.2
Florence (Faravelli et al., 1990)	1000	—	12.4
Beirut (Karam, 1992)	528	—	19.0
Taiwan (Hwu et al., 1989)	11 004	0.8	1.5
Korea (Lee et al., 1990)	5100	2.3	2.9
Christchurch, New Zealand (Oakley-Browne et al., 1989)	1498	5.8	11.6

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<sup>1</sup> Aged 26–64.

Data from Weissman et al. (1996). References in table are to base papers from original studies.

**Table 1.5** Prevalence rates for depressive disorders: recent large-scale surveys

Survey	N	Prevalence	Notes
National Comorbidity Survey (Kessler et al., 1993)	8098		Age 15–54; 1-year prevalence University of Michigan version of CIDI DSM-IV major depressive disorder
Australian National Survey (Henderson et al., 2000)	10 600	5.1%	1-year prevalence ICD-10 depressive episode Automated presentation of CIDI
Finnish National Survey (Lindeman et al., 2000)	5993	9.3%	1-year prevalence Automated presentation of short form of UM—CIDI
First British National Survey (Jenkins et al., 1997)	10 108	2.3%	1-week prevalence—CIS-R ICD-10 depressive disorder
Second British National Survey (Singleton et al., 2001)	8580	2.6%	1-week prevalence—CIS-R ICD-10 depressive disorder

(Robins et al., 1988). The British Surveys also used lay interviewers, but was based on the revised version of the Clinical Interview Schedule (CIS-R) (Lewis et al., 1992), an interview that provides ICD-10 diagnoses (WHO, 1992). It can be seen from Table 1.5 that despite the similar procedure of the CIDI and the DIS, the prevalences in the ECA studies, which used the latter, are closer to those in the British National Survey of Psychiatric Morbidity than to the CIDI-based surveys. The rate of affective disorders with CIDI in Ethiopia was low, and it is not clear whether this represents a methodological problem or a real difference (Kebede & Alem, 1999).

Some community psychiatric studies using SCAN have now been published (WHO, 1992). Two are British and are located in Camberwell (inner south London) and Derry (Londonderry), Northern Ireland, respectively (Bebbington et al., 1997; McConnell et al., 2002). The 1-year prevalence rates of ICD-10 depressive episode were 6% and 7%, respectively. The rate in Derry would be expected to be higher than in towns of comparable size, given its considerable poverty and legacy of sectarian violence. The multinational ODIN project also used SCAN, but the results so far published are difficult to interpret, as the authors provide prevalences for depressive disorder of all types, whether identified according to ICD-10 or DSM-IV (Ayuso-Mateos et al., 2001). Not surprisingly, in view of this confused decision, the prevalences are among some of the highest quoted, and cannot be compared with any other studies.

What, then, can be concluded from this exercise in counting? First, if we are going to establish a category of depressive disorder, we should be consistent. There is no real way of choosing between ICD-10 and DSM-IV criteria, although they differ somewhat in the cases they identify, but one or other system should be adhered to, as they are the most commonly used. The criteria for depressive disorder (DSM-IV) are more restrictive than those of ICD-10 major depressive episode, and, in principle, should result in lower prevalences. However, epidemiological studies presenting DSM-IV major depressive disorder (MDD) often use CIDI, and this probably results in quoted prevalences around 50% above what they would be if a semi-structured clinical interview were used. The short form of the CIDI, as used

in the Finnish study (Lindeman et al., 2000), may result in particularly high prevalences (Patten, 1997; 2000).

The consequence of these two countervailing influences is that we cannot use the epidemiological surveys to make very sensible statements about whether the different locations in which they were carried out are characterized by true differences in prevalence. For that, we have to rely on studies that cover more than one area, in a way that permits inferences about consistent influences; for instance, the relatively low rates of depression in rural areas (Paykel et al., 2000).

My best guess is that annual prevalence rates of ICD depressive episode may be around 4%, and that of DSM depressive disorder around 5%. Prevalence related to shorter periods (1-week, 1-month) will be around one-half to two-thirds these rates.

