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The Validity of the Family History Screen for Assessing Family History of Mental Disorders

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Abstract

There is a need to collect psychiatric family history information quickly and economically (e.g., for genome-wide studies and primary care practice). We sought to evaluate the validity of family history reports using a brief screening instrument, the Family History Screen (FHS). We assessed the validity of parents' reports of seven psychiatric disorders in their adult children probands from the Dunedin Study (n=959, 52% male), using the proband's diagnosis as the criterion outcome. We also investigated whether there were informant characteristics that enhanced accuracy of reporting or were associated with reporting biases. Using reports from multiple informants, we obtained sensitivities ranging from 31.7% (alcohol dependence) to 60.0% (conduct disorder) and specificities ranging from 76.0% (major depressive episode) to 97.1% (suicide attempt). There was little evidence that any informant characteristics enhanced accuracy of reporting. However, three reporting biases were found: the probability of reporting disorder in the proband was greater for informants with versus without a disorder, for female versus male informants, and for younger versus older informants. We conclude that the FHS is as valid as other family history instruments (e.g., the FH-RDC, FISC), and its brief administration time makes it a cost-effective method for collecting family history data. To avoid biasing results, researchers who aim to compare groups in terms of their family history should ensure that the informants reporting on these groups do not differ in terms of age, sex or personal history of disorder.

Keywords

family history; sensitivity; specificity; accuracy; bias

INTRODUCTION

Family history is a major risk factor for most psychiatric disorders [Kendler et al., 1997; Miles et al., 1998; Sullivan et al., 2000; Bandelow et al., 2002, 2004; Byrne et al., 2002; Qin et al., 2002; Klein et al., 2003; Newman and Bland, 2006; Coelho et al., 2007]. Increasingly, psychiatric family history data are being collected on very large samples, for example, for candidate gene and genome-wide studies [Prescott et al., 2005; Chen et al., 2007]. In

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addition, family history is being promoted for use by primary care clinicians [Yoon et al., 2003], for whom time constraints place restrictions on the information that can be collected. Thus, there is a need for assessment tools which enable psychiatric family history information to be collected quickly and economically.

Commonly used family history instruments, such as the Family History Method for Research Diagnostic Criteria (FH-RDC) [Andreasen et al., 1977], the Family Interview for Genetic Studies (FIGS) [Nurnberger et al., 1994], and the Family Informant Schedule and Criteria (FISC) [Chapman et al., 1994], take several hours to complete for an average sized family. The reasons for these instruments' lengthy administration times are twofold. First, because diagnoses of disorder are made for each disorder, a large number of items are required to assess all diagnostic criteria, so administration time for each relative is long (10–50 min). Second, relatives are assessed one-at-a-time, so even average-sized families can take a long time to assess.

Here we report on the validity of a brief screening instrument, the Family History Screen (FHS) [Weissman et al., 2000], which cuts administration time by assessing only key symptom items per disorder, and assessing relatives "in parallel" (i.e., each item is asked about all relatives at the same time). The validity of the FHS has been demonstrated by the developers of the instrument [Lish et al., 1995; Weissman et al., 2000], but it is important to have replication by an independent team.

We assessed the validity of reports for seven psychiatric disorders: major depressive episode, anxiety, schizophreniform disorder, conduct disorder, suicide attempt, alcohol dependence and drug dependence; and two non-psychiatric conditions: smoking and asthma. We chose smoking and asthma in order to compare family history reports of psychiatric disorders against two different benchmarks. Smoking, on the one hand, is an externally observable behavior that is not as stigmatized as psychiatric conditions, and that can be reported with high validity [Kendler et al., 2002]. Asthma, on the other hand, is reported with less validity than other non-psychiatric disorders: for example, cardiovascular disease [Bensen et al., 1999], cancers [Chang et al., 2006], smoking [Kendler et al., 2002]. Moreover, like psychiatric disorders, asthma is diagnosed according to a syndrome of symptoms, some of which may be difficult to observe. Therefore, smoking might be considered a "highest possible" benchmark against which to compare the validity of family history reports of psychiatric disorders, whereas asthma might be considered a more attainable benchmark.

