Maternal and Child Health and the Architecture of Daily Life among Rural Nicaraguans: A Biocultural Investigation

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Goal: To improve the health of mothers and children in rural Nicaragua by documenting their health challenges and their associated cultural practices.al

Summary: Each year millions of pregnant women, mothers, and children experience severe illness or death, largely from preventable or treatable causes. Of these, 99% occur in the developing world. Consequently, attention to maternal and child health (MCH) has been growing, and improving MCH is seen as critical to fostering economic development. The urgency of this issue is reflected in the fact the MCH is a top international development priority for the Canadian government and one of the three strategic priorities of the United States government. It was also reflected in two of the Millennium Development Goals (MDGs); MDG 4-reduce child mortality and MDG 5-improve maternal health. Of the eight MDGs, by the 2015 deadline these two goals were the furthest from being met. Further, in 2015 the 2 goals have were combined in the UN's Sustainable Development Goal #3 "Good Health and Well-being". Efforts to improve maternal and child health have been hobbled by two problems. First, decades of research demonstrates that health outcomes are strongly influenced by culture, yet maternal and child health data are generally collected without a clear understanding of the cultural context in which these women and children live. Second, challenges such as poverty, food insecurity, low social capital, and psychological stress affect a wide array of physiological systems, causing diverse health problems. However, most maternal and child health research focuses on a single health outcome at a time, obscuring the bigger picture of how stressors are affecting general health. The first problem can be addressed via participant observation in the community of interest, an approach taken by anthropologists who conduct ethnographic research. The second problem can be addressed by pooling variables in an innovative model known as allostatic load. Allostatic load captures the cumulative dysregulation of biological systems confronting chronic environmental challenges, providing a holistic consideration of the well-being of a population. Addressing both of these gaps in the literature is essential for improving maternal and child health. Toward that end, in collaboration with a Nicaraguan NGO and front-line health workers in the region, this project is designed to document health outcomes and causes of these outcomes

among rural women and children who inhabit Nicaragua's poorest region. The first round of fieldwork for this project was completed in January-June & November-December 2015 during which time health outcome variables (nutritional status, mental health, blood pressure, and biomarkers of immune function, stress, diet, and metabolism) and predictor variables (food insecurity, social capital, and other cultural and demographic factors) were collected for 250 caregiver-child dyads. In 2017 a second line of work was initiated, combing ethnography with the One-Health approach to assess the impact of household animals on the gut microbiome and health in children. The immediate outcome of the project will be the identification of barriers to maternal and child health in this region and, in the long term, the development of new evidence-based and locally-relevant solutions.

Narrative: Improving maternal and child health is a critical population health issue, particularly relevant in developing country settings where mothers and children suffer high rate of illness and premature mortality. This research advances our understanding of maternal and child health by investigating the effects of low levels of SES, social capital, and food security on an integrated measure of physiological status (allostatic load) based on biomarkers collected in a sample of mothers and children in rural Nicaragua. The findings will inform health disparities research and policies aimed at improving maternal and child health in developing countries.

Background: Maternal and child health remains unacceptably poor: daily, nearly 830 women die from causes related to pregnancy and childbirth and every three seconds a child dies, almost all in poor countries and most often due to preventable causes. Exacerbating this issue is the emergence in developing countries of chronic disease and the increasingly important role of psychosocial stress and mental health, creating a double burden of both infectious and chronic disease in these already under-resourced regions. The unfinished agenda concerning maternal and child health is particularly concentrated in developing countries, with dire, long-term implications for social cohesion, stability, and development. In 2014, the WHO's Director General emphasized that from a technical standpoint *we know how to tackle the persistent causes of maternal and child mortality, "but we must find the right approach in each and every setting".* Indeed, the causes of death differ substantially from one country to another, highlighting the need to expand understanding of child and maternal health and predictors at a local level rather than in geopolitical regions. Moreover, decades of research have documented that health varies in relation to culture. The collection and analysis of data on cultural variables which mediate health outcomes in each setting is consequently required to save the lives of women and children. The disciplines of biological anthropology and sociology, with their consideration of both cultural and biological variables associated with health outcomes, are well-suited to such research.

