1

What Constitutes an MRI Indicative of Axial Spondyloarthritis? A Systematic Literature Review by the Spondyloarthritis Research and Treatment Network and the Society of Skeletal Radiologists

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Objectives: MRI indicative of axSpA in the sacroiliac joints (SIJ) is the highest ranked variable in the 2025 ASAS-SPARTAN Revised Classification Criteria for AxSpA (Maksymowych et al. Arthritis Rheumatol 2025;77[suppl 9]:0854) and requires consideration of both inflammatory and structural lesions. But it lacks guidance as to the type of lesion, its location and extent. We aimed to conduct a systematic literature review (SLR) to form the evidence base for a guidance document that defines what constitutes a positive MRI indicative of axSpA.

Methods: The primary question for the SLR was 'Which MRI lesion, or combination of lesions, in the SIJ is most sensitive and specific for an MRI considered indicative of axSpA in the SIJ?'. Three additional questions addressed an endpoint of clinician diagnosis of axSpA and the extent and location of the lesion(s). The SLR included all studies from January 2017 to July 27,2025 that included patients with clinically suspected axial SpA undergoing MRI. Studies from a previously published SLR up to January 2017 were also included. Each study selected for data extraction was assessed independently for risk of bias (RoB) by three reviewers using the Quality Assessment of Diagnostic Accuracy Studies-2 tool.

Results: Searches in Ovid MEDLINE, Ovid Embase, Scopus, Web of Science Core Collection, and the Cochrane Library gave 1871 unique results for screening in the Covidence tool, of which 35 were selected for data extraction, and 7 were excluded. Only 2 reports described 'MRI global indicative of axSpA' as reference criterion for the assessment of MRI lesion definitions and only 5 reports described assessment of MRI lesion definitions in an inception cohort study design. The quantitative component for BME of the ASAS 2009/2016 definitions of a positive MRI lacked specificity. Bone marrow edema (BME) in <4 SIJ quadrants was seen in anterior SIJ slices of antepartum and postpartum women, health individuals, and athletes but in ≥4 SIJ quadrants was specific for axSpA. Erosion and fat lesion were uncommon (<5%) in health individuals and disorders that mimic axSpA (DISH). Erosion in ≥3 SIJ quadrants and fat lesion in ≥5 SIJ quadrants had high specificity for axSpA and was rarely seen in conditions that mimic axSpA. BME adjacent to erosion and/or fat lesion was highly specific for axSpA.

Conclusion: These results reinforce the need to revise previously reported definitions of a positive MRI for axSpA towards more stringent MRI cut-offs that detail the extent and location of MRI lesions.

2

Performance of the 2025 ASAS-Spartan Revised Classification Criteria for Axial Spondyloarthritis in a Canadian Multicenter Inception Cohort with Psoriasis, Uveitis, or Colitis Presenting with Undiagnosed Back Pain

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Objectives: To test the performance of the 2025 ASAS-SPARTAN Revised Classification Criteria for Axial Spondyloarthritis (axSpA) (Maksymowych et al. Arthritis Rheumatol 2025;77[suppl 9]:0854) in a multicenter inception cohort of patients with undiagnosed chronic back pain attending dermatology, ophthalmology, and gastroenterology clinics with psoriasis (PsO), acute anterior uveitis (AAU), or inflammatory bowel disease (IBD) referred to a rheumatologist with special expertise in axSpA.
Methods: The multicenter Screening for Axial Spondyloarthritis in Psoriasis, Iritis, and Colitis (SASPIC) Study at 9 sites is aimed at early detection of axSpA in consecutive patients presenting with undiagnosed back pain to the rheumatologist. Consecutive patients ≤45 years of age with ≥3 months undiagnosed back pain with any one of psoriasis, acute anterior uveitis (AAU), or colitis diagnosed by the relevant specialist had routine clinical evaluation by a rheumatologist for axial SpA. The rheumatologist determined the presence or absence of axial SpA at 3 consecutive stages: 1. After clinical evaluation; 2. After results of labs (B27, CRP), radiography; 3. After results of MRI evaluation. All MRI scans were evaluated by 3 central readers whether the MRI was indicative of axSpA. In SASPIC 1 patients had MRI done as deemed appropriate by the rheumatologist, whereas all patients in SASPIC-2 had MRI. Final diagnosis by the rheumatologist was used as gold standard to test the performance of the criteria according to sensitivity and specificity [95%CI], emphasis being on attainment of high specificity.
Results: A total of 363 patients were recruited to the SASPIC cohorts (n=212 SASPIC 1, n=151 SASPIC 2) of whom 308 had MRI evaluation. The proportions of patients diagnosed with axSpA were 46.7%, 61.6%, and 46.8% for those with PsO, AAU, and IBD, respectively, in SASPIC-1, whereas the respective proportions were 23.5%, 57.9%, and 23.3% for SASPIC-2. Patient demographics and disease characteristics were similar between those with and without an MRI scan and with the patients recruited to the 2025 ASAS-SPARTAN cohort from which the criteria were developed. Sensitivity/specificity [95%CI] were 56.5 [47.3-65.3]/ 98.9 [96.1-99.9] for the entire cohort, and 59.7 [46.4-71.9]/ 97.6 [87.1-99.9], 52.8 [35.5-69.6]/ 100.0 [95.8-100.0], 53.9 [33.4-73.4]/ 98.3 [90.8-100.0] for the subgroups with AAU, IBD, or PsO, respectively. Performance in the 2025 ASAS-SPARTAN cohort using central reader imaging data was 56.6 [49.2, 63.7]/ 98.5 [96.5, 99.4] in testing data and 63.1 [56.1, 69.5]/ 98.7 [96.8, 99.5] in validation data.
Conclusion: The revised axSpA criteria perform with consistently high specificity in the 2025 ASAS-SPARTAN and SASPIC cohorts.
3
Autoantibodies to 14-3-3η Improves Discriminative Performance of CRP and HLA-B27 to

Differentiate People with Radiographic axSpA from Those with Mechanical Back Pain

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Objectives: Reducing diagnostic delay for people presenting with back pain but who have axial spondyloarthritis (axSpA) has become a clinical imperative. The absence of a simple blood test that is accessible by referring physicians contributes to this delay. This study evaluates the performance of auto-antibodies to 14-3-3η in combination with existing clinical parameters in an established Edmonton radiographic (r-axSpA) patient cohort.

Methods: Serum samples from 159 patients with a rheumatologist confirmed diagnosis and classified as r-axSpA (AS-modified New York criteria) were tested on the anti-14-3-3η multiplex assay. The serum differential expression of autoantibodies to 14-3-3η, CRP and HLA-B27 between patients with r-axSpA and MBP was evaluated by ROC AUC. Regression models combining the auto 14-3-3η AAb Score derived from the Bath study were tested in two predictive models: one with CRP and HLA-B27 markers only and the other adding Age and Sex variables. Corresponding specificity (SP), sensitivity (SN), predictive values (PPV, NPV), likelihood (LR) and diagnostic odds ratios (DxOR) are provided. The Akaike Information Criterion (AIC) statistical measure was reported to compare the relative quality of predictive models.

Results: Mean age of patients with r-axSpA was 42 (69% male) and for MBP, 30 years (59% male). Differential expressions of each of the biomarkers delivered significant ROC AUCs; 0.70 for autoantibodies to 14-3-3η, 0.81 for CRP and 0.84 for HLA-B27. The latter two delivered respectively higher DxOR (6.2, 11.1, 24.1) as expected, considering that they were used in patient diagnosis. The model that included the auto 14-3-3η AAb score with CRP and HLA-B27 added had better discrimination of patients with axSpA versus MBP with an AUC of 0.93 and DxOR of 39.6 that further improved to an AUC of 0.94 and DxOR of 95.3 when age and sex variables were added. As shown below (Table), the AIC of the predictive models supported the full model as the best fit.

Conclusion: This study demonstrates that auto 14-3-3η AAb score when added to currently used CRP and HLA-B27 markers, improves the differentiation of people with MBP from established r-axSpA. While the pretest probability of CRP and HLA-B27 performance is higher in this cross-sectional study than would be expected in an early referral cohort, including 14-3-3η AAb score may reduce diagnostic delay and potentially enable more confident and prompt initiation of therapy to improve outcomes.

4

The Immunomodulatory Role of Math-Only Proteins (MOPs) in Macrophages and Ankylosing Spondylitis

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Objectives: Inflammation is a fundamental immune defense that protects the body from

infection, injury, and tissue damage. However, exacerbated or unresolved inflammation contributes to chronic autoimmune disorders such as spondyloarthritis and rheumatoid arthritis.[1] Meprin and TRAF-C Homology (MATH) domain–containing proteins, including TRAF1–6 and Speckle-type POZ protein (SPOP), regulate immune signaling through Toll-like receptor (TLR)–NF-κB pathways (Figure 1).[1–3] Recent evidence demonstrates that SPOP suppresses inflammation by promoting MyD88 degradation, underscoring the anti-inflammatory potential of MATH-containing proteins.[2,3] Both TRAF and SPOP contain additional catalytic or adaptor domains, leaving the function of proteins composed exclusively of the MATH domain unexplored. In both human and mouse genomes, genes encoding only the MATH domain have been identified; we designate these as MATH-only proteins (MOPs). This study aims to characterize MOPs and investigate whether their overexpression mitigates inflammatory responses in macrophages.

Methods: A mixed-methods design integrating in vitro and in vivo approaches was employed. Bone-marrow-derived macrophages (BMDMs) from C57BL/6 and SKG mice, and human THP-1 macrophages, were stimulated with LPS (100 ng/mL). MOP isoforms (murine: 37, 11, 246; human: 212, 217, 220) and cytokines (IL-1β, IL-10) were quantified by RT-qPCR. Lentiviral constructs (pLenti-MOP 212, 220) were packaged in HEK293T cells (psPAX2 + pMD2.G) and used to transduce THP-1 cells. Phospho-flow cytometry assessed NF-κB (p65) and MAPK (ERK1/2) activation, while curdlan-treated SKG mice served as an in vivo model of autoimmune inflammation (Figure 1.2).

Results: Our results demonstrate that MOPs expression were significantly induced upon LPS stimulation in both murine and human macrophages (Figure 1. 3–4). In BMDMs, MOP 37, 11, and 246 peaked at 6 h post-LPS, paralleling IL-10 expression. In THP-1 cells, MOP 212 and 217 were progressively upregulated to 48 h. In the SKG in-vivo model, MOPs were elevated, validating the relevance of these pathways (Figure 1.5). MOP-220 overexpression in THP-1 cells selectively enhanced NF-κB and reduced ERK signaling (Figure 1.6), leading to upregulation of inflammatory cytokines (IL-1β, TNF-α) at the mRNA level. Together, findings highlight MOPs as potential modulators of inflammatory signaling (Figure 1.7).

Conclusion: This study identifies and characterizes MATH-only proteins (MOPs) as novel regulators of inflammation. MOPs expression is dynamically induced by TLR activation in murine and human systems and correlates with cytokine responses in vivo. These findings suggest that MOPs may modulate NF-κB and MAPK-driven cytokine signaling, providing a new molecular framework for immunoregulation. Ongoing MOPs overexpression and knockout studies aim to delineate their mechanisms in chronic inflammation and autoimmune disease.

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5

Work Productivity and Activity Impairment Across Functional Disability Levels in Patients with Inflammatory Arthritis

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Objectives: Inflammatory arthritis (IA) can progressively compromise physical function, leading to reductions in work productivity and daily activity. However, the thresholds at which productivity loss becomes clinically meaningful remain unclear, particularly across different IA types and within the Canadian healthcare context. This study quantified productivity and activity impairment across levels of functional disability to identify thresholds for intervention and inform early, function-preserving care strategies.
Methods: Data from the Rheum4U Precision Health Registry, including adults (> 18 years) with IA receiving care at a rheumatology clinic in Calgary/Canada, were analyzed. The first registry visit with complete Clinical Health Assessment Questionnaire (ClinHAQ) and the Work Productivity and Activity Impairment questionnaire (WPAI) was included. ClinHAQ scores categorized participants into minimal/no, mild, moderate, or severe disability. WPAI domains (absenteeism, presenteeism, overall work impairment, and activity impairment) were scored ranging 0-100%, with higher values indicating greater impairment. Kruskal–Wallis tests evaluated differences across disability levels, and Dunn's post-hoc tests with Bonferroni correction identified pairwise differences.
Results: Among 1,337 participants (68% women; median age 52 [IQR 39–62] years), 59% had minimal/no disability, 18% mild, 21% moderate, and 2.5% severe functional disability. The median time since diagnosis was 7.2 [IQR 2.5-13.1] years. Significant differences were observed across all WPAI domains ($p<0.001$), with activity impairment showing the largest differences. Post-hoc analyses revealed that absenteeism, presenteeism, overall work impairment, and activity impairment increased progressively with functional disability, with the most consistent and statistically significant differences observed at moderate levels compared with minimal/no disability. Comparison involving mild disability also showed significant, though smaller, differences relative to minimal/no disability. Differences involving severe disability compared with minimal/no disability were generally smaller or non-significant, likely due to the small number of participants in this group. Activity impairment differed significantly across all disability levels, including comparisons involving severe disability.
Conclusion: In adults with IA, work productivity and activity impairment worsen progressively with increasing functional disability. Most notable productivity declines were detected at moderate ClinHAQ levels. These begin at mild disability but reach a clinically meaningful threshold once functional limitations are moderate. These results offer practical insights for early interventions aimed at preserving physical function. Implementing strategies when patients have minimal/no or mild disability may help maintain productivity and support patients' participation in daily and work-related activities.

