JOURNAL OF WOMEN'S HEALTH
Volume 34, Number 10, 2025

DOI: 10.1177/15409996251365000

Abstracts from the NIH Office of Research on Women's Health 2025 Annual BIRCWH Meeting: Building Interdisciplinary Research Careers in Women's Health November 4, 2025

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Building Interdisciplinary Research Careers in Women's Health (BIRCWH)

Introduction to the Scientific Abstracts for the 2025 Annual BIRCWH Meeting

Xenia Tigno, MS, PhD[1] and Marquitta White, MS, PhD[2]

The Building Interdisciplinary Research Careers in Women's Health (BIRCWH) program is now in its 25th year and has produced more than 800 highly qualified and successful junior investigators. The BIRCWH program was created in 2000 by the Office of Research on Women's Health (ORWH) in collaboration with several other National Institutes of Health (NIH) institutes and centers. The program is funded through an institutional career development grant and is focused on providing mentorship, career development opportunities, and research experience to junior faculty who have recently completed clinical training or postdoctoral fellowships. The overall mission of the BIRCWH program is to increase the number and skillset of these junior faculty researchers (called BIRCWH Scholars) to support their continued advancement in the scientific workforce as well as to promote and advance research on women's health.

The BIRCWH program supports the ORWH mission and advances its goal of creating a diverse and robust workforce well prepared to advance science for the health of women, and where appropriate, further our understanding of the influence and impact of biological sex on health and disease.

When the BIRCWH program was originally created, most of the scientific abstracts focused on reproductive health research. Over the years, the abstract topics have greatly expanded across many areas of science. For 2025, nine categories were created to enable clustering of abstracts during the poster session on November 4, 2025. Many of our Scholars engage in transdisciplinary research, and therefore abstract categories often overlap significantly; readers may find it informative to peruse abstracts in all categories.

The numbers of abstracts in each of the nine categories, from highest to lowest are Clinical Research (8), Sex Differences (8), Public Health (7), Basic Research (6), Bioengineering/Bioinformatics (6), Reproductive Health (5), Cancer (5), Health Disparities (5), and Neuroscience (4). Last year, most abstracts centered on Public Health research. The shift toward Clinical Research and Sex Differences research for this year reflects the enthusiasm and dedication to research that examines the myriad structural, environmental, and biological factors, and the intersection of these factors, that influence the health of women.

Also of note, the number of abstracts focused on Bioengineering/Bioinformatics research—an abstract category that was introduced in 2024—increased by greater than 50%. This increased focus on the use of bioengineering and/or bioinformatic methods, and in some cases, the development of novel methods, showcases the diligence and ingenuity of the BIRCWH Scholars as they explore ever more inventive and cutting-edge technologies and methodologies to address issues affecting women's health.

The career development associated with these BIRCWH abstracts is built around three pillars: interdisciplinary research, mentorship, and career development. Studies have shown that interdisciplinary science teams that bring insight from multiple disciplines to tackle scientific questions are more productive. These teams advance our fundamental understanding of women's health and address gaps in knowledge in a way that would not be possible only working within the confines of any single discipline. The highly variable toolkit of research methods and experience that our Scholars gain from engaging in interdisciplinary research is invaluable, and many Scholars leverage this training to obtain independent NIH grant funding following their participation in the BIRCWH program.

Interdisciplinary mentoring teams are essential to the BIRCWH program. Diversity in training and perspective is the hallmark of these teams, which may include individuals with backgrounds and training in medicine, dentistry, pharmacy, nursing, veterinary medicine, biotechnology, social sciences, anthropology, genetics, public health, and any number of other STEM (science, technology, engineering, and mathematics) disciplines. These teams collaborate as a unit, with the common goal of supporting a BIRCWH Scholar in the transition from trainee to independent researcher. To further bolster these invaluable collaborations, this year we have focused on supporting collaboration not only within BIRCWH sites but also across several sites to ensure that Scholars can benefit from the full breadth of research training and experience that the BIRCWH program has to offer.

The 2025 Annual BIRCWH Meeting will be held in person at NIH on November 4, 2025. Poster sessions for all abstracts will occur in the morning in the Atrium area of the Natcher Conference Center. An afternoon plenary session will be videocast worldwide and will feature two special talks—the Ruth L. Kirschstein Memorial Lectureship and the Legacy of Leadership lecture. There will also be three Podium talks for the top Scholar abstracts, which are listed first in the abstract file below. More information about the November 4, 2025, meeting, the videocast link, and the complete BIRCWH program can be found on the ORWH website, https://orwh.od.nih.gov/events/building-interdisciplinary-research-careers-in-womens-health-bircwh-annual-meeting.

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2025 BIRCWH Scholar Podium Abstracts

O-1. Sex Disparities in Adaptive and Innate Immune Cells and Kidney Function in the Health and Retirement Study (HRS)

Shannon M. Sullivan (presenting author),[1] Charles Silkin,[1] Shweta Sharma,[2] Jessica D. Faul,[3] Bharat Thyagarajan[1]

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Background: Chronic kidney disease (CKD) exhibits sex disparities, with females having a higher age- adjusted prevalence than males. However, mechanisms underlying these differences remain unclear.

Given the known sex differences in immune cells, immune-related pathways may contribute to CKD disparities.

Objectives: To evaluate sex differences in immune cells subsets and estimated glomerular filtration rate (eGFR) in the Health and Retirement Study (HRS).

Methods: We used eGFR measures and 29 immune cell subsets from the 2016 HRS Venous Blood Study. Multinomial logistic and linear regression models estimated the association between immune cell subsets and eGFR (categories and continuous), stratified by sex. Models were adjusted for survey design and age, race/ethnicity, body mass index (BMI), hypertension, diabetes, alcohol use, smoking status, cytomegalovirus, and inflammation. Significance was determined using false discovery rate (FDR)-adjusted *P* value.

Results: Among 8966 HRS participants (aged 56-107 y) with complete data, 54% were female. Of females, 24% had eGFR less than 60 mL/min/1.73 m^2, compared to 19% of males. Notably, after adjustment, CD8+ T cell subsets showed opposing sex-specific effects, with CD8+ effector memory T cell (Tem) showing pronounced divergence. In females, higher CD8+Tem was associated with decreasing eGFR (β-trend = − 0.98; P_{FDR}-trend = 0.034); whereas in males, higher CD8+Tem was nonsignificantly associated with increasing eGFR (β-trend = 0.63; P_{FDR}-trend = 0.158). Additionally, in males, higher NK cells:CD56LO and plasmacytoid dendritic cells were significantly associated with increasing eGFR and myeloid dendritic cells with decreasing eGFR but not in females. In females, higher neutrophils were associated with increasing eGFR.

Conclusions: CD8+Tem exhibits sex-specific associations with kidney function, suggesting potential immune-mediated mechanisms underlying CKD disparities.

O-2. Cardiac Index Is Longitudinally Associated With Cerebrospinal Fluid Beta-Amyloid, a Core Alzheimer's Disease Biomarker, in Women but Not Men

Amalia Peterson (presenting author),[1,2] Panpan Zhang,[1,3] Dandan Liu,[1,3] Kimberly R. Pechman,[1] Deepak Gupta,[4] Kaj Blennow,[5,6] Henrik Zetterberg,[5,6,7,8,9,10] Timothy J. Hohman,[1,2] Angela L. Jefferson,[1,2,4]

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Background: Subclinical reductions in cardiac index are associated with lower cerebral blood flow and faster cognitive decline and may precede abnormal protein accumulation in Alzheimer's disease (AD).

Objectives: To examine the relationship between cardiac index and cerebrospinal fluid (CSF) biomarkers of core AD pathology (β-amyloid [$A\beta_{42}$] and phosphorylated tau [p-tau]).

Methods: Vanderbilt Memory and Aging Project participants (n = 153, 73 ± 8 y, 41% female) without dementia at baseline underwent echocardiogram at study entry and serial lumbar punctures over a 5-year period (mean follow-up = 4.0 y). CSF $A\beta_{42}$ and p-tau were analyzed in batch. Linear mixed-effects regression models related cardiac index to longitudinal CSF $A\beta_{42}$ and p-tau levels adjusting for baseline age, sex, race/ethnicity, education, modified Framingham Stroke Risk Profile, baseline cognitive status, and apolipoprotein E-ε4 status. Models were repeated with a sex interaction term and stratified by sex.
Results: In main effect models, cardiac index was unrelated to CSF $A\beta_{42}$ or p-tau levels (*P* values > .05). Cardiac index interacted with sex on CSF $A\beta_{42}$ levels (*P* = .03). In stratified models, lower cardiac index related to longitudinal decline in CSF $A\beta_{42}$ levels in females (β = 34.3; *P* = .05) but not males (β = −8.3; *P* = .31). There was no significant interaction with sex on CSF p-tau levels (*P* > .05).

Conclusions: In females, lower cardiac index may relate to progressively lower CSF $A\beta_{42}$ (but not p-tau levels) over time. Lower CSF levels of $A\beta_{42}$ are indicative of more accumulation of Aβ plaques in the brain. Future work on sex differences in the association between cardiac index and other AD biomarkers is warranted.

O-3. Sex-Specific Prediction of 1-Year Medication Nonadherence Using Machine Learning: Analysis of Medicare Fee-for-Service Ischemic Stroke Survivors

Hend Mansoor (presenting author),[1] Daniel Manion,[1] Daniela C. Moga,[1] Jeffery C. Talbert,[1,2] Wei-Hsuan Lo-Ciganic[3,4]

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Background: Nonadherence to guideline-directed medications (GDMs) is prevalent among stroke survivors, particularly in women.

Objectives: To develop and validate sex-specific machine-learning algorithms (MLA) to predict 1-year nonadherence to GDMs among Medicare stroke survivors.

Methods: Medicare beneficiaries discharged after a primary diagnosis of acute ischemic stroke between January 2013 to December 2020 and with a prescription filled for secondary prevention GDMs (i.e., statins and antihypertensives) were included. Patients were randomly divided into training, testing, and validation samples. Potential predictors included socio-demographics, medical history, area-level social factors, and filling prescription patterns. We evaluated 7 MLAs to predict nonadherence to GDMs, defined as the proportion of days covered less than 0.80 (i.e., prescription filling gaps) at 1 year. Prediction performance was assessed using C-statistic, and SHAP values were reported for the top 20 predictors.

Results: Our final cohort included 10 848 patients; of which 5589 (51.5%) were women. In both sexes, the gradient boosting machine (GBM) and histogram-based gradient boosting were best performing (C = 0.80 and 0.81, respectively) in the testing cohort. The GBM had a specificity of 86.4%, and negative predictive value (NPV) of 73.5% in women, and a specificity of 87.6%, and NPV of 74.7% in men. Among both sexes, top predictors included polypharmacy and adherence to GDMs in the first 3 months post-discharge and 12 months prior. Less than high school education and proportion of households receiving food stamps were among top predictors in women.

Conclusions: MLAs appear to perform well for risk prediction of nonadherence to GDMs among stroke survivors in women and men.

2025 BIRCWH Scholar Poster Abstracts

Basic Research

1. Timing Regenerative Therapeutics: ECM Remodeling by Stage of Prolapse

Nisha Shetty,[1] Natalie Sayers,[1] Pamela A. Moalli,[1–3] Amanda M. Artsen (presenting author)[1,3]

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Background: Regenerative extracellular matrix (ECM) therapies are a promising treatment for pelvic organ prolapse (POP), but ideal timing of administration is unknown.

Objectives: To quantify critical ECM degradative enzymes by stage of POP compared to controls.

Methods: Patients undergoing POP surgery (≥ stage 2) or benign gynecologic surgery were offered enrollment and underwent a full thickness vaginal biopsy. To detect a 30% difference with 80% power and alpha of 0.05, 10 control and 30 POP samples were analyzed. MMP2, MMP9, and TIMP3, a potent MMP inhibitor, were quantified by ELISA and compared by POP stage using ANOVA and Bonferroni posthoc comparisons.

Results: Because of known risk factors, women with POP were older, more likely to be menopausal, and had slightly higher median parity. The POP group was 100% White, while controls were 70% White, 20% Black, and 10% Black and American Indian. POP subjects were less likely to be smokers. 30% of postmenopausal women were on hormone replacement therapy (HRT). Regardless of HRT use, MMP2 decreased with worsening POP, reaching half the MMP2 concentration of controls at the worst stage ($P < .05$). MMP9 showed a similar trend that was significant in women on HRT ($P < .05$). An MMP2+MMP9/TIMP3 ratio confirmed decreasing levels of degradative potential across worsening stages of POP ($P < .05$).

Conclusions: ECM remodeling changes with severity of POP with early degradation followed by absence of remodeling in later stages are likely due to diminished mechanical loading and loss of key structural proteins. Regenerative therapies may be more successful at earlier stages.

2. Targeting Estrogen Signaling in Tumor Associated Myeloid Cells to Enhance Radiotherapy Responses

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Background: There are sex differences in immunological responses both in the initial and secondary response during tumor progression. We have shown that 17-β-Estradiol (E2) promotes tumor growth and resistance to immunotherapy by polarizing tumor associated macrophages (TAMs) toward an immune- suppressive state, both of which can be reversed with the anti-estrogen fulvestrant. However, how sex hormones shape tumor immunity and effect the responses to immunotherapy is currently unknown.

Objectives: To determine how E2 influences TAM functionality intratumorally by exploring key regulatory nodes downstream or parallel to the E2/ER [estrogen receptor] axis.

Methods: Lewis lung carcinomas (LLC1) were implanted in ovariectomized animals treated ± E2. Tumor cells were sorted to isolate myeloid cells for RNA sequencing and chromatin accessibility sequencing.

Results: E2 exposure led to enhanced engulfment and accelerated degradation of apoptotic cancer cells by TAM, thus limiting the activation of type I interferon (IFN) axis within myeloid cells. Mechanistically, E2-ERα signaling activates the NFATC1-CX3CR1 signaling axis to promote efferocytosis. Efferocytosis following radiation therapy (RT) limits the efficacy of RT in an E2-exposed tumor microenvironment. Using clinically approved endocrine therapy, fulvestrant and a small molecule inhibitor of CX3CR1, we reversed E2-induced efferocytosis within irradiated tumor microenvironment, thus leading to an increased efficacy of RT.

Conclusions: E2/ER via the NFATCI-CX3CR1 pathway results in an immune-suppressed tumor microenvironment. This can be exploited pharmacologically to improve the effects of

RT. Future studies will determine whether the TAM intrinsic NFATC1-CX3CR1 signaling axis can be targeted to enhance immunotherapy sensitivity across other solid tumor types.

3. The Role of IL-12 in Sjogren's Disease

Rachael A. Gordon (presenting author),[1] Leah Wunsch,[1] Aiden Brown,[1,2] Robyn T. Domsic,[1] Mark J. Shlomchik[2]

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Background: Sjogren's disease (SjD) is a common systemic autoimmune disorder characterized by loss of tolerance to self-antigens and inflammation of the exocrine glands. There are no U.S. Food and Drug Administration–approved disease-modifying therapies. SjD-associated polymorphisms in IL12A, TYK2, and STAT4 suggest that the IL-12–STAT4–IFNγ signaling axis plays a key role in SjD. Supporting this idea, serum IL-12p70 levels are elevated in patients carrying the IL12A rs485497*A risk allele. We hypothesize that IL-12 is a key pathogenic driver in SjD.

Objectives: To determine whether IL-12 drives SjD and the mechanisms by which it exacerbates autoimmunity.

Methods: IL-12 was targeted in vivo by treating 28-week-old NOD.B10 SjD-prone mice with a rat anti- mouse IL-12p70 neutralizing antibody or control for 4 weeks. Sialadenitis, dacryoadenitis, and immune composition were assessed. A murinized version of the antibody was engineered to reduce immunogenicity. As a complementary strategy, we generated Il12rβ1$^{-/-}$mice on the NOD.B10 background using CRISPR/Cas9. These mice lack IL-12 signaling and are being aged in parallel.

Results: Administration of rat anti–IL-12p70 antibody resulted in premature death in ∼50% of female mice, likely due to anti-drug antibody responses, as evidenced by the presence of anti-drug antibodies in serum.

To circumvent this problem, we successfully engineered a murine version of this antibody. In parallel, we have generated the Il12rβ1$^{-/-}$ NOD.B10 mouse. Il12rβ1$^{-/-}$ mice lack Il12rβ1 mRNA expression and exhibit impaired IL-12-induced plasmablast and Th1 differentiation. Cohorts are currently aging for disease assessment.

Conclusions: These novel tools enable direct investigation of IL-12 in SjD and may guide the development of IL-12-targeted therapies for autoimmune diseases.

4. The Genes & Hormones Initiative: A Biobank to Elucidate the Effects of the Sex Chromosomes and Sex Hormones in Humans

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Background: Sex chromosomes and sex hormones impact human traits and diseases. However, it has proven challenging to understand the sex chromosomal and hormonal basis of sex-differential biology.

Objectives: To create a biobank with associated clinical data from participants with alterations in sex chromosomes and/or sex hormones.

Methods: We recruited participants from the Boston Children's Hospital Pediatric Endocrinology clinic. After obtaining informed consent/assent, participants completed a demographic questionnaire and provided blood and urine samples. We isolated peripheral blood mononuclear cells, serum, and plasma and generated lymphoblastoid cell lines. Additionally, we extracted clinical data from the electronic medical record.

Results: Between 2019 and 2025 we recruited 33 participants aged 5-20 years. Fourteen participants had Turner syndrome: 6 participants had a 45,X karyotype, 2 had mosaic Turner syndrome (45,X/46,XX), and 6 had more complex karyotypes (45,X/46,X del Xq24; 45,X/46,X,r(X)(p22.3q21.2); 45,X/46,X,idic(X)(p11.2); 45,X/46,X,+r; and 2 had 45,X/46,X,i(X)(q10)). Seven participants had Klinefelter syndrome (47,XXY), 3 had Kabuki syndrome due to a mutation in the X-chromosomal gene *lysine-specific demethylase 6A (KDM6A)*, 3 had sex chromosome mosaicism, 2 had complete androgen insensitivity syndrome due to a mutation in the gene encoding the *androgen receptor (AR)*, 2 had gonadal dysgenesis, 1 had a duplication of Xpter to Xp21.3, and 1 had testicular regression.

Conclusions: We have created a biobank from participants with alterations in sex chromosomes and/or sex hormones, and recruitment is ongoing. In the future, we will use these biospecimens in translational research to further elucidate the effects of the sex chromosomes and hormones in humans.

5. LRIG1 as a Pan-Negative RTK Regulator in Endocrine-Therapy Resistant ER+ Breast Cancer

Brittany D. Jenkins-Lord (presenting author),[1] Kayla S. Ingram,[1] Jaclyn Morgan,[1] Eleanor Liu,[1] Aashna Saxena,[1] Utthara Nayar[1]

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Background: Estrogen-receptor positive (ER+) breast cancer (BC) accounts for approximately 70% of all BCs. Although most ER+ BCs initially respond to endocrine treatment, 30% to 40% acquire resistance to these drugs. Resistance mechanisms include alterations in the ERBB receptor tyrosine kinase (RTK) family, particularly HER2/ERBB2. The ERBB RTK family represents approximately 10% to 15% of clinical endocrine resistance cases but lacks a unified targeting strategy.

Objectives: To investigate the mechanistic and therapeutic relevance of a pan-RTK negative regulator, LRIG1, in promoting sensitivity to endocrine therapies in treatment-resistant ER+ BC cell lines, specifically those with acquired *ERBB* and *FGFR* family alterations.

Methods: Our analysis uses gene expression data (bulk RNA sequencing [RNAseq]) from publicly available databases from ER+ fulvestrant-resistant breast cancer cell lines (MCF7 and T47D). We specifically focused on tumors with acquired alterations in HER2/ERBB2 and FGFR2 after first-line therapy. We evaluated changes to the LRIG1 gene and protein expression after combinatorial therapies in these cell lines.

Results: HER2-overexpressing mutant ER+ BC cell lines demonstrate downregulation of LRIG1 across all mutants. With the addition of neratinib, a tyrosine kinase inhibitor, LRIG1 gene expression increased significantly, indicating its potential role in modulating RTK inhibition. Initial investigations at the protein level revealed variation in LRIG1 expression in HER2-activating mutants compared to controls. RNAseq data from FGFR2-altered cell lines also show similar results after treatment with an FGFR- inhibitor.

Conclusions: Our results will be clinically informative in providing an actionable target for overcoming endocrine therapy resistance in ER+ BC.

6. Herpesvirus Seroprevalence Between Males and Females With Different Forms of Interstitial Lung Diseases

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Background: Herpesviruses are viruses that can establish latent infections and are found at high rates in individuals with interstitial lung disease (ILD). Many reports indicate that herpesvirus can be a "second hit" micro injury to the lung epithelium. Among the different types of ILDs, males are more often diagnosed with idiopathic pulmonary fibrosis (IPF) and females with autoimmune-mediated ILD. The influence of herpesvirus in these different forms of ILDs remains unclear.

Objectives: To investigate the incidence of latent herpesvirus infection in males and females among patients with ILD.

Methods: We performed cytomegalovirus (CMV) and Epstein-Barr virus (EBV) serology analysis on 161 individuals with ILD enrolled in a longitudinal cohort. Pulmonary function testing (predicted force vital capacity [FVC]%) was performed at baseline and 1 year following enrollment.

Results: Among all participants, 90 were positive for CMV (53% females and 46% males), and 141 were positive for EBV (47% females and 52% males). Female patients who were positive for either type of herpesvirus were more often diagnosed with non-IPF ILDs (72%) when compared to IPF (28%). Male patients who were CMV+ or EBV+ were more often diagnosed with IPF (65%) compared to non-IPF ILDs (35%). However, changes in FVC% were not associated with CMV serostatus in both IPF and non- IPF ILD.

Conclusions: A history of herpesvirus infection is prevalent in males with IPF and females with non-IPF ILD. Detecting virus reactivation in the lungs is essential to investigating the roles of these viruses in disease progression.

Bioengineering/Bioinformatics

7. Assessing and Compensating for Motion Artifact on Near Infrared Spectroscopy in Bladder and Brain

Linda S. Burkett (presenting author),[1,3] Avani Venkatesh,[1] Nuhame Mulugeta,[1] Mina P. Ghatas,[2] Alice Strawn,[2] Ethan Casto,[2] Nyasia Jones,[1,2] John E. Speich, Adam P. Klausner[1,2]

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Background: Near infrared spectroscopy (NIRS) is a technique to assess oxyhemoglobin (O2Hb) concentration in the anterior bladder wall with device placement on the abdomen. NIRS signals can be disrupted by motion artifacts. Disturbances can be mitigated using accelerometers or inertia motion units (IMUs).

Objectives: To evaluate differences during natural bladder filling between NIRS signals and motion artifacts using both headcap-mounted and abdominal wall–mounted IMUs.

Methods: Participants without voiding dysfunction, comprising both biological sexes, underwent a validated natural filling protocol using both headcap- and abdominal-mounted IMUs to continuously measure bladder O2Hb. During high sensation (after first desire to void), NIRS signals were compared using motion segmentation from either the headcap or abdominal IMUs using a Pearson correlation.

Results: Ten participants (5 female, 5 male) completed the protocol, providing sufficient data for paired analysis. In 8/10 samples, the Pearson correlation between fNIRS headcap IMU and NIRS abdominal IMU was greater than 0.75. Those with lower correlations (0.51-0.55) had notable phase shifts and very similar visual NIRS patterns. Similar O2Hb patterns as functions of filling were obtained with NIRS signals obtained with both the headcap and abdominal devices.

Conclusions: This study indicates that data from both a headcap IMU and a abdominal IMU can reliably identify and correct for motion artifact during natural filling studies. The strong correlations observed in the NIRS signal demonstrate the relative consistency of NIRS in capturing bladder hemodynamics measurements using both devices and helps control for intrinsic variability in NIRS analytics.

8. Computational Modeling of Estrogen and Type I Interferon Signaling in Valve Interstitial Cells

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Background: There are no pharmacotherapies for calcific aortic valve disease (CAVD), the most prevalent heart valve disease in the United States. The current consensus suggests that endothelial dysfunction and inflammation precede the fibrocalcific remodeling that define CAVD and that women typically exhibit higher degrees of fibrosis and less calcification than men for similar levels of hemodynamic dysfunction. Moreover, the increase in the rate of CAVD after menopause is large, suggesting that estrogen may protect against the development of CAVD. Sex differences in type I interferon signaling, a major inflammatory pathway, exhibited by the resident valve interstitial cells (VICs) have recently been reported, but the underlying mechanisms behind these differences have not been elucidated.

Objectives: To elucidate the contributions of female sex and 17β-estradiol (E2) crosstalk to type I interferon (IFNα) signaling in VICs.

Methods: A mechanistic computational model of canonical type I interferon signaling and nuclear estrogen receptor signaling was developed to quickly interrogate potential crosstalk mechanisms. The mechanistic model was calibrated to human VIC responses via fitting to Western blotting and immunocytochemistry time courses.

Results: Pre-stimulation with 100 nM E2 leads to a doubling of STAT1 phosphorylation and corresponding increase in STAT1 protein levels by IFNα in female VICs (n = 2 male, 2 female). Computational modeling suggests that STAT2 inhibition plays a larger role than IRF9 inhibition in facilitating the increased STAT1 activation.

Conclusions: Estrogen and female sex synergize to bias IFNα signaling toward STAT1 homodimers and away from STAT2 and IRF9 complexes.

9. Impact of Menstrual Cycle on Skin Inflammation and Spironolactone Effectiveness in Hidradenitis Suppurativa: Mechanistic Insights

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Background: Hidradenitis suppurativa (HS) is a chronic, incurable inflammatory skin disorder characterized by painful nodules and abscesses.

Objectives: To evaluate the impact of menstrual cycle stages and hormone-modulating therapy (spironolactone) on HS-disease activity and on gene expression within skin lesions.

Methods: We collected patient- and physician-reported measures from 28 HS-women during the early follicular and luteal phases of the menstrual cycle. Seven patients were treated with spironolactone for 12 to 16 weeks. RNA sequencing was performed on skin biopsies from 10 HS-women, 5 healthy controls, and 3 spironolactone-treated women. Significance criteria for differentially expressed genes were false discovery rate (FDR) < 0.05; | log2fold-change | > 1.5.

Results: Patient-reported outcomes worsened significantly during the early follicular phase compared to luteal phase. In spironolactone-treated patients, 4 (57%) achieved HiSCR50 (50% reduction in abscess/nodule count). Comparing the follicular to the luteal phase: in healthy control skin, genes were upregulated in immunoregulatory pathways, while in lesional HS-skin, genes were upregulated in keratinization and microbial defense response pathways. Genes in keratinization and microbial defense pathways were conversely downregulated in follicular phase lesional skin after individuals achieved HiSCR50 following spironolactone treatment.

Conclusions: Our study offers novel mechanistic insights into hormone modulation affecting skin inflammation. The identification of genes in these relevant pathways that are affected by hormone modulation will lead to improved understanding of skin inflammation in HS and enable development of improved treatment options.

10. A Genome-wide Association Study of Perinatal Depression Reveals Novel Genetic Risk Factors

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Background: Perinatal depression (PD) is a common complication of pregnancy. Though moderate heritability estimates suggest that genetics plays a role in development of PD, genetic research is limited and often focuses solely on postpartum depression.

Objectives: To identify genetic determinants of PD.

Methods: Data on females who had been pregnant and delivered at Vanderbilt University Medical Center were obtained from BioVU, a DNA biobank linked to electronic health records. PD cases were defined using billing codes. Individuals with preexisting depression were excluded. We performed a genome- wide association study (GWAS) for PD, adjusting for 10 principal components. Bonferroni corrected *P* values were used to determine significance.

Results: The study cohort included 3614 individuals, with an average age at delivery of 29.3 years. Most individuals identified as Non-Hispanic Black (30.4%) or Non-Hispanic White (59.1%). Roughly 19.0% (N = 677) experienced PD. We identified 2 significant variants (rs7830243 and rs111668725) in the *TRAPPC9* gene. Although this finding is novel for PD, variants in this gene have previously been linked to major depressive disorder in females. There were 72 variants with suggestive significance (P value $< 5 \times 10^{-6}$), many with strong biologic plausibility supporting an association with PD. One variant lies within the *SPATA17* gene, which previous research found to be differentially expressed based on depressive symptoms at 2 months postpartum. Eight variants are within a gene (*PRKCH*) related to prolactin signaling, a hormone known to increase throughout the peripartum.

Conclusion: We identified novel genetic associations and multiple suggestive associations that require additional investigation to determine the mechanisms linking them to PD.

11. Elucidating the Role of Tension and Mesh Deformation on Vaginal Smooth Muscle Morphology and Contractile Function

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Background: Tension applied to polypropylene mesh used in repairs of prolapse can result in mesh deformation, which is associated with vaginal degeneration and complications. It is unclear whether tensioning mesh or deformation is the major contributing factor driving the vaginal response.

Objectives: To define the impact of tension and deformation on vaginal smooth muscle (VSM) morphology and contractile function.

Methods: Mesh was implanted flat on the vagina of rhesus macaques (IACUC 22091549) on no tension (NT, N = 9) and high tension (HT, N = 8) and was also implanted deformed with no tension (DNT, N = 9) and on high tension (DHT, N = 10). Sham animals served as controls (N = 8). After 12 weeks, the mesh-vagina complexes (MVCs) were excised and analyzed for VSM morphology and vaginal contractile function. Kruskal-Wallis followed by pairwise comparisons were used to compare groups.

Results: The density and spatial homogeneity of VSM bundles diminished with mesh implantation compared to Sham. Overall, vaginal contractility significantly decreased by 61% to 66% with deformed mesh (DNT, $P = .015$ and DHT, $P = .028$) but not flat mesh (P values > .05 NT) relative to Sham. Similarly, contractility was 69% ($P = .015$) and 64% ($P = .024$) reduced for DNT and DHT relative to NT, respectively. Vaginal

contractility was not different between NT vs HT nor DNT vs DHT (P values > .05).

Conclusions: Mesh implantation impairs VSM morphology and contractile function, particularly with deformed mesh irrespective of tension. These results suggest that deformation has a greater impact on the vaginal response to mesh. Future studies will quantify smooth muscle density, bundle size, and innervation of the smooth muscle to further probe changes in VSM morphology.

12. Increasing Metabolic Burden Has a Larger Impact on Atrial Fibrillation Risk in Females Than Males

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Background: Obesity and metabolic derangements (MetD) are key modifiable risk factors for atrial fibrillation (AF) management.

Objectives: To evaluate the influence of height-adjusted weight and diagnostic time for specific modifiable MetD on AF risk in a real-world clinical population using time-to- event analyses.

Methods: Using landmark methods, we ascertained MetD prior to ("chronic") or during ("developed") a 3-year baseline period in 95 160 adult-patients with no history of AF from Vanderbilt University Medical Center. Overall and sex-specific risk of incident AF was assessed using Cox regression analyses adjusted for age, sex, race, height, and MetD as well as Kaplan-Meier analyses for individual MetD abnormalities.

Results: Incident AF occurred in 9094 (9.6%) patients over a median follow-up of 6.35 years. Ten-year AF risk was lowest in patients with a body mass index between 18.5 kg/m^2 and 25 kg/m^2 and elevated with MetD regardless of exposure time. There were slight differences in the patterns of risk associated with MetD. Chronic or developed low high-density lipoprotein (HDL) significantly increases risk in females (HR,1.27 and 1.21, respectively, $P < 0.0001$) but in males only developed low HDL increases risk (HR, 1.26, $P < 0.0001$). We observed a step-wise increase in AF risk with increasing MetD burden for all individuals. Females consistently had higher hazard ratios than males (e.g., 4 MetD components, HR = 2.53 for females compared to HR = 2.05 for males).

Conclusions: MetD is a significant driver of risk for AF in male and female patients; however, increasing burden of MetD appears to have a greater impact of females than males.

Cancer

13. Individual and Contextual Factors Associated with Incidence of Ovarian Cancer in the United States

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Background: Ovarian cancer (OC) has the worst prognosis and highest death rate of all gynecological cancers in the United States. Because data on incidence and risk factors are important for strategic program planning, we sought to determine the independent effects of individual- and contextual-level factors on the incidence of OC in the United States.

Objective: To examine the independent effects of individual-, neighborhood- and state level factors on the incidence of ovarian cancer in the US.

Methods: This retrospective cohort study used de-identified data from the *All of Us* research database to identify women aged 18 years and older without OC before January 2017. The cohort was followed up from January 2017 to July 2023. Mixed-effects Cox regression models were used to analyze data on 78 770 individuals, nested within 974 neighborhoods and 50 states across the United States.

Results: Approximately 4 out of every 1000 patients in this study had OC. After all other factors were adjusted for in the final model, individuals aged 50-59 years (aHR, 1.94; 95% CI, 1.27-2.98) and 60-69 years (aHR, 1.69; 95% CI, 1.07-2.66) had increased risks of developing OC compared to those younger than 40 years. Being a retiree, using hormone replacement therapy, and having annual income of greater than or equal to $100,000/year increased the risks of OC. Compared to individuals residing in the Midwest region neighborhoods, those residing in the Northeast region neighborhoods of the United States had increased risks of having OC (aHR, 1.66; 95% CI, 1.09-2.53). There was significant clustering of OC at the neighborhood and state levels.

Conclusions: This study showed that individual- and contextual-level factors were associated with increased risk of OC in the United States. Interventions and programs designed to lower the risk of OC should be directed at both individual- and contextual-level factors.

14. Feasibility Pilot Study of a Standardized Extract of Cultured Lentinula edodes Mycelia (AHCC®) on Quality of Life for Ovarian Cancer Patients on Adjuvant Chemotherapy

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Background: Quality of life for women with ovarian cancer is affected by their disease and the treatment. Two-thirds of gynecologic oncology patients in the United States are using integrative medicine to improve symptoms. AHCC®, a shiitake mushroom supplement, has been shown to upregulate CD4 and CD8 T-lymphocytes and increase cytokines such as IFN-γ while

alleviating chemotherapy side effects in small preclinical and clinical studies.

Objectives: To determine feasibility of a randomized controlled trial (RCT) evaluating the effects of AHCC® on health-related quality of life (HRQOL) and immune function for ovarian cancer patients receiving chemotherapy.

Methods: This is a pilot feasibility RCT for newly diagnosed ovarian cancer patients receiving chemotherapy after surgery. Participants are randomized 1:1 to AHCC® or placebo. HRQOL will be measured by validated assessments. Side effects from chemotherapy will be collected from the electronic medical record. Immune cell components and function will be evaluated using RNA sequencing and flow cytometry. For feasibility testing, women with ovarian cancer will be approached for participation. We will evaluate the time needed to recruit participants. We will also evaluate adherence and acceptability of participating in a supplement trial.

Results: This trial has been open for 12 months. To date, 26 of the 37 ovarian cancer patients identified have been eligible. Eight participants have been consented, and 6 have been enrolled in the trial.

Conclusions: This pilot study will determine the feasibility of conducting a larger RCT of the effect of AHCC® on quality of life and cancer outcomes for women with ovarian cancer.

15. Obesity-Linked Endothelial Dysfunction and Proteomic Alterations in Breast Cancer Survivors

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Background: Breast cancer survivors (BCS) face a significantly elevated cardiovascular disease (CVD) risk. Obesity further amplifies this risk, yet its effects on early markers of vascular injury and dysfunction remain unexplored.

Objectives: To evaluate the relationship between obesity and preclinical markers of CVD in BCS.

Methods: We conducted 2 complementary studies in postmenopausal BCS without CVD. In a pilot cohort (n = 12) of BCS with obesity, endothelial function was assessed using the EndoPAT-derived reactive hyperemia index (RHI), a strong predictor of CVD risk. Linear regression examined associations with adiposity (reported as parameter estimates [PE] and 95% CI). In a separate proteomics study, we used the Olink Cardiovascular III panel to identify differentially expressed proteins (DEPs) in plasma from BCS with (n = 56) and without obesity (n = 56), using principal component analysis and false discovery rate-corrected Wilcoxon tests.

Results: In the EndoPAT cohort, greater adiposity was significantly associated with lower RHI, reflecting poorer endothelial function: weight PE –.01 (–0.02; –0.01), BMI –0.03 (–0.06; –0.11), waist circumference –0.02 (–0.03; –0.01), and hip circumference –0.02 (–0.03; –0.01); all $P < .01$. Proteomic analysis identified 26 DEPs, with obesity linked to upregulation of pro-inflammatory and vascular injury markers (e.g., TNF- R1/R2, vWF) and downregulation of protective proteins (e.g., PON3, IGFBPs).

Conclusions: Obesity in BCS is associated with impaired endothelial function and a proteomic profile associated with inflammation and vascular injury, highlighting its contribution to elevated CVD risk in this population. These findings underscore the need for early CVD risk assessment and targeted interventions in BCS with obesity to improve long-term cardiovascular outcomes.

16. The Influence of Sex on the Size of Cytologically Indeterminate Thyroid Nodules

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Background: Women have higher incidence of thyroid nodules. However, the role of sex on nodule size and risk of molecularly suspicious findings in cytologically indeterminate nodules has not been characterized.

Objectives: To determine the impact of sex on size of cytologically indeterminate thyroid nodules and their molecular classification.

Methods: We assessed patients with thyroid nodules evaluated at our institution's nodule clinic from 2017 to 2023 with a fine needle aspiration biopsy yielding indeterminate cytological findings that subsequently underwent molecular testing with Afirma Genomic Sequencing Classifier.

Results: The cohort consisted of 823 thyroid nodules, the average age of patients was 57.2 years and the prevalence of female sex was 74.6%. We divided thyroid nodules in 3 groups: 650 nodules under 3 cm, 114 3-4 cm, and 59 larger than 4 cm. The mean nodule size in each group was 1.82, 3.33, and 4.53 cm, respectively. We observed a significantly lower prevalence of female sex in larger nodules (>4 cm) (52.53%), when compared to nodules 3-4 cm (74.56%) and those <3 cm (76.61%) ($P < .01$). The mean age was significantly lower in nodules <3 cm (49.35 years), compared to the 3-4 cm group (60.70 y) and the >4 cm group (60.72 y) ($P < .05$). Using logistic regression analysis, no significant association was observed between age and sex in this cohort. The prevalence of suspicious molecular findings was not significantly different between the 3 nodule groups ($P = 0.166$).

Conclusions: We observed a significantly lower percentage of females in the group of large (>4 cm) thyroid nodules, not associated with patients' age nor rate of molecularly suspicious results.

17. A Current Unmet Need for Staging in the Setting of Recurrent Breast Cancer

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Background: For patients with recurrent breast cancer (RBC), post-recurrence survival varies, and the current

prognostic staging guidelines do not offer a standardized system for patients with RBC. In addition, it is unclear whether this gap in standardization is important to breast oncology providers.

Objectives: To assess the perceived need by breast oncology providers for a standardized staging system for RBC.

Methods: A Qualtrics survey was distributed to 329 breast oncology providers at 4 major cancer centers, and 108 responses were received (32.8% response rate), with 24 responses excluded due to incomplete surveys. Response data were summarized with frequencies and percentages.

Results: Among the 84 respondents with completed surveys, the mean age was 47 years (range 28-82), and the majority were women (75.9%), White (65.5%), and physicians (79.8%). Overall, 74.2% agreed that there is an unmet need for an RBC staging system, and 84.8% of those who frequently use staging agreed. Participants who perceived a need for a novel RBC staging system believed that it could be important for communication, informing treatment decisions, predicting prognosis, and research. The lack of clear and standardized guidelines was identified as the most significant barrier when discussing prognosis for RBC. Although neither developed for nor validated in the setting of RBC, 48.8% use the tumor/nodal/metastases (TNM) staging system to counsel patients with RBC.

Conclusions: These findings highlight the need for a novel RBC staging system, which could address gaps in current guidelines and improve clinical and nonclinical decision-making for patients.

Clinical Research

18. Better Together: Implementation of Combined Contingency Management for Stimulant Use and HIV in Women's Health HIV Primary Care

Ayesha Appa (presenting author),[1] Gabriela Steiner,[1] Stefan Baral,[2] Elise Riley,[1] Lauren Suchman,[1] Kate Roberts,[3] Kelly Knight,[1] Meghan Murphy,[1] Gabriel Chamie,[1] Steve Shoptaw,[4] Phillip Coffin,[5] Monica Gandhi[1]

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Background: Among women living with HIV (WLWH), stimulant use disorder (StUD) reduces anti- retroviral therapy (ART) adherence and accelerates progression to AIDS. Contingency management (CM), where patients receive prizes for measurable behavior change, effectively reduces stimulant misuse and improves HIV medication adherence. A novel urine assay for tenofovir (TFV) has been developed.

Objectives: To describe the feasibility, acceptability, and preliminary effectiveness of CM embedded into primary care serving WLWH to reduce stimulant use and optimize ART adherence.

Methods: We conducted a 12-week, single-arm, implementation-effectiveness, pilot trial of weekly CM in a safety-net HIV clinic for people at risk for or living with HIV (PWH) who had StUD. We recruited from a women's subclinic, but enrolled both women and men. We offered escalating incentives for sustained stimulant non-reactive and/or TFV-reactive point-of-care urine assays, evaluating Reach and Effectiveness using the RE-AIM framework.

Results: We enrolled 37 participants with severe StUD (43% Black, 30% Latino/a, 41% White; 51% women, 49% men; 52% experiencing homelessness). Most (84%) were PWH, with 45% virally nonsuppressed pre-intervention. Participants attended 42% of scheduled visits, with 57% of stimulant tests nonreactive during intervention. Among PWH, 96% of TFV tests were positive. Qualitative interviews revealed strong appreciation for colocation of CM within their regular clinic setting and stigma-free therapeutic relationships, as well as interest in gender-concordant services.

Conclusions: CM for stimulant use and/or ART adherence embedded into HIV care demonstrated effectiveness in reducing stimulant use and improving HIV viral suppression, including among women.

19. Impact of Maternal Depression Intervention During Pregnancy on Infant Subcortical Brain Development: A Randomized Clinical Trial

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Background: Research spanning decades has established a compelling link between prenatal maternal mental health and long-term offspring health outcomes, supporting the Fetal or Developmental Origins of Health and Disease Hypothesis. However, existing human research has been limited by its reliance on correlational evidence. Experimental control through intervention is needed.

Objective: The current innovative study employed a randomized clinical trial (RCT) to rigorously test the fetal origins hypothesis, aiming to determine whether alleviating maternal depression during pregnancy can yield significant effects on child brain development.

Methods: A prospective RCT, the Care Project, was conducted among pregnant individuals who reported elevated depressive symptoms. Participants were randomized to receive brief interpersonal psychotherapy (IPT; n = 52) or enhanced usual care (EUC; n = 57). Infant hippocampal and amygdala volumes were assessed using structural magnetic resonance imaging.

Results: Infants in the IPT treatment group had significantly lower right hippocampal volume than those in the EUC group (P = .002; d = 0.62). No significant group differences were observed in left hippocampus (P = .16, d = 0.28) or bilateral amygdala volume (all Ps > .49).

Conclusions: Treating maternal depression during pregnancy exerts intergenerational effects on infant brain structure, with potential long-term implications for cognitive and emotional development. This study offers the first experimental evidence linking prenatal mental health interventions to alterations in early brain development, highlighting critical pathways for prevention and underscoring the potential of early intervention strategies to promote improved health outcomes across generations.

20. Regulatory Actions of Follicle Stimulating Hormone on Cerebrovascular Function in Postmenopausal Women: A Pilot Study

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Background: Menopause is a sex-specific risk factor that increases the risk of Alzheimer's disease (AD) in women. However, the mechanisms remain poorly understood. Declines in cerebral blood flow contribute to the development of AD neuropathology. AD neuropathology is increased after menopause, presumably due to estradiol (E2) deficiency, but the effects of E2-based therapy on AD neuropathology are mixed, suggesting the involvement of other mechanisms. Recent preclinical data suggest that follicle stimulating hormone (FSH) blockade prevents AD neuropathology.

Objective: To determine whether FSH contributes to cerebral blood flow regulation in menopause.

Methods: A model of short-term ovarian hormone suppression (gonadotropin releasing hormone antagonist [$GnRH_{ant}$]) was used to explore the independent actions of E2 and FSH on cerebrovascular function (cerebral blood velocity [CBV], transcranial Doppler ultrasonography) in early postmenopausal women (n = 22, 55 ± 3 y). CBV was measured at baseline and after 12 weeks of randomization to (1) saline placebo (PL) injection with placebo patch (PL+PL), (2) GnRHant with placebo add-back (GnRHant+PL), or (3) GnRHant with transdermal E2 (0.075 mg/d) add-back (GnRHant+E2) to alter E2 and FSH.CBV was normalized to blood pressure (cerebrovascular conductance index [CVCi]), with higher values indicative of greater cerebral blood flow.

Results: There was a marginal effect of the treatment by time interaction ($P = .09$). Exploratory within-group analyses reveal that CVCi was increased in postmenopausal women randomized to GnRHant+PL (0.58 ± 0.18 vs 0.64 ± 0.14 cm/s/mmHg^2, $P = .04$) to suppress FSH concentrations but was not altered in the other groups ($P > .481$).

Conclusions: FSH may regulate cerebral blood flow in postmenopausal women; additional studies are needed.

21. Factors Associated With Low Statin Prescription for Primary and Secondary Prevention Among Women: A National VA Study

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Background: Statins are first-line treatment for primary and secondary prevention of cardiovascular disease (CVD), the leading cause of death for women in the United States.

Objectives: To analyze prevalence of statin prescription and differences in treatment.

Methods: We conducted an electronic health record (EHR)-based epidemiological cohort study of women aged 18 years and older in Veterans Affairs (VA) care from 2009 to 2019 with cardiovascular disease, diabetes (aged 40-75 y), or dyslipidemia using the national VA database and Centers for Medicare & Medicaid Services data. Multivariable logistic regression models evaluated patient- and system-level factors associated with statin prescription.

Results: Among 188 240 women, 55% with an indication for a statin or dyslipidemia diagnosis were prescribed statin therapy (62% with CVD, 56% with diabetes, and 47% with dyslipidemia). Asian (37.9%) and Hispanic/Latina (37.8%) women were prescribed a statin less frequently compared to White and non-Hispanic/Latina women (45.9%, $P < .001$). A third (33%) of patients who had 2 or less primary care visits received a statin versus 52.3% who had 6 or more visits ($P < .0001$). In adjusted analyses, Hispanic/Latina and other racial minority women had lower odds of receiving statin therapy (OR 0.88, 95% CI, 0.84-0.92; OR, 0.94, 95% CI, 0.91-0.96, respectively) compared to non-Hispanic/Latina and White women. Women with 6 or more visits had over twice the odds of statin prescription compared to those with 2 or less visits (OR, 2.16; 95% CI, 2.10-2.22).

Conclusions: In a national sample of women, statin prescription for prevention of atherosclerotic disease was low. Our findings suggest a need to increase first-line hyperlipidemia treatment among women, address differences in treatment for minority women, and bolster primary care follow-up to improve adherence to guideline-based recommendations.

22. Association Between Biological Sex and Chronic Rhinosinusitis: Insights from the *All of Us* Research Program

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Background: Chronic rhinosinusitis (CRS) is an inflammatory sinonasal condition affecting 2% to 14% of adults in the United States and costing more than $10 billion annually. It is phenotypically divided into without (CRSsNP) and with (CRSwNP) nasal polyps. The inflammation-modulating properties of sex hormones provide a pathophysiological basis for anticipating biological sex-based differences in CRS, but this has not been thoroughly studied.

Objective: To investigate the association between biological sex and CRS among adults in the United States using a large national database.

Methods: This study was conducted among 393 890 participants from the *All of Us* Research Program. Data on CRS diagnoses and covariate data, including sociodemographics, risk factors, and comorbidities, were extracted. These variables were included in a multivariable logistic regression model to determine the independent association between biological sex and CRS. Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated. CRS prevalence was plotted by age group, stratified by sex.

Results: Female sex was associated with higher odds of CRSsNP (OR, 1.32; 95% CI, 1.28-1.32) but lower odds of CRSwNP (OR, 0.62; 95% CI, 0.57-0.68) compared to male sex after controlling for covariates. Analyzing sex differences by age revealed a shift among older participants (>69 y), where CRS prevalence dropped dramatically among females compared to males ($P < .001$).

Conclusions: Female sex was associated with higher odds of CRSsNP, but lower odds of CRSwNP compared to males. More research is needed to establish causation and better understand the mechanisms underlying this association.

23. Understanding Barriers and Preferences for Diabetes Management Support Among Youth With Type 2 Diabetes and Their Caregivers

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Background: Youth-onset type 2 diabetes (T2D) disproportionately affects females, with incidence rates nearly twice that of males. Youth-onset T2D progresses more aggressively than adult-onset T2D, making adherence critical to prevent complications. Yet, up to 70% of youth do not follow their prescribed regimens.

Objectives: To understand the barriers that influence diabetes-management behaviors and to identify the intervention needs and preferences of youth with T2D and their caregivers.

Methods: Youth (11-19 y) with T2D completed 2 weeks of ecological momentary assessment (EMA) surveys on daily barriers to medication, diet, and physical activity. Following EMA completion, caregiver-youth dyads participated in qualitative interviews designed to contextualize EMA findings and share perspectives on intervention needs and preferences.

Results: To date, 12 caregiver-youth dyads have completed interviews. Youth participants (mean age = 14.1 ± 2.5 y; 58% female) reported at least 1 barrier related to medication, dietary, or physical activity adherence during the EMA period. Preliminary qualitative findings reveal key emerging themes: (1) frequent day-to-day disruptions to diabetes management, (2) preference for digital platforms, (3) desire for youth-friendly education on T2D and treatment strategies, (4) importance of practical and emotional social support, and (5) interest in learning concrete adherence skills.

Conclusions: Youth with T2D encounter multifaceted challenges to treatment regimen adherence. Intervention development for this population should be tailored to their developmental stage and include strategies for fostering social support, delivering engaging education, and building adherence skills. Digital platforms are a promising and preferred option for delivering interventions and warrant consideration in future program design.

24. Cardiac Index Is Longitudinally Associated With Cerebrospinal Fluid Beta-Amyloid, a Core Alzheimer's Disease Biomarker, in Women but Not Men

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Background: Subclinical reductions in cardiac index are associated with lower cerebral blood flow and faster cognitive decline and may precede abnormal protein accumulation in Alzheimer's disease (AD).

Objectives: To examine the relationship between cardiac index and cerebrospinal fluid (CSF) biomarkers of core AD pathology (β-amyloid [$A\beta_{42}$] and phosphorylated tau [p-tau]).

Methods: Vanderbilt Memory and Aging Project participants (n = 153, 73 ± 8 y, 41% female) without dementia at baseline underwent echocardiogram at study entry and serial lumbar punctures over a 5-year period (mean follow-up = 4.0 y). CSF $A\beta_{42}$ and p-tau were analyzed in batch. Linear mixed-effects regression models related cardiac index to longitudinal CSF $A\beta_{42}$ and p-tau levels adjusting for baseline age, sex, race/ethnicity, education, modified Framingham Stroke Risk Profile, baseline cognitive status, and apolipoprotein E-ε4 status. Models were repeated with a sex interaction term and stratified by sex.

Results: In main effect models, cardiac index was unrelated to CSF $A\beta_{42}$ or p-tau levels (P values > .05). Cardiac index interacted with sex on CSF $A\beta_{42}$ levels ($P = .03$). In stratified models, lower cardiac index related to longitudinal decline in CSF $A\beta_{42}$ levels in females ($\beta = 34.3$; $P = .05$) but not males ($\beta = -8.3$; $P = .31$). There was no significant interaction with sex on CSF p-tau levels ($P > .05$).

Conclusions: In females, lower cardiac index may relate to progressively lower CSF $A\beta_{42}$ (but not p-tau levels) over time. Lower CSF levels of $A\beta_{42}$ are indicative of more accumulation of Aβ plaques in the brain. Future work on sex differences in the association between cardiac index and other AD biomarkers is warranted.

25. Discrepancies in Gestational Age by Dating Methods and Risk of Loss in a Prospective Pregnancy Cohort With First Trimester Research Ultrasounds

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Background: Interruption of normal pregnancy development noted on ultrasound is detectable prior to symptoms of pregnancy loss and could serve as a clinical indicator of future risk.

Objectives: To estimate the risk of pregnancy loss associated with discrepancies between last menstrual period (LMP)-based and ultrasound-based gestational dating in a prospective pregnancy cohort.

Methods: Participants in a community-based, prospective pregnancy cohort were recruited preconceptionally or in early pregnancy and underwent a standardized research ultrasound targeted for the sixth week of gestation. We calculated the difference between LMP-based and ultrasound-based gestational dating at the research ultrasound. Cox proportional hazard models were used to estimate the association between this difference and pregnancy loss. To assess for effect modification, analyses were stratified by week of research ultrasound, developmental stage, and menstrual regularity.

Results: Among 4935 participants, the median difference between LMP-based and ultrasound-based dating was 1 day (interquartile range: −1, 5 days) and 9.3% of pregnancies ended in loss. Risk of pregnancy loss increased exponentially with each additional day ultrasound-based dating lagged LMP- based dating ($P < .001$). A discrepancy of more than 5 days was associated with a notably elevated risk of loss (HR, 6.99; 95% CI, 5.78-8.44). These finding persisted when analyses were restricted to individuals with regular cycles and certain LMP dates.

Conclusions: Increasing discrepancy between LMP-based and ultrasound-based dating among asymptomatic patients strongly associates with pregnancy loss risk. This clinically quantifiable measure can substantiate concern for pregnancy loss prior to symptom onset among individuals who know their LMP.

Health Disparities

26. Racialized Income Inequality, the Cardiovascular Disease Continuum, and Black–White Disparities in Premature Mortality Among U.S. Adult Women

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Background: Black adults experience a disparate risk of outcomes along the cardiovascular disease continuum (CC)—the sequelae of conditions beginning with the onset of hypertension. This excess risk is largely attributable to income inequality. Black women are particularly at risk due to the economic consequences of existing as both Black and female in the United States. However, it is unclear to what extent income inequality impacts CC-related premature mortality among Black women relative to their White counterparts.

Objectives: To estimate the association between racialized income inequality and Black–White disparities in CC-related premature mortality among U.S. adult women.

Methods: This pooled cross-sectional analysis (2018 -2022) merged county-level income inequality data from the IPUMS Contextual Determinants of Health project with county-level mortality data for Black and White women aged 25-64. Linear regression estimated whether increased racialized income inequality significantly increased Black–White disparities in CC-related mortality—calculated as the county-level CC-related mortality rate among Black women divided by the rate among White women.

Mortality rates included hypertension, ischemic heart disease, atherosclerosis, atrial fibrillation, myocardial infarction, stroke, or heart failure.

Results: We examined 815 counties across 42 states and the District of Columbia. Average mortality rate was significantly higher among Black women compared to White women (179.6 vs 116.8, respectively), and the average mortality rate ratio was 1.7. Racialized income inequality was associated with a significant increase in Black–White disparities in CC-related premature mortality ($\beta = 0.79$; $P < .001$).

Conclusions: Income inequality is an intervenable determinant of Black–White cardiovascular disparities in premature mortality among U.S. women.

27. Geographic Patterns of HIV Risk Behaviors Among Older Adults: A Strategy for Identifying Space as a Risk Exposure

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Background: HIV prevention research among older adults remains limited, particularly with regard to how geographic variation influences risk. This study explores spatial patterns in HIV risk behaviors among adults aged 60 and older using national surveillance data.

Objectives: To examine regional differences in HIV risk behaviors among older adults and assess the influence of demographic and health-related factors across U.S. census regions and divisions.

Methods: Data from the 2019 Behavioral Risk Factor Surveillance System (BRFSS) were analyzed to assess self-reported HIV risk behaviors among adults aged 60 and older (n = 62 852). A dichotomous HIV risk behavior variable was examined using weighted logistic regression models to explore geographic variation across regions and divisions.

Results: Findings revealed significant geographic variation in HIV risk behaviors. The East North Central division of the Midwest had fewer significant predictors compared to other divisions. Across all regions, identifying as female, Hispanic, or not having a history of depression was associated with lower odds of reporting HIV risk behaviors. These results underscore the importance of considering geographic context when evaluating HIV risk among older adults.

Conclusions: Substantial variation exists in HIV risk behaviors by region, highlighting how large geographic units may obscure localized vulnerability. This study emphasizes the value of spatial mapping to capture contextual influences—such as structural disadvantage, partner access, and emotional health—that shape behavioral risk. Findings support the need for geographically informed HIV prevention strategies and suggest that older adults must be more explicitly reflected in spatial and implementation science research agendas.

28. Identification of Key Symptoms for a Core Outcome Set for Research in Vulvar Lichen Sclerosus: A CORALS Symptom Domain Initiative

Erin L. Foster (presenting author),[1] Maya Davis,[1] Amy X Li,[2] Jan Kottner,[3] Kim Thomas,[4] Rosalind Simpson,[4] Catherine Leclair[1]

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Background: Genital lichen sclerosus (LS) is a chronic inflammatory skin disease affecting men, women and children. It is most common in females, with an estimated 1% to 3% of women affected across their lifetime. Vulvar LS can cause significant symptoms and impact quality of life. To enhance the quality of clinical research and practice, core outcome domains have been identified including quality of life, clinical signs, and symptoms by the Core Outcome Set for Research in Lichen Sclerosus (CORALS) initiative.

Objectives: To identify key symptoms for the core outcome symptom domain for research in LS.

Methods: An international multidisciplinary steering committee was convened to define and discuss LS symptoms. A modified electronic Delphi process was conducted among experts to reach consensus on priority symptoms. An online patient survey was distributed to rank symptoms. A scoping review was performed to identify commonly measured symptoms in LS studies. Results from all 3 sources were analyzed and symptoms selected.

Results: Expert consensus identified 5 key symptoms: itch, pain with vaginal penetration, cuts and tears in the skin, pain, and irritation. The patient survey (n = 863) ranked itch, burning, pain, and cuts or tears in the skin as the most important symptoms, with pain with sex being most important to some, and least important to others. The scoping review of 93 manuscripts showed itch, pain with penetration, and burning/burning pain as the most frequently measured symptoms. Itch emerged as the most important symptom across all 3 data sources, with pain also consistently prioritized.

Conclusions: This study identified 5 key symptoms for evaluating LS. Based on the results, we suggest measurement of itch, pain, skin cuts and tears, burning, and (when relevant) pain with sex within the symptoms core outcome domain for LS. These findings will be used to inform content validity studies when evaluating potential measurement instruments for the Core Outcome Set. Both the survey and scoping review had a small population of male participants, highlighting the need for further research in this population.

29. Sex Differences in Clinical History Among Emergency Department Patients Tested for Pulmonary Embolism

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Background: For reasons that are complex and not well understood, women undergo diagnostic testing for pulmonary embolism (PE) at far greater rates than men, despite the disease incidence being higher in men overall. It is unknown whether differences in clinical presentation by sex contribute to this disparity in testing.

Objectives: To determine whether differences in clinical history between male and female emergency department (ED) patients are associated with testing patterns for PE.

Methods: This is a prospective, observational cohort study, conducted at a regional tertiary care hospital. Nonpregnant adult patients (aged 18 y and older) were eligible for inclusion if they presented to the ED between April 1, 2024, and February 1, 2025, with an eligible chief complaint (chest pain, shortness of breath, hemoptysis, syncope) and had objective testing for PE (imaging/laboratory). Patients who consented to participate completed a symptom survey at the time of enrollment. Data analysis was performed using Stata Statistical Software Version 18. This study was approved by the local institutional review board.

Results: We enrolled 129 patients with a mean age of 55.8 years; most patients (53.5%, 69/129) were female. Women and men had no statistically significant differences across 11 discrete symptoms. They were also equally likely (female 63.7%, 34/69; male 52.6%, 31/59; $P = .49$) to have delayed presentations. There were no significant differences in pretest risk by patient sex. The yield of testing (presence of PE) was similar for women (7.2%, 5/69) and men (5.1%, 3/59; $P = .61$).

Conclusions: Men and women tested for PE had similar symptoms and pretest risk. Differences in clinical presentation do not appear to account for the disparity in testing for PE by patient sex.

30. Sleep Quality and BMI: The Role of Menopausal Status in Patients in Low-Income Settings

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Background: Poor sleep quality is linked to adverse cardiometabolic outcomes, both of which deteriorate in menopause. Patients in low-income settings may experience poorer sleep and worse health outcomes due to adverse social determinants of health. Understanding associations between determinants, sleep quality, and cardiometabolic health across sex-menopausal status in low-income settings may inform targeted interventions to improve sleep and reduce cardiometabolic disparities.

Objectives: To identify determinants associated with poor sleep quality in federally qualified health center (FQHC) patients and associations between sleep quality and body mass index (BMI), overall and stratified by sex-menopausal status.

Methods: A cross-sectional survey was completed by 530 patients of 2 Louisiana FQHCs. Sleep quality was measured using the Pittsburgh Sleep Quality Index; poor sleep quality = score > 5. Multivariable logistic and linear regression estimated associations between determinants and poor sleep quality, and poor sleep quality and BMI, respectively, overall and by sex-menopausal status.

Results: Participants were predominantly Black (66.8%), with mean age 44.7 years and mean BMI 32.2; 52.6% reported poor sleep quality. Having a disability, loneliness, financial hardship, cost-related health care delays, perceived health care discrimination, and alcohol consumption were associated with poor sleep quality in the total sample. Poor sleep quality was associated with a 3.48-point (95% CI, 1.08-5.88) higher BMI among premenopausal women but not menopausal women (b = –0.25; 95% CI, –4.12-3.61).

Conclusions: In patients in low-income settings, poor sleep quality was associated with higher BMI among premenopausal women. Research with larger samples is needed to further explore how menopause impacts associations between sleep quality and cardiometabolic health.

Neuroscience

31. Relationship of Brain GABA and GABA/Glutamate Ratio with Circulating Progesterone

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Background: The GABAergic and glutamatergic systems in the prefrontal cortex of the brain are implicated in neurodegenerative conditions and psychiatric disorders such as depression. Preclinical studies of major depression have shown decreased $GABA_A$ receptor function and dysregulated glutamate levels in the frontal cortex and limbic areas. Progesterone acts as a positive modulator of $GABA_A$ receptors, possibly impacting the inhibition/excitation balance (i.e., GABA/glutamate ratio). However, limited knowledge exists on the effect of circulating progesterone on brain GABA and the GABA/glutamate ratio, in humans in vivo.

Objectives: To examine the association of brain GABA and GABA/glutamate ratio with circulating progesterone.

Methods: GABA and glutamate were measured using magnetic resonance spectroscopy (MRS) at 7 Tesla in the dorsal anterior cingulate cortex (ACC), ventromedial prefrontal cortex (VMPFC), and left dorsolateral prefrontal cortex (DLPFC) in 31 females. Pearson correlations were used to determine the association of brain metabolites levels with circulating progesterone concentrations.

Results: We observed a significant positive correlation of progesterone with VMPFC GABA as well as a trend positive correlation of progesterone with VMPFC GABA/glutamate ratio in females.

Conclusions: Our study provides evidence of increased VMPFC and VMPFC GABA/glutamate ratio in females with higher progesterone, suggesting that circulating sex hormones may be important factors to consider in future studies examining brain GABA levels in psychiatric and other disorders. Further, future studies should consider the interplay of progesterone and inhibition/excitation balance when examining mechanisms of depression in women.

32. The Role of Endogenous and Exogenous Hormones in Borderline Personality Disorder Symptom Severity and Treatment Response

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Background: Borderline Personality Disorder (BPD) is a chronic mental health disorder characterized by rapidly shifting emotional, interpersonal, and behavioral symptoms. Females are more likely to be diagnosed with BPD than males and exhibit more significant functional impairment. Ovarian hormone fluctuations may influence the manifestation of BPD symptoms.

Objectives: To examine how endogenous and exogenous hormones (from hormonal contraception) contribute to BPD symptoms.

Methods: The study includes 123 females aged 18-50 undergoing residential treatment for psychiatric disorders. Patients were categorized based on their contraceptive method: ovulation-suppressing contraceptives (e.g., oral contraceptives, Depo-Provera; N = 39) and naturally cycling (e.g., no contraceptives; N = 56). Estradiol (E2), progesterone (P4), testosterone (T), luteinizing hormone (LH), and follicle-stimulating hormone (FSH) levels were measured in a subset of 38 participants at admission and discharge. BPD symptom severity and emotional dysregulation were assessed by the McLean Screening Instrument for BPD (MSI-BPD) and Difficulties in Emotion Regulation Scale (DERS), respectively.

Results: Females using ovulation-suppressing contraceptives had higher emotional dysregulation at admission ($\beta = 5.9$; $P = .01$), had lower emotional dysregulation at discharge ($\beta = -5.7$; $P = .03$), and showed greater overall improvement compared to naturally cycling females ($\beta = -10.2$; $P = 1.6e\text{-}04$). Lower E2 at admission was associated with greater BPD symptom severity ($\beta = -1.39$; $P = .01$), and both lower E2 ($\beta = -3.89$; $P = .03$) and LH ($\beta = -2.39$; $P = .03$) were associated with higher emotional dysregulation. Moreover, decreases in LH ($\beta = -0.09$; $P = .04$) and FSH ($\beta = -0.12$; $P = .05$) were associated with greater improvement in BPD symptoms.

Conclusions: These findings suggest that hormonal regulation, through ovulation-suppressing contraceptives or reductions in gonadotropins, may support symptom improvement in BPD.

33. Sex-Specific Prediction of 1-Year Medication Nonadherence Using Machine Learning: Analysis of Medicare Fee-for-Service Ischemic Stroke Survivors

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Background: Nonadherence to guideline-directed medications (GDMs) is prevalent among stroke survivors, particularly in women.

Objectives: To develop and validate sex-specific machine-learning algorithms (MLA) to predict 1-year nonadherence to GDMs among Medicare stroke survivors.

Methods: Medicare beneficiaries discharged after a primary diagnosis of acute ischemic stroke between January 2013 to December 2020 and with a prescription filled for secondary prevention GDMs (i.e., statins and antihypertensives) were included. Patients were randomly divided into training, testing, and validation samples. Potential predictors included socio-demographics, medical history, area-level social factors, and filling prescription patterns. We evaluated 7 MLAs to predict nonadherence to GDMs, defined as the proportion of days covered less than 0.80 (i.e., prescription filling gaps) at 1 year. Prediction performance was assessed using C-statistic, and SHAP values were reported for the top 20 predictors.

Results: Our final cohort included 10 848 patients; of which 5589 (51.5%) were women. In both sexes, the gradient boosting machine (GBM) and histogram-based gradient boosting were best performing (C = 0.80 and 0.81, respectively) in the testing cohort. The GBM had a specificity of 86.4%, and negative

predictive value (NPV) of 73.5% in women, and a specificity of 87.6%, and NPV of 74.7% in men. Among both sexes, top predictors included polypharmacy and adherence to GDMs in the first 3 months post-discharge and 12 months prior. Less than high school education and proportion of households receiving food stamps were among top predictors in women.

Conclusions: MLAs appear to perform well for risk prediction of nonadherence to GDMs among stroke survivors in women and men.

34. Collision Sports Participation and Acoustic Startle Reflex in Female Adolescent Athletes

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Background: Collision and contact sports carry a greater risk of concussion and repetitive head impacts, and female athletes are significantly underrepresented in this area of research. Recent concussions and concussion history are both associated with acoustic startle suppression in adolescent athletes, but it is unknown how exposure to repetitive head impacts from collision sports participation may influence startle response post-concussion.

Objectives: To investigate the influence of collision and contact sports participation on acoustic startle reflex in female adolescent athletes following concussion.

Methods: We conducted a cross-sectional study on 16 adolescent athletes with a recent concussion (age: 15.1 ± 2.6 y, time since concussion: 35.3 ± 17.2 d). All participants self-reported their sport type (collision/contact vs limited contact/noncontact). Acoustic startle probes were administered to participants through noise-canceling headphones. The startle reflex was recorded via electromyography using electrodes placed under the right eye. The dependent variable was mean startle magnitude (μV), and sport type was the independent variable. We used an independent samples t-test to compare acoustic startle magnitude between the sport types.

Results: Mean startle magnitude was not statistically significantly different ($t(14) = -1.28$; $P = .22$) between the collision/contact sport athletes (77.0 ± 25.9 μV) and limited contact/noncontact sport athletes (98.6 ± 38.9 μV).

Conclusions: Collision sports participation does not appear to influence acoustic startle magnitude in female adolescent athletes. However, the collision/contact sport athletes did have a lower startle magnitude compared to other sport types. Future research should continue to investigate the consequences of repetitive head impacts in female athletes.

Public Health

35. Association Between Social Support and Clinical Outcomes in Older Adults with Kidney Disease

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Background: Older adults with chronic kidney disease (CKD) face a higher risk of adverse clinical outcomes. Social support, a modifiable factor, has been understudied in this population.

Objectives: To assess the association between social support and hospitalization, mortality, and CKD progression (50% decline in estimated glomerular filtration or transition to kidney failure) among older adults with non-dialysis-dependent CKD.

Methods: We analyzed data from the Chronic Renal Insufficiency Cohort study. Social support was assessed among adults aged 65 years and older using the Lubben Social Network Scale (LSNS), administered between 2013 to 2018 (baseline). Follow-up occurred until death, study withdrawal, or October 2024. Poisson and Cox regression analyses examined associations between social support and clinical outcomes, with stratification by sex and race/ethnicity.

Results: Among 2616 participants who completed the LSNS (mean age[SD] 71[5], 43% female, 45% White, 41% Black, 11% Hispanic), 23% had low social support (LSNS score < 12). After adjusting for sociodemographic and clinical factors, greater social support was linked to lower hospitalization risk in the full cohort (IRR, 0.89; 95% CI, 0.85-0.94), and women (IRR, 0.75; 95% CI, 0.70-0.81), Black (IRR, 0.90; 95% CI, 0.85-0.96), Hispanic (IRR, 0.84; 95% CI, 0.71-0.98), and White (IRR, 0.90; 95% CI, 0.82-0.98) subgroups. Social support was also associated with lower mortality in the full cohort (HR, 0.83; 95% CI, 0.71-0.98), women (HR, 0.76; 95% CI, 0.58-0.998), and Hispanic individuals (HR, 0.57; 95% CI, 0.35- 0.92). Social support was not associated with CKD progression.

Conclusions: In this cohort of older adults with CKD, increased social support was associated with a reduced risk of hospitalizations and mortality.

36. A Telehealth Family-focused Lifestyle Change Program for Rural Dwelling Caregivers and Their Children at Risk for Diabetes: Results of a Pilot Test

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Background: Family-based programs acknowledge that health behaviors are shaped and influenced by familial and environmental contexts. Because family history is a risk factor for type 2 diabetes (T2DM), focusing on the family unit could

address modifiable risk factors in adults while also engaging younger generations in developing healthy health habits.

Objectives: We present the results of a pilot test of a 3-month telehealth program that focused on positive behavior change strategies and a strength-based approach to improve the family health climate while reducing modifiable diabetes risk factors.

Methods: Rural-dwelling caregiver and child dyads with T2DM family history were enrolled. Data were collected pre- and post-intervention and included objective measures of physical activity (PA) and self-reported global health, family cohesion, social support, and family health. Post-intervention interviews assessed feasibility.

Results: Seventeen dyads (N = 34) were enrolled. Fifteen dyads completed the study with 86% adherence. Caregivers' moderate to vigorous PA increased post-intervention by 40.0 minutes ($P = .01$), and children's mean daily step counts increased by 1226.3 steps ($P = .08$). Caregiver reported measures showed improvements post-intervention to child global health ($P = .052$) and to adult global health ($P = .12$) and social support ($P = .004$). Interviews indicated that the program was feasible and acceptable.

Conclusions: This telehealth family-focused lifestyle change program was found to be feasible, with promising results for PA, global health, and social support. Programs that include both children and caregivers have the potential to not only impact adult health outcomes but also improve the health habits of youth at higher risk for developing T2DM.

37. Describing the Suspected Cardiac Arrest to a Telecommunicator: Does Sex Make a Difference?

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Background: Prompt delivery of bystander cardiopulmonary resuscitation (B-CPR) doubles survival from out-of-hospital cardiac arrest (OHCA). Females are less likely than males to receive B-CPR in public. Few studies have explored the impact of caller description of the suspected OHCA and sex differences.

Objectives: To examine caller's description of the suspected OHCA and differences by sex.

Methods: We performed a retrospective study of 9-1-1 calls of suspected nontraumatic adult OHCAs in a U.S. suburban county. Characteristics of the caller were analyzed descriptively to assess the association of caller sex and description of the suspected OHCA as unclear/vague or clear/detailed. Descriptive statistics were used.

Results: From April 2023 to September 2023, 197 suspected OHCA calls (188 patients) were recorded; 49% of the patients received B-CPR. Mean patient age was 56 ± 20, and 37% were female. Of these, 114 (58%) were identified as unclear/vague (73% patient male, 73% patient female), while 52 were identified as clear/detailed (36% patient male, 37% patient female). Of those that were unclear for female patients, 49% occurred when the caller was a male, while 51% occurred when the caller was female. Examples of unclear descriptions include "I don't know if he's dead or alive or just really out of it." and "I don't know what's going on." Reasons for an unclear/vague explanation included high emotional involvement, not wanting to touch the patient, not witnessing the arrest, and focus on demanding medical assistance.

Conclusions: This study suggests that the initial description of suspected cardiac arrest does not differ by caller or patient sex.

38. Addressing Opioid Mortality Among Pregnant and Parenting Populations in Virginia: Integrating Socioecological and Qualitative Data to Perform a Needs Assessment and Gap Analysis

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Background: More than 100 000 drug overdose deaths occurred nationally, profoundly impacting women and children. We received a grant from the Virginia Opioid Abatement Authority to develop an online toolkit to help local officials implement evidence-based strategies to reduce opioid-related mortality, including strategies focused on maternal and child health.

Objectives: To employ a strengths-based approach to opioid mortality and conduct a needs assessment and gap analysis for 1 region (Henrico, Chesterfield, and Hanover Counties, and the City of Richmond) for substance use disorder (SUD) resources for pregnant and parenting women.

Methods: We performed a mixed-methods evaluation guided by a community stakeholder-engaged process, including in-depth interviews with community stakeholders, community needs assessment survey, and socioecological data analysis. We used 2016-2022 data from the Virginia All-Payer Claims Database, 2016-2023 Virginia Department of Health opioid mortality data, and 2015-2022 American Community Survey data.

Results: The claims-level analysis identified improvement in rates of counseling services, access to recovery housing, and prescriptions for medications for opioid use disorder (OUD) among maternal populations between 2016 and 2021. Community needs assessment survey participants (n = 89) reported needs related to OUD treatment, including recovery residences/safe housing (91%), safe childcare (91%), and peer recovery services (85%). Stakeholders (n = 35) provided key insights to inform the SUD treatment system for pregnant/parenting populations.

Conclusions: Leveraging existing community resources through community-engaged approaches is essential for reducing opioid-related deaths among women and children. These findings provide valuable insights to inform strategies for addressing opioid mortality in Virginia and across the nation.

39. Exploring the Intersection of Recovery Capital and Sexual and Reproductive Autonomy for Women With Substance Use Disorder

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Background: Women with substance use disorder (SUD) have unique sexual and reproductive health disparities. Specifically, they have higher rates of unintended pregnancies (>75%) and are 3 to 5 times more likely to be victimized by violence and reproductive coercion than women without SUD. One avenue to reduce risks associated with SUD, while improving health and access to resources, is through building recovery capital (RC). RC is an asset-based, ecological model whereby human, financial, social, and community factors can enable well-being, mitigate harms associated with addiction, and promote long-term recovery. Sex work is an understudied and complex determinant of sexual and reproductive health and autonomy that potentially impacts RC.

Objectives: To explore experiences and perceptions related to the intersection of RC, autonomy, sexual and reproductive health, and sex work.

Methods: We are currently conducting a descriptive qualitative study consisting of focus groups of peer support specialists who work in recovery community centers. Peers will be asked to share their expertise related to their own lived experiences and experiences of participants with whom they have worked.

Descriptive content analysis will be used to code and interpret the social context to develop meaningful conclusions as themes.

Results: We anticipate this study will yield valuable insights into issues surrounding the context of sex work and SUD, specifically nuances related to choice, circumstance, and coercion, and the impact on recovery capital.

Conclusions: Enabling trusted community partners to describe lived experiences can inform the science of RC, lead to effective strategies in peer support services, and reduce disparities for people with SUD.

40. Real-World Use of Fezolinetant, a Novel Nonhormonal Neurokinin 3 Receptor Antagonist for Treating Moderate-to-Severe Vasomotor Symptoms From Menopause

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Background: In May 2023, Veozah (fezolinetant) was approved as a nonhormonal treatment for moderate-to-severe vasomotor symptoms of menopause, providing a treatment option for those with contraindications to hormone replacement therapy. To our knowledge, no studies have been conducted on the real-world utilization of fezolinetant and uptake among breast cancer survivors, for whom hormone replacement is contraindicated given the risk of cancer recurrence.

Objective: To characterize the uptake of fezolinetant in A real-world setting.

Methods: We conducted a retrospective cohort study using TriNetX data, which includes 69 health care organizations and more than 60 million patients. Females aged 18 years and older with an initial prescription for fezolinetant between June 1, 2023, and November 1, 2024, were included. We described baseline patient characteristics and examined the monthly trends in the number of fezolinetant prescriptions over time.

Results: The total number of fezolinetant prescriptions increased over time, from 489 prescriptions in the June-August 2023 quarter to 2812 prescriptions in the September-November 2024 quarter. Our cohort included 7283 women initiating fezolinetant 45 mg, including 1363 (18.7%) with breast cancer or breast cancer history. The mean age was similar between the overall cohort and those with breast cancer history (56.4 y vs 56.0 y, respectively). Among those with breast cancer history and hormone receptor testing, 44.8% had estrogen receptor positive status and 7.3% had progesterone receptor positive status.

Conclusions: Our findings show a dramatic increase in fezolinetant uptake since its approval and highlight a need for future postmarketing safety and efficacy studies, especially among breast cancer survivors, who were excluded from the fezolinetant randomized controlled trials.

41. Sex-Specific Changes to Overnight Blood Pressure With Transition to Early-Morning Shiftwork

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Background: Impairments to overnight blood pressure (BP) dipping (i.e., "non-dipping", <10% decrease from daytime BP) occur rapidly when transitioning into a shift working occupation. The misalignment of behaviors (i.e., sleeping) with the internal circadian clock (i.e., circadian misalignment) likely contributes to these adverse cardiovascular consequences. We have shown that circadian misalignment affects sex- specific cardiometabolic mechanisms in healthy, non-shift working adults; however, it is unclear whether transition to shiftwork affects BP dipping in a sex-specific fashion.

Objectives: To determine the sex-specific changes to BP dipping with transition to shiftwork.

Methods: Using a natural experiment whereby newly hired bus operators began day-oriented onboarding training at baseline followed by transition into an early-morning shiftwork schedule, 24-hour ambulatory BP was measured in 10 participants (5 female). Sex differences at baseline were assessed using independent t-tests. Mixed effects linear models were used to examine the changes in BP dipping, with fixed factors for sex and time (baseline vs 90 d of early-morning shiftwork) and subject as a random intercept.

Results: There were no sex differences at baseline in age (mean ± SD, females vs males, respectively; 33.6 ± 6.8 y vs 36.7 ± 7.6 y; $P = .26$), but there was a nonsignificant trend for females having greater BP dipping (12.7 ± 3.1% vs 8.33 ± 5.5%; $P = .08$). A significant sex-by-time interaction ($F(1,20) = 5.8$'; $P = .02$) showed that compared to baseline, females had significantly worse BP dipping at 90 days (3.1 ± 5.5%) than males (7.1 ± 2.1%).

Conclusions: Females exhibited worse BP dipping profiles following 90 days of early morning shiftwork. Future work is needed to identify how circadian misalignment associated with shiftwork affects sex-specific health mechanisms.

Reproductive Health

42. Artificial Intelligence Powered Electrocardiograms as a Novel Digital Biomarker in Cardio-Obstetric Care

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Background: Cardiovascular disease (CVD) is the leading cause of maternal death in the United States, with cardiomyopathy being the primary cause of death in the late postpartum period. Cardiomyopathy symptoms can mimic those seen with normal pregnancy, leading to diagnostic delays and poor outcomes.

Objectives: To examine the impact of artificial intelligence (AI)-guided screening on cardiomyopathy diagnosis and the association between AI-predicted metrics and cardiovascular outcomes among pregnant and postpartum women.

Methods: A pragmatic randomized controlled trial was conducted among pregnant and postpartum women (median age, 31 y) in Nigeria from August 2022 to September 2023, with follow-up until May 2024. The trial randomized 587 women to intervention and 608 to control. The intervention arm had digital stethoscope recordings with real-time AI predictions for cardiomyopathy and asynchronous 12-lead electrocardiogram (ECG) predictions. Logistic regression was used to estimate odds ratio (OR) for cardiomyopathy (primary endpoint), any CVD, and mortality.

Results: Screening with the digital stethoscope had ORs of 12.9 (95% CI, 3.04-54.90), 11.2 (95% CI, 2.62-48.16), and 9.6 (95% CI, 2.21-41.49) for detection of cardiomyopathy at ejection fraction thresholds <45%, <40%, and ≤35% respectively. Within the full study cohort, delta-age (adjusted AI- predicted age − chronological age) greater than the 75th percentile had ORs of 2.06 for any CVD, 4.98 for cardiomyopathy, and 32.81 for all-cause mortality ($P < .001$).

Conclusions: AI-guided screening improved the diagnosis of cardiomyopathy in obstetric patients. Additionally, AI-derived biological age appears to be a valuable indicator of maternal cardiovascular health status. Its utility in obstetric care will require additional studies.

43. Rooted in Health: Characterizing Nutrition Context to Inform a Plant-Forward Dietary Intervention for Gestational Diabetes Mellitus Prevention in Black Pregnant Women

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Background: Black women with gestational diabetes mellitus (GDM) face greater cardiometabolic risk during and after pregnancy compared to those without GDM. Yet, few interventions target GDM prevention in this population through dietary behavior change.

Objectives: To explore the relationship between food security, fruit/vegetable intake, and perceived nutrition environment among Black pregnant women at risk/affected by GDM.

Methods: Chicago Black pregnant women at risk/affected by GDM were recruited to complete a 136- item online survey. The National Cancer Institute's Dietary Screener Questionnaire II, U.S. Department of Agriculture Household Food Security Questionnaire, Chicago Health Atlas Data, and Perceived Nutrition Environment surveys were used to assess fruit/vegetable intake, food security/access, and perceived neighborhood/primary food shopping outlet healthiness. Descriptive and correlative analyses were performed using SPSS.

Results: Eighty-two participants completed the online survey, including 17 with GDM. On average, most participants were aged 18-41 years, experienced a body mass index (BMI) of greater than 30 kg/m^2 (69%), were single (54%), earned less than $50,000 (78%), and lived in neighborhoods with low food access (65%) and limited access to fruits/vegetables (78%). Most participants consumed 3.25 (SD ± 0.19) cups of fruits/vegetables/day, indicated food insecurity without hunger (μ score = 2.6 ± 2.9), and perceived neighborhood/primary food shopping outlets as moderately healthy (77%). The measures examined showed no significant differences between individuals at risk or affected by GDM.

Conclusions: These findings highlight structural and contextual challenges, such as food insecurity and limited access to healthy foods, influencing dietary intake among Chicago Black pregnant women, underscoring the need for collaborative, community-driven solutions to develop effective and sustainable interventions.

44. The Oviduct and Mesometrium Trigger Uterine Contractions in Labor

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Background: Improved understanding of uterine contraction physiology could guide design of better therapies for managing labor and treating preterm birth. Labor contractions are quasi-periodic, but the basis of this periodicity is unknown. Traditional techniques have not revealed clear origins of activity; therefore new approaches are needed.

Objectives: To visualize contraction-associated calcium dynamics in live mice during labor.

Methods: The calcium sensor GCaMP6s was expressed using a transgenic mouse line. Transgene expression pattern was characterized with immunofluorescence and confocal microscopy. Pregnancies in transgenic animals were achieved with time-restricted breeding. GCaMP6 signals were captured intrapartum (between birth of first and last pup), using an open surgical

approach and an ultra-widefield imaging system. Image processing and analysis were performed in MatLab.

Results: GCaMP6s showed uniform staining in the longitudinal and circular muscle layers of the uterus in fixed tissue sections from intrapartum animals. Transgenic animals had a gestational length of 19.0 ± 0.2 days and litter size of 7.3 ± 1.3 pups, similar to wildtype C57 mice. Uterine activity with distant propagation (>1 mm) occurred every 1 to 3 minutes. Most (~85%) of these events originated either in the oviduct or discrete locations in the mesometrium. Both sites showed higher activation frequencies than the uterine horn. A subset (25-50%) of activations generated only highly localized uterine calcium responses, suggesting horn refractoriness.

Conclusions: We have identified the origin sites for most labor contractions in a mouse model. Future work will study the molecular and cellular mechanisms operating at these sites.

45. Identifying Psychosocial Risk Factors of Postpartum Depressive Symptoms: A Data-Driven Approach

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Background: A wide range of psychosocial risk factors of postpartum depression (PPD) have been identified. However, few studies have leveraged data-driven approaches to determine which factors have the highest predictive utility for predicting depressive symptoms both dimensionally and in terms of classification (individual has "elevated depressive symptoms" or "non-elevated depressive symptoms").

Objectives: We used a data-driven approach to determine (1) the psychosocial risk factors with the highest predictive utility for postpartum depressive symptoms dimensionally, via regression, and (2) the risk factors with the highest predictive utility for classifying individuals as "elevated" or "non-elevated" for depressive symptoms.

Methods: Participants (n = 102) were enrolled in a study of PPD, and inclusion criteria required them to have experienced at least 1 major depressive episode. Psychosocial risk factors and depressive symptoms (CES-D) were collected at 6 weeks postpartum (mean = 7.0, SD = 5.79). A CES-D cutoff of 16 defined elevated symptoms. Perceived stress, social support, trauma history, mindfulness, and discrimination were tested as psychosocial risk factors. Models used logistic and LASSO regression with 3-fold cross-validation, with 68/34 train/test splits.

Results: Perceived stress and mindfulness were features with high predictive utility for classifying participants as "elevated" versus "non-elevated" depressive symptoms (AUC = 0.92). Only perceived stress was identified to have high predictive utility for depressive symptoms dimensionally ($R^2 = 0.48$).

Conclusions: Elevated perceived stress is a potential risk factor for elevated depressive symptoms postpartum. However, it is unclear whether increases in perceived stress across the postpartum period can forecast future depressive symptom increases. Determining this will be the focus of this BIRCWH project.

46. A Mixed Methods Study to Explore the Integration and Function of Social Workers in the Maternal Health Care of Women with Pregnancy-related Cardiovascular Disease

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Background: Cardiovascular disease is the leading cause of death for women before, during, and after pregnancy, accounting for 20% of female deaths and 30% of maternal deaths. Social workers are professionally trained to address social drivers of health that can impact risk for cardiovascular disease; however, they are grossly underutilized in health care delivery. With mental health conditions as a correlate and consequence of cardiovascular disease accounting for a significant proportion of pregnancy- related deaths, the intersection of physical and mental health must be prioritized in maternal health care.

Objectives: To investigate the integration and function of social workers in maternal health care of women with cardiac severe maternal morbidity (SMM).

Methods: Clinical social worker (CSW) notes were abstracted from electronic health records (EHRs) of patients with cardiac SMM diagnoses who gave birth at Duke Hospital from 2016 to 2021. We determined (1) how many patients interacted with CSWs before and/or after delivery, (2) interaction frequency, and (3) frequency of social worker-generated referrals.

Results: Among 201 patients, 80 patients (40%) received a CSW referral from their OB provider; 98 patients had CSW interactions with the majority (85%) with only 1 interaction. Black patients were less likely to receive a CSW referral, more likely to have a CSW interaction, and more likely to have multiple CSW interactions. Analysis of referrals from CSWs is ongoing.

Conclusions: Further assessment of CSW interactions is needed to understand the underutilization of social workers and to develop strategies to leverage their potential to improve maternal health outcomes at the patient-, provider-, and system levels.

Sex Differences

47. Sex-Specific Association Between Maternal Anemia and Neonatal Hemoglobin

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Background: Insufficient iron accrual in utero can permanently impair infant neurodevelopment. Low neonatal hemoglobin (Hb) may indicate inadequate fetal iron capture and storage. Prior studies differ on whether and under what conditions maternal anemia predicts neonatal Hb.

Objectives: To identify maternal determinants of neonatal Hb and sex differences therein.

Methods: Maternal and infant Hb, sociodemographic, and health data were abstracted from the electronic medical records

of biorepository participants at a tertiary academic medical center in 2020 to 2023.

Results: In 228 participants, the prevalence of maternal anemia at delivery (Hb <11 g/dL) was 44%. Neonatal hematology was available for 50% of newborns. Median (IQR) neonatal Hb was 16.7 g/dL (14.9, 18.0) and did not differ by sex. Median Hb was lower among infants of mothers with anemia versus without (15.9 g/dL vs 17.1 g/dL; $P = .032$), and among infants of Black mothers (16.0 g/dL) versus Hispanic (17.9 g/dL), or Other (17.0 g/dL) ($P = .003$). In multivariable models, maternal anemia and Black (vs Hispanic) race and ethnicity were each associated with lower neonatal Hb in male but not female infants.

Conclusions: Sex-specific associations were observed between maternal characteristics and neonatal Hb. Sex differences may elucidate conflicting evidence regarding maternal and prenatal determinants of neonatal iron endowment. Future studies will replicate these findings with a more comprehensive panel of iron biomarkers in mothers and neonates and investigate the functional consequences of observed lower neonatal Hb in male infants of anemic mothers.

48. Sex Differences in Training Characteristics and the Relationship to Performance Among Boston Marathon Runners

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Background: Physical training influences competitive marathon performance. However, sex-based differences in training modes and changes (TMCs), and the relationship with endurance performance, have not been well described.

Objectives: To compare training modes and TMCs between male and female marathon runners, and the relationship with performance by sex.

Methods: Adult Boston Marathon registrants completed an electronic survey pre-race for demographics, experience, and training pre-race. TMCs were calculated comparing 12-4 and 4-0 month timeframes of pre-race training. Race performance was obtained from chip timing data. Separate multivariate analyses of covariance (age, experience) were used to compare training modes by sex. Separate linear regressions were used to assess the effects of pre-race training and TMCs on performance by sex.

Results: There were 917 respondents (495 female and 422 male; performance: 3:45 ± 0:39 hr:min). Females completed more bouts of cross-training per week ($P < .001$) and total bouts of weekly training (running + cross-training; $P = .003$) compared to males. Females completed less weekly running distance compared to males ($P = .03$). TMCs did not differ by sex ($P = .06$). Training modes explained 48.6% of the variance in performance for females, and 61.9% for males. Running volume was associated with improved performance among males ($P < .001$). Running more quality sessions (i.e., workouts) was associated with improved performance among females ($P = .01$). Increased cross-training bouts per week were associated with better performance across sexes (P range: < 0.001-0.02). TMCs of reduced weekly runs pre-race was associated with better performance for females ($P < .001$).

Conclusions: Training modes for a competitive marathon differed by sex, which were significantly associated with performance, suggesting sex-specific advantageous training adaptations.

49. Sex Differences in Response to Bariatric Surgery

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Background: Obesity is associated with hyperandrogenism in women and hypogonadism in men. Decreased gut microbiome diversity and altered composition are also seen in obesity. While bariatric surgery is the most effective treatment for obesity and improves microbiome alterations, clinical outcomes differ by sex. It is unclear whether postoperative microbiome changes may improve obesity- related hormonal dysregulation.

Objectives: To examine how bariatric surgery affects obesity-related hyper/hypoandrogenism and microbiome alterations, and whether sex-dependent microbiome differences contribute to sex-specific outcomes.

Methods: In an exploratory study of participants undergoing gastric bypass, feces and blood were collected preoperatively and 2 months postoperatively. Fecal shotgun metagenomic microbiome analyses and ultra-performance liquid chromatography/mass spectrometry will measure plasma sex hormone levels. Weight loss and metabolic outcomes (e.g., glycemic dysregulation, hyperlipidemia) categorized by sex will be correlated with differences in microbiome and androgen patterns using PLS-DA to identify changes discriminant of sex.

Results: Fifty-one participants were enrolled with completed collection of biospecimens. Preoperative and 2-month postoperative mean age, body mass index, low-density lipoprotein (LDL), triglyceride, fasting glucose, and hemoglobin A1c (HbA1c) were similar between sexes. Total cholesterol, high-density lipoprotein (HDL), and HbA1c significantly decreased in women while only HbA1c decreased in men. Shotgun metagenomic microbiome and metabolomic analyses will be performed next.

Conclusions: This proposal examines the biologic underpinnings of sex-specific differences in bariatric surgery outcomes. Understanding postoperative microbiome differences by sex and the impact of surgery on microbiome-mediated hormonal alterations may lead to further mechanistic studies to understand sex-specific outcomes and allow for possible pre/probiotic interventions to aid in the multidisciplinary care of obesity.

50. Administrative Burden Impacts Care for Young Women with Congenital Heart Disease

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Background: Women with congenital heart disease (CHD) face compounding clinical risks during transition from pediatric to adult care; disruptions in cardiac monitoring, insurance, and reproductive and mental health management are common.

Objectives: This observational mixed methods study evaluates sex differences in transition education encounters among youth aged 12-26 years with CHD to improve transition to adult care.

Methods: A representative sample (n = 16) of patients referred to a CHD Transition Clinic from 2024 to 2025 tested adapted transition readiness assessments. Transition education was observed, and a total sample of participants (schedulers, nurses, care coordinators, patients, family members, physicians; n = 78) were interviewed. Qualitative ethnographic data were collected, transcribed, and analyzed with NVivo14.

Results: Participants described referral delays, burdensome paperwork, and confusion about insurance coverage. Clinic observations revealed patterns of indexical alignment and temporal deixis by speaker sex and role. Females frequently used proxy speech—as intermediaries for patients or institutions—while males rarely spoke on behalf of others. Female speakers more often anchored utterances in lived experience linked to administrative requirements, a difference that persisted in interviews.

Conclusions: Bureaucratic barriers substantially hinder effective transition care for CHD patients. Women bear a disproportionate communicative burden, an index of their structural position in the transition process. Reducing administrative complexity through streamlined systems and education interventions may improve access over the life course.

51. Sex Disparities in Adaptive and Innate Immune Cells and Kidney Function in the Health and Retirement Study (HRS)

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Background: Chronic kidney disease (CKD) exhibits sex disparities, with females having a higher age- adjusted prevalence than males. However, mechanisms underlying these differences remain unclear. Given the known sex differences in immune cells, immune-related pathways may contribute to CKD disparities.

Objectives: To evaluate sex differences in immune cells subsets and estimated glomerular filtration rate (eGFR) in the Health and Retirement Study (HRS).

Methods: We used eGFR measures and 29 immune cell subsets from the 2016 HRS Venous Blood Study. Multinomial logistic and linear regression models estimated the association between immune cell subsets and eGFR (categories and continuous), stratified by sex. Models were adjusted for survey design and age, race/ethnicity, body mass index (BMI), hypertension, diabetes, alcohol use, smoking status, cytomegalovirus, and inflammation. Significance was determined using false discovery rate (FDR)-adjusted *P* value.

Results: Among 8966 HRS participants (aged 56-107 y) with complete data, 54% were female. Of females, 24% had eGFR less than 60 mL/min/1.73 m^2, compared to 19% of males. Notably, after adjustment, CD8+ T cell subsets showed opposing sex-specific effects, with CD8+ effector memory T cell (Tem) showing pronounced divergence. In females, higher CD8+Tem was associated with decreasing eGFR (β-trend = –0.98; P_{FDR}-trend = 0.034); whereas in males, higher CD8+Tem was nonsignificantly associated with increasing eGFR (β-trend = 0.63; P_{FDR}-trend = 0.158). Additionally, in males, higher NK cells:CD56LO and plasmacytoid dendritic cells were significantly associated with increasing eGFR and myeloid dendritic cells with decreasing eGFR but not in females. In females, higher neutrophils were associated with increasing eGFR.

Conclusions: CD8+Tem exhibits sex-specific associations with kidney function, suggesting potential immune-mediated mechanisms underlying CKD disparities.

52. Sex Differences in Exercise Participation Among Veterans: A LIMBIC-CENC Study

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Background: National physical activity guidelines for adults include weekly moderate-to-vigorous aerobic exercise (MVAE) and strength training (STR) targets for health-related benefits. These exercise targets are not sex specific; however, male and female military Veterans may engage in exercise-related activities differently, which may inform the need for sex-specific education or other interventions to meet those targets.

Objectives: To describe MVAE and STR participation among military Veterans and compare odds of meeting MVAE and STR recommendations between sexes.

Methods: Veterans from the Long-term Impact of Military-relevant Brain Injury Consortium—Chronic Effects of Neurotrauma Consortium prospective longitudinal study (n = 1715; aged 42.0 ± 10.7 y; n = 228 [13.3%] female) self-reported exercise activities via the Behavioral Risk Factor Surveillance Survey. Responses were examined to determine whether they met MVAE or STR recommendations, both recommendations, or neither recommendation (referent group). Associations in meeting MVAE and STR recommendations by sex were tested with a multinomial logistic regression model covarying for age, military service years, pain interference, depression symptoms, education attainment, and relationship status. Odds

ratios (ORs) with 95% confidence intervals (95% CI) were calculated and considered statistically significant if they did not include 1.0.

Results: Overall, 33 (14.5%) and 251 (16.9%) female and male Veterans, respectively, met both recommendations; 48 (21.1%) and 229 (15.4%) met only MVAE; 33 (14.5%) and 343 (23.1%) met only STR; and 114 (50.0%) and 664 (44.7%) met neither. Female Veterans had lower odds of meeting only STR recommendations relative to males (OR, 0.48; 95% CI, 0.32-0.73).

Conclusions: Most female and male Veterans reported not meeting both exercise recommendations, and female Veterans were significantly less likely to meet STR recommendations than males.

53. Sedentary Behavior, Self-Efficacy, and Diabetes Management in Older Women and Men With Type 2 Diabetes: Baseline Data from the STEP Up T2D Study

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Background: Prior research demonstrates that interrupting or breaking up sedentary behavior (SB) benefits cardiovascular health, particularly in people with type 2 diabetes (T2D). However, most people with T2D are highly sedentary. The STEP Up T2D study is an ongoing, randomized crossover trial evaluating sex differences in the acute effects of SB interruptions on vascular function.

Objectives: To examine relationships between SB, self-efficacy, and diabetes management among women and men aged 60 and older with T2D.

Methods: Data were collected on hemoglobin A1c (HbA1c) and medical history. Participants completed questionnaires evaluating diabetes self-management (Problem Areas in Diabetes [PAID]) and self- efficacy to reduce SB (Self-Efficacy to Reduce Sedentary Behavior Scale [SRSB]) and increase exercise (Exercise Confidence Scale [ECS]). Sedentary time and sit-to-stand transitions were measured via thigh- mounted accelerometer. Analyses were conducted with R (v.4.3.2); $P < .05$ was statistically significant.

Results: The sample (N = 31 adults, 58% women) had a mean (SD) age of 72.4 (5.7) years and HbA1c of 6.9% (0.8). Men were more sedentary than women (12.3 vs 10.6 h; $P = .04$). There was a moderate negative correlation between sit-to-stand transitions and HbA1c ($r = –0.45$; $P = .03$). ECS and PAID were significantly correlated among women ($r = –0.74$; $P = .003$) but not men ($r = 0.15$; $P = .67$). Similarly, ECS and SRSB were significantly related in women ($r = 0.58$; $P < .001$) but not men ($r = 0.21$; $P = .50$).

Conclusions: Among older women with T2D, self-efficacy to reduce SB and increase exercise are related yet distinct constructs that warrant consideration in SB interventions. Future research is needed to target SB and thereby reduce cardiovascular risk in people with T2D.

54. Microglia Density in the Thalamus Is Influenced by Sex in Multiple Sclerosis

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Background: Chronic microglia activity in the central nervous system (CNS) promotes neurodegeneration and progression in multiple sclerosis (MS). 18-translocator protein (TSPO) PET using a third-generation tracer, ^{11}C-ER176, can quantify microglia density in CNS, including in the thalamus, a key CNS relay commonly affected in patients with MS (pwMS).

Objectives: To investigate age and sex differences in thalamic microglia density in pwMS and controls.

Methods: In a prospective case-control study, 50 pwMS and 55 controls underwent ^{11}C-ER176 PET.

Results: Age and sex were similar between controls (mean ± SD age: 48.2 ± 15.4 y; 65% female) and pwMS (49.6 ± 12.9 y; 72% female) ($P > .05$). Age did not correlate with thalamus ^{11}C-ER176 uptake in controls ($r = 0.19$; $P = .17$) or pwMS ($r = –0.05$; $P = .73$). A gradient of increase was observed in thalamus ^{11}C-ER176 uptake among male controls (1.13 ± 0.06), female controls (1.18 ± 0.06), male pwMS (1.25 ± 0.10) and female pwMS (1.22 ± 0.07; $P < .001$). Thalamus ^{11}C-ER176 uptake was higher in females than males within controls ($P = 0.009$), whereas it was similar in pwMS ($P = .24$). Within females ($P = .015$) and within males ($P < .001$), thalamus ^{11}C-ER176 uptake was higher in pwMS than controls.

Conclusions: Sex influences thalamus ^{11}C-ER176 uptake and should be accounted for as a biological variable in future studies and trials using ^{11}C-ER176 PET. The sex difference in controls was nullified in pwMS, possibly due to a more significant increase in thalamus ^{11}C-ER176 uptake in male pwMS than female pwMS compared to controls. The higher difference gradient in thalamus ^{11}C-ER176 uptake in males may be related to more severe and progressive MS course in males compared to females.