Nevertheless, one can use these essentially questionable procedures to come to certain limited but interesting conclusions concerning the factors that influence prevalence.

## **DEPRESSION AND SEX**

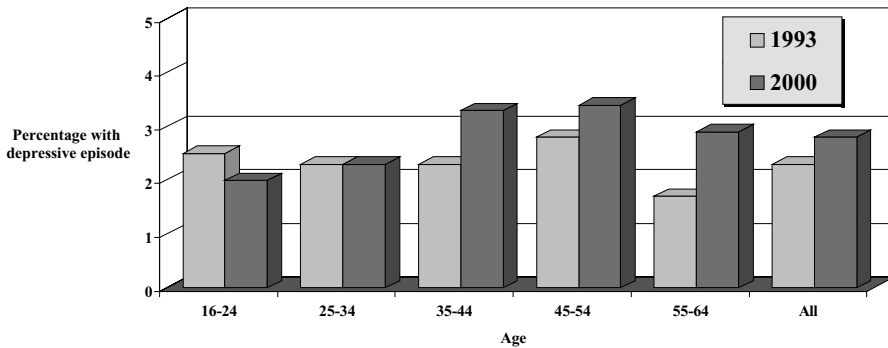
One of the most consistent findings in the whole of psychiatric epidemiology is that women are more likely to suffer from depression than men. Thus, in the summary of the DIS studies (Weissman et al., 1996), the sex ratio for the lifetime prevalence of depression ranged from 1.6 to 3.0. The two British national surveys gave a sex ratio for 1-week prevalence on the low side, at 1.5 and 1.2, respectively. The Finnish national study gave a value of 1.5 (Lindeman et al., 2000). There have been numerous reviews (Bebbington, 1996; Maier et al., 1999; Merikangas, 2000; Piccinelli & Wilkinson, 2000). The very large, six-nation European study DEPRES (Depressive Research in European Society) (Angst et al., 2002) establishes the sex difference at the level both of MDD (F:M = 1.7) and of the various depressive symptoms. Very few studies have shown ratios close to unity, and they have usually been in restricted populations.

This consistency of the sex ratio is not matched by any clarity of explanation. Before considering the possible causes, we must consider the influence of age on depression.

## **DEPRESSION AND AGE**

There are clear general statements that can be made about the relationship between age and depression. First, the propensity for depression is rare before adolescence (Birmaher et al., 1996). Secondly, the prevalence of depression declines in late middle age or early old age (e.g., Figure 1.2). Thirdly, the female to male sex ratio for depression is not constant over the lifespan, being around unity in childhood, rising during adulthood, and declining once again in elderly groups (Jorm, 1987).

The relationship between sex differences and age is of interest, as it may be linked to explanations for the former. The onset of the difference in adolescence may be related to the emergence of adult hormonal status. However, adolescence is both a biological and a social transformation. Some authors have argued that the social process of 'gender intensification' may be responsible for additional stresses on girls. Others adhere to the idea that hormonal changes increase female vulnerability. Until recently, the burden of evidence favoured the social hypothesis, as the sex ratio appeared to be related to chronological age



**Figure 1.2** Prevalence of depressive episode by age in 1993 and 2000 for all adults. Data taken from Meltzer et al. (1995) and Singleton et al. (2001)

rather than to hormonal development (Bebbington, 1996). However, two very good, recent epidemiological studies (Angold et al., 1999; Patton et al., 1996) are both in favour of a relationship with menarche rather than social transition.

The issue nevertheless remains unresolved, as does the age at which the sex ratio once again tends towards unity. One possibility is that the rate of depression in women declines (thus reducing the sex ratio) after the menopause. This would be interesting, in view of the idea that in women the hormonal status of the child-rearing years is particularly associated with vulnerability to depression. Because the menopause coincides with a number of social transitions, and is in any case an event of psychological significance, it is necessary to try to control for confounding by social variables that serve to mark these transitions. Using data from the first British National Survey, Bebbington and his colleagues (1998) found that the decline in prevalence rates of depression after age 55 could not be accounted for by obvious social factors, such as the end of involvement in childcare or changes in marital or employment status. This would be consistent with a possible hormonal influence. However, in the second national survey, the decline in female depression occurred to a greater degree after age 65. Such a shift is easier to explain in (unspecified) social terms.