6

STK17B/DRAK2 in Axial Spondyloarthritis: Expression Patterns in Blood and Tissue

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Objectives: T cells play a central role in axial spondyloarthritis (axSpA). The serine-threonine kinase DRAK2, encoded by STK17B, modulates T cell activation and survival. In autoimmune

models, it promotes autoreactive T cell persistence and reduces regulatory T cell (Treg) abundance.[1,2] We previously found STK17B upregulation in peripheral blood mononuclear cells (PBMCs) of axSpA patients who were non-responders to tumor necrosis factor inhibitors (TNFi).[3] To clarify whether this reflects disease-associated inflammation or treatment resistance, we compared STK17B/DRAK2 expression (i) between axSpA patients and healthy controls and (ii) between responders and non-responders to IL-17 inhibitor (IL-17i) therapy. We also examined STK17B/DRAK2 expression in the SKG mouse model of SpA.
Methods: Human spinal tissue from axSpA patients and spinal trauma controls was analyzed by immunohistochemistry (IHC) to localize DRAK2 expression, and by immunofluorescence (IF) to compare expression between $CD4^+$ and $CD8^+$ T cells. PBMCs from patients and controls were sorted by fluorescence-activated cell sorting (FACS), and STK17B expression in each subset was quantified by qPCR. Parallel IHC was performed on ankle, tail, and ileum of curdlan-treated and PBS-treated SKG mice. To corroborate findings at higher resolution, STK17B expression in mature $CD4^+$ and $CD8^+$ T cells was queried from our pre-biologic single-cell RNA-sequencing and multiome datasets.
Results: In human spinal tissue, $DRAK2^+$ immune infiltrates were more abundant in axSpA than in controls (Figure 1A), with stronger IF staining in $CD4^+$ than $CD8^+$ T cells. In PBMCs, STK17B was preferentially expressed in $CD4^+$ T cells and trended higher in axSpA compared with controls. Single-cell and multiomic analyses confirmed this pattern, showing modest STK17B increases in CD8+ T cells but markedly higher levels in CD4+ T cells of axSpA patients, particularly in effector T cells and Tregs. Notably, pre-biologic STK17B expression was higher among patients who were later identified as non-responders to IL-17i compared with responders (Figure 1B). Consistent with the human findings, curdlan-treated SKG mice exhibited increased $DRAK2^+$ infiltrates in ankle, tail, and ileum relative to PBS-treated controls, paralleling the observation in human tissues (Figure 1C).
Conclusion: Across humans and mouse models, STK17B/DRAK2 expression is increased in inflammatory lesions and enriched in $CD4^+$ effector and regulatory T cells, particularly in patients with inadequate IL-17i response. These findings suggest that DRAK2 upregulation contributes both to axSpA-related inflammation and to treatment resistance, warranting further mechanistic investigation.
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7

Real-World Effectiveness of Upadacitinib on Early and Sustained Pain Control in Canadian Patients with Axial Spondyloarthritis: Interim Results from the Upstand Study

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Objectives: To prospectively assess the real-world effectiveness of upadacitinib (UPA) on early and sustained pain control in Canadian patients with axial spondyloarthritis (axSpA) participating in the UPSTAND study.
Methods: UPSTAND (NCT04846244) is a 12-month, multi-country observational study in adult patients with axSpA for whom, prior to and independent of the study enrolment, the treating physician has decided to prescribe UPA, per local label. Patients had Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) and total back pain scores ≥4 at baseline and an inadequate response or intolerance/contraindication to NSAIDs. Co-primary endpoints are 1) total spinal pain score <4 and ≥2-unit improvement from baseline at Week 12, and 2) maintenance up to Week 52 (not available). Secondary endpoint measures include patient assessment of spinal, total back, and nocturnal back pain, painDETECT for capturing neuropathic pain, Widespread Pain Index (WPI) and Symptom Severity Scale (SSS) for capturing nociplastic pain, Ankylosing Spondylitis Disease Activity Score (ASDAS), and BASDAI. This interim analysis reports data through 20-Jun-2024; at cutoff, all patients had completed at least the Week 12 visit. Results are presented as observed cases using descriptive statistics.
Results: A total of 71 Canadian patients were included in this analysis (mean age: 51.3 years [SD: 12.5]; female gender: 52.1%; mainly White [90.1%] or Asian [8.5%]). Most patients had radiographic axSpA (97.1%) and 70.1% experienced symptoms of axSpA for ≥10 years (mean duration 18.3 years). The primary endpoint of a total spinal pain score <4 and a ≥2-point improvement from baseline at Week 12 was achieved by 31.7% (n/N = 13/41) of patients with a baseline score ≥4. The mean total (7.0 to 5.3) and nocturnal (6.6 to 5.0) back pain decreased rapidly over the first 2 weeks of treatment with further reduction up to Week 52 (Figure 1A/B). Treatment with UPA reduced both painDETECT (12.8 to 9.0) and WPI (7.6 to 6.1) from baseline to Week 52 (Figure 1C). Similarly, improvement in axSpA composite measures of disease activity was observed using the ASDAS and BASDAI (Figure 1D). UPA was generally well-tolerated, and its safety profile was consistent with observations made across randomized clinical trials (RCTs).
Conclusion: These interim results show that Canadian patients with axSpA treated with UPA in the real-world setting have rapid and consistent improvement in pain (including measures reflecting neuropathic and nociplastic components) and in disease activity. This improvement in pain and disease control is consistent with data from RCTs.

8

Injection Site Pain and Adherence in Patients Switching from Reference Adalimumab to AVT02 – Ease Pain Trial (Full Analysis)

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Objectives: AVT02, a biosimilar to reference product (RP) adalimumab, is formulated at high concentration and with citrate-free excipients. The EASE PAIN trial is a Phase IV study in Canada evaluating the impact of switching from RP or an alternative adalimumab biosimilar to AVT02 on patient outcomes.[1–3] The primary objective examines the impact of switching on injection site pain (ISP) across patients in Canada. Secondary objectives include describing the impact of switching on patient perception of change in ISP, injection site reaction (ISR),

treatment Adherence, patient satisfaction, quality of life, disease activity, and healthcare utilization.
Methods: The study enrolled patients with gastrointestinal conditions (Crohn's disease [CD], ulcerative colitis [UC]), rheumatological conditions (rheumatoid arthritis [RA], ankylosing spondylitis [AS], psoriatic arthritis [PsA]), or dermatological conditions (hidradenitis suppurativa [HS], psoriasis [PsO]). Participants were eligible if their treating physician had decided to switch them from low-concentration RP or alternative adalimumab biosimilar to AVT02. The study assessed ISP measured via the Visual Analog Scale (VAS), adherence via the compliance rate, patient satisfaction and perception of change in pain via the Likert scale, quality of life based on EQ-5D-5L, and disease activity via the patient and physician global assessment scores for participants up to Day 180 after switching.
Results: The intention-to-treat (ITT) population comprised 324 participants. Following the first administration of AVT02, injection site VAS pain score decreased by an average of -19.9 ± 26.13 across the whole population. Supporting this, 76% of the participants perceived AVT02 as less painful as measured by the 5-Likert scale. Moreover, a significantly lower number of patients experienced ISRs after their first dose of AVT02 (36 patients; 12.4%) compared with their last dose of low-concentration adalimumab (124 patients; 42.3%). Adherence rate was 93.4% overall. The ITT population maintained a high patient satisfaction (more than 74.4% reported being 'mostly or completely satisfied') and a high quality of life score (EQ-5D-5L score of >82 on a scale of 1-100) after switching from RP to AVT02. There were generally no changes in patient and physician reported outcomes nor in healthcare utilization.
Conclusion: The results of this study demonstrate that switching from RP or alternative biosimilar adalimumab to AVT02 leads to decreased ISP across all indications, fewer numbers of ISRs, and a maintenance of high adherence rates, patient satisfaction, and quality of life among patients.
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9
Effectiveness of Upadacitinib in Patients with Rheumatoid Arthritis in Canadian Real-World Practice: Final Results from the Close-Up Post-Marketing Observational Study
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Objectives: To evaluate the real-world effectiveness and safety of upadacitinib (UPA) among Canadian patients with rheumatoid arthritis (RA) with prior exposure to conventional synthetic (cs)DMARD, biologic (b)DMARD, and targeted-synthetic (ts)DMARD in real-world settings**.**
Methods: CLOSE-UP was a prospective, observational post-marketing study conducted at 33 sites in Canada in adults with moderate-to-severe RA who were treated with UPA 15 mg once

daily. UPA initiation was decided before study participation. Patients were followed for 24 months after UPA initiation with data collected at routine clinic visits. The primary endpoint was the proportion of patients achieving a Disease Activity Score 28 Joint Count – C-reactive protein (DAS28-CRP) < 2.6 at 6 months. Secondary endpoints included pain score using a visual analog scale, fatigue (FACIT-F), physical function as measured by the Health Assessment Questionnaire-Disability Index (HAQ-DI), and other assessments of disease activity including Clinical Disease Activity Index (CDAI) score. Patients were grouped by prior/most recent exposure to no b/tsDMARDs (bio-naïve), ≤2 bDMARDs but no tsDMARD (bio-experienced), and a maximum of 1 bDMARD followed by a tsDMARD (tsDMARD-experienced). Data are presented as observed and summarized descriptively.

Results: Analysis included 412 patients, with 47.1% identified as bio-naïve, 41.3% as bio-experienced, and 10.7% as tsDMARD-experienced. At baseline, most patients (84.5%) exhibited a DAS28-CRP > 3.2. After 6 months of UPA treatment initiation, 60.7% of patients achieved a DAS28-CRP < 2.6 (primary endpoint) and 75.6% achieved a DAS28-CRP ≤ 3.2 with a response rate maintained for up to 24 months (Figure 1a). Similar trends were observed using CDAI definitions for clinical remission and low disease activity. The type of prior/most recent DMARD exposure did not impact response. Additionally, the proportion of patients achieving a DAS28-CRP < 2.6 at the 6-month visit were similar between those on UPA monotherapy (62.7%) and those on UPA in combination with a csDMARD (60.1%). Improvements in pain score, fatigue, and physical function were observed throughout the study (Figure 1b). At 6 months, 86.5% of patients persisted in their treatment on UPA and 67.5% persisted up to Month 24. The safety profile of UPA was consistent with that seen in Phase 3 trials with no new safety signals.

Conclusion: Consistent with clinical trial findings, this real-world Canadian study demonstrated a reduction in disease activity and improvements in patient-reported outcomes, supporting a favorable benefit-risk profile for patients treated with UPA. Notably, response rates were consistent irrespective of prior bDMARDs/tsDMARDs use or concomitant csDMARD.

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Bimekizumab Demonstrated Comparable One-Year Efficacy in Male and Female Patients with Axial Spondyloarthritis: Results from Two Phase 3 Studies

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Objectives: To assess bimekizumab (BKZ) efficacy to Week (Wk)52 across the full axial spondyloarthritis (axSpA) disease spectrum, focusing on potential sex-based differences in treatment response.

Methods: BE MOBILE 1/2 (NCT03928704/NCT03928743) included a 16-wk double-blind and 36-wk maintenance period. Patients received BKZ 160mg every 4 wks (Q4W) or placebo (PBO) to Wk16; thereafter, all received BKZ. Sex-stratified outcomes reported to Wk52: ASAS40,

ASDAS<2.1, BASDAI, Ankylosing Spondylitis Quality of Life Questionnaire (ASQoL), and objective signs of inflammation (OSI; MRI SPARCC SIJ, MRI Berlin spine, hs-CRP). Wk16 BKZ vs PBO efficacy between males vs females were compared using adjusted relative odds ratios (rOR; logistic regression) and relative differences (RD; ANCOVA). Analyses were post-hoc (no p values).
Results: 220/254 BE MOBILE 1 (male: 124/138 [89.9%]; female: 96/116 [82.8%]) and 298/332 BE MOBILE 2 patients (male: 215/240 [89.6%]; female: 83/92 [90.2%]) completed Wk52. At baseline, females had longer mean symptom duration (years; non-radiographic [nr]-axSpA: 11.1 vs 7.2; radiographic [r]-axSpA: 15.0 vs 12.9) and lower HLA-B27 positivity (%) (nr-axSpA: 69.0 vs 84.8; r-axSpA: 78.3 vs 88.3) than males; males had lower mean ASQoL scores (nr-axSpA: BKZ: 8.5 vs 10.8, PBO: 8.6 vs 10.2; r-axSpA: BKZ: 8.3 vs 11.1, PBO: 8.4 vs 9.0), and generally higher OSI values than females. Across ASAS40, ASDAS<2.1, and BASDAI, rORs and RDs demonstrated greater Wk16 BKZ vs PBO treatment effect in males vs females (Figure 1). At Wk52, responses were higher in males with nr-axSpA than females, but comparable in r-axSpA. Overall, at Wk52, both sexes responded well in both trials, with >50% of BKZ-randomized patients achieving ASAS40, >40% achieving ASDAS <2.1, and BASDAI score improvements. For ASQoL, both males and females demonstrated substantial improvements with BKZ at Wk16 (nr-axSpA: −5.5 vs −4.8; r-axSpA: −4.8 vs −5.5) compared with PBO (nr-axSpA: −2.1 vs −2.9; r-axSpA: −3.1 vs −3.7). Improvements continued to Wk52 with BKZ (nr-axSpA: BKZ: −5.7 vs −6.2, PBO/BKZ: −5.5 vs −5.1; r-axSpA: BKZ: −5.4 vs −6.5, PBO/BKZ: −5.5 vs −5.8). For change from baseline in OSI outcomes, RDs indicated a higher Wk16 BKZ vs PBO treatment effect in males than females; absolute OSI values were comparable between males/females and maintained or improved to Wk52 with BKZ.
Conclusion: Wk16 BKZ vs PBO treatment effect trended higher among males than females. By Wk52, females showed improvement in longer-term BKZ response, approaching levels comparable to males. Overall BKZ efficacy was demonstrated across clinical, patient-reported, and OSI outcomes in both sexes across the full axSpA disease spectrum.