The health outcome variables considered here include nutritional status, mental health of the mother, blood pressure, patterns of illness, and immune and metabolic function. Of these, nutritional status, blood pressure, patterns of illness, and immune and metabolic function will be combined to create an index of overall health outcomes, allostatic load. The predictive variables considered in this study which may explain these health outcomes include diet, social capital and other cultural factors. With regard to the latter, we focus on cultural characteristics which have the potential to influence diet (e.g. agricultural practices, coffee prices, membership in agricultural cooperatives, etc.), social capital (e.g. extent of family networks, family contexts, membership in groups, social identity, power relationships, educational and wage-labor

opportunities, relationship with partners, etc.), and views concerning mental health (e.g. culture of blame, etc.) and health (e.g. use of traditional vs. biomedical treatment).

We combine the outcome variables in an allostatic load model to provide an integrative framework for understanding the physiological processes through which chronic stress affects health. The allostatic load model describes the biologic cost exacted by the regulatory systems such as the sympathetic and parasympathetic nervous systems, hypothalamic-pituitary-adrenocortical system, and inflammatory response, as an organism attempts to maintain allostasis (i.e., physiological homeostasis) in the face of ecological, psychological, and behavioral challenges. The cost of this cumulative stress is manifest in damaging effects on multiple downstream physiological functions. Elevated allostatic load is associated with compromised health and all-cause mortality in adults and children. Any operational definition of allostatic load must include some combination of markers that can gauge how much cumulative burden has developed. Over time, stressors are likely to affect many physiological systems through many proximal pathways, which is why the effects of poverty, food insecurity, low social capital, psychological stress, etc., are so pervasive and cause so many different types of health problems. However, if one examines only a single marker - like cortisol or height-for-age alone - the bigger picture regarding how stressors are affecting general health can easily be lost. The more systems we capture, the better we're doing at gauging the overall health of the population. Not surprisingly, a strength of the allostatic load model is its ability to detect systemic effects that are obscured by looking at a single outcome at a time. In this study we cast a broad net, using seven health outcome markers to create a comprehensive measure of the well-being of these mothers and children.

Specific Aims:

Specific Aim #1: To assess how objective and subjective socioeconomic status (SES) are associated with maternal and child allostatic load. The rationale for this aim is to quantify SES disparities in allostatic load among mothers and children, and SES as a fundamental cause of biological disadvantage in this setting. We hypothesize that low objective SES (education, economic resources) will be associated with both maternal and child allostatic load. Maternal reports of subjective SES may be particularly detrimental to maternal allostatic load, and may also produce higher allostatic load in children through lower maternal mental health.

Specific Aim #2: To determine the role of maternal social capital in reducing allostatic load directly, and as a moderator of SES. The rationale for this aim is to test the importance of social support and participation as a buffer to physiological dysregulation in stressful environments. We hypothesize that social capital will have a direct effect on reducing allostatic load among mothers and children by providing social and psychological resources needed for healthy development. Further, we hypothesize a moderating role of social capital, where it may be most effective at reducing allostatic load among mothers and children in very low SES conditions.

Specific Aim #3: How is access to food associated with allostatic load in mothers and their children? The rationale for this aim is to study the specific effects of food insecurity on allostatic load, given research that suggests the lack of sufficient quality and quantity of food reduces adequate nutritional intake and increases psychosocial stress, net of economic resources. Based on our own and others' research, we hypothesize that lower access to food (higher food insecurity and lower food frequency) to be associated with higher allostatic load in children and

mothers, and a potentially important leverage point for policy efforts to improve maternal and child health.

Innovation: Our failure to address the maternal and child health crisis is a significant public health and humanitarian issue. In the face of the emerging dual burden of infectious and chronic disease, this crisis will only deepen without innovative solutions. Heeding both the WHO Director General's call for contextually grounded research and the recognition that focusing on one or even two health outcomes alone can easily obscure the impact of environmental challenges on health, this project is couched in a clear understanding of relevant cultural variables and utilizes an integrative model of health outcomes, allostatic load, to generate a broad understanding of the cumulative burden of stress experienced by these mothers and children. The combination of ethnographic data, cutting-edge protocols, a multidisciplinary team with vast experience researching health inequities, and extensive collaborative networks of Nicaraguan health workers, NGO's, and focal populations represents a novel, ground-breaking approach to a seemingly intractable problem. In sum, this project addresses a pressing local need in Nicaragua in an innovative manner, providing new opportunities this team to contribute to improving the lives of women and children in our global community.

Research Methods: In this work, we build upon and improve similar work the Co-PIs have completed in Brazil, Tanzania, Guyana, and elsewhere in Nicaragua. Data collection for this project commenced in 2015 and is ongoing.