## OTHER SOCIODEMOGRAPHIC VARIABLES THAT INFLUENCE RATES OF DEPRESSION

The age effects confirm the embarrassing situation that we have no clear explanation of the sex difference: we cannot say for sure what weight should be accorded to biological, social, and psychological explanations (Bebbington, 1996, 1998).

Nevertheless, social factors may well be of considerable importance because the sex ratio is not universally maintained across all sociodemographic categories. It is, for instance, much more marked in married than in never-married groups (Bebbington et al., 1981; Lindeman et al., 2000; Weissman & Klerman, 1977). Young married women looking after small children appear to be particularly at risk, at least in some societies (Brown & Harris, 1978; Ensel, 1982). Unsupported mothers appear to be even more at risk (Targosz et al., 2003). However, marital status has different associations with affective disorder in different

cultures. Married women are at low risk of disorder in Mediterranean countries (Mavreas et al., 1986; Vazquez-Barquero et al., 1987), in rural New Zealand (Romans-Clarkson et al., 1988), and among British Orthodox Jews (Lowenthal et al., 1995). These societies all accord a high value to the home-making role.

This variation in the impact of marital status on the sex ratio of depression might be taken as merely epiphenomenal, a sort of froth on the central fact that women are inherently vulnerable to depression for biological reasons. Alternatively, it might suggest not only that social variables are important in determining the sex ratio for depression, but also that the association with relatively simple sociodemographic factors is itself affected by more subtle sociocultural influences. The pervasiveness of the sex ratio could then be seen as a reflection of the all-pervading hydra of social disadvantage experienced by women worldwide.

In most Western societies, women are even now less likely to be employed than men. Employment generally has beneficial effects on psychological health: it brings interest, income, fulfilment, social contacts, and status, and provides structure and a sense of control (Jahoda, 1982; Krause & Geyer-Pestello, 1985). The availability of these benefits is likely to differ both among women, and between men and women. The advantages of employment are weaker in married women (Roberts & O'Keefe, 1981; Roberts et al., 1982; Warr & Parry, 1982), more so if they have children (McGee et al., 1983; Parry, 1986), most so when the children are of pre-school age (Haw, 1995). Full-time employment is particularly demanding (Cleary & Mechanic, 1983; Elliott & Huppert, 1991). The most likely explanation for these findings is role conflict and overload. Thus, part of the excess of depressive disorders in women may be related both to their reduced involvement in employment and to the particular strains they are exposed to if they do work.

## **BIOLOGICAL EXPLANATIONS FOR THE SEX RATIO IN DEPRESSION**

My interpretation of the evidence for a specific biological vulnerability to depression in women may be politically driven, since the choice between social and biological theories can be represented at the choice between seeing women either as universally disadvantaged, or as inherently vulnerable with all the associated implications of inferiority.

Direct evidence linking hormone status to depressive disorder has some face validity: oestradiol and progesterone seem to modulate the neurotransmitter and neuroendocrine systems, including those involving monamines, and there are transitions in women's lives characterized by hormonal shifts that may also be associated with mood disturbance (child-birth and the menopause).

The evidence in this area is extremely complicated (Bebbington, 1996). Moreover, there is a more plausible neuroendocrine hypothesis for depression involving glucocorticoids. This offers an explanation for a range of other neurohumoral phenomena, and a mechanism whereby extrinsic stress may result in the features of depressive disorder (Checkley, 1998; Dinan, 1994). It links overactivation of the hypothalamico-pituitary-adrenal (HPA) axis and the associated hypercortisolism with the changes in the central monoaminergic pathways thought to underlie depression and the actions of antidepressants. These changes will probably turn out to be the major hormonal concomitants of depressive disorder. Unfortunately



for our purpose, they cannot explain the sex difference: specifically, the function of the HPA axis in general does not differ by sex in the required manner (Allen & Pitts, 1984; Ansseau et al., 1987; Hunt et al., 1989; Maes et al., 1989).