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Screening Tools for Spondyloarthropathies Among Patients with Inflammatory Bowel Disease: A Scoping Review

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Objectives: Inflammatory bowel disease (IBD), including Crohn's disease and ulcerative colitis, is a systemic chronic inflammatory disease of the gastrointestinal tract where extraintestinal manifestations (EIMs) are common. The musculoskeletal system is the most common EIM with spondyloarthropathies (SpA) seen in up to 39% of patients with IBD. Despite its prevalence, there remain challenges in early identification of SpA in patients with IBD. The aim of this scoping review was to identify and describe the validity of screening tools for IBD-related arthritis.
Methods: We searched MEDLINE and Embase (inception to August 15, 2025) to identify studies of screening tools used to detect SpA in both pediatric and adult IBD patient populations. Review articles, opinion-based articles, conference abstracts, incomplete publications and non-

English studies were excluded. Screening of studies for eligibility was performed on Covidence, with conflicts resolved by consensus amongst three reviewers. Data was extracted and synthesized.
Results: Of 568 studies identified, 14 studies were included. All identified studies reported on adults with IBD. Six studies reported on the validation of SpA screening tools, including DETAIL (n=3), IBIS-Q (n=2), and structured clinical screening criteria used in individual studies. Validation studies demonstrated that screening tools such as DETAIL and IBIS-Q showed moderate–high sensitivity ranged 43–92.7% and specificity 62–89.8%, with ≥3 positive items consistently corresponding to a high post-test probability of SpA ranging from 75.0–81.9%. These same scales, along with diagnostic imaging, were used to determine the prevalence of SpA among people with IBD. The prevalence of SpA or sacroiliitis among adults with IBD ranged from approximately 5–30%, with many cases previously unrecognized in routine care. All included studies were conducted in academic or tertiary referral centres.
Conclusion: DETAIL and IBIS-Q are validated tools that can be used for early detection and referral of SpA among adults living with IBD. Study design evaluating the prevalence of SpA using these tools were heterogenous, leading to varied prevalence estimates. All included studies were from referral centres where patients often have more complex IBD presentations which may influence prevalence estimates and limit generalizability to community practice. Coordinated efforts between gastroenterology and rheumatology will be critical to refine, validate, and implement IBD-appropriate tools that support integrated, patient-centered care. This is critical in the pediatric population where there is a complete absence of screening tools.

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Mental Health Concerns in Patients with Juvenile Idiopathic Arthritis and Their Caregivers: A Systematic Review

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Objectives: The COVID-19 pandemic has amplified mental health (MH) challenges among youth, with one in five children reporting their MH to be “fair” or “poor”.[1] Children with chronic disease, including Juvenile idiopathic arthritis (JIA), the most common pediatric rheumatic disease, are at particular risk for anxiety and depression. Despite this, the epidemiology of broader MH concerns in children with JIA (CWJIA) and their caregivers remain poorly characterized, particularly in the post-pandemic era. This systematic review will evaluate the epidemiology and scope of MH concerns among CWJIA and their caregivers, including MH disorders (e.g. anxiety, depression), MH symptoms (e.g. stress), cognitive functioning, positive MH indicators (e.g. resilience).
Methods: Following PRISMA guidelines, an initial search was completed on MEDLINE (Ovid) to generate keywords and was followed by extensive searches on MEDLINE, Embase, PsychINFO and CINAHL (1806-August 2025). Eligible studies examined MH concerns for CWJIA and/or their caregivers reporting on the incidence or prevalence of MH disorders, symptoms, cognitive functioning, or positive MH indicators. Four reviewers independently screened and extracted data using Covidence, with quality assessment planned using JBI critical appraisal tools.

Results: A total of 30 studies met the inclusion criteria, with most studies being of cross-sectional design. MH disorders (n=18) and MH symptoms (n=17) were most frequently evaluated. Anxiety and depression were the most reported MH disorders, consistently showing higher prevalence among CWJIA than healthy controls. JIA was shown to impact cognitive functioning (n=7), with several studies exploring its impact on school performance. Positive MH indicators (n=3 studies) such as resilience and adaptive coping emerged as potential protective mechanisms against poor MH outcomes. Caregiver MH was evaluated in three studies, all describing elevated distress associated with caring for CWJIA (Figure 1).
Conclusion: This systematic review highlights the scarcity of literature describing the burden of MH concerns among CWJIA and their caregivers. The higher prevalence of negative MH indicators in this population, along with the protective effects suggested by positive MH indicators underscores the need for studies of family-centered interventions to strengthen the psychosocial well-being of CWJIA and their caregivers.
References: [1.] Rising mental health. 2025; https://www.statcan.gc.ca/o1/en/plus/7642-rising-mental-health-concerns-among-youth. Berkelbach van der Sprenkel EE. Psychosocial functioning. 2021; 181(2):763–73.

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Long-Term Uveitis Rates with Bimekizumab Treatment Across Pooled Phase 2B and Phase 3 Studies in Patients with Axial Spondyloarthritis or Psoriatic Arthritis: 3-Year Update

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Objectives: To report updated uveitis incidence in bimekizumab (BKZ)-treated patients with axial spondyloarthritis (axSpA) or psoriatic arthritis (PsA) in Phase 2b/3 studies over a treatment duration of three years in Phase 3 studies.
Methods: Data are reported for two pools, each comprising one Phase 2b and two Phase 3 studies and their open-label extensions, in patients with axSpA and PsA, respectively (data cut-off in axSpA: September 2024; PsA: August 2024). Uveitis events were identified using the preferred terms "autoimmune uveitis", "iridocyclitis", "iritis", and "uveitis", classified using the MedDRA v19.0; "acute anterior uveitis" was not a specific preferred term available in MedDRA v19.0. Uveitis rates and exposure-adjusted incidence rates (EAIR) per 100 patient-years (PY) for patients who received ≥1 BKZ 160 mg every four weeks (Q4W) dose are reported separately for axSpA and PsA, respectively.
Results: Patients with axSpA (N=848) and PsA (N=1,409) had a mean (standard deviation [SD]) age of 40.3 (11.9) and 49.3 (12.4) years, respectively. Mean (SD) time since diagnosis was 6.1 (7.8) years in patients with axSpA and 7.0 (8.0) in patients with PsA. Of patients with axSpA, 130 (15.3%) had a history of uveitis (PsA: 21 [1.5%]). Most patients with axSpA were HLA-B27 positive (717/848 [84.6%]). In patients with axSpA across the pooled Phase 2b/3 data, BKZ exposure was 2,748.9 PY. In total, uveitis occurred in 33/848 (3.9%; EAIR [95% CI]: 1.2/100

PY [0.8, 1.7]) patients overall and in 20/130 (15.4%; 5.0/100 PY [3.0, 7.7]) patients with history of uveitis. In patients without a history of uveitis, 13/718 (1.8%; 0.6/100 PY [0.3, 1.0]) patients had uveitis events (Figure 1). Most events were mild/moderate, one was severe; two (0.2%) patients discontinued treatment due to uveitis. Incidence of uveitis in patients with PsA was low across the pooled Phase 2b/3 data (total BKZ exposure: 4,264.7 PY); uveitis occurred in 4/1,409 (0.3%; 0.1/100 PY [0.0, 0.2]) patients overall; two had a history of uveitis. No uveitis events led to treatment discontinuation.
Conclusion: Over three years of BKZ treatment, the incidence of uveitis in patients with spondyloarthritis receiving BKZ long-term was low.

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Maternal and Fetal Outcomes Associated with Interleukin-17 Inhibitor Exposure During Pregnancy in Patients with Seronegative Arthritis: A Case Series of Nine

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Objectives: Interleukin-17 (IL-17) inhibitors, such as ixekizumab and secukinumab, are increasingly used in the treatment of seronegative inflammatory arthritis, including psoriatic arthritis and axial spondyloarthritis. However, data on their safety and outcomes during pregnancy remain limited. Given the expanding use of IL-17 inhibitors in individuals of reproductive age, further characterization of maternal and fetal outcomes is needed to inform clinical decision-making.
Methods: Nine pregnant individuals with seronegative inflammatory arthritis who were treated with IL-17 inhibitors were identified through the Pregnancy and Rheumatic Diseases Clinics at two Canadian centers. Clinical data were prospectively extracted by a trained research assistant using REDCap, electronic medical records, and relevant consult notes. Outcomes of interest included maternal disease activity during pregnancy, pregnancy complications, neonatal outcomes, and the presence of congenital anomalies.
Results: These patients were managed throughout all trimesters of pregnancy and followed for six weeks postpartum. The mean maternal age at conception was 34 years. Patient characteristics are summarized in Table 1. Pregnancy complications included gestational diabetes, preeclampsia, chorioamnionitis, gestational hypertension, and COVID-19 infection. Ankyloglossia was noted in one infant (P5). Neonatal complications included jaundice not requiring intervention (P4) and transient hypoglycemia and transaminitis (P7) (Table 1).
Conclusion: In this prospective case series, IL-17 inhibitor exposure during pregnancy was not associated with an increased risk of major congenital anomalies or serious adverse neonatal outcomes. Although encouraging, these results are preliminary and do not establish safety. Confirmation in larger, controlled cohorts is needed. Larger, multicenter studies are needed to confirm these observations and better inform clinical guidance.

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Diagnostic Delays in Axial Spondyloarthritis: Identifying Diagnostic Inequities in Immigrant Patients

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Objectives: In Axial spondyloarthritis (AxSpA), diagnostic delays remain a persistent challenge. Socioeconomic, cultural, and systemic factors may contribute to inequities in access to timely diagnosis, particularly among immigrant populations. This study aims to generate pilot data on diagnostic delays among immigrant patients with AxSpA and to compare these delays with those observed in non-immigrant populations.

Methods: This study is part of an ongoing prospective data collection using a single-visit, cross-sectional design. Participants were consecutively recruited from two clinical settings within our rheumatology program: (1) the AxSpA Triage Clinic (FASTRAX*), which evaluates patients with suspected AxSpA, and (2) the ORCHESTRA (Ottawa Rheumatology CompreHEnSive TReatment and Assessment) Clinic, which follows patients with established, active AxSpA requiring biologic therapy and managed through a standardized approach. Demographic and clinical data were collected, including place of birth, and symptom duration. Diagnostic confirmation of AxSpA was made by a rheumatologist based on clinical evaluation and imaging findings. The primary outcome was diagnostic delay, defined as the time interval from symptom onset to rheumatologist-confirmed diagnosis of AxSpA. Immigrant status was determined by country of birth (Canada-born vs. foreign-born). Comparative analyses were performed between immigrant and non-immigrant patients.

Results: A total of 81 patients were enrolled to date (44 females and 37 males). AxSpA was confirmed in 51 patients, while 30 were determined to have non-SpA back pain. The mean duration from symptom onset to final diagnosis (or exclusion) was 10.1 years (SD ±10.8) overall, 9.6 ±10.8 years among patients diagnosed with AxSpA, and 11.1 ±11.2 years among those with non-SpA back pain. Of the total cohort, 67 patients were Canadian-born and 14 were immigrants. Among Canadian-born patients, 41 were diagnosed with AxSpA, with a mean diagnostic delay of 8.8 years (SD ±10.7). Among immigrants, 10 were diagnosed with AxSpA, with a longer mean diagnostic delay of 12.7 years (SD ±10.9). In parallel, perceived delays in care showed same trends: within immigrant patients, 40% stated moderate-severe delays for access to rheumatology and 30% for imaging, compared to non-immigrants (22% for access to rheumatology; and 7.5% for the imaging) (Table 1).

Conclusion: Our pilot data suggest longer diagnostic delays in AxSpA among immigrant patients compared with those born in Canada. Although the sample size is small and lacks statistical power, consistent trends indicate potential inequities in access to rheumatology assessment and imaging. These findings highlight the importance of considering social and systemic factors that may contribute to diagnostic disparities.

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Proteome-Wide Mendelian Randomization in Ankylosing Spondylitis

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Objectives: While numerous proteins have been linked to ankylosing spondylitis (AS), the

causal nature of these associations remains unconfirmed. This study employed a Mendelian randomization (MR) approach to evaluate whether circulating plasma protein levels, derived from large-scale international dataset, are causally associated with AS risk.
Methods: The study analyzed genetic summary data from 1,462 AS patients and 164,682 controls, all of whom had undergone genome-wide association scans, as identified from the FinnGen consortium. Large-scale plasma protein quantitative trait locus (pQTL) data were sourced from the UK Biobank Proteomics Project (UKB-PPP; 2,923 unique proteins), the INTERVAL study (2,995 unique proteins), and the Icelandic study (Ferkingsatad et al. 2021; 4,719 proteins). Potential protein candidates were identified based on SNP associations with proteins ($p < 5x10^{-8}$), followed by linkage disequilibrium (LD) clumping to identify independent pQTLs for each protein ($r^2 < 0.001$), and defining SNPs when the leading SNP was located within 500kb of the transcription site of the protein-coding gene. A two-sample MR analysis was then conducted, using the Wald ratio for genes with one SNP and inverse variance weighting (IVW) for those genes with multiple SNPs. Sensitivity analyses, including tests for pleiotropy and heterogeneity, were performed to ensure robustness of the causal estimates.
Results: A total of 21 unique proteins were identified as being associated with the risk of AS. In the UKB-PPP dataset, three proteins were linked to an increased risk of AS (DXO, LTA, AGER), while six proteins associated with a decreased risk (TRIM40, LTB, AIF1, HLA-E, MICB_MICA, CFB). The INTERVAL dataset identified five proteins correlated with an elevated risk of AS (IL-23R, TNXB, CFB, MICB, ERAP1) and AGER protein was linked to a reduced risk (Table 2). From Ferkingsatad et al. 2021 dataset, MR identified eight proteins significantly associated with AS (HLA-DQA2, ERAP1, MICB, BTN3A3, TAPBP, C2, CFB, TNXB and seven proteins with decreased risk NCR3, HSPA1L, MICA, VARS, APOM, AIF1, AGER). The top six Reactome pathways identified from pathway enrichment analysis included Immune system, cytokine signaling, adaptive immune system, adaptive immune system, innate immune system and signaling by interleukins (1 x10-6)
Conclusion: This proteome-wide MR study identified 21 unique proteins associated with AS risk, offering novel insights into the disease's pathogenesis. These prioritized proteins also present potential druggable targets, warranting further investigation to explore novel therapeutic opportunities.