We had two additional aims. First, we sought to investigate whether any characteristics of the informant who reported family history were associated with accuracy of reporting (that is, correctly identifying the true disorder status). Second, we sought to investigate whether any characteristics of the informant who reported family history were associated with "informant reporting biases," that is, whether the probability of reporting a positive history of disorder in a relative varies according to some characteristic of the informant. For example, it is known that the probability of an informant reporting a disorder in a relative is greater if the informant has a history of that disorder than if they do not [Kendler et al., 1991; Chapman et al., 1994; Roy et al., 1996; Heun et al., 1997; Coelho et al., 2006]. This can lead to inflated estimates of association if family history reports provided by disordered cases are compared with family history reports provided by non-disordered controls. There have been few investigations of the extent to which other informant characteristics increase or decrease the probability of reporting disorder in relatives. An investigation of other sources of informant reporting biases is therefore warranted.

We tested whether four informant characteristics were associated with accuracy of reporting and informant reporting biases: psychiatric history, sex, age, and education. We chose to investigate these characteristics either because they have been shown previously to be associated with accuracy of reporting (e.g., informant's sex and age) [Andreasen et al., 1986; Kosten et al., 1992; Fogelson et al., 2004; Hardt and Franke, 2007]; they have been shown previously to be associated with informant reporting biases (e.g., informant's psychiatric history) [Kendler et al., 1991; Chapman et al., 1994; Roy et al., 1996; Heun et al., 1997; Coelho et al., 2006]; or because they have implications for those planning family history studies (e.g., informant's education).

MATERIALS AND METHODS

Participants

Participants are probands from the Dunedin Study and their parents. All participants gave written informed consent for this research. Study protocols were approved by the Otago Ethics Committee.

Probands—Probands are members of the Dunedin Study, a longitudinal investigation of health and behavior in a complete birth cohort [Moffitt et al., 2001]. One thousand thirty-seven children (52% male) participated in the first assessment at age 3, constituting the base sample for the remainder of the study. These children comprise 91% of children born in Dunedin between 1 April 1972 and 31 March 1973 and who still resided in the local province (Otago) when the first assessments took place at age 3. Proband families are representative of the general population of New Zealand's South Island and are primarily white. Follow-ups with high rates of participation have been carried out at ages 5 (n=991), 7 (n=954), 9 (n=955), 11 (n=925), 13 (n=850), 15 (n=976), 18 (n=993), 21 (n=992), 26 (n=980), and 32 (n=972, 96% of the living sample of 1,015). Here we report data from 959 probands (94% of the living sample of 1,015) on whom health history data were available.

Parents—As part of a family history assessment that took place between 2003 and 2006, when probands were aged 30–33 years old, parents of probands were interviewed about their own health history and the health history of the proband. Interviews typically took place in the home of the parent, and were conducted by trained research interviewers who were blind to the data provided by the proband.

We aimed to interview the biological mother and father of all living probands (n=1,015), but sought alternative informants when a biological mother or father was either deceased or unable to be interviewed. Eight hundred eighty-two biological mothers provided reports on probands. Of the 133 living probands for whom a biological mother did not report, 51 had a non-biological mother or a maternal aunt or uncle who agreed to provide reports on probands. Thus, we achieved maternal informants for 933 of the 1,015 living probands (92%). Seven hundred fifty-three biological fathers provided reports on probands. Of the 262 living probands for whom a biological father did not report, 97 had a non-biological father or a paternal aunt or uncle who agreed to provide reports on probands. Thus, we achieved paternal informants for 850 of the 1,015 living probands (84%). Nine hundred fifty-nine probands were reported on by at least one parent; 824 probands were reported on by both parents.

Measures

Family history reports—Parents reported the psychiatric health history of the proband using the Family-History Screen (FHS) [Weissman et al., 2000]. To minimize under-reporting, the FHS uses pairs of questions to ascertain each symptom. A broadly sensitive

"introductory-screen" question is first asked to stimulate memory and give the informant time to reflect (e.g., "Has___ever had a sudden spell or attack in which they felt frightened or panicked?"). A positive response is followed by a second, narrower "symptom-definition" question (e.g., "Has___had several attacks of extreme fear or panic, even though there was nothing to be afraid of?"). For data analysis purposes, only the second question in a pair is used.

To broaden the FHS's coverage, we added items drawn from the Diagnostic Interview Schedule (DIS) [Robins et al., 1981, 1995], the Short Michigan Alcoholism Screening Test [Selzer et al., 1975], and the Drug Abuse Screening Test [Skinner, 1982]. We also added a checklist of psychiatric conditions commonly understood by the public (e.g., "alcoholism," "depression," etc.), the asthma item from the NHLBI Family Heart Study [Higgins et al., 1996], and an item asking whether family members were ever a smoker.

