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Study Protocol

Official Study Title:
Indigenous Supported Agriculture Study (ISA) “Go Healthy”

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Research Protocol

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Principal Investigator: Valarie Blue Bird Jernigan, DrPH, MPH, Professor of Rural Health and Director of the Center for Indigenous Health Research and Policy at Oklahoma State University Center for Health Sciences

Co-Investigators: Ying Zhang, PhD, MD, Jessica Reese, PhD, MS, Robert Rosenman, PhD, Tvli Jacob, PhD, Jann Hayman, PhD, Susan B. Sisson, PhD, RDN, CHES, FACSM,

1. SPECIFIC AIMS

The proposed study will implement an agricultural and health education program in which American Indian (AI) residents of Osage Nation will receive a weekly share of healthy fresh fruit and vegetables for four months, coupled with healthy recipes and cooking materials. These types of programs, referred to as "Community Supported Agriculture (CSA)" programs, have improved diet and health in non-AI populations, and are evidence-based strategies recommended by the Centers for Disease Control and Prevention and the Institute of Medicine to reduce health disparities. However, no randomized controlled trial of a CSA program has been conducted in the AI population. Accordingly, we will test the efficacy of a CSA program- which we refer to as the Go Healthy Indigenous Supported Agriculture (ISA) program- combined with culturally-tailored nutrition and cooking education on diet and health outcomes among AI households. We will evaluate its cost-effectiveness, and develop a multimedia toolkit for disseminating findings. Our specific aims are to: 1) Conduct a randomized controlled trial to test the newly developed ISA program's effect on diet, blood pressure, and blood lipids (primary outcomes) and on body mass index (BMI), hemoglobin A1c (HbA1c), food insecurity, health status, and Skin carotenoid measurement by Veggie Meter (secondary outcomes) among 200 AI households with an index adult (aged 18-75) identifying as AI with overweight/obesity; 2) Perform an economic evaluation for individual (e.g., health-related quality of life), organizational (e.g., healthcare utilization costs), and community-level (e.g., prevention of cardiometabolic diseases) outcomes; and 3) Document and disseminate study processes and findings using participatory video methods, and compile a web-based toolkit for other AI communities to use to improve tribal food systems. This study is the first to rigorously intervene across all components of the food system to address poor diet and health among AIs. Building upon Osage Nation assets and priorities, guided by a participatory research and Indigenous food sovereignty orientation, and based upon recommended strategies to eliminate disparities, study findings will inform research and policy efforts to create sustainable food access in reservations with high rates of chronic disease as well as urban AI communities where ISAs are available and could be tailored to AIs.

2. RESEARCH TEAM AND SETTING

This study will be led by an experienced research team with diverse and complementary expertise and a long and positive history of collaboration.

Valarie Blue Bird Jernigan, DrPH, MPH (Choctaw), Principal Investigator (PI), Professor of Rural Health and Director of the Center for Indigenous Health Research and Policy (CIHRP) at Oklahoma State University Center for Health Sciences (OSU-CHS), is an Indigenous researcher trained in intervention science. Dr. Jernigan uses participatory research to address diet-related health disparities among AIs. She is the PI of several NIH-funded studies and currently co-leads three NIH trials.

Ying Zhang, PhD, MD, Co-I, Associate Professor in the Department of Biostatistics and Epidemiology at OUHSC, will serve as the methods lead of the study. Dr. Zhang has two decades of experience using CBPR in

Native communities across the United States and currently serves as the PI of the Strong Heart Study Coordinating Center. Dr. Zhang will provide methodological oversight and oversee statistical analysis for the ISA study. Dr. Zhang will attend virtual or in-person monthly research team methods meetings with OSU-CHS.

Jessica Reese, PhD, MS, Co-I, Assistant Professor of Research in the Department of Biostatistics and Epidemiology at OUHSC, will serve as the lead analyst for the heath outcomes of study. Dr. Reese has expertise in clinical research, epidemiologic methods, and data analysis and currently conducts research with the Strong Heart Study, which is an NIH-funded, multi-centered cohort study of CVD in AIs. Dr. Reese will attend virtual or in-person monthly research team methods meetings with OSU-CHS.

Robert Rosenman, PhD**,** Co-I, Professor Emeritus of Economic Sciences at WSU, will lead the health economics analyses. Dr. Rosenman is performing economic analyses on seven behavioral intervention studies involving AIs led by Dr. Jernigan. Dr. Rosenman will develop customized instruments for measuring direct and indirect costs and benefits associated with the intervention at individual, organizational, and community levels and across domains (e.g., health-related quality of life and clinical outcomes).

Susan B. Sisson, PhD, RDN, CHES, FACSM, Co-I Behavioral Scientist, Research Dietician, and Professor at the University of Oklahoma Health Sciences Center (OUHSC), will oversee all dietary components of the study. Dr. Sisson will determine appropriate dosage for each ISA box and calculate associated nutritional content. Dr. Sisson will also provide dietary and nutritional guidance for curriculum development, study implementation, and evaluation. Dr. Sisson will attend virtual or in-person monthly research team meetings with OSU-CHS and Osage Nation research partners.

Tvli Jacob, PhD (Choctaw)**,** Assistant Professor in the Department of Psychiatry at OSU-CHS, is an Indigenous qualitative researcher and filmmaker who uses video and other media to effect social change. He has been a Co-I on several NIH-funded studies led by Dr. Jernigan, including the THRIVE and FRESH studies. Dr. Jacob will use participatory videography techniques to teach AI community members how to use video to tell their stories and lead the development of the web-based multimedia manual and “how-to” toolkit for dissemination to AI communities locally and nationally.

