The epidemiology of major depressive episodes: results from the International Consortium of Psychiatric Epidemiology (ICPE) Surveys

LAURA ANDRADE, Institute and Department of Psychiatry, School of Medicine, University of São Paulo, São Paulo, Brazil
JORGE J. CARAVEO-ANDUAGA, Division of Epidemiogical and Social Research, National Institute of Psychiatry Ramón de la Fuente, Mexico City, Mexico
PATRICIA BERGLUND, Institute for Social Research, University of Michigan, Ann Arbor MI, USA
ROB V. BIJL, Research and Documentation Centers (WODC) Ministry of Justice, The Hague, Netherlands
RON DE GRAAF, WILMA VOLLEBERGH, Monitoring and Epidemiology Department, Trimbos Institute, Utrecht, The Netherlands
EVA DRAGOMIRECKA, Psychiatric Demography Unit, Prague Psychiatric Center, Prague, Czech Republic
ROBERT KOHN, MARTIN KELLER, Department of Psychiatry and Human Behavior, Brown University, Providence RI, USA
RONALD C KESSLER, Department of Health Care Policy, Harvard Medical School, Boston MA, USA
NORITO KAWAKAMI, Okayama University Graduate School of Medicine and Dentistry, Okayama, Japan
CENGIZ KILIÇ, Section of Trauma Studies, Institute of Psychiatry, University of London, London, UK
DAVID OFFORD, Chedoke-McMaster Hospital, Hamilton, Canada
T. BEDIRHAN USTUN, World Health Organization (WHO), Geneva, Switzerland
HANS-ULRICH WITTCHEN, Institute of Clinical Psychology and Psychotherapy, Technical University of Dresden and Max Planck Institute of Psychiatry, Munich, Germany

ABSTRACT *Absence of a common diagnostic interview has hampered cross-national syntheses of epidemiological evidence on major depressive episodes (MDE). Community epidemiological surveys using the World Health Organization Composite International Diagnostic Interview administered face-to-face were carried out in 10 countries in North America (Canada and the US), Latin America (Brazil, Chile, and Mexico), Europe (Czech Republic, Germany, the Netherlands, and Turkey), and Asia (Japan). The total sample size was more than 37,000.*

Lifetime prevalence estimates of hierarchy-free DSM-III-R/DSM-IV MDE varied widely, from 3% in Japan to 16.9% in the US, with the majority in the range of 8% to 12%. The 12-month/lifetime prevalence ratio was in the range 40% to 55%, the 30-day/12-month prevalence ratio in the range 45% to 65%, and median age of onset in the range 20 to 25 in most countries. Consistent socio-demographic correlates included being female and unmarried. Respondents in recent cohorts reported higher lifetime prevalence, but lower persistence than those in earlier cohorts. Major depressive episodes were found to be strongly co-morbid with, and temporally secondary to, anxiety disorders in all countries, with primary panic and generalized anxiety disorders the most powerful predictors of the first onset of secondary MDE.

Major depressive episodes are a commonly occurring disorder that usually has a chronic-intermittent course. Effectiveness trials are needed to evaluate the impact of early detection and treatment on the course of MDE as well as to evaluate whether timely treatment of primary anxiety disorders would reduce the subsequent onset, persistence, and severity of secondary MDE.

Key words: major depression, epidemiology, ICPE surveys

Introduction

Community epidemiological surveys of mental disorders, using some combination of structured screening scales and clinical interviews, have been carried out since the end of the Second World War (see, for example, Lin, 1953 and Helgason, 1964). However, in the absence of a common format for diagnostic interviews, few cross-national syntheses were made until the past decade. The foundation for recent syntheses was laid in the early 1980s with the development of the Diagnostic Interview Schedule (DIS) (Robins et al., 1981), the first fully structured research diagnostic interview that could be used by lay interviewers to generate diagnoses according to the definitions and criteria of the *Diagnostic and Statistical Manual of Mental Disorders*, third edition (DSM-III) (American Psychiatric Association, 1980). The DIS was first used in the Epidemiologic Catchment Area (ECA) Study (Robins and Regier, 1991), a landmark survey of the prevalences and correlates of mental disorders in the US. The widespread dissemination of the ECA results led to a number of similar studies in other countries (Canino et al., 1987; Bland et al., 1988a; Hwu et al., 1989; Lépine et al., 1989; Wells et al., 1989; Lee et al., 1990; Wittchen et al., 1992). These surveys were subsequently brought together in a series of important cross-national comparative papers that focused on specific disorders (Cross-National Collaborative Group, 1992; Weissman et al., 1996, 1997).

Beginning in the mid-1980s, the World Health Organization (WHO), in collaboration with the US Public Health Service, attempted to build on the success of the DIS and to encourage further cross-national collaboration by developing a fully structured research diagnostic interview based on the DIS that could generate reliable and valid diagnoses in many different languages throughout the world. This new instrument, known as the Composite International Diagnostic Interview (CIDI), was created by an international WHO working group that expanded and refined the DIS to include ICD (International Classification of Diseases) criteria (Robins et al., 1988). Cross-national field trials showed the CIDI to be reliable and valid cross-nationally (Wittchen, 1994). Version 1.0 of the CIDI was released in 1990 (World Health Organization, 1990) and was subsequently revised to include DSM-IV criteria (World Health Organization, 1997).

In the decade since it first became available, the CIDI has been used in a number of large-scale community epidemiological surveys throughout the world (Kessler et al., 1994; Andrade et al., 1996; Bijl et al., 1998; Caraveo et al., 1998; Kılıç, 1998; Vega et al., 1998; Offord et al., 1994; Dragomirecká et al., 2002; Wittchen et al., 1998).

In recognition of this widespread use, the WHO created a research consortium – the WHO International Consortium in Psychiatric Epidemiology (ICPE) – to co-ordinate comparative analyses of these data (Kessler, 1999). This article presents findings from the first generation of ICPE surveys on the epidemiology of major depressive episodes (MDE). Data are presented from surveys carried out between 1990 and 1999 in 10 countries with a combined sample size of approximately 37,000 respondents.

Methods

Samples

A total of 10 surveys were carried out in North America (Canada and the USA), Latin America (Brazil, Chile and Mexico), Europe (Czech Republic, Germany, Netherlands, and Turkey), and Asia (Japan). All the surveys were based on probability samples of the general population, and all interviews were carried out face-to-face by trained lay interviewers. As shown in Table 1, the pooled sample included respondents as young as 14 years of age. Across surveys, the response rates were in the range 56.9% to 90.3%. The data sets in Canada, Chile, Germany, the Netherlands, and the US were weighted to adjust for differences between the socio-demographic characteristics of the samples and the populations from which they were selected. These adjustments were not possible in the other data sets because of a lack of population data.

Measures

The surveys used either the WHO-CIDI (in Brazil, Chile, Czech Republic, Netherlands, Turkey), the University of Michigan version of CIDI (UM-CIDI) (Kessler et al., 1998a) (Canada, Japan, Mexico and the USA), or the Munich version of CIDI (M–CIDI) (Wittchen et al., 1996) (Germany). The UM-CIDI added a series of commitment and clarification probes to the original CIDI in order to increase the accuracy of responses about lifetime prevalence. It also included

Table 1. Sample characteristics of the ICPE surveys in the 10 study countries

Country	Name and type	Sample characteristics	Field dates	Age range (years)	Sample size	Response rate
Brazil	The Epidemiologic Catchment Area Study in the city of São Paulo (ECAS-SP) WHO-CIDI with DSM-III-R	Stratified area probability sample of the catchment area of the university of São Paulo Medical Centre. Oversampling of ages 18–24 years and 59+.	1994–6	18+	1,464	62.5%
Canada	The Mental Health Supplement to the Ontario Health Survey (MHS-OHS) UM-CIDI with DSM-III-R	Stratified subsample of residents of households that participated in the Ontario Health Survey (OHS). The OHS was based on a stratified, multistage clustered area probability sample representative of the Ontario household populations.	1990–1	18+	6,902	88.1%
Chile	Chile Psychiatric Prevalence Study (CPPS) CIDI 1.1 with DSM-III-R	Stratified sample of household residents aged 15 and older, representative of the national population distribution and selected from four provinces representing geographically distinct regions of the country: Santiago, Concepcion, Iquique, and Cautin.	1992–9	15+	2,978	90.3%
Czech Republic	National Probability Survey of Mental Health and Comorbidity (Czech CIDI Survey) CIDI 2.1 with DSM-IV	A two-stage, nationally representative sample in population aged 18 and over in the Czech Republic. First sample drawn from the register of places of residence. Second sample drawn from Central Register of Inhabitants.	1998–9	18–79	1,534	66.0%
Germany	Early Developmental Stages of Psychopathology Study (EDSP) M-CIDI with DSM-IV	Stratified one-stage sample representative of Munich residents. Sample drawn from official population registry of the Greater Munich area. Stratification based on demographic characteristics available in registry.	1995	14–25	3,021	71.1%
Japan	The Gifu Interview Survey on Stress, Lifestyle and Health (GISSH) UM-CIDI with DSM-III-R	A simple random sample of residents drawn from those aged 20+ (with no upper limit) in Gifu prefecture, Japan with a population of 410,000.	1997–9	20+	1,029	56.9%
Mexico	Epidemiology of Psychiatric Comorbidity Project (EPM) UM-CIDI with DSM-III-R	Stratified multistage clustered area probability sample of household residents in a subsample of the 16 political divisions of Mexico City.	1995	18–54	1,734	60.4%
Netherlands	Netherlands Mental Health Survey and Incidence Study (NEMESIS) WHO CIDI with DSM-III-R	Nationally representative stratified multistage clustered area probability sample of household respondents.	1996	18–64	7,076	70.0%
Turkey	Mental Health Profile of Turkey WHO CIDI with DSM-III-R	Nationally representative stratified multistage clustered area probability sample of household residents that included interviews with all adult respondents in each sample household.	1996	18–54	6,095	72.6%
US	US National Comorbidity Survey (NCS) UM-CIDI with DSM-III-R	Nationally representative stratified multistage clustered area probability sample of household residents with a supplemental sample of students living in campus group housing.	1990–2	15–54	5,877	82.4%

a review of lifetime diagnostic stem questions at the beginning of the interview in order to facilitate active memory search. Experimental evidence shows that these modifications led to a substantial increase in lifetime prevalence estimates (Kessler et al., 1998a). Compared with the original CIDI, the expanded questions in the M-CIDI helped to investigate disorder subtypes and to increase accuracy of assessing diagnostic criteria. Diagnostic assessments were based on DSM-III-R (American Psychiatric Association, 1987) criteria in all countries other than Germany, where DSM-IV (American Psychiatric Association, 1994) criteria were used.