In total, there were symptom-definition items pertaining to major depressive episode (4 items), anxiety (13 items on generalized anxiety, panic, agoraphobia, phobia and obsessive–compulsive disorder), schizophreniform disorder (8 items), conduct disorder (8 items), alcohol dependence (3 items), drug dependence (3 items), suicide attempt (2 items), smoking (1 item), and asthma (1 item). Following FHS protocol [Weissman et al., 2000], a proband for whom one or more of a disorder's symptom-definition items was endorsed was considered to have a positive history of that disorder.

Criterion outcomes—We report on three criterion outcomes in the proband:

1. Psychiatric disorders: The psychiatric assessment of Dunedin probands has been described in detail elsewhere [Kim-Cohen et al, 2003]. Briefly, proband psychiatric disorder was assessed using the Diagnostic Interview Schedule for Children (DISC-C) [Costello et al., 1982] at younger ages (11–15 years) and the DIS [Robins et al., 1981, 1995] at older ages (18–32 years), with a past-year reporting period at each age. At ages 11, 13, and 15 years diagnoses were made using the then-current *Diagnostic and Statistical Manual of Mental Disorders, Version 3* (*DSM-III*) [American Psychiatric Association, 1980], at ages 18 and 21 years according to the then-current *DSM-III-R* [American Psychiatric Association, 1987] criteria, and at ages 26 and 32 years according to *DSM-IV* [American Psychiatric Association, 1994] criteria. Diagnoses were derived as follows. We assessed conduct disorder in childhood: those who were diagnosed with conduct disorder at any of ages 11, 13, 15, or 18 were considered to have a childhood diagnosis of conduct disorder. In adulthood we assessed major depressive episode, anxiety (generalized anxiety disorder, phobia, agoraphobia, panic disorder, obsessive compulsive disorder and post-traumatic stress disorder), schizophreniform disorder, alcohol dependence, and drug dependence. For each disorder, those who were diagnosed with that disorder at any of ages 21,26, or 32 were considered to have an adult diagnosis of disorder. We assessed suicide attempt in adolescence and adulthood: those who reported a lifetime suicide attempt at any of ages 15, 18, 21, 26, or 32 were considered to have attempted suicide in their lifetime.
2. Smoking: Those who reported that they had smoked daily for at least a month of the previous year at *any* of the assessments at ages 15,18,21,26, and 32 were considered to have "ever been a smoker."
3. Asthma: Those who presented with current asthma at *any* of the assessments at ages 9, 11, 13, 15, 18, 21, 26, and 32 were considered to have "ever had asthma." Further details on the assessment of asthma are available in Sears et al. [2002].

As described above, we based diagnoses for each outcome on a cumulative count of cases, each of which was ascertained in a past-year assessment. Using this prospective approach, cases are not under-counted due to failure to recall criterion symptoms from years past, as occurs in retrospective surveys [Simon and VonKorff, 1995]. Moreover, we have shown that there is very little case under-counting as a result of the gaps between past-year assessments. For example, only eight cohort members who had received mental-health services in the years between assessments had not been diagnosed by the study's repeated psychiatric interviews [Moffitt et al., 2007]. These eight cases had received services for either depression or anxiety; no cases of psychosis, suicide or substance abuse were missed.

Informant characteristics—We investigated whether the following informant characteristics were associated with accuracy of reporting and informant reporting biases: (1) personal history for each disorder (0=negative history of symptoms, 1=positive history of symptoms); (2) sex (0=male, 1=female); (3) age (in 10 year increments); and (4) education (0=no educational qualifications or basic school qualifications only, 1=high school, trade or tertiary qualifications).