Jann Hayman, PhD (Osage), Tribal PI, Director of Natural Resources for the Osage Nation, and Director of Harvest Land, has over a decade of experience leading tribal agricultural initiatives that include sustainable agriculture program development and implementation, agricultural marketing and communications, and agriculture education programs for youth and adults. Dr. Hayman will oversee all aspects of the ISA program, with extensive support from Harvest Land staff.

This research will take place in two locations – the Osage Nation and OSU-CHS. Located in northeastern Oklahoma, Osage Nation occupies the state’s only federally recognized reservation, which is coterminous with Osage County. Osage Nation has a healthcare system that includes a main healthcare center providing comprehensive primary and specialty care. Recruitment will be conducted at community locations (e.g. health fairs, powwows, and community dances) and within the healthcare center. Data will be collected via REDCap and stored and analyzed at both OSU-CHS and WSU.

3. RESEARCH METHODS

This study will be overseen by the OSU-CHS IRB, which will serve as the official IRB of record for the study. It will also be reviewed and approved by the Osage Nation Historic Preservation Department prior to implementation. This Department serves as a research review body for the Osage Nation. No research will take place without both the OSU-CHS IRB review and approval and the Osage Nation Preservation Department review and approval. This study will be registered in ClinicalTrials.gov no later than 21 calendar days after enrollment of the first participant and primary summary results reported in ClinicalTrials.gov, no later than one year after the completion date.

All surveys and data collection protocols are included within this document.

We summarize the study aims, methods, and measures, as follows.

Aim 1. Conduct a randomized controlled trial to test the Go Healthy ISA program's effect on diet, blood pressure, and blood lipids (primary outcomes) and on body mass index (BMI), hemoglobin A1c (HbA1c), food insecurity, and health status (secondary outcomes) among AI households.

This is a five-year study. During years one and two of the study we will finalize research protocol and survey measures. In years two and three of the study, we will recruit and follow a cohort of 200 AI households over a four-month period (400 adults and up to 400 children).

Specifically, one AI adult will be recruited as an "index" participant. This individual must be aged 18-75 years, identify as AI, reside within Osage Nation, and be overweight or obese (BMI ≥ 25 kg/m^2) based on height and weight information collected onsite by a research staff member. The individual should also have no plans of moving within the next year and must not be pregnant or plan to become pregnant within the next year.

We will also enroll up to two additional adults living within the index participant's household and up to four children (aged 3-17 years) living within the index participant's household. These individuals are not required to be AI or overweight/obese but must reside within the index participant's household.

Households will be randomized to either immediately receive four months of weekly ISA produce plus culturally-tailored nutrition education, website links to Indigenous cooking demonstration videos, and basic kitchen supplies (intervention group), or to receive equally valued gift cards to use at Harvest Land (gift cards loaded in small increments over four months) and education after completing the study (wait-list control group).

The primary outcomes assessed for adult participants are diet, systolic and diastolic blood pressure, and blood lipids. Secondary outcomes are BMI, HbA1c, food insecurity, health status, and skin carotenoid measurement by Veggie Meter. For children, only BMI and dietary intake.

Data collection for all measures will be conducted at baseline and four months and for adults will comprise self-report questionnaires, blood panels, 24-hour dietary recalls, and biometrics measured by the research staff.

For children, only BMI and dietary intake will be assessed. BMI will be assessed by measuring height and weight. Dietary intake will be assessed using a Pediatric-Adapted Liking Survey and a "Veggie Meter", which is a noninvasive research-grade instrument that detects and quantifies carotenoids in the skin, a class of phytochemical compounds found in fruits and vegetables and therefore commonly used as a biomarker for fruit/vegetable intake. The Veggie Meter will also be used with adults.

The study uses a wait-list control group, and all participants assigned to the control group will have the opportunity to receive an Osage Nation Harvest Land Farm gift card of equal monetary value during the completion of the trial. An overview of the randomized control trial study design is shown in **Figure 1**.

Staff Training, Recruitment, Screening, and Enrollment

Recruitment, screening, and enrollment of study participants will be conducted by a **research team that comprises both university and tribal staff. All research team members will be trained in one standard screening and data collection protocol developed for and implemented in our previous studies.** The protocol includes the use of standard study equipment, regularly monitored and calibrated, and a standardized protocol for the collection of blood pressure, height and weight, and the administration of dietary recalls and survey questions. The blood panel and HbA1c data will be collected and analyzed using Point of Care Testing (POCT) at the Osage Health System, which uses a standard protocol.

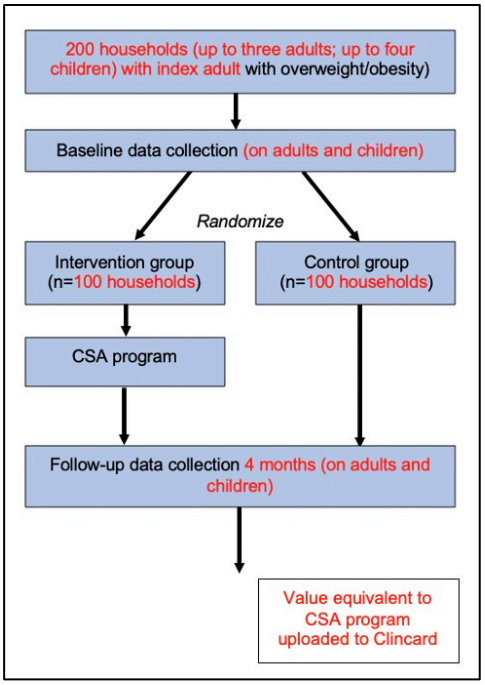

Figure 1: Randomized control trial study design

The research team will recruit, screen, and enroll study participants **in both community and clinic settings**. In the community setting, the team will advertise the study through the media (e.g., Osage television, Osage newspaper, and Osage websites) and attend town hall meetings and community events, such as powwows, gatherings, community dinners, and health fairs. The team will also set up recruitment tables in the waiting rooms at the Osage Health System main clinic.

