An aerial photograph of a vast, flat, snow-covered landscape, likely a frozen body of water or a tundra. The ground is marked with numerous tracks from vehicles or sleds, creating a grid-like pattern. In the distance, there are some small, dark structures or equipment, possibly part of a research or mining operation. The sky is a pale, overcast blue.

How Two Decades of Community-engaged Research Informed an Alaska DOHaD Project

Bert Boyer and Scarlett Hopkins
Oregon Health & Science University
August 7, 2023

Presentation Outline

- Establishment of a biomedical research center
- Building respectful research partnerships
- Research findings
- DOHaD focused research in Alaska
- Summary

Establishment of a Community-based Participatory Research Center

- NIH-funded Center for Alaska Native Health Research (CANHR) initiated in 2001 at the University of Alaska Fairbanks.
- Focus on understanding risk and protective factors for obesity and related cardiometabolic disease in Yup'ik Alaska Native people.
- Strengths-based approach.
- This multidisciplinary approach included genetic, nutritional and behavioral factors.
- Engaged community in development and implementation of research activities.

Yukon-Kuskokwim Delta

- Home to more than 23,000 Yup'ik, Cup'ik and Athabascan people.
- Central Yup'ik is the first language of over 14,000 people.
- 58 rural communities located in a 75,000 square mile area.
 - Each community is a federally-recognized Tribe
 - Range from 25 to over 1,000 community members
- Regional hub in Bethel.
- Travel by plane, boat, snowmachine or 4-wheeler.
 - No road system
- Access to health care services is limited.
 - Small community clinics
 - Advanced health care at regional hub



Initial Discussions & Approvals

- Multiple Interactions with Native health corporation to:
 - Identify communities
 - Develop respectful research protocols
 - Establish referral criteria
- Four IRB's and Tribal Oversight
 - Yukon-Kuskokwim Health Corporation
 - Traditional Councils
 - Community-wide approvals



Genetic Education for Native Americans (GENA)

- Tribal leadership requested information about genetics
 - To define the basic terminology used in genetics research
 - To discuss the risks and benefits of genetics research
 - To understand the concerns and thoughts of Tribal leadership and Elders before gaining approval for the study



Engaging Community & Building Capacity

Spent **2 years** prior to data collection:

- Making frequent visits to study communities
- Hiring local research assistants in each community
- Door to door visits to discuss proposed research activities and address any concerns
- Learning about the subsistence lifestyle and community activities
- Learning culturally respectful recruitment and data collection activities
 - Advertising
 - Timing
 - Location



Community Planning Group (CPG)

- Composed of past participants in our genetic studies.
- Co-researchers
 - Explore Yup'ik understandings of heredity
 - Assist in development of research instruments
 - Co-facilitate focus groups
 - Participate in interpretation of research findings
 - Directed future research
 - Asked *“Can the foods we eat change DNA?”*



Ciuliat Group

- A group of 4 Yup'ik bicultural consultants and translators.
- To help facilitate communication, translate and bridge the conversation between the CPG and University researchers.



Over 2,000 Yup'ik people have participated in our studies since 2003

Cross-sectional (2003-2007) → Longitudinal/Cross-sectional (2007-present)

Demographic, Nutritional, Behavioral, Anthropometric & Biochemical data

Genomic, Pharmacogenomic, and Epigenomic Studies



Traditional Diet

- Yup'ik traditional diet rich in n-3 PUFA's
 - Marine mammals
 - Cold water fish
- Active hunting and gathering lifestyle



How does a traditional dietary pattern rich in PUFAs modify disease risk?



n-3 PUFA intake is associated with several cardiometabolic disease risk factors

- n-3 PUFA intake is positively associated with:
 - HDL-cholesterol
 - Adiponectin
 - IGFBP-3
 - Vitamin D levels
- n-3 PUFA intake is negatively associated with:
 - Triglycerides, total cholesterol and non-HDL cholesterol
 - Systolic and diastolic blood pressure
 - Leptin and the ratio of Leptin:Adiponectin
 - Inflammatory cytokines including TNF α , IL-6, MCP-1 and CRP