Statistical Methods

Two analyses were undertaken—First, we assessed the validity of informant reports for each outcome by computing *sensitivity* (the proportion of probands *with* a diagnosis who were correctly identified by informant report) and *specificity* (the proportion of probands *without* a diagnosis who were correctly identified by informant report). We assessed validity for single reports (maternal informant on proband; paternal informant on proband) as well as for combined reports from maternal and paternal informants. We combined reports using an "Or" rule, where the proband is classified as disordered if *either* maternal or paternal informant reported a positive history. When analyzing the validity of combined reports, we included all cases in which at least one parent reported, so these validity statistics are based on the reports of two parents when they exist and on the reports on one parent when they do not. We took this approach because it is likely that researchers attempting to obtain two informants will be unable to do so for all families in their study [e.g., Roy et al., 1994, 1996; Weissman et al., 2000; Vandeleur et al., 2008]. As such, we believe the statistics presented in this way represent what might be achieved by researchers who attempt to recruit two informants, and so will be of interest to researchers considering undertaking family history studies.

Second, we investigated the effects of informant characteristics on accuracy of reporting and informant reporting biases. We did this by conducting, for each disorder, the following logistic regression model:

$$Y_i=\beta_0+\beta_D X_i+\beta_C Z_{ij}+\beta_{DC}(X_i \times Z_{ij})$$

where Y_i is the informant report of disorder for proband i (0=no disorder, 1=disorder), X_i is the disorder status for proband i (0=no disorder, 1=disorder), and Z_{ij} is the characteristic of the informant (as scored above) for each informant characteristic j.

Accuracy of reporting is tested by the parameter β_{DC}, which tests whether the strength of the association between having a disorder and being rated as having that disorder differs according to some characteristic of the informant. Thus, a significant positive association for this parameter (odds ratio >1) indicates that an informant characteristic is associated with increased accuracy of reporting, whereas a significant negative association for this parameter (odds ratio<1) indicates that an informant characteristic is associated with decreased accuracy of reporting.

Informant reporting bias is tested by the parameter β_C, which tests whether there is an association between an informant characteristic and making a positive report of disorder, *controlling for* the disorder status of the proband. Thus, a significant positive association for this parameter (odds ratio >1) indicates that an informant characteristic is associated with an *increased* probability of reporting a positive history of disorder in the proband, irrespective of the proband's actual disorder status. Conversely, a significant negative association for this parameter (odds ratio <1) indicates that an informant characteristic is associated with a *decreased* probability of reporting a positive history of disorder in the proband, irrespective of the proband's actual disorder status.

Because these analyses contained two reports on the same person (i.e., maternal informant's report on proband, paternal informant's report on proband), standard error estimates were adjusted based on the sandwich or Huber/White variance estimator [Williams, 2000], to account for the dependence in the data.

All analyses were conducted using Stata 9.1 [StataCorp, 2005].

RESULTS

Proband Characteristics

Prevalence of psychiatric disorders, smoking and asthma for probands is shown in Table I. Female probands had significantly higher prevalence rates of major depressive episode and anxiety. Male probands had significantly higher prevalence rates of alcohol dependence, drug dependence, and conduct disorder.

Informant Characteristics

Demographic characteristics and prevalence of psychiatric symptoms, smoking and asthma for parental informants are shown in Table II. Compared to paternal informants, maternal informants self-reported significantly higher rates of major depressive episode, anxiety and asthma. Paternal informants were approximately 3 years older at interview than maternal informants, were more likely to have educational qualifications, and they also self-reported significantly higher lifetime rates of alcohol dependence, conduct disorder, and smoking.

Is Informant-Reported Psychiatric Family History Valid?

For single reports, sensitivities for psychiatric disorders ranged from 21.7% (alcohol dependence) to 48.4% (schizophreniform disorder, Table III, panel A). Most sensitivities fell between 30.0% and 50.0%. Specificities for psychiatric disorders ranged from 84.6% (depression) to 98.2% (suicide attempt), with 5/7 disorders having specificities >90.0%. For combined maternal-or-paternal reports, sensitivities for psychiatric disorders ranged from 31.7% (alcohol dependence) to 60.0% (conduct disorder), and specificities ranged from 76.0% (major depressive episode) to 97.1% (suicide attempt, Table III, panel B).

For both single and combined reports, sensitivity was greater for smoking and asthma than for any psychiatric disorder. Specificity for smoking and asthma was similar to specificities for psychiatric disorders.

Are There Informant Characteristics Associated With Accuracy of Reporting or With Informant Reporting Biases?