The failure to find a convincing sex-related biological mechanism for depression that would account for the sex difference has its parallel in genetic studies. It is extremely unlikely that biological differences between women would be unaffected by intrafamilial (specifically, genetic) factors. The most plausible model is one based on multiple threshold liability. This assumes that the familial liability to a disorder is continuously distributed, comprising both genetic factors and familial-environmental effects. Depression in women can be conceived as a broad form of disorder with a lower threshold than the narrow male form, thus accounting for the higher prevalence rate in women. Under this model, the relatives of male probands will be more frequently affected, because in them the loading of familial factors will be greater (Carter, 1969). In practice, the relatives of male depressives are not at higher risk than the relatives of female depressives (Kupfer et al., 1989; Merikangas et al., 1985). Kendler and Prescott (1999) and Sullivan and colleagues (2002) were led to conclude that the heritability of the liability to depression was similar in men and women, even though the specific genetic factors might not overlap completely. Thus, it seems that the sex ratio must be explained in terms of extra-familial influences. This still allows for genetic effects in the transmission of depression, we merely assert that they do not cause the sex difference.

## **LIFE STRESS AND DEPRESSION**

Life event research has been a major topic in the aetiology of depression for more than 30 years. The idea is intuitively appealing, and this is exactly why there is a conceptual problem with this type of research. Humans try to make sense of their experience by identifying patterns of apparent cause and effect, and this applies to the relationship between social circumstances, feelings, and behaviour. People understand that individuals are often distressed when upsetting things happen. Sociologists and social psychiatrists developed the concept of significant life events from the upset that can be caused by rapid adverse changes in circumstances, while psychiatrists' conceptualization of affective disorders derives from the features that characterize distress. Distress is recognized from emotional and cognitive responses that, in severe or persistent forms, strongly resemble the symptoms of depressive disorder.

At a technological level, 'life events' differ from ordinary experience, and depressive disorder differs from ordinary distress only in degree. So what is the status of the assertion 'life events cause depression'? It could be regarded as definitional: things defined as being likely to distress people often do cause distress. At the very best, it is a hypothesis with low information value. Popper (1959) particularly admired theories (such as relativity) that were of inherently low a priori probability: the change in knowledge if they were corroborated, was thus great. However, our theory about life events has high a priori probability: everybody already believes it, not just the scientists, and thus corroboration does not add much to our knowledge. Given this preamble, it is not surprising that studies in both clinical and general populations, whether methodologically sophisticated or not, display remarkable consistency in finding that life events are associated with the onset of depressive disorder.

While this finding is not very interesting in itself, it does lead to more interesting questions. Thus, although there is an overall association, some people put up with considerable stress without becoming depressed. What is the nature of this resilience? People may vary in the way they handle events (coping), or particular individuals may have been exposed to events that happen not to be very threatening to them. Vulnerability itself may be the consequence of exposure to prior experiences that caused particular psychological predispositions. Alternatively, relevant temperamental variation may be under genetic control. Finally, genetic inheritance may influence the frequency with which individuals experience life events, even those that do not appear to be under their control.

## THE CHILDHOOD ANTECEDENTS OF LATER DEPRESSION

There are clear associations between certain childhood experiences, circumstances, and characteristics, and later depression. This is despite the rarity of childhood depressive disorder. What links there are must therefore usually be indirect—the causal connection appears to operate over a gap of years. This suggests some enduring change that mediates the later propensity to depression. Such changes might include psychological, temperamental, and biological predispositions, and an increased sensitivity to adult stress is a plausible mechanism. For example, the tendency of women to become depressed in response to domestic violence in adulthood is increased if they had also experienced abuse in childhood (Roberts et al., 1998).

The identification of childhood antecedents is an essentially epidemiological task, particularly when it involves longitudinal cohorts with follow-up over many years. Later depression is associated with childhood neuroticism, childhood symptoms of depression and anxiety, and reduced cognitive abilities. It has been suggested that these antecedents render individuals more sensitive to later life events (van Os et al., 1997; van Os & Jones, 1999).