In addition, Osage Health System clinical staff will conduct chart reviews to identify individuals who may be eligible for the study and refer them to the research team to learn more information and, if interested and eligible, to enroll (see Letter of Support from Osage Health System). Research team members will explain the study goals, study design, and requirements of participation to potential participants. Individuals who are screened as eligible and choose to enroll will provide written informed consent and complete baseline data collection prior to being randomized to a treatment group. All baseline data will be collected by research team members. Based on retention rates in our previous studies with AIs, we expect at least 80% of potential families to participate. We are highly confident that we can successfully achieve a final sample size of 160 households after accounting for attrition.

Baseline Data Collection

After completing all baseline data collection, participants will be told whether they have been selected to receive the ISA program in the first round (intervention group) or a Harvest Land gift card of equal value in the second round (wait-list control group). Intervention group participants will be provided with an informational folder about the ISA program, including pick-up times and dates and in-person meetings. **Data will be collected on all 200 index participants and participating household members, up to two additional adults and up to four children per household (intervention and wait-list control) at the two time points.**

Randomization. Households will be randomized using variable-size block randomization in a 1:1 ratio with a computer-generated randomization sequence. Treatment group assignment will be concealed from field staff until the moment when a household is ready for randomization. Dr. Muller, lead biostatistician, will work with study staff to conduct regular audits to ensure that randomization is being accurately implemented.

Immediate Intervention. Households in the intervention group will receive the ISA program during a four-month growing period (January-May 2024). The ISA program consists of both didactical education as well as practice-based learning, informed by an ecological model to influence multiple levels of eating behavior and designed by our research group in partnership with Osage community health planners. The program consists of five components: 1) ISA produce boxes from Osage's Harvest Land Farm and a local food supply company available weekly for pick-up at one of the three Osage Nation Districts; 2) a healthy eating and traditional foods curriculum

that will be available inside the box with the history and preparation options for the foods in the weekly box; 3) a monthly in-person healthy eating and traditional Indigenous foods cooking workshop during which Osage staff and Osage cooks (a position of leadership and prominence within Osage culture and held exclusively by women) will prepare and feature a healthy, traditional meal with ISA foods and then facilitate a discussion guided by the Indigenous food sovereignty principles; 4) Indigenous cooking demonstration video website links (provided through QR codes) to accompany suggested recipes; and 5) a kitchen starter kit that includes kitchen cooking supplies.

ISA Produce Boxes. The study will purchase a Harvest Land ISA membership for intervention group households. The ISA will provide each household with 12 servings of vegetables and eight servings of fruits per day, which is the recommended daily serving for four adults, for the duration of the four-month intervention. The average household size in Osage Nation is 2.5, according to the most recent US Census data. In a given week, each ISA will contain at least 6–12 types of produce. Example foods include carrots, scallions, cucumbers, squash, tomatoes, pumpkins, kale, spinach, celery, salad greens, beets, sweet peppers, hot peppers, tomatillos, and melons. The produce will be picked up by a household participant at one of three pickup locations closest to the participant's residence each week.

Healthy Eating and Traditional Foods Curriculum. Each ISA box will include healthy recipes, incorporating as many traditional Osage foods and recipes as possible, due to the high nutrient content. As part of the FRESH study with Osage Nation and in preparation for the proposed study, our research team compiled a list of recipes incorporating Osage traditional foods and preparation processes. We worked with the Osage Nation Language Department to translate all recipes into Osage language. We will incorporate these recipes and their nutritional profiles into a finalized curriculum to be reviewed and approved by the Osage Nation Congress and the Osage Historic Preservation Department. The recipes will be available in the ISA box and on our study website, to which participants will receive a link.

Healthy Eating and Traditional Indigenous Foods Cooking Workshops. Interactive workshops will be offered monthly to intervention households during the course of the four-month intervention period. Osage Nation staff and cooks will teach healthy eating and traditional Indigenous foods cooking workshops that integrate traditional and locally grown foods with Osage language and culture. One recipe will be demonstrated each month. Along with the recipes, basic information about the featured foods will be provided, including the Osage name of the food and history of the food in relation to Osage Nation (e.g., when the food was first used by Osage people and how it was prepared). The monthly workshops will be held at Harvest Land and will include basic nutritional information, a cooking demonstration, and sharing of the meal with the participant and his/her family. They will be filmed and put online for viewing for intervention participants (initially) and then for the community once the intervention is complete.

Indigenous Cooking Demonstration Videos. Indigenous cooking demonstration videos will be made available through a QR code and will accompany weekly ISA boxes. The videos will highlight healthy, Indigenous recipes.

Kitchen Starter Kit. A kitchen starter kit will be provided to households in the intervention group at the first pickup of their ISA box. Each kitchen starter kit will include kitchen utensils and small appliances to promote the use of the ISA box produce and reduce barriers to using the produce in the provided recipes. Some of the suggested recipes require the use of a knife, blender, or crock pot, items a family might not have readily available for their use. These items will increase household capacity to utilize the produce and to try the suggested recipes. Each kitchen starter kit is valued at about $75.