Associations between informant characteristics and accuracy of reporting, and between informant characteristics and informant reporting biases, are shown in Table IV. The table reveals five main findings. First, there was little evidence that any informant characteristic was associated with accuracy of reporting. Only two (of 36) associations were significant:

female sex was associated with increased accuracy in reporting smoking, and having (vs. not having) educational qualifications was associated with decreased accuracy in reporting alcohol dependence. Second, as expected, informants with (vs. without) a history of disorder were more likely to report that same disorder in probands. This bias was significant for major depressive episode, anxiety, schizophreniform disorder, and drug dependence. Third, female informants were more likely than male informants to report disorder in the proband, and this bias was significant for major depressive episode, alcohol dependence and conduct disorder. Fourth, age of informant was negatively associated with the likelihood of reporting disorder across all disorders, and this bias was significant for two disorders: conduct disorder and smoking. Fifth, there was no evidence that education of the informant was associated with reporting biases.

DISCUSSION

This study sought to evaluate the validity of reports of psychiatric family history using the FHS. We found that psychiatric disorders were reported with low-moderate sensitivity (median=35.9) but high specificity (median=94.0). This indicates that, as in prior family-history research, under-reporting is a more serious problem than over-reporting [Kosten et al., 1992; Weissman et al., 2000; Hardt and Franke, 2007]. Previous investigations of the validity of these disorders using longer diagnostic instruments have found similar levels of sensitivity and specificity. For example, compared to studies using the FH-RDC and FISC (reviewed by Hardt and Franke [2007]), the estimates of sensitivity in the present study were 2% better (median difference across disorders), and the estimates of specificity in the present study were 6% worse (median difference across disorders). Thus, while brief screening instruments, such as the FHS, are subject to the same failings as other informant-based instruments (i.e., low sensitivity), they do not appear to be affected to any greater extent.

Specificity tended to be high across all disorders (>90% for all but two disorders), while sensitivity varied widely. Perhaps reflecting their degree of observability, smoking and asthma were detected with good sensitivity (90% and 60%, respectively), while sensitivity for all psychiatric disorders was lower (all <50%). In general, the family history literature shows little consensus about the relative sensitivity of different psychiatric disorders, so comparisons are difficult. However, two comparisons can be made. First, our finding that anxiety was reported with low sensitivity is in line with most previous research [Kosten et al., 1992; Heun et al., 1996; Weissman et al., 2000; Kendler et al., 2002]. This perhaps highlights the difficulty of reporting on a disorder whose symptoms are largely hidden from view. Second, most previous research reports higher sensitivity estimates for alcohol dependence than we do [e.g., Andreasen et al., 1986; Kosten et al., 1992; Lish et al., 1995; Roy et al., 1996; Weissman et al., 2000; Kendler et al., 2002]. Reasons for our lower estimate are unclear, although it could be that by using DSM criteria with young-adult probands we diagnosed less severe forms of alcohol dependence that were not detected by parental informants.

Combining reports from multiple informants resulted in greater sensitivity (median=44.6) with only a slight loss in specificity (median=91.1). As in most previous studies [e.g., Kosten et al., 1992; Roy et al., 1996; Weissman et al., 2000; Hardt and Franke, 2007], we combined reports from multiple informants using an “Or” rule, where the proband is classified as disordered if *either* maternal or paternal informant reported a positive history. Additional analyses (available from the author) demonstrate that this rule improves sensitivity, whereas sensitivity is reduced by “stricter” combination rules, such as those that require *both* informants to report a positive history, or those that increase the threshold number of symptoms required to be endorsed for a positive history.

We investigated the influence on accuracy and bias in family-history reporting of four informant characteristics: personal history of psychiatric disorders, sex, age, and educational qualifications. These will be discussed in turn.

Regarding informants' disorder history, we found no evidence that informants with a history of disorder reported with any greater accuracy than those without a history. However, in line with previous research [e.g., Kendler et al., 1991; Chapman et al., 1994; Roy et al., 1996; Heun et al., 1997; Coelho et al., 2006], we found that the probability of reporting disorder in the proband was greater for informants with versus without a history of disorder for major depressive episode, anxiety, schizophreniform disorder, and drug dependence. We found no evidence for such biased reporting of the non-psychiatric outcomes we investigated, suggesting that this phenomenon may be specific to reporting of psychiatric disorders.

