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Age-specific familial risks of depression: A nation-wide epidemiological study from Sweden

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Abstract

Objective—Familial risks of depression have been assessed in small case-control studies, usually based on reported, but not medically verified, depressions in family members; thus the degree of familial clustering of these diseases remains to be established.

Methods—The Multigeneration Register, in which all men and women born in Sweden from 1932 onward are registered together with their parents, was linked to hospital admission data. Standardized incidence ratios (SIRs) were calculated as the ratio of the observed to the expected number of cases in men and women with mothers or fathers affected by depression, compared with men and women whose mothers or fathers were not affected by depression.

Results—A total of respectively 60,477 and 79,969 depressions were recorded in offspring and parents. In 6.44% of all families, an offspring and a parent were affected, giving a population-attributable proportion of 4.04% and a familial SIR of 2.68. The parental transmission of depression was similar for both men and women (2.72 and 2.66).

Conclusions—This study has provided the first data on age-specific familial clustering of depressions, based on medically confirmed records. The risks were so high that hereditary factors were considered to be likely to contribute to depression, possibly modified by environmental factors. Age-specific risk tables would be helpful for clinical counseling.

Keywords

Familial risk; depression; hereditary factors; population-attributable fraction; genetics

INTRODUCTION

Depression is one of the most common psychiatric disorders with prevalence estimates ranging from 5% to a maximum of 20%. Despite its high prevalence and socioeconomic impact (Sundquist et al., 2004a; Sundquist et al., 2004b), little is known about the etiology. The risk factors of depression are most likely to be a combination of biological, environmental, and genetic factors. In one epidemiological meta-analysis, a 2.8-fold risk of depression was observed in first-degree relatives (Sullivan et al., 2000) and a 5.2-fold risk in another analysis of three generations of relatives (Weissman et al., 2005). A population-based sample of twins

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DECLARATION OF INTEREST

There are no conflicts of interest.

from Virginia showed a modest genetic influence of 39–42% (Kendler & Prescott, 1999). Another study of twins recruited from psychiatric treatment centers demonstrated strong genetic influences on the development of depression even up to 70% (McGuffin et al., 1996). Major depression in parents increases the overall risk in offspring for depression and seems to influence the natural course of depression (Lieb et al., 2002a), recurrence and impairment (Lieb et al., 2002b). Results from family and epidemiological studies have led to the suggestion that early-onset depression may be more strongly genetically influenced than adult-onset major depression (Fombonne et al., 2001; Wickramaratne et al., 2000). For example, more early-onset patients tended to have a family history of mood disorders in a study of 289 outpatients with chronic major depression (Klein et al., 1999). These findings have not been reported consistently (Eley & Stevenson, 1999; Thapar & McGuffin, 1994). The influence of genetic factors has been reported to have significantly greater transmissibility of depression in women than in men (Faraone et al., 1987; Merikangas et al., 1985; Reich et al., 1987), but not in twins (Bierut et al., 1999; Kendler & Prescott, 1999). Consequently, there is a need for further research into the genetic etiology of depression with specific attention paid to age and sex effects.

The patterns of inheritance of depression are probably complex, and environmental factors are also important, based on other correlations of the risk between spouses (Hippisley-Cox et al., 2002). For the future success of the gene identification efforts, it is important that the familial risks are characterized and the genetic and environmental components are delineated. Because of the limited amount of population-based data on familial clustering of depression, we examine here age-specific familial risks for depression using the nationwide Swedish MigMed Research Database. Age-specific data have been shown to facilitate therapeutic decisions and clinical counseling. We also estimated the population-attributable fraction (PAF) for the familial risk, i.e., the amount of the disease that could be prevented if the cause could be removed. The Swedish data on family relationships and on medically diagnosed depressions were obtained from register sources with practically complete coverage. The Swedish family dataset, i.e., the Multigeneration Register, is a well-validated source that has been found to be reliable in the study of familial cancer (Hemminki & Li, 2004a; Hemminki & Li, 2004b; Hemminki & Li, 2004c; Li & Hemminki, 2004; Li & Hemminki, 2005). The new contribution of the present study is its large-scale approach and the elimination of self-report and recall bias in the assessment of family history.