A variety of childhood traumas are associated with later depressive episodes (De Marco, 2000). Childhood abuse, whether physical, emotional, or sexual, is associated with later psychopathology (Bifulco et al., 1991; Fergusson et al., 1996; Mullen et al., 1996). This seems particularly likely to be mediated through low self-esteem and later difficulties in forming relationships (Romans et al., 1995, 1996). In these New Zealand studies, only the most severe forms of abuse were unequivocally related to adult affective disorder. Abuse usually occurs in the context of other problems, and it may be this matrix that leads to adult disorder (Finkelhor et al., 1990; Higgins & McCabe, 1994; Rind & Tromovitch, 1997). Abuse is associated with many types of adult psychopathology, indicating a less than specific relationship with depression.

Childhood sexual abuse is associated with adult-onset depression in both men and women, but abuse is much more frequent in girls (Weiss et al., 1999). It may be mediated by its effects on psychological disparities, but also by dysregulating the HPA axis. Moreover, in females, the HPA axis may be inherently vulnerable to dysregulation by early stress (Weiss et al., 1999).

The link between child sexual abuse and adult depression is all too plausible. There has been some debate, however, whether parenting style in itself is sufficient to account for much of the variance in adult depression. One school of thought is that children have a built-in plasticity in the face of quite considerable disparities in levels of care. However, it is becoming increasingly clear that parenting style does have considerable impact. Much of

this work has resulted from the development of simple methods of assessment. The Parental Bonding Instrument (PBI) (Parker, 1990; Parker et al., 1979) is a self-report inventory designed to measure perceived parental care. It divides parenting style into the aspects of *care* and *overprotection*, and these seem stable over time. Optimal parenting comprises high care and low overprotection (Parker, 1990). While lack of care is consistently related to adult depression, the association of overprotection is less consistent (Parker et al., 1995).

Clearly, the PBI is a self-report measure, and might merely represent a querulous response set in people whose mood is depressed, but in fact, there is little evidence of this (Parker, 1981). Parker (1981) assessed the validity of the PBI by showing correspondence between sibling ratings of the subject's parenting with the subject's own. It is of interest that perceived parental care of twins correlates better for monozygotic than dizygotic twins (Kendler, 1996). Finally, it is possible that a third variable (neuroticism, for instance) might lead to a spurious relationship between reports of parenting and depression, by itself, being responsible for the propensity towards both. It is also possible that neuroticism might mediate between the experience of poor parenting and depression (Kendler et al., 1993). However, Duggan and his colleagues (1998) found that poor parenting and neuroticism had effects on later depression that were independent of each other.

Of course, it is possible that suboptimal parenting style may be linked to child sexual abuse. Hill and his colleagues (2001) demonstrated that low care was associated with sexual abuse, not only by relatives, but also by non-relatives. However, low care and child sex abuse were independently related to depression. However, this led Hill and his colleagues (2001) to suggest that the links between childhood sexual abuse and poor parenting with adult depression are mediated through different pathways.

## THE EPIDEMIOLOGY OF TREATMENT FOR DEPRESSION

There are various ways in which the delivery of treatment for depression can be assessed (Bebbington et al., 1996). One is to assume that identified depressive disorders need treatment of one sort or another, and to establish how often they actually received it. This is technically a measure of *utilization*. Another approach is to establish directly whether treatment was actually needed before quantifying how often it was delivered. Need can be defined either by experts, or by the individual in question (when it is called want, demand, or subjective need). Investigations of general population samples are the obvious source of such information. The obvious questions are as follows. Did this person have a need for professional treatment? Did he or she seek psychiatric help at either primary or secondary care level? Was he or she then prescribed treatment? Did he or she take the treatment prescribed? Studies of any kind are rare, but give a clear picture of under-treatment.

The Australian National Survey of Mental Health and Well-Being (Andrews *et al.*, 2001) reports data on service utilization. Thus, two-thirds of all subjects had no contact with services in the previous year, while 29% had seen GPs and 7.5% psychiatrists (Henderson et al., 2000). However, the survey gives data only from the combined category of major depressive disorder and dysthymia—the use of a broad category like theirs would reduce the likelihood of service contact.

