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Role of Family Health History in Predicting Midlife Chronic Disease Outcomes

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Abstract

Introduction: The generational relevance for determining disease risk for the leading causes of morbidity and mortality for U.S. adults is a source of debate.

Methods: Data on 12,300 adults (Add Health Study members [AHSMs]) participating in Wave V (2016–2018) of the National Longitudinal Study of Adolescent to Adult Health (Add Health) were merged with data from respondents' parents (n=2,013) participating in the Add Health Parent Study (AHPS, 2015–2017). Analyses beginning in January 2020 examined concordance in lifetime occurrence of chronic conditions across 4 generations, including cardiovascular disease, diabetes, hypertension, hyperlipidemia, obesity, cancer, and depression; and associations between individual disease history and ones' family health history for the same condition.

Results: Mean ages were 37.4 years for AHSMs and 62.9 years for AHPS mothers. AHPS mother hyperlipidemia (AOR=1.61, 95% CI=1.04, 2.48), obesity (AOR=1.77, 95% CI=1.27, 2.48), and depression (AOR=1.87, 95% CI=1.19, 2.95) histories were significantly associated with increased odds of AHSM report of these conditions. Maternal great grandparent hyperlipidemia history was significantly associated with AHSM hyperlipidemia (AOR=2.81, 95% CI=1.51, 5.21). Maternal grandfather (AOR=2.41, 95% CI=1.24, 4.69) and maternal great grandparent (AOR=3.05, 95% CI=1.45, 6.43) diabetes histories were significantly associated with AHSM diabetes. Each additional point in the AHPS mothers' cardiometabolic risk factor index was

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associated with an 11% increase (incidence rate ratio=1.11, 95% CI=1.04, 1.19) in the expected count of cardiometabolic risk conditions for AHSMs.

Conclusions: Multigenerational health histories have value for quantifying the probability of diabetes, obesity, depression, and hyperlipidemia in early mid-adulthood. Family health history knowledge is relevant for health promotion and disease prevention strategies.

INTRODUCTION

Family health history (FHH) is a metric by which healthcare providers disseminate recommendations for screening and disease surveillance and help determine long-term goals for optimal health.[1–4] Community- and clinic-based education interventions target individuals' awareness of their FHH, to facilitate understanding of disease risk and to motivate healthy lifestyle choices.[5–10] Indeed, the Centers for Disease Control and Prevention champions knowledge of ones' FHH and health-related behavior as critical for the development of lifelong wellness.[11,12]

The intergenerational transmission of health represents a variable contribution from heritable factors and mutual health behaviors, values, and beliefs. Risks for conditions such as heart disease, diabetes, cancer, and depression run in families[11,13–16]; however, the relative value ones' FHH contributes to the prediction of disease occurrence remains a source of debate. For example, parental history of cardiovascular disease (CVD) is an established risk factor for heart disease in adult offspring[17–19]; and cardiovascular risks track across parent and offspring generations.[20,21] However, in the case of CVD, existing U.S. cohort-formulated traditional risk assessment measures do not use FHH as a component of risk score calculations.[22–27] In the case of CVD, separating the influences of FHH from traditional risk factors such as smoking, activity, and diet-related behaviors to improve risk prediction calculations has proven challenging.[26,28,29]

Determining the level of generational complexity needed may further complicate risk prediction. In the example of CVD and some cancers, evidence exists for the importance of knowledge about first-degree relatives.[29,30–38] However, there is increasing recognition of the relevance of histories from multiple generations in assessing risk for malignancies, CVD, hypertension, and depression,[16,39–43] particularly for early onset of these conditions.[39,41–44]

To date, FHH studies generally have focused on single conditions and diagnostic categories for prediction. To the authors' knowledge, no population-representative studies assessing disease risk have used histories from 3 preceding generations to understand better the contribution of FHH to individual disease risk for multiple causes of morbidity and mortality for U.S. adults, including heart and other vascular diseases, cancers, diabetes, and poor mental health. Improved estimation of the contribution of FHH for a range of causes of adult morbidity and mortality may inform goal metrics for health and well-being at individual, community, and population levels.