Retrospective reports were used to estimate age of onset. The core disorders included in the surveys were anxiety disorders (panic disorder, agoraphobia with and without panic, social anxiety disorder, simple phobia, generalized anxiety disorder, obsessive-compulsive disorder, post-traumatic stress disorder), mood disorders (major depressive disorder, dysthymia, mania), and substance-use disorders (alcohol and drug abuse/dependence). The CIDI organic exclusion rules were imposed in making all diagnoses. Diagnostic hierarchy rules were used for substance-use disorders but not for mental disorders. Methodological evidence gathered in the WHO-CIDI field trials showed that all the lifetime DSM/CIDI disorders considered here were assessed with acceptable reliability and validity in the WHO-CIDI (Wittchen, 1994). Clinical reappraisal studies carried out in conjunction with two of the ICPE surveys, the US National Comorbidity Survey (Kessler et al., 1998a) and the German Early Developmental Stages of Psychopathology study (Wittchen et al., 1996; Reed et al., 1998), documented acceptable reliability and validity for lifetime diagnoses based on the UM–CIDI and M–CIDI. No validity data are available for the 12-month or 30-day prevalence estimates.

Analysis methods

Data are reported here on prevalences, co-morbidities, cohort effects, age-of-onset distributions, demographic correlates, effects of temporally primary disorders in predicting the subsequent first onset of an MDE, speed of initial treatment contact, and patterns of 12-month service use. Simple cross-tabulations were used to calculate prevalences. Odds-ratios (ORs) were used to calculate co-morbidities. The Kaplan–Meier method (Kaplan and Meier, 1958) was used to generate age-of-onset curves. Logistic regression analysis (Hosmer and Lemeshow, 1989) was used to study demographic correlates. Discrete-time survival analysis (Efron, 1988) with the person-year as the unit of analysis was used to study cohort effects, the effects of temporally primary disorders on secondary MDE, and predictors of speed of initial treatment contact.

Owing to the complex sample designs and weighting of the surveys, standard errors of the various descriptive statistics were estimated using the jacknife repeated replications (JRR) method (Kish and Frankel, 1974) implemented in an SAS macro. The JRR estimates adjust for the clustering and weighting of cases. The logistic regression and survival coefficients were transformed to ORs and are reported below as ORs with 95% confidence intervals (CIs). The 95% CIs were adjusted for design effects. Multivariate tests were based on Wald χ^2 tests computed from coefficient variance–covariance matrices that were adjusted for design effects using JRR. Statistical significance was based on two-sided design-based tests evaluated at the 0.05 level of significance.

Results

Demographic characteristics of the samples

The demographic distributions of the samples are presented in Table 2. As noted above, the results were weighted to approximate the population census distribution in five of the samples (Canada, Chile, Germany, Netherlands and the US), but were weighted only for differential probability of selection in households in the other samples. It is therefore not legitimate to compare the patterns across all the samples. Nonetheless, some general observations are worth making. Age distributions varied considerably owing to differences in the age restrictions of sample participation. Distribution between the sexes was fairly evenly divided. Distribution in education varied dramatically because of cross-national differences in schooling. The majority of respondents in most surveys were married at the time of interview, although this was not the case in Germany because of the young age range of this sample. Rural–urban distribution was predominantly urban in all the surveys but was 100% urban, by definition, in the surveys carried out in Brazil, Chile, Japan, and Mexico. Although the German sample was also largely urban, non-urban areas were included in the sampling frame.

Table 2. Distributions of sociodemographic variables in the ICPE surveys

	Brazil		Canada		Chile		Czech Republic		Germany		Japan		Mexico		Netherlands		Turkey		US	
	%	SE	%	SE	%	SE	%	SE	%	SE	%	SE	%	SE	%	SE	%	SE	%	SE
Gender																				
Female	57.4	1.5	50.5	1.2	52.1	0.7	51.5	1.1	50.6	1.1	53.1	1.4	56.8	1.0	49.3	0.6	55.8	0.5	50.1	1.2
Male	42.6	1.5	49.5	1.2	47.9	0.7	48.5	1.1	49.4	1.1	46.9	1.4	43.2	1.0	50.7	0.6	44.2	0.5	49.9	1.2
Education																				
0-11	39.4	1.4	30.2	1.0	50.2	3.9	40.9	1.5	58.3	1.1	33.4	1.5	60.8	1.7	43.5	1.0	78.5	1.1	21.6	0.9
12	4.8	0.5	25.6	0.8	19.5	0.9	25.1	1.1	6.8	0.5	31.2	1.3	18.4	1.1	28.8	0.6	13.9	0.7	35.0	1.1
13-15	20.0	1.4	27.7	0.7	16.9	1.9	21.5	1.2	34.0	1.1	17.2	1.1	6.9	0.7	19.0	0.6	0.0	—	23.2	1.1
16+	35.8	1.8	16.5	0.6	13.4	2.2	12.5	1.0	0.9	0.2	18.1	1.2	13.9	1.1	8.7	0.7	7.6	0.7	20.2	1.0
Marital status																				
Not married	52.9	1.9	36.0	1.1	48.8	1.8	36.7	1.2	96.6	0.4	28.0	1.4	42.8	1.1	30.8	0.8	18.9	0.6	46.0	1.1
Married	47.1	1.9	64.0	1.1	51.2	1.8	63.3	1.2	3.4	0.4	72.0	1.4	57.2	1.1	69.2	0.8	81.1	0.6	54.0	1.1
Urbanicity																				
Rural	0.0	—	12.8	0.5	6.8	(0.5)	49.8	3.6	24.9	0.8	0.0	—	0.0	—	16.9	1.1	29.3	0.9	21.2	3.2
Urban	100.0	—	87.2	0.5	93.2	(0.5)	50.2	3.6	75.1	0.8	100.0	—	100.0	—	83.1	1.1	70.7	0.9	78.8	3.2
Age group (years)																				
14–24	15.5	0.8	24.9	0.8	25.3	1.4	15.8	1.0	99.8	0.1	7.7	1.3	28.0	1.0	14.1	0.6	20.3	0.6	24.8	0.9
25–34	23.8	1.3	30.8	1.2	25.2	1.0	18.4	1.2	0.2	0.1	18.0	1.4	34.3	1.3	26.1	0.6	33.0	0.8	30.6	0.8
35–44	21.9	1.1	26.0	0.8	18.3	1.6	17.8	0.9	0.0	—	16.0	1.2	23.1	0.8	24.1	0.6	30.3	0.8	27.7	0.8
45+	38.8	1.5	18.3	1.1	31.1	1.4	48.0	1.3	0.0	—	58.2	1.8	14.5	1.0	35.6	0.7	16.5	0.5	16.9	0.9
(n)	(1,464)		(6,902)		(2,978)		(1,534)		(3,021)		(1,029)		(1.734)		(7,076)		(6,095)		(5,877)	

Prevalence

The lifetime prevalence of MDE based on DSM-III, DSM-III-R, DSM-IV, and ICD-10 criteria has been estimated in a number of community epidemiological surveys, most of them carried out in industrialized countries (Weissman and Myers, 1978; American Psychiatric Association 1980, 1987, 1994; Bebbington et al., 1981; Canino et al., 1987; Lee et al., 1987; Bebbington, 1988; Bland et al., 1988a,b; Cheng, 1989; Hwu et al., 1989; Wells et al., 1989; Wittchen et al., 1992).

There is enormous variation in these estimates, between 4% and 20% lifetime prevalence. This variation is presumably due to differences in populations studied, criteria used to generate diagnoses, survey response rates, and methodological features of the surveys that influence accuracy of response. However, little is known about the relative importance of these different factors. Twelve-month MDE prevalence estimates in these epidemiological surveys are generally between one-third and half as high as lifetime prevalence estimates, whereas 30-day prevalence estimates are usually between one-third and half as high as 12-month prevalence estimates.

As shown in Table 3, the range of lifetime prevalence estimates in the ICPE surveys is similar to previous literature reports, from a low of 3% in Japan to a high of 16.9% in the US. Only in the Japanese survey was lifetime prevalence less than 5%, compared with five surveys with lifetime prevalence in the range 5% to 10%, two in the range 10% to 15%, and two greater than 15%. Twelve-month prevalence estimates range from 1.2% (Japan) to 10% (US), with seven of the 10 estimates clustered in the range 3.5% to 5.9%. Thirty-day prevalence estimates range from 0.9% (Japan) to 4.6% (US), with six of the 10 estimates clustered in the range 1.9% to 3.9%.