Makhoul et al., Eur. J. Clin. Nutr 2011

O'Brien et al 2014, J. Nutr

Fohner et al 2016 J. Nutr

Boyer et al 2022 J. Nutr

Boyer et al 2023 J. Nutr

Epigenetics

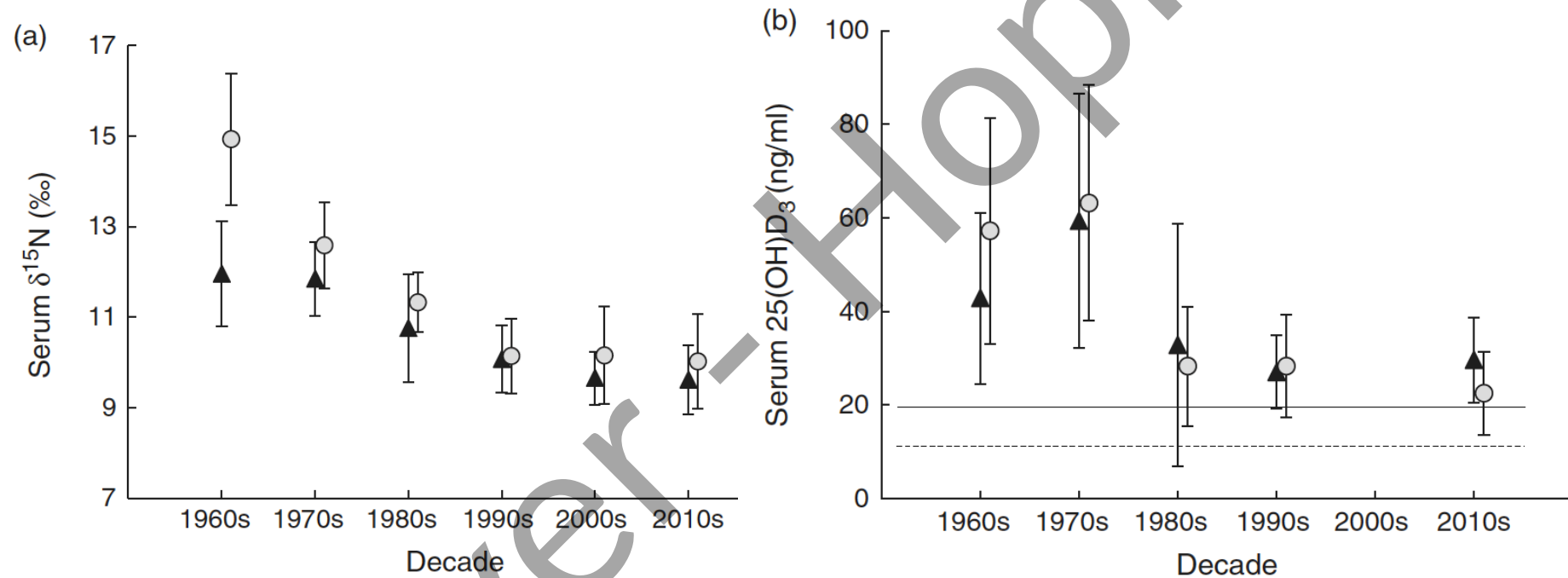
- In response to the question, “*Can the foods we eat change our DNA?*”
- We have identified several differentially methylated regions associated with PUFA intake.
- One of the more interesting differentially methylated regions is located in the fatty acid desaturase gene cluster.
 - These genes are responsible for n-3 PUFA synthesis from plant-derived n-3 and n-6 PUFAS.

The Big Question

What is protecting the population from T2D?

- The prevalence of overweight and obesity is similar to the overall U.S. population.
- Prediabetes is on the rise and is equal to the U.S.
- However, the prevalence of T2D is less than one-fourth in the U.S.
- **We have not found a direct association between glucose parameters and n-3 PUFA intake.**

Declining traditional food intake and Vitamin D levels over time



Diet in Transition

- We believe the traditional diet rich in n-3 PUFA's that was eaten in the previous 2 generations is protecting the current generation from T2D.
- Younger people are transitioning to more energy-dense, highly processed market foods.
- Prediabetes is increasing.
- While all of our previous research was in non-pregnant adults, we are now investigating diet and pregnancy-related health outcomes.