Using data from the National Longitudinal Study of Adolescent to Adult Health (Add Health) Waves I and V, and the Add Health Parent Study (AHPS), research objectives were to: (1) evaluate concordance in lifetime occurrence of chronic conditions related to the

leading causes of morbidity and mortality among U.S. adults,[45,46] including CVD (heart attack, stroke), diabetes, hypertension, hyperlipidemia, obesity, cancer, and depression, across 4 generations, G4 (Add Health Study members [AHSMs], average age=37.4 years), G3 (Add Health mothers, average age=62.9 years), G2 (AHSM maternal grandparents), and G1 (AHSM maternal great grandparents [MGGPs]); and (2) evaluate associations between G4 disease outcomes and FHH for the same condition. Independent associations were hypothesized for FHH of chronic conditions and G4 disease outcomes.

METHODS

Study Population

Data were from Add Health, a nationally representative study covering the life-course periods of adolescence to mature adulthood for individuals living in the U.S.[47] Data were first collected from a national cohort of 7th–12th graders during the 1994–1995 school year; in-home data were collected from adolescents on participating schools' rosters (n=20,745) in 1995, along with a primary caregiver (usually the mother) who was interviewed separately (n=17,670). Follow-up in-home data for AHSMs have been collected across 4 additional waves, the most recent wave (2016–2018) when the cohort was in their mid-30s to early 40s (Wave V, n=12,300). In 2015–2017, data were collected on a probability sample of the parents who were interviewed in 1995, the AHPS (n=2,013). As part of the AHPS, parents (70.2%) returned an FHH form. The majority of mothers (84.2%) completing the FHH were non-Hispanic White (71% FHH completion rate). Among non-Hispanic Black and Hispanic mothers, the FHH completion rate was approximately 50%. The final analytic sample consisted of Wave V AHSM with Wave I mothers represented in the AHPS who completed an FHH (n=1,094). Additional details on Add Health and the AHPS are published elsewhere.[47,48] All Add Health and AHPS study protocols have received Human Subjects IRB approval (University of North Carolina at Chapel Hill).

Measures

For each health outcome, AHSMs indicated if they had *ever been told by a health care provider that they have or had*: (1) *a heart attack or have had heart surgery for clogged coronary arteries*; (2) *a stroke, mini-stroke, or have had surgery for clogged neck arteries*; (3) *high blood sugar or diabetes*; (4) *high blood pressure or hypertension*; (5) *high blood cholesterol, triglycerides, or lipids*; (6) *obesity, BMI ≥30*; (7) *cancer, lymphoma, or leukemia*; and (8) *depression*. Responses were dichotomized to reflect "any" versus "no" history of each condition. A cardiometabolic risk factor index (RFI) was created as the sum of the number of categorical risk factors[49]: diabetes, hypertension, hyperlipidemia, and obesity (range=0–4).

In the AHPS, Add Health mothers (G3) completed questions about their own health, including histories for the 8 aforementioned diagnoses. AHPS mothers also completed an FHH for the same conditions for their mother and father (G2, separately), and any grandparent (G1, collectively). For AHPS mothers, responses were dichotomized to reflect "any" versus "no" history of each condition. Sensitivity analyses (available upon request) revealed no significant differences in associations between FHH and AHSM disease

outcomes when *no* and *don't know* responses were combined for AHPS mother report on G2 and G1 conditions. As a result, in all analyses, *no* and *don't know* responses were combined such that each health condition for G2 and G1 reflects "any" versus "no known" history of each condition. A cardiometabolic RFI was also created for each generation: G3, G2, and G1 members.

