

Accuracy of Offspring Reports of Parental Cardiovascular Disease History: The Framingham Offspring Study

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Background: Family history is used to infer the risk for heart disease; however, little is known about the accuracy of family history reports.

Objective: To examine the accuracy of offspring reports of parental cardiovascular disease.

Design: Validation study.

Setting: Framingham Heart Study.

Participants: Offspring participants of the multigenerational Framingham Heart Study with both parents in the original cohort.

Measurements: 791 men and 837 women (mean age, 57 years) completed a family history questionnaire from 1995 to 1998. Offspring reports were compared with confirmed medical evidence of parental status, and positive and negative predictive values and likelihood ratios were calculated.

Results: Positive reports of high blood pressure, diabetes, and high cholesterol levels in fathers were accurate: Positive predictive values were 83% (95% CI, 80% to 86%), 76% (CI, 70% to 82%), and 78% (CI, 73% to 83%), respectively. Corresponding positive predictive values for reports in mothers were 91% (CI, 89% to 93%), 79% (CI, 73% to 85%), and 88% (CI, 84% to

92%), respectively. Positive predictive values for reports of paternal heart attack occurring before 55 years of age and for stroke occurring before 65 years of age were 28% (CI, 22% to 34%) and 43% (CI, 33% to 53%), respectively, whereas the positive likelihood ratios were 8.6 (CI, 6.8 to 10.9) and 11.2 (CI, 9.2 to 13.6), respectively. Negative predictive values for parental history reports were greater than 90%, except for high blood pressure and high cholesterol level (negative predictive values, 33% to 55%, and negative likelihood ratios, 0.47 to 0.88).

Limitations: This study does not determine whether more accurate measures of family history would meaningfully improve estimation of cardiovascular risk.

Conclusions: Negative parental history reports were reliable, except for hypertension and high cholesterol levels. Although reports of parental premature heart attack and stroke had high likelihood ratios, their predictive values were low because the prevalence of these conditions was low in parents. If patients were more aware of their parents' medical illnesses, they might be able to estimate their risk for disease more accurately and perhaps motivate themselves to follow a healthy lifestyle.

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A report of a positive family history confers an increased risk for cardiovascular disease and risk factors in first-degree relatives (1–10). Therefore, physicians use self-reported information about family history to infer the risk for cardiovascular disease in their patients, develop screening strategies, and target primary prevention efforts (11). Although most of the information about family history that is available to physicians is limited to individual patient reports of their family members' disease status, little is known about the accuracy of these reports. Previous work has largely evaluated a person's reported family history compared with the relatives' self-reported medical history (12).

Few studies have validated the reported family history information with medical record information (13–15) or direct clinical assessment of the affected relatives (16). These studies have been limited to reports provided by high school students (15, 16), accounts of deceased relatives using data from death certificates (14), or small case-control studies restricted to male reporters (15). A better understanding of the magnitude of misreporting of family history information and the factors related to misreporting is needed to enhance physicians' ability to reliably use a patient's reported family history and identify those at increased risk for disease. This will allow prevention efforts to be focused most effectively.

The multigenerational design of the Framingham Heart Study provides the unique opportunity to examine the accuracy of reported parental history information because of the availability of validated events and objective clinical assessments in a 2-generation population-based sample. We also sought to evaluate the effects of age, sex, and birth order on offspring reports of parental history. In addition, we assessed whether a less restrictive definition of cardiovascular disease might improve reporting.

METHODS

Study Sample

The Framingham Heart Study was established in 1948 when 5209 residents of Framingham, Massachusetts, 28 to 62 years of age, were enrolled in a prospective epidemiologic cohort study. Members of the original cohort have undergone follow-up examinations every 2 years. In 1971, 5124 offspring of the original cohort members and offspring spouses were enrolled in the Framingham Offspring Study. These participants undergo follow-up examinations approximately every 4 years. Study design and entry criteria have been reported elsewhere (17, 18). The Institutional Review Board at Boston Medical Center approved the examination content for both offspring and original cohort examinations.