MATERIAL AND METHODS

MigMed Research Database

Data used in this study were retrieved from the MigMed database, located at the Center for Family and Community Medicine at the Karolinska Institute in Stockholm. MigMed is a single, comprehensive database that has been constructed using several national Swedish data registers, including, but not limited to, the Total Population Register, National Census Data (1960–90), the Swedish Hospital Discharge Register (1987–2004), and the Multigeneration Register (Rosen & Hakulinen, 2005; Statistics Sweden, 2005; The National Board of Health and Welfare). The Multigeneration Register includes all individuals born in Sweden in 1932 and thereafter, i.e. the second generation, which constituted the index persons or the offspring. Individuals in the second generation are registered shortly after birth and linked to their parents, i.e. the first generation. Since the database contains information from the Multigeneration Register, it is possible to link more than 9 million index persons (persons born in or after 1932 and registered in Sweden at any time since 1961) with their biological parents. The latest version of the Multigeneration Register, which has been incorporated in the MigMed database, includes supplementary data from church records on index persons domiciled in Sweden

between 1947 and 1961, including information about biological parents, children, siblings, and adoptions.

Information from the various registers in the database is linked at the individual level via the national 10-digit national registration number assigned to each person in Sweden for his or her lifetime. Prior to inclusion in the MigMed database, national registration numbers were replaced by serial numbers to ensure the anonymity of all individuals.

Follow-up was started for each offspring at birth, immigration or on January 1, 1987, whichever came last. Follow-up was terminated at hospital diagnosis of depression, death, emigration, or the end of the study on December 31, 2004.

Outcome variable

Depressions were retrieved from hospital discharge records reported according to the 9th (1987–1996) and 10th (1997–2004) versions of the International Classification of Diseases. The following ICD codes were included for both parents and offspring: 296 and 311 (ICD-9) and F30 to F39 (ICD-10). Only the first hospitalization for depression was considered.

Individual variables

Gender: males and females

Age at diagnosis was categorized as follows: under 15, 15–29, 30–39, 40–49, 50–59, and over 59 years of age.

Depression in father/mother was dichotomized into Yes and No.

Socioeconomic status was divided into six groups according to occupation: (1) Farmers; (2) Unskilled/Skilled workers; (3) White-collar workers; (4) Professionals; (5) Self-employed; and (6) All others.

Geographic region was divided into large cities (cities with a population of more than 200,000, i.e., Stockholm, Gothenburg, and Malmö), Southern Sweden, and Northern Sweden. Geographic region was included as an individual variable to adjust for possible differences between geographic regions in Sweden with regard to hospital admissions for depression.

Statistical analysis

Age-standardized incidence ratios were calculated for the whole follow-up period, divided into six 3-year periods (1987–1989, 1990–1992, 1993–1995, 1996–1998, 1999–2001, and 2002–2004). Standardized incidence ratios (SIRs) were calculated as the ratio of the observed to the expected number of cases (Rothman & Greenland, 1998). The expected number of cases was calculated for age (in 5-year groups), sex, period (in 3-year groups), socioeconomic status (in gender groups), and region (in three groups). Familial risks were calculated for men and women with mothers or fathers affected by depressions, compared with men and women whose mothers or fathers were not affected by depressions (i.e. the reference group). Each parent-offspring pair was included only once in the analysis, which implies that an individual could be classified only as a parent or an offspring. Confidence intervals (95% CI) were calculated assuming a Poisson distribution. The population-attributable fraction (PAF) of cases with a family history of depression was estimated as follows: $\text{proportion of familial cases} \times (\text{familial SIR} - 1) / \text{familial SIR}$ (Rothman & Greenland, 1998).

Ethical Considerations

This study was approved by the Ethics Committee of the Karolinska Institute, Stockholm, Sweden.

RESULTS

The family depression database covered the years 1987 to 2004 in the Swedish Hospital Discharge Register and included 25,678 male and 34,799 female depressions between the ages 0 and 72 years, in addition to 29,820 paternal and 50,149 maternal depressions (Table 1). The mean age at the diagnosis of depression was 55.8 and 56.1 for fathers and mothers and 40.8 and 39.2 for sons and daughters. The mean age at the diagnosis of depression was 36.9 and 35.9 for sons and daughters when a parent was affected with depression.