Maternal Health Disparities

- >30% in YK region are below the poverty level
- Geographically isolated
 - Travel restricted due to extreme weather
- Only 31% of Yup'ik women receive adequate prenatal care
- Preterm birth is 14% in Yup'ik women compared to 7.9% in AK whites
- Prenatal care in regional hub
 - First prenatal and ~20 week visit, more if needed.
 - Travel at 36 weeks to prematernal home to await delivery at the hospital in Bethel.
 - About 600 births per year, 400 of these deliver in Bethel.
 - High-risk pregnancies and scheduled c-sections have to travel to Anchorage (500 miles) for delivery
 - ~200/year

Source: <http://anthctoday.org/epicenter/healthdata.html>



Yup'ik Feasibility Study

- Completed a feasibility study with 15 pregnant Yup'ik women.
- Focus on the role of maternal diet on the health of the mother and unborn child.
- Following offspring for 5 years via EHR data.
- We have received funding to expand our research with pregnant women.



Challenges to DOHaD Research

- Geographic distance
 - Time and cost
- Missed appointments due to weather
- Research infrastructure
 - Facility
 - Trained Ob/Gyn nurses and US staff
 - Need liquid nitrogen to process samples
- Cultural and environmental considerations
 - Beliefs and practices during pregnancy
 - Environmental exposures
 - Long-term follow-up is challenging



Building YK Research Infrastructure

- Building research infrastructure for future pregnancy-related research in the region.
 - Research facility at UAF Kuskokwim Campus (2010)
 - Liquid nitrogen plant for processing placental samples
- Working with the YKHC staff for recruitment and data collection.
- Training obstetric nurses in research methodology.
- Training sonographers in advanced fetal measurements.



Current Pregnancy Study

- Recruit 70 pregnant women, 18 – 40 yrs. over the next 3 years
 - Understand how maternal diet and stress affects health of mother and child
 - Have recruited 36 women, and recruitment is ongoing.
- Data collected at four timepoints, 14, 20, 36 weeks and delivery
 - Demographic and stress questionnaires
 - Dietary assessment using a validated Yup'ik FFQ and NIR
 - Fetal ultrasounds
 - Blood, hair, and placenta sampling
 - Anthropometric measures – Maternal and infant
 - Electronic Health Record review
 - Maternal – Medical history, including prior and current pregnancy.
 - Infant – Birth to 5 years

Importance of this study

- Builds on known health benefits of a traditional Yup'ik diet.
- Diet is transitioning to more unhealthy market foods.
- The current population appears to be protected but for how long?
- Future generations may be at greater risk for developing cardiometabolic diseases
- This study builds research capacity in the region and provides critical preliminary data to develop a sustainable DOHaD research program in Southwestern Alaska.