Family History Questionnaire

From 1995 to 1998, offspring participants who attended a routine research examination (1656 men and 1875 women) were asked to complete a self-administered Awareness of Coronary Factors questionnaire that included questions about cardiovascular risk factors and disease for themselves and their parents. Participants were asked, "Did your parents . . . and did you . . . ever have high blood pressure, ever have high blood cholesterol >6.2 mmol/L (>240 mg/dL), ever have diabetes mellitus, have a heart attack before age 55, have a stroke before age 65, or die of heart disease?" Participants reported separately for their father and mother.

Final Study Sample

Only offspring participants who had both natural parents in the original cohort of the Framingham Heart Study were eligible for inclusion in this study. Exclusions included 682 offspring with only one parent in the original cohort, 15 offspring with neither parent in the original cohort, and 1079 offspring spouses. An additional 10 offspring participants were excluded because parental data were unavailable. Reports of parental history information were missing for 117 participants who were excluded. Therefore, the study sample consisted of 791 male offspring reporters and 837 female offspring reporters.

Ascertainment of Risk Factors

Research examinations included 2 measurements of resting blood pressure obtained by physicians, a physician-administered medical history questionnaire and physical examination for the presence of symptoms and signs of cardiovascular disease, resting electrocardiography, and blood specimens for glucose and cholesterol levels. Parental hypertension was defined as a blood pressure of 160/95 mm Hg or greater or the use of antihypertensive medications on at least 2 research examinations. We did not use criteria for hypertension recommended in the sixth report of the Joint National Committee on Prevention, Detection, and Treatment of High Blood Pressure because many original cohort members died before publication of these criteria (19). Diabetes mellitus was defined as a random blood glucose level of 11.1 mmol/L (200 mg/dL) or greater or the use of insulin or oral hypoglycemic agents. High blood cholesterol level was considered present if the total cholesterol level was 6.2 mmol/L (240 mg/dL) or greater or if the parent was using cholesterol-lowering medications on at least 2 research examinations.

Risk factors in offspring reporters were defined by using more contemporary criteria and were considered to be present if criteria were met at 2 or more research examinations attended or at the examination at which the parental history data were collected. Offspring hypertension was defined as a blood pressure reading of 140/90 mm Hg or greater or use of blood pressure-lowering medication. Diabetes was defined as a fasting blood glucose level of

Context

Although physicians use the family history in their assessment of cardiovascular disease risk, the accuracy of patient reports of family history is unknown.

Contribution

Using Framingham Heart Study data spanning 2 generations, the authors compared participant reports of parental history with parents' health records. Specificity was high and sensitivity was low for all items.

Conclusion

A positive family history item is probably accurate. A negative family history item is often inaccurate.

—The Editors

7.77 mmol/L (140 mg/dL) or greater or use of insulin or oral hypoglycemic agents. Current recommendations to diagnose diabetes by using a fasting glucose of 6.99 mmol/L (126 mg/dL) or greater were not in effect at the time of this study (20). High blood cholesterol level was considered present for a total cholesterol level of 6.2 mmol/L (240 mg/dL) or greater or use of cholesterol-lowering medication.

Validation of Cardiovascular Outcomes

An end point committee panel of 3 senior physician investigators reviewed all available information (Framingham Heart Study research examination records, outside personal physician and hospital records, and next-of-kin interviews) to determine the presence of myocardial infarction and to assign a cause of death. A panel of study neurologists reviewed all available information for suspected cases of stroke and transient ischemic attack. Uniform criteria for all cardiovascular disease end points and causes of death have been in place for both the original cohort and offspring since study inception.

