



The Influence of Informant Characteristics on the Reliability of Family History Interviews

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Family history interviews are widely used in psychiatric research, as well as in genetic and twin studies, and provide a way to collect family history information quickly and economically. To obtain a valid assessment of family history, it is important to investigate which family member will be able to provide accurate information. Previous research shows that the validity of family history reporting can be influenced by characteristics of the informant, such as age, gender and personal history of psychiatric disorder. The aim of this study was to investigate the role of a subject's position in a pedigree on the validity of data collection. Family history data on diabetes and psychiatric disorders were collected in three generations of 33 families by interviewing both an index subject (3rd generation) and his or her mother (2nd generation). Mothers were shown to report higher rates of diabetes and psychiatric disorder in the family compared to the index subjects. There was no significant difference in the disease rate reported by male and female index subject. Mothers who experienced a depressive episode indicated significantly more family members as having a psychiatric disorder than mothers who never experienced such an episode. This could be explained by the presence of informant bias, but may also result from the fact that depression is a heritable disorder and is therefore actually more prevalent in these families. Our findings suggest that family interview data should be collected by interviewing subjects who have a central position in the pedigree and can therefore provide information on his/her own generation, the previous and the next. In addition, psychiatric status of the informant should be carefully addressed.

■ **Keywords:** family history interview, age, gender, psychiatric disorder

The assessment of family history is widely used in psychiatric research, as well as in primary care practice (Bensen et al., 1999). Since the acknowledgment that the risk to develop a psychiatric disorder is influenced by genetic factors, many family studies have been conducted. Accurate information about the presence or absence of psychiatric disorders in family members is needed to study these genetic factors. For such a purpose, it is important to assess all members of a pedigree for as many generations as possible.

Family history interviews provide a way to collect family history information quickly and economically. The main advantage is that only one informant provides information on his or her relatives. In this way, information on all the members of a pedigree can be collected. This is important, because Heun and colleagues (Heun et al., 1995) showed that family members willing to participate in research can differ from those who are unwilling. A disadvantage may be reduced validity of data collection, and

it is therefore crucial to interview a subject who is capable of providing valid information. This is of particular importance when some of the potential informants may suffer from a psychiatric (e.g., psychotic) disorder.

Past research shows that the validity of family history reporting can be influenced by characteristics of the informant, such as age, gender, personal history of psychiatric disorder, and familial relationship (Bensen et al., 1999; Chang et al., 2006; Coelho et al., 2006; Devi et al., 1998; Heun et al., 1997; Heun & Muller, 1998; Milne et al., 2009). In addition, the validity of data collection may

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depend on the specific disease or disorder of interest. Milne et al. (2009) showed that the assessment of family history information on smoking and asthma was more reliable than the assessment of the family history information on psychiatric disorders. Hardt and Franke (2007) further showed that family history interview data on severe mental disorders are more reliable than family history data on less severe disorders.

One way to study the validity of family history data collection is to compare disease rates as reported by different informants. For example, a subject might not be informed on the disease status of a grandparent, while he or she is probably more likely to be informed on the disease status of his or her parent. In addition, gender and personal psychiatric history may influence the validity of the collected information. The aim of this study is to compare family history interview data on diabetes and psychiatric disorders assessed in subjects of different generations in a pedigree. Thirty-three families with no family history of psychosis participating in the Genetic Risk and Outcome of Psychosis (GROUP) study were included (Genetic Risk and Outcome in Psychosis (GROUP) Investigators, 2010). Data were collected in index subjects, being a member of the third generation, and in their mothers, being a member of the second generation. We will test whether the reported rates of diabetes and psychiatric disorder are different between these two types of informants. In addition, we will assess whether gender and psychiatric status influence the assessment of family history.

