

Increased Risk of Affective Disorders in Males after Second Trimester Prenatal Exposure to the Dutch Hunger Winter of 1944–45*

ALAN S. BROWN, EZRA S. SUSSER, SHANG P. LIN, RICHARD NEUGEBAUER and JACK M. GORMAN

Background. Prenatal and perinatal factors have been linked to affective disorders. We therefore undertook an exploratory study to determine whether prenatal exposure to severe famine was associated with an increased risk of affective disorders.

Method. Monthly birth cohorts that were exposed and unexposed to the Dutch Hunger Winter of 1944–45 were identified. The cumulative incidences of affective psychoses and neurotic depression (ICD–9 criteria) were compared between exposed and unexposed cohorts during each trimester of gestation.

Results. The relative risk (RR) of affective psychosis (broad and restricted definitions) among persons exposed to famine during the second trimester was significantly increased (broad: RR (95% confidence interval) = 1.62 (1.19, 2.20); restricted: 1.59 (1.14, 2.21)). Separate analysis by gender showed a significant association among males (broad: 2.26 (1.43, 3.57); restricted: 2.40 (1.49, 3.89)), but not females (broad: 1.28 (0.84, 1.94); restricted: 1.17 (0.73, 1.86)). The risk of neurotic depression was not increased after prenatal famine exposure.

Conclusions. These results suggest a possible relationship between prenatal famine during the second trimester and affective psychosis, lending plausibility to reports that have associated affective psychoses with prenatal exposures. Further studies of this relationship are warranted.

A growing number of investigations suggest a link between prenatal factors and subsequent risk of psychiatric disorders in the offspring (Meyer-Bahlburg *et al*, 1985; Susser & Lin, 1992; Buka *et al*, 1993; Susser *et al*, 1995). Some of these studies have indicated a potential relationship between prenatal/perinatal factors and affective disorders (Salk *et al*, 1985; Jacobson *et al*, 1987; Crow *et al*, 1991; Done *et al*, 1991). Prenatal exposures, including influenza and obstetric complications, have been associated with affective psychosis (Crow *et al*, 1991; Done *et al*, 1991) and Lewis & Murray (1987) have reported obstetric complications in 11% of bipolar depressives. In addition, prenatal and perinatal disturbances have been associated with suicide during adolescence (Salk *et al*, 1985) and adulthood (Jacobson *et al*, 1987).

In recent follow-up investigations of the original Dutch famine study (Stein *et al*, 1975), the relationship between prenatal exposure to famine and schizophrenia in adulthood has been tested (Susser & Lin, 1992; Susser *et al*, 1995). The well-demarcated period of food deprivation, documentation of the severity of famine and relatively complete case ascertainment enabled the investigators to compare the risk of schizophrenia between cohorts exposed and unexposed to

nutritional deprivation during the first trimester. They demonstrated that cohorts exposed to famine in early gestation had a more than twofold increase in the risk of schizophrenia in both men and women, suggesting that prenatal nutritional deficiency may play a causal role in this disorder.

We sought to capitalise on the virtually unique opportunity afforded by the tragedy of the Dutch famine to examine the possible contribution of prenatal famine exposure to risk for affective disorders in adulthood. Data from the Dutch Psychiatric Registry on affective disorders in these cohorts have been obtained. We compared the incidence of affective disorders between cohorts exposed and unexposed to nutritional deprivation during each trimester. Because prior studies have indicated that prenatal exposures during the first (Susser & Lin, 1992) and second (Crow *et al*, 1991) trimesters, and events during the perinatal period (Lewis & Murray, 1987; Done *et al*, 1991) are associated with the later occurrence of psychiatric disorders, we had no a priori reason to expect a differential effect according to trimester of exposure. Although we did not hypothesise that there would be a gender difference in the effect of prenatal famine on affective disorders, we explored this possibility in our analyses.

*Presented in part at the 146th Annual Meeting (New Research) of the American Psychiatric Association, San Francisco, CA, 24 May 1993.