Course

The finding in previous community epidemiological surveys that the 12-month prevalence of MDE is between one-third and half as large as the lifetime prevalence suggests that MDE is a very chronic disorder. The finding in these same surveys that the 30-day prevalence is between one-third and one-half as large as 12-month prevalence suggests that MDE is an intermittent disorder. That is, people with the disorder typically have recurrent episodes that persist for less than a full year. Longitudinal studies in clinical samples find similar patterns (Solomon et al., 2000).

Table 4 presents ratios of the lifetime, 12-month, and 30-day prevalence estimates of MDE in the ICPE surveys. The ratio of 12-month to lifetime prevalence ranges from 24.4% (Czech Republic) to 62.6% (Chile), with six of the 10 estimates clustered in the range 42% to 55.5%. The ratio of 30-day to 12-month prevalence ranges from 24.4% (Germany) to 88.1% (Turkey), with seven of the 10 estimates clustered in the range 44.9% to 67.2%. The ratio of 30-day to lifetime prevalence ranges from 11.0% (Germany) to 63.6% (Turkey), with six of the 10 estimates clustered in the range 23.3% to 37.4%. These results are generally consistent with those of previous studies in suggesting that MDE is a chronic disorder (high 12-month/lifetime prevalence ratio) that is usually intermittent in its course (30-day/12-month prevalence ratio considerably lower than 1).

Disaggregation of the lifetime/12-month and 30-day/12-month prevalence ratios as a function of number of years since first onset of MDE (results not shown, but available on the ICPE Web page www.hcp.med.harvard.edu/icpe) show that the ratios typically decline, but nonetheless remain substantial, across the distribution of time since onset. For example, in seven of the 10 countries, among respondents whose first onset of MDE was more than a decade ago, at least one-third of people with lifetime MDE had an episode in the 12 months before the interview. This shows that recurrence risk continues for years after first onset. It is also noteworthy that the 30-day/12-month prevalence ratio remains fairly stable over time in most countries, suggesting that the average duration of episodes does not change over time.

Further evidence along the same lines comes from reports of respondents who met criteria for lifetime MDE about the course of their illness. Recurrent episodes were reported by nearly 75% of respondents with lifetime MDE. The mean and median numbers of lifetime episodes among recurrent cases were four and 16, respectively. The mean duration of the longest lifetime episode was approximately three months, whereas fewer than one in eight respondents with lifetime MDE reported ever having an episode that lasted as long as two years, this being the minimum duration for a chronic depressive episode in the DSM-IV system (American Psychiatric Association, 1994).

Table 3. Prevalence of major depressive episodes in the ICPE surveys

	Brazil		Canada		Chile		Czech Republic		Germany		Japan		Mexico		Netherlands		Turkey		US	
	%	SE	%	SE	%	SE	%	SE	%	SE	%	SE	%	SE	%	SE	%	SE	%	SE
Lifetime	12.6	0.9	8.3	0.6	9.0	0.6	7.8	0.9	11.5	0.7	3.0	0.5	8.1	1.2	15.7	0.5	6.3	0.5	16.9	0.0
12-month	5.8	0.6	4.3	0.4	5.6	0.6	2.0	0.4	5.2	0.5	1.2	0.4	4.5	0.8	5.9	0.3	3.5	0.4	10.0	0.6
30-day	3.9	0.6	1.9	0.3	3.3	0.4	1.0	0.3	1.3	0.2	0.9	0.3	2.2	0.6	2.7	0.2	3.1	0.4	4.6	0.4
(n)	(1,464)		(6,902)		(2,978)		(1,534)		(3,021)		(1,029)		(1,734)		(7,076)		(6,095)		(5,877)	

Table 4. The persistence of major depressive episodes in the ICPE surveys

	Brazil		Canada		Chile		Czech Republic		Germany		Japan		Mexico		Netherlands		Turkey		US	
	%	SE	%	SE	%	SE	%	SE	%	SE	%	SE	%	SE	%	SE	%	SE	%	SE
12-month/ Lifetime	46.5	3.6	51.8	2.9	62.6	3.8	26.1	3.4	44.9	2.6	42.0	5.4	55.5	5.3	37.4	1.3	72.1	2.6	59.2	1.8
30-day/12-month	67.2	4.5	44.9	4.2	59.7	5.2	49.9	8.5	24.4	2.7	74.2	0.0	48.5	6.2	46.8	2.5	88.1	1.1	46.0	2.2
30-day/Lifetime	31.2	3.6	23.3	2.4	37.4	3.2	13.0	2.6	11.0	1.7	31.1	3.7	27.0	3.9	17.5	1.1	63.6	2.8	27.3	1.6
(n)	(1,464)		(6,902)		(2,978)		(1,534)		(3,021)		(1,029)		(1,734)		(7,076)		(6,095)		(5,877)	

Age of onset

Previous epidemiological studies have found that MDE has a much earlier age of onset than most other chronic conditions, with risk beginning to appear in early adolescence. The median age of onset is in the early-to-mid twenties, but risk of MDE continues throughout the life course (Christie et al., 1988; Blazer et al., 1994). Data about the age of onset from the ICPE survey were acquired by using retrospective age-of-onset reports obtained from respondents who met lifetime criteria for MDE. Age-of-onset curves were generated from these reports using the Kaplan–Meier method (Kaplan and Meier, 1958). Country-specific results are shown graphically in Figure 1. Results have been standardized for between-country differences in lifetime prevalence. The median age of onset of MDE is predominantly in the early to mid-twenties in all countries other than Japan (late twenties) and the Czech Republic (early thirties). The curves have a consistent shape across all the countries, with risk being fairly low in the early years of life, rising during adolescence and through the middle-to-late twenties, and then decreasing in later years.

Sociodemographic correlates

Previous epidemiological studies have found that MDE is more common among women than men, among people with lower than higher socioeconomic status (low income and education), and among the unmarried than the married (Canino et al., 1987; Bland et al., 1988a; Hwu et al., 1989; Lépine et al., 1989; Wells et al., 1989; Lee et al., 1990; Wittchen et al., 1992). The results in Table 5 show the associations of 12-month MDE with these sociodemographic correlates in the ICPE surveys. (Results were found to be very similar across the lifetime, 12-month, and 30-day time frames, so only the predictors of 12-month prevalence are presented here.) The most consistent association in the table is with gender. Women have higher rates of MDE than men in all 10 countries, with ORs ranging from 1.2 in the Czech Republic to 2.5 in Japan. ORs for female:male in eight of the 10 countries are statistically significant at the 0.05 level and 9 of the 10 are tightly clustered in the range 1.9–2.5.

The associations of socioeconomic status with 12-month MDE are considerably weaker than those involving gender. Education is significantly related to

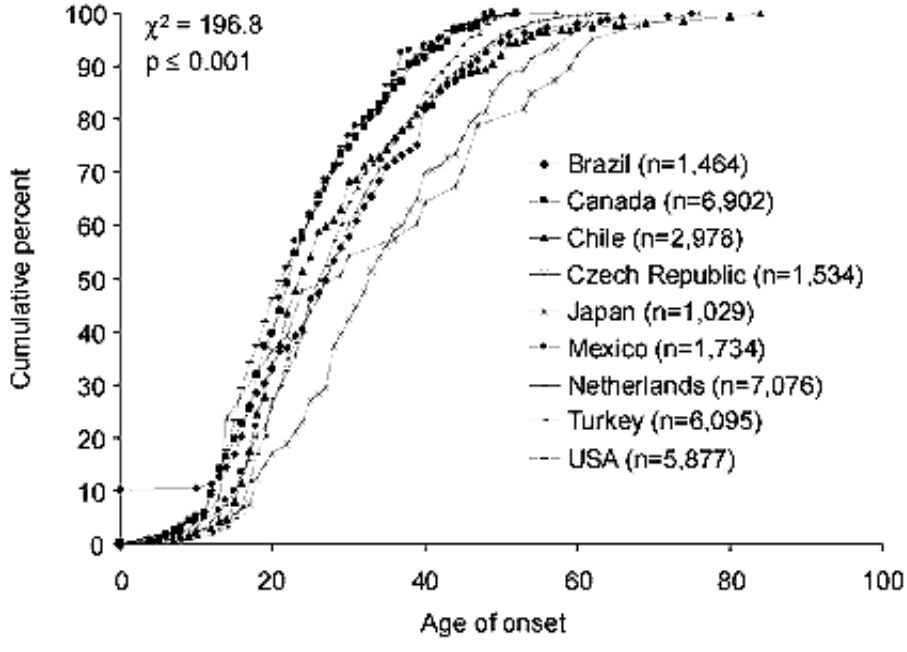

Figure 1. Age-of-onset distributions of major depressive episodes in the ICPE surveys.

MDE in only two of the 10 countries (the US and the Netherlands), whereas family income (divided into within-country quartiles) is significantly related to MDE in three of the five countries in which income was assessed (US, Canada, and the Netherlands). Unmarried people have higher rates of MDE than those that are married in all 10 surveys, with ORs ranging from 1.1 in Brazil and Turkey to 2.5 in Germany. The ORs for four of the 10 countries are statistically significant at the 0.05 level and seven of the 10 are meaningfully elevated in the range 1.5 to 2.5. Urban-rural difference was also studied. Rural respondents were slightly less likely than urban respondents to have MDE in five of the six countries where urbanicity could be studied, with ORs ranging from 0.6 in The Netherlands to 1 in Germany. Only one of the six (the Netherlands) was statistically significant at the 0.05 level.