In Figure 1 the age-specific incidence is plotted by parental family history. The incidence rate of familial depression was higher than that of sporadic depression, with an upward bend between the ages 20–24 and 40–44 and after age 60. There were statistical differences in all age groups with the exception of the age group 70–72 years (data not shown).

Familial risks were calculated separately for depression in men (sons) and women (daughters) according to the father's and mother's depression histories (Table 2). All the models are adjusted for all the explanatory variables simultaneously, i.e., age, socioeconomic status, period, and region. The overall SIRs were similar in men with a father who had had depression (2.64, 95% CI, 2.43–2.86) and in men with a mother who had had depression (2.68, 95% CI, 2.53–2.84). Maternal transmission of depression was stronger than paternal transmission in women. The overall SIRs were 2.70 (95% CI, 2.56–2.84) for maternal transmission and 2.38 (95% CI, 2.22–2.56) for paternal transmission. A gradient was found for both men and women, so that with increasing age the SIRs decreased but remained significant in all age groups; in both men and women, depressions diagnosed at an early age (<30 years) showed marginally higher SIRs than the total SIRs.

Table 3 shows the SIRs for men and women according to parental depression. We combined fathers and mothers as family (parental) history. The overall risk was 2.72 (95% CI, 2.59–2.85) for men and 2.66 (95% CI, 2.55–2.77) for women. When both parents were affected by depression, the SIRs were even higher, i.e., 5.08 (95% CI, 3.45–7.21) for men and 7.92 (95% CI, 6.15–10.05) for women. The highest SIR was found in the youngest age groups among men and women when both parents were affected with depression; for example, the SIR was 8.22 (95% CI, 4.58–13.59) for men and 11.03 (95% CI, 7.44–15.76) for women aged 15 to 29 years.

The familial percentage of affected offspring with an affected parent for depression was calculated based on the familial cases of depression from Table 3 in relation to the total number of cases of depression in offspring from Table 1. The familial proportion of depression was also age-dependent and fell from 9.51 to 3.30% for men and from 9.73% to 3.24% for women (Table 4). The SIR from a parental proband was derived from the same data as in Table 3. These figures were used to calculate familial PAFs of depression, which ranged in an age-dependent manner from 7.03% to 1.89% for men and from 7.75% to 1.79% for women. The overall SIR for depression was 2.68 in offspring aged 0 to 72 years when a parent was affected by depression, with a familial proportion of 6.44% and a PAF of 4.04%. We compared the risk of depression in parents (spouses) and found similar risks in both husbands and wives (data not shown). There were no significant interactions by gender.

DISCUSSION

Familial clustering of disease has been studied traditionally in the clinical setting where probands and their multiply affected relatives have been identified (Kendler et al., 1999; Reich et al., 1987; Weissman et al., 2005). This approach has also been very productive in terms of understanding the genetic factors. The disadvantages include difficulties in obtaining large numbers of cases and in securing unbiased risk estimates. These problems can be overcome in population datasets where depression data on cases and probands are medically verified. The largest population-based dataset on familial depression is the Swedish familial depression database, covering 10.2 million people and 79,969 cases of depressions in the first generations and 60,477 cases of depressions in the second generation, that was used in our study. The use of hospital data eliminated potential self-report and recall bias in the assessment of family history.

This study has a number of strengths. For example, the study population included a well-defined open cohort, the entire population of Sweden. Because of the national registration number assigned to each individual in Sweden, it was possible to track the records of every person for the whole follow-up period. The unique Swedish Population Registers are almost entirely complete with very little missing data. For example, data on occupational status were nearly 100% complete (99.2%), which enabled us to adjust our models for socioeconomic status. The use of a personal identification number made it possible to track each individual in different registers, e.g. the Migrant Register, which allowed calculation of exact risk periods.

In addition, the data in the Swedish Hospital Discharge Register is also nearly complete. In 2001, the main diagnosis was missing in only 0.9% of cases and the national registration number in 0.4% of hospitalizations (Rosen & Hakulinen, 2005). Finally, the accuracy of the multigenerational part of the MigMed database is very reliable. It includes information about parents, children, siblings, and adoptions for index persons domiciled in Sweden born from 1932 onward and at any time between 1947 and 2001.