NUTRITION
in pregnancy
LIFELONG CONSEQUENCES

In Summary

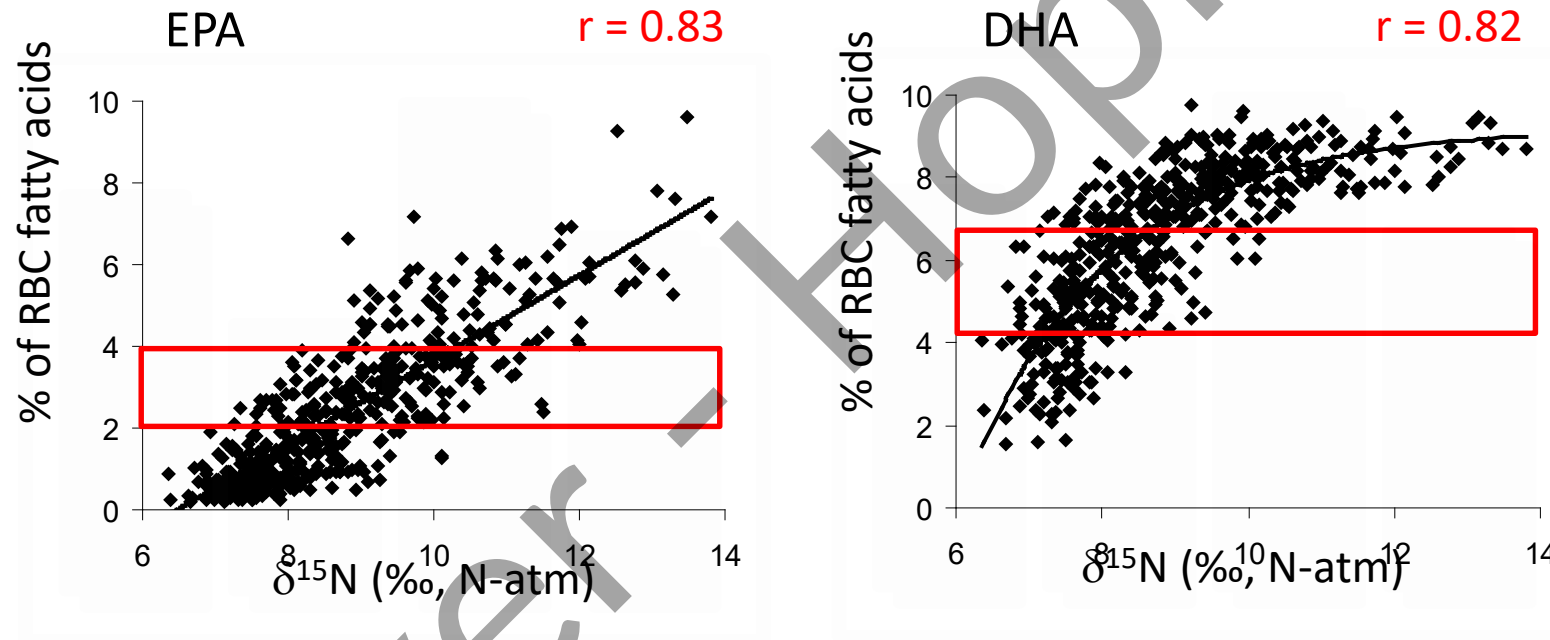
- Research relationships take time and require frequent face-to-face interaction.
- Important to understand cultural and environmental factors influencing health.
- Bi-directional learning and **dialog** is essential
 - Scientific Knowledge ↔ Indigenous Knowledge
- Building on prior research enhances our ability to conduct meaningful DOHaD research to reduce health disparities in underserved and vulnerable populations.
- While these examples are specific to Yup'ik communities, these considerations can apply to other underserved communities.

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- The M. J. Murdock Charitable Trust