The final sociodemographic correlate studied was age. A number of epidemiological surveys have shown that age is inversely related to MDE (Weissman and Myers, 1978; Canino et al., 1987; Bland et al., 1988b) although an earlier analysis of the ICPE surveys that focused on overall mood disorders found that this relationship is more true for lifetime prevalence than for recent prevalence (WHO International Consortium of Psychiatric Epidemiology, 2000). As shown in the last rows of Table 5, the association of age with 12-month MDE is not apparent in the ICPE surveys. This association is statistically significant in only one of the 10 countries (the Netherlands). Even in this one case, the highest risk was not found in the youngest cohort. There were only two countries (Japan and the US) where the risk was highest in the youngest cohort.

Cohort effects

As noted in the last paragraph, previous analyses of the ICPE data found a much stronger inverse relationship between age and lifetime than recent mood disorders (MDD, bipolar disorder, or dysthymia). The association between age and lifetime risk, which was evaluated in a survival framework that adjusted for age differences in time at risk, can be interpreted substantively as a 'cohort effect', by which we mean an increase in the lifetime prevalence of mental disorders across successive generations. This possibility was evaluated using retrospective age-of-onset reports to estimate a series of survival models for lifetime prevalence as a function of age at interview. The results are presented in Table 6, which shows consistent and statistically significant evidence for increasing lifetime prevalence of MDE in more recent cohorts across all nine of the countries in which cohort effects were estimated (Germany was excluded from this part of the analysis because of the restricted age range in this sample). The ORs for the youngest cohorts compared with the oldest cohorts range from 2.2 in Brazil to 10.9 in Japan, with the ORs for seven of the nine countries being greater than 5.

There is a striking discrepancy between the insignificant associations between age and recent MDE in Table 5 and the strongly consistent associations between age and lifetime risk of MDE in Table 6. Statistically, this discrepancy means that whereas younger cohorts have higher reported rates of MDE, it is less persistent (as indicated by the ratio of 12-month to lifetime prevalence) in the younger than the older cohorts. This lower persistence is not due to an inverse relationship between time since onset and persistence, as no such pattern was found in the data. A more likely interpretation is that the increase in the proportion of people who have a lifetime depressive episode in recent cohorts is accompanied by a decrease in the persistence of these new cases of depression.

Co-morbidity

Previous epidemiological studies have shown that MDE is highly co-morbid with other mental disorders, especially with anxiety disorders (Merikangas et al., 1996; Kessler, 1997). The same is true for the ICPE surveys. There were statistically significant co-morbidities between MDE and all the anxiety disorders assessed in the ICPE surveys (results not shown, but available on the ICPE Web page www.hcp.med.harvard.edu/icpe). Consistent with previous research (Kessler et al., 1998b, 1999a), these associations were strongest with generalized anxiety disorder (ORs in the range 3.0 to 20.7) and panic disorder (ORs in the range 4.3 to 23.9). In most surveys, between one-third and half of respondents with a lifetime history of MDE also had a history of at least one anxiety disorder.

Previous research suggests that the age of onset of anxiety disorders is typically earlier than the age of onset of MDE among people with co-morbid anxiety and depression (Kessler, 1995; Merikangas et al., 1996). This is also the case in the ICPE surveys

Table 5. Bivariate sociodemographic correlates of 12-month major depressive episodes in the ICPE surveys

	Brazil		Canada		Chile		Czech Republic		Germany		Japan		Mexico		Netherlands		Turkey		US	
	OR[a]	95% CI[a]	OR[a]	95% CI[a]	OR[a]	95% CI[a]	OR[a]	95% CI[a]	OR[a]	95% CI[a]	OR[a]	95% CI[a]	OR[a]	95% CI[a]	OR[a]	95% CI[a]	OR[a]	95% CI[a]	OR[a]	95% CI[a]
Gender																				
Female	2.1*	1.2–3.7	2.0*	1.5–2.7	2.1*	1.4–3.1	1.2	0.6–2.5	2.3*	1.5–3.4	2.5	0.7–9.0	1.9*	1.0–3.6	1.9*	1.4–2.4	2.3*	1.6–3.3	2.0*	1.6–2.5
Male	1.0	—	1.0	—	1.0	—	—	—	1.0	—	1.0	— 1.0	—	1.0	—	1.0	—	1.0	—	
χ^2_1	*7.5***		*24.0***		*13.9***		*0.4*		*15.4***		*2.1*		*3.7*		*23.9***		*20.0***		*40.1***	
Education																				
0–11	0.9	0.5–1.5	1.1	0.9–1.5	1.3	0.7–2.3	0.8	0.2–3.9	0.3	0.0–2.6	0.7	0.2–3.0	1.5	0.5–4.7	1.3	0.9–1.8	1.6	0.9–2.9	1.8*	1.4–2.5
12	1.0	0.4–2.5	0.9	0.6–1.4	1.5	0.8–2.9	1.6	0.5–5.0	0.2	0.0–2.2	0.3	0.0–1.9	0.7	0.2–1.9	0.9	0.6–1.3	1.2	0.7–2.1	1.5*	1.1–2.0
13–15	0.9	0.4–2.2	1.1	0.7–1.7	1.2	0.7–2.2	1.0	0.3–3.4	0.5	0.1–4.1	1.1	0.2–6.0	0.4	0.1–2.4	0.8	0.5–1.2	—	—	1.5*	1.1–2.1
16+	1.0	—	1.0	—	1.0	—	1.0	—	1.0	—	1.0	— 1.0	—	1.0	—	1.0	—	1.0	—	
χ^2_3	*0.5*		*2.1*		*1.5*		*2.1*		*5.9*		*2.4*		*6.2*		*16.1***		*3.1*		*17.5***	
Family income																				
0–25%			1.4	0.8–2.4							1.7	0.5–6.2	1.0	0.3–3.3	2.1*	1.6–2.8			1.8*	1.3–2.5
26–50%			2.1*	1.2–3.5							0.9	0.1–5.9	1.3	0.4–4.0	1.3	1.0–1.8			1.5*	1.1–2.1
51–75%	not assessed		1.1	0.7–1.6	not assessed		not assessed		not assessed		1.7	0.5–6.2	1.2	0.4–3.0	0.6	0.4–1.0	not assessed		1.3	1.0–1.8
76–100%			1.0	—							1.0	— 1.0	—	1.0	—	—			—	1.0
χ^2_3			*12.8***								*1.2*		*0.4*		*35.9***				*14.0***	
Marital status																				
Not married	1.1	0.7–1.6	1.7*	1.3–2.1	1.7*	1.1–2.8	1.5	0.7–3.3	2.5	0.6–10.7	1.2	0.3–4.9	1.6	0.9–2.9	2.0*	1.6–2.3	1.1	0.8–1.5	1.6*	1.3–2.1
Married	1.0	—	1.0	—	1.0	—	1.0	—	1.0	—	1.0	— 1.0	—	1.0	—	1.0	—	1.0	—	
χ^2_1	*0.1*		*17.1***		*4.7***		*1.3*		*1.5*		*0.1*		*2.8*		*54.5***		*0.1*		*16.5***	
Urbanicity																				
Rural			0.8	0.6–1.1			0.6	0.3–1.3	1.0	0.6–1.6				0.6*	0.3–0.9	0.9	0.6–1.4	0.9	0.7–1.3	
Urban	not assessed		1.0	—	not assessed		1.0	—	1.0	—	not assessed		not assessed	1.0	—	1.0	—	1.0	—	
χ^2_1			*1.8*				*2.0*		*0.0*					—	*6.2***		*0.2*		*0.1*	
Age group (years)																				
14–24	1.0	0.6–1.8	1.0	0.6–1.8	1.0	0.5–1.9	1.0	0.4–2.8	—	—	4.4	0.9–20.8	1.2	0.4–3.5	1.2	0.8–1.8	1.0	0.6–1.6	1.6*	1.1–2.4
25–34	1.0	0.4–2.2	1.2	0.7–2.1	1.1	0.7–1.7	1.4	0.6–3.6	—	—	1.2	0.3–4.7	1.1	0.3–3.8	1.3	1.0–1.8	0.8	0.6–1.2	1.2	0.9–1.9
35–44	1.4	0.8–2.5	1.3	0.8–2.0	0.9	0.5–1.5	0.6	0.2–1.7	—	—	—	—	1.5	0.4–5	11.5*	1.2–2.0	1.1	0.7–1.7	1.2	0.9–1.9
45+	1.0	—	1.0	—	1.0	—	1.0	—	—	—	1.0	— 1.0	—	1.0	—	1.0	—	1.0	—	
χ^2_3	*1.5*		*0.5*		*0.7*		*3.1*		—		*3.7*		*0.9*		*11.0***		*2.1*		*6.5*	
(n)	–1,464		–6,902		–2,978		–1,534		–3,021		–1,029		–1,734		–7,076		–6,095		–5,877	

[a] OR = odds ratio, 95% CI = 95% confidence interval

* Significant at the .05 level, two-sided test

** Significant at the .05 level

Table 6. The effect of cohort (age at interview) in predicting lifetime major depressive episodes in the ICPE surveys