The present study provided evidence on familial risks of depression in the 0-72-year-old population. The risk in offspring with parental depression was 2.68 and is in line with earlier publications on depression (Sullivan et al., 2000). Our results indicated that there was no gender difference in the transmission of depression from mothers and fathers. However, it was found that maternal transmission of depression is stronger than paternal transmission in women. In addition, the risk of depression was especially high for men and women with both parents affected by depression. Because of the large numbers, we were able to describe age-specific familial risks to some extent. In the offspring of affected parents, the risk was maximized at ages under 30 years and remained stable in the older risk groups around 2.0. Previous studies have suggested that the etiology of depression in adults may differ from that of early-onset depression and may be more strongly genetically influenced than adult-onset depressions (McGuffin et al., 1996; Rice et al., 2002; Thapar & McGuffin, 1994). In a ten-year follow-up study, it was shown that a positive parental history of depression predicted the risk of early-onset depression in subjects under 30 years of age (Wickramaratne & Weissman, 1998).

A large age-specific familial risk for depression is demonstrated in the present study. It could be assumed that this is due to a genetic basis for depression. However, it is also possible that depression running in families is due to children learning depressive strategies from their parents. This refers to the fact that genetic and environmental influences coverage, which means that children inherit genes from their parents but are also exposed to environments that are shared by their own and their parent's genetic makeup. Several previous studies have demonstrated associations of the psychological functioning of the children of depressed parents that suggest possible mechanisms for the transmission of maternal depression to the offspring

of dysfunctional and erratic parenting behavior, exposure to negative cognitions, and increased family disruption (Beardslee et al., 2003; Cummings & Davies, 1994; Goodman & Gotlib, 1999; Kim-Cohen et al., 2005). However, mechanisms of transmission of depression from parents to children also include genetic effects.

Another feature of our study is that we were able to give gender-specific familial risk estimates. Although differences in the lifetime prevalence of depression in men and women are demonstrated consistently in epidemiological studies, we found no significant differences in familial risks of depression between the sexes, including transmission from father and mother, separately. This result is consistent with prior evidence in twins (Bierut et al., 1999; Kendler & Prescott, 1999).

Since 6.44% of the parents were affected by depression, the population-attributable risk for depression was 4.04%. The population-attributable fraction is an epidemiological concept which indicates the proportion of disease that could be prevented if familial causes could be removed. PAFs have been used to calculate environmental exposures; however, only limited are available for familial depression (Prigerson et al., 2002). If environmental factors have been excluded or quantified, the PAF values give an estimate of the inherited effects for disease when only nuclear families can be studied. However, because of low penetrance, familial PAFs underestimate true heritable effects. An interesting question is the correspondence of familial PAFs to the heritability estimates derived from twin studies (Kendler & Prescott, 1999; McGuffin et al., 1996). In the twin study, the heritability estimates for depression were some 10 times higher than the familial PAFs. One obvious reason for the difference between these estimates is the inability of the PAF calculations to fully cover recessive, low-penetrant and polygenetic effects. Low-penetrant gene effects will make familial patterns difficult to observe, but they may be detected in twin studies.

An important limitation of our study is the lack of information on environmental risk factors for depression (e.g., alcohol). However, we were able to adjust for socioeconomic status and regions (Sundquist et al., 2004a). Another limitation is that the mean age at diagnosis was higher among the parents than among the studied men and women because the Swedish Hospital Discharge Register began recording complete data on all discharges in Sweden only in 1987. We were unable to test for the validity of the depression diagnoses because our data were based on the entire population. However, we only used main diagnoses for depression recorded in the hospital registers, i.e., all patients were hospitalized mainly for depression, which increases the possibility that the diagnoses for depression are valid. We also investigated the number of subsequent hospitalizations for depression. Two or more admissions for depression were recorded in 44% of the cases, whereas 56% had only one admission for depression. However, this bias is present in both the compared groups, i.e., the parental history of the depression probands and the parents of the control probands. We have no reason to believe that the magnitude of this bias differed between the two groups and, therefore, it ought to be of minor importance. Data on out-patients were not available to us, which means that only the most severe forms of depression were included in the study, i.e. those that required hospitalization.

