Associations of Pregnancy History and Complications with Incident Cardiovascular Disease Among American Indian Women: The Strong Heart Family Study

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Abstract

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In the United States, cardiovascular disease is a leading cause of death among American Indian women. We examined the associations of parity (0/1, 2-4, >=5) and pregnancy complications (history of preeclampsia, protein in urine; eclampsia or seizures; gestational diabetes, hypertension) with incident cardiovascular disease (myocardial infarction, coronary heart disease, congestive heart failure, ischemic stroke) among American Indian women in the Strong Heart Family Study. Baseline information was collected between January 2006 and December 2009. Cardiovascular disease events were evaluated through December 2022. We used clustered logistic regression analyses to assess these associations among women free of cardiovascular disease at baseline (N=1,203). American Indian women with >=5 parity (grand multiparous) represented 25.5% of the sample size. Grand multiparous participants were 33% more likely to develop cardiovascular disease when compared to those with 0/1 parity (OR=1.33, 95% CI: 0.65, 2.71; p=0.44). Participants with pregnancy complications were 8% more likely to develop cardiovascular disease when compared to women with no pregnancy complications (OR=1.08, 95% CI: 0.62, 1.88; p=0.78). While the findings were not statistically significant, they support potential positive associations of grand multiparity and pregnancy complications with cardiovascular disease in American Indian women. This work suggests that American Indian women with grand multiparity and/or pregnancy complications should be followed closely and screened for cardiovascular disease.

INTRODUCTION

In the United States, cardiovascular disease is a leading cause of death among American Indian and Alaska Native women.[1] During 2015-2018, the prevalence of cardiovascular disease was 49.9% among Medicare-enrolled American Indian women, and 8% of American Indian women died from cardiovascular disease each year.[2] However, these statistics likely underestimate cardiovascular disease burden among American Indian women due to underreporting and misclassification of race/ethnicity in Medicare databases.[3] This increased risk of cardiovascular disease among American Indian women may be attributed, at least in part, to a higher burden of risk factors (e.g., obesity, diabetes), geographic isolation from preventative services in many communities, and underfunding of Indian Health Services.[4-5] As American Indian women in the United States experience significant risk of cardiovascular disease, it is important to better understand predisposing risk factors.[1-5]

In addition to traditional cardiovascular disease risk factors,[6] a developing body of research suggests that women have additional unique risk factors for cardiovascular disease related to parity and history of pregnancy complications.[7-8] The burden of pregnancy related morbidity and mortality is high in American Indian women.[7-8] For instance, the overall pregnancy-related mortality (per 100,000 live births) rate among American Indian women was 2.3 times higher than White women between 2007 and 2016.[9-10] Additionally, hypertensive disorders present in delivery hospitalizations,[7] gestational diabetes mellitus,[8] and average family size[11] were higher among American Indians as compared to White individuals in the United States.[7,8,11] Previous literature has demonstrated positive associations of multiparity and pregnancy complications with cardiovascular disease risk.[7-8] Endothelial dysfunction, increased coronary calcium, high body mass index, and impaired fasting glucose are both risk factors and consequences of pregnancy complications, and can also lead to cardiovascular diseases.[12] To date, few studies have investigated associations of multiparity or pregnancy complications with cardiovascular disease outcomes among American Indians.[7-11]

The primary aim of this project was to examine the associations of parity and pregnancy complications with incident cardiovascular disease among American Indian women who participated in the Strong Heart Family Study (SHFS), a large cohort study of cardiometabolic health in 12 Tribal communities throughout the United States. We hypothesized that cardiovascular disease incidence will be higher among American Indian women with multiparity or self-reported history of pregnancy complications.[7-12] Secondarily, we evaluated whether underlying cardiovascular health (as assessed with achievement of the American Heart Association's Life's Essential 8 modified these associations.[13] We hypothesized that associations are stronger among American Indian women with a lower cardiovascular health risk score.[13-14]

METHODS

Study Design, Setting, and Participants

The Strong Heart Family Study (SHFS) is a large cohort study designed to better understand cardiovascular disease and its risk factors in 12 American Indian communities in Arizona, Oklahoma, North Dakota and South Dakota.[15] The cohort comprised 2,462 participants (974 male and 1,448 female). Participants completed two examinations over an eight year period between 2001 through 2003 and 2006 through 2009 with ongoing annual phone calls and surveillance for cardiovascular disease events. The current analysis included SHFS participants free of cardiovascular disease in 2007 to 2009 who had available data on parity and/or pregnancy complications. Participants with prevalent cardiovascular disease during 2006 to 2009 (N=117) or who did not provide data on parity (N=135) were excluded from the current analysis. The final analytic sample size was 1,203 participants [Figure 1].The institutional review board from each Indian Health Service region and all 12 communities approved the SHFS. Written informed consent was obtained from all participants.