Sociodemographic covariates consistently linked to individual and population health and health disparities across the life course[50,51] were included in analyses. Covariates included AHSM age, self-identified biological sex, and race/ethnicity (non-Hispanic Black, African, or African American; non-Hispanic White [ref group in multivariable models]; and other/multiple races [inclusive of respondents self-identifying as Hispanic ethnicity and multiple racial/ethnic categories]). AHSM and AHPS mother education were categorical variables, dummy coded to represent high school completion or less, some college, and college degree or more (ref group).

Multivariable analyses included additional covariates representing modifiable risk factors for AHSMs measured at Wave V, including moderate-to-vigorous physical activity (e.g., walking, team sports, strength training) in the past week (count=0–6),[52] smoking (i.e., any cigarette use during the past 30 days), and excessive drinking (i.e., drinking every day/almost every day, or binge drinking ≥2 days/month during the past 12 months).[46] Obesity status (calculated from AHSM self-reported height and weight at Wave I) was also included in final multivariable models as a childhood risk indicator for adult morbidity and mortality.[53,54]

Statistical Analysis

Sociodemographic characteristics (AHSMs, AHPS mothers) and chronic disease histories of AHSMs (G4), their mothers (G3), maternal grandmothers and grandfathers (G2: MGMs, MGFs), and MGGPs (G1) are reported. Descriptive statistics for chronic conditions across generations are stratified by sex where available (G4, G2). Owing to limited variability in self-identified race/ethnicity for AHPS mothers, prevalence estimates across generations were not stratified by race/ethnicity.

Logistic regression was used to examine each AHSM chronic condition outcome and the cardiometabolic RFI as a function of their FHH. In Model 1, each AHSM outcome at Wave V was regressed onto the corresponding history of each condition in AHPS mothers. In Model 2, each outcome was regressed onto AHSM FHH (mother + MGM + MGF + MGGP). Life-course socioeconomic indicators were added to analyses in Model 3 (AHPS mother education, AHSM education, AHSM age, sex, and race/ethnicity). Final multivariable models (Model 4) included AHSM FHH, sociodemographic covariates, and other risk factor measures (modifiable factors and childhood obesity status). Additional models were estimated with the inclusion of AHSM household income and insurance status. Inclusion of these variables did not contribute additional explanatory power to analytic models or change parameter estimates; as such, the parsimonious models are presented. Logistic regression models were estimated for each outcome except heart attack, stroke, and the cardiometabolic RFI. Models were not estimated for heart attack and stroke given too

few cases of this diagnosis among AHSMs. Poisson regression models were estimated for the cardiometabolic RFI.

There was insufficient power to conduct analyses stratified by race/ethnicity. Analyses stratified by sex showed no significant differences in observed associations. Accordingly, results for the non-stratified analyses are presented.

In sensitivity analyses, to assess the potential impact of age differentials driving AHPS mothers' knowledge about FHH, a series of regression models incorporating AHPS mother (G3) age, MGF age (G2, at time of FHH or age at death), and MGM age (G2, at time of FHH or age at death) into Model 4 were performed. Inclusion of the 3 age variables did not contribute additional explanatory power to analytic models or change parameter estimates. Thus, the analytic models are presented without these age variables.

All analyses were weighted and adjusted for the complex survey design of Add Health.[55] Respondents with missing data on dependent variables and covariates were excluded from the analysis. Separate analyses revealed any observed differences in model variables between included and excluded cases were statistically negligible. All statistical modeling was 2-sided, setting a significance level at 0.05. All analyses were performed using Stata SE, version 14.2.

RESULTS

The mean age of AHSMs was 37.4 years; the mean age of their mothers was 62.9 years (Table 1). The majority of AHSMs were male (53.6%), non-Hispanic White (82.9%), and had completed some college (38.7%) or had a college degree or more (43.8%). Approximately, 26.4% were current smokers, 35.1% reported excessive drinking behaviors, and on average they participated in 2.4 moderate-to-vigorous physical activities in the past week. The majority of AHPS mothers were non-Hispanic White (84.2%) and had completed less schooling than their children: some college (31.5%) and college degree or more (26.2%).