	Brazil		Canada		Chile		Czech Republic		Japan		Mexico		Netherlands		Turkey		US	
Cohort	OR[a]	95% CI[a]	OR[a]	95% CI[a]	OR[a]	95% CI[a]	OR[a]	95% CI[a]	OR[a]	95% CI[a]	OR[a]	95% CI[a]	OR[a]	95% CI[a]	OR[a]	95% CI[a]	OR[a]	95% CI[a]
14–24	2.2*	1.2–4.2	3.5*	2.1–6.0	8.3*	5.0–14.0	5.3*	2.0–13.5	10.9*	4.3–27.7	6.4*	1.9–21.8	8.4*	6.1–11.5	10.3*	5.7–18.6	5.5*	4.0–7.4
25–34	2.3*	1.3–4.1	1.7*	1.1–2.6	4.3*	2.9–6.4	2.6*	1.3–5.2	0.6	0.0–4.0	2.6	0.9–7.3	4.7*	3.7–5.9	2.9*	1.8–4.6	2.4*	1.9–3.1
35–44	2.0*	1.3–2.9	2.1*	1.5–2.9	1.8*	1.2–2.8	1.2	0.8–1.8	2.6	1.0–6.3	1.9	0.8–4.4	2.8*	2.3–3.4	2.1*	1.3–3.4	1.6*	1.2–2.1
45+	1.0	—	1.0	—	1.0	—	1.0	—	1.0	—	1.0	—	1.0	—	1.0	—	1.0	—
χ^2_3	15.3**		26.2**		87.6**		14.1**		28.6**		12.2**		210.7**		71.4**		159.9**	
(n)	(1,464)		(6,902)		(2,978)		(1,534)		(1,029)		(1,734)		(7,076)		(6,095)		(5,877)	

[a] OR = odds ratio, 95% CI = 95% confidence interval
* Significant at the 0.05 level, two-sided test
** Significant at the 0.05 level

(results not shown, but available on the ICPE Web page www.hcp.med.harvard.edu/icpe). The proportion of respondents with lifetime co-morbid anxiety-depression, whose anxiety began at an earlier age than their MDE, ranged from 53% in Germany to 80% in the Czech Republic, while the proportion of those whose MDE began at an earlier age than their anxiety ranged from 16% in the US to 32% in Mexico. The remainder had same-year onsets. It is noteworthy that the same-year onsets, although smaller in number than time-lagged onsets, were much more common than one would expect on the basis of chance alone.

Temporally primary anxiety disorders as predictors of subsequent MDE

A previously published analysis of the ICPE survey carried out in the US showed that temporally primary anxiety disorders are powerful predictors of the subsequent first onset of MDE (Kessler et al., 1996). A detailed analysis of the association between temporally primary panic and subsequent MDE in the US survey also showed that subsequent MDE was predicted as strongly by panic attacks as panic disorder, and as strongly by remitted panic as by active panic (Kessler et al., 1998c). These results suggest that panic is more likely to be a risk marker than a causal risk factor for subsequent MDE. In other cases, though, only active anxiety appears to predict MDE. This is true, for example, for primary social anxiety disorder in the US survey data (Kessler et al., 1999b).

The results in the ICPE surveys for the associations of primary anxiety with later MDE are presented in Table 7. These results are based on a series of discrete-time survival equations (Efron, 1988) in which active and remitted anxiety disorders were treated as time-varying predictors of the first onset of MDE, controlling for person-year, cohort, and gender. Several consistent patterns can be seen in the data. Firstly, all active primary anxiety disorders consistently and powerfully predict the subsequent first onset of MDE, with weighted mean ORs ranging from 9.4 for post-traumatic stress disorder to 81.6 for generalized anxiety disorder. Secondly, the associations between primary anxiety and secondary MDE consistently decrease significantly as the duration of the anxiety increases. Thirdly, although remitted primary anxiety disorders are substantially less powerful predictors than active primary anxiety disorders, the weighted mean ORs associated with most remitted anxiety disorders are nonetheless greater than 2. The exceptions are remitted post-traumatic stress disorder and agoraphobia, neither of which significantly predicts MDE.

More elaborate analyses of these data (results not shown) reveal that the decrease in the effects of active disorders is consistently non-linear across all countries and disorders. This is due to the extremely strong same-year association noted above. If we divide each measure of active anxiety disorders into two analyses – (i) first onset in the same year as the onset of MDE and (ii) onset at least one year prior to the onset of MDE – the OR for the first of these two coefficients is consistently much larger than that for the second. The second OR in each pair is consistently significant in these specifications and the evidence of temporal decay in the magnitude of effects decreases substantially. These last two results mean that statistically significant effects of active primary anxiety in predicting first onset of subsequent MDE persist for many years after the onset of the anxiety.

Speed of initial treatment contact

The ICPE surveys did not include a consistent set of questions on treatment of MDE. As a result, it is impossible to compare the rates of treatment across countries. However, the surveys in Canada and the US were carried out collaboratively and included identical questions on service use. It is consequently possible to say a few words about treatment that apply to these two countries. We focus on only one aspect of treatment: speed of initial treatment contact after the first onset of MDE. This is an aspect of treatment that is seldom examined, but one that can be studied. In the Canadian and US surveys, respondents were asked both about the age of onset of their MDE and about the age at which they first consulted a professional about their MDE.

Previous analyses of these data compared the age-of-onset reports to the age-of-contact reports and revealed that delays in initial treatment seeking of more than a decade were normal for both Canada and the US (Olfson et al., 1998). These previous analyses also showed that treatment contact has increased in recent cohorts in both Canada and the US, and that the speed of initial treatment contact is inversely related to age-of-onset of MDE in both countries (Olfson et al., 1998; Kessler et al., 1998d). The first of these results is important because it means that treatment rates are increasing over time. The second

Table 7. The effects of temporally primary anxiety disorders in predicting first onset of major depressive episodes, all countries combined

	Active				Remitted			
	Average effect		Time trend for onset in years		Average effect		Time trend for years since onset	
	OR[a]	95% CI[a]	OR[a]	95% CI[a]	OR[a]	95% CI[a]	OR[a]	95% CI[a]
I. Weighted mean associations across all 10 countries								
Agoraphobia	16.8*	13.5–21.0	0.8*	0.8–0.9	1.7	0.8–3.5	1.0	0.8–1.1
Generalized anxiety disorder	81.6*	62.2–107.1	0.7*	0.6–0.7	4.7*	1.1–20.6	0.7	0.4–1.2
Obsessive-compulsive disorder	52.7*	25.5–109.0	0.7*	0.6–0.8	3.2	0.4–23.8	0.7*	0.7–0.8
Panic disorder	43.5*	29.8–63.4	0.8*	0.7–0.8	2.8	0.9–9.3	0.8	0.7–1.1
Post-traumatic stress disorder	9.4*	6.2–14.2	0.9*	0.8–0.9	0.9	0.4–2.27	1.1	1.0–1.3
Simple phobia	10.7*	8.6–13.3	0.9*	0.9–0.9	3.6*	2.2–5.7	1.0	0.9–1.0
Social anxiety disorder	11.9*	9.6–14.8	0.9*	0.8–0.9	2.1*	1.2–3.8	1.0	0.9–1.1
II. Range of within country associations								
Agoraphobia	3.3–47.3*		0.7*–1.1		0.2*–56.3*		0.0*–1.3	
Generalized anxiety disorder	20.7*–876.8*		0.1*–0.9		0.0*–33.5*		0.0*–1.1	
Obsessive-compulsive disorder	3.0–877.3*		0.4*–0.9		—		0.0*–0.4*	
Panic disorder	6.8*–110.9*		0.6*–1.0		2.1–20.6*		0.5*–1.0	
Post-traumatic stress disorder	3.6–23.6*		0.9*–1.0		0.2–1.1		1.1–1.4*	
Simple phobia	0.6–43.2*		0.8*–1.2		0.2–47.6*		0.7–1.6*	
Social anxiety disorder	5.9*–28.2*		0.8*–0.9*		1.0–8.9*		0.1*–1.3	

[a] OR = odds ratio, 95% CI = 95% confidence interval
* Significant at the 0.05 level, two-sided test

result is also important because it suggests that early onset cases, which are often more persistent and severe than later-onset cases (Rothschild and Zimmerman, 2002), have the longest delays in obtaining treatment. Some limited information about the generalizability of this pattern was obtained by including questions about age of onset and speed of initial treatment contact in a cross-national survey of members of patient advocate groups in 11 countries around the world. This survey was carried out by the Global Alliance of Mental Illness Advocacy Networks (GAMIAN), an international consortium of patient advocacy groups. Consistent with the results reported in the ICPE surveys, a strong inverse relationship between age of onset and speed of initial treatment contact was found across all countries in the GAMIAN survey (Christiana et al., 2000).

Discussion

Caution is needed in interpreting the prevalence estimates reported here because of limited evidence on the reliability and validity of the different versions of the CIDI in the countries where the surveys were carried out. The lifetime prevalence estimates obtained in the surveys carried out in the US (UM–CIDI) and Germany (M–CIDI) are similar to those obtained by clinicians in confirmatory re-interviews administered in conjunction with these two surveys (American Psychiatric Association, 1994; Kessler et al., 1998a). However, similar clinical confirmation interviews were not carried out in the other countries. It is conceivable that the prevalence estimates based on the original WHO–CIDI are less accurate than those generated by the enhanced versions of the instrument (UM-CIDI and M-CIDI) or

that the CIDI diagnoses are less consistent with clinical diagnoses for other time frames (12-month and 30-day prevalence) than for lifetime prevalence.

The substantial cross-national variation in the estimated prevalence of MDE in the ICPE surveys is broadly consistent with the results of the previous cross-national epidemiological surveys that were reviewed in the introduction. It is interesting to note that these previous surveys consistently find the lowest prevalence estimates in Asian countries (Weissman et al., 1996), as do cross-national surveys of depression in primary care samples (Simon et al., 2002). The finding that Japan has by far the lowest prevalence in the ICPE surveys is consistent with this fact. It is not clear why prevalence is lower in Asian countries, nor why the larger pattern of cross-national differences exists. The broad substantive possibilities include cross-national differences in genetic vulnerability and environmental risk factors, and methodological possibilities include cross-national differences in the relevance of DSM criteria, in the sensitivity and specificity of the CIDI symptom questions, and in the willingness of respondents to admit depressive symptoms in an interview.