Table 1.6 lists two direct studies of expert-defined need that provide data for depression. While the proportion of the population requiring treatment for depression was similar in Camberwell and Derry, it does appear that people were more likely to receive treatment in

**Table 1.6** Need and utilization of treatment for depressive disorders

Study	Location	N stage2/stage 1	One-year treatment needs for depression	Proportion of needs met			
Bebbington et al., 1997	Camberwell, London	408 (760)	6.0%	20%			
McConnell et al., 2002	Derry, N. Ireland	307 (923)	7.1%	48%			
Study	Location	N	Contact with primary care services	Proportion treated	Antidepressant treatment	Other drugs	Counselling
Bebbington et al., 2000	First British National Survey	10 108	48%	28%	16%	9%	15%
Singleton et al., 2001	Second British National Survey	8580	62%	44%	34%	12%	17%

the latter: Derry appears to have inner-city levels of depression, but small-town levels of primary-care services.

The other results listed in Table 1.6 are of particular interest—the two British National Surveys used the same methods, but the data were gathered seven years apart (1993 and 2000). There are significant improvements in the treatment of cases of depressive disorder at primary-care level: more people saw their GP with their mental health problem, and more received appropriate treatment, indicated by the noteworthy rise in antidepressant drug prescription.

Large surveys of this type offer rather crude indications of treatment levels, but the general finding of under-treatment is so marked that it clearly represents a serious public health problem, requiring education both of primary-care physicians and of the public at large.

## THE GENETIC EPIDEMIOLOGY OF MAJOR DEPRESSION

The study of genetic epidemiology is of interest because it seeks to attribute a relative weight to the effects of genes, the shared and non-shared environment, and gene–environment interactions. Sullivan and colleagues (2002) have recently reviewed the literature on the genetic epidemiology of major depression, using specific inclusion criteria. On the basis of the five family studies that met their criteria, they concluded that the odds ratio of being affected with major depression in the first-degree relatives of probands compared with those of unaffected comparison subjects was around 2.8.

Twin studies are capable of providing estimates for the relative strength of genetic effects and the effects of the shared and non-shared environments. Sullivan and colleagues (2002) reviewed five studies covering 21 000 individuals that met their criteria. Although the studies showed appreciable variation in the heritability of major depression, all reported significant heritability estimates, while the estimates for *shared* environmental effects were non-significant in all the studies. There were no consistent sex differences in the results.

Despite problems in aggregating data of this type from different studies, it did prove possible. The best-fitting model included only genetic and individual-specific environmental factors, with the former contributing about 37% of variance. Heritability may be particularly increased in depression with an early onset, and is almost certainly so in recurrent depression. It should be noted that, as calculated, heritability estimates would cover gene–environment interactions as well as purely genetic effects.

## CONCLUSIONS

In this chapter, I have considered the practical difficulties facing the epidemiological study of depression. Epidemiology is a medical approach that relies initially on the conceptualization of impaired functions as disorders, followed by a requirement to identify these disorders in a reliable way. Depression as conceived shades both into normal experience and into other affective disorders. Distinguishing it in a way at once useful and consistent is thus difficult, as I have argued in some detail. In particular, the comparability of studies is jeopardized by differences between classifications and instruments and in the way these are applied. The consequence is that no two research teams are likely to identify the same sets of respondents

as cases; indeed, in practice, the overlap is small, and there may be systematic over- or under-identification, resulting in different prevalence rates. I now think these obstacles to precise case identification are probably insuperable. Nevertheless, the arguments remain strong for doing the best we can. Two things alleviate this rather miserable conclusion. Because most cases identified in general populations are around the threshold that distinguishes them from non-cases, different studies are likely to end up with case groups that have similar characteristics. Robust associations—for example, the association of depression with life events or with poverty—will therefore survive the inadequacies of our instrumentation.

The second way around these inadequacies is to supplement the medical case approach with studies that look at the correlates of total symptom score. In this way, important findings can be triangulated, as they are in the study of blood pressure.

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