Purpose: The purpose of this presentation is two-fold: first to briefly describe the emerging technology of metabolomics and illustrate how this technology can be leveraged by nursing scientists and clinicians to advance nursing assessment, diagnosis, and intervention, and second, to present data for the first time describing the metabolites and metabolic pathways activated by exposure to chronic stress during pregnancy. To address the first purpose, an overview of the procedures for conducting metabolomics will be presented, including a description of the sophisticated analyses required. To address the second, the relevance and power of metabolomics will be reviewed within the exemplar of chronic stress exposure experienced by a cohort of pregnant African American women at high risk of adverse birth outcomes. Adverse birth outcomes occur at unacceptably high rates around the world, with socially disadvantaged women at the greatest risk and severe consequences for offspring all too common. Although a worldwide problem, the pathways by which chronic stress influences adverse birth outcomes remain unknown; however, in their most recent report on preterm birth, the United States Institute of Medicine (IOM) identified exposure to chronic stress as the most significant unexplained contributor.

Methods: To address the first purpose, we will briefly review the technology of metabolomics, describing what it is, how it works, and why it offers a powerful real-time picture of the physiological processes occurring in a given individual, including the real-time production of metabolites and activation of metabolic pathways associated with chronic stress. Important clinical examples wherein metabolomics has been shown to provide unique and variable prognostic and diagnostic data will be presented, focusing on nursing assessment, diagnosis, and intervention. This will be followed by an exemplar of chronic stress exposure in pregnant African American women enrolled in our NIN-funded study (R01NR014800) investigating risk factors for preterm birth. In this study, African American women enroll during their first trimester of pregnancy and are followed through delivery. During their 1st and 3rd trimesters, participants complete demographic and health questionnaires, as well as questionnaires related to acute and chronic stress exposure including: perceived stress; lifetime stressful life events; childhood stressors; and exposure to racism and discrimination. Participants also provided a blood sample for measurement of dexamethasone suppression, a biological indicator of chronic stress exposure, following standard techniques published previously. Serum samples are then analyzed for metabolites using a Thermo Scientific Orbitrap Fusion Mass Spectrometer with dual ionization/dual liquid chromatography. Three technical replicates are run for each sample along with pooled reference samples. Metabolic features are extracted after preliminary statistical analyses and feature selection. Medical record review after delivery is conducted to gather empirical evidence of birth outcomes. Big data mummichug software is used for pathway enrichment analysis to identify associations between metabolites and metabolic pathways with self-report and biological indicators of chronic stress exposure. Metabolite features from untargeted LC-MS are then ranked by their Pearson correlation with DexIC50 levels. Pathways with p<0.05 and more than 3 significant metabolites are considered significant. Strategies for utilizing this knowledge for future nursing assessment, diagnosis and intervention will be discussed.

Results: Currently, 486 women are enrolled in the prenatal study and metabolomics analyses have been conducted on samples from the first 320 women. Findings indicate that the metabolomic pathways related to chronic stress with p<0.05 and more than 3 significant metabolites: include: anti-oxidant pathways including those related to vitamin C; metabolomic pathways related to the metabolism of tryptophan, the precursor to serotonin; and pathways related to mitochondrial enzymes and energy production. A discussion of how nursing assessment, diagnosis, and intervention strategies can be
leveraged from the knowledge generated regarding these metabolites and metabolic pathways will follow, and symposium attendees will gain a better understanding of how this emerging technology can be leveraged by both nurse researchers and nurse clinicians.

**Conclusion:** Until a better understanding of the underlying biology by which chronic stress exposure contributes to adverse birth outcomes is achieved, an unacceptably high number of the world's most vulnerable women and infants will continue to be at risk. Applying a metabolomic approach to expose the metabolites and metabolic pathways associated with chronic stress during pregnancy provides increasing opportunities for targeted nursing assessment, diagnosis, and intervention. By gaining exposure to cutting-edge technologies such as metabolomics, nurse scientists can better lead and/or participate in innovative interdisciplinary research initiatives in the future and can better provide a precision nursing approach to patient care: the very essence of nursing science.

**Title:**
Leveraging Metabolomics to Advance Nursing Assessment, Diagnosis, and Intervention Exemplar: Chronic Stress and Birth Outcomes

**Keywords:**
Chronic stress during pregnancy, Metabolomics and the nursing process and Stress-related metabolites and metabolic pathways

**References:**

Abstract Summary:
In this presentation, we will review the emerging technology of metabolomics, describing what it is and its implications for nursing science. Within the exemplar of chronic prenatal stress exposure and birth outcomes, we will then describe how metabolomics can be leveraged by nurses to improve patient assessment, diagnosis, and management.

Content Outline:

I. Introduction
   A. Metabolomics: What it is and How Nurses can Leverage it to Improve Nursing Assessment, Diagnosis, and Intervention
   B. Chronic Stress and Birth Outcomes
   C. Exemplar: Metabolites and Metabolic Pathways Associated with Chronic Stress & Implications

II. Body
   A. Metabolomic Technology
      1. What it is
      2. How to leverage metabolomics to improve nursing assessment, diagnosis and intervention
   B. Chronic Stress and Birth Outcomes
      1. The physiology of chronic stress
      2. Chronic stress and birth outcomes in African American Women
      3. Pathways by which chronic stress exerts adverse effects remain unclear
   C. Exemplar: The Metabolites and Metabolic Pathways Associated with Chronic Stress & Implications
      1. Key metabolites and pathways associated with chronic stress
      2. Implications for nursing research and practice
         a. Discovery
         b. Targeted interventions
         c. Longitudinal evaluation of intervention efficacy

III. Summary/Conclusions
   1. Metabolomics: A Powerful technology to answer complex questions
      a) Interdisciplinary
b) Holistic

2. Targeting metabolites and/or pathways may improve nursing care and patient outcomes
   a) Identify the metabolites and pathways then develop targeted interventions
   b) Evaluate the intervention by following the metabolites and looking for change

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Professional Experience: I am a PhD prepared Physiologist, a bachelor-prepared nurse, and a masters-prepared nurse practitioner. I have been conducting research on maternal health and nursing science for nearly 20 years.

Author Summary: Elizabeth Corwin, PhD, RN, FAAN, is the Associate Dean for Research and Professor at the Nell Hodgson Woodruff School of Nursing at Emory University. She is a PhD-prepared Physiologist and a family nurse practitioner. Dr. Corwin is leading pioneering, interdisciplinary research aimed at uncovering the biological mechanisms responsible for adverse outcomes including symptoms, with a focus on the contributions of exaggerated inflammation, chronic stress, the microbiome, and metabolomic pathways on patient and family outcomes.

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Author Summary: Dr. Dunlop is a physician with decades of caring clinically for high risk populations of women and infants. She is also a well-respected researcher, focused on exploring the contribution of nutrition, the microbiome, metabolites, and chronic stress on preterm birth and adverse infant and family outcomes. Dissemination of her research has impacted maternal infant health worldwide.