Simon et al. (2002), in a report from the WHO Psychological Problems in General Health Care (PPGHC) study (Christiana et al., 2000), shed some light on the methodological possibilities by showing that the clustering of depressive symptoms is consistent across PPGHC sites in 15 countries worldwide. This finding argues indirectly that DSM criteria are equally relevant and CIDI questions equally sensitive and specific across these countries. Simon and colleagues also found a strong dose-response relationship between the number of depressive symptoms and role impairment in all parts of the world. However, the level of role impairment among people with a given number of depressive symptoms was found to be inversely related to the estimated prevalence of depression, raising the possibility that cross-national prevalence differences might be due, at least in part, to cultural differences in the threshold for reporting depressive symptoms. This possibility cannot be investigated in the ICPE surveys due to between-survey differences in the specific items used to assess disorders.

Within the context of this limitation in the accuracy of between-country prevalence differences, the ICPE prevalence estimates are consistent with those of other community epidemiological surveys in suggesting that MDE is a commonly occurring disorder in many countries throughout the world (Weissman et al., 1996). Furthermore, the results of our indirect evaluation of persistence are consistent with long-term prospective studies (Hagnell and Grasbeck, 1990; Murphy et al., 1986; Steinhausen et al., 1998) in suggesting that MDE is a chronic episodic disorder that often persists throughout the life course. Our results regarding early age of onset are consistent with the finding of high prevalence of MDE in epidemiological studies of adolescents (Murphy et al., 1986).

The substantial persistence of MDE is especially important in light of the evidence that persistent depression can have a devastating effect on role functioning and quality of life (Rice et al., 1990; Wohlfarth et al., 1993; Kessler and Frank, 1997). For example, Wells and colleagues showed that the effects of MDE are comparable with, and in some cases greater than, the effects of such chronic physical disorders as hypertension, diabetes, and arthritis, to name only a few (Wells et al., 1989). Moreover, because of its early age of onset compared with most chronic disorders, MDE has powerful adverse effects on critical life-course transitions such as educational attainment (Kessler et al., 1995), teenage childbearing (Kessler et al., 1997a) and marital instability (Kessler et al., 1998e). It is surprising, in light of the evidence about these effects of MDE on subsequent life adversity, that evidence for a socioeconomic gradient in MDE is less clear in the ICPE surveys than in previous epidemiological studies (Canino et al., 1987; Bland et al., 1988a; Hwu et al., 1989; Lépine et al., 1989; Wells et al., 1989; Lee et al., 1990; Wittchen et al., 1992). Twelve-month MDE is inversely related to family income in the ICPE surveys carried out in the US and the Netherlands, but there is no meaningful income gradient in 12-month MDE in the other countries that assessed family income. Nor is there a meaningful association between education and 12-month MDE in any of the ICPE countries other than the US. This intriguing difference between countries in the effects of socioeconomic status requires more in-depth investigation. The ICPE surveys are consistent with previous surveys in confirming the finding that MDE is more common among women than men and among the unmarried than the married.

The consistent finding of increasing lifetime prevalence of MDE across successively more recent cohorts

is broadly consistent with the results of other recent epidemiological surveys (Robins and Regier, 1991; Cross-National Collaborative Group, 1992). Methodological factors, such as age-related differential recall or differential willingness to disclose the disorder, could play an important part in accounting for this pattern (Giuffra and Risch, 1994; Simon and Von Korff, 1995). However, other data patterns discussed elsewhere (Kessler et al., 1994; Kessler, 2000) are also consistent with there being a genuine increase in the prevalence of MDE in recent cohorts. One of the most telling of these patterns is the finding that the effects of early life adversities in predicting MDE are consistent across cohorts (Kessler et al., 1997b), a finding one would not expect if the apparent cohort effect was due entirely to recall failure. At the same time, it is likely that at least part of the apparent cohort effect is due to recall failure. It is noteworthy in this regard that the ICPE surveys show consistent evidence of lower persistence of MDE in recent cohorts, a finding that could be due to respondents in older cohorts selectively remembering more persistent and severe disorders. If this is so, then the actual lifetime prevalence of MDE might be considerably higher than estimated in the ICPE surveys and the actual chronicity of MDE might be lower than estimated in the ICPE surveys.

The finding that MDE is highly co-morbid with anxiety disorders is consistent with studies in both community samples (Merikangas et al., 1996) and clinical samples (Stein et al., 1995), as is the finding that anxiety disorders typically have an earlier age of onset than MDE (Bebbington, 1998). The kind of analysis reported here on primary anxiety disorders predicting subsequent MDE, however, has not been carried out in previous epidemiological surveys with the exception of the US survey (Kessler, 1997; Kessler et al., 1996; Kessler et al., 1998f). The results show that temporally primary anxiety disorders are powerful predictors of the subsequent first onset of MDE. It is less clear, though, whether this is true because anxiety disorders are causal risk factors for MDE or only markers of other more fundamental causes. If anxiety disorders are causal risk factors, we would expect that treatment and resolution of the anxiety disorders would help reduce the risk of the subsequent onset of MDE, while this would not be true if anxiety disorders were risk markers.

It is tempting to draw the conclusion that anxiety disorders are causal risk factors, based on the finding that active anxiety disorders are more powerful predictors of MDE than are remitted anxiety disorders. However, several other plausible causal mechanisms could bring about this specification. It might be, for example, that persistent anxiety disorders are associated with greater environmental adversity and/or genetic predisposition to MDE than remitted anxiety disorders, in which case the persistence of anxiety would be a marker of underlying causal factors that would not be affected by the treatment and resolution of the anxiety. However, there are at least two broad possibilities that are consistent with the assertion that persistent anxiety creates genuine risk for MDE. The first possibility is that MDE might, in some cases, be a resignation response that occurs once other attempts to resolve anxiety have been exhausted (Aksikal, 1984). The second possibility is that primary anxiety disorders might have neurological effects that predispose to MDE (Wittchen et al., 2000). If either of these possibilities is true, we would expect that resolution of the anxiety prior to the onset of the MDE would be successful in preventing the proportion of MDE cases that occur as a result of these processes.

The obvious broad-gauged test of these possibilities – an experimental treatment effectiveness trial that treats primary anxiety disorders and follows up both cases and controls for a sufficiently long period of time to determine whether the intervention has significantly reduced the risk of secondary MDE – has never been carried out. Given the age-of-onset distributions of anxiety and depression, such a study would ideally focus on screening, outreach, and treatment of adolescents with primary anxiety disorders and would follow these adolescents through the transition into early adulthood in order to track intervention effects. Even if the intervention did not prevent the onset of secondary MDE, there is the question of whether it might influence the course of MDE. We know that anxious-depression is generally more persistent and severe than pure depression (O'Leary et al., 2000). This being the case, a reasonable question is whether the course of depressive episodes would be less persistent and severe if previously existing anxiety disorders were effectively treated prior to the onset of the MDE.

We have little non-experimental evidence to go on in making even a provisional evaluation of the likely effects of the treatment of primary anxiety on subsequent depression. An exception is the work of Goodwin and Olfson (2001), which showed that the risk of subsequent MDE among survey respondents

with prior panic disorder was lower for those who received treatment for their panic than for those who did not. Based on this result, Goodwin and Olfson argued that treatment of primary panic might reduce the risk of developing MDE. It is noteworthy that this finding runs counter to the obvious non-causal interpretation of the association between primary anxiety and later MDE, which is that persistent-severe anxiety is a risk marker rather than a causal risk factor. If this non-causal interpretation were true, we would expect to find that survey respondents who received treatment for their panic would have a higher risk of subsequent MDE than those whose panic was untreated due to the selection bias for the most severe cases to have the highest probability of seeking treatment. Indeed, Goodwin and Olfson found the opposite pattern suggests that the causal interpretation has some plausibility.

Finally, the evidence reviewed from the ICPE Canadian and US surveys regarding speed of initial treatment contact is encouraging in that it shows an increase in treatment over successively more recent cohorts. This result is consistent with recent reports of increases in treatment of MDE based on trend studies of treatment records (Zito et al., 2002; Olfson et al., 2002). However, the finding that, despite this secular trend, treatment delays are longer for retrospectively reported early onset cases than later onset cases is discouraging. This is especially true in light of evidence concerning adverse effects of early-onset disorders on critical life-course transitions, such as schooling (Kessler et al., 1995), teen childbearing (Kessler et al., 1997a), marital timing (Forthofer, 1996), and marital stability (Kessler et al., 1998e).

Importantly, the vast majority of early-onset depressives experience these adverse life effects before they obtain any professional treatment (Christiana et al., 2000). There is no systematic research on the effectiveness of early outreach and treatment of early onset MDE in preventing these adverse effects, or on the impact of the prevention of such effects on the subsequent course of early onset MDE. As noted above, we do know that early onset MDE is more persistent and severe than later onset MDE. It is conceivable that at least part of the reason for this is that early onset MDE has structural effects (for example, effects on educational attainment, teen childbearing, marital disruption) that create lifelong structural vulnerabilities to recurrence. If so, then early treatment of MDE might be effective in influencing the subsequent illness course by reducing the risk of the onset of structural vulnerabilities. Another potentially important benefit of early outreach and treatment is that it might reduce the probability of neurological effects that are associated with depressive episodes becoming endogenous as the number of episodes increases (Weiss et al., 1998).

A great practical appeal of outreach and treatment of early onset MDE from a public health perspective is that most such cases occur during the school years. This means that screening and outreach can be carried out inexpensively by using schools for group screening. It might also be possible to co-ordinate treatment with the school system either by using school nurses to participate in outreach and treatment or by using the physical space of school classrooms during evenings and weekends as a site for delivering services. The availability of effective treatments for adolescent depression, reviewed by Ryan in this volume, adds to the appeal of this approach. In light of these considerations, the development and evaluation of the long-term effects of such school-based early screening, outreach, and treatment programs are important areas for future work.