The ISA boxes, healthy eating and traditional foods curriculum, and kitchen starter kits are designed to strengthen and reconnect participants with the principles of Indigenous food sovereignty and increase self-efficacy and daily participation in healthy eating. The monthly cooking workshops and Indigenous cooking

demonstration videos aim to increase community-efficacy and cultural connectedness and improve diet and health outcomes.

Pilot intervention. In order to test the feasibility of the intervention and reduce potential food waste, a pilot intervention will be conducted in July 2023, before household randomization. A small sample of individuals enrolled in the ISA study (N = 5) will be invited via email to participate in the pilot intervention. Participants will receive 2 weeks of the ISA program, which will include, as described above, 1) a weekly ISA produce box for 2 weeks, 2) the healthy eating and traditional foods curriculum, and 3) Indigenous cooking demonstration videos. After receiving the 2-week pilot intervention, participants will be invited to an in-person focus group, where researchers will solicit verbal feedback from participants regarding their experiences of the intervention, what improvements could be made to the intervention, and any necessary adjustments to the number of servings per box. Participants will receive a $40 gift card for attending the focus group. Focus group feedback will be incorporated to the ISA program before the full intervention begins in January 2024.

Wait-list Control Group. At the time of their initial randomization assignment, households in the waitlist control group will be told that they will receive compensation equal in value to the intervention after completion of the trial, after data collection is complete, in approximately 10 months. They will be contacted periodically during the study period to update contact information and to remind them about the four-month follow-up data collection visits. After completing the four-month data collection visit, wait-list control group participants will be offered the option to receive compensation equal in value to the intervention uploaded to their ClinCard.

Follow-up Data Collection. The four-month follow-up visit will take place directly after the intervention group receives the ISA (May-July 2024). Staff will contact participants to schedule the visit beginning in April. Staff will contact individuals by telephone and text up to 10 times (five phone calls and five text messages). They will also send up to two letters as well as two emails. Appointments will be made at a time of convenience to the participant including weekends and evenings.

Process Evaluations. We will administer 16 weekly process evaluation surveys via REDCap to index adults in the intervention group to assess the fidelity of the intervention. Questions will ask about the produce (consumption, quality, etc.), recipes, curriculum, and costs and expenses. The survey will take no more than five minutes to complete.

Retention and Compensation. Our participatory research approach will be essential for maintaining participation during the intervention. We will employ strategies that have been successful in retaining participation in our previous research. For example, research staff will work with the same participants for the duration of the study. The relationships that they establish with these participants will be critical for retention. In addition to each participating household receiving the ISA program, valued at approximately $800, individual adult participants will receive gift cards totaling $150 for completing baseline ($75) and four-month post intervention data collection ($75). Additionally, index adults will receive an additional $25 if they complete all 16 of the weekly process evaluations. Children will be compensated with a small toy (ages 3-10) or $20 gift card (ages 11-17) for completing BMI, Veggie Meter, and survey data collection.
In order to meet our recruitment goal and account for retention, we aim to recruit 440 adults. We plan to offer additional compensation for enrolled participants who refer adults to enroll in the ISA study. Adults will be compensated $10 for each adult who is eligible and enrolls in the “Go Healthy” study, and will be compensated up to $50.

Primary Outcomes. Study outcomes are shown in **Table 1.** The National Cancer Institute’s Automated Self-Administered 24-hour Recall (ASA-24) 2022 will be used to assess **diet**. This self-report instrument generates a “healthy eating index” (HEI), with scores ranging from 0 (least healthy) to 100 (healthiest). We will use the most recent version, the HEI-2015 with adult participants, which has been updated to reflect recent US dietary guidelines and has been demonstrated to have good validity and reliability. The HEI has been widely used in public health research with diverse populations, including one analysis that used the previous version (HEI-2010)

to assess diet of the FDPIR recipients administered by the US federal government. Continuous values of the overall HEI score will constitute our primary outcome, but we will also evaluate subscores for diet adequacy and moderation, and an ordinal categorical outcome that reflects conventional letter grades ranging from "A" (score = 90-100) to "F" (score = 0-59). **Blood pressure** will be measured using a rigorous standardized protocol previously developed for similar intervention projects. All research staff will be trained to measure blood pressure for adult participants. A total of three measurements, separated by 30 seconds, will be obtained on participants' right arm, using a cuff of appropriate size, after they rest quietly in the seated position for at least five minutes. **Blood lipid panels** for adult participants will be assayed from a finger stick sample that is collected and processed using a point of care testing (POCT) machine, CardioCheck PA analyzer. Staff will be trained on proper finger stick and POCT procedures to collect instant blood lipid results.