Few AHSMs (G4) reported conditions such as history of heart attack, stroke, diabetes, and cancer (Table 2). The lifetime occurrence of these conditions was greater among G2 and G1 compared with G3 and G4. By contrast, obesity was more often identified among the more recent G4 and G3 generations, corresponding to AHSMs and their mothers. Report of depression diagnosed by a healthcare provider was highest among the G4 generation (especially female participants) and lower among their mothers, MGPs, and MGGPs.

Table 3 shows the multivariate associations between AHSM report of a health condition and FHH. Net the influence of covariates and modifiable risk factors (Model 4), AHPS mother histories for hyperlipidemia (AOR=1.61, 95% CI=1.04, 2.48), obesity (AOR=1.77, 95% CI=1.27, 2.48), and depression (AOR=1.87, 95% CI=1.19, 2.95) were significantly associated with increased odds of AHSM report of these conditions. MGGP history (G1) of hyperlipidemia was also significantly associated with AHSM report of this condition (AOR=2.81, 95% CI=1.51, 5.21). Older generation diabetes histories were significantly associated with AHSM report of this chronic condition (MGF [G2]: AOR=2.41, 95%

CI=1.24, 4.69; MGGP [G1]: AOR=3.05, 95% CI=1.45, 6.43). AHPS mother report of cancer was significantly associated with AHSM report of cancer (AOR=3.10, 95% CI=1.19, 8.11); however, given low report of cancer among Wave V AHSMs, these models should be interpreted with caution. Generational histories for hypertension were not significantly associated with AHSM Wave V report of this condition.

In fully adjusted models (Model 4), each additional cardiometabolic condition that AHPS mothers reported was associated with an 11% increase (incidence rate ratio=1.11, 95% CI=1.04, 1.19) in the expected count of cardiometabolic risk conditions for AHSMs.

Each generation's health history seemed to have an independent association with G4 AHSM health outcomes such that controlling for the presence of a condition across generations in Model 2 did not generally change the magnitude of the association between the G3 mother's health condition with G4 AHSM health condition in Model 1. Moreover, the addition of demographic controls in Model 3 and modifiable risk factors in Model 4 did not explain much of the association between the FHH conditions and AHSM conditions, and in several cases (e.g., diabetes, depression), these covariates acted to suppress the association, which became stronger with the addition of these controls. There was some attenuation in the AHPS mother condition with the AHSM condition when covariates were included for obesity, cancer, and the cardiometabolic RFI, suggesting that these factors represent confounders in this relationship (i.e., they are related to both the AHPS mothers' and AHSMs' chronic condition). Finally, covariates included in Models 3 and 4 in Table 3 were associated with each AHSM health outcome in expected ways (Appendix Table 1 provides full model results).

DISCUSSION

Using new and novel national data from Add Health and the AHPS, health histories across 4 generations for conditions contributing to significant chronic disease burden among U.S. adults are presented. Generational histories exhibit some interesting patterns, including greater prevalence of obesity in more recent G4 and G3 generations, reflecting the contemporary period rise in obesity risk that began in the 1980s when the G4 cohort was in childhood and their G3 mothers were entering midlife.

A value for FHH in CVD risk for the Add Health cohort could not be quantified owing to low prevalence of CVD to date; however, findings do reveal notable relationships between FHH and other outcomes that contribute to significant morbidity and mortality for U.S. adults and increase risk for CVD, including diabetes, hyperlipidemia, and obesity.[45,46] In their examination of the value added by including FHH across 2 generations to a standard 10-year CVD risk assessment using the Framingham-based tool, Qureshi and colleagues[56] found that systematically including FHH in assessments for primary care patients significantly increased the proportion of individuals deemed at high risk for CVD and eligible for further targeting of prevention efforts.