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Sacroiliac-Only MRI Protocol for Detection of Axial Spondyloarthritis: A Quality Improvement Study

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Objectives: St. Joseph’s Healthcare Hamilton (SJHH) changed its MRI protocol for axial spondyloarthritis (axSpA), shifting from full imaging of the spine and sacroiliac joints (SI) to an SI joint-only protocol. This study aimed to evaluate whether the diagnostic accuracy for axSpA would be reduced with this limited MRI protocol.
Methods: This was a retrospective chart review. Using electronic medical records from four community rheumatologists in Southwestern Ontario, a computerized search was performed to identify all patients newly diagnosed with axSpA between January 2011 to January 2021 who had an MRI-axSpA protocol performed at SJHH. MRI reports were reviewed to determine the presence of isolated spondylitis vs sacroiliitis with or without spondylitis. Patient characteristics

including age, sex, HLA-B27 status, CRP and ESR at the time of MRI, personal and family history of psoriasis or psoriatic arthritis, personal and family history of inflammatory bowel disease, and family history of axial spondyloarthritis/ankylosing spondylitis, were also extracted. Data analysis was performed using logistic regression with missing data imputed using the CART method.
Results: A total of 1,356 patient charts were identified and 135 patients fulfilled inclusion criteria. The mean age was 42 (± 14) and 55% were female. Of these, 126 patients (93%) had sacroiliitis with or without spondylitis and 9 (7%) had spondylitis alone. A sacroiliac-only protocol would have identified 93% of axSpA cases. Patients with isolated spondylitis were more likely to have a personal or family history of psoriatic arthritis (OR 6.77, 95% CI [1.18, 38.76]). We further approximated cost and time savings to be $700 and 30 minutes per scan, or ~$94,500 and 67.5 hours, respectively, over 10 years for this study cohort.
Conclusion: A sacroiliac-only MRI protocol maintains high diagnostic yield while reducing costs and the time an MRI machine is occupied. However, clinicians should consider spine imaging in select patients specifically those with a personal or family history of psoriasis or psoriatic arthritis. Larger studies are warranted to validate these findings and to better define the role of spinal MRI in patients with suspected axial PsA.

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T Cell Interferon and Cytotoxic Pathways in Axial Spondyloarthritis: Relationship to Secukinumab Response Profiles

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Objectives: Our study aims to define the difference in granzyme (GZMs) expression in axial spondyloarthritis (axSpA) patients that predisposes secukinumab treatment response.
Methods: Secukinumab treatment response, as determined using BASDAI50 scoring at week 24, stratified patients into responders (SEC-R) and nonresponders (SEC-NR). Multiome Sequencing was performed on CD4+ T cells from 3 SEC-R patients, 3 SEC-NR patients, and 2 healthy controls.
Results: SEC-R patients had an increased PU.1 CD4+ T cell cluster that had high expression of genes associated with the type 1 interferon (IFN) pathway. SEC-R patients have transcripts elevated in ATP synthesis and cytotoxic molecular functions. SEC-R patients have increased cytotoxic gene transcripts compared to SEC-NR patients. SEC-NR patients appear to have an altered TGFβ signaling pathway likely mediated through RELA and NFKB1. Although SEC-NR Tregs appears more responsive to TGFβ, there is higher expression of IFNγ genes in the Treg cluster compared to SEC-R.
Conclusion: SEC-NR patients demonstrate enhanced IFNγ production that is dissociated from cytotoxic potential. This may occur due to increased SMAD7 activation of NFKB1 which prevents cells from differentiating into cytotoxic T cells and maintains a pro-inflammatory effector phenotype. Type 1 IFN is overrepresented in SEC-R patients before secukinumab treatment and elevated after treatment in SEC-NR patients. Regulation of type 1 interferons may therefore play an important role in influencing treatment response to secukinumab in axSpA.

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Characterizing Mental Health Burden of Patients with Juvenile Spondyloarthritis

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Objectives: To describe the frequency of mental health issues in Juvenile Spondyloarthritis (JSpA) patients attending the SickKids rheumatology clinic and to explore potential relationships between mental health symptoms and disease activity.
Methods: A cross-sectional retrospective study was conducted among children aged 12–18 years diagnosed with JSpA/Enthesitis Related Arthritis (ERA) using the 2019 PRINTO criteria. Patients attending the SickKids JSpA Clinic (Oct 2024-Sept 2025) were screened for mental health symptoms using the Patient Health Questionnaire-9 (PHQ-9), Generalized Anxiety Disorder-7 (GAD-7), and PROMIS 37 v1.1 tools, as part of a hospital-wide measurement-based care initiative. Additional data included demographics, disease characteristics (age of onset, duration, joint/entheseal involvement), disease activity scores (cJADAS, BASDAI), and Physician Global Assessment (MDPGA). Descriptive statistics were calculated, and Spearman correlations determined relationships between PROMIS measures and disease variables. Ethics approval was obtained from the SickKids REB.
Results: Thirty-one patients were included (Table 1). 84% were male, mean ± SD age at onset was 15.7 ± 1.7 years, and mean disease duration was 47 ± 36.4 months. Joint involvement at diagnosis was peripheral (32%), axial (26%), or mixed (39%). Over 90% were on biologics; only 23% had active joints at the screening visit. The PHQ-9 and GAD-7 were completed by n=20, and PROMIS-37 by n=26. Elevated depressive symptoms on the PHQ-9 were reported by 65% (n=13) - 40% mild, 5% moderate and 20% severe. Elevated anxiety symptoms on GAD-7 were reported by 60% (n=12)- 30% mild, 15% moderate, and 15% severe. On average, PROMIS scores indicated good physical functioning and peer relationships. Correlation analysis showed significant positive associations between self-reported disease activity (BASDAI) and depression ($\rho = 0.690$, $p = 0.001$), fatigue ($\rho = 0.807$, $p < 0.001$), pain interference ($\rho = 0.672$, $p = 0.001$) and pain intensity ($\rho = 0.744$, $p = 0.001$). cJADAS scores were significantly correlated with pain intensity ($\rho = 0.734$, $p = 0.001$) and pain interference ($\rho = 0.721$, $p = 0.001$). Anxiety and depression scores were highly correlated with each other ($\rho = 0.880$, $p < 0.001$) and both correlated with fatigue and pain interference ($p < 0.001$).
Conclusion: Mental health symptoms were highly prevalent in this male predominant cohort of JSpA, even in the context of well-controlled disease. Furthermore, mental health symptoms correlated with self-reported disease related measures. These findings support routine mental health screening to identify at-risk JSpA patients and provide timely interventions, potentially improving overall outcomes.

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The Ink Strikes Back: Tattoo-Associated Uveitis Syndrome. A Five-Case Series

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Objectives: Tattoo-Associated Uveitis Syndrome (TAUS) is a rare immune-mediated condition characterized by synchronous inflammation, including some cases with granulomatous

involvement, of tattooed skin and ocular structures, reflecting a hypersensitivity to pigment antigens. This series details the clinical manifestations of five patients with TAUS managed at a multidisciplinary tertiary centre.[1][2]
Methods: Five patients were identified through the Uveitis–Rheumatology Collaborative Program (Toronto, Canada) between 2019 and 2025. Demographic, ophthalmologic, dermatologic, and immunologic data were reviewed, including the timing of tattoo reactivation, uveitis phenotype, systemic work-up, treatment, and outcomes. Infectious and systemic autoimmune etiologies were excluded by comprehensive testing such as angiotensine-converting enzyme (ACE), autoantibodies, chest imaging, tuberculosis screening, and biopsy when indicated.
Results: The cohort comprised five adults (three women, two men; mean age 34 years) who all developed ocular inflammation within months of inflammatory changes in long-standing tattoos—manifesting as erythema, induration, or swelling, most often in black or multicoloured pigments on the arms, shoulders, or trunk. Latency between tattoo placement and uveitis onset ranged from 6 months to > 5 years (Table 1). Uveitis phenotypes included bilateral anterior (n = 1), anterior–intermediate (n = 1), and panuveitis (n = 3). Two presented with optic-disc edema and one with subretinal fluid. Diagnosis was confirmed by biopsy-proven non-caseating granulomas in two cases and by elevated ACE with concordant tattoo–ocular activity in three; none developed systemic sarcoidosis. All received systemic corticosteroids for induction with topical therapy for local control. Methotrexate was first line in four, with adalimumab escalation in two partial responders. One patient required mycophenolate mofetil after steroid-induced hyperglycemia, maintaining remission thereafter. Four achieved ≥12 months of steroid-free quiescence; one remains on taper with preserved vision and inactive tattoos.
Conclusion: TAUS represents a distinctive cutaneous–ocular inflammatory syndrome characterized by concurrent inflammatory activity in tattoos and uveal tissue. Diagnosis relies on the simultaneous inflammation of skin and eye and, although is not always a granulomatous-type inflammation, it is important to rule out this type of involvement with histologic or biochemical evidence due to its particular severity and also to exclude systemic sarcoidosis. Management should combine early systemic corticosteroids with timely transition to steroid-sparing agents—methotrexate or mycophenolate—and escalation to biologics such as adalimumab for refractory or recurrent cases. Continuous communication between ophthalmology, rheumatology, and dermatology is essential. Prompt recognition and multidisciplinary immunosuppression can achieve durable remission, prevent visual loss, and mitigate systemic overtreatment in this pigment-driven disease.
References: [1.] Kesav, N. P. et al. J Vitreoretin Dis 8, 339–342 (2024). [2.] Siebert, E. et al. Clin Exp Ophthalmol https://doi.org/10.1111/ceo.70012 (2025)

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A Rare Case of Tumor Induced Osteomalacia from Phosphaturic Mesenchymal Tumor in a Patient with Ankylosing Spondylitis

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Background: Tumor Induced Osteomalacia (TIO) is a rare, paraneoplastic syndrome often caused by phosphaturic mesenchymal tumors (PMT). Tumoral overproduction of fibroblast growth factor 23 (FGF23) results in renal phosphate wasting, hypophosphatemia, and defective bone mineralization (osteomalacia). Symptoms are vague and include bone pain, myalgias, or fragility fractures.[1] Diagnosis is often delayed and misdiagnoses are common; mean disease

duration before diagnosis is greater than 4 years. The most frequent misdiagnoses include osteoporosis and spondyloarthritis (37.2 % and 26.3% of patients respectively).[2]
Case Report: A 51-year-old man presented to rheumatology with severe, progressive inflammatory back pain since age 34, in addition to heel and rib border enthesitis. HLA-B27 was positive. There was a family history of ankylosing spondylitis in his father. MRI of the sacroiliac joints was negative for sacroiliitis. He was diagnosed with clinical spondyloarthritis. Trials of NSAIDs were ineffective. He trialed multiple biologics that were either ineffective or partially effective including etanercept, golimumab, secukinumab, adalimumab, upadacitinib. In November 2024, he presented to clinic with severe hip pain and antalgic gait in spite of upadacitinib and full dose oral diclofenac. In December 2024, repeat MRI SI joints and whole spine showed fatty metaplasia at bilateral SI joints suggestive of chronic sacroiliitis without active inflammation and no evidence of spinal involvement. In April 2025, an MRI bilateral hips and subsequent bone scan revealed an undisplaced right femoral neck stress fracture as well as a 2.4 x 2.5 x 3.2 cm enhancing mixed cystic and solid lesion within the left thigh involving the neurovascular bundle. He underwent open reduction internal fixation of the right femoral fracture in May 2025. A bone density scan revealed osteoporosis (femoral neck T score -3.5). The left thigh mass was biopsied and consistent with a PMT. Endocrinology consultation noted very low serum phosphate (0.45 mmol/L, ref. range 0.70-1.50) and diagnosed TIO. Surgical resection of the tumor was performed in August 2025. The patient noted a dramatic improvement in bone pain following PMT resection and has been able to taper both diclofenac and upadacitinib. There are plans to attempt discontinuation of upadacitinib in the future.
Conclusion: This case demonstrates an example of TIO due to a PMT mimicking spondyloarthropathy. Long-term hypophosphatemic osteomalacia can have axial involvement and cause enthesopathy.[2] This rare diagnosis should be considered in those with suspected spondyloarthropathy who have persistent pain despite biologic therapy, fragility fractures, and hypophosphatemia.
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Co-Developing a Flexible Care Delivery Model for Inflammatory Arthritis (Flexcare): Results from Patient Focus Groups

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Objectives: To improve how inflammatory arthritis (IA) care is delivered in Canada and the outcomes obtained, we are co-designing FlexCAre in partnership with adults living with IA and health care providers. FlexCAre aims to better meet the individual needs of patients and achieve better health outcomes. We conducted focus groups with adults with IA across Canada to learn about their experiences, values and preferences, informing the timing, modality, and nature of healthcare visits to optimize IA care.
Methods: Focus groups were held with adults in English and French. Structured online groups lasting 90 minutes used predefined questions to explore how IA care delivery could be changed to better meet their needs. Transcripts were thematically coded and analysed to identify patterns to inform new approaches, interventions, and policy.