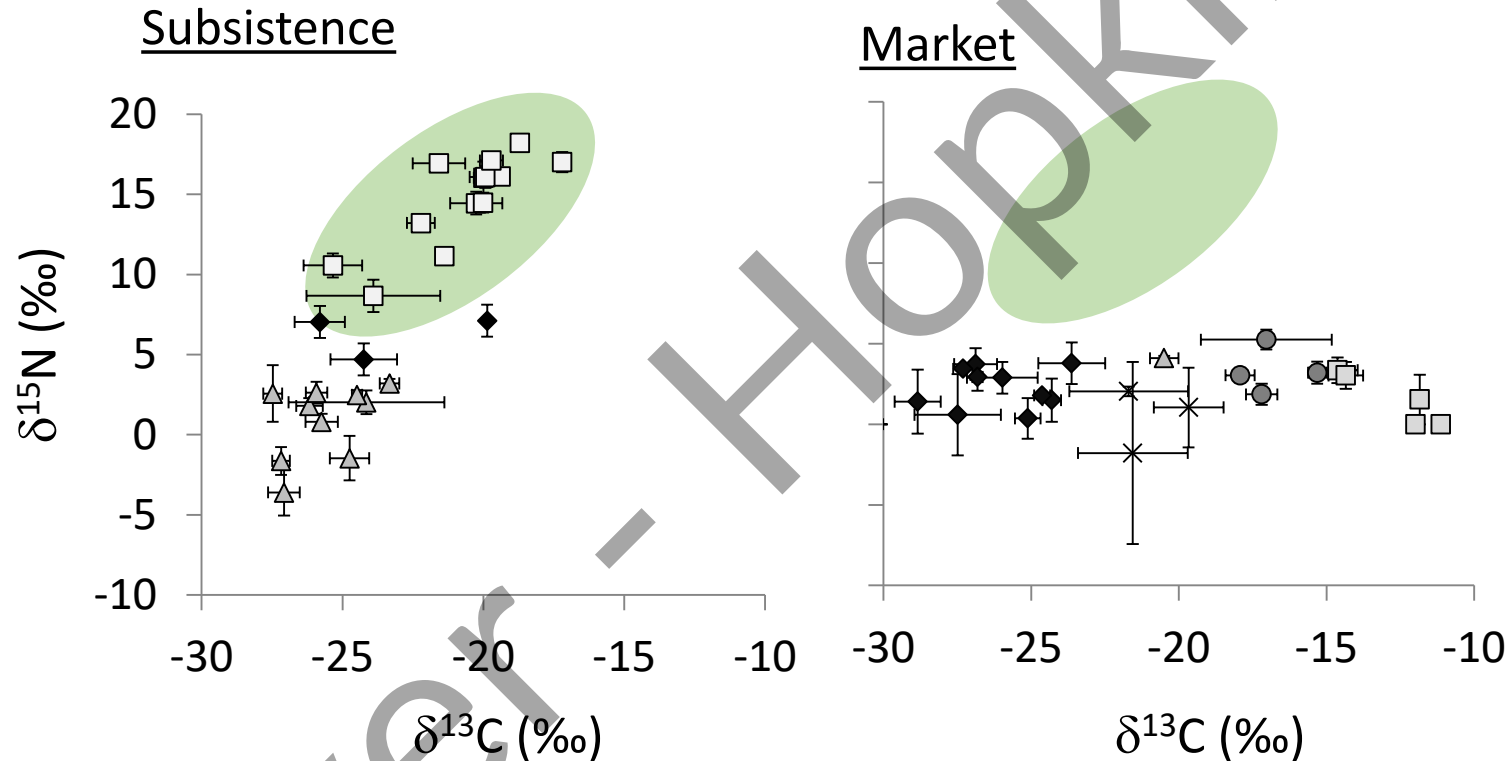
Email: hopkisca@ohsu.edu
boyerbe@ohsu.edu

RBC NIR is strongly associated with RBC EPA & DHA ($n = 496$)



*US population mean +/- SD
Sun et al 2007 AJCN

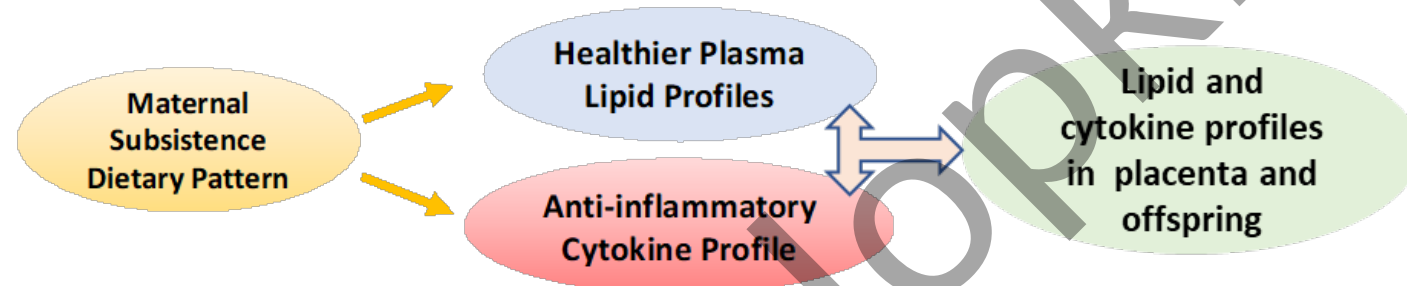
Fish and marine mammals have high NIR



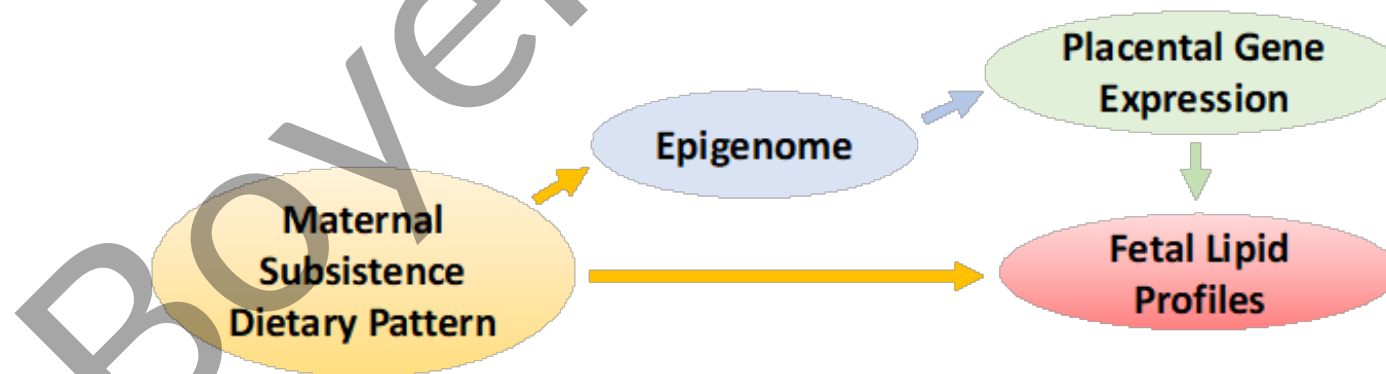
We used NIR as an objectively measured biomarker of the traditional dietary pattern in blood, but it can also be measured in nails, hair and breath!

Aims of the Study

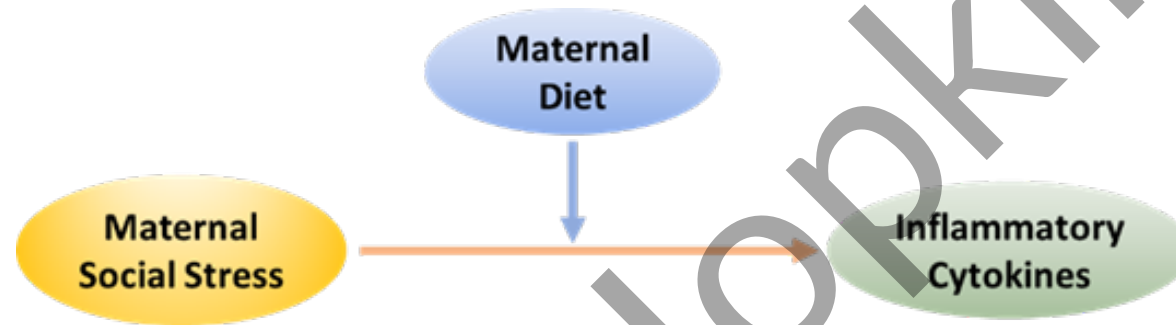
Aim 1: Determine the degree to which a maternal subsistence dietary pattern correlates with maternal, placental and fetal plasma lipid profiles and inflammatory markers.



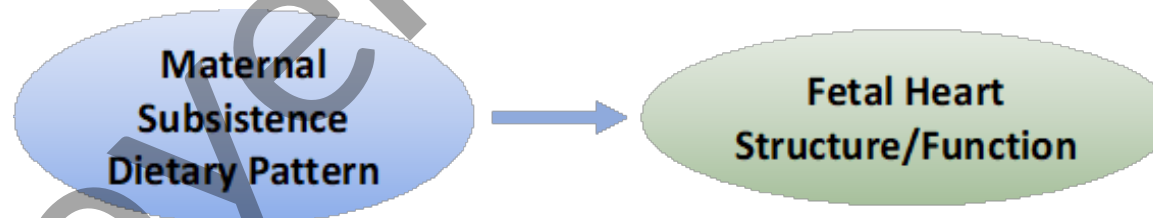
Aim 2: Determine the degree to which a maternal subsistence dietary pattern affects epigenomic profiles of maternal leukocytes, placental trophoblast cells and fetal leukocytes and influences subsequent expression patterns of genes that regulate the transport of glucose, amino acids, and long chain free fatty acids from mother to fetus.



Aim 3: Determine the degree that maternal diet moderates the association between maternal social stress and markers of inflammation in mother and offspring.



Aim 4: Determine the degree to which maternal dietary patterns correlate with fetal heart structure and function.



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