Sample (2015): The unit of analysis for this study is households with the mother and one child between the ages of 0.0-11.0 years present. Our age criteria are based on our interest in understanding the impact of the household food environment on children who are still young enough to be heavily dependent on adults for securing food. Data were collected in 250 opportunistically recruited households in Los Robles, an agricultural community of approximately 2,200 individuals in rural Nicaragua's Department of Jinotega. Sample size calculations are based on the expected relationship between food insecurity and child allostatic load, because this is likely to be the weakest effect tested. The sample was selected for 5 reasons: 1) women and children are the cohorts most at risk cohorts for poor health outcomes in developing countries; 2) populations in rural regions are more at risk for poor health outcomes than those in urban areas; 3) globally, agriculture is the main occupation of 80% of poor populations in rural areas; 4) the Department of Jinotega manifests the worst maternal and child health in Nicaragua; 5) this study provides an opportunity to compare the same health outcomes and predictors collected in 2013-14 by Piperata and Schmeer in Leon, an urban setting in Nicaragua.

Sample (2017): Please see Appendix A.

Maternal and child health outcomes considered:
■ *Self-Reported Health & Maternal-reported health of child* (2015): Mothers were interviewed about their health and that of their child.
■ *Anthropometrics* (2015): Standard procedures were implemented to collect anthropometric measures for each mother and child. Anthropometry provides the single most portable, precise,

replicable, universally applicable, inexpensive and non-invasive technique for assessing the health and nutritional status of populations.

■ *Microbiome analysis* (2017): Following the One-Health Initiative the project explores how domestic-animal husbandry shapes children's microbiota during the 7 years of life, a critical developmental window for children's microbiota. A number of disease conditions, such as inflammatory bowel diseases, type-2 diabetes, diarrhea, obesity, allergies and colorectal cancer are linked with altered microbiota composition. Moreover, domestic animal husbandry, a common practice in rural Nicaragua, can alter a child's microbiota and lead to zoonotic transmission of diarrhea causing pathogens. In 2017, we collected swabs from household animals and fecal samples from 40 individuals 0-2 years of age, conducted direct observations of time allocation for 20 of these 40 individuals, observations of the interactions between children aged 3-7 years and household animals (focusing on the potential for microbiome exchange), 18 interviews with mothers concerning child care practices, water and soil samples from 51 households. 16S sequencing of the animal and fecal swabs, water, and soil samples is underway. See Appendix A for more details concerning this aspect of the work.

■ *Blood Pressure* (2015): Blood pressure, an established marker of stress, was measured for mothers with the respondent seated and the right arm supported at heart level.

■ *Maternal mental health* (2015): Mental health was assessed using the SRQ-20, a validated 20-question symptoms checklist designed to screen for psychiatric disturbance, especially in developing countries. The questionnaire is used to measure symptoms of poor mental well-being and not as a diagnostic tool. The SRQ-20 has successfully been used in León by members of this research team in studies of domestic violence elsewhere.

■ *Immune & metabolic function & Iron levels via Dried Blood Spots* (2015): Field-based research on morbidity often relies on caregiver or self-reports of overt symptoms typically recalled over a 7- or 21-day period. This approach, however, is subject to underreporting, particularly for longer periods of time. Additionally, linguistic and cultural factors help define idealized states of health, and may contribute to variation in the experience and reporting of symptoms. Physical examinations by healthcare professionals can provide a more objective assessment of morbidity, but are time-intensive and not generally feasible in remote settings. Morbidity can be assessed via the collection of blood, but the collection is invasive. In addition, once collected, these samples must be immediately centrifuged, separated, and quick-frozen or assayed, requiring ready access to lab facilities. Recent developments in dried blood spot protocols surmount these obstacles, requiring only a finger prick with the resulting drops of blood placed on filter paper. The filter paper can be easily transported and subsequently assayed for markers of health and diet. For this project 10 drops of blood were collected for 250 mother-child dyads and will be assayed for immune function indicators of both acute stress (C-reactive protein) and chronic stress (cytomegalovirus antibodies) and immunoglobulin E (IgE).

    ● *C-reactive protein* (CRP) is an inflammatory protein produced by liver hepatocytes in response to messenger cytokines, primarily IL-6. CRP is an important component of innate immunity and has been used clinically for decades as an indicator of active infection. Since CRP has been shown to increase in response to a wide array of pathogenic agents as well as psychological stressors, it is a potentially useful marker of stress. Elevated CRP concentrations have been associated with detrimental health outcomes across all age cohorts.

    ● *Cytomegalovirus* (CMV) specific antibodies provide an indirect, functional measure of cell-mediated immune activity). CMV is a nearly ubiquitous herpesvirus and in non-

Western contexts, CMV infection at an early age - as early as infancy - is common. CMV is generally asymptomatic, becomes latent, and can be reactivated by chronic stress, in turn leading to higher antibody titers and potentially higher chronic disease risk. Individual and population-level variation in responses to CMV can provide a subtle portrait of immune system ecology. Working with healthy and well-nourished populations of older adults, college students, and adolescents in the US and Samoa, high CMV antibody titers have been associated with chronic psychosocial stressors including caretaking of a sick relative, exams, and status inconsistency. The proposed mechanism is that chronic stress reduces CMV surveillance, allowing viral reactivation that requires a humoral (antibody) response, a pattern evident in relatively affluent settings. By contrast, in ecological settings characterized by poverty, poor nutrition, and high infectious disease load, herpesvirus antibodies are often unrelated to other markers of stress. Most intriguingly, in a study of children in Nepal, EBV antibody titers were highest among the healthiest subset of children. The authors proposed that only the healthier children have the physiological capacity to mount an effective antibody response in the first place, in effect turning the stress model of viral reactivation on its head.

● *Immunoglobulin E* (IgE) is known to be an important mediator with regard to both allergic and gastrointestinal parasitic disease. Even mild-to-moderate loads of gastrointestinal parasitic infection have been associated with compromised health in children and adolescents. Exposure to these parasites provokes the activation of Th-2 cells which in turn promote B cell production and IgE. Hence, IgE levels were determined as a proxy measure of parasitic infection using standard methods.

Between September 2015 and July 2017, the dried blood spots were assayed at Dr. Jason DeCaro's Developmental Ecology and Human Biology Lab at the University of Alabama, Tuscaloosa. Dr. DeCaro is a leader in this field, has conducted similar research with WW in Tanzania, and assisted with data collection in Nicaragua.

■ *Metabolic function* (2015): Following WHO protocols, metabolic function was measured with a random capillary whole blood glucose test (aka non-fasting or casual blood glucose test) for all mothers, to screen for metabolic function with a focus on those at risk for diabetes. Those who had not eaten in the 3 hours prior to the test were excluded from the study.

Predictors of maternal and child health considered: Anticipated predictors of maternal and child health were selected based on their power to explain health outcomes in similar settings. We prioritized diet as it has been found to have the strongest predictive power of health outcomes in low-to-middle income countries (LMICs).

■ *Ethnography* (2015, 2016, 2017):
● Participant observation by the PI and U. Calgary graduate students living in the Los Robles (January-July 2015, May-July 2016, May-July 2017) and graduate students from Ohio State University (June-July 2017). Participant observation connects the researcher to the most basic of human experiences, discovering through immersion and participation the hows and whys of human behavior in a particular context. Their observations were complemented by frequent questions designed to uncover the meaning behind observed behaviors. They participated in a wide range of community activities, such as domestic

chores, travel to the nearby town to shop and sell produce, the harvesting and transport of coffee, home and road repair, and the cultivation of maize. Villagers were aware that all the researchers were interested in health. Qualitative observations were recorded daily in field journals. As above, cultural variables of particular import here include those most likely to articulate with diet, social support networks, and health.

● Direct focal follows (2017): Second-by-second recorded activity was collected for 20 infants and 17 children. Each individual infant/child was observed for 2 hours. This was complemented by interviews with the infant/child's caregiver concerning household illness histories and demographics. These data will be combined with the infant/children's microbiome data to see how their interactions with their environment (soil, water, food, animals) affects their gut microbiome and incidence of diarrhea.

● Infant care & child development practices (2017): 18 interviews were conducted with mothers to explore cultural beliefs and practices surrounding infant care and child development.

■ *Sociodemographics* (2015): Age, marital status, family size data, etc. were collected for each household. In addition, as it has been found to influence health, objective socioeconomic status (OSS) were determined on the basis of household production, composition, wage labor, and assets.

■ *Social networks and status* (2015): Social capital, a strong predictor of morbidity, was assessed following. Subjective social status, also strongly associated with morbidity, was measured using the MacArthur Subjective Social Status Scale, an instrument validated for use in developing countries with minor adaptations to local contexts.

■ *Food insecurity* (2015): Perceived food insecurity was measured using the Latin American and Caribbean Food Security Scale (ELCSA), an instrument validated throughout Latin America, including in Nicaragua.

■ *Food Frequency* (2015): Dietary intake data were collected using a food frequency questionnaire comprised of 95 Nicaraguan food items. The questionnaire was developed by Piperata and Schmeer in Leon and refined prior to use in Los Robles in focus groups. The questionnaire was administered in an interview format to reduce issues of misinterpretation and illiteracy, and allow for the interviewer to continually provide clarification and check responses.

■ *Water quality* (2017): Coliform levels in water were measured in 51 households and at the source, the water treatment plant, both as water entered and left the plant.

■ *Microbiome of household animals and soil* (2017): To better understand the etiology of the children's microbiome, samples for microbiome analysis were collected from animals in homes (n=27 chickens (fecal), n = 15 pigs (skin/snout swab), n=58 dogs (skin snout swab), and soil (n=39 samples).

Data collection:

2015: The data collection team in consisted of the PI, four local, female assistants (aka *Brigidistas*) with years of experience in public health, a local physician, Dr. Alfredo Alaniz,

employed in the Los Robles clinic and four North American university and graduate students (U. Calgary, Dept. Anthropology & Archaeology and Emory U., Rollins School of Public Health). WW worked closely with the *Brigidistas* and Dr. Alaniz from January to June 2015 as described below, trained the N. American students in data collection procedures and subsequently supervised data collection. *Instrument refinement and team training:* From January through April, the team adapted all instruments to the local context in four steps: (1) January—March: team practice with and refine the instruments for eight days, (2) April: focus groups were held over 3 days with 3 different focus groups, each with 4 Los Robles mothers, to further refine the instruments, (3) April: the refined instruments were used in individual interviews with 6 Los Robles mothers whose pooled respondent feedback to was used to rephrase portions of the interview that were unclear, (4) the team spent 2 days conducting practice interviews using the refined questionnaires. Practice elements included explanation and discussion of each item, learning how to interview by role playing and with real respondents.

2016: The data collection team included the PI and two graduate students from the U. Calgary (Dept. Anthropology & Archaeology).

2017: The data collection team included one graduate student from the U. Calgary (Dept. Anthropology & Archaeology), four graduate students from Ohio State U. (Dept. Anthropology, College of Veterinary Medicine, and College of Public Health), one graduate student from U. Alabama (Dept. Anthropology), and a paediatrician from the Centro de Investigaciones en Demografía y Salud (CIDS) Universidad Nacional Autônoma de Nicaragua.

Data analyses: For mothers, self-reported health, body-mass-index (BMI), waist-hip ratio, blood pressure, and markers of metabolic function and stress will be combined to a construct multi-measure, cumulative-burden, index of maternal well-being as the main dependent variable. For children, maternal reported child health and markers of stress will be combined with standardized measures of growth and nutritional status will be combined with to construct multi-measure, cumulative-burden, index of child well-being as the main dependent variable. This approach is more attractive than a single measure because it quantifies the cumulative burden of adversity reflected in the body's responses to multiple stressors across developmental time. Ordinary least squares regression will be used to test the model, relying on procedures developed to identify mediation.

Institutional Ethical Clearance: The research was approved by the Nicaraguan Comité Institucional de Revisión Ética (CIRE), del Centro Nacional de Diagnóstico y Referencia (CNDR) del Ministerio de Salud de Nicaragua (MINSA) (Ethics ID: NIC-MINSA/CNDR CIRE-25/05/15-060) and the Conjoint Health Research Ethics Board in the Faculty of Medicine at the University of Calgary (Ethics ID: REB15-0232 and REB15-0232_MOD1). Ethical clearance for the microbiome work conducted in 2017 was obtained from The Ohio State University and the Universidad Nacional Autônoma de Nicaragua– León (Appendix A).

Long-term outcomes: Our long term plans include the development of a larger-scale project that assesses social and economic stressors and biomarkers of health and stress in multiple

populations across Nicaragua. We will then expand our study to better capture the types of resources and insecurities that are likely to be the drivers of poor physiological conditions, poor microbiota, and dysregulated immune systems and potential leverage points for public health policy. We also plan to expand geographically to increase the diversity of settings in which we can understand these processes. As of now, we have been invited by public health workers in in two communities which neighbor Los Robles, San Esteban and La Laguna, to complete the same study in their villages. This invitation was seconded in June 2017 by the Jinotega regional director of MINSA, who offered their support in growing the project. This is a tremendous opportunity to conduct interdisciplinary and international research on an urgent global issue.

Significance: Poor maternal and child health is a complex problem that urgently requires multidisciplinary, innovative approaches. This project, pooling resources from academics across disciplines and partners such as the front-line public health workers of Los Robles and local NGOs, provides a multidisciplinary approach. Further, this study fills a gap in our understanding of maternal and child health by couching our findings on both an understanding of the cultural context of the focal population and a multi-measure, cumulative-burden, index of maternal and child health. This diversity of expertise and innovative approach is imperative to ensure the development of effective public-health interventions in Los Robles.

APPENDIX A: 2017 MICROBIOME PROJECT

Title: Cultural Models of Child Development and Risk of Zoonotic Diseases in Nicaragua

In 2017, in collaboration with the Centro de Investigaciones en Demografía y Salud (CIDS) Universidad Nacional Autônoma de Nicaragua – León, a team of anthropologists, public health experts, and veterinary school students from Ohio State University began a new phase of this study following the One-Health Initiative to learn how the rearing of domesticated animals and water quality may influence diarrheal disease in young children. The One-Health Initiative recognizes that human health, animal health, and environmental health are inextricably linked. This project builds upon data collected in Los Robles in 2015-16 **to understand how the home environment especially pathogen exposure (water, soil) and the presence of domestic animals shapes children's microbiota**. In other words, the project seeks to understand how children's environment and activities influence their microbiota and disease risk.

Sample:
■ <u>Children aged 0-2 years –early child rearing practices and gut microbiome formation</u>: In 2017 researchers visited 40 of the 250 households surveyed in 2015 that currently have a child between 0-2 years of age and asked the residents about the home, pet and livestock interactions, and drinking water. Biological samples collected included 1 fecal sample from the infant, 1 drinking water sample from household, and 1-2 soil samples (depending on house floor type). Researchers administered a survey (30-45 min) in all n=40 households to document household infrastructure, human and domesticated animal demography, and illness histories of people and domesticated animals in the home. This was followed by a ~1-hour interview with a subsample of 12 mothers concerning beliefs, ideals, and practices regarding child development during the first two years of life. As well, over a period of 4 days for 3 hours per day, researchers were in the home to conduct direct observations of infant routines with a subsample of 15 infants.
■ <u>Children aged 3-7 years -child interactions with animals and effect on their microbiome</u>: Researchers visited 30 of the 250 households surveyed in 2015 that currently have children between 3-7 years of age, as well as a dog and a pig. Biological sample collection included a fecal sample from one child, a Swiffer swab of a household dog with which the child interacts, a Swiffer swab of a dog from another home with which the child does NOT interact (e.g. a neighbor's dog), and a Swiffer swab of a household pig. Observational survey data collected included a basic assessment of the household infrastructure and, on a subset of 17 of the children, observations of the children's interactions with animals in the home. Interview data included household human and animal demography and an illness history of human and animals in the home over the previous month. In-depth interviews were conducted with a sub-set of 18 mothers. These ~1-hour conversations focused on understanding local beliefs and practices regarding child development and rearing practices including infant and maternal care in the postpartum period. An additional set of interviews with mothers focused on the human-animal bond and importance of animals in human life in rural Nicaraguan communities.

Short-term outcomes: The expected, short-term outcome of this work is several high-level publications in population health journals in addition to scholarly presentations at professional meetings. As noted above, knowledge translation was initiated as soon as the first round of data collection was complete in July 2015 and is ongoing via multiple meetings with stakeholders in

the community and elsewhere. The use of biomarker data to assess maternal and child health in low-income, high-stress settings such as Los Robles is unusual and will provide new insights into both health inequalities and how social and economic conditions may contribute to system dysregulation in mothers and children. The findings have the potential to set a new agenda for international maternal/child health research, with a focus on chronic stress and altered physiological systems that contribute to chronic disease and disability.

<u>Institutional Ethical Clearance</u>: The research was approved by the Universidad Nacional Autônoma de Nicaragua– León (Ethics ID: No ethics ID number is provided by this institution.) and the Human Research Protection Program at The Ohio State University (Ethics ID: U2016B0192).