Methods

The families participating in this study are a subset of the control group from the Genetic Risk and Outcome of Psychosis (GROUP) study (Genetic Risk and Outcome in Psychosis (GROUP) Investigators, 2010). Controls were selected through a system of random mailings to addresses in the catchments areas of the schizophrenia cases. Inclusion criteria for the index subjects were: (1) age between 18 and 50 years, (2) no psychotic disorder, and (3) no first- or second-degree relatives with psychosis. After complete description of the study, all participants provided written informed consent. The Family Interview for Genetic Studies (FIGS) was administered (Maxwell, 1992) to assess diabetes and psychiatric disorders, including depression, mania, personality disorders, and alcohol or drug abuse. Both the index subject and his or her mother were interviewed. This resulted in 33 completed interviews by the index subject and 33 completed interviews by his or her mother. The index subjects had a mean age of 32.5 years and 52% were male. Mothers had a mean age of 61.7 years. The 33 families comprised 507 relatives from three generations in whom information on diabetes and psychiatric disorders was obtained. Index subjects were members of the third generation and their mothers of the second generation.

We assumed that a disorder was present if at least one of the informants responded positively. To compare the disease rates of diabetes and psychiatric disorder reported by the index subjects with the disease rates reported by the mother, the McNemar's Test for comparing dependent samples was used as the mothers and the index subjects reported on the same family members. In contrast, the effect of gender and psychiatric status on the assessment of family history was tested with a chi-squared test for independent samples. Data were analyzed using R version 2.12.0 for Windows software.

Results

In total 22 of the 451 relatives were reported to have diabetes according to at least one of the informants (see Table 1 for a summary of the results). Of these 22 relatives, the mother identified 19 of the 22 (86%) family members with diabetes and the subject identified 9 of the 22 (41%) family members with diabetes. The mother indicated significantly more family members with diabetes than the index subject, $\chi^2(1) = 5.06, p = .02$. In total, mothers indicated 3.5% of the family members as having diabetes compared to 1.8% indicated by the index subject. For psychiatric disorders including depression, mania, personality disorders and alcohol or drug abuse, mothers and index subjects reported on 480 family members. The mother recognized 38 (88%) of the 43 cases and the index subjects 18 (42%) of the 43 cases. In total mothers indicated 7.0% of the family members as having a psychiatric disorder compared to 3.5% indicated by the index subjects. This implies that mothers report significantly higher rates on psychiatric disorders compared to index subjects, $\chi^2(1) = 12.03, p < .0005$.

Seventeen of the index subjects are male and 16 are female. The male index subjects reported on 270 family members, while females reported on 240 family members. Male index subjects rated 1.9% of their relatives as having diabetes and 3.7% as having a psychiatric disorder. Female index subjects reported that 1.7% of their relatives had diabetes and 3.3% had a psychiatric disorder. There was no significant difference in the disease rates reported by male and female index subjects for diabetes, $\chi^2(1) = 03, p = .86$, or psychiatric disorders, $\chi^2(1) = .01, p = .91$.

Of the 33 mothers, seven experienced a depressive episode and 26 did not. The mothers who experienced a depressive episode reported on 129 family members while mothers who did not have a depressive episode reported on 411 family members. Mothers who experienced a depressive episode indicated significantly more family members as having a psychiatric disorder (12.4%) than mothers who never experienced such an episode (5.8%) $\chi^2(1) = 5.25, p = .02$. No difference was found for diabetes $\chi^2(1) = .25, p = .62$. Note that the rate of depression in the index subjects was low ($N = 3$) and we could therefore not perform this analysis in index subjects.

TABLE 1

The Reported Rates of Diabetes and Psychiatric Disorder Assessed in Different Types of Informants

	Diabetes N affected/total N (%)	Psychiatric disorder N affected/total N (%)
Index subjects	9/451 (2.0%)	18/480 (3.8%)
Mothers	19/451 (4.2%)	38/480 (7.9%)
	$\chi^2(1) = 5.06, p = .02$	$\chi^2(1) = 12.03, p < .001$
Male index subjects	5/270 (1.9%)	10/270 (3.7%)
Female index subjects	4/240 (1.7%)	8/240 (3.3%)
	$\chi^2(1) = .03, p = .86$	$\chi^2(1) = .01, p = .91$
Mothers with depression	7/129 (5.4%)	16/129 (12.4%)
Mothers without depression	16/411 (3.9%)	24/411 (5.8%)
	$\chi^2(1) = .25, p = .62$	$\chi^2(1) = 5.25, p = .02$
Subjects with depressed mother	1/127 (0.8%)	8/127 (6.3%)
Subjects without depressed mother	8/383 (2.1%)	10/383 (2.6%)
	$\chi^2(1) = .33, p = .56$	$\chi^2(1) = 2.80, p = .09$