CONCLUSION

There was an age-specific familial risk of depression by parental proband. We showed an age-dependent familial risk for depression and an overall 2.68-fold increase in depression among 0-72-year-old offspring of parents with depression. There was a similar familial risk of depression for men and women with parental depression. The population-attributable proportion for familial clustering was 4.04%. Further progress in the understanding of the

heritable basis of depression requires coordinated efforts in genetic epidemiology and molecular genetics.

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REFERENCES

- Beardslee WR, Gladstone TR, Wright EJ, Cooper AB. A family-based approach to the prevention of depressive symptoms in children at risk: evidence of parental and child change. *Pediatrics* 2003;112:e119–e131. [PubMed: 12897317]
- Bierut LJ, Heath AC, Bucholz KK, Dinwiddie SH, Madden PA, Statham DJ, Dunne MP, Martin NG. Major depressive disorder in a community-based twin sample: are there different genetic and environmental contributions for men and women? *Arch Gen Psychiatry* 1999;56:557–563. [PubMed: 10359473]
- Cummings EM, Davies PT. Maternal depression and child development. *J Child Psychol Psychiatry* 1994;35:73–112. [PubMed: 8163630]
- Eley TC, Stevenson J. Exploring the covariation between anxiety and depression symptoms: a genetic analysis of the effects of age and sex. *J Child Psychol Psychiatry* 1999;40:1273–1282. [PubMed: 10604405]
- Faraone SV, Lyons MJ, Tsuang MT. Sex differences in affective disorder: genetic transmission. *Genet Epidemiol* 1987;4:331–343. [PubMed: 3692133]
- Fombonne E, Wostear G, Cooper V, Harrington R, Rutter M. The Maudsley long-term follow-up of child and adolescent depression. 1. Psychiatric outcomes in adulthood. *Br J Psychiatry* 2001;179:210–217. [PubMed: 11532797]
- Goodman SH, Gotlib IH. Risk for psychopathology in the children of depressed mothers: a developmental model for understanding mechanisms of transmission. *Psychol Rev* 1999;106:458–490. [PubMed: 10467895]
- Hemminki K, Li X. Familial renal cell cancer appears to have a recessive component. *J Med Genet* 2004a; 41:E58. [PubMed: 15121786]
- Hemminki K, Li X. Familial risk of cancer: data for clinical counseling and cancer genetics. *Int J Cancer* 2004b;108:109–114. [PubMed: 14618624]
- Hemminki K, Li X. Familial risks of cancer as a guide to gene identification and mode of inheritance. *Int J Cancer* 2004c;110:291–294. [PubMed: 15069696]
- Hippisley-Cox J, Coupland C, Pringle M, Crown N, Hammersley V. Married couples' risk of same disease: cross sectional study. *Bmj* 2002;325:636. [PubMed: 12242177]
- Kendler KS, Gardner CO, Prescott CA. Clinical characteristics of major depression that predict risk of depression in relatives. *Arch Gen Psychiatry* 1999;56:322–327. [PubMed: 10197826]
- Kendler KS, Prescott CA. A population-based twin study of lifetime major depression in men and women. *Arch Gen Psychiatry* 1999;56:39–44. [PubMed: 9892254]
- Kim-Cohen J, Moffitt TE, Taylor A, Pawlby SJ, Caspi A. Maternal depression and children's antisocial behavior: nature and nurture effects. *Arch Gen Psychiatry* 2005;62:173–181. [PubMed: 15699294]
- Klein DN, Schatzberg AF, McCullough JP, Dowling F, Goodman D, Howland RH, Markowitz JC, Smith C, Thase ME, Rush AJ, LaVange L, Harrison WM, Keller MB. Age of onset in chronic major depression: relation to demographic and clinical variables, family history, and treatment response. *J Affect Disord* 1999;55:149–157. [PubMed: 10628884]
- Li X, Hemminki K. Inherited predisposition to early onset lung cancer according to histological type. *Int J Cancer* 2004;112:451–457. [PubMed: 15382071]
- Li X, Hemminki K. Familial multiple primary lung cancers: a population-based analysis from Sweden. *Lung Cancer* 2005;47:301–307. [PubMed: 15713513]