Method

Definition of exposure

The definition of exposed and unexposed birth cohorts has already been presented (Susser & Lin, 1992), and will thus be summarised here. During World War II, the Nazi blockade of occupied Holland created a sharp decline in food intake in the western or 'famine' region from October 1944 to May 1945. All six cities in this region with populations greater than 40 000 were included in the original study by Stein *et al* (1975). These cities were Amsterdam, The Hague, Haarlem, Leiden, Rotterdam and Utrecht. Official food rations fell to very

Table 1
Food rations by trimester in monthly birth cohorts

Year of birth	Month of birth	Average daily intake (kcal)		
		First trimester	Second trimester	Third trimester
1944	January	1697	1717	1743
	February	1670	1727	1747
	March	1713	1713	1717
	April	1717	1743	1633
	May	1727	1747	1567
	June	1713	1717	1563
	July	1743	1633	1578
	August	1747	1567	1512
	September	1717	1563	1462
	October	1633	1578	1405
	November	1567	1512	1414
	December	1563	1462	1277
1945	January	1578	1405	1011
	February	1512	1414	740
	March	1462	1277	590
	April	1405	1011	618
	May	1414	740	670
	June	1277	590	868
	July	1011	618	1361
	August	740	670	1757
	September	590	868	2045
	October	618	1361	1995
	November	670	1757	2083
	December	868	2045	2127
1946	January	1361	1995	2171
	February	1757	2083	2514
	March	2045	2127	2857
	April	1995	2171	3200
	May	2083	2514	3200
	June	2127	2857	3200
	July	2171	3200	3200
	August	2514	3200	3200
	September	2857	3200	3200
	October	3200	3200	3200
	November	3200	3200	3200
	December	3200	3200	3200

Source: Stein *et al* (1975).

low levels in this famine region, less than 4200 kJ (1000 kcal) per person per day between February and April 1945. In the original Dutch famine study, the mean intake (kcal/day) in the official ration in the first, second and third trimesters was calculated for each of the 36 monthly birth cohorts in 1944–1946 (Stein *et al*, 1975) (Table 1). These data were used in the present study to identify the monthly birth cohorts that were exposed to severe food deprivation (average rations < 4200 kJ (1000 kcal)/day) during each trimester. Cohorts exposed during the first trimester were born between August and December, 1945; those exposed during the second trimester were born between May and September, 1945; and those exposed during the third trimester were born between February and June, 1945. Unexposed cohorts had average daily rations that were greater than 4200 kJ (1000 kcal)/day, and consisted of those cohorts born in all other months in 1944 and 1946 less the respective periods of exposure for each trimester.

Estimation of numbers at risk for affective disorders

The number of men and women who survived to at least age 18, and thus were potentially at risk for hospitalised affective disorders in adulthood, was calculated from the number of live births and deaths up to age 18 for each monthly birth cohort (Stein *et al*, 1975; Susser & Lin, 1992).

Estimation of numbers with affective disorders

The numbers of men and women in each monthly birth cohort with in-patient admissions for affective disorders from 1978 to 1991 were obtained from the Dutch Psychiatric Registry, which contains information on all in-patient psychiatric admissions to psychiatric and university hospitals in Holland since 1978. The abstracted data comprised month and municipality of birth, and most recent psychiatric discharge diagnosis, based on the *International Classification of Diseases*, ninth revision (ICD-9) (World Health Organization, 1978).

Classification of affective disorders

Affective disorder diagnoses were categorised a priori into two main groups for the primary analyses: affective psychosis and neurotic depression (ICD-9, 1978). Affective psychosis consists of all 296 ICD-9 diagnoses, which are defined as "severe disturbances of mood (mania and/or depression) accompanied by mood-congruent psychotic symptoms". We also examined a subcategory of 296, "affective psychosis, restricted", consisting of

296.0–296.4. This subcategory excluded those conditions denoted as ‘other’ or ‘not specified’. Neurotic depression (300.4, ICD–9) is characterised by “disproportionate depression without psychotic symptoms”.

Measures of effect

For each birth cohort, we calculated the risk or cumulative incidence of hospitalisation for affective disorder (the number of men and women with a diagnosis of affective disorder in the psychiatric registry from 1978 through 1991 divided by the number who survived to age 18). Separate calculations were made for “affective psychosis, restricted”, “affective psychosis, broad”, and neurotic depression. The relative risk (with 95% confidence intervals) was obtained by calculating the ratio of the risk of each affective disorder diagnosis in exposed v. unexposed birth cohorts. Relative risks were calculated for first, second and third trimester famine exposure.

Males and females may differ in terms of vulnerability to prenatal insult (Kline *et al*, 1989) and rates of affective disorder (Weissman *et al*, 1991), the latter suggesting that risk factors may exert differential effects on males and females. As a result, we decided to explore possible gender differences in the risk of affective disorders after prenatal famine exposure.