Secondary Outcomes. We will measure **food insecurity** among adults using the Household Food Security Survey Module. This instrument contains 18 items to capture the qualitative and quantitative dimensions of household food supply, including psychological and behavioral responses of household members. To compute levels of food security and insecurity, we will total the number of affirmative responses to these items, counting "Often" and "Sometimes" as affirmative. Consistent with USDA guidelines, 0-2 affirmatives indicate food security, and 3 or more affirmatives indicate food insecurity**. BMI** will be evaluated on adults and children by measuring height with a portable stadiometer (Hopkins) to the nearest 0.1 centimeter. Height will be taken twice and averaged. We will measure weight to the nearest 0.1 kilogram on an electric digital scale (Health Morbius Health Meter). Weight will be taken with clothing on and without shoes. Scales will be calibrated monthly. We will calculate adult BMI as a continuous variable by dividing weight in kilograms by height in meters squared and categorize participants according to CDC guidelines: 1) underweight (BMI < 18.5); 2) healthy weight (BMI = 18.5-24.9); 3) overweight (BMI = 25.0-29.9); 4) obese (BMI = 30.0-39.9), and 5) morbidly obese (BMI ≥ 40.0). Note that all index participants will have BMI ≥ 25 kg/m^2 at baseline. Child BMI will be calculated as a continuous variable using the CDC Child and Teen BMI Calculator. **HbA1c** will only be collected for adult participants. The Osage Nation Health System estimates that approximately 20% of their total population may have undiagnosed diabetes. Using a CardioChek PA analyzer, we will collect a blood sample by finger stick to assess HbA1c at baseline and four months. Values reflect the percentage of red blood cells with attached glucose molecules and will be recorded both as a continuous value (%) to the tenths digit and as a binary indicator of HbA1c < 8%. Adult **Health status** will be assessed using a general overall health question from the Short Form-36 (SF-36), which participants rate their overall health as excellent, very good, good, fair, or poor. The SF-36 has been widely used and validated with AIs. In addition, we will also administer the EuroQuol 5 Dimension – 5 Level Questionnaire (EQ-5D-5L). The EQ-5D-5L is a self-assessment of overall health and quality of life, measuring five dimensions of participant's health today, including mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. **Skin carotenoids** will be measured in adult and child participants using a Veggie Meter machine. The Veggie Meter uses a LED light to measure carotenoids. Three scans will be taken with the average entered into the database.

Table 1 Randomized controlled trial measures

Variables	Role
Diet	Primary outcome
Blood pressure	Primary outcome
Blood lipids	Primary outcome
Food insecurity	Secondary outcome
Body mass index	Secondary outcome
Hemoglobin A1c	Secondary outcome
Health status	Secondary outcome
Skin carotenoids	Secondary outcome
Self-efficacy	Mediator
Social support	Mediator
Cultural connection	Mediator

Community efficacy	Mediator
Food environment	Mediator
Mindful eating	Mediator
Age	Covariate
Sex	Covariate
Education	Covariate
Marital status	Covariate
Household income	Covariate
Employment status	Covariate
Smoking and alcohol use	Covariate
Comorbidities*	Covariate
Healthcare access	Covariate
Healthcare utilization	Covariate
Physical activity	Covariate
Public assistance programs	Covariate
Health economics†	Specific Aim 2

*Chronic kidney disease, cardiovascular disease, diabetes, prediabetes, depression, anxiety, hypertension at baseline
†Financial and non-financial costs and outcomes measured at the level of individual, organization, and community (see Section 4.F).

Mediators. We will assess the following mediators among adults to facilitate a comprehensive analysis of the ability of diet-related food system intervention to improve AI health. **Self-efficacy** will be measured using the Healthy Eating and Weight Self Efficacy scale. This scale measures the consumption of healthy foods on a five-point Likert scale, with a higher score indicating a higher healthy eating and weight self-efficacy. **Social support** will be measured using the Social Support for a Healthy Diet survey. This survey evaluates how a participant's family supports and either encourages or discourages healthy diet maintenance using a five-point Likert scale. A higher score indicates higher levels of social support from family**. Cultural connection** will be measured using an Osage Traditional Food Frequency questionnaire and a Cultural Identity Scale. Questions include the frequency of following tribal ways of life, importance of Indigenous values and practices, and involvement in traditional and cultural events and practices. **Community efficacy** will be measured using the Community Health and Climate Survey and a Food Sovereignty and Health survey. These questions are adapted to the Osage Nation community and include interest, involvement and importance of cultural practices and climate change. These items have both been used with AIs. **Food environment** will be measured using the First Nations Food Nutrition and Environment Survey, which evaluates traditional Indigenous foods, and the Perceived Nutrition Environment Survey (NEMS-P). The NEMS-P will assess home food environment, food shopping, and thoughts and habits about food. **Mindful eating** will be measured using the Mindful Eating Behavior Scale (MEBS). MEBS measures the attention element of mindful eating. We will also assess exposure to the intervention by assessing log-in sheets during the ISA pick-ups and website metrics for logging on to the study site for weekly recipes and video narratives as well as intervention participation questions on a six-month post-intervention survey.

Covariates. Additional covariates assessed via study questionnaires will include age, sex, education, marital status, household composition and income, employment status, cigarette and alcohol use (coded current, former, and never), comorbidities (e.g., chronic kidney disease, cardiovascular disease, diabetes, pre-diabetes, depression, anxiety), healthcare access and utilization, and physical activity. We will also ask about participation in public assistance programs such as Temporary Assistance for Needy Families, SNAP, Women, Infants, and Children, and Supplemental Security Income.

Child Measures. BMI and dietary intake will be assessed in households with up to four children, aged 3-17. Dietary intake will be measured using the Veggie Meter and the Pediatric-Adapted Liking Survey (PALS). PALS assesses a child's level of liking or disliking a list of 33-items, shown in both words and pictures, using a visual scale from -100 to 100 with seven different faces corresponding with the level of liking of the item. Additional demographic questions including age and sex will also be asked.

Data Security. All databases and computers will be password-protected in accordance with OSU-CHS IRB requirements, and all data will be stored on a secure server operated by OSU-CHS and WSU. Nightly incremental backups and weekly full backups will ensure optimal recovery of data in the event of a disaster. On all data files, individuals will be identified only by a unique participant identification code. Similarly, paper records will identify the participant only by identification code and will be kept in a locked filing cabinet at OSU-CHS. A key associating the participant identification codes with the participants' names and contact information will be kept separately in a locked drawer. All audit and survey data collected on iPads using REDCap will be automatically uploaded to a secure server when an Internet connection is available. Identification codes will be used to merge datasets for statistical analysis. All personal identifiers will be redacted before data transmission.