Results: The 42 adults (English n=30); French n=12) had a mean (SD) age of 64 (13) years and disease duration of 9 (15) years. They were mostly white (88%) women (88%) from BC (21%), AB (10%), ON (29%), QC (36%) and NS (5%) living in urban locations (60%). Most had RA (50%), PsA (14%), axSpA (10%), and/or other rheumatic diseases (26%). Three overarching themes were identified: 1) IA affects all aspects of life. Participants described the physical, mental, and social burden of IA and need for co-ordinated, holistic care – ideally at one site. They regarded nurses as essential valued team members providing clinical and psychosocial support. 2) Information needs are dynamic and often go unmet. Patients reported limited preparedness for managing their IA and have difficulty accessing timely, relevant information. They identified opportunities for improved education through online and direct engagement with different rheumatology team members. 3) Care must be individualized. Health care needs and preferences vary based on disease activity and duration, life context, and social determinants. They discussed the need to take into consideration individual circumstances and preferences in addition to results of between-visits remote monitoring.
Conclusion: Advances in IA treatment and access to interprofessional care have significantly improved IA outcomes for many. While physical aspects of IA can be controlled, important gaps persist with emotional and social health needs. Findings will help inform the development and initial testing of FlexCAre, a new IA care model that integrates education, remote monitoring, and flexible visit schedules to better meet the diverse needs of individuals with IA. A patient-informed approach has the potential to improve engagement, equity, and outcomes in Canadian IA care.

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Co-Developing Flexcare: Insights from Canadian Health Care Providers on Optimizing Care Delivery

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Objectives: To improve the delivery and outcomes of inflammatory arthritis (IA) care in Canada, we are co-designing FlexCAre in partnership with adults living with IA and arthritis health care providers (HCPs). FlexCAre aims to provide flexible delivery of care to better meet the individual needs of patients and achieve better health outcomes. This study reports findings from focus groups conducted with Canadian IA HCPs to explore their experiences, values, and preferences regarding the timing, modality, and nature of IA healthcare visits.
Methods: Structured online 90-minute focus groups were conducted with HCPs using a predefined question guide to explore opportunities to optimize IA care delivery. Transcripts were thematically coded and analysed to identify patterns to inform new approaches, interventions, and policy.
Results: The 30 HCPs had a mean (SD) age of 64 (13) years. They included rheumatology nurses (67%), rheumatologists (30%) and pharmacists (3%) in BC (60%) and AB (40%) who had been practicing on average 16 years. Three overarching themes were identified: 1) The challenge of whole person care. HCPs noted that when patients lack access to primary care, providing whole person care can feel overwhelming and limits their ability to focus on complex, dynamic disease-specific needs. Equity gaps are greatest among older adults, racialized groups, individuals with mobility limitations, and in rural areas. Unrealistic patient expectations

regarding the scope of services rheumatologists can offer were noted, particularly when patients lack a family doctor and/or mental health services. 2) The need for education and support from IA interprofessionals. Sustaining interprofessional teams remains challenging, even with provincial funding. HCPs emphasized the value of rheumatology team members to educate patients and fill gaps by providing virtual visits, responding to messaging systems, and returning calls. 3) Individualizing care through flexible tools and strategies. HCPs varied in their use of and preferences for virtual care and between-visit monitoring, and tailoring approaches to patient needs, disease status, and life context. Flexibility regarding visit scheduling, type, and monitoring was deemed essential. Several noted that when medication approval depends on symptom assessments, patients are more likely to complete questionnaires. E-health systems can provide disease education and self-management skills training.
Conclusion: HCPs identified key challenges and opportunities to improve IA care delivery. Findings underscore the importance of flexible, integrated, and patient-centered approaches to meet diverse needs, support whole person care, and reduce the burden on providers and meet patient needs. These insights are helping inform the co-design of FlexCAre.

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Evaluation of Baseline Sonographic Enthesitis as a Predictor of Clinical Enthesitis Response to TNF-α and IL-17 Inhibitors Among Patients with Psoriatic Arthritis

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Objectives: Enthesitis is a hallmark feature of psoriatic arthritis (PsA), contributing to pain, disability, and radiographic damage. Detection of clinical enthesitis (CE), defined as tenderness on palpation of entheseal sites, is influenced by non-inflammatory pain and examiner variability. Sonographic enthesitis (SE) provides a more objective assessment of inflammatory and structural lesions at the enthesis but has seldom been used as an outcome in clinical trials.[1] This study aimed to assess whether baseline SE is associated with clinical response after 3 months of TNF-α or IL-17 inhibitor therapy and whether this association differs across biologic classes
Methods: In a single-centre cohort of PsA patients fulfilling CASPAR criteria, those initiating systemic therapy for active musculoskeletal disease were invited to an ultrasound sub-study. A retrospective analysis of stored ultrasound scans included participants treated with TNF-α or IL-17 inhibitors. CE was assessed at baseline and 3 months using the SPARCC Enthesitis Index. SE was evaluated at 16 bilateral sites for grayscale and power Doppler abnormalities following a standardized protocol,[2] including quadriceps, distal patella, tibial tuberosity, Achilles, plantar fascia, triceps, lateral epicondyle, and supraspinatus insertions. Elementary lesions (hypoechogenicity, thickening, erosion, enthesophyte, calcification, Doppler signal) were scored individually using a semi-quantitative score, then combined into composite scores representing total lesion burden, inflammation, and structural damage. An active SE count was calculated based on sites with a Doppler signal plus hypoechogenicity or thickening. A multivariable logistic regression model was used to assess associations between baseline SE scores and resolution of CE at follow-up, adjusting for age, sex, baseline SPARCC score, prior advanced therapy, and biologic therapy class.
Results: Seventy-eight patients were included in the analysis, with 42 on TNF-α inhibitors and 36 on IL-17 inhibitors. At baseline, mean SPARCC score was 1.8 (SD 1.8), with 68% showing at least one CE site. Mean active SE count was 1.4 (SD 1.7), with 65% showing at least one SE site. After 3 months of treatment, mean SPARCC decreased to 1.1 (SD 1.6; p=0.01), and 42%

still had at least one CE site. None of the SE composite scores, nor biologic class (OR 1.31, 95% CI 0.48-3.58; p=0.603), were significantly associated with CE resolution (Table 1).
Conclusion: Baseline composite SE scores were not associated with CE responses to treatment, likely reflecting the limited correlation between SE and CE at baseline. Further studies are needed to evaluate associations at individual entheses and determine whether serial sonographic assessments can better capture treatment response.
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Changes in HAQ Scores over Time in Indigenous Patients with Inflammatory Arthritis

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Objectives: Inflammatory Arthritis (IA) conditions affect Indigenous and First Nations people more than non-Indigenous people. Conditions such as rheumatoid arthritis, axial spondyloarthritis, and psoriatic diseases are more prevalent among First Nations people and have higher healthcare utilization compared to non-First Nations people. Our study looked at the differences that are noted at initial presentation and during treatment for Indigenous people with IA conditions compared to non-Indigenous people.
Methods: Participants are enrolled into the Rheum4U database. The Rheum4U database was first implemented in 2016 as a longitudinal database of patients with inflammatory arthritis conditions, including rheumatoid arthritis, psoriatic arthritis, axial spondyloarthritis, juvenile idiopathic arthritis, and gout. The database now consists of over 1300 patient profiles. We used a linear mixed effects model to identify the correlation between the Health Assessment Questionnaire (HAQ) score and time since baseline (Table).
Results: There were 68 patients in the Rheum4U registry who self-identified as Indigenous. From the Rheum4U registry, Indigenous people were identified using self-reported Indigenous status. IA conditions included rheumatoid arthritis, psoriatic arthritis, spondyloarthritis, and juvenile idiopathic arthritis. Patients are 18 years old and older. Median follow-up time per individual is 26 months (IQR 9, 49). Average HAQ at baseline is 0.86 SD (0.79). The average HAQ score at baseline (time 0) is approximately 0.87. As time increases, the HAQ score changes by 0.00076 per month, but this is not statistically significant.
Conclusion: Among Indigenous people with IA conditions, there is no evidence that HAQ scores changed over time.

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A Pilot Randomized Controlled Trial of a Tailored Internet-Delivered Cognitive-Behavioural Therapy for Insomnia in Persons with Inflammatory Rheumatic Diseases

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Objectives: Sleep disturbances are reported in up to 80% of persons with inflammatory arthritis

(IA) and are poorly addressed. Cognitive-behavioural therapy for insomnia (CBTi) is the first-line insomnia treatment in the general population, but access is limited. Internet-delivered CBT for insomnia (ICBTi) overcomes accessibility barriers. A randomized waitlist-controlled pilot trial was conducted to determine the acceptability and preliminary efficacy of ICBTi for individuals with inflammatory arthritis and insomnia symptoms.
Methods: Participants with IA and symptoms of insomnia were recruited through social media and patient-partner organizations and randomly assigned to the ICBTi treatment group (n= 24; 6 modules over 8 weeks) or the waitlist-control group (n= 26). Participants completed surveys at baseline, 8 weeks (post-treatment), and 3 months later. Treatment group participants completed questions about treatment perceptions. The Insomnia Severity Index (ISI) (maximum score of 28) assessed insomnia symptoms at each time point. Paired sample t-tests were used to analyze changes in ISI scores over time for each group.
Results: The sample included 50 participants with IA and insomnia symptoms (Table). Post treatment completion, most participants in the treatment group rated the ICBTi modules as moderately or extremely useful (84%) and were moderately or extremely satisfied (89%) with the program. Seventy-three percent of treatment group participants self-reported moderate or extreme improvements in sleep. However, only 52% of the treatment group completed the entire program. Feedback included wanting more relevance to arthritis and chronic pain, and a guide alongside the intervention. The mean baseline ISI score was 16.7 in the treatment group and 14.9 in the control group. Twenty treatment groups and 24 control group participants completed the 8-week survey. The mean (95% CI) change in ISI scores pre- to post-treatment in the treatment group was -4.95(-6.77,-3.13), $p<.001$, and -0.94(-.38,2.26) in the control group, a non-significant difference. Eighteen treatment group and 21 control group participants completed the 3-month survey. The mean (95% CI) change in ISI scores from pre-treatment to the 3-month follow-up was -5.28(-7.62,-2.93, $p<.001$) in the treatment group and -0.83(-1.53,3.20) in the control group, a non-significant difference.
Conclusion: The Internet-delivered CBTi program was acceptable and perceived as useful by most participants but could benefit from further adaptation to arthritis-specific needs. The results suggest efficacy of ICBTi among individuals with arthritis. A larger randomized-controlled trial with a larger, more diverse sample is needed to determine the effectiveness of using ICBTi to help people manage the double-burden of insomnia and arthritis. **Supported by a CIORA grant**
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Individuals Using Cannabis for Inflammatory Arthritis Report Similar Symptoms Levels, but Worse Anxiety and Depression than Non-Users
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Objectives: The use of cannabis among individuals with rheumatologic conditions has gained increasing attention due to potential effects on pain, mood, and overall quality of life. However, data on its frequency of use, motivations, and patient-reported outcomes remain limited. We compared cannabis users and non-users by sociodemographic and arthritis characteristics and HRQL, and explored motivations for use, and assessed differences in HRQL among people with rheumatic diseases.

Methods: Data is from the baseline visit of a pilot study of people with inflammatory rheumatic diseases who volunteered for an internet-based intervention to improve sleep. Participants self-reported cannabis use, reasons for consumption, and completed the PROMIS-29 questionnaire (physical function, anxiety, depression, fatigue, sleep disturbance, pain interference, and social participation). Characteristics were compared between cannabis users and non-users using t-test and chi-square. Associations between cannabis use, demographics, and clinical characteristics were examined using multivariable regression.
Results: Our sample had a mean (SD) age of 54 (14) and all were female. Most had RA or PsA, with a mean disease duration of 10 (11) years; many also had OA (30%) (Table). One third reported have used cannabis in the past year, and 24% in the past 3 months (of which 38% used weekly and 31% daily/almost daily). All participations indicated they were using for medicinal reasons only (100%), with primary motivations being to improve pain (19%), sleep (17%), fatigue (<5%) or anxiety (<5%). Nearly half (46%) reported a little improvement in arthritis symptoms with use, 15% reported a lot of improvement, 31% no change, and 8% were unsure. Users reported similar levels of physical function, pain, fatigue, sleep disturbance, and social participation, but significantly higher anxiety (p=.046) and depression (p=.014) than non-users.
Conclusion: One in three participants in an online intervention to improve sleep reported using cannabis in the past year to improve their arthritis symptoms, with nearly a quarter using cannabis regularly to improve pain, sleep, fatigue and anxiety. Users did not report different PROMIS-29 outcomes, although 61% reported a little to a lot of symptom improvement. Understanding the motivations and health impact of cannabis use can help guide patient counseling and future research on alternative management strategies for pain and mood disorders. **Supported by a CIORA grant**

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Use and Perceived Accuracy of Artificial Intelligence (ChatGPT) for Self-Leaning in Inflammatory Arthritis: Opportunities for Equitable Access to Appropriate Information?