In the calculation of the above relative risks, cohorts listed as exposed during a particular trimester usually included individuals who were exposed during an adjacent trimester(s). For example, those listed as second trimester exposed included individuals exposed during the second plus either the first or third trimesters. Thus, it was necessary to separate the effects of first, second and third trimester famine exposure on the risk of affective psychosis. We addressed this difficulty by fitting a logistic regression model with first trimester, second trimester and third trimester famine as independent variables and affective psychosis as the dependent variable. We then calculated the odds ratios for exposure to famine during each individual trimester by their fitted regression coefficients in the model (Model I). Given the possible gender differences in prenatal disturbances and rates of affective disorder (see above), it was also necessary to control for the possible confounding effect of gender. This was accomplished by including the gender variable along with the three trimester famine variables in the logistic regression model (Model II). Finally, to determine whether the effect of prenatal famine differed significantly between men and women, we included additional

terms that represented the interaction between famine variables and gender in the model (Model III). A significant interaction term in this stage would necessitate reporting the results separately for men and women. For each procedure described above, two analyses were performed, one for “affective psychosis, broad”, and the other for “affective psychosis, restricted”.

Results

Univariate analysis

The relative risks of “affective psychosis, broad”, “affective psychosis, restricted” and neurotic depression after famine exposure during each trimester are presented in Tables 2–4. For males and females combined, there was a large and significant association between second trimester exposure to famine and the risk of affective psychosis, both ‘broad’ and ‘restricted’; a lesser association was found between affective psychosis and famine exposure during the third trimester. There was no indication of a first trimester effect. When genders were analysed separately, the relative risk of affective psychosis after second trimester famine exposure was significantly elevated only in men; a lesser association was found between affective psychosis in men and third trimester exposure.

Multivariate analysis

The results of the logistic regression analyses are presented in Tables 5 and 6. Model I analyses showed that, controlling for the effects of first and third trimester famine, the risks of both “affective psychosis, broad” and “affective psychosis, restricted” were significantly increased after second trimester famine exposure. The odds ratios of both affective psychosis categories were not increased by either first trimester or third trimester famine exposure (Table 5).

We next examined the effect of gender on risk of affective psychosis (Table 5). As expected, when the gender variable was included in the logistic model (Model II), its effect on risk of affective psychosis was significant; women were at higher risk than men. Moreover, the effect of second trimester famine exposure remained significant. Having established independent effects of second trimester famine and gender, we entered a term representing famine-by-gender interaction into the model (Model III), and found a significant interaction between famine and gender for “affective psychosis, restricted” ($P=0.03$) and a nearly significant

Table 2
Affective disorders after exposure to famine in the first trimester

	All				Men				Women			
	Incidence ¹		RR (95% CI)	Exposed	Incidence ¹		RR (95% CI)	Exposed	Incidence ¹		RR (95% CI)	Exposed
	Unexposed	Exposed			Unexposed	Exposed			Unexposed	Exposed		
No. in cohort	136 691	9656	-	69 943	4984	-	66 748	4672	-	-	-	
Affective psychosis, broad	2.15 (294)	2.17 (21)	1.01 (0.65, 1.57)	1.52 (106)	1.81 (9)	1.19 (0.60, 2.35)	2.82 (188)	2.57 (12)	0.91 (0.51, 1.63)	0.97 (0.53, 1.79)	2.35 (11)	
Affective psychosis, restricted	1.86 (254)	1.97 (19)	1.06 (0.66, 1.69)	1.32 (92)	1.61 (8)	1.22 (0.59, 2.51)	2.43 (162)	2.35 (11)	0.97 (0.53, 1.79)	0.74 (0.34, 1.57)	1.50 (7)	
Neurotic depression	1.62 (226)	1.66 (16)	1.00 (0.60, 1.66)	1.29 (90)	1.81 (9)	1.40 (0.71, 2.78)	2.04 (136)	2.04 (136)	0.91 (0.51, 1.63)	0.97 (0.53, 1.79)	1.50 (7)	

1. Cumulative incidence per 1000, 1978-1991. Numbers in parentheses are numbers of cases.

Unexposed: ration > 4200 kJ per day; exposed ration < 4200 kJ per day. RR, relative risk; CI, confidence interval.