Statistical Analysis

Offspring parental history reports were compared with parental data recorded in the research database. Sensitivity, specificity, positive and negative predictive values (and their 95% CIs) of offspring reports for parental risk factors, and cardiovascular events were calculated. Sensitivity measures the proportion of the offspring sample with a parent with the condition that has a positive offspring report, and specificity measures the proportion of the offspring sample with a parent free of the condition that has a negative offspring report. Positive predictive value estimates the probability that the parent has the condition, given a positive offspring report, whereas negative predictive value measures the probability that the parent does not have the condition, given a negative offspring report. Because predictive values depend on the prevalence of disease or no

parental events, the positive likelihood ratios for all parental events were high. The likelihood ratio for a positive offspring report of paternal heart attack was 8.6, indicating that a positive offspring report is 8.6 times more likely to come from an offspring with a father who had a heart attack before age 55 years than from an offspring with a father free of the condition. Furthermore, the positive likelihood ratios for parental heart attack and stroke were actually greater than the positive likelihood ratios for high blood pressure and high blood cholesterol level, risk factors with high positive predictive values. Thus, the low positive predictive values for parental history of heart attack and stroke may in part reflect the low prevalence of these conditions in parents rather than solely low predictive value.

Negative offspring reports of parental history of diabetes, early-onset heart attack, and death from heart disease were associated with negative predictive values of 92% to 99% and negative likelihood ratios significantly less than 1.0 (Table 2). For a parental history of high blood pressure and high blood cholesterol level, negative reports were associated with low negative predictive values of 53% to 55% for high blood pressure and less than 50% for high blood cholesterol levels. The negative likelihood ratios for these conditions ranged from 0.47 to 0.64 for high blood pressure and approximately 0.9 for high blood cholesterol level. For offspring reports of early-onset stroke in a parent, the negative predictive values were high ($\geq 96\%$); however, the negative likelihood ratios were 0.51 to 0.61.

We examined the effect of several offspring characteristics on reporting. The accuracy of parental history reports did not differ significantly between male and female offspring reporters for any cardiovascular disease risk factor or event (Figure 1). Age affected the accuracy of offspring parental history reports for some conditions. Men with incorrect reports were on average 2 years older and women with incorrect reports were on average 4 years older than

their counterparts with correct reports. No significant differences in the accuracy of reporting of parental history were seen in the oldest compared with the youngest sibling.

The presence of a risk factor in the offspring reporter did not affect the accuracy of a report for the same condition in the parent. Positive predictive values for parental hypertension were similar in offspring reporters having and not having high blood pressure; however, negative predictive values were lower in offspring reporters who had high blood pressure than in those who did not (negative predictive values of 44% and 57%, respectively, for fathers and 43% and 59%, respectively, for mothers). No differences were seen in reporting of parental diabetes mellitus in offspring reporters with and without diabetes mellitus.

The positive predictive value of an offspring report of a heart attack before age 55 years in a father improved as we broadened the definition of correct response for heart attack. In broadening the definition of a correct response, a false-positive response was changed to a true-positive response if the criteria for the broadened definition were met. When the definition of heart attack assigned a correct response included a heart attack at any age or coronary heart disease at any age, the recalculated positive predictive value increased from 28% to 54% or to 86%, respectively. When the definition of stroke assigned a correct response was broadened to stroke at any age, the positive predictive value of offspring reports improved from 43% to 64% for reports about fathers and from 54% to 75% for reports about mothers. Similarly, when we broadened the definition of a correct response to “die of heart disease” to include both validated coronary heart disease and cardiovascular deaths, the positive predictive values improved to 79% for reports about fathers and to 70% for reports about mothers.