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Objectives: Our study identified demographic, clinical, and educational factors associated with using ChatGPT (an artificial intelligence, AI application) for self-learning, and the perceived accuracy of information provided by ChatGPT among adults with inflammatory arthritis (IA).
Methods: Between March and July 2025, we conducted a cross-sectional survey of 410 adults with IA followed at the McGill University Health Centre. Self-reported diagnoses included rheumatoid arthritis (61.5%), spondyloarthritis (13.4%), psoriatic arthritis (9%), systemic lupus erythematosus (7.3%), juvenile idiopathic arthritis (5.1%), and others (3.2%). The primary outcome ‘frequency of AI/ChatGPT use to inquire about their medical condition’ was categorized as an ordered outcome (never rarely/occasionally; somewhat /very frequently) and alternatively as a dichotomous outcome (never used versus ever used AI). The secondary outcome ‘accuracy of information provided by AI’ was categorized dichotomously as rarely/never accurate versus always/mostly accurate. Potential correlates included sociodemographic characteristics, disease duration, prior access to educational resources, reported barriers to education, prior educational resources, and preference for online formats. We built multivariate logistic regressions with either ordered or dichotomous outcomes.

Results: Participants were predominantly middle-aged (mean ± SD 49.6 ± 18.8 years), female (72.7%), urban residents (87.3%), with established IA (77.6%, >5 years). Overall, 59% reported never using AI, 31.7% used it rarely/occasionally, 8.5% used it somewhat/very frequently. In multivariate ordered (logit) models, older age (per-year aOR 0.64, 95% CI 0.51–0.79), established IA (>5 years; aOR 0.51, 95% CI 0.32–0.83), and prior arthritis education (aOR 0.58, 95% CI 0.33–0.99) were associated with lower AI use, while preference for online formats for educational resources predicted greater AI use (aOR 2.06, 95% CI 1.28–3.36). In dichotomous logistic models, female sex (aOR 0.61, 95% CI 0.38–0.97), older age (per-year aOR 0.98, 95% CI 0.97–0.99), and established IA (>5 years; aOR 0.54, 95% CI 0.32–0.89) were associated with lower odds of AI use, whereas online preference again correlated with AI use (aOR 2.25, 95% CI 1.39–3.71). Among AI users, older age was associated with lower perceived information accuracy (per-year aOR 0.96, 95% CI 0.94–0.98). No other covariates were significant.
Conclusion: Many patients with IA use ChatGPT for self-learning, especially younger ones and those preferring online resources. In contrast, women, older patients, those with long-standing disease, or relying on traditional education were less likely to use it. Among users, older age was associated with lower perceived accuracy. Future work should explore how to best integrate AI while ensuring accuracy and equity.

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Confidence in Arthritis Self-Management Correlates Positively with Prior Access to Educational Resources and Negatively with Financial and Access Barriers

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Objectives: To identify demographic, clinical, and educational factors associated with confidence in self-management among individuals living with inflammatory arthritis.
Methods: We conducted a cross-sectional survey in Quebec of 410 participants with inflammatory arthritis, including rheumatoid arthritis (61.5%), spondyloarthritis (13.4%), psoriatic arthritis (9.0%), systemic lupus erythematosus (7.3%), and other (8.3%). The primary self-reported outcome was confidence in managing arthritis, categorized as: confident (very/somewhat), neutral, or unconfident (very/somewhat). Potential correlates included sociodemographic characteristics, disease duration, prior use of educational resources, reported barriers to education, and preferred modes of learning. We assessed possible associations of these factors with confidence using multivariate ordered logistic regression.
Results: Participants were predominantly middle aged (mean ± SD: 49.6 ± 18.8 years) female (73%) residing in urban areas (87%) with established arthritis (78% >5 years). Overall, 48% of respondents reported being very confident, 32% somewhat confident, 12% neutral, and 7% somewhat or very unconfident in their ability to manage their condition. The majority (81%) reported at least one barrier to accessing or understanding educational materials, most commonly lack of time (31%) and complexity of information (25%). In the multivariable model, prior access to educational resources and preference for online resources as a primary mode of learning were strongly associated with higher confidence in self-management (adjusted OR 2.91, 95% CI: 1.29–7.84 and 2.05, 95% CI: 1.20–3.52, respectively). Conversely, financial or access-

related barriers were negatively associated with higher confidence (adjusted OR 0.56, 95% CI 0.31–0.99). Sex, age, residence, primary language, disease duration, and rheumatoid arthritis diagnosis were not significantly associated with confidence in arthritis self-management.
Conclusion: Prior exposure to educational materials and preference for online learning platforms was associated with confidence in arthritis self-management. In contrast, financial and access barriers negatively correlate with confidence. These findings highlight the importance of improving equitable access to patient education and tailoring delivery formats to align with patient preferences.

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Machine Learning Assessment of Cost-Related Medication Nonadherence Among Canadians with Arthritis

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Objectives: Cost is a well-established barrier to treatment adherence, contributing to poorer health outcomes.[1] While cost-related nonadherence (CRNA) has been studied in the general population, it remains under-characterized among Canadians with arthritis, a group with distinct treatment needs and financial burdens. This study applied machine learning to identify and rank factors associated with higher probability of CRNA in this population and to estimate its prevalence and burden.
Methods: Data were sourced from the 2016 Canadian Community Health Survey. Responses from 23,687 individuals with arthritis were analyzed for CRNA, defined as self-reported skipping or not filling prescriptions due to cost in the past 12 months. Sixteen demographic and health/health-system variables were examined using case-weighted random forest models to estimate variable importance (via permutation-based assessment) in the overall and sex-stratified populations. Missing data were imputed using multiple imputations by chained equations. For enhanced interpretability and burden assessment, case-weighted multivariable logistic regression models (overall and sex-stratified) estimated the direction and magnitude of associations. Prevalence estimates and 95% confidence intervals (CIs) were calculated using survey weights and 1,000 bootstrap replicates.
Results: The weighted prevalence of CRNA was 7.5% (95% CI:6.9–8.1), with higher prevalence among females (8.5%, 95% CI:7.7–9.4) than males (6.1%, 95% CI:5.3–6.9). In random forest models, the most influential factors associated with higher probability of CRNA in the overall population were age, insurance coverage, household income, and satisfaction with life (Figure 1). Within the top quartile of factors for both males and females independently were age and insurance coverage. However, remaining top variables differed: among females, household income and education ranked highly, whereas among males, perceived health and satisfaction with life were more prominent (Figure 1). In the multivariable logistic regression, higher odds of CRNA were observed among females (OR= 1.37, 95% CI:1.13–1.66), younger adults ≤34 years (OR=5.22, 95% CI:3.53–7.70), non-white individuals (OR=1.53, 95% CI:1.01–2.32), those with lower income (<$20,000; OR=2.49, 95% CI:1.76–3.52), ≥4 chronic conditions (OR=2.22; 95% CI:1.56–3.14), uninsured (OR=3.31, 95% CI:2.72–4.02), and those residing in British Columbia (OR=1.58, 95% CI:1.15–2.18) or the Prairies (OR=1.37, 95% CI:1.0–1.86). Respondents reporting poor/fair health or dissatisfaction with life also had greater odds of nonadherence.
Conclusion: Findings highlight socioeconomic and regional disparities in cost-related

nonadherence among Canadians with arthritis, with age and insurance coverage being the most influential correlates. While financial and systemic barriers remain central, sex-stratified differences suggest additional psychosocial and health-related factors. Therefore, policies to improve medication affordability and equitable access are warranted.

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In their Own Words: Patient Experiences with Patient Support Programs

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Objectives: The Canadian Arthritis Patient Alliance (CAPA), an independent and patient-led organization, developed, launched, and analyzed results of a national survey to evaluate the experiences of people with rheumatic diseases using Patient Support Programs (PSPs). PSPs were introduced in the early 2000s alongside biologic medications due to gaps in publicly funded healthcare services as a way to provide infusions and nursing support to patients needing these medications.[1] Despite their necessity, limited evidence exists on how patients experience these programs. This project aimed to understand the value, accessibility, and gaps in PSP services through a patient lens, and to generate recommendations to improve patient support, education, and engagement in care.

Methods: The survey was co-developed by people living with inflammatory arthritis, many with firsthand experience using PSPs. It explored domains such as patient–provider communication, consent, and information sharing, and access to pharmacy and insurance services. The survey was open from June 2023 to January 2024, with 375 respondents across Canada. Descriptive statistics were used to analyze quantitative data, while open-ended comments were thematically reviewed to contextualize experiences and recommendations. Findings were presented to a patient advisory group to co-develop key recommendations for improving PSP design and delivery.

Results: Survey respondents represented diverse rheumatic diseases, including rheumatoid arthritis, psoriatic arthritis, and lupus, with the largest proportion aged 30–49 years. Over half of respondents (57%) received consent forms before PSP enrollment, yet only 60% fully understood the program's role. Approximately two-thirds felt they received the necessary information about medication use, though 50% reported inadequate nursing support. Respondents emphasized the value of individualized education and consistent points of contact, noting frequent turnover among PSP staff as a barrier to trust and continuity. Key patient-identified recommendations included simplifying insurance systems, improving communication between PSPs and healthcare teams, ensuring informed consent, enhancing patient education, and developing independent monitoring of PSP effectiveness (Figure).[2]

Conclusion: This patient-led review demonstrates that while PSPs fill critical gaps in Canada's healthcare system, improvements are needed to enhance equity, clarity, and patient-centeredness. People with arthritis and related diseases want programs that prioritize relationship-based care, clear information, and holistic support. Ongoing collaboration between patient organizations, PSP providers, and policymakers can improve these services and ensure they benefit patients in meaningful and impactful ways.

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Hacking Arthritis: Innovation and Adaptation in Daily Life

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Objectives: The Hacking Arthritis project aimed to explore how people living with arthritis adapt to maintain independence, participation, and well-being in daily life. Guided by the Person–Environment–Occupation (PEO) model, the study sought to identify practical, patient-driven strategies that support self-management and participation in meaningful activities. It also aimed to understand how creativity, community support, and systemic factors influence adaptation. Ultimately, the project intended to generate patient-led insights to inform occupational therapy (OT) practice, inclusive design, and broader approaches to arthritis care.

Methods: This initiative synthesized qualitative findings from multiple Canadian Arthritis Patient Alliance (CAPA) projects led by occupational therapy students. which employed qualitative designs (e.g. photovoice) and quantitative design involving an online survey. Participants were individuals living with different forms of arthritis who shared personal stories, photographs, and adaptive “life hacks” demonstrating how they navigate daily challenges. To synthesize the data, we conducted an interpretive, cross-project analysis that merged the qualitative themes generated identifying convergent ideas around adaptation, creativity, and participation. Thematic analysis was guided by Braun and Clarke’s (2012) framework and informed by the PEO model to examine how personal, environmental, and occupational factors intersect to support or hinder participation.

Results: Findings highlighted that people living with arthritis experience functional limitations in a wide range of tasks and occupations, yet they exhibited creativity and resilience when adapting to daily life despite a range of PEO barriers: - Person: Participants reframed loss into adaptation, using creativity as empowerment and self-expression. Emotional resilience, acceptance, and humour were key to sustaining mental health. - Environment: Peer networks, community programs, and digital spaces provided vital social and emotional support, while barriers such as limited OT access, high equipment costs, and stigma persisted. - Occupation: Engagement in meaningful activity—through adaptive tools, modified routines, or personalized strategies—was central to maintaining identity and autonomy. Incremental successes in everyday

tasks reinforced confidence and control.
Conclusion: The Hacking Arthritis project demonstrates the power of patient-driven, co-creative approaches that centre lived experience in arthritis care. It shows how people with arthritis can struggle with tasks but that those that were interviewed were creative in adapting daily tasks. CAPA will continue to find ways to support people living with arthritis in collaboration with occupational therapists, designers, makers, and others and will add to its repository of tools and life hacks on its website,[1] to provide practical hands-on tools and advice for people with arthritis to live independently.
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Factors Associated with Waiting Time for a First Consultation in Rheumatology from a Centralized Referral System.