Table 3
Affective disorders after exposure to famine in the second trimester

	All				Men				Women			
	Incidence ¹		RR (95% CI)	Exposed	Incidence ¹		RR (95% CI)	Exposed	Incidence ¹		RR (95% CI)	Exposed
	Unexposed	Exposed			Unexposed	Exposed			Unexposed	Exposed		
No. in cohort	131 702	14 645	-	67 467	7460	-	64 235	7185	-	-	-	
Affective psychosis, broad	2.03 (267)	3.28 (48)	1.62 (1.19, 2.20)	1.36 (92)	3.08 (23)	2.26 (1.43, 3.57) ²	2.72 (175)	3.50 (25)	1.28 (0.84, 1.94)	1.17 (0.73, 1.86)	2.78 (20)	
Affective psychosis, restricted	1.76 (232)	2.80 (41)	1.59 (1.14, 2.21)	1.17 (79)	2.82 (21)	2.40 (1.49, 3.89) ²	2.38 (153)	2.78 (20)	1.17 (0.73, 1.86)	0.97 (0.56, 1.68)	1.95 (14)	
Neurotic depression	1.63 (215)	1.84 (27)	1.13 (0.76, 1.68)	1.27 (86)	1.74 (13)	1.37 (0.76, 2.45)	2.01 (129)	1.95 (14)	0.97 (0.56, 1.68)	0.97 (0.56, 1.68)	1.95 (14)	

1. Cumulative incidence per 1000, 1978-1991. Numbers in parentheses are numbers of cases.

2. The 95% confidence interval does not include 1.

Unexposed: ration > 4200 kJ per day; exposed ration < 4200 kJ per day. RR, relative risk; CI, confidence interval.

Table 4
Affective disorders after exposure to famine in the third trimester

	All				Men				Women			
	Incidence ¹		RR (95% CI)	Exposed	Incidence ¹		RR (95% CI)	Exposed	Incidence ¹		RR (95% CI)	Exposed
	Unexposed	Exposed			Unexposed	Exposed			Unexposed	Exposed		
No. in cohort	128 659	17 668	-	65 966	8941	-	62 693	8727	-	-	-	
Affective psychosis, broad	2.04 (262)	3.00 (53)	1.47 (1.10, 1.98)	1.42 (94)	2.35 (21)	1.65 (1.03, 2.64) ²	2.68 (168)	3.67 (32)	1.37 (0.94, 2.0)	1.16 (0.75, 1.78)	2.75 (24)	
Affective psychosis, restricted	1.78 (229)	2.49 (44)	1.40 (1.01, 1.93)	1.21 (80)	2.24 (20)	1.84 (1.13, 3.01) ²	2.38 (149)	2.75 (24)	1.16 (0.75, 1.78)	0.91 (0.54, 1.52)	1.83 (16)	
Neurotic depression	1.66 (214)	1.58 (28)	0.95 (0.64, 1.41)	1.32 (87)	1.34 (12)	1.02 (0.56, 1.86)	2.03 (127)	1.83 (16)	0.91 (0.54, 1.52)	0.91 (0.54, 1.52)	1.83 (16)	

1. Cumulative incidence per 1000, 1978-1991. Numbers in parentheses are numbers of cases.

2. The 95% confidence interval does not include 1.

Unexposed: ration > 4200 kJ per day; exposed ration < 4200 kJ per day. RR, relative risk; CI, confidence interval.

Table 5
Affective psychosis after prenatal exposure to famine:
logistic regression models

Risk factors and covariates	Affective psychosis, broad		Affective psychosis, restricted	
	Odds ratio	(95% CI)	Odds ratio	(95% CI)
Model I				
First trimester	0.87	(0.53, 1.42)	0.91	(0.54, 1.52)
Second trimester	1.53	(1.05, 2.22) ¹	1.52	(1.01, 2.28) ¹
Third trimester	1.25	(0.89, 1.76)	1.19	(0.82, 1.73)
Model II				
Gender	1.82	(1.45, 2.30) ¹	1.81	(1.42, 2.32) ¹
First trimester	0.87	(0.53, 1.42)	0.91	(0.54, 1.52)
Second trimester	1.53	(1.05, 2.22) ¹	1.52	(1.01, 2.27) ¹
Third trimester	1.24	(0.88, 1.75)	1.19	(0.82, 1.72)

1. Confidence limits do not include 1: indicates statistical significance.

interaction for “affective psychosis, broad” ($P=0.07$).