Regarding informant sex, we found that females reported smoking more accurately than males. A number of previous studies have demonstrated that females report with greater accuracy [e.g., Andreasen et al., 1986; Kosten et al., 1992; Fogelson et al., 2004], though a recent meta-regression has suggested no overall effect [Hardt and Franke, 2007]. In addition, we found that, controlling for the proband's actual disorder status, females were more likely than males to report that the proband suffered from major depressive episode, conduct disorder and alcohol dependence. This is in line with one previous report of a sex-specific reporting bias [Roy et al., 1994]. Thus, researchers should be aware of the potential for sex-specific reporting biases, and should take steps to ensure this does not bias measures of association (e.g., by ensuring that the sex-ratio of informants among compared groups is roughly similar).

Regarding informant age, we found no age-associated increase in accuracy of family history reporting, but did find that age was negatively associated with the likelihood of reporting two outcomes: conduct disorder and smoking. Previous studies of the effect of age on family history reporting have yielded inconsistent conclusions [Roy et al., 1994, 1996; Weissman et al., 2000; Hardt and Franke, 2007]. Notably, the ages of the samples in these studies were very different: the mean age of informants in our sample was around 58, compared to 40–50 in the Roy et al. [1994, 1996] studies, around 34 across samples in the meta-regression by Hardt and Franke [2007], and 23 in the study by Weissman et al. [2000]. The different findings might therefore be a function of the unique parts of the age distribution that each study sampled, especially if the association between age and family history reporting is U-shaped or even more complex.

Regarding informant education, we found evidence that alcohol dependence was reported more accurately by informants without (vs. with) educational qualifications, but no evidence for any reporting bias associated with the informant's education. This perhaps suggests that low (vs. high) education parents may be more willing to accept—and therefore to report—that their adult child has a drinking problem. Though there have been previous investigations of the role of informant education on quality of family history reporting [e.g., Roy et al., 1994, 1996], to our knowledge this is the first report to find a significant association.

This study has a number of strengths. First, because we studied a longitudinal sample, we could prospectively assess disorder in the probands at a number of ages, and derived diagnoses by combining data across ages. In this way we were able to evaluate the validity of family history reports against a measure of disorder that is not prone to the under-detection of cases associated with retrospective recall [Simon and VonKorff, 1995]. Second, our findings were derived from a representative, population-based sample, so are likely to be applicable to population-based uses of family history (e.g., whole genome scans, public

health screening programs). Third, we assessed validity and bias across a number of psychiatric disorders as well as two non-psychiatric outcomes, so were able to test the generality of our findings. This proved particularly beneficial for our analyses of the informant characteristics associated with reporting biases, as we were able to demonstrate that the bias associated with informant age was in a consistent direction across all disorders studied.

Our study also has limitations. First, our estimates of validity and bias were derived from family history reports by parental informants on their 32-year-old child. Replication is therefore needed using different informant–subject combinations to test the robustness of our findings. We can report on the validity of probands' reports on parents, and parents' reports on the other parent, as assessed against the parents' lifetime DSM-IV diagnosed major depressive episode (these data were collected as part of the larger family history study, see Milne et al., 2008). The sensitivity and specificity of proband-reported depression in parents was 45.0% and 76.7%, respectively, while the sensitivity and specificity of parent-reported depression in the other parent was 38.5% and 84.8%, respectively. These estimates of sensitivity and specificity are similar to those we found for parent-reported depression in probands (35.9% and 84.6%, respectively). Moreover, estimates of sensitivity and specificity similar to ours have been demonstrated for 17- to 33-year-old probands reporting on a wide range of psychiatric disorders in their parents, siblings and children [Weissman et al., 2000], suggesting the estimates of sensitivity and specificity reported in this paper generalize to other informant–subject combinations.