- Lieb R, Isensee B, Hofler M, Pfister H, Wittchen HU. Parental major depression and the risk of depression and other mental disorders in offspring: a prospective-longitudinal community study. *Arch Gen Psychiatry* 2002a;59:365–374. [PubMed: 11926937]
- Lieb R, Isensee B, Hofler M, Wittchen HU. Parental depression and depression in offspring: evidence for familial characteristics and subtypes? *J Psychiatr Res* 2002b;36:237–246. [PubMed: 12191628]
- McGuffin P, Katz R, Watkins S, Rutherford J. A hospital-based twin register of the heritability of DSM-IV unipolar depression. *Arch Gen Psychiatry* 1996;53:129–136. [PubMed: 8629888]
- Merikangas KR, Weissman MM, Pauls DL. Genetic factors in the sex ratio of major depression. *Psychol Med* 1985;15:63–69. [PubMed: 3991835]
- Prigerson HG, Maciejewski PK, Rosenheck RA. Population attributable fractions of psychiatric disorders and behavioral outcomes associated with combat exposure among US men. *Am J Public Health* 2002;92:59–63. [PubMed: 11772762]
- Reich T, Van Eerdewegh P, Rice J, Mullaney J, Endicott J, Klerman GL. The familial transmission of primary major depressive disorder. *J Psychiatr Res* 1987;21:613–624. [PubMed: 3440960]
- Rice F, Harold G, Thapar A. The genetic aetiology of childhood depression: a review. *J Child Psychol Psychiatry* 2002;43:65–79. [PubMed: 11848337]
- Rosen, M.; Hakulinen, T. Use of disease registers. In: Ahrens, W.; Pigeot, I., editors. *Handbook of epidemiology*. Berlin: Springer-Verlag; 2005.
- Rothman, KJ.; Greenland, S. *Modern Epidemiology*. 2nd ed.. Philadelphia: Lippincott-Raven; 1998.
- Statistics Sweden. The Swedish Multi Generation Register (1960–1990). 2005. http://www.scb.se/templates/Standard_22842.asp (In Swedish: Registret över totalbefolkningen/RTB)
- Sullivan PF, Neale MC, Kendler KS. Genetic epidemiology of major depression: review and meta-analysis. *Am J Psychiatry* 2000;157:1552–1562. [PubMed: 11007705]
- Sundquist K, Frank G, Sundquist J. Urbanisation and incidence of psychosis and depression: follow-up study of 4.4 million women and men in Sweden. *Br J Psychiatry* 2004a;184:293–298. [PubMed: 15056572]
- Sundquist K, Johansson LM, Johansson SE, Sundquist J. Social environment and psychiatric illness: A follow-up study of 9,170 women and men in Sweden. *Soc Psychiatry Psychiatr Epidemiol* 2004b;39:39–44. [PubMed: 15022045]
- Thapar A, McGuffin P. A twin study of depressive symptoms in childhood. *Br J Psychiatry* 1994;165:259–265. [PubMed: 7953041]
- The National Board of Health and Welfare. The Swedish Hospital Discharge Register and the Cause of Death Register (1961–2001). <http://www.sos.se/epc/english/ParEng.htm>
- Weissman MM, Wickramaratne P, Nomura Y, Warner V, Verdelli H, Pilowsky DJ, Grillon C, Bruder G. Families at high and low risk for depression: a 3-generation study. *Arch Gen Psychiatry* 2005;63:29–36. [PubMed: 15630070]
- Wickramaratne PJ, Greenwald S, Weissman MM. Psychiatric disorders in the relatives of probands with prepubertal-onset or adolescent-onset major depression. *J Am Acad Child Adolesc Psychiatry* 2000;39:1396–1405. [PubMed: 11068895]
- Wickramaratne PJ, Weissman MM. Onset of psychopathology in offspring by developmental phase and parental depression. *J Am Acad Child Adolesc Psychiatry* 1998;37:933–942. [PubMed: 9841243]

Figure 1.
Age-specific incidence rate of depression in offspring of parents with and without depression