Acknowledgements

Preparation of this article was supported by grants from the US Public Health Service (RO1 DA11121) and the US National Institute of Drug Abuse (U01 MH60220) and by unrestricted educational grants from the Pfizer Foundation and from the GRAD network through Wyeth Pharmaceuticals. This report presents data from 10 countries. The ECAS-SP study (Brazil) was funded by FAPESP, an agency of the State of São Paulo (Projecto Temático no. 93/0501-4). The MHS-OHS (Canada) was funded by the Ontario Ministry of Community and Social Services. The CPPS (Chile) was funded by FONDECYT (Nº 90-229, 92-233, 1971315, 1990325); Dirección de Investigación de la Universidad de Concepción (Nº 201.087.027-1.0); and the Pan American Health Organization / World Health Organization. The Czech CIDI Survey was funded by the Grant Agency (GA_R 313/97/9052) and the Internal Grant Agency of the Ministry of Health (IGA MZ _R _. NF/4978-3) of the Czech Republic. The EDSP was funded by the German Ministry of Research and Education (BMBF) as part of the Addiction Research Initiative (01EB94056). The GISSH (Japan) was supported by the Grant-in-Aid for Scientific Research (C) 1996-1999 (08670422 and 10670346) from the Ministry of Education, Science, Sports and Culture and by grants for the Comprehensive Research on Aging and Health (1996-2000) and for the Research on Pharmaceutical and Medical Survey (1999-2001) from the Ministry of Health

and Welfare. The EPM (Mexico) was funded by grant 2077-H9302 of the National Council of Science and Technology (CONACYT). NEMESIS was funded by the Netherlands Institute of Mental Health and Addiction (Trimbosinstituut) in Utrecht, the Netherlands Ministry of Health, Welfare and Sport (VWS), the Medical Sciences Department of the Netherlands Organization of Scientific Research (NWO), and the National Institute for Public Health and Environment (RIVM). The Mental Health Profile of Turkey was funded by the Turkish Ministry of Health. The NCS was funded by the US National Institute of Mental Health (RO1 MH46376 and RO1 MH 49098) and the W.T. Grant Foundation (90135190).

Excerpts from this paper were presented at the Major Depressive Disorders Consensus Conference, Edgartown, Martha's Vineyard, USA, 31 May 2002. This symposium was sponsored by the Global Research on Anxiety and Depression (GRAD) Network. The preparation of this paper was partially supported by the GRAD Network through an unrestricted educational grant by Wyeth-Ayerst Pharmaceuticals.

References

Akiskal HS. The interface of chronic depression with personality and anxiety disorders. Psychopharmacol Bull 1984; 20: 393–8.

American Psychiatric Association. Diagnostic and statistical manual of mental disorders, 3 edn Washington DC: American Psychiatric Association, 1980.

American Psychiatric Association. Diagnostic and statistical manual of mental disorders. 3 edn revised. Washington DC: American Psychiatric Association, 1987.

American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders. 4 edn. Washington DC: American Psychiatric Association, 1994.

Andrade L, de Lolio C, Gentil V, et al. Lifetime prevalence of mental disorders in a catchment area in São Paulo, Brazil. Paper presented at: VII Congress of the International Federation of Psychiatric Epidemiology Santiago, Chile, August 1996.

Bebbington PE. The social epidemiology of clinical depression. In Henderson AS, Burrows GD (eds) Handbook of Social Psychiatry. Amsterdam: Elsevier Science, 1988, pp. 87–102.

Bebbington PE, Hurry J, Tennant C, et al. Epidemiology of mental disorders in Camberwell. Psychol Med 1981; 11: 561–79.

Bijl RV, van Zessen G, Ravelli A, et al. The Netherlands Mental Health Survey and Incidence Study (NEMESIS): objectives and design. Soc Psychiatry Psychiatr Epidemiol 1998; 33: 581–6.

Bland RC, Newman SC, Orn H. Period prevalence of psychiatric disorders in Edmonton. Acta Psychiatr Scand Suppl 1988b; 338: 33–42.

Bland RC, Orn H, Newman SC. Lifetime prevalence of psychiatric disorders in Edmonton. Acta Psychiatr Scand Suppl 1988a; 338: 24–32.

Blazer DG, Kessler RC, McGonagle KA, et al. The prevalence and distribution of major depression in a national community sample: The National Comorbidity Survey. Am J Psychiatry 1994; 151: 979–86.

Canino GJ, Bird HR, Shrout PE, et al. The prevalence of specific psychiatric disorders in Puerto Rico. Arch Gen Psychiatry 1987; 44: 727–35.

Caraveo J, Martinez J, Rivera B. Un modelo para estudios epidemiológicos de la salud mental y la morbilidad. Salud Mental 1998; 21: 48–57.

Cheng TA. Sex difference in the prevalence of minor psychiatric morbidity: a social epidemiological study in Taiwan. Acta Psychiatr Scand 1989; 80: 395–407.

Christiana JM, Gilman SE, Guardino M, et al. Duration between onset and time of obtaining initial treatment among people with anxiety and mood disorders: an international survey of members of mental health patient advocate groups. Psychol Med 2000; 30: 693–703.

Christie KA, Burke JD Jr, Regier DA, et al. Epidemiologic evidence for early onset of mental disorders and higher risk of drug abuse in young adults. Am J Psychiatry 1988; 145: 971–5.

Comstock GW, Helsing KJ. Symptoms of depression in two communities. Psychol Med 1976; 6: 551–63.

Cross-National Collaborative Group. The changing rate of major depression. Cross-national comparisons. JAMA 1992; 268: 3098–105.

Dragomirecká E, Baudiš P, Smolová E, et al. Psychiatrická nemocnost obyvatel České republiky.[Psychiatric morbidity of inhabitants of the Czech Republic]. Čes. a Slov. Psychiat 2002; 98: 72–80.

Efron B. Logistic regression, survival analysis, and the Kaplan-Meier curve. Journal of the American Statistical Association 1988; 83: 414–25.

Forthofer MS, Kessler RC, Story AL, et al. The effects of psychiatric disorders on the probability and timing of first marriage. J Health Soc Behav 1996; 37: 121–32.

Giuffra LA, Risch N. Diminished recall and the cohort effect of major depression: a stimulation study. Psychol Med 1994; 24: 375–83.

Goodwin R, Olfson M. Treatment of panic attack and risk of major depressive disorder in the community. Am J Psychiatry 2001; 158: 1146–8.

Hagnell O, Grasbeck A. Comorbidity of anxiety and depression in the Lundby 25-year prospective study: the pattern of subsequent episodes. In Maser JD, Cloninger CR (eds) Comorbidity of Mood and Anxiety Disorders. Washington, D.C.: American Psychiatric Press, 1990: 139–52.

Helgason T. Epidemiology of mental disorders in Iceland. Acta Psychiatr Scand 1964; 40(173, suppl): 115–32.

Hosmer DW, Lemeshow S. Applied Logistic Regression. New York: John Wiley & Sons, 1989.

Hwu HG, Yeh EK, Chang LY. Prevalence of psychiatric disorders in Taiwan defined by the Chinese Diagnostic Interview Schedule. Acta Psychiatr Scand 1989; 79: 136–47.

Kaplan EL, Meier P. Nonparametric estimation from incomplete observations. J Am Stat Assoc 1958; 53: 281–4.

Kessler RC. Epidemiology of psychiatric comorbidity. In Tsuang MT, Tohen M, Zahner GEP, eds. Textbook in Psychiatric Epidemiology. New York: John Wiley & Sons; 1995: 179–97.

Kessler RC. The prevalence of psychiatric comorbidity. In Wetzler S, Sanderson WC (eds) Treatment Strategies for Patients with Psychiatric Comorbidity. New York: John Wiley & Sons, 1997: 23–48.

Kessler RC. The World Health Organization International Consortium in Psychiatric Epidemiology (ICPE): Initial work and future directions – the NAPE lecture 1998. Acta Psychiatr Scand 1999; 99: 2–9.

Kessler RC. Gender differences in major depression: epidemiologic findings. In Frank E (ed.) Gender and its Effect on Psychopathology. Washington DC: American Psychiatric Press, 2000, 61–84.

Kessler RC, Avenevoli S, Merikangas KR. Mood disorders in children and adolescents: An epidemiologic perspective. Biol Psychiatry 2001; 49: 1002–14.

Kessler RC, Berglund PA, Foster CL, et al. Social consequences of psychiatric disorders. II. Teenage parenthood. Am J Psychiatry 1997a; 154: 1405–11.

Kessler RC, Davis CG, Kendler KS. Childhood adversity and adult psychiatric disorder in the US National Comorbidity Survey. Psychol Med 1997b; 27: 1101–19.

Kessler RC, DuPont RL, Berglund PA, et al. Impairment in pure and comorbid generalized anxiety disorder and major depression at 12 months in two national surveys. Am J Psychiatry 1999a; 156: 1915–23.

Kessler RC, Foster CL, Saunders WB, et al. Social consequences of psychiatric disorders. I. Educational attainment. Am J Psychiatry 1995; 152: 1026–32.

Kessler RC, Frank RG. The impact of psychiatric disorders on work loss days. Psychol Med 1997; 27: 861–73.

Kessler RC, McGonagle KA, Nelson CB, et al. Sex and depression in the National Comorbidity Survey. II. Cohort effects. J Affect Disord 1994; 30: 15–26.