Second, we are obliged to offer an explanation of the high prevalence of certain disorders in the Dunedin probands. For example, the prevalence of at least one major depressive episode by age 32 was approximately twice the lifetime prevalence of major depressive episode of 16% in the NCS for the 15–34 age-group [Kessler et al., 1993]. Several factors may contribute to the Dunedin Study's higher prevalence. First, we diagnose regardless of the presence of other disorders, eschewing exclusionary criteria followed in many studies. Second, the 96% participation rate in this study lets us count disordered individuals overlooked in most studies: data from our own study suggests that our prevalence estimates would be 6–28% lower had we achieved a 77% instead of a 96% participation rate (data available on request). Third, after more than 30 years of participation with no confidentiality violation, longitudinal study members are more forthcoming about psychiatric symptoms than participants in single-wave surveys. Fourth, Dunedin diagnoses are based on prospective symptom reports. Although prospective and retrospective studies disagree markedly about cumulative prevalence, they agree very well about past-year prevalence. For example, the average past-year major depressive episode prevalence was 14% in Dunedin, similar to 12% past-year for the similar age group in the NCS [Kessler et al., 1993]. Fifth, the Dunedin Study's prospective diagnoses are not prone to the effects of recall failure to the same extent as the retrospective diagnoses of other studies [Simon and VonKorff, 1995]. Interestingly, when cross-sectional depression data have been modeled to take account of the effects of recall failure, lifetime prevalence rates similar to ours have been achieved [Kruijshaar et al., 2005]. Sixth, cumulative prevalence in Dunedin is based on the sum of past-year cases. Virtually identical high cumulative prevalence rates have been reported by others who followed adolescent cohorts to adulthood while conducting repeated diagnostic assessments in North Carolina, New York, and Oregon [Lewinsohn et al., 1993; Costello et al., 2003; Jaffee et al., 2005].

How might high prevalence for disorders have affected our findings? In terms of our sensitivity estimates, identifying disordered cases (i.e., achieving high sensitivity) might be more difficult when there is high prevalence because there are more disordered cases to identify. Conversely, in terms of our specificity estimates, identifying non-disordered cases

(i.e., achieving high specificity) might be less difficult when there is high prevalence because there are fewer non-disordered cases to identify. However, the fact that our estimates of sensitivity and specificity are very similar to those found in other family history studies [Miles et al., 1998; Weissman et al., 2000; Hardt and Franke, 2007] suggests that the high prevalence for disorder in this sample cannot have had a major impact.

With these limitations in mind, implications of our findings can be noted. First, the FHS is useful tool for assessing family history of disorder. We are not suggesting that the FHS—or, for that matter, *any* informant-based family history instrument—is a substitute for direct interviews when accurate case-identification is required. However, if the goal is to identify cases with a family history of disorder (e.g., for genome-wide association studies), the FHS appears to work as well as other informant-based instruments, and, because it is quick to administer, it is likely to be more cost-effective. Second, multiple informants are necessary when collecting data on psychiatric family history to reduce under-reporting. Third, researchers should be aware of the biases associated with informant characteristics, specifically those associated with having a personal history of disorder, informant sex and informant age. Thus, researchers who aim to compare groups in terms of their family history should ensure that the informants reporting on these groups do not significantly differ in terms of age, sex, and personal history of disorder.

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TABLE I

Prevalence of Psychiatric Disorders, Smoking and Asthma Among Dunedin Study Probands

	Female (n=471)	Male (n=488)
Psychiatric disorders		
Major depressive episode, %	44.1*	25.4
Anxiety, %	52.9*	32.8
Schizophreniform disorder, %	2.8	4.4
Alcohol dependence, %	187	37.1*
Drug dependence, %	9.2	25.3*
Suicide attempt, %	7.1	6.6
Conduct disorder, %	13.9	27.9*
Non-psychiatric outcomes		
Ever been a smoker, %	46.7	45.8
Ever had asthma, %	26.5	25.3

Asterisks indicate significantly higher prevalence among that sex group:

* $P < 0.001$ from Chi-squared tests.

TABLE II

Demographic Characteristics and Prevalence of Lifetime Psychiatric Disorder Symptoms, Smoking and Asthma in Parental Informants

	Maternal (n=933)	Paternal (n=850)
Demographics		
Age at interview, mean (SD)	56.6 (5.3)	59.5 (6.0)**
Educational qualifications, %	59.2	74.3**
Psychiatric disorders, lifetime symptoms[a]		
Major depressive episode, %	68.1**	51.8
Anxiety, %	66.2**	50.2
Schizophreniform disorder, %	16.3	172
Alcohol dependence, %	2.6	8.3**
Drug dependence, %	1.9	1.6
Suicide, %	10.3	7.6
Conduct disorder, %	20.8	49.7**
Non-psychiatric outcomes		
Ever been a smoker, %	54.6	69.8**
Ever had asthma, %	18.8*	13.9

[a]Prevalence is based on self-report of at least one key symptom per disorder following the protocol of the Family History Screen.