Since depression is influenced by genetic factors, it is possible that the prevalence of depression is indeed higher in the families of the mothers with a depressive episode. We therefore compared the prevalences as reported by index subjects with a mother who experienced a depressive episode and index subjects with a mother who did not experience such an episode. The prevalence of having a psychiatric disorder was 6.3% in index subjects of whom the mother had a depressive episode compared to a prevalence of 2.6% in index subjects with mothers who never had a depressive episode, $\chi^2(1) = 2.80, p = .09$.

Discussion

We have studied family history interview data on diabetes and psychiatric disorders assessed both in an index subject and in his or her mother and showed that mothers report significantly higher disease rates. As disease status was not confirmed by clinical diagnosis we do not have a gold standard for comparison. However, the percentages as reported by the mother closely resembled the prevalence of diabetes (3.9%¹) for the global Dutch population in 2008, provided by the Dutch state institution for health and environment. Although the family history interview was administered to assess depression, mania, personality disorders, and alcohol or drug abuse, the majority of the family members indicated as having a psychiatric disorder were suffering from depression. The reported prevalence of depression by the mothers resembles the lifetime risk of 10% mentioned by Andrews et al. (2005). These findings indicate that the mothers in this study were likely to be more valid informants.

Index subjects had slightly more difficulty with identifying family members with diabetes than family members with psychiatric disorders. This is in contrast with the finding of Milne et al. (2009), who report that information collected on a physical disorder like asthma is more valid than information about psychiatric diseases. This can pos-

sibly be explained by the fact that the occurrence of a somatic disease such as diabetes is more common in elderly (i.e., first generation) family members and therefore unknown by the young index subjects (i.e., third generation). So the finding by Bensen et al. (1999) that older subjects are less accurate informants than younger ones may be explained by generation rather than age.

Previous research shows that gender, personal history of psychiatric disorder and age of the informant influences the validity of data collection (Bensen et al., 1999; Chang et al., 2006; Coelho et al., 2006; Devi et al., 1998; Heun et al., 1997; Heun & Muller, 1998; Milne et al., 2009). In contrast to the findings of Milne et al. (2009), gender did not appear to influence the reliability of the collection of family history data in our study. In agreement with earlier findings, we showed that mothers who had a depressive episode reported significantly higher rates of depression in their family members than mothers who had never had a depressive episode. This finding could be due to informant bias but may also result from the fact that depression is a heritable disorder. The latter hypothesis was supported by the finding that index subjects with a mother who experienced a depressive episode also reported higher rates of a psychiatric disorder compared to index subjects who did not have a mother who experienced a depressive episode. In the index subjects themselves, it was not possible to compare subjects with or without psychiatric disorder as only three of the 33 subjects had ever experienced a depressive episode.

In addition to the absence of a gold standard for clinical diagnosis, a second limitation of this study is the fact that the family history interviews were conducted in a cohort of subjects selected for the absence of psychosis in the family. As the presence of mania, personality disorders, and alcohol or drug abuse was low, we mainly focused on depression. Future studies should reveal if the results can be generalized to families with psychosis.

In conclusion, studying the collection of family history in a pedigree consisting of three generations, members of the second generation were shown to provide more valid information on family history data compared to the third generation. It could therefore be hypothesized that it is not age but generation that influences the validity of family history data collection. Our findings suggest that interviewing mothers about her own generation, the previous generation and the next generation is to be preferred over interviewing the younger index subjects. In addition, the psychiatric status of the informant should be carefully addressed, although we have not conclusively shown a reporter bias in informants suffering from a psychiatric disorder.

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Endnote

- 1 <http://www.nationaalkompas.nl/gezondheid-en-ziekte/ziekten-en-aandoeningen/endocriene-voedings-en-stofwisselingsziekten-en-immuniteitsstoornissen/diabetes-mellitus/verschillen-internationaal/>

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