Thus, we analysed the effect of second trimester famine (adjusting for first and third trimester famine) on the risk of affective psychosis separately in men and women (Table 6). Our results indicated a significantly increased risk of “affective psychosis, broad” and “affective psychosis, restricted” after second trimester famine exposure in males but not females.

Analysis controlling for season of birth

In order to control for any possible season of birth effect that could account for our findings, we compared the risk of affective disorders between male birth cohorts who had been exposed to famine in the second trimester (born May–September, 1945) with unexposed male birth cohorts born in the same months in 1944 and 1946. Rather than diminishing, the relative risk (with 95% CI) of “affective psychosis, broad” increased to 2.81 (1.62, 4.85) and of “affective psychosis, restricted” to 2.75 (1.56, 4.87). The relative risk (with 95% CI) of neurotic depression was 1.15 (0.62, 2.15), similar to the result of our prior analysis (see Tables 2–4).

Discussion

There have been several recent reports of associations between affective disorders and exposures during the prenatal and perinatal periods. In a study of pregnancy and birth complications in the British perinatal mortality survey sample, Done *et al* (1991) found an increased risk of factors predisposing to perinatal death among patients with affective psychosis; specific associations were observed between affective psychosis and two factors, diminished length of gestation and vitamin K treatment at the time of birth. Crow *et al* (1991), in an investigation of individuals in whom prenatal influenza exposure was documented by maternal interview and medical records at the time of birth, reported an almost threefold risk (although not significant at $P<0.05$) of second trimester influenza exposure among patients with hospitalised affective illness; a gender-specific analysis was not reported.

Our finding may also help to clarify the results of prior studies of prenatal famine exposure and schizophrenia (Susser & Lin, 1992; Susser *et al*, submitted). In these investigations, other psychiatric diagnoses were not examined for their potential association with famine. Since first trimester exposure to famine does not increase the risk of the hospitalised affective disorders, systematic misclassification of affective disorder as schizophrenia cannot account for the observed association between early prenatal exposure to famine and schizophrenia.

There may be no direct link between our previous findings for schizophrenia and first trimester famine exposure, and our present findings for affective psychosis and second trimester famine. As was evident in the results of the original Dutch famine study, the effects of famine on reproductive outcomes are very different depending upon the timing of the exposure during gestation (Stein *et al*, 1975). Thus, disorders that follow from exposure to famine at different time points in gestation may not necessarily be aetiologically related. For instance,

Table 6
Affective psychosis after prenatal exposure to famine: logistic regression analysis conducted separately by gender

	Affective psychosis, broad Odds ratio (95% CI)		Affective psychosis, restricted Odds ratio (95% CI)	
	Males	Females	Males	Females
	First trimester	0.85 (0.39, 1.85)	0.88 (0.46, 1.66)	0.90 (0.40, 2.03)
Second trimester	2.20 (1.23, 3.91) ¹	1.19 (0.73, 1.96)	2.19 (1.19, 4.02) ¹	1.15 (0.66, 1.99)
Third trimester	1.19 (0.67, 2.09)	1.28 (0.83, 1.96)	1.33 (0.74, 2.41)	1.10 (0.68, 1.78)

1. Confidence limits do not include 1: indicates statistical significance.

in the original Dutch famine study, reduced mean birthweight was related to famine exposure in late gestation, while neural tube defects, stillbirths and very low birthweight were associated only with famine during early gestation (Stein *et al*, 1975).

Given the exploratory nature of the study, these results must be regarded as preliminary. Further research is necessary in order to attempt replication of our findings, to address the specificity of type and timing of prenatal exposures, and to clarify and elucidate their effects with respect to gender and diagnosis. However, these results do provide some support for the view that prenatal experience may be related to the risk of affective disorders.

Limitations

A discussion of several important limitations inherent in studies of the Dutch famine cohort may be found in Susser & Lin (1992). These include: (a) the ascertainment of the population at risk, (b) the ascertainment of cases, (c) the reliability of diagnosis, (d) the degree of food deprivation, (e) the control of coincident factors, (f) the use of group *v.* individual data, and (g) the control of social class. We note here two additional limitations. Firstly, it is possible that second trimester famine exposure may not increase the risk of affective psychosis *per se* but only increase the duration or severity of affective episodes in men, thereby increasing the likelihood of hospitalisation. Secondly, prenatal malnutrition might also enhance the chronicity or delay the age of onset of episodes in men, thus enhancing the probability of a psychiatric hospitalisation after 1978.