Kessler RC, McGonagle KA, Zhao S, et al. Lifetime and 12-month prevalence of DSM-III-R psychiatric disorders in the United States: results from the National Comorbidity Survey. Arch Gen Psychiatry 1994; 51: 8–19.

Kessler RC, Nelson CB, McGonagle KA, et al. Comorbidity of DSM-III-R major depressive disorder in the general population: Results from the US National Comorbidity Survey. Br J Psychiatry Suppl 1996; 30: 17–30.

Kessler RC, Olfson M, Berglund PA. Patterns and predictors of treatment contact after first onset of psychiatric disorders. Am J Psychiatry 1998d; 155: 62–9.

Kessler RC, Stang P, Wittchen H-U, et al. Lifetime panic-depression comorbidity in the National Comorbidity Survey. Arch Gen Psychiatry 1998b; 55: 801–8.

Kessler RC, Stang PE, Wittchen H-U, et al. Lifetime panic-depression comorbidity in the National Comorbidity Survey. Arch Gen Psychiatry 1998c; 55: 801–8.

Kessler RC, Stang P, Wittchen H-U et al. Lifetime panic-depression comorbidity in the National Comorbidity Survey. Arch Gen Psychiatry 1998f; 55: 801–8.

Kessler RC, Stang P, Wittchen H-U, et al. Lifetime comorbidities between social phobia and mood disorders in the US National Comorbidity Survey. Psychol Med 1999b; 29: 555–67.

Kessler RC, Walters EE, Forthofer MS. The social consequences of psychiatric disorders. III. Probability of marital stability. Am J Psychiatry 1998e; 155: 1092–6.

Kessler RC, Wittchen HU, Abelson JM, et al. Methodological studies of the Composite International Diagnostic Interview (CIDI) in the U.S. National Comorbidity Survey. Int J Methods Psychiatr Res 1998a; 7: 33–55.

Kılıç C. Mental Health Profile of Turkey: Main Report. Ankara: Ministry of Health Publications, 1998.

Kish L, Frankel MR. Inferences from complex samples. J R Stat Soc 1974; 36: 1–37.

Lee CK, Han JH, Choi JO. The epidemiological study of mental disorders in Korea (IX): Alcoholism, anxiety and depression. Seoul J Psychiatry 1987; 12: 183–91.

Lee CK, Kwak YS, Yamamoto J, et al. Psychiatric epidemiology in Korea. Part I. Gender and age differences in Seoul. J Nerv Ment Dis 1990; 178: 247–52.

Lépine JP, Pariente P, Boulenger JP, et al. Anxiety and depressive disorders in a French population: methodology and preliminary results. Psychiatric Psychobiology 1989; 4: 267–74.

Lin TY. A study of incidence of mental disorders in Chinese and other cultures. Psychiatry 1953; 16: 315–35.

Merikangas KR, Angst J, Eaton W, et al. Comorbidity and boundaries of affective disorders with anxiety disorders and substance misuse: results of an international task force. Br J Psychiatry Suppl 1996; (30): 58–67.

Murphy JM, Olivier DC, Sobol AM, et al. Diagnosis and outcome: depression and anxiety in a general population. Psychol Med 1986; 16: 117–26.

O'Leary D, Costello F, Gormley N, et al. Remission onset and relapse in depression. An 18-month prospective study of course for 100 first admission patients. J Affect Disord 2000; 57: 159–71.

Offord DR, Boyle M, Campbell D, et al. Mental health in Ontario: Selected Findings from the Mental Health Supplement to the Ontario Health Survey. Toronto, Queen's Printer for Ontario, 1994

Olfson M, Kessler RC, Berglund PA, et al. Psychiatric disorder onset and first treatment contact in the United States and Ontario. Am J Psychiatry 1998; 155: 1415–22.

Olfson M, Marcus SC, Druss B, et al. National trends in the outpatient treatment of depression. JAMA 2002; 287: 203–9.

Reed V, Gander F, Pfister H, et al. To what degree does the Composite International Diagnostic Interview (CIDI) correctly identify DSM-IV disorders? Testing validity issues in a clinical sample. Int J Methods Psychiatr Res 1998; 7: 142–55.

Rice DP, Kelman S, Miller LS, et al. The Economic Costs of Alcohol and Drug Abuse and Mental Illness: 1985. Rockville MD: Alcohol, Drug Abuse, and Mental Health Administration; 1990

Robins LN, Helzer JE, Croughan J, et al. National Institute of Mental Health Diagnostic Interview Schedule: its history, characteristics and validity. Arch Gen Psychiatry 1981; 38: 381–9.

Robins LN, Regier DA (eds). Psychiatric disorders in America: the Epidemiologic Catchment Area Study. New York: Free Press, 1991.

Robins LN, Wing J, Wittchen H-U, et al. The Composite International Diagnostic Interview: an epidemiologic instrument suitable for use in conjunction with different diagnostic systems and in different cultures. Arch Gen Psychiatry 1988; 45: 1069–77.

Rothschild L, Zimmerman M. Borderline personality disorder and age of onset in major depression. J Person Disord 2002; 16: 189–99.

Simon GE, Goldberg DP, Von Korff M, et al. Understanding cross-national differences in depression prevalence. Psychol Med 2002; 32: 585–94.

Simon GE, Von Korff M. Recall of psychiatric history in cross-sectional surveys: implications for epidemiologic research. Epidemiol Rev 1995; 17: 221–7.

Solomon DA, Keller MB, Leon AC, et al. Multiple recurrences of major depressive disorder. Am J Psychiatry 2000; 157: 229–33.

Stein MB, Kirk P, Prabhu V, et al. Mixed anxiety-depression in a primary-care clinic. J Affect Disord 1995; 34: 79–84.

Steinhausen HC, Meier M, Angst J. The Zurich long-term outcome study of child and adolescent psychiatric disorders in males. Psychol Med 1998; 28: 375–83.

Üstün T, Sartorious N. Mental Illness in General Health Care. New York: John Wiley & Sons, 1995.

Vega WA, Kolody B, Aguilar-Gaxiola S, et al. Lifetime prevalence of DSM-III-R psychiatric disorders among urban and rural Mexican Americans in California. Arch Gen Psychiatry 1998; 55: 771–8.

Weiss SR, Post RM. Kindling: separate vs. shared mechanisms in affective disorders and epilepsy. Neuropsychobiology 1998; 38:167–80.

Weissman MM, Bland RC, Canino GJ, et al. Cross-national epidemiology of major depression and bipolar disorder. JAMA 1996; 276: 293–9.

Weissman MM, Bland RC, Canino GJ, et al. The cross-national epidemiology of panic disorder. Arch Gen Psychiatry 1997; 54: 305–9.

Weissman MM, Myers JK. Affective disorders in a US urban community. The use of research diagnostic criteria in an epidemiological survey. Arch Gen Psychiatry 1978; 35: 1304–11.

Wells JE, Bushnell JA, Hornblow AR, et al. Christchurch Psychiatric Epidemiology Study. Part I. Methodology and lifetime prevalence for specific psychiatric disorders. Aust N Z J Psychiatry 1989; 23: 315–26.

Wells K, Stewart A, Hays RD, et al. The functioning and well-being of depressed patients: results from the Medical Outcomes Study. JAMA 1989; 262: 914–19.

WHO International Consortium of Psychiatric Epidemiology. Cross-national comparisons of the prevalences and correlates of mental disorders. Bull World Health Organ 2000; 78: 413–26.

Wittchen H-U. Reliability and validity studies of the WHO-Composite International Diagnostic Interview (CIDI): a critical review. J Psychiatr Res 1994; 28: 57–84.

Wittchen H-U, Essau CA, Von Zerssen D, et al. Lifetime and six-month prevalence of mental disorders in the Munich Follow-up Study. Eur Arch Psychiatry Clin Neurosci 1992; 241: 247–58

Wittchen, H-U, Kessler, RC, Pfister H, et al. Why do people with anxiety disorders become depressed? A prospective-longitudinal community study. Acta Psychiatr Scan Suppl 2000 (406): 14–23.

Wittchen H-U, Perkonigg A, Lachner G, et al. Early Developmental Stages of Psychopathology study (EDSP): objectives and design. Eur Addict Res 1998; 4: 18–27.

Wittchen H-U, Zhao S, Abelson JM, et al. Reliability and procedural validity of UM-CIDI DSM-III-R phobic disorders. Psychol Med 1996; 26: 1169–77.

Wohlfarth TD, Van den Brink W, Ormel J, et al. The relationship between social dysfunctioning and psychopathology among primary care attenders. Br J Psychiatry 1993; 163: 37–44.

World Health Organization. Composite International Diagnostic Interview (CIDI, Version 1.0). Geneva: World Health Organization, 1990

World Health Organization. Composite International Diagnostic Interview (CIDI, Version 2.1). Geneva: World Health Organization, 1997.

Zito JM, Safer DJ, DosReis S, et al. Rising prevalence of antidepressants among US youths. Pediatrics 2002; 109: 721–7.

Correspondence: R.C. Kessler, Harvard Medical School, 180 Longwood Avenue, Boston MA 02115, USA.
Telephone (+1) 617 432 3587.
Fax (+1) 617 432 3588.
Email: kessler@hcp.med.harvard.edu.
Also:
T.B. Ustun, Assessment, Classification and Epidemiology, WHO, 1211 Geneva 27, Switzerland.
Telephone (+41) 4122 79 13609.
Fax: (+41) 4122 791 3610.
Email: ustunt@who.ch.

Further information is available on the WHO ICPE Web site at URL www.hcp.med.harvard.edu/icpe and on the Global Research on Anxiety and Depression (GRAD) network at URL www.gradnetwork.com. Additional results archived at http://www.hcp.med.harvard.edu/icpe/relatedmaterials.htm.