Statistical Analysis. Dr. Muller will attend team meetings, oversee methods-related implementation and potential changes to study design, and work with the research team during data analysis. Quantitative analyses will be conducted using R (version 3.3 or later) or Stata (version 14 or later) software packages. All analyses will use the intent-to-treat principle, with results reported as point estimates with 95% confidence intervals. For **descriptive statistics**, we will describe all variables by using counts and frequencies for categorical factors, and means, medians, standard deviations, and ranges for continuous factors. We will use chi-square and t tests to compare baseline distributions across the two treatment groups to identify factors that might be unbalanced by chance. We will plot primary and secondary outcomes during follow-up in the intervention and wait-list control groups and calculate descriptive statistics for primary outcomes stratified by potential mediators (**Table 1**). For **inferential analysis** we will conduct the following:

Intervention Effectiveness. We will use linear mixed models to test the effect of the ISA intervention on within-person change in primary and secondary outcomes. For each outcome, the initial model will include a fixed effect for group assignment, a random intercept for individual participant, and a fixed effect for time (baseline and four-month follow-up). We will run models with and without a participant-level random effect for slope associated with the intervention and will include the effect if it provides a better fit to the data. Next, we will add a term for the intervention × time interaction to determine whether the intervention is associated with divergence between the two treatment groups during the four-month follow-up period. Separate models will be fit where time is considered a continuous variable vs. indicator variables. A likelihood ratio test will be used to determine the best-fitting model. This analysis will be the **primary test of the effectiveness** and will be interpreted as estimating the average within-person change for the intervention group, beyond any change that participants would have experienced without the ISA program. If necessary, we will conduct sensitivity analyses in which models are adjusted for covariates that showed imbalance between treatment groups at baseline. We will also **conduct exploratory analyses to examine if the intervention has a differential effect according to biological group.** These analyses will follow the same approach described above except analyses will be stratified by biological group.

Mediation Analysis. **First**, we will estimate the effect of the ISA intervention on the potential mediating factors at four-month follow-up to establish whether a temporal effect exists as would be necessary for a mediating influence. **Second**, we will evaluate whether baseline levels of the mediators predict the outcome at four-month follow-up among control participants only, adjusting for baseline outcome values. Although this analysis will not establish causality, it will address whether associations are present in the control group consistent with mediation. **Third,** we will evaluate whether the magnitude of association between treatment group and outcome attenuates after adjusting for the potential mediating factors. This model estimates the controlled direct effect of the ISA intervention and will include adjustment for potential confounders of the association between the mediators and the outcome. Given well-established limitations in causal inference from mediation analysis, we will emphasize a qualitative interpretation in which we evaluate whether the results of these models are consistent with a mediating influence of the interim factor on the effect of the intervention on outcome variables, rather than attempting to quantify the precise percentage of the overall effect that is "explained by" the mediators.

Missing Data. We will carefully check for non-random patterns of missing data and determine whether analytic methods are necessary to adjust for informative missingness. Our preferred method is multiple imputation, in which participants with complete data are sampled repeatedly to generate probability distributions, allowing unbiased parameter estimates with appropriate standard errors. Multiple imputation assumes that data are missing at random, but is robust to violation of this assumption and performs well even with large amounts

of missing data (> 50%). Dr. Muller has the necessary expertise to consider other methods, such as the full maximum likelihood estimator, which does not require the assumption of missing at random.

Power. A sample size of 200 households will provide at least 80% power to detect between-group differences (e.g., intra-individual change compared between the two treatment groups) as small as 2.6 for the HEI score, 3.7 mmHg for systolic blood pressure, and 8.6 mg/dL for low density lipoproteins. These calculations assume three data collection points per person, 15% attrition over four months, an alpha error rate of 0.05, within-person correlation of 0.6, and standard deviation estimates obtained from prior studies. These minimum detectable differences correspond to standardized effect sizes of 0.2, which are conventionally considered indicative of strong statistical power.

Aim 2. Perform an economic evaluation to estimate the ISA's cost-effectiveness and cost-benefit. We will conduct a health economics analysis for individual (e.g., health-related quality of life), organizational (e.g., healthcare utilization costs), and community-level (e.g., prevention of cardiometabolic diseases) outcomes.

For the health economics analysis, we will use measures collected at baseline and four months follow-up to estimate the cost benefit of the ISA intervention in improving expected quality adjusted life years (QALYs), reducing direct medical costs associated with overweight/obesity, hypertension, and dyslipidemia, and a cost-effectiveness analysis of clinical improvements based on glycemic control, QALYs, and other secondary outcomes.