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Objectives: In Québec, general practitioners are required to submit patient referrals for initial rheumatology consultations through the regional centralized referral system (CRDS). This system assigns appointments based on the reason for consultation and priority level indicated by the GP, using a standardized referral form. This study aims to identify the factors associated with the waiting time for CRDS-assigned rheumatology appointments.
Methods: We conducted a retrospective analysis using data from two regional CRDS over four 4-month periods, over four consecutive years (n=1768 referrals). We examined the characteristics of rheumatology referrals, including system delays calculated as the interval between the referral receipt date at the CRDS and the date of first appointment allocation. Cox regression models were used to identify factors associated with these delays. Waiting times for initial consultations were compared against CRDS target wait time benchmarks.
Results: Median waiting times were 7 days [3-14] for priority B referrals (target wait time <10 days), 31 days [17-70] for priority C (target <28 days), 286 days [128-464] for priority D (target <90 days), and 548 days [347-548] for priority E (target <365 days). Beyond priority level ($p<0.001$), several factors were associated with delays in accessing an initial rheumatology consultation. These included the period ($p<0.001$), with the pandemic year (2020-21) showing longer delays in comparison to the reference year (2019-20); the source of the referral ($p<0.001$), as referrals originating from family medicine groups having longer waits than those from other practice settings; reason for consultation ($p=0.021$), with fibromyalgia linked to longer delays and vasculitis and connective tissue disease to shorter ones; sex assigned at birth ($p<0.001$), with female patients facing longer delays than men; and age ($p=0.021$), older individuals experiencing longer waits. In the multivariable model, the low priority level, the pandemic period, the referrals from family medicine groups and older age were significantly associated with longer delays.
Conclusion: These results suggest that, beyond medical priority, both patient- and system-level factors may influence delays for rheumatology consultations. The next phase of the study will

investigate the circumstances under which these inequities in access arise, by analyzing CRDS demand and supply data, and conducting a comprehensive classification analysis of the additional clinical background and personal history information included in individual referral forms. The findings will inform triage and prioritization strategies in centralized referral systems, including potential extensions and refinements to the standardized referral forms, to support efforts aimed at reducing disparities and promoting equitable access to care. **Supported by a CIORA grant**

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Novel Treatment of Rapidly Progressive ILD in Anti-Pl7 Associated Antisynthetase Syndrome: A Case Report

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Background: Antisynthetase syndrome (ASS) is a rare autoimmune disorder characterized by the presence of antisynthetase antibodies and variable clinical features, including myositis, arthritis, Raynaud's phenomenon, and interstitial lung disease (ILD).[1] Among its subtypes, PL-7-associated ASS, representing approximately 3-4% of cases, is particularly associated with rapidly progressive ILD (RP-ILD) and poor prognosis.[1] Corticosteroids remain the mainstay of therapy; however, steroid-resistant disease is common, and evidence guiding optimal adjunctive immunosuppressive strategies remains limited.[2] In the absence of randomized trials, treatment is often extrapolated from other connective tissue disease-related ILDs. Data from anti-MDA5-associated ILD suggest that early, aggressive combination therapy with corticosteroids, cyclophosphamide, and tacrolimus can improve survival compared to stepwise escalation.[3]

Case Report: We describe a 77-year-old man with atrial fibrillation and prior stroke who presented with a 3-week history of progressive dyspnea, dry cough, and fatigue unresponsive to outpatient therapy. He had no relevant exposures but reported a 2-year history of Raynaud's phenomenon. High-resolution CT revealed right-predominant ground-glass opacities with early fibrosis (Figure 1). Serology demonstrated high-titer anti-PL7 and anti-Ro52/TRIM21 antibodies, confirming ASS. Despite initial corticosteroids, his oxygen requirements worsened to 10 L via non-rebreather, prompting escalation to pulse methylprednisolone (250 mg IV x 3 days), cyclophosphamide (500 mg/m² IV monthly), and tacrolimus (target trough 5-10 ng/mL). His respiratory status improved, and by discharge, he required oxygen only with exertion. During admission, workup revealed rectal adenocarcinoma with a hepatic metastasis, for which neoadjuvant FOLFOX chemotherapy was initiated with curative intent. Cyclophosphamide was discontinued to minimize toxicity, while tacrolimus and prednisone were continued. Within 10 weeks, he no longer required supplemental oxygen.

Conclusion: To our knowledge, this represents the first reported case of colorectal cancer-associated anti-PL7/anti-Ro52-positive ASS presenting with rapidly progressive ILD successfully treated with early triple-agent immunosuppression. This case highlights two key observations: (1) early combination therapy with corticosteroids, cyclophosphamide, and tacrolimus may be lifesaving in severe, steroid-refractory anti-PL7/anti-Ro52-positive RP-ILD; and (2) The coexistence of metastatic colorectal cancer raises the possibility of a paraneoplastic variant of ASS, a rare but described phenomenon. New-onset ASS should prompt evaluation for underlying malignancy, even in amyopathic presentations.

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Monozygotic Triplets Discordant for Cardiac Neonatal Lupus Erythematosus: Case Report and Epigenetic Pilot Study

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Objectives: Infants born to anti-Ro/La antibody positive mothers are at risk of neonatal lupus erythematosus (NLE). These maternal antibodies are necessary but not sufficient to cause NLE, indicating other risk factors contribute to NLE development. Here we present the first recorded case of monozygotic (MZ) triplets discordant for cardiac NLE. We hypothesize that epigenetic changes contribute to the development of cardiac NLE. We also conducted an epigenetic study of infants with and without cardiac NLE, to evaluate the association between epigenetics and cardiac NLE.

Methods: We conducted a retrospective chart review of the triplets referred to the Hospital for Sick Children. Peripheral blood DNA of the triplets, as well as unrelated infants with and without cardiac NLE, was run on Infinium methylation EPIC array (at 850,000 methylation sites) analysis. We identified 39 infants seen in the SickKids NLE clinic with and without cardiac NLE, matched for sex, gestational age (GA) at birth, and age at blood sampling. Differential methylation between infants with and without cardiac NLE was performed and methylation changes were visualized using principal component analyses (PCA) and heatmaps.

Results: The MZ female triplets were identified at 18 weeks GA. Triplet A had endocardial fibroelastosis (EFE), a non-nodal manifestation associated with cardiac NLE. Triplet B was healthy, and triplet C had complete heart block (CHB) and EFE. The triplets (blood sampling at 24 days of life) demonstrated segregation on a heatmap based on methylation patterns concordant with cardiac NLE status. The subsequent study included 39 infants (12 cardiac NLE) born to high titer anti-Ro positive mothers, with a mean 37 weeks GA at birth. Ten infants had CHB, one had EFE, and one had both. PCAs and heatmaps demonstrated segregation of the cardiac NLE infants from those without cardiac manifestations (Figure). The triplets' methylation patterns were not concordant with methylation segregation patterns observed in the unrelated infants, which may have been a consequence of age differences.

Conclusion: We present the first recorded case of MZ triplets discordant for cardiac NLE and observed differences in methylation profiles between the triplets with and without cardiac NLE. In an epigenetic study of cardiac NLE, we observed segregated methylation profiles between infants with cardiac NLE and healthy infants. We acknowledge that sample collection following cardiac NLE manifestations and treatment may impact results. Further research is required to investigate and validate our findings.

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Kinesin Family Member 20B is Upregulated in a Murine Peripheral Nerve Injury Model

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Objectives: Kinesin Family Member 20B (KIF20B) is a cytokinesis-involved motor protein.[1] We have previously shown that antibodies directed against KIF20B (anti-KIF20B) are associated with cranial and peripheral neuropathies in systemic lupus erythematosus (SLE).[2,3] In the central nervous system, KIF20B is essential for normal cortical development in mice;[1] however, the role of KIF20B in the peripheral nervous system has not been explored. The aim of this study was to assess changes in KIF20B expression in a murine model of peripheral nerve injury.
Methods: Right sciatic nerve crush injury was performed in male and female C57BL/6 mice (young, age 2 months, n=4; old, 16 months, n=3) on day 0, with euthanasia and bilateral sciatic nerve collection on day 7. Spatial transcriptomics with single cell resolution was performed on both ipsilateral (injured) and contralateral (non-injured) nerves (Xenium, 10x Genomic, Pleasonton, CA, USA). Cells expressing KIF20B were labelled as positive. Chi square tests were used to compare the proportion of KIF20B positive cells between injured and non-injured nerves, as well as between the nerve segments proximal and distal to the site of injury. Study protocol was approved by the University of Calgary Animal Ethics Committee.
Results: When KIF20B expression was compared across all cell types between injured and non-injured nerves, there was significantly greater expression in injured nerves (2.87%) when compared to non-injured nerves (0.83%; p=0.0000011), (Figure 1). In injured nerves, the proportion of KIF20B expressing cells was significantly increased in the segment distal to site of injury (3.51%) when compared to the proximal segment (1.28%; p=0.000000003), (Figure 1). There was no significant difference in KIF20B expression between non-injured nerves and the proximal segment of injured nerves (proximal, 1.28%; non-injured, 0.83%; p=0.16); (Figure 1). When KIF20B expression was assessed in individual cell types between injured and uninjured nerves, the greatest difference was seen in Schwann cells (injured, 4.90%; non-injured, 1.00%; p=0.0000087). There were no significant differences in KIF20B expression when old and young mice were compared.
Conclusion: KIF20B expression is increased in the distal segment of mouse sciatic nerves following crush injury and these changes are greatest in Schwann cells. Future studies are needed to characterize how Schwann cell expressed KIF20B contributes to peripheral nerve healing, as well as how anti-KIF20B antibodies might disrupt this process and potentially contribute to cranial and peripheral neuropathies in SLE.
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Longitudinal Serum Proteomic Profiles – A Step Closer to Personalized Monitoring in Dermatomyositis
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Objectives: Dermatomyositis (DM) is a multisystemic immune mediated disease presenting with

heterogeneous clinical features. Disease activity relies on biomarkers such as creatine kinase (CK) which can be unreliable, notably in cases with extra-muscular manifestations.
Novel proteomic platforms have the potential to identify inflammatory biomarkers for personalized monitoring. The objective of this study was to identify proteins associated with disease activity in DM by using the Olink Target 96 Inflammation panel.
Methods: Six DM patients from a multicenter inflammatory myopathy registry with available longitudinal biobanked sera were identified. All patients met the 2017 EULAR/ACR criteria for adult idiopathic inflammatory myopathy. Disease activity was categorized based on the International Myositis Assessment and Clinical Study (IMACS) physician global assessment (PhGA) as low (PhGA 0-3) or moderate/high (PhGA 4-10). The IMACS core set measures used for the 2016 ACR/EULAR Total Improvement Score were extracted. Serum samples were analyzed using proximity extension technology (Olink Proteomics Inc., Watertown, MA), simultaneously targeting 92 proteins involved in inflammatory processes. Results were reported as normalized protein expression (NPX) values (log2 scale) with higher NPX values representing higher protein concentrations. Mean NPX difference (ΔNPX) for each protein comparing moderate/high and low disease activity were calculated using paired t-tests with Benjamini-Hochberg correction for multiple testing.
Results: Six female DM patients with ages ranging from 34 to 53 years were included (Table 1). Clinical features at timepoint 1 included rash (n=6), muscle weakness (n=5), interstitial lung disease (n=5), Raynaud's (n=3), arthritis (n=1) and dysphagia (n=1). CK values ranged from 37-6039 U/L. Autoantibodies included anti-MDA5, -TIF1y, -Mi2, -Ro52, and -Ku. At timepoint 1, 5 patients had moderate/high disease activity and at the timepoint 2, 5 patients had low disease activity. Eleven proteins were significantly upregulated when comparing moderate/high vs. low disease activity. The strongest ΔNPX was observed for monocyte chemoattractant proteins, MCP-2 (3.0), MCP-1 (2.4), MCP-4 (2.2) (all adj. p=0.02) and C-X-C motif chemokine 11 (CXCL11, 3.0, adj. p=0.05). Other upregulated proteins included CX3CL1 (1.57), CCL11 (1.42), PD-L1 (1.27), IL-4 (1.1), CD40 (0.92), IL-15RA (0.9) and CSF-1 (0.61) (all adj. p=0.05).
Conclusion: Using serum inflammatory profiles, we identified proteins upregulated in DM patients with moderate/high disease activity compared to low disease activity in a small exploratory cohort. Those included chemokines involved in monocyte and T-cell recruitment that could represent potential biomarkers for disease activity monitoring. Further studies in larger DM cohorts are warranted to evaluate the role of longitudinal proteomic profiling in personalized disease activity monitoring.

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Double Trouble: A Retrospective Chart Review of Patients with Immune-Related Myositis and Myasthenia Gravis

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Objectives: 1. Describe the clinical characteristics of patients presenting with an overlap of immune-related myositis and myasthenia gravis (MG) secondary to immune checkpoint inhibitors (ICIs).
2. Evaluate the management strategies utilized to care for these patients.
3. Identify clinical and treatment-related factors associated with patient outcomes.
Methods: Clinical data was abstracted from medical records, including demographics, oncologic history, pre-existing autoimmune conditions, manifestations of disease, laboratory findings,

treatment, and outcomes.
Results: 18 patients were identified with overlapping myositis and MG. 50% of MG diagnoses were supported by positive electromyography (EMG) or MRI, and 50% were diagnosed clinically by ocular or bulbar symptoms, and/or fatigable muscle weakness. Myositis was diagnosed by CK elevation, MRI or EMG, and physical findings of sustained proximal muscle weakness. All patients received initial high-dose glucocorticoids, with improvement in 12 of 18 patients. In addition to glucocorticoids, 7 received intravenous immunoglobulins, 1 plasma exchange, 8 acetylcholinesterase inhibitor therapy (pyridostigmine), and 3 disease-modifying antirheumatic drug (DMARD) therapy. DMARD therapies included mycophenolate (symptom improvement in 2 of 3 patients), infliximab (improvement in 1 of 3 patients), and rituximab (deterioration in 1 patient). 7 patients received pyridostigmine, of which 6 had symptom improvement. None required ventilatory support. 3 of 18 patients died from MG/myositis syndrome. Mortality was associated with Grade 4 symptom severity, bulbar involvement, and profound muscle weakness. The presence of MG- or myositis associated antibodies did not predict mortality.
Conclusion: This multi-centre study characterizes a spectrum of clinical presentations among patients with overlapping immune-related myositis and MG. Mortality was associated with Grade 4 symptom manifestations, bulbar symptoms, and need for ventilatory support, highlighting the critical role of early recognition and aggressive management in severe cases.[1] All patients received high-dose glucocorticoids, with some receiving additional immunosuppressive therapies and supportive care. Addition of acetylcholinesterase inhibitor therapy improved overlap symptoms more than DMARD therapy alone. Among those with EMG-confirmed MG, the majority improved with pyridostigmine, further suggesting true neuromuscular junction pathology and arguing against the interpretation that MG diagnoses merely represent severe myositis, which reinforces the concept of distinct overlap syndrome rather than a single disease spectrum. As in previous studies, clinical outcomes were influenced by disease severity and organ involvement rather than serologic markers, as antibody positivity did not correlate with mortality.[2] These findings support the need for multidisciplinary care, early diagnostic evaluation, and individualized treatment strategies to optimize outcomes in patients with overlap syndromes.
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Obinutuzumab Demonstrates Steroid-Sparing Effects and Consistent Benefit in Patients with Lupus Nephritis when Using Multiple Primary Endpoint Definitions: A Secondary Analysis of Phase III Trial Results

