lead to increased mutual understanding of CER principles, enhanced appreciation for diverse forms of expertise, and strengthen trust.

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Comparative cardiovascular risk burden across autoimmune diseases: Evidence from a primary care cohort

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OBJECTIVES/GOALS: To generate phenotype-specific insights that support tailored prevention strategies and advance precision cardiovascular risk management within Gulf health systems. METHODS/STUDY POPULATION: We analyzed collected primary care records and retained 14,616 complete cases. A composite CV risk index was constructed using a Framingham-based general CVD algorithm from standard clinical variables. "High risk" was defined as the top cohort quartile. Between-group differences were tested with the Kruskal–Wallis test followed by Dunn's multiple comparisons with Benjamini–Hochberg adjustment. We then modeled (i) the binary high-risk outcome using multivariable logistic regression and (ii) the continuous index using linear regression. Adjusted models included body mass index (BMI), log(ESR + 1), log(CRP + 1), and statin use; variables embedded in the index were not re-adjusted to avoid over-adjustment. RESULTS/ANTICIPATED RESULTS: The proportion above the high-index threshold differed by group: RA 29.4%, no autoimmune 25.7%, multiple-autoimmune 23.9%, SLE 19.8%, and Hashimoto's 12.7%. The Kruskal–Wallis test was significant ($H=68.6$, $df=4$, $p<10-13$), with Dunn tests (BH-adjusted) showing RA > no autoimmune and SLE, and Hashimoto < all groups. In adjusted logistic regression, odds of high index were higher in RA (OR 1.20, 95% CI 1.06–1.37), lower in Hashimoto (OR 0.49, 95% CI 0.40–0.60), and not clearly different in SLE or multiple-autoimmune. Higher BMI (OR/unit 1.08), ESR (OR/log 1.06), and statin use (OR 4.97) were strongly associated. DISCUSSION/SIGNIFICANCE OF IMPACT: In a large primary care cohort, RA showed modestly higher CV risk than non-autoimmune patients after adjustment, while Hashimoto's showed lower burden. Findings support targeted control of risk factors, especially blood pressure, weight, and inflammation in autoimmune populations.

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Pregnancy outcomes following hormonal intrauterine device discontinuation: A prospective cohort study

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OBJECTIVES/GOALS: The objective is to determine the relationship between prior progestin intrauterine device (IUD) use, duration of use, and adverse pregnancy outcomes and also to examine the return-time to fertility and whether demographic factors modify the effect of IUD use on pregnancy outcomes. METHODS/STUDY POPULATION: This is a prospective cohort study of 600 pregnant adults between 10 and 28 weeks of gestation who have not delivered a fetus. We will compare participants with and without prior progestin IUD use. Participants are recruited via flyers posted in university-associated OB-GYN clinics and via the health portal, MyChart. Participants complete a comprehensive contraception, medical, and pregnancy history and receive compensation. Pregnancies are followed until 6 weeks post-delivery, and outcomes are collected via the electronic health record. Pregnancy outcomes will be analyzed using multivariable logistic regression with adjustment for confounders, with sensitivity analyses stratified by duration of prior progestin IUD use. RESULTS/ANTICIPATED RESULTS: We will characterize the prevalence and duration of progestin IUD use in the cohort and evaluate demographic factors associated with IUD use compared to other contraceptive methods. We will compare the rates of placental abnormalities, as well as miscarriage, preterm birth, hypertensive disorders of pregnancy, including preeclampsia and gestational hypertension, and other complications, between participants with prior progestin IUD use versus non-use. Among participants with prior IUD use, we will examine whether the risk of adverse pregnancy outcomes is associated with the length of use. We will also examine the time between the last contraceptive use and conception. DISCUSSION/SIGNIFICANCE OF IMPACT: An association between prior progestin IUD use and pregnancy outcomes would be a novel finding and will have clinical implications for how contraceptive history may inform counseling and reproductive care. We hope that this study will rationalize the need for well-powered, larger studies to investigate the robustness of our study findings.

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Dual roles of β2-adrenergic signaling in the progression of acute myeloid leukemia*

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OBJECTIVES/GOALS: To determine how loss of sympathetic nerves and β2-adrenergic receptor (Adrb2) signaling remodels the leukemic bone marrow niche, alters immune responses against leukemia, and influences acute myeloid leukemia (AML) progression. METHODS/STUDY POPULATION: AML was modeled using MLL-AF9-driven murine leukemia and human AML xenografts (MOLM-13 and patient-derived samples) in NOD scid gamma (NSG) mice. Sympathetic signaling was disrupted chemically with 6-hydroxydopamine or genetically using Adrb2 knockout mice. Leukemic burden,

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survival, and immune composition were analyzed by flow cytometry and imaging. Public RNA-seq and clinical datasets were used to assess ADRB2 expression and its prognostic value in AML patients. RESULTS/ANTICIPATED RESULTS: AML induces sympathetic neuropathy in both mouse and human bone marrow. Denervation or Adrb2 loss accelerated AML and reduced survival in immune-competent mice, correlating with decreased $CD8^+$ T cell activity. In contrast, denervation reduced leukemia burden in immunodeficient NSG mice, and β2-adrenergic agonist treatment enhanced AML proliferation *in vitro*. High ADRB2 expression in AML patients predicted worse survival, particularly in M5/MLL-rearranged subtypes. DISCUSSION/SIGNIFICANCE OF IMPACT: Sympathetic signaling exerts dual roles in AML, supporting immune surveillance but directly acting on leukemic cells to promote AML progression. These findings identify β2-adrenergic signaling as a potential therapeutic target, especially in immunodeficient or chemotherapy-treated AML patients.

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Translating research into clinical practice: Pre-implementation assessment of an AI-enabled same-day diagnostic workflow for breast screening*

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OBJECTIVES/GOALS: Asynchronous imaging workflows delay follow-up for abnormal screening mammograms. Real-time artificial intelligence (AI) flags high-risk scans for synchronous, immediate review. We present pre-implementation qualitative and quantitative assessments to inform AI-enabled workflow redesign and improve outcomes. METHODS/STUDY POPULATION: We conducted a workflow study in the largest of 14 breast imaging centers in our health system. A multidisciplinary team of experts in breast imaging, implementation science, and AI/informatics conducted four clinical shadowing visits held on different weekdays (August 2023) and a time-motion study (February 2024) to identify opportunities for optimization in the current breast cancer screening imaging workflows. To determine the optimal time for potential AI workflow integration, we used statistical process control (SPC) charts to visualize patient volumes based on 2022 to 2023 scheduling data. RESULTS/ANTICIPATED RESULTS: The selected site had an average daily patient volume of 67, including 29 screening mammography patients, 3 of whom with abnormal findings prompting a diagnostic workup. During shadowing, observers recorded time stamps for each breast imaging exam step, from check-in to check-out, to calculate exam duration and estimate waiting room capacity for diagnostic and screening mammography or ultrasound. We analyzed workflow to identify unnecessary tasks and radiologists' disruptions that, if changed, could create the space for real-time reading without more difficult changes to workflow, for example, the number of radiologists and their deployment. SPC charts indicated that selected clinic days would be most promising for testing the new real-time workflows without major disruption to the system. DISCUSSION/SIGNIFICANCE OF IMPACT: A detailed understanding of the workflow ensures future implementations achieve intended outcomes. This analysis helped identify modest opportunities in radiologist and staff downtime to support the new workflow, potentially improving satisfaction, reducing anxiety, and shortening time to diagnosis.

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Clinical translation of quantitative ultrasound for nail disease: Bridging imaging biophysics and dermatology

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OBJECTIVES/GOALS: To translate quantitative ultrasound (QUS) from imaging biophysics into clinical dermatology by evaluating its reproducibility, diagnostic differentiation, and potential as a non-invasive, point-of-care tool for nail disease assessment. METHODS/STUDY POPULATION: Diagnosing nail disease is difficult due to overlapping features and the invasiveness of biopsy. In a prospective study (recruitment ongoing), patients with onychomycosis, inflammatory nail disease (psoriasis or lichen planus), and controls underwent 15-MHz ultrasound of fingernails and toenails (n = 26 patients, 152 nails). Raw radio-frequency data were processed to derive three QUS parameters: Homodyned-K [α] (microstructural organization), effective scatterer diameter (ESD) (scatterer size reflecting tissue texture), and effective acoustic concentration (EAC) (scatterer density reflecting compactness). Metrics were analyzed with t-tests and mixed-effects models. Within-patient consistency and parameter reproducibility were evaluated to assess clinical translation feasibility. RESULTS/ANTICIPATED RESULTS: Diseased fingernails (33 vs 54 controls) showed reduced α (−1.11, $p < 0.001$), reflecting loss of microstructural organization. Onychomycosis had the largest change (−1.25), while inflammatory nails were moderately reduced (−0.93). ESD showed opposite trends (+0.85, $p = 0.02$) indicating coarser scatterers in fungal disease, and EAC was uniquely elevated in lichen planus (+1.30, $p < 0.01$), consistent with fibrotic regions. In the toenail cohort (16 diseased vs 49 controls), onychomycosis showed parallel changes (α −0.9, $p < 0.001$; ESD +1.0, $p = 0.02$), supporting reproducibility across nail sites.

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