Measures and Analysis. The costs of the RCT include both programmatic costs and the costs for participants. Programmatic costs include the ISA subsidy, the cost of education materials, videos and workshops, kitchen starter kit, and administration. The ISA subsidy is easily available as the direct costs paid by the study to Harvest Land and Go Fresh. The personnel time and material costs for education, videos, and research will be collected by direct interaction between Dr. Rosenman and the research staff. Administrative costs will be assessed similarly. Participant costs primarily consist of time and effort spent to obtain the ISA boxes and learn new recipes, offset by any reduction in grocery costs since the ISA provides food which may displace the participants' normal diets. At each data collection point, participants will be asked to report their time spent and any indirect costs (e.g., taking time off from work or extra childcare) associated with obtaining the ISA boxes. Participants will also be asked to monitor their time spent on educational activities. The value of time will be either the participant's actual hourly wage or, if not working, the prevailing minimum wage. Finally, participants will be asked to estimate any change in their spending on foods (offset or augmentation instigated by receiving the ISA boxes). At the participant-level, cost-benefit analyses (CBA) and cost-effectiveness analyses (CEA) will be conducted. The CBA will compare the direct and indirect costs the participants incur to any change in food spending that results from receiving the ISA boxes, as well as reduction in out-of-pocket healthcare costs, and gains is QALYs from health improvements. The CEA will compare the costs per unit improvement in the primary outcomes: diet, blood pressure, blood lipids, and QALYs (as measured by the EQ5D, a six-item instrument that has been widely used internationally for this purpose) and three of the four secondary outcomes (excluding health status because of any lack of comparison outside the study). This analysis assesses the economic value of the intervention to the participants. Economics at the organizational level will be assessed with CBA and CEA similarly by adding the programmatic costs to the participant costs and performing the same analytics that will be done at the participant level. This analysis assesses the economic value of the intervention to Osage Nation. Finally, at the community-level, the economic analysis will forecast savings in healthcare expenditures due to improved health. Using changes in adult participants' blood pressure, blood lipids, HbA1c, and BMI, Dr. Rosenman will predict changes in cardiovascular events. He will conduct a CEA on these outcomes and will also translate these health status changes into healthcare resources saved through a CBA.

Aim 3. Document and disseminate study processes and findings using participatory video methods and compile a web-based toolkit for other AI communities to use CBPR to improve tribal food systems.

We will document and disseminate study processes and findings using participatory video methods and compile a web-based toolkit for other AI communities to use participatory research to improve tribal food systems. Once the web-based toolkit is complete, we will partner with local and national groups, including the NCAI Tribal Food

Sovereignty Advancement Initiative (TFSAI), to broadly disseminate the toolkit to Indigenous communities across the US and assess its appropriateness and potential for supporting tribes to improve their food systems and positively impact health. The TFSAI supports the development and strengthening of tribal nations' efforts to build and protect Indigenous food systems. The TFSAI currently provides the broadest forum and network in the US to share best practices for advancing Indigenous food sovereignty and assisting tribal governments with developing food sovereignty and related policies that improve the health of tribal citizens.

Toolkit Development. The toolkit and dissemination process will be guided by the Social Impact Model for Creative Media, which begins with a culturally-appropriate and compelling story and uses awareness raising, engagement methods and best practices for dissemination from our previous work, such as video voice, photovoice, and digital storytelling. Dr. Jacob will lead our study partnership in creating the toolkit, which will include a documentary-style film and multimedia manual of intervention materials including study processes, measures, and findings. We will use video footage and materials developed in Specific Aims 1 and 2 (e.g., cooking demonstrations and community gatherings) to create culturally-relevant and engaging material that will raise awareness about food systems and health with the goal to increase tribal communities' readiness and capacity to assess and improve their food systems. In addition, community members who are enrolled in the study and participating in the intervention component of the study will be invited to share their stories as part of the toolkit and documentary. Dr. Jacob will interview interested participants prior to and after each of the healthy eating and traditional Indigenous foods cooking workshops, as well as during ISA pick-ups, and at other times of convenience for study participants, to include participant perspectives within the toolkit. In addition, participants will be invited to submit video narratives via the study website, to which they will be given an individual link. They will be provided with guidelines, including release forms to complete for themselves and all individuals included within their videos. To assist in creating engaging video narratives, participants will be prompted with questions that pertain to their experiences in the different components of the intervention and their perspectives on Indigenous food sovereignty. The documentary will share the story of Osage Nation's Harvest Land Farm, our research and ISA intervention, and the ways in which working to improve the food system impacted Osage Nation. We successfully used these participatory video methods in previous studies which were featured in the PBS documentary ***Blood Sugar Rising*** and in the online associated learning materials. In the proposed study, we will implement similar methods with NCAI TFSAI to disseminate our study processes and findings.

Assessment of Community Engagement and Impact. Upon completion of the web-based toolkit and documentary, we will work in close partnership with NCAI TFSAI to disseminate the toolkit to Indigenous communities across the US via community events, conferences, listservs, and websites, screen the documentary film, and assess its impact via surveys, focus groups, and interviews with tribal citizens and leaders. We will evaluate the usefulness, appropriateness, and potential impact of the toolkit in partnership with the TFSAI. Specifically, we will use website metrics to track the number of downloads of the toolkit and offer a small incentive ($10 gift card) for completing a brief online survey. We aim to survey 500 Indigenous adults from diverse Indigenous communities to assess the broad feasibility and readiness of tribal communities to implement ISAs and food system interventions across diverse Indigenous communities, including both rural and urban communities. In addition, we will distribute toolkit materials and host small screenings (approximately 10 participants per screening) of the documentary film at Indigenous conferences and national meetings. After the screenings, we will facilitate talking circles to evaluate usefulness, appropriateness, and feasibility of the toolkit within participants' communities. We will host approximately six screenings with diverse tribal community members including tribal citizens, health planners, and leaders, and offer a $100 gift card to each participant. We will also follow-up with organizations that have used the toolkit to obtain feedback about how these materials were used and what impact they had on improving the tribe's food system and health. We will use the study website and the TFSAI networks to share success stories.

