# Collecting pregnancy data in the Strong Heart Study

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# Background

- Pregnancy complications such as hypertensive disorders of pregnancy (gestational hypertension and pre-eclampsia; HDP) and gestational diabetes (GDM) predict cardiovascular morbidity and mortality
- Most studies addressing the relationship between CVD and pregnancy have been conducted in White populations, even though studies suggest racial variation in likelihood of progression from GDM to type 2 diabetes or from prehypertension to hypertension
- American Indian women are at high risk for pregnancy complications and adverse birth outcomes, although there is substantial variation by state and tribe
- AIAN women are at particularly higher risk for complications linked to higher BMI: GDM, pre-eclampsia, and macrosomia
- Few or no large-scale studies that address reproductive health in this population

# The Strong Heart Study

- A study of cardiovascular disease and its risk factors among American Indian men and women
- Started in 1988, NHLBI-supported
- The largest epidemiologic study of American Indians ever undertaken
- Designed to estimate cardiovascular disease mortality and morbidity and the prevalence of cardiovascular disease risk factors in American Indians and to assess the significance of these risk factors in a longitudinal analysis.
- Included 12 American Indian tribes and communities in three geographic areas: an area near Phoenix, Arizona; the southwestern area of Oklahoma; and western and central North and South Dakota.

# The Strong Heart Study - methods

- Initial stages (Phase I: 1989-1991; Phase II: 1993-1995; Phase III: 1998-1999)
  - Survey to determine cardiovascular disease mortality rates from 1984 to 1994 among tribal members aged 35-74 years of age residing in the 3 study areas (the community mortality study).
  - Clinical examination of 4,549 eligible tribal members
  - Morbidity and mortality surveillance of these participants
- Phase III study included a pilot family study of approximately 30 families
- Phase IV recruited additional 18 to 25 extended families from each of the field centers (2001-2003)
  - 3,776 individuals from 94 families, of whom 825 were re-examined Phase III participants
- Phase V completed the second exam on over 90% of the living family cohort and continued surveillance of the original cohort.
  - Phase IV and V included echocardiograms
- Phase VI: morbidity and mortality surveillance of the family cohort and the original cohort (no physical exam; completed 2019)
  - Cardiovascular disease, cancer, liver disease, and inflammatory disease
- Phase VII is currently underway: continued surveillance; basic clinical follow-up examination of approximately 3,500 participants
- The present authors received an IDeA women's health supplement to examine pregnancy data in this cohort

# Women's health supplement aims

- To assess quality of self-report of reproductive health in an American Indian cohort
- To characterize pre-eclampsia and gestational diabetes in an American Indian cohort
  - The combined burden of pre-existing diabetes and GDM will be substantially higher than comparable numbers in other ethnic groups.
  - HDP and GDM will predict later cardiovascular disease and type 2 diabetes.
  - Pre-pregnancy cardiovascular risk factors will predict pregnancy complications.

# The Strong Heart Study – pregnancy data

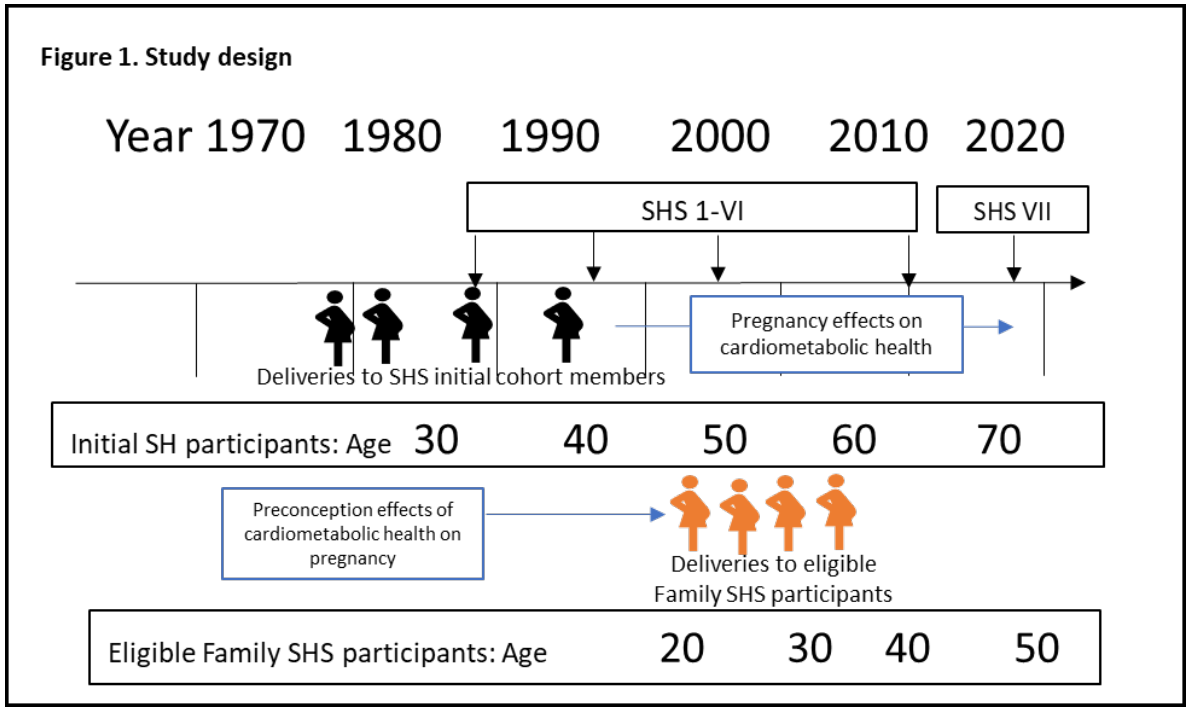
- In phases 1, 2, 4, and 5, female participants were asked about the number of times they had given birth, living children, and “lost pregnancies” (miscarriage and stillbirth)
- When participants were asked about high blood pressure and diabetes, “only during pregnancy” was one option
- Phase 3 – participants asked about high blood pressure during pregnancy
- Phase 4 – participants asked if currently pregnant/breastfeeding
- Phase 5 – participants asked about history of hypertension during pregnancy and preeclampsia
- Phase 6 – medical history included parity, gravidity, stillbirth, pre-eclampsia in first or later pregnancies, GDM in first or later pregnancies (also dates of first pregnancy and complicated pregnancies)