Data Collection

Study participants completed a personal interview that included questionnaires on medical and reproductive history, demographic information, and health habits at each study exam.[16] Participants also completed a brief clinical examination that included measurements of weight, height, and blood pressure.[16] A fasting blood draw was also done to measure lipids and glucose.[16] At the exam, participants were asked to wear a pedometer for 3 or more days at all times (except while bathing or swimming) to estimate usual levels of activity.[16] A past year Block Food Frequency Questionnaire was administered to estimate usual diet quality.[17]

Exposures

The exposures of interest were parity and pregnancy complications. Parity, or the number of live births, was ascertained during the 2007-2009 study examination.[16] The variable "parity" was created with observations of "zero or one," "two, three, or four," and five or more" live births. The reference group was individuals of “zero or one” parity.[18] Pregnancy complications were also ascertained through clinical examinations and personal interviews, and included history of preeclampsia, protein in the urine; eclampsia or seizures during childbirth; gestational diabetes, and hypertension.[18] The variable "pregnancy complications" was created and dichotomized into "pregnancy complication" and "no pregnancy complication." Respondents were categorized as "pregnancy complication" if they answered "yes" or "only during pregnancy" to one or more of the following questions: "Did you develop hypertension during your first pregnancy?" "During that (first) pregnancy, were you told you had preeclampsia, toxemia or protein in your urine?" "Did you have preeclampsia, toxemia, or both hypertension and protein in your urine in one or more subsequent pregnancies?" "Did you ever have eclampsia, i.e. a seizure (convulsion or “fit”) along with hypertension during a pregnancy or around the time of delivery?" "Diabetes?" "Hypertension?"[18] Respondents who indicated none of the above were categorized in the reference group as "no pregnancy complications."[18]

Outcomes

The outcome of interest was incident cardiovascular diseases, including fatal and non-fatal myocardial infarction, coronary heart disease, congestive heart failure, or ischemic stroke (categorized as yes/no).[18] Incident cardiovascular disease was ascertained by annual morbidity surveillance of cardiovascular events through annual telephone calls, mail contacts, home visits, and review of medical records. All identified events were verified in medical records reviewed by study physicians on an ongoing basis through December 2022.

Covariates

The covariates of interest were cardiovascular risk behaviors and factors consistent with the American Heart Association's *Life's Essential 8*[13] guidelines between March 2001 and June 2009. These included diet quality (as assessed with the Alternative Healthy Eating Index),[19] physical activity (average number of daily steps),[18] cigarette smoking (current, former, never) and secondhand smoke exposure,[19] body mass index,[18] non-HDL cholesterol,[18] fasting blood glucose,[19] and systolic and diastolic blood pressure.[18] To assess cardiovascular health, participants were assigned a score from 0 to 100 based on achievement of each Life's Essential 8 guideline.[13] We assessed potential confounding by each metric separately. The Alternative Healthy Eating Index and passive smoking variable were assessed using data from the 2001-2003 exam.[19]; this was used as a proxy for diet and second hand smoke exposure at the 2006-2009 exam since limited diet and second hand smoke exposure data were available at that exam.[18-19] The remaining variables were assessed at the 2006-2009 exam. Participant age (continuous),[20] clinical site (AZ, OK, ND/SD),[21] marital status (currently married, never married, divorced or separated, widowed, Adult Roommate, Partners, Significant Other, or Not Specified),[22] and education (years)[23] were considered as potential confounders since they may impact both parity/pregnancy complications and risk of cardiovascular disease.

Statistical Analyses

Baseline demographic, health behaviors, and clinical characteristics of study participants according to parity and pregnancy complications prevalence were summarized using descriptive analyses. Multivariate logistic regression was used to examine the associations of parity and pregnancy complications with cardiovascular disease incidence. As the SHFS comprises large families, all analyses included a cluster indicator for families to address potential correlation within individual family-units. Two models were fit for each analysis: (1) a crude model that adjusted for participant age and clinical center; (2) a multivariate (primary) model that additionally adjusted for potential confounders, including marital status, educational attainment, and each risk factor of the Life's Essential 8 framework, including smoking, BMI, physical activity, diet quality, non-HDL cholesterol, blood pressure, and fasting glucose. Multiple imputations were used (5 replicates) to address occasional missing values for passive smoking (N=5), active smoking (N=13), BMI (N=19), physical activity (N=320), diet quality (N=127), non-HDL cholesterol (N=20), systolic and diastolic blood pressure (N=13), baseline diabetes status (N=15), fasting glucose (N=20), hypotensive medication (N=400), and lipid-lowering medication (N=400) using information on cardiovascular disease incidence, parity frequency, pregnancy complications history, educational attainment, marital status, clinical site, and participant age. The MICE package in R was used for all imputations. In sensitivity analyses, we re-ran all models using a complete-case approach. Odds ratios, confidence intervals, and p-values were reported with a significance level of 0.05. All analyses were completed using RStudio 2023.09.0+463.

RESULTS

The mean age of participants was 46 years old (SD=15.5 years; Range: 19-90 years old). About 44.7% (N=583) of participants were from North Dakota or South Dakota; 43.1% of study participants were from OK (n=518); and, 12.2% (N=147) of participants were from AZ [Table 1A].