Asterisks indicate significantly higher prevalence among that group:

*P<0.01;

**P<0.001.

TABLE III

Sensitivity and Specificity of Single and Combined Informant Reports of the Proband's Psychiatric Disorders, Smoking and Asthma

	(A) Single reports			(B) Combined reports		
Disorder	**N**	**Sensitivity %**	**Specificity %**	**N**	**Sensitivity %**	**Specificity %**
Psychiatric disorders						
Major depressive episode	1,745	35.9	84.6	953	50.8	76.0
Anxiety	1,745	24.1	90.8	953	357	84.3
Schizophreniform disorder	1,707	48.4	96.6	932	55.9	94.5
Alcohol dependence	1,766	21.7	94.0	954	31.7	91.1
Drug dependence	1,765	32.2	96.2	953	44.0	94.8
Suicide attempt	1,740	38.9	98.2	950	44.6	97.l
Conduct disorder	1,743	45.8	85.7	951	60.0	79.5
Non-psychiatric outcomes						
Ever been a smoker	1,760	89.5	93.8	956	95.0	90.5
Asthma	1,720	59.6	94.0	935	73.6	90.6

TABLE IV

Associations Between Informant Characteristics and (i) Accuracy of Reporting (ACC), and (ii) Informant Reporting Biases (BIAS)

		Major depressive episode	Anxiety	Schizophreniform disorder	Alcohol dependence	Drug dependence	Suicide attempt	Conduct disorder	Ever been a smoker	Asthma
Personal history of the same disorder	ACC	0.88 (0.49–1.57)	0.63 (0.33–1.22)	0.54 (0.15–1.95)	1.46 (0.40–5.37)	0.53 (0.08–3.67)	0.83 (0.15–4.65)	1.47 (0.82–2.65)	1.81 (0.84–3.91)	1.13 (0.52–2.43)
	BIAS	2.59 (174–3.86) ***	3.21 (1.89–5.46) ***	2.08 (1.17–3.71) *	1.23 (0.44–3.42)	6.19 (2.06–18.59) **	1.12 (0.35–3.62)	1.11 (0.77–1.60)	0.94 (0.54–1.65)	1.53 (0.87–2.70)
Female sex	ACC	0.96 (0.60–1.52)	1.49 (0.85–2.61)	0.50 (0.18–1.42)	0.74 (0.40–1.39)	1.67 (0.91–3.07)	0.58 (0.23–1.48)	0.97 (0.58–1.64)	3.12 (1.58–6.15) **	1.64 (0.93–2.89)
	BIAS	1.87 (1.33–2.62) ***	1.02 (0.64–1.61)	1.30 (0.79–2.15)	1.59 (1.04–2.44) *	0.97 (0.63–1.50)	2.01 (0.98–4.09)	1.64 (1.21–2.22) **	0.93 (0.57–1.52)	1.34 (0.87–2.08)
Age (10-year increments)	ACC	0.85 (0.50–1.44)	0.89 (0.50–1.60)	0.58 (0.12–2.87)	0.69 (0.32–1.50)	1.93 (0.72–5.17)	0.55 (0.18–1.73)	1.73 (0.95–3.16)	1.67 (0.72–3.84)	1.44 (0.73–2.85)
	BIAS	0.74 (0.52–1.05)	0.86 (0.57–1.30)	0.87 (0.44–1.73)	0.73 (0.42–1.28)	0.45 (0.20–1.01)	0.87 (0.43–1.76)	0.52 (0.35–0.78) **	0.45 (0.22–0.92) *	0.80 (0.48–1.34)
Educational qualifications	ACC	0.59 (0.34–1.00)	0.77 (0.41–1.42)	1.11 (0.27–4.46)	0.46 (0.23–0.93) *	0.65 (0.28–1.49)	0.98 (0.31–3.11)	0.62 (0.34–1.14)	0.56 (0.24–1.30)	0.97 (0.50–1.89)
	BIAS	1.40 (0.96–2.04)	1.04 (0.63–1.73)	1.27 (0.68–2.35)	1.22 (0.72–2.09)	1.34 (0.69–2.59)	1.21 (0.52–2.84)	1.26 (0.88–1.81)	1.18 (0.65–2.17)	1.17 (0.70–1.96)

For ACC, panels show the increased odds (95% CI) of correctly identifying a proband as disordered associated with each informant characteristic. For BIAS, panels show the odds (95% CI) of reporting that a proband is disordered associated with each informant characteristic, controlling for the proband's actual disorder status

* $P<0.05$.

** $P<0.0l$.

*** $P<0.001$.