Sprint for Women's Health
Full Description of Topics

Late Updated: March 1st, 2024
Note: This document is subject to change

This request for solution invites Solution Summary submissions on the following topics of interest in Women's Health for either the Spark or Launchpad tracks. Please note that submissions outside of topics listed below will not be considered at this time.

- **Women's Health Topic 01:** Women's Health at Home
- **Women's Health Topic 02:** Preserving Ovarian Health Past Reproductive Age
- **Women's Health Topic 03:** ARTEMIS – Advancing Research Through Enhanced Models for Investigating Sex Differences
- **Women's Health Topic 04:** Modulating Women's Brain Health Via Lymphatic Targeting
- **A Women's Health Topic 05:** Objective and Quantitative Measurement of Chronic Pain in Women
- **Women's Health Topic 06:** WILD CARD: Revolutionary Breakthroughs in Women's Health

1. Women's Health Topic 01: Women's Health at Home

What If Statement: What if women were empowered to address their healthcare needs through diagnostics and treatments at home across all ages and stages of life?

Problem Statement and Opportunity:
Many women are facing considerable barriers to accessing routine preventive healthcare, which is crucial for early detection and management of potential health issues. Primary obstacles include childcare responsibilities, which often prevent women from prioritizing their personal health needs; financial constraints, which can make regular healthcare visits unaffordable; transportation issues, which can make it challenging to reach healthcare facilities; and cultural or family perceptions, which may discourage women from seeking medical attention. There is an urgent need to address these barriers and develop comprehensive strategies and innovative solutions to ensure that all women have access to routine preventive healthcare. Although technologies capable of diagnosing and possibly treating diseases across all ages and stages of a woman's life within the privacy of one's own home are increasingly possible, very few are currently available in the marketplace, or are not designed with the customer in mind.

ARPA-H aims to catalyze the development of innovative and impactful platform technologies capable of diagnosing and/or treating women's health issues in the home

environment. Novel platform technologies that monitor, diagnose, administer, treat, or maintain healthy status across all ages and stages of women's health are of interest. These novel capabilities should empower women to take control of their health and detect and treat disease early, in the privacy of their own home. Successful concepts will improve quality of life by decreasing the complexity and time spent to access healthcare, and measurably improve health outcomes.
Examples of potential capabilities may include, but are not limited to: devices or wearable sensors to assess breast, hormonal, cervical, and pelvic health; diagnose infectious disease (UTIs, STDs); vaginal specimen collection and drug delivery innovations; predicting and preventing premature labor; postpartum health; mental health and wellness; nutritional support; maternal health; innovations in telehealth; and healthy microbiomes to support a broad range of women's health topics.

2. Women's Health Topic 02: Preserving Ovarian Health Past Reproductive Age

What If Statement: What if prioritizing ovarian health throughout a woman's life could actively prevent or delay the onset of a diverse array of acute and chronic conditions and diseases, and ultimately challenge the paradigm that ovarian aging is an inevitable factor in women's health?

Problem Statement and Opportunity:
Ovarian aging is an ongoing physiological process, culminating in menopause, which signifies the cessation of ovarian function. As women age through mid-life and beyond, the decline in estrogen levels following peri-menopause and menopause results in both short-term and long-term health implications for women. Short-term effects involve hot flashes, night sweats, palpitations, headaches, vaginal discomfort, and urinary issues, while long-term consequences include osteoporosis and a higher risk of cardiovascular and neurological diseases. While Hormone Replacement Therapy (HRT) is the primary treatment for these symptoms, risks including the potential for venous thromboembolism can dissuade physicians from prescribing HRT. Further, the lack of solutions that enable simple, timely (continuous or time of need), and cost-effective measurement of hormone levels further exacerbates the challenges of understanding and regulating ovarian, hormone, endocrine, and metabolic health.

ARPA-H seeks revolutionary solutions to enhance women's health span by proactively addressing both short and long-term health effects associated with ovarian aging. This initiative aims to explore novel treatments, interventions, and research that prioritize conservation of ovarian function, maintaining or restoring hormone levels, including exploration of solutions that promote natural ovarian health past reproductive age. By prioritizing the development of groundbreaking solutions that improve the ovarian function through mid- and later stages of a woman's life, we aim to prevent and mitigate diseases and conditions associated with women's aging, ensuring a healthier and extended quality of life.

Examples of promising innovations may include but are not limited to: safe and accessible pharmaceutical interventions to promote ovarian health; cell and gene therapies; implantable bioelectronics; and ovarian tissue preservation and

reimplantation**.** It is anticipated that this topic will require the development of novel capabilities to non-invasively measure or modulate hormone- or hormone-like substance levels at home to augment and inform the use of treatment interventions; these capabilities may be proposed here as a companion to a given intervention, or as a stand-alone effort under the Women's Health at Home topic (Topic 1).

3. **Women's Health Topic 03: ARTEMIS – Advancing Research Through Enhanced Models for Investigating Sex Differences**

What If Statement: What if we could revolutionize female-specific research models to ensure equitable and effective treatments?

Problem Statement and Opportunity:
Despite the well-known sex differences between males and females, research often neglects the impact of sex on study outcomes, with a predominant reliance on male animal tissues and cell models in pre-clinical research. This oversight has led to flawed and biased results, particularly affecting women by contributing to safety issues, healthcare disparities, data bias, and inequity, especially in diseases more prevalent in females. The absence of female-specific models poses a significant barrier in understanding female biology and in developing safe and effective drugs and medical devices. The FDA Modernization Act 2.0, enacted in 2023, marks a pivotal shift by endorsing alternatives to traditional animal testing, including *in vitro* and *in silico* models, such as organ-on-a-chip systems and computational approaches. These advancements promise to enhance the development of therapies that are more effective and predictive for women, addressing a critical gap in women's healthcare.
ARPA-H aims to catalyze the development of innovative female-specific model platforms, which are tailored and optimized to study women's health issues. The aim is to enable a transformative leap forward in how women's health issues are modeled and subsequently addressed. While developing women-specific models, the platform technology should adequately represent female biology and physiology including the reproductive system, hormonal fluctuations, and genetic and epigenetic differences between males and females. Further proposals could consider how female-specific behavioral and psychological factors may influence research outcomes, such as stress responses or social behaviors.

Examples of potential capabilities for physical or digital female models may include, but are not limited to:

- Development of customizable "healthy" models that emulate the response of a tissue, organ, or organ system that is critical for women's health over the life course.
- Development of customizable disease models that accurately mimic how diseases manifest and progress in females, considering conditions that predominantly affect women or present differently in women compared to men.
- Development of models that facilitate an improved understanding of disease heterogeneity based on sex and gender.

- Development of models that include novel features, functions, and design choices that improve the ability to predict the response of women to therapies and interventions.

4. **Women's Health Topic 04: Modulating Women's Brain Health Via Lymphatic Targeting**

   What If Statement: What if targeting our brain's lymphatic system improved outcomes for women at risk for neurogenerative diseases?

   Problem Statement and Opportunity:
   Neurodegenerative diseases like Alzheimer's Disease (AD), Parkinson's disease, and Multiple Sclerosis (MS) exhibit distinct sex differences in prevalence or disease course. For example, women represent nearly two-thirds of the 6.7 million Americans living with AD, and they often bear the brunt of caregiver responsibility, leading to significant emotional, physical, and financial impacts. Meningeal lymphatics and glymphatics play a crucial role in maintaining brain health by facilitating waste clearance, regulating immune responses, and supporting brain fluid balance. Impairment of these systems, common in aging individuals, has been linked to various neurodegenerative diseases like AD and MS, as well as major depressive disorder. Despite this, the influence of sex differences in the lymphatic system on brain health has not been extensively investigated as a potential prevention or treatment approach for the millions of women affected by these diseases. There is a pressing need to explore the lymphatic system's potential for the prevention, early detection, and treatment of many neurodegenerative diseases, including AD, Parkinson's Disease, MS, and depressive disorders.

   ARPA-H aims to catalyze neurodegenerative disease research by investing in innovative technology that addresses the key challenges in meningeal lymphatics and glymphatic research, diagnosis, treatment, and care. We aim to bring together an interdisciplinary group of researchers, clinicians, and technology experts to accelerate these solutions. All proposed solutions should be developed to ensure fit to the onset, phenotype, and presentation of these disease states in women.
   Examples of promising innovations may include, but are not limited to: novel diagnostics leveraging the lymphatic and glymphatic systems' unique functions for disease prediction and monitoring; high-throughput drug studies using advanced discovery methods to identify compounds that penetrate the blood-brain barrier, targeting the lymphatic and glymphatic system to enhance waste clearance; and research focusing on the impact of sex and age on lymphatic vasculature variability, which could shed light on neurodegenerative disease pathology.

5. **Women's Health Topic 05: Objective and Quantitative Measurement of Chronic Pain in Women**

   What If Statement: What if women's pain were taken seriously?

   Problem Statement and Opportunity:

Women experience pain and pain mitigation differently than men do. There are measurable, sex-based differences in the perception of a variety of pain stimuli, hormone-mediated effects on pain perception, psychosocial effects on pain perception and sex-based differences in response to opiates. The etiology of these differences is not well understood. Women are also more likely to suffer from chronic pain conditions, rheumatoid arthritis, and migraines. Gender stereotypes can lead clinicians to underestimate and undertreat women's pain, resulting in prolonged suffering, delayed diagnosis and treatment, and a reluctance to seek medical care. The challenge is exacerbated by the absence of objective, quantitative markers of pain, and pain assessment primarily relies on self-reporting. The lack of biomarkers complicates the stratification of patients and the prediction of disease progression or response to treatment, reducing the success rate of pain treatment clinical trials by nearly 20%. Addressing this, a recent NIH-led workshop highlighted the urgent need for developing and validating objective pain biomarkers to advance pain management and contribute to resolving the opioid crisis.

ARPA-H seeks to develop methods to objectively, quantitatively and longitudinally measure pain across a variety of chronic conditions, including nociceptive pain, neuropathic pain, and pain due to central nervous system sensitization. These methods should enable clinicians to evaluate disease evolution and to determine how well a patient's course of treatment is addressing their pain. The pain measurement method should be simple, inexpensive and deployable in a range of settings.

Solutions that enable time-resolved, at-home pain monitoring are highly encouraged. While it is acknowledged that a multitude of markers may be needed for a precise and accurate evaluation, it is desired for these markers to be of similar origin (e.g. multiple blood or urine biomarkers, as opposed to MRI exam + genomic screen + blood based biomarkers + urine based biomarkers). The design and intended use of the pain measurement method should consider the psychosocial component of pain and the fact that gender, background, and life circumstances affect a person's response to pain (e.g. a person who cannot afford to skip a day of work may force themselves to be more mobile despite high pain levels). The solution is intended to quantify and support a patient's claims about their comfort and wellbeing and must agree with self-reported assessments. Methods that accurately identify the location of the pain generator and that distinguish between different pain types are encouraged, as are wearables.

6. Women's Health Topic 06: WILD CARD : Revolutionary Breakthroughs in Women's Health

What If Statement: What if we could shatter the glass ceiling of women's health research with innovations so bold, they rewrite the rules of the game?

ARPA- H recognizes that some revolutionary advances in women's health may be hindered by the inability to secure public or private sector funding because the concepts are considered too technically challenging, and are not covered in the topics above. In the WILD CARD topic, we seek to catalyze breakthroughs that will completely transform the paradigm of women's health, acknowledging the critical gaps in data, the historical underrepresentation in clinical trials, and the lack of focused research on the

unique health needs of women throughout their lives. By advocating for innovative solutions that transcend mere data collection, ARPA-H aims to revolutionize the methodologies for data generation, analysis, and application in women's health. We invite proposals that employ cutting-edge research, novel technologies, new business models to sustain investment, and interdisciplinary approaches to forge personalized and effective strategies, addressing the comprehensive and specific health challenges women face. This topic is dedicated to reshaping women's health research into a more comprehensive, inclusive, and forward-thinking endeavor, ensuring significant improvements in global health outcomes for women. If successful, the concepts pursued under this topic will change the conversation – and more importantly the practice – of how we engage women's health day-to-day.

Specifically excluded from this topic are iterative and standard approaches, including traditional clinical trials and work that is already well-supported by other private and public funds, or is otherwise specifically described and solicited in Sprint Topics 1-5.