In total, 14.8% of participants reported parity of 0/1 (N=178), 59.7% of participants reported parity of 2-4 (N=718), and 25.5% of participants reported >=5 parity (N=307) [Table 1A]. The prevalence of pregnancy complications was similar across all parity groups. The mean systolic blood pressure was higher among participants who reported >=5 (grand multiparous) as compared to participants with 0/1 and 2-4 parity. The average daily pedometer steps were lowest among participants who reported >=5 parity as compared to participants with 0/1 and 2-4 parity.

In total, 21.5% of participants reported a history of pregnancy complications (N=247) at baseline examination from 2006 to 2009 (N=956) [Table 1B]. The prevalence of active and/or passive smoking exposure was highest among participants with history of pregnancy complications as compared to participants with no history of pregnancy complications. Participants with history of pregnancy complications were more likely to have lower diet quality than participants with no history of pregnancy complications.

During follow-up, 113 participants developed cardiovascular diseases (9.4% of total sample) [Table 1C]. The average daily pedometer steps was lower among participants who developed cardiovascular disease events as compared to participants who did not develop incident cardiovascular disease during the study period. No other meaningful differences were observed.

In the primary model adjusted for age, clinical site, marital status, educational attainment, and the AHA's Modified LE8 risk factors, participants who reported 2-4 parity experienced lower odds of incident or fatal definitive cardiovascular disease as compared to those with 0/1 parity (OR = 0.76; 95% CI: 0.39, 1.46; p=0.41). Grand multiparous participants exhibited higher odds of incident or fatal cardiovascular disease incidence as compared to those with 0/1 parity (OR = 1.33; 95% CI: 0.65, 2.71; p=0.44). The associations were not statistically significant in either comparison [Table 2]. For the pregnancy complications analysis, participants who reported one or more pregnancy complications had 1.08 higher odds of incident or fatal definitive cardiovascular disease as compared to women who reported no pregnancy complications (OR = 1.08; 95% CI: 0.62, 1.88; p=0.78). This association was also not statistically significant [Table 2]. Results of sensitivity analyses using complete-case analyses were in general similar to those reported above [Table 3].

DISCUSSION

The findings herein indicate that American Indian women with a history of >=5 parity and/or pregnancy complications experience a potential higher risk of developing cardiovascular disease during a 13 to 16 year follow-up when compared to participants who reported 0-1 parity or no history of pregnancy complications, respectively. The findings also indicate that American Indian women with a history of 2-4 parity experience a potential lower risk of developing cardiovascular disease as compared to participants who reported 0-1 parity.
Although the findings did not reach statistical significance (likely due to a small number of cardiovascular events during follow-up), they are consistent with past studies and relevant biological mechanisms, warranting future research in this area.

The reported risk estimates are consistent with previous research that assessed the relationship of pregnancy events and cardiovascular mortality in non-American Indian populations.[24-26] In a large meta-analysis that consisted of cohort and case-control studies evaluating the association of pregnancy complications and cardiovascular disease incidence among women, gestational diabetes mellitus (OR = 1.7; 95% CI: 1.1, 2.5), gestational hypertension (OR = 1.7; 95% CI: 1.3, 2.2), placental abruption (OR = 1.8; 95% CI: 1.4, 2.3), and preeclampsia (OR = 2.7; 95% CI: 2.5,3.0) were associated with increased cardiovascular disease incidence.[24] A retrospective cohort study in Sweden also found that pregnancy complications including preeclampsia or eclampsia (OR = 2.10, 95% CI: 1.47, 2.99; $p < 0.005$), gestational hypertension (OR = 1.79, 95% CI: 1.20, 2.66; $p < 0.005$), and gestational diabetes (OR = 3.03, 95% CI: 1.49, 6.16; $p < 0.005$) were positively associated with cardiovascular disease incidence and mortality.[25] Our findings complement both studies as the magnitude of the observed risk estimates indicated a potential positive association. However, our reported confidence intervals were large and associations were not statistically significant (likely due to a small number of events). Similarly, our work supports findings from previous cohort studies that reported positive associations of multiparity (RR = 1.14; 95% CI: 1.09, 1.18; $p = 0.002$) with development of non-fatal cardiovascular disease compared to nulliparity.[26] Overall, our findings of how grand multiparity and pregnancy complication history can potentially elevate risk of cardiovascular disease onset is comparable to this previous work and advances the field by expanding to American Indian women.[24-26]

The biological mechanisms that may explain the potential association between parity and/or pregnancy complications and risk of cardiovascular disease is complex.[12,27] Previous research suggests that higher parity is associated with impaired metabolic lipid and glucose functioning, which may increase future risk of coronary heart disease.[27] Previous literature suggests that abnormal metabolic environments prior to and during pregnancy complications could be biologically linked to cardiovascular disease onset in women.[12] An abnormal metabolic environment can exacerbate fetal health, placental artery development, and maternal organ function through delivery and postpartum, increasing physiological stress and overall cardiovascular disease risk.[12] Pregnancy-induced hypertensive disorders characterized by elevated serum acid levels and microalbuminuria have been shown to be related to cardiovascular disease onset.[12]

This study has many strengths. To our knowledge, this is the first study to examine the relationship of parity and pregnancy complications in a multi-tribal cohort of American Indian women. Our study presented a novel analysis evaluating the association between two preventable and underreported health conditions, pregnancy complications and cardiovascular diseases, that disproportionately burden American Indian women.[1, 7-11] It can provide insight for improving prevention programming and risk profiling in tribal communities to decrease pregnancy and cardiovascular disease morbidity.

This study is not without limitations. Given the young age of the cohort (mean age: 46.6 years) and small sample size (N=1,203), power to examine associations was limited However, the magnitude of multivariate estimates aligned with previous literature showing a positive

association of pregnancy complications[24-25] and parity.[26] The Block Food Frequency (FFQ) questionnaire used to evaluate diet quality in our study is well-known for validity and reliability, however there is a possibility that participants did not accurately recall their usual diet.[28] Using a reference group of 0/1 parity instead of comparing nulliparous to 1-parity due to smaller sample size women may have obscured significant associations. Another limitation of our analysis was potential for residual confounding by unmeasured factors that may be associated with parity and/or pregnancy complications and cardiovascular health.

Our findings suggest that American Indian women with a history of >= 5 parity and/or pregnancy complications could experience potential higher risk of cardiovascular disease onset. These findings demonstrate that American Indian women in the United States may experience increased burden of cardiovascular disease onset as a result of multiparity and/or history of pregnancy complications. Our work suggests that American Indian women with multiparity and/or pregnancy complications should be followed closely and screened for cardiovascular disease. Future research should assess the impact of multiparity and/or pregnancy complications on cardiovascular disease in other states with significant American Indian communities and larger studies.

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TABLES AND FIGURES

Figure 1: Study Enrollment and Participant Selection of SHFS American Indian Women

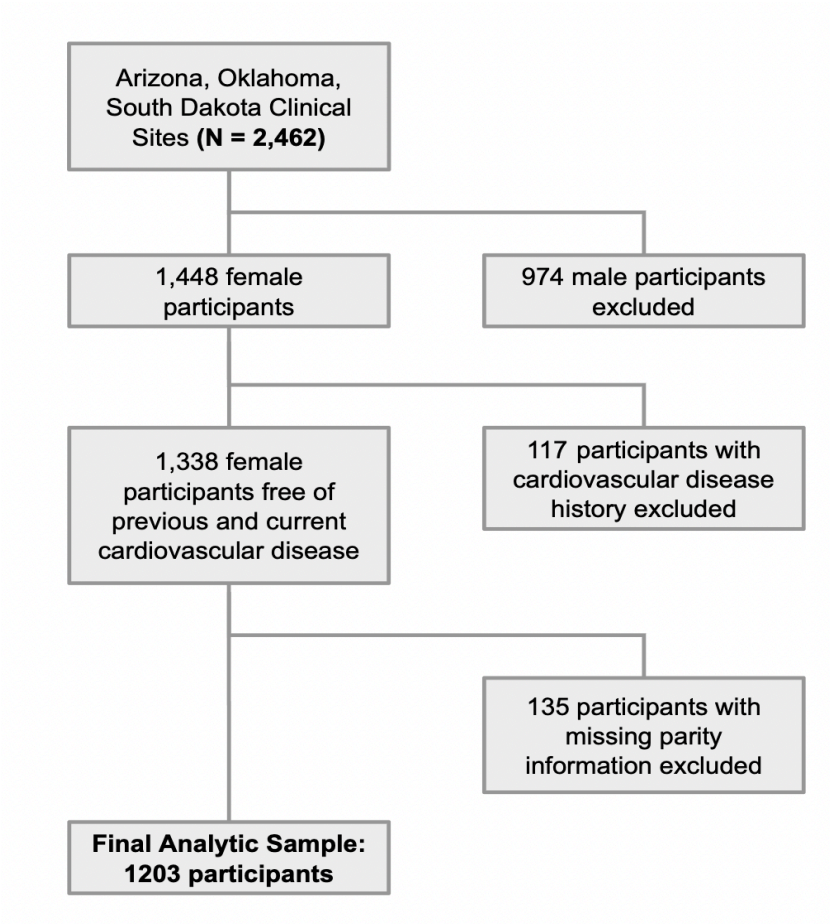

Table 1a Baseline Characteristics of SHFS Participants Stratified by Parity (N = 1203)

	Zero or One (N=178)	Two, Three, or Four (N=718)	Five or More (N=307)	Total (%) (N=1203)
Cardiovascular Disease Incidence or Fatality				
No Incident or Fatal Definitive CVD	166 (93.3%)	670 (93.3%)	254 (82.7%)	1090 (90.6%)
Incident or Fatal Definitive CVD	12 (6.7%)	48 (6.7%)	53 (17.3%)	113 (9.4%)
History of Pregnancy Complication(s)				
No Pregnancy Complications	148 (83.1%)	565 (78.7%)	243 (79.2%)	956 (79.5%)
Pregnancy Complications	30 (16.9%)	153 (21.3%)	64 (20.8%)	247 (20.5%)
Age (Years)				
Mean (SD)	38.0 (14.2)	45.0 (14.0)	55.3 (15.5)	46.6 (15.5)
Median [Min, Max]	35.4 [19.2, 85.2]	44.4 [19.7, 88.1]	54.3 [23.2, 90.2]	45.8 [19.2, 90.2]
Strong Heart Family Study Site				
South Dakota	69 (38.8%)	302 (42.1%)	167 (54.4%)	538 (44.7%)
Arizona	26 (14.6%)	64 (8.9%)	57 (18.6%)	147 (12.2%)
Oklahoma	83 (46.6%)	352 (49.0%)	83 (27.0%)	518 (43.1%)
Marital Status				
Currently Married	45 (25.3%)	334 (46.5%)	111 (36.2%)	490 (40.7%)
Never Married	75 (42.1%)	119 (16.6%)	32 (10.4%)	226 (18.8%)
Divorced or Separated	28 (15.7%)	150 (20.9%)	81 (26.4%)	259 (21.5%)
Widowed	12 (6.7%)	56 (7.8%)	56 (18.2%)	124 (10.3%)
Adult Roommate, Partners, Significant Other, or Not Specified	18 (10.1%)	59 (8.2%)	27 (8.8%)	104 (8.6%)
Education Level				
High School/VoTech/GED	72 (40.4%)	324 (45.1%)	141 (45.9%)	537 (44.6%)
Less Than High School or Not Specified	22 (12.4%)	92 (12.8%)	86 (28.0%)	200 (16.6%)

Some College	8 (4.5%)	44 (6.1%)	11 (3.6%)	63 (5.2%)
Junior College	48 (27.0%)	151 (21.0%)	46 (15.0%)	245 (20.4%)
Bachelor's Degree	21 (11.8%)	78 (10.9%)	21 (6.8%)	120 (10.0%)
Graduate or Professional Degree	7 (3.9%)	29 (4.0%)	2 (0.7%)	38 (3.2%)
Active and/or Passive Smoking Exposure				
Active and/or Passive Nicotine Exposure	134 (75.3%)	557 (77.6%)	221 (72.0%)	912 (75.8%)
No Active and/or Passive Nicotine Exposure	42 (23.6%)	157 (21.9%)	79 (25.7%)	278 (23.1%)
Average Pedometer Steps for Greater Than or Equal to Three Days				
Mean (SD)	5810 (3790)	5760 (4210)	4900 (3650)	5570 (4040)
Median [Min, Max]	5330 [571, 24500]	5080 [243, 58600]	4050 [631, 22200]	4880 [243, 58600]
Alternative Healthy Eating Index (No Alcohol) Risk Measurement				
Mean (SD)	41.4 (9.22)	41.0 (8.54)	41.4 (8.55)	41.2 (8.65)
Median [Min, Max]	40.4 [22.4, 75.1]	40.4 [20.5, 74.6]	40.9 [20.2, 73.1]	40.5 [20.2, 75.1]
Body Mass Index (kg/m^2)				
Mean (SD)	34.1 (9.40)	32.6 (7.48)	32.0 (6.74)	32.6 (7.64)
Median [Min, Max]	32.6 [18.1, 76.7]	31.9 [16.2, 73.3]	30.8 [17.8, 54.6]	31.6 [16.2, 76.7]
Non-HDL Blood Cholesterol (mg/dL)				
Mean (SD)	128 (36.1)	131 (34.8)	132 (35.1)	131 (35.1)
Median [Min, Max]	126 [62.0, 271]	130 [42.0, 314]	131 [32.0, 288]	130 [32.0, 314]
Systolic Blood Pressure (mm Hg) Measurement				
Mean (SD)	118 (15.7)	120 (17.6)	125 (19.0)	121 (17.8)

Median [Min, Max]	115 [88.0, 191]	117 [83.0, 202]	121 [78.0, 184]	117 [78.0, 202]
Diastolic Blood Pressure (mm Hg) Measurement				
Mean (SD)	72.1 (10.5)	71.6 (10.6)	71.6 (11.3)	71.7 (10.8)
Median [Min, Max]	71.0 [44.0, 109]	71.0 [41.0, 108]	72.0 [40.0, 110]	71.0 [40.0, 110]
Diabetes Status				
DM	43 (24.2%)	137 (19.1%)	99 (32.2%)	279 (23.2%)
IFG	20 (11.2%)	142 (19.8%)	64 (20.8%)	226 (18.8%)
NFG	111 (62.4%)	432 (60.2%)	140 (45.6%)	683 (56.8%)
Hemoglobin A1C % (Measurement)				
Mean (SD)	7.34 (2.29)	6.88 (2.11)	7.20 (2.25)	7.04 (2.18)
Median [Min, Max]	6.40 [4.80, 13.4]	6.00 [4.70, 17.5]	6.30 [4.70, 17.3]	6.10 [4.70, 17.5]
Hemoglobin A1C % (Calculation for Participants with Missing Measurement)				
Mean (SD)	1.16 (3.97)	0.631 (3.57)	1.84 (4.46)	1.02 (3.91)
Median [Min, Max]	-1.00 [-1.00, 13.8]	-1.00 [-1.00, 20.7]	-1.00 [-1.00, 20.5]	-1.00 [-1.00, 20.7]
Fasting Blood Glucose (mg/dL)				
Mean (SD)	112 (51.3)	108 (46.7)	122 (62.7)	112 (52.2)
Median [Min, Max]	93.0 [70.0, 349]	93.0 [60.0, 548]	99.0 [61.0, 542]	95.0 [60.0, 548]
American Heart Association (Modified) Life's Essential 8 Risk Level				
Elevated CVD Risk	36 (20.2%)	142 (19.8%)	71 (23.1%)	249 (20.7%)
Moderate CVD Risk	58 (32.6%)	255 (35.5%)	90 (29.3%)	403 (33.5%)
Lower CVD Risk	27 (15.2%)	93 (13.0%)	20 (6.5%)	140 (11.6%)

**Column percentages may not equal 100% due to additional missingness of presented variables*

Table 1b: Baseline Characteristics of SHFS Participants Stratified by Pregnancy Complication(s) History (N = 1203)

	No Pregnancy Complications (N=956)	Pregnancy Complications (N=247)	Total(%) (N=1203)
Cardiovascular Disease Incidence or Fatality			
No Incident or Fatal Definitive CVD	866 (90.6%)	224 (90.7%)	1090 (90.6%)
Incident or Fatal Definitive CVD	90 (9.4%)	23 (9.3%)	113 (9.4%)
Parity (Number of Live Births)			
Zero or One	148 (15.5%)	30 (12.1%)	178 (14.8%)
Two, Three, or Four	565 (59.1%)	153 (61.9%)	718 (59.7%)
Five or More	243 (25.4%)	64 (25.9%)	307 (25.5%)
Age (Years)			
Mean (SD)	47.4 (15.7)	43.7 (14.1)	46.6 (15.5)
Median [Min, Max]	46.5 [19.2, 90.2]	42.9 [20.1, 84.1]	45.8 [19.2, 90.2]
Strong Heart Family Study Site			
South Dakota	414 (43.3%)	124 (50.2%)	538 (44.7%)
Arizona	113 (11.8%)	34 (13.8%)	147 (12.2%)
Oklahoma	429 (44.9%)	89 (36.0%)	518 (43.1%)
Marital Status			
Currently Married	393 (41.1%)	97 (39.3%)	490 (40.7%)
Never Married	177 (18.5%)	49 (19.8%)	226 (18.8%)
Divorced or Separated	207 (21.7%)	52 (21.1%)	259 (21.5%)
Widowed	104 (10.9%)	20 (8.1%)	124 (10.3%)
Adult Roommate, Partners, Significant Other, or Not Specified	75 (7.8%)	29 (11.7%)	104 (8.6%)
Education Level			
High School/VoTech/GED	426 (44.6%)	111 (44.9%)	537 (44.6%)
Less Than High School or Not Specified	164 (17.2%)	36 (14.6%)	200 (16.6%)
Some College	47 (4.9%)	16 (6.5%)	63 (5.2%)
Junior College	193 (20.2%)	52 (21.1%)	245 (20.4%)

Bachelor's Degree	92 (9.6%)	28 (11.3%)	120 (10.0%)
Graduate or Professional Degree	34 (3.6%)	4 (1.6%)	38 (3.2%)
Active and/or Passive Smoking Exposure			
Active and/or Passive Nicotine Exposure	726 (75.9%)	186 (75.3%)	912 (75.8%)
No Active and/or Passive Nicotine Exposure	220 (23.0%)	58 (23.5%)	278 (23.1%)
Average Pedometer Steps for Greater Than or Equal to Three Days			
Mean (SD)	5560 (4080)	5600 (3870)	5570 (4040)
Median [Min, Max]	4850 [243, 58600]	5130 [461, 30800]	4880 [243, 58600]
Alternative Healthy Eating Index (No Alcohol) Risk Measurement			
Mean (SD)	41.4 (8.56)	40.5 (8.96)	41.2 (8.65)
Median [Min, Max]	40.7 [20.2, 75.1]	39.4 [22.0, 74.6]	40.5 [20.2, 75.1]
Body Mass Index (kg/m^2)			
Mean (SD)	32.4 (7.72)	33.5 (7.28)	32.6 (7.64)
Median [Min, Max]	31.3 [16.2, 73.3]	32.9 [16.8, 76.7]	31.6 [16.2, 76.7]
Non-HDL Blood Cholesterol (mg/dL)			
Mean (SD)	131 (35.2)	129 (34.8)	131 (35.1)
Median [Min, Max]	130 [42.0, 314]	128 [32.0, 240]	130 [32.0, 314]
Systolic Blood Pressure (mm Hg) Measurement			
Mean (SD)	120 (17.8)	122 (17.8)	121 (17.8)
Median [Min, Max]	117 [78.0, 202]	119 [84.0, 180]	117 [78.0, 202]
Diastolic Blood Pressure (mm Hg) Measurement			
Mean (SD)	71.2 (10.7)	73.5 (11.0)	71.7 (10.8)
Median [Min, Max]	71.0 [40.0, 109]	73.0 [44.0, 110]	71.0 [40.0, 110]
Diabetes Status			
DM	224 (23.4%)	55 (22.3%)	279 (23.2%)

IFG	169 (17.7%)	57 (23.1%)	226 (18.8%)
NFG	550 (57.5%)	133 (53.8%)	683 (56.8%)
Hemoglobin A1C % (Measurement)			
Mean (SD)	7.08 (2.22)	6.88 (2.05)	7.04 (2.18)
Median [Min, Max]	6.20 [4.70, 17.5]	6.00 [4.70, 13.3]	6.10 [4.70, 17.5]
Hemoglobin A1C % (Calculation for Participants with Missing Measurement)			
Mean (SD)	1.04 (3.96)	0.912 (3.73)	1.02 (3.91)
Median [Min, Max]	-1.00 [-1.00, 20.7]	-1.00 [-1.00, 12.2]	-1.00 [-1.00, 20.7]
Fasting Blood Glucose (mg/dL)			
Mean (SD)	112 (53.9)	111 (45.5)	112 (52.2)
Median [Min, Max]	94.0 [67.0, 548]	95.0 [60.0, 304]	95.0 [60.0, 548]
American Heart Association (Modified) Life's Essential 8 Risk Level			
Elevated CVD Risk	189 (19.8%)	60 (24.3%)	249 (20.7%)
Moderate CVD Risk	323 (33.8%)	80 (32.4%)	403 (33.5%)
Lower CVD Risk	119 (12.4%)	21 (8.5%)	140 (11.6%)

**Column percentages may not equal 100% due to additional missingness of presented variables*

Table 1c: Baseline Characteristics of SHFS Participants Stratified by Cardiovascular Disease Definitive Incidence or Fatality (N = 1203)

	No Incident or Fatal Definitive CVD (N=1090)	Incident or Fatal Definitive CVD (N=113)	Total (%) (N=1203)
History of Pregnancy Complication(s)			
No Pregnancy Complications	866 (79.4%)	90 (79.6%)	956 (79.5%)
Pregnancy Complications	224 (20.6%)	23 (20.4%)	247 (20.5%)
Parity (Number of Live Births)			
Zero or One	166 (15.2%)	12 (10.6%)	178 (14.8%)
Two, Three, or Four	670 (61.5%)	48 (42.5%)	718 (59.7%)
Five or More	254 (23.3%)	53 (46.9%)	307 (25.5%)
Age (Years)			
Mean (SD)	45.3 (14.9)	59.5 (14.7)	46.6 (15.5)
Median [Min, Max]	44.5 [19.2, 90.2]	58.6 [22.9, 89.1]	45.8 [19.2, 90.2]
Strong Heart Family Study Site			
South Dakota	482 (44.2%)	56 (49.6%)	538 (44.7%)
Arizona	141 (12.9%)	6 (5.3%)	147 (12.2%)
Oklahoma	467 (42.8%)	51 (45.1%)	518 (43.1%)
Marital Status			
Currently Married	451 (41.4%)	39 (34.5%)	490 (40.7%)
Never Married	212 (19.4%)	14 (12.4%)	226 (18.8%)
Divorced or Separated	231 (21.2%)	28 (24.8%)	259 (21.5%)
Widowed	98 (9.0%)	26 (23.0%)	124 (10.3%)
Adult Roommate, Partners, Significant Other, or Not Specified	98 (9.0%)	6 (5.3%)	104 (8.6%)
Education Level			
High School/VoTech/GED	485 (44.5%)	52 (46.0%)	537 (44.6%)
Less Than High School or Not Specified	178 (16.3%)	22 (19.5%)	200 (16.6%)
Some College	58 (5.3%)	5 (4.4%)	63 (5.2%)

Junior College	227 (20.8%)	18 (15.9%)	245 (20.4%)
Bachelor's Degree	108 (9.9%)	12 (10.6%)	120 (10.0%)
Graduate or Professional Degree	34 (3.1%)	4 (3.5%)	38 (3.2%)
Active and/or Passive Smoking Exposure			
Active and/or Passive Nicotine Exposure	829 (76.1%)	83 (73.5%)	912 (75.8%)
No Active and/or Passive Nicotine Exposure	253 (23.2%)	25 (22.1%)	278 (23.1%)
Average Pedometer Steps for Greater Than or Equal to Three Days			
Mean (SD)	5740 (4080)	3720 (2950)	5570 (4040)
Median [Min, Max]	5110 [243, 58600]	3090 [250, 16500]	4880 [243, 58600]
Alternative Healthy Eating Index (No Alcohol) Risk Measurement			
Mean (SD)	41.0 (8.61)	42.9 (8.87)	41.2 (8.65)
Median [Min, Max]	40.4 [20.2, 75.1]	41.2 [20.5, 73.1]	40.5 [20.2, 75.1]
Body Mass Index (kg/m^2)			
Mean (SD)	32.7 (7.70)	32.5 (7.07)	32.6 (7.64)
Median [Min, Max]	31.6 [16.2, 76.7]	31.6 [16.8, 54.4]	31.6 [16.2, 76.7]
Non-HDL Blood Cholesterol (mg/dL)			
Mean (SD)	130 (34.6)	137 (39.3)	131 (35.1)
Median [Min, Max]	129 [32.0, 314]	139 [53.0, 271]	130 [32.0, 314]
Systolic Blood Pressure (mm Hg) Measurement			
Mean (SD)	120 (17.1)	132 (20.8)	121 (17.8)
Median [Min, Max]	117 [83.0, 202]	129 [78.0, 184]	117 [78.0, 202]
Diastolic Blood Pressure (mm Hg) Measurement			
Mean (SD)	71.7 (10.6)	71.8 (12.4)	71.7 (10.8)
Median [Min, Max]	72.0 [40.0, 110]	71.0 [41.0, 99.0]	71.0 [40.0, 110]

Diabetes Status			
DM	218 (20.0%)	61 (54.0%)	279 (23.2%)
IFG	209 (19.2%)	17 (15.0%)	226 (18.8%)
NFG	649 (59.5%)	34 (30.1%)	683 (56.8%)
Hemoglobin A1C % (Measurement)			
Mean (SD)	6.91 (2.14)	7.71 (2.29)	7.04 (2.18)
Median [Min, Max]	6.00 [4.70, 17.5]	6.75 [4.90, 13.6]	6.10 [4.70, 17.5]
Hemoglobin A1C % (Calculation for Participants with Missing Measurement)			
Mean (SD)	0.732 (3.67)	3.80 (4.93)	1.02 (3.91)
Median [Min, Max]	-1.00 [-1.00, 20.5]	4.83 [-1.00, 20.7]	-1.00 [-1.00, 20.7]
Fasting Blood Glucose (mg/dL)			
Mean (SD)	109 (48.5)	141 (73.9)	112 (52.2)
Median [Min, Max]	94.0 [60.0, 542]	111 [71.0, 548]	95.0 [60.0, 548]
American Heart Association (Modified) Life's Essential 8 Risk Level			
Elevated CVD Risk	204 (18.7%)	45 (39.8%)	249 (20.7%)
Moderate CVD Risk	384 (35.2%)	19 (16.8%)	403 (33.5%)
Lower CVD Risk	133 (12.2%)	7 (6.2%)	140 (11.6%)

**Column percentages may not equal 100% due to additional missingness of presented variables*

Table 2: Association of Pregnancy Parity and Complications with Incident or Fatal Cardiovascular Disease Among SHFS Native American Women

Variables	Incident or Fatal Definitive CVD Frequency	Total Sample Frequency	OR[1] (95% CI)	p-value[1]	OR[2] (95% CI)	p-value[2]
Parity (Number of Live Births)						
Zero or One	12 (6.8%)	178	*ref*		*ref*	
Two, Three, or Four	48 (6.7%)	718	0.65 (0.32, 1.29)	0.22	0.76 (0.39, 1.46)	0.41
Five or More	53 (17.2%)	307	1.17 (0.58, 2.35)	0.66	1.33 (0.65, 2.71)	0.44
Pregnancy Complications						
No Pregnancy Complications	90 (9.5%)	956	*ref*		*ref*	
One or More Pregnancy Complications	23 (9.3%)	247	1.28 (0.78, 2.11)	0.33	1.08 (0.62, 1.88)	0.78

*Adjusted for Age and Clinical Site (Crude Model, OR[1]); Adjusted for Age, Clinical Site, Marital Status, Educational Attainment, and the AHA's Modified LE8 Individual Risk Factor Metrics (Multivariate Adjusted Model, OR[2])

*OR = Odds Ratio, CI = Confidence Interval | * Indicates Statistical Significance ($p<0.05$)

Table 3: Sensitivity analysis: Complete Case Analysis of Associations of Pregnancy Parity and Complications with Incident or Fatal Cardiovascular Disease in SHFS Native American Women (N = 1203)

Variables	Incident or Fatal Definitive CVD Frequency	Total Sample Frequency	OR[1] (95% CI)	p-value[1]	OR[2] (95% CI)	p-value[2]
Parity (Number of Live Births)						
Zero or One	12 (6.8%)	178	*ref*		*ref*	
Two, Three, or Four	48 (6.7%)	718	0.65 (0.32, 1.29)	0.22	0.94 (0.39, 2.25)	0.89
Five or More	53 (17.2%)	307	1.17 (0.58, 2.35)	0.66	1.47 (0.55, 3.91)	0.44
Pregnancy Complications						
No Pregnancy Complications	90 (9.5%)	956	*ref*		*ref*	
One or More Pregnancy Complications	23 (9.3%)	247	1.28 (0.78, 2.11)	0.33	0.69 (0.33, 1.43)	0.32

*Adjusted for Age and Clinical Site (Crude Model, OR[1]); Adjusted for Age, Clinical Site, Marital Status, Educational Attainment, and the AHA's Modified LE8 Individual Risk Factor Metrics (Multivariate Adjusted Model, OR[2])

*OR = Odds Ratio, CI = Confidence Interval | * Indicates Statistical Significance (p<0.05)