Table 1
Number of cases of depression in men and women and parents

Age at diagnosis (years)	Men		Women		Father		Mother	
	No.	%	No.	%	No.	%	No.	%
<15	163	0.6	329	0.9	9	0.0	26	0.1
15-29	5624	21.9	9240	26.6	1585	5.3	3973	7.9
30-39	5778	22.5	7754	22.3	3841	12.9	7121	14.2
40-49	6783	26.4	8682	24.9	6207	20.8	8842	17.6
50-59	5570	21.7	6662	19.1	6057	20.3	7859	15.7
60-69	1704	6.6	2036	5.9	4503	15.1	7152	14.3
70-79	56	0.2	96	0.3	4750	15.9	9439	18.8
80+					2868	9.6	5737	11.4
All	25678	100.0	34799	100.0	29820	100.0	50149	100.0

Table 2
SIR for depression in offspring of father/mother with depression

Age at diagnosis (years)	Men						Women					
	Father with depression			Mother with depression			Father with depression			Mother with depression		
	O	SIR	95%CI	p-value	O	SIR	95%CI	p-value	O	SIR	95%CI	p-value
<15	7	4.27	1.69	8.85	7	3.16	1.25	6.54	9	2.72	1.23	5.19
15–29	215	3.44	3.00	3.93	335	3.83	3.43	4.26	285	2.73	2.42	3.07
30–39	156	2.49	2.12	2.92	266	2.70	2.39	3.05	216	2.55	2.22	2.92
40–49	158	2.61	2.22	3.06	292	2.36	2.09	2.64	171	2.17	1.86	2.52
50–59	54	1.57	1.18	2.05	176	2.01	1.72	2.33	67	1.65	1.28	2.10
>=60	11	1.74	0.86	3.12	47	2.49	1.83	3.32	12	1.62	0.84	2.85
All	601	2.64	2.43	2.86	1123	2.68	2.53	2.84	760	2.38	2.22	2.56

O = observed number of cases; SIR = standardized incidence ratio; CI = confidence interval. Bold type: 95% CI does not include 1.00.

Table 3

SIR for depression in offspring of parents (father/mother) with depression

Age at diagnosis (years)	Men						Women					
	Father/mother with depression			Both parents with depression			Father/mother with depression			Both parents with depression		
	O	SIR	95%CI	O	SIR	95%CI	O	SIR	95%CI	O	SIR	95%CI
	p-value			p-value			p-value			p-value		p-value
<15	13	3.61	1.92	6.20	1	18.76	32	4.93	3.37	2	18.30	67.29
15-29	535	3.83	3.51	4.16	15	8.22	751	3.22	2.99	30	11.03	7.44
30-39	417	2.60	2.36	2.86	5	3.12	526	2.59	2.37	22	10.41	15.76
40-49	442	2.51	2.28	2.75	8	5.19	540	2.46	2.26	11	4.85	8.71
50-59	228	1.93	1.69	2.20	2	2.22	284	2.11	1.87	2	1.65	6.06
>=60	58	2.35	1.78	3.04	0		69	2.23	1.74	1	6.31	36.17
All	693	2.72	2.59	2.85	31	5.08	2202	2.66	2.55	68	7.92	10.05

O = observed number of cases; SIR = standardized incidence ratio; CI = confidence interval. Bold type: 95% CI does not include 1.00.

Table 4
Familial proportions (% of affected cases with affected parents), SIR, and PAFs for parental history

Age at diagnosis (years)	Men			Women			All			
	Familial proportion (%)		SIR	Familial proportion (%)		SIR	Familial proportion (%)		SIR	PAF
<15	7.98	3.61	5.77	9.73	4.93	7.75	9.15	4.46	7.10	
15–29	9.51	3.83	7.03	8.13	3.22	5.60	8.65	3.44	6.14	
30–39	7.22	2.60	4.44	6.78	2.59	4.16	6.97	2.59	4.28	
40–49	6.52	2.51	3.92	6.22	2.46	3.69	6.35	2.48	3.79	
50–59	4.09	1.93	1.98	4.26	2.11	2.24	4.19	2.03	2.12	
>=60	3.30	2.35	1.89	3.24	2.23	1.79	3.26	2.29	1.84	
All	6.59	2.72	4.17	6.33	2.66	3.95	6.44	2.68	4.04	

SIR = standardized incidence ratio; PAF = population-attributable fraction.