It should be noted that Susser & Lin (1992) reported a non-significant trend toward increased risk of schizophrenia in famine-exposed birth cohorts in the northern and southern regions of Holland. The small numbers of hospitalised psychiatric cases in these regions precluded a useful analysis of the data; in the present study, however, available cases do not indicate any increased risk of affective psychosis or neurotic depression after famine exposure (results available on request).

Alan S. Brown, MD; Ezra S. Susser, MD; Jack M. Gorman, MD; Richard Neugebauer, PhD, Department of Psychiatry, Columbia University, New York State Psychiatric Institute, New York, USA; Shang P. Lin, PhD, Statistical Sciences and Epidemiology Division, Nathan Kline Institute for Psychiatric Research, Orangeburg, NY, USA

Correspondence: Dr Brown, New York State Psychiatric Institute, Unit 2, 722 West 168th St., New York, NY 10032, USA

(First received 25 October 1993, final revision 12 April 1994, accepted 18 May 1994)

Acknowledgements

Supported by the Frontier Fund, Columbia University (Dr Brown), a NIMH National Research Service Award, MH10483-01 (Dr Brown), a National Alliance for Research on Schizophrenia and Depression Young Investigator Award (Dr Brown), and a NIMH Research Scientist Award, MH-00416 (Dr Gorman). The authors would like to thank the Dutch Centre for Health Care Information (Peter Bosch and Constance van Rooijen) for the data abstraction from the Dutch Psychiatric Registry, and Sonia Montiel-Perez for her assistance in preparation of the manuscript.

References

- BUKA, S. L., TSUANG, M. T. & LIPSITT, L. P. (1993) Pregnancy/delivery complications and psychiatric diagnosis. *Archives of General Psychiatry*, **50**, 151–156.
- CROW, T. J., DONE, D. J. & JOHNSTONE, E. C. (1991) Schizophrenia and influenza. *Lancet*, **338**, 116–117.
- DONE, D. J., JOHNSTONE, E. C., FRITH, C. D., *et al* (1991) Complications of pregnancy and delivery in relation to psychosis in adult life: data from the British perinatal mortality survey sample. *British Medical Journal*, **302**, 1576–1580.
- JACOBSON, B., EKLUND, G., HAMBERGER, L., *et al* (1987) Perinatal origin of adult self-destructive behavior. *Acta Psychiatrica Scandinavica*, **76**, 364–371.
- KLINE, J., STEIN, Z. & SUSSER, M. (1989) *Conception to Birth. Epidemiology of Prenatal Development*. Monographs in Epidemiology and Biostatistics, vol. 1. New York: Oxford University Press.
- LEWIS, S. W. & MURRAY, R. M. (1987) Obstetric complications, neurodevelopmental deviance and schizophrenia. *Journal of Psychiatric Research*, **21**, 413–421.
- MEYER-BAHLBURG, H. F. L., EHRHARDT, A. A., ENDICOTT, J., *et al* (1985) Depression in adults with a history of prenatal DES exposure. *Psychopharmacology Bulletin*, **21**, 686–689.
- SALK, L., LIPSITT, L. P., STURNER, W. Q., *et al* (1985) Relationship of maternal and perinatal conditions to eventual adolescent suicide. *Lancet*, **i**, 624–627.
- STEIN, Z., SUSSER, M., SAENGER, G., *et al* (1975) *Famine and Human Development: The Dutch Hunger Winter of 1944–45*. New York: Oxford University Press.
- SUSSER, E. S. & LIN, S. P. (1992) Schizophrenia after prenatal exposure to the Dutch Hunger Winter of 1944–1945. *Archives of General Psychiatry*, **49**, 983–988.
- , NEUGEBAUER, R., HOEK, H. W., *et al* (1995) Schizophrenia after prenatal exposure to famine. *Lancet* (submitted).
- WEISSMAN, M. M., LIVINGSTON, B. M., LEAF, P. J., *et al* (1991) Affective disorders. In *Psychiatric Disorders in America: The Epidemiologic Catchment Area Study*, New York (eds L. N. Robin & D. A. Regier). New York: The Free Press.
- WORLD HEALTH ORGANIZATION (1978) *Mental Disorders: Glossary and Guide to their Classification in Accordance with the Ninth Revision of the International Classification of Diseases*. Geneva: WHO.