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Objectives: The Phase III REGENCY study (NCT04221477) demonstrated superiority of obinutuzumab (OBI) over placebo (PBO) in achieving complete renal response (CRR) at Week 76 when added to standard therapy (ST) in patients with active lupus nephritis (LN). There is no standardized CRR definition. These post hoc analyses evaluated OBI+ST vs PBO+ST across different renal response definitions from recent studies, the efficacy of OBI+ST vs PBO+ST on each component of the REGENCY CRR definition and the oral prednisone intake over time.
Methods: REGENCY, BLISS-LN and AURORA-1 renal response endpoint definitions were used for analysis of the REGENCY dataset at Week 76. The Cochran–Mantel–Haenszel test, stratified by region and race, was used for treatment comparisons. All patients received oral prednisone as part of ST, tapered to 5 mg/day by Week 24.
Results: At Week 76, 46.4% of patients in the OBI+ST (n=135) and 33.1% in the PBO+ST arm (n=136) achieved CRR (adjusted difference: 13.4%, 95% CI, 2.0 to 24.8%; P=0.0232). The proportions of OBI+ST vs PBO+ST achieving modified BLISS-LN primary efficacy renal response were 51.8% and 39.7% (adjusted difference: 12.1%, 95% CI, 0.5 to 23.8%; P=0.0432); modified BLISS-LN CRR were 48.7% and 33.1% (adjusted difference: 15.7%, 95% CI, 4.3 to 27.2%; P=0.0084); modified AURORA-1 CRR were 48.7% and 33.8% (adjusted difference: 15.0%, 95% CI, 3.6 to 26.5%; P=0.0117). A higher number of patients achieved the individual components of CRR at Week 76 in the OBI vs PBO arm for all three components (UPCR <0.5 g/g: 47.4% vs 36.0%; eGFR ≥85% of baseline: 83.7% vs 75.7%; no occurrence of intercurrent events: 88.9% vs 75.0% for OBI+ST and PBO+ST, respectively). In both arms, the main reasons for not attaining CRR were UPCR ≥0.5 or eGFR <85% of baseline (54.8% OBI+ST vs 65.4% PBO+ST). The mean daily prednisone intake was consistently lower in patients in the OBI vs PBO arm from Week 24-76 (Figure 1). The proportions of patients achieving a daily prednisone (or equivalent) dose of ≤5 mg/day were consistently higher in the OBI vs PBO arm from Week 36, reaching a 10 percentage point absolute difference from Week 64-76 (78.5% vs 68.4% for OBI+ST vs PBO+ST; adjusted difference (95% CI): 10.1% (−0.5 to 20.4), P=0.0589).
Conclusion: In a post hoc analysis of the REGENCY trial outcomes, OBI showed consistent benefit across patient subgroups, utilizing multiple alternative definitions of CRR and exhibited steroid-sparing properties.
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Infusion-Related Reactions (IRRs) and Hematologic Events Associated with Obinutuzumab in Lupus Nephritis: A Secondary Analysis of a Phase III Trial

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Objectives: The REGENCY (NCT04221477) trial demonstrated superior efficacy of obinutuzumab and standard therapy (OBI+ST) over placebo and ST (PBO+ST) in patients (pts) with active lupus nephritis (LN). Insights related to IRRs and hematologic effects of OBI would help guide future management of LN. This study characterized the IRR profile and occurrence of neutropenia in the REGENCY trial.
Methods: Incidence, severity and attribution of IRRs and hematologic abnormalities, including drug-related neutropenia, were determined based on investigator and NCI CTCAE v5.0 adverse event grading.
Results: The proportion of pts who experienced at least one IRR was higher in the OBI+ST vs the PBO+ST arm (21 [15.4%] vs 15 [11.4%]). In the OBI+ST arm, the majority (19 [14.0%]) experienced IRRs of Grade (Gr) 1-2, which resolved. In the OBI+ST arm, 2 pts (1.5%) experienced Gr 3-4 IRRs; both events resolved. No Gr 5 IRRs were observed. The most frequently reported symptoms of IRRs in the OBI vs PBO arms respectively were nausea (4 [2.9%] vs 4 [3.0%]), headache (4 [2.9%] vs 3 [2.3%]) and vomiting (4 [2.9%] vs 2 [1.5%]). IRR incidence and severity was highest at first infusion, with Gr 3-4 observed only then (Table 1). The shifts observed from Gr 1-2 at baseline to Gr 3-4 post-baseline were notably different between the treatment arms for neutrophils and lymphocytes. As lymphopenia is an expected pharmacologic effect of anti-CD20 therapies, this analysis focused on drug-related neutropenia. The proportion of pts who experienced at least one drug-related neutropenia was higher in the OBI+ST arm vs the PBO+ST arm (17 [12.5%] vs 5 [3.8%]). Most cases of neutropenia were incidentally detected during routine hematology labs at scheduled study visits. Median time for resolution was 16 days (d) (min-max: 4-378 d) and 50.5 d (min-max: 21-371 d) in the OBI+ST and PBO+ST arm, respectively. Seven pts (4.1%) had Gr 3-4 drug-related neutropenia (including 1 febrile neutropenia), while none occurred in the PBO+ST arm. All drug-related neutropenia resolved with treatment except for one PBO pt where it was resolving at clinical cutoff. No Gr 5 neutropenia was observed. Five patients received G-CSF treatment for drug-related neutropenia (4 in the OBI+ST arm vs 1 in the PBO+ST arm).
Conclusion: The incidence of IRRs and drug-related neutropenia was higher in pts receiving OBI+ST but risks remained low overall; many were Gr 1-2, self-limited, easily manageable and without consequence. These data provide insights into adverse events related to OBI.

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Idiopathic AA Renal Amyloidosis Treated with Tocilizumab — A Case Report

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Background: Amyloidosis represents a heterogeneous group of disorders characterized by the deposition of misfolded protein. Among its subtypes, serum amyloid A (AA) amyloidosis arises when persistent systemic inflammation drives hepatic production of SAA. Excess SAA misfolds into insoluble fibrils that deposit in organs such as the kidneys, causing progressive proteinuria, loss of renal function and eventual renal failure. Standard management aims to control the underlying inflammation to reduce SAA production and halt further amyloid deposition. For example, interleukin-6 blockade with tocilizumab, which suppresses SAA production, has shown encouraging results in small series of patients with secondary amyloidosis.[1,2] In rare cases without an identifiable source of inflammation, however, no targeted therapies have been shown to be effective.
Case Report: We report a 48-year-old female first found incidentally at the age of 37 to have renal impairment. Over the past decade, her eGFR had declined to 12mL/min/1.73m², with 3g/L

of proteinuria. Renal biopsy in 2020 confirmed widespread AA amyloid deposits with severe interstitial fibrosis and 11/16 glomeruli globally sclerosed, with SAA concentrations exceeding 16,000ng/mL. Throughout her entire course, she had no infectious, rheumatologic or constitutional symptoms. Other than a RF titer of 30 IUx103/L, extensive investigations were negative, including bone marrow biopsy, rheumatologic markers (CCP, ANA, dsDNA, C3/C4, ANCA, ESR, CRP) and infectious serologies (hepatitis, syphilis, schistosoma, strongyloides, whipples, tuberculosis, HIV, HTLV, filariasis). A thorough genetic investigation was also negative including sequencing for the SAA1 gene, panels containing genes associated with hereditary amyloidosis and autoinflammatory diseases, as well as a research exome. A brief trial of colchicine was initially trialed but stopped due to worsening kidney function. Tocilizumab 160mg SC every two weeks was initiated in December 2024 in an attempt to suppress hepatic SAA production. A year after, SAA levels fell from >16,000 to 5,427ng/mL. Her GFR stabilized at 13 mL/min/1.73m², and dialysis has not yet been required at the time of writing.
Conclusion: Idiopathic AA amyloidosis is a therapeutic challenge due to the condition's rarity and lack of standard therapies. While there are numerous publications demonstrating the efficacy of tocilizumab in secondary AA amyloidosis,[1,2,3] our case is the first we are aware of, describing this therapeutic effect in idiopathic AA amyloidosis. This case underscores the central role of interleukin-6 in SAA production and may form the foundation for future studies with more patients over a longer duration to further explore the disease-modifying benefits of tocilizumab in idiopathic AA amyloidosis.
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Adults with Unclassified Systemic Autoinflammatory Disease: Insights from a Canadian Autoinflammatory Clinic

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Objectives: 1) Describe the clinical and genetic characteristics of adult patients with Unclassified Systemic Autoinflammatory Disease (USAID). 2) Hypothesize on potential causal factors behind USAID.
Methods: Inclusion criteria were age ≥18 years, with unexplained recurrent or chronic inflammation (≥1 of: fevers, serositis, peritonitis, pharyngitis, mucocutaneous ulceration, skin lesions, elevated CRP, response to colchicine or IL-1 blockade). Gene panel testing was performed via Next Generation Sequencing at the Hospital for Sick Children. All patients provided written consent to be included in a case series.
Results: A total of 48 patients were included (85% female). The cohort was ethnically diverse, including Caucasian (77%), South Asian (10%), East Asian, African and Middle Eastern (each 4%). The median age at enrollment was 36 years, and first symptom onset at 25 years. A family history of similar symptoms was present in 23%. Prior to first onset, an antecedent event was recalled in 40% of patients. The most common were concussion (8/48, 17%), and frequent viral

infections (6/48, 12.5%). The most common manifestations were joint pain/swelling (83%), dermatologic lesions (77%), and recurrent fevers >38°C (75%). In those with dermatologic lesions, the most subtypes were nonspecific rash (62%), mucocutaneous ulcerations (57%) and urticaria-like lesions (38%). Skin biopsy was performed in 11, with neutrophilic infiltration found in 5. CRP was elevated during flares in 32/39 (82%) of patients, and in 9/48 (19%) at baseline. Autoinflammatory gene variants were found in 40/48 (83%) patients. MEFV variants were present in 30/48 (63%) for which the most common was E148Q (12/30, 40%). NOD2 variants were present in 25/48 (52%), the most common being L1007fs (5/25, 25%). NLRP12 variants were present in 5/48 (10%). Variants were also found (in fewer numbers) in NLRP3, TNFRSF1A, NLRC4, and MVK. Colchicine was beneficial in 32/39 patients. IL-1 inhibitor was trialed in 9 patients, with 8 showing clinical and biochemical improvement.
Conclusion: USAID remains an important area of study given the large number of autoinflammatory patients that lack a monogenic explanation. It remains unclear whether USAID patients have a monogenic disease in a yet unknown gene, or a multifactorial condition with genetic susceptibility factors. Indeed, a '2 hit hypothesis' appears plausible given the significant proportion of patients carrying a genetic variant and recalling a triggering event. Only one patient in the cohort denied any antecedent events and lacked autoinflammatory gene variants, highlighting these as likely important factors in disease pathogenesis.

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Lenalidomide-Induced Large Vessel Vasculitis and Pachymeningitis Complicating Treatment of Follicular Lymphoma: A Case Report

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Background: Lenalidomide is a cornerstone therapy for hematologic malignancies with direct antineoplastic effects via modification of ubiquitin ligation as well as pleiotropic immunomodulatory effects. Increased T cell and natural killer cell proliferation and Th1 polarization induced by lenalidomide with upregulation of pro-inflammatory cytokines IL-2, IL12 and IFN-y is thought to amplify antitumor immune responses.[1] Although confounded by underlying treatment indication, there are reports of secondary autoimmune diseases evolving during therapy with lenalidomide.[2] To our knowledge, no reports have yet described large vessel vasculitis or meningeal involvement.
Case Report: A 66-year-old male was hospitalized with acute fever, headache and back pain one month after initiation of rituximab and lenalidomide for relapsed lymphoma. Five years prior after diagnosis of stage IVA follicular lymphoma, he achieved complete radiographic remission with bendamustine and rituximab, and further maintenance was deferred. Six months before his hospitalization, he developed abdominal distension with CT findings of bulky diffuse mesenteric and retroperitoneal lymphadenopathy presumed to reflect lymphoma recurrence. At admission, MRI demonstrated new diffuse pachymeningeal thickening and enhancement with scattered nodularity, and restaging CT noted stable lymphadenopathy but new ill-defined perivascular fat stranding and circumferential wall thickening of the aortic arch and left subclavian artery. At time of lumbar puncture for concern of relapsed lymphoma, he received an empiric single dose of intrathecal methotrexate, cytarabine and hydrocortisone. However, extensive microbiologic and malignancy workup subsequently returned negative including two bland CSF samples and an unrevealing retroperitoneal lymph node biopsy. He received no other empiric treatment beyond an initial 3 days of antibiotics. His initial CRP of 255 mg/L steadily decreased and normalized over 2 weeks alongside his symptoms. Repeat imaging at 4 weeks from initial presentation

demonstrated a reduction in lymphadenopathy, near resolution of aortitis and no significant dural thickening or enhancement. PET CT body scan subsequently found no abnormal FDG avidity to suggest active large vessel vasculitis, meningitis or malignancy.
Conclusion: The temporal relationship with lenalidomide exposure and a complete clinical, biochemical and radiographic resolution without ongoing aggressive systemic therapy suggests his large vessel vasculitis and pachymeningitis were caused by lenalidomide. This case is particularly unique as neither manifestