Published in final edited form as:

Am J Prev Med. 2017 May ; 52(5): 640–644. doi:10.1016/j.amepre.2016.11.018.

Put the Family Back in Family Health History: A Multiple-Informant Approach

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Abstract

Introduction—An accurate family health history is essential for individual risk assessment. This study uses a multiple-informant approach to examine whether family members have consistent perceptions of shared familial risk for four common chronic conditions (heart disease, Type 2 diabetes, high cholesterol, and hypertension) and whether accounting for inconsistency in family health history reports leads to more accurate risk assessment.

Methods—In 2012–2013, individual and family health histories were collected from 127 adult informants of 45 families in the Greater Cincinnati Area. Pedigrees were linked within each family to assess inter-informant (in)consistency regarding common biological family member's health history. An adjusted risk assessment based on pooled pedigrees of multiple informants was evaluated to determine whether it could more accurately identify individuals affected by common chronic conditions, using self-reported disease diagnoses as a validation criterion. Analysis was completed in 2015–2016.

Results—Inter-informant consistency in family health history reports was 54% for heart disease, 61% for Type 2 diabetes, 43% for high cholesterol, and 41% for hypertension. Compared with the unadjusted risk assessment, the adjusted risk assessment correctly identified an additional 7%–13% of the individuals who had been diagnosed, with a <2% increase in cases that were predicted to be at risk but had not been diagnosed.

Conclusions—Considerable inconsistency exists in individual knowledge of their family health history. Accounting for such inconsistency can, nevertheless, lead to a more accurate genetic risk assessment tool. A multiple-informant approach is potentially powerful when coupled with technology to support clinical decisions.

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INTRODUCTION

More than a decade ago, the Surgeon General launched the Family History Initiative, which included a series of efforts to increase public awareness about the value of family health history (FHH) for tailored disease prevention and medical care.¹ This was motivated by research showing that FHH tapped into the joint effect of shared genetic and environmental risk factors clustered in families, making it a robust predictor of many conditions.^{2–4} Accordingly, many advocate using FHH for preventing complex diseases such as heart disease and Type 2 diabetes mellitus (T2DM).^{5–7}

In clinical practice, FHH is routinely collected but underutilized, owing in part to inaccuracy in self-reports.^{8–12} When validated with medical records, accuracy of individuals' reports of parental history is 74% for heart disease, about 60% for T2DM, about 50% for hypertension, and less than 20% for high cholesterol.¹¹ New tools such as pedigree workbooks and online software support better FHH collection,^{13–16} but focus on individuals as opposed to harnessing the potential of families. Informants may have different perceptions of a common biological family member's health history. Capitalizing on a multiple-informant approach, this report addresses two questions:

1. Do informants have consistent perceptions of common family members' health history?
2. Does accounting for (in)consistency lead to more accurate risk assessment?

METHODS

Study Population

Initial participants were recruited as part of a study of families affected by T2DM in the Greater Cincinnati Area. They were asked to refer biological relatives with or without T2DM into the study. This process generated a sample of 155 participants from 70 families of diverse backgrounds, with 39% African American and 14% self-reported Appalachian heritage. Data were collected in 2012–2013 by interviewers specialized in genetic counseling. This 2015–2016 analysis, conducted using Stata, version 13, was based on the 45 families with two or more informants (N=127; sample characteristics presented in Appendix Table 1). The IRBs at the University of Cincinnati and National Human Genome Research Institute approved the study.

Measures

Individual and family histories on heart disease, T2DM, high cholesterol, and hypertension were collected. Responses to each question included *yes*, *no*, and *don't know*. Linking pedigrees within families yielded 581 instances where two or more informants reported on the same family member. Four categories described inter-informant (in)consistency:

1. consistent—both responded *yes* or *no*;
2. inconsistent/mixed responses—one responded *yes* and the other responded *no*;

3. inconsistent/one *don't know*—one responded *yes* or *no* and the other responded *don't know*; and
4. both responded *don't know*.

Statistical Analysis

For each condition, mean inter-informant (in)consistency was calculated by aggregating all informant dyad comparisons with respect to common biological relatives (Appendix Figure 1). Combining FHH reports on comorbid conditions heart disease and T2DM,¹⁷ individual risk scores were calculated as a standardized weighted sum of disease risk that an informant's first- and second-degree relatives could confer. The scores were dichotomized into a risk assessment (at risk if ≥ 0.5). In the unadjusted assessment, risk scores were based on individually reported pedigrees. The adjusted assessment reweighted the risk scores, substituting the disease risk a relative could confer with a weighted average of reports by multiple informants. Reports for first-degree relatives were given a greater weight, assuming that they were more accurate than those for second-degree relatives.^{18,19} The method for risk assessment calculation is detailed in Appendix Figure 2. Each assessment was cross-tabulated with the informant's self-reported disease diagnoses, to evaluate whether the adjusted assessment could more accurately identify individuals with disease.

RESULTS

Reports about common family members' T2DM diagnosis showed the highest degree of consistency (61%) and lowest degree of mixed response (5%, Figure 1). Consistency was slightly lower for reports on heart disease (54%, $p < 0.01$ versus T2DM) and remarkably lower for high cholesterol and hypertension (43% and 41%, respectively; $p < 0.001$ versus T2DM). Although there were mixed responses for all four conditions (5%–16%), inconsistency largely resulted from one informant not knowing FHH (21%–30%).

The unadjusted risk assessment correctly identified 67% of the individuals who, according to their self-report, had been diagnosed with heart disease (Figure 2). By contrast, the adjusted risk assessment correctly identified 80% of the individuals diagnosed with heart disease. This improvement was accompanied by a modest 2% increase in cases that were predicted to be at risk but had not been diagnosed. Similarly, correctly identified cases increased by 7% for T2DM, 12% for high cholesterol, and 8% for hypertension when risk assessment was adjusted, with almost no increase in cases that were predicted to be at risk but not diagnosed.

DISCUSSION

Consistent with previous studies,^{9–12} the results suggest inaccuracy in self-reported FHH data, evidenced by inconsistent reports within families. Linking pedigrees within families yields a risk assessment that can uncover a sizable proportion of individuals at risk for complex diseases. These findings have both research and clinical implications. Rather than discarding discrepant data from multiple informants, researchers can assign proper adjustments, so that information from more-reliable informants is weighted more heavily in risk calculation. Future research can generalize this multiple-informant approach to a

multiple-source approach. For example, self-reports and medical records can complement each other. By linking self-reports and diagnostic codes in electronic health records for related individuals, this approach would draw strengths from synthesizing the convenience, accuracy, and availability of each source.

Similarly, practitioners such as genetic counselors may receive inconsistent FHH reports when serving multiple related family members. They can use a simple weighting scheme to integrate discrepancies and generate more-accurate genetic risk assessments for patients. As clinicians increasingly adopt electronic health records in their practice, future work advancing the multiple-informant approach can best serve them by consolidating these records. Health Insurance Portability and Accountability Act Privacy Rules allow providers to share protected health information with another provider for the purpose of treating other patients, unless individuals request additional restriction.²⁰ Therefore, linking health records for treatment purposes is not against the Rule and such an effort can create a better evidence base for clinical decisions. Nevertheless, measures for obtaining consent must be developed before information can be freely linked between individuals for research and clinical use, thereby posing a major challenge to implementing this approach.

Limitations

The current study has two limitations. First, the results may be biased toward higher consistency. This study targets families at risk for T2DM, who are presumably more knowledgeable about T2DM and related health conditions. These families also tend to be more cohesive and are more likely to have consistent perceptions about their shared FHH, as isolated family members often do not get referred. Second, a simple weighting scheme based on degree of relations is applied when calculating risk scores, assuming that reports of first-degree relatives are more accurate than those of second-degree relatives. Future studies should consider alternative scenarios and account for other factors that might influence FHH reporting, such as SES and patterns of family risk communication.

CONCLUSIONS

This report links FHH reports within families to obtain a more informed risk assessment tool with improved accuracy. Despite the limitations, it provides one example of realizing the potential of a family-oriented approach to FHH, echoing the repeated call to “put the family back in family health history.”⁸ Future research should continue to leverage this approach to ensure better utilization of this clinical tool.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

This research is supported by the National Human Genome Research Institute’s Intramural Research Program (ZIAHG200335 to LMK) and a National Institute of Diabetes and Digestive and Kidney Diseases grant (K18DK095473 to MFM). The views expressed in this article are those of the authors and do not reflect the official policy or positions of NIH, DHHS, or the U.S. Government.

IRBs at the University of Cincinnati (2013-4924) and National Human Genome Research Institute (12-HG-N149) approved the study. Written and verbal consent were obtained before study participation.

JL, CSM, MFM, and LMK conceived and designed the study. JL performed the statistical analysis, interpreted the results, and wrote the manuscript. CSM and LMK oversaw the statistical analysis, contributed to the interpretation of the results, and revised drafts of the manuscript. MFM supervised data collection and revised drafts of the manuscript. All authors read and approved the final version of the submitted manuscript.

No financial disclosures were reported by the authors of this paper.

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Figure 1.

Inter-informant (in)consistency.

^aH=Heart Disease; D=Type 2 Diabetes; C=High cholesterol; P=Hypertension. Differences in proportions across conditions for each (in)consistency category tested using independent sample equality of proportions tests (two-tailed). All p -values <0.01.

Figure 2.
 Comparison of unadjusted and adjusted FHH-based risk assessments.
Note: Self-report diagnoses used as the validation criterion.