Table 2. Accuracy of Offspring Parental History Reports Compared with Parents' Confirmed Medical History

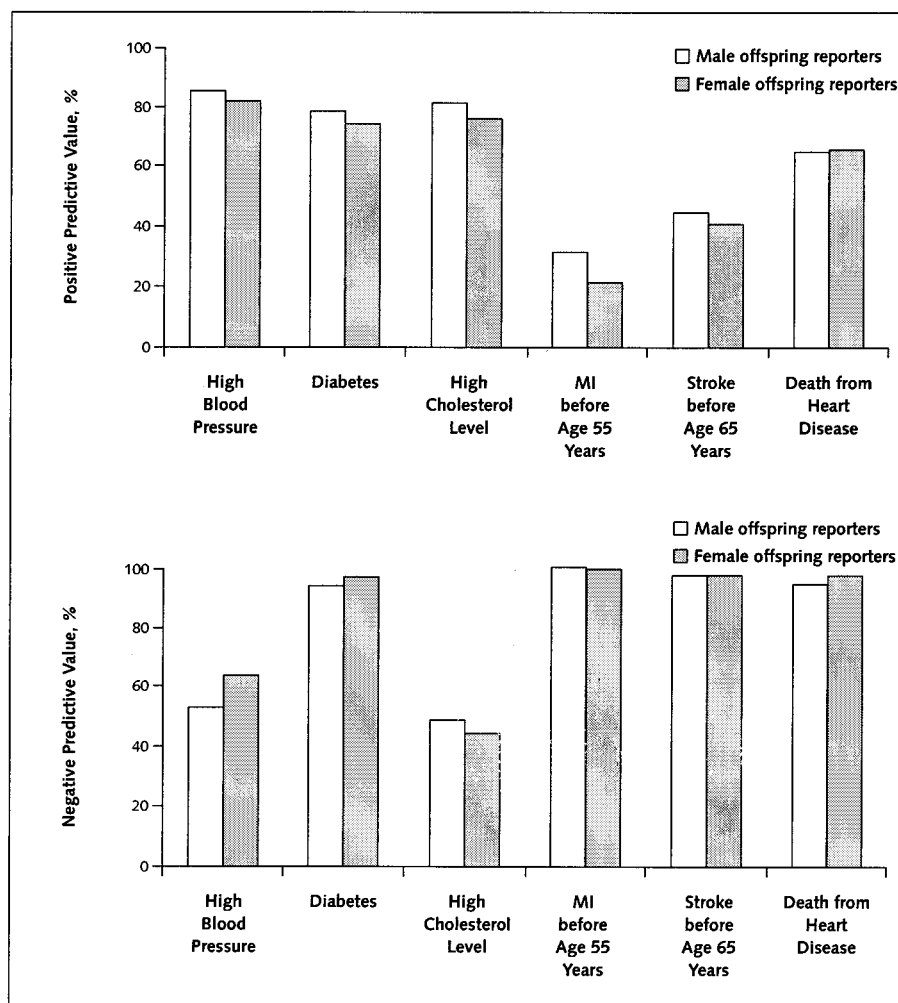
Condition	Prevalence	Positive Predictive Value (95% CI)	Negative Predictive Value (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)	Positive Likelihood Ratio (95% CI)*	Negative Likelihood Ratio (95% CI)†
← % →							
Offspring reports about fathers							
High blood pressure	58	83 (80–86)	53 (50–56)	44 (41–47)	88 (86–90)	3.6 (3.3–4.0)	0.64 (0.58–0.70)
Diabetes mellitus	16	76 (70–82)	92 (91–93)	56 (50–62)	97 (96–98)	16.6 (14.5–18.9)	0.46 (0.40–0.52)
High blood cholesterol level‡	61	78 (73–83)	42 (39–45)	19 (17–21)	92 (90–94)	2.3 (2.1–2.6)	0.88 (0.80–0.97)
Heart attack age < 55 y	4	28 (22–34)	99 (98–100)	74 (64–84)	91 (90–92)	8.6 (6.8–10.9)	0.28 (0.22–0.36)
Stroke age < 65 y	6	43 (33–53)	96 (95–97)	42 (32–52)	96 (95–97)	11.2 (9.2–13.6)	0.61 (0.50–0.74)
Death from heart disease	24	66 (62–70)	93 (92–94)	81 (77–85)	86 (84–88)	5.9 (5.3–6.6)	0.22 (0.20–0.25)
Offspring reports about mothers							
High blood pressure	64	91 (89–93)	55 (52–58)	57 (54–60)	90 (88–92)	5.6 (5.0–6.2)	0.47 (0.43–0.53)
Diabetes mellitus	14	79 (73–85)	95 (94–96)	65 (59–71)	97 (96–98)	24.0 (20.8–27.7)	0.36 (0.31–0.42)
High blood cholesterol level‡	70	88 (84–92)	33 (31–35)	18 (16–20)	95 (93–97)	3.3 (3.0–3.7)	0.87 (0.78–0.96)
Heart attack age < 55 y	<0.01			Too few events to analyze			
Stroke age < 65 y	5	54 (43–65)	97 (96–98)	51 (40–62)	98 (97–99)	22.4 (17.9–28.0)	0.51 (0.40–0.63)
Death from heart disease	10	47 (41–53)	97 (96–98)	72 (65–79)	91 (90–92)	8.1 (6.9–9.6)	0.31 (0.26–0.37)

* Positive likelihood ratio is the quotient of sensitivity/(1 – specificity).

† Negative likelihood ratio is the quotient of (1 – sensitivity)/specificity.

‡ More than half of reporters responded “unsure” or “unknown” for this condition in the parent.

Figure. Offsprings' reports of cardiovascular risk factors and disease in their fathers.



Top. Positive predictive values. Bottom. Negative predictive values. MI = myocardial infarction.

DISCUSSION

We examined the accuracy of offspring-reported parental history of cardiovascular risk factors and events by using objective medical records and clinical assessments of parents in the population-based multigenerational Framingham Heart Study. Negative offspring parental history reports were reliable (high negative predictive value) for diabetes, early-onset heart attack and stroke, and death from heart disease, but not for high blood pressure and high blood cholesterol level. Positive offspring parental history reports were very accurate (high positive predictive value) for cardiovascular risk factors but relatively inaccurate (low positive predictive value) for positive reports of early-onset heart attack and stroke. The low positive predictive value for these parental events may be more reflective of the low prevalence of these conditions in parents in our sample than solely low predictive power, as evidenced by the high likelihood ratios. Offspring with positive paternal reports of early-onset heart attack and stroke were 8.6 and 11.2 times as likely to have a father with these conditions than offspring with fathers free of heart attack

and stroke, respectively. However, the parents in our study sample were derived from a community-based sample and are thus likely to be representative of the general population of patients presenting to a physician's office.

To our knowledge, this is the largest study in middle-aged adults that compared self-reported and validated information for both male and female offspring reporters and included both fatal and nonfatal parental events. Our expectation that offspring reporters in our study sample would have good knowledge of cardiovascular risk factors and diseases as a result of their participation and their parents' participation in a longitudinal study of cardiovascular disease was confirmed by their ability to report accurately on the same conditions for themselves. Thus, our findings probably represent the best-case scenario regarding accuracy of offspring-reported parental history.

The true magnitude of risk for offspring cardiovascular disease associated with a positive parental history is uncertain in part because available data rely on offspring reports with limited validation of parental history. Misreporting of parental history may lead to an underestimation of the

associated risk for cardiovascular disease in offspring. It remains unclear whether more accurate offspring reporting of parental history would substantially change the associated relative risks or improve patient care. Despite these limitations, current national practice guidelines for clinicians recommend ascertaining a parental history of premature onset of heart disease when deciding whether to begin drug therapy for hypertension and high blood cholesterol level (11, 20). Preliminary work from the Framingham Heart Study supports this strategy because parental history of cardiovascular disease was shown to add predictive value to individual established risk factors in determining offspring risk for disease (23).

Studies that use data from death certificates or general practitioner records to validate parental history reports have yielded higher estimates of the accuracy of family history reports of coronary heart disease (14, 15, 24) than did our study. For this purpose, data from death certificates are problematic because of incorrect diagnoses. Previous work from the Framingham Heart Study has demonstrated that coronary heart disease as a cause of death may be overrepresented on death certificates, particularly in older persons (25). The difference in accuracy between our study and earlier reports is probably related to alternate methods used to confirm family history reports, the definition of coronary heart disease that is used to indicate a positive report, and restriction of reports to deceased family members.

The prevalence of early-onset heart attack and stroke in parents in our study was low (<6%), and reliable negative reporting (high negative predictive values) would be expected because most of the reporters have disease-free parents. Myocardial infarction and stroke often result in hospitalization and can be associated with substantial disability. Therefore, the degree of awareness among family members may be greater for these conditions. Hypertension and high blood cholesterol level usually lack signs or symptoms, and a significant fraction of those affected are unaware of these conditions (11, 26). All original cohort participants of the Framingham Heart Study routinely had periodic screening for cholesterol level, but the role of cholesterol in predicting heart disease was not established until the 1970s and 1980s (27, 28). Therefore, original cohort participants may not have been treated for high cholesterol level in their lifetime. These factors may in part explain the low negative predictive value observed for offspring reports of parental high blood pressure and high blood cholesterol level.

The positive predictive value for offspring reports of early-onset heart attack was low and increased by broadening the definition of a correct report. Other investigators have hypothesized that a broad definition of coronary disease, encompassing a larger number of events rather than heart attack alone, may lead to greater accuracy in family history reports (12). The phrasing of the question may affect the accuracy of the family history report. For exam-

ple, others have used phrases such as “did you ever have . . .” (12), instead of asking about premature disease onset. However, guidelines for physicians that incorporate family history as a risk factor for disease often include age at onset of the disease in the family history definition. For example, the National Cholesterol Education Program assigns family history risk factor status if coronary heart disease occurred in a first-degree male relative before age 55 years and in a first-degree female relative before age 65 years (11).

Older offspring, both male and female, were more likely to report incorrectly on some of their parents' conditions. This may reflect that older reporters had older parents who were unaware of some medical conditions. We expected that offspring reporters with a particular condition would be better able to report the presence or absence of the condition in their parents. Our study findings demonstrated that reporters with hypertension were more likely to underreport the condition in the parent (lower negative predictive value) than were reporters without hypertension. Other investigators have also found that reporters with a health condition did not report disease status in their relatives more accurately (12). Therefore, although a person with a particular medical condition may have more knowledge of the condition, this cannot be associated with better reporting of the condition within the family.

Our study has several limitations. First, the accuracy of offspring reports of parental history may have been higher if the questionnaire had been administered by an interviewer. The offspring participant may have been aware of his or her parental history of heart attack and the age at which it occurred, but failed to attend to the portion of the question that required the heart attack to occur before age 55 years. Second, reporting accuracy may also have been affected by the stringent research criteria used at the Framingham Heart Study to assign cardiovascular disease end points. It is possible that the parent's personal physician discussed with the parent or offspring reporter the occurrence of a heart attack or stroke, but the Framingham Heart Study end point committee did not find evidence that met the standardized criteria required to assign the event. Our results cannot be generalized to other ethnicities because our sample primarily consisted of white participants and reflects family interactions and living patterns up to the 1990s in a suburban area. Greater mobility in society and different degrees of awareness of cardiovascular health status across generations may now be operative.

Our study has several clinical implications. Direct administration of the questionnaire and broadening the definition of a particular cardiovascular event may improve reporting. Identification of persons with a positive family history is important because family history is a recognized risk factor for cardiovascular disease and national screening and treatment guidelines have included a reported family history of premature cardiovascular disease in the criteria for initiating drug treatments (11). Physicians and other

health care professionals need to educate their patients on the presence and relevance of a family history of disease to clarify within families the associated risks and in turn enhance adherence with primary prevention interventions.

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