Timeline

Study activities in six-month intervals are shown in **Table 2.**

Table 2 Study timeline in six-month intervals (red signifies changes from the original table)

Project Phase	Year 1		Year 2		Year 3		Year 4		Year 5	
Development										
Obtain regulatory approvals										
Finalize study protocols										

Assemble intervention materials										
Train research staff										
Randomized Controlled Trial										
Recruit and randomized participants										
Baseline data collection										
Pilot intervention ISA										
Intervention group ISA										
Wait-list control group ISA equivalent										
Four-month follow-up data collection										
Process evaluation										
Data Analysis and Dissemination										
Data cleaning and management										
Data analysis										
Documentary and dissemination										

4. PROTECTION AGAINST RISKS

All university and tribal research staff will be required to complete the CITI (Collaborative Institutional Training Initiative) program in ethical use of human participants in research. All research protocols and activities will be co-developed by the tribal/university study partnership and reviewed and approved by the OSU-CHS IRB. It will also be reviewed and approved by the Osage Nation Historic Preservation Department prior to implementation. This Department serves as a research review body for the Osage Nation. No research will take place without both the OSU-CHS IRB review and approval and the Osage Nation Preservation Department review and approval.

Adequacy of Protection Against

Risks Informed Consent and Assent. Standard language in our consent and assent procedures assures the participants understand the nature of the study. Trained university/tribal research staff members will obtain informed consent during the first research encounter and prior to any data collection. Eligible child participants 17 or younger will have a guardian complete the Child Consent Form on their behalf. For children between the ages of 7 and 17, the child participant will sign an Assent Form. The informed consent and assent documents will be clearly written in accordance with the OSU-CHS IRB guidelines. If subjects being enrolled cannot read the consent form or HIPAA form due to low literacy levels or age, consent materials will be presented orally. Sufficient time will be allowed for questions to be asked and answered both by the subject and the person obtaining the consent to ensure the subject comprehends the consent information. Research staff will verbally review the consent forms including voluntary participation, confidentiality, ability to withdraw from the study or videotaping at any time. The consent form will be orally reviewed with each participant and they will be given a copy of the signed consent form. The original signed consent forms will be maintained by Dr. Jernigan, study PI, for documentation. Consent forms will be stored separately from participant data and contact information

Protections Against Risk. All surveys and data collection from study participants will be identified by an identification code only, and will be stored in password protected databases, maintained on a secure server for which only research staff have access. Passwords will be changed in the event of a staff member leaving the research team and/or bi-yearly, whichever occurs earlier. Published results will be presented as group data, without identifiers. The Osage Nation Congress will review all presentations and manuscripts prior to dissemination or submission.

In the event of unanticipated adverse events or reactions, Dr. Jernigan, the study PI, will attempt to contact the participant and ascertain the need for services (e.g., psychological reassurance). A full report will be made to the OSU-CHS IRB, Osage Nation, and to the NIH program officer (PO). Participants will be informed that, should they pose a potential threat to themselves, (e.g., suicide), they will be given a mental health referral number and are encouraged to make contact immediately. Serious adverse events will be reported to the OSU-CHS IRB

within 24 hours and to the appropriate NIH PO within 48 hours. Non-serious adverse events will be reported to the NIH PO within 15 days.

Loss of Privacy. All university and tribal staff will complete CITI training and will be trained in all participant consent processes, such as informing community members of the potential risks of participation (e.g., loss of privacy) and benefits (e.g., opportunity to share experiences and ideas). They will also be trained in how to identify and report potential human subjects' issues and/or concerns.

For the video data collected, Dr. Jacob, and other staff who assist him, will be trained in the participant consent process to inform community members of the risks of participating in the video recordings, such as loss of privacy, and benefits, such as an opportunity to share experiences and ideas. They will explain to potential interviewees that footage, if they provide consent, may appear on the study and tribal websites, in the web-based toolkit, and in the documentary film about the study. The footage and the products in which it may be used may be shared at community and online screenings. All participants who are video recorded will sign consent forms. At the start of each video recording, and otherwise when necessary, we will explain to participants that they have the right to stop participating at any time. To date, in our five previous research studies that have used video in a similar manner, we have never experienced an incident that resulted in participants asking us to stop videotaping or that needed to be reported to tribal authorities or to the IRB. The likelihood of such an incident is extremely low. In the rare and unlikely event that such an incident is observed during video recording, the study PI will work with the Osage Nation Historic Preservation Department to report it to appropriate tribal officials. She will also report the incident to the OSU-CHS IRB.

Embarrassment. Though unlikely, participants may feel embarrassed or uncomfortable in responding to some of the survey questions or from participating in research activities, such as getting weighed. At the start of each survey session, and otherwise when necessary, we will explain to participants that they have the right to withdraw from the study at any time, and that they can refuse to answer any question or to decide not to participate in a study activity, but still continue their participation. Likewise, participants who are video recorded may also feel embarrassment, though unlikely. They will be informed that they can refuse to be video recorded at any time or can ask for the camera to be turned off at any time.

Disclosing Psychopathology. Though highly unlikely, participants may disclose psychopathology or distress, and may request help for their distress. At the conclusion of each survey, all telephone survey participants will be provided with contact information for the tribal health clinics that offer food assistance and mental health services, independent of any expression of concern on their parts. Disclosing information that requires intervention by research staff (e.g., statements of intent to commit suicide) is unlikely, because we do not ask about mental health or suicide. Nevertheless, if this should happen, the study PI will be on-call during all data collection times. She will assess and make appropriate referrals if needed. All of the research staff are or will be fully trained in relevant ethical principles and procedures, including confidentiality. We will report all situations or potential situations to the OSU-CHS IRB.

Out-of-range results that might indicate uncontrolled or previously undiagnosed pathology will be flagged and explained in lay terms to emphasize the need for immediate medical attention. For urgent levels of HbA1c (≥ 10.5%) or blood pressure (≥ 200/120 mmHg) participants will be referred immediately to their physician during clinic hours or to a hospital emergency department. These individuals will still be eligible for participation in the randomized controlled trial, with the consent of their physician.