Some risk prediction models include parent history, but do not extend beyond the parent generation, including the Framingham Study 8-year risk prediction model for type 2

diabetes[22,57] and Framingham prediction models for hypertension.[22] Findings for the current study suggest the relevance of G2 (MGF) and G1 (MGGP) for diabetes risk among a nationally representative cohort of adults in early midlife. Study findings also identify the importance of maternal history for obesity risk, which is a correlate of diabetes. Results point to the independent significance for mother history in overall offspring cardiometabolic risk. Notably, the salience of maternal history for cardiometabolic risk is evident in analytic models that adjust for education and lifestyle behaviors (smoking, physical activity, and excess alcohol), which may be representative of values and beliefs acquired via shared early-life contexts.

Study findings did not reveal significant associations between FHH and AHSM hypertension. A recent study examining risk for hypertension using data from 3 generations of Framingham Heart Study participants found early-onset hypertension (age <55 years) in parents or grandparents conferred risk to children/grandchildren.[41] However, in this same study, late-onset hypertension in either parents or grandparents did not consistently confer risk.[41] As the current study does not account for age of hypertension onset across generations, significant variations in relationships between FHH and AHSM hypertension risk may be obscured.

Beyond cardiometabolic risk, FHH of depression in mothers (G3) was associated with AHSM depression history. These findings are consistent with findings from Weissman et al.[16] in their longitudinal cohort family study. By contrast, the authors also found an association between grandparent depression and respondent major depression.[16]

Deepening the understanding of intergenerational links for chronic disease may provide more personalized and targeted health guidance, before permanent biological damage is done; it may also support provider confidence in taking a family history and improve the ability to interpret FHH information. Given the prevalence and costs of chronic diseases for U.S. adults,[58] including healthcare spending, loss of economic productivity, and loss of a sense of well-being, the importance of examining multigenerational risks for chronic conditions seems critical. Addressing disease risks in early midlife may promote family economic stability and the health of a workforce at the peak of their careers.

Limitations

Add Health parents are primarily mothers in Wave I; as such, mothers represent the majority of respondents in the AHPS. For the current study, father report (n=39) revealed limited FHH knowledge, yielding low-quality data; thus, fathers were excluded from analyses. Relationships between FHH and AHSM history of heart attack and stroke could not be examined in this study. In later waves of Add Health, it will be important to revisit the contribution of FHH to CVD outcomes. There may be sociodemographic correlates of FHH knowledge that could not be addressed via tests of interaction effects in these analyses. Owing to limited AHPS racial/ethnic diversity, examination of outcomes by racial/ethnic stratification with the current G3 mother sample could not be performed. Increasing diversity of the AHPS sample in later waves of data collection will facilitate examination of sociodemographic correlates of FHH knowledge as well as the strength of associations between AHSM outcomes in midlife and later life, and FHH stratified by race/ethnicity.

Analytic models were not able to address age of onset of conditions across generations as these data were not available, knowledge that may support greater precision of probability estimates.

CONCLUSIONS

Using a nationally representative and contemporaneous population-based study with novel health data across 4 generations, findings reveal the value of FHH for quantifying the probability of development of diabetes, obesity, depression, and hyperlipidemia in mid-adulthood. Results demonstrate disease risks in an early midlife cohort are linked to the presence of similar disease conditions in the parent, grandparent, and great grandparent generations. As such, findings support continued efforts to prioritize knowledge of FHH for health promotion and disease prevention strategies.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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All authors participated in the concept and design, analysis and interpretation of data, and drafting and revising of the manuscript.

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Table 1.

Demographic Characteristics (Weighted)

Characteristic	AHSM Mean or % (95% CI)	AHPS: Mother Mean or % (95% CI)
Age	37.4 (37.1, 37.7)	62.9 (62.3, 63.4)
Sex		
Female	46.4 (42.9, 45.0)	100
Male	53.6 (50.0, 57.1)	_[a]
Race/Ethnicity		
NH White	82.9 (77.6, 87.1)	84.2 (79.6, 88.0)
NH Black/African/African American	7.7 (5.2, 11.4)	7.0 (4.7, 10.2)
NH Asian	1.0 (0.4, 2.0)	1.0 (0.5, 2.2)
NH Other/Native American	1.1 (0.5, 2.3)	2.1 (1.3, 3.3)
Hispanic	7.4 (5.2, 10.4)	5.7 (3.7, 8.6)
Education		
High school or less	17.5 (13.9, 21.9)	42.3 (37.5, 47.3)
Some college	38.7 (34.9, 42.6)	31.5 (28.3, 35.0)
College degree or more	43.8 (38.0, 49.7)	26.2 (21.3, 31.7)
Physical activity	2.4 (2.3, 2.5)	_[b]
Smoking	26.4 (22.2, 30.5)	_[b]
Excessive drinking	35.1 (31.0, 39.2)	_[b]
Obesity (Wave I)	5.9 (4.2, 7.7)	_[b]

[a]Respondents are all AHPS mothers.

[b]Information not included in analyses.

AHSM, Add Health Study Member (Wave V, 2016−2018); AHPS, Add Health Parent Study (2015−2017).

Table 2.

Multigenerational Health Conditions (Weighted)

Condition	AHSM (G4, Wave V self-report)	AHPS mother (G3, self-report)	AHSM maternal grandparent (G2, AHPS mother report)	AHSM maternal great grandparent (G1, AHPS mother report)
	% (95% CI)	% (95% CI)	% (95% CI)	% (95% CI)
Heart attack				30.5 (26.7, 34.3)
Female	0.1 (0.0, 1.0)	12.2 (9.6, 14.9)	16.0 (13.4, 18.5)	
Male	1.3 (0.2, 2.3)	_[a]	31.4 (27.1, 35.6)	
Stroke				21.3 (17.5, 25.1)
Female	0.1 (0.0, 0.3)	3.0 (1.8, 4.2)	16.9 (14.3, 19.5)	
Male	0.2 (0.0, 0.6)	_[a]	15.7 (12.5, 18.9)	
Diabetes				23.3 (20.0, 27.1)
Female	4.6 (2.6, 6.6)	19.0 (16.0, 22.0)	26.4 (23.3, 29.5)	
Male	5.2 (3.1, 7.3)	_[a]	21.8 (18.9, 24.6)	
Hypertension				23.8 (21.2, 26.5)
Female	15.6 (12.6, 18.5)	44.1 (40.7, 47.6)	48.9 (45.1, 52.7)	
Male	21.6 (17.3, 25.9)	_[a]	41.0 (37.4, 44.6)	
Elevated lipids				11.2 (9.1, 13.3)
Female	11.3 (7.7, 14.9)	48.1 (43.3, 52.9)	30.2 (26.3, 34.2)	
Male	15.5 (11.5, 19.5)	_[a]	25.6 (22.2, 29.1)	
Obesity				15.4 (13.2, 17.6)
Female	38.9 (34.3, 43.5)	40.3 (35.0, 45.7)	19.5 (16.2, 22.8)	
Male	41.2 (37.2, 46.7)	_[a]	10.5 (8.5, 12.5)	
Cancer				33.7 (30.3, 37.2)
Female	2.5 (1.0, 4.1)	13.7 (11.4, 16.0)	33.4 (29.1, 37.7)	
Male	2.1 (0.8, 3.5)	_[a]	34.6 (31.5, 37.6)	
Depression				6.5 (4.9, 8.2)
Female	34.1 (29.4, 38.9)	25.5 (22.2, 28.8)	25.1 (21.8, 28.4)	
Male	18.9 (14.3, 23.5)	_[a]	11.0 (8.5, 13.6)	
Cardiometabolic risk factor index, M (95%CI)				0.7 (0.6, 0.8)
Female	0.7 (0.6, 0.8)	1.5 (1.4, 1.6)	1.2 (1.1, 1.3)	
Male	0.8 (0.7, 0.9)	_[a]	1.0 (0.9, 1.1)	

Notes: The cell for males in the AHPS Mother column is blank because the analytic sample includes only AHSM whose mothers provided data in the AHPS. Only one statistic is displayed for G1 AHSM great grandparent generation because the family health history asked AHPS mothers to report on any grandparent, so the sex of the AHSM's great grandparent cannot be determined.

[a]Respondents are all AHPS mothers.

AHSM, Add Health Study Member (Wave V, 2016−2018); AHPS, Add Health Parent Study (2015−2017); G4, AHSM generation; G3, AHPS mother; G2, AHSM maternal grandparent generation; G1, AHSM maternal great grandparent generation.

Table 3.

AHSM Health Condition at Wave V Regressed on Multigenerational Family History of Same Condition (Weighted)

Variable	Model 1[c] AOR (95% CI)	Model 2[d] AOR (95% CI)	Model 3[e] AOR (95% CI)	Model 4[f] AOR (95% CI)
Diabetes				
AHPS mother had (G3 self-report)[a]	2.13 (1.00, 4.56)	1.63 (0.73, 3.64)	1.27 (0.52, 3.06)	1.21 (0.50, 2.92)
AHSM maternal grandfather had (G2, AHPS mother report)[a]	_[b]	**2.44 (1.29, 4.59)**	**2.49 (1.32, 4.70)**	**2.41 (1.24, 4.69)**
AHSM maternal grandmother had (G2, AHPS mother report)[a]	_[b]	0.97 (0.45, 2.07)	0.68 (0.35, 1.34)	0.68 (0.35, 1.33)
AHSM maternal great grandparent had (G1, AHPS mother report)[a]	_[b]	**2.40 (1.24, 4.61)**	**3.03 (1.46, 6.30)**	**3.05 (1.45, 6.43)**
Hypertension				
AHPS mother had (G3 self-report)[a]	1.19 (0.77, 1.82)	1.12 (0.71, 1.75)	1.13 (0.71, 1.78)	1.07 (0.66, 1.72)
AHSM maternal grandfather had (G2, AHPS mother report)[a]	_[b]	1.21 (0.80, 1.82)	1.18 (0.77, 1.82)	1.18 (0.75, 1.85)
AHSM maternal grandmother had (G2, AHPS mother report)[a]	_[b]	1.14 (0.73, 1.77)	1.21 (0.76, 1.92)	1.26 (0.79, 2.00)
AHSM maternal great grandparent had (G1, AHPS mother report)[a]	_[b]	1.38 (0.86, 2.21)	1.38 (0.86, 2.23)	1.29 (0.79, 2.11)
Elevated lipids				
AHPS mother had (G3 self-report)[a]	**1.66 (1.11, 2.47)**	**1.63 (1.08, 2.45)**	**1.57 (1.03, 2.40)**	**1.61 (1.04, 2.48)**
AHSM maternal grandfather had (G2, AHPs mother report)[a]	_[b]	**0.55 (0.32, 0.94)**	0.58 (0.33, 1.01)	0.57 (0.32, 1.01)
AHSM maternal grandmother had (G2, AHPS mother report)[a]	_[b]	1.02 (0.63, 1.65)	1.10 (0.69, 1.78)	1.10 (0.67, 1.79)
AHSM maternal great grandparent had (G1, AHPS mother report)[a]	_[b]	**2.88 (1.60, 5.19)**	**2.89 (1.59, 5.27)**	**2.81 (1.51, 5.21)**
Obesity				
AHPS mother had (G3 self-report)[a]	**2.26 (1.69, 3.01)**	**2.27 (1.65, 3.11)**	**1.92 (1.39, 2.67)**	**1.77 (1.27, 2.48)**
AHSM maternal grandfather had (G2, AHPS mother report)[a]	_[b]	0.96 (0.53, 1.75)	1.04 (0.54, 1.97)	1.07 (0.56, 2.06)
AHSM maternal grandmother had (G2, AHPS mother report)[a]	_[b]	0.87 (0.51, 1.48)	0.88 (0.52, 1.49)	0.95 (0.56, 1.62)
AHSM maternal great grandparent had (G1, AHPS mother report)[a]	_[b]	1.27 (0.82, 1.95)	1.44 (0.91, 2.27)	1.40 (0.91, 2.15)
Cancer				
AHPS mother had (G3 self-report)[a]	**3.44 (1.15, 10.27)**	**3.86 (1.21, 12.31)**	**3.30 (1.16, 9.37)**	**3.10 (1.19, 8.11)**
AHSM maternal grandfather had (G2, AHPS mother report)[a]	_[b]	0.82 (0.30, 2.21)	0.77 (0.28, 2.10)	0.85 (0.32, 2.24)

Variable	Model 1[c] AOR (95% CI)	Model 2[d] AOR (95% CI)	Model 3[e] AOR (95% CI)	Model 4[f] AOR (95% CI)
AHSM maternal grandmother had (G2, AHPS mother report)[a]	_[b]	0.36 (0.11, 1.19)	0.39 (0.11, 1.30)	0.39 (0.12, 1.29)
AHSM maternal great grandparent had (G1, AHPS mother report)[a]	_[b]	0.50 (0.16, 1.57)	0.53 (0.16, 1.78)	0.56 (0.17, 1.86)
Depression				
AHPS mother had (G3 self-report)[a]	**1.97 (1.30, 3.00)**	**1.82 (1.20, 2.76)**	**1.84 (1.19, 2.85)**	**1.87 (1.19, 2.95)**
AHSM maternal grandfather had (G2, AHPS mother report)[a]	_[b]	1.15 (0.70, 1.91)	1.05 (0.65, 1.71)	1.07 (0.64, 1.76)
AHSM maternal grandmother had (G2, AHPS mother report)[a]	_[b]	1.48 (0.95, 2.30)	1.50 (0.96, 2.33)	1.52 (0.96, 2.40)
AHSM maternal great grandparent had (G1, AHPS mother report)[a]	_[b]	0.63 (0.32, 1.23)	0.70 (0.38, 1.30)	0.74 (0.42, 1.32)
Cardiometabolic risk factor index, IRR (95% CI)				
AHPS mother had (G3 self-report)[a]	**1.17 (1.10, 1.24)**	**1.17 (1.10, 1.25)**	**1.13 (1.05, 1.21)**	**1.11 (1.04, 1.19)**
AHSM maternal grandfather had (G2, AHPS mother report)[a]	_[b]	0.99 (0.91, 1.08)	1.01 (0.93, 1.09)	1.01 (0.93, 1.09)
AHSM maternal grandmother had (G2, AHPS mother report)[a]	_[b]	0.98 (0.90, 1.07)	0.99 (0.91, 1.07)	0.99 (0.91, 1.07)
AHSM maternal great grandparent had (G1, AHPS mother report)[a]	_[b]	1.07 (0.99, 1.17)	**1.08 (1.00, 1.17)**	1.07 (1.00, 1.15)

Notes: Boldface indicates statistical significance at $p<0.05$.

[a] Binary variables indicating the health condition for mothers, maternal grandmothers, maternal grandfathers, and any maternal great grandparent (0=No/Don't Know, 1=Yes).

[b] Model includes AHPS mother condition only.

[c] Model 1: AHPS mother health condition only.

[d] Model 2: AHSM multigenerational history (mother + maternal grandfather + maternal grandmother + any maternal great grandparent).

[e] Model 3: Model 2 + AHPS mother education; AHSM education, sex, age, and race-ethnicity.

[f] Model 4: Model 3 + AHSM Wave V physical activity, smoking, excessive drinking, and Wave I obesity.

AHSM, Add Health Study Member (Wave V, 2016−2018); AHPS, Add Health Parent Study (2015−2017); G3, Add Health mother; G2, AHSM maternal grandparent generation; G1, AHSM maternal great grandparent generation; IRR, incidence rate ratio (estimated from Poisson model).