# The Strong Heart Study – other sources of pregnancy data

- Medical records – requested for cases of PE and a subset as controls
  - Previous study included some members of the cohort
  - Requested based on data provided in phase VI
  - Abstracted and reviewed
- National Data Warehouse of Indian Health Service
- Birth certificates

# Integrating Strong Heart Study and pregnancy data

- Retrospective report – all female members
- Prospective – women of reproductive age
  - Pregnancies occur randomly relative to study visits



# The Strong Heart Study – validation of pre-eclampsia data

- Self-report vs. NDW data

| | | Pre-eclampsia IHS Code | | |
|---|---|---|---|---|
| | | Yes | No | Total |
| Pre-eclampsia self-report | Yes | 7 | 26 | 33 |
| | No | 15 | 1733 | 1748 |
| | Total | 22 | 1759 | 1781 |

Kappa=0.24

| | | Pre-eclampsia/HTN/Proteinuria IHS Code | | |
|---|---|---|---|---|
| | | Yes | No | Total |
| Pre-eclampsia self-report | Yes | 11 | 22 | 33 |
| | No | 39 | 1709 | 1754 |
| | Total | 50 | 1731 | 1781 |

Kappa=0.25

- Self-report vs. medical records (study 1)

| | | Medical records | | |
|---|---|---|---|---|
| | | Yes | No | Total |
| Pre-eclampsia self-report | Yes | 13 | 1 | 14 |
| | No | 6 | 3 | 9 |
| | Total | 19 | 4 | 23 |

Kappa=0.29

- Self-report vs. medical records (study 2)

| | | Medical records | | |
|---|---|---|---|---|
| | | Yes | No | Total |
| Pre-eclampsia self-report | Yes | 8 | 18 | 25 |
| | No | 1 | 7 | 9 |
| | Total | 9 | 25 | 34 |

Kappa=0.11

# GDM and pre- and post-pregnancy CVD – study population

| | women with a pre-pregnancy visit (n=294) | | women with a post-pregnancy visit (n=1710) | |
|---|---|---|---|---|
| | mean | SD | mean | SD |
| age at first visit | 22.0 | 5.7 | 41.6 | 13.4 |
| age at first birth | 21.9 | 4.4 | 21.1 | 4.1 |
| BMI at first visit | 29.1 | 8.0 | 31.2 | 7.1 |
| | | | | |
| | N | % | N | % |
| highest reported education | | | | |
| <HS | 58 | 19.7 | 300 | 17.6 |
| HS | 122 | 41.5 | 627 | 36.7 |
| AA, some college | 89 | 30.3 | 535 | 31.3 |
| college+ | 25 | 8.5 | 246 | 14.4 |
| | | | | |
| income | | | | |
| <$5K | 64 | 28.2 | 362 | 24.4 |
| $5K-15K | 66 | 29.1 | 416 | 28.1 |
| >$15K | 97 | 42.7 | 705 | 47.5 |
| missing/refused/don't know | 67 | | 227 | |

# GDM and pre- and post-pregnancy CVD – study population

| parity | women with a pre-pregnancy visit (n=294) | | women with a post-pregnancy visit (n=1710) | |
|---|---|---|---|---|
| 0 | 152 | 52.1 | 20 | 1.2 |
| 1 | 43 | 14.7 | 227 | 13.3 |
| 2 | 58 | 19.9 | 325 | 19.0 |
| 3 | 19 | 6.5 | 371 | 21.7 |
| 4-5 | 15 | 5.1 | 445 | 26.1 |
| 6+ | 5 | 1.7 | 320 | 18.7 |
| | | | | |
| smoking | | | | |
| Current | 107 | 36.4 | 674 | 39.5 |
| Former | 46 | 15.7 | 412 | 24.1 |
| Never | 141 | 48.0 | 622 | 36.4 |
| | | | | |
| alcohol visit | | | | |
| Current | 210 | 71.4 | 921 | 54.0 |
| Former | 45 | 15.3 | 579 | 34.0 |
| Never | 39 | 13.3 | 205 | 12.0 |

# Pre-pregnancy risk factors predicting GDM

GDM at any pregnancy – pre-pregnancy sample – 23, 7.8%; additional 6.8% with DM prior to pregnancy

| | OR* | 95% CI |
|---|---|---|
| BMI | 1.03 | 0.98-1.09 |
| systolic blood pressure | 1.01 | 0.96-1.05 |
| diastolic blood pressure | 1.02 | 0.98-1.08 |
| cholesterol | 1.00 | 0.98-1.02 |
| LDL | 1.00 | 0.98-1.02 |
| HDL | 1.00 | 0.97-1.04 |
| glucose | 1.06 | 1.01-1.12 |
| triglycerides | 1.00 | 0.99 -1.01 |

*adjusted for age, BMI (non-BMI models), smoking, alcohol use, parity, education, income at pre-pregnancy visit.

# GDM predicting later cardiovascular health

| | N | % | | mean age of occurrence/ onset | aHR | 95% CI |
|---|---|---|---|---|---|---|
| coronary heart disease | 203 | 12.1 | | 59.4 | 1.47 | 0.85-2.53 |
| cardiovascular disease | 269 | 16.0 | | 59.2 | 1.32 | 0.81-2.17 |
| myocardial infarction | 118 | 7.0 | | 59.8 | 1.17 | 0.58-2.46 |
| stroke | 63 | 3.7 | | 59.9 | 1.67 | 0.58-4.82 |
| diabetes* | 741 | 44.0 | | 53.5 | 1.98 | 1.51-2.59 |

adjusted for time on study, smoking, BMI, education, income, menopausal status, age at birth for GDM

*Hazards were not proportional for diabetes. HR provided is for age 50.

# Covariates predicting progression from GDM to T2DM

| | Progressed to DM (N=100) | | Did not progress (n=42) | | |
|---|---|---|---|---|---|
| | mean | SD | mean | SD | p |
| age at first birth | 21.5 | 4.5 | 21.8 | 5.6 | 0.73 |
| BMI at first visit | 33.5 | 7.0 | 30.2 | 6.8 | 0.01 |
| BMI at post-pregnancy visit | 33.8 | 6.8 | 31.5 | 7.4 | 0.08 |
| SBP at post-pregnancy visit (n=125) | 119.1 | 13.6 | 114.6 | 10.7 | 0.08 |
| total cholesterol at post-pregnancy visit (n=111) | 184.2 | 37.7 | 189.4 | 34.4 | 0.50 |
| LDL at post-pregnancy visit (n=111) | 103.7 | 29.2 | 105.0 | 22.5 | 0.82 |
| HDL at post-pregnancy visit (n=111) | 47.8 | 9.2 | 48.0 | 11.1 | 0.91 |
| HbA1c at post-pregnancy visit (n=73) | 6.9 | 2.2 | 5.1 | 0.5 | <0.01 |
| glucose at post-pregnancy visit (n=100) | 139.2 | 70.3 | 93.3 | 9.6 | <0.01 |
| triglycerides at post-pregnancy visit (n=111) | 138.5 | 74.8 | 181.2 | 130.8 | 0.09 |

# Limitations

- Self-report of GDM
- Limited number of cases
- Limited pre-pregnancy data
- Incomplete pregnancy history

# Conclusions

- Accessing pregnancy data, even with records and appropriate permissions, is difficult
- Developing an accurate retrospective diagnosis of pre-eclampsia is difficult
- Major predictors and consequences of GDM relate to glucose and BMI
  - Limited associations with other CV risk factors
- High prevalence of diabetes
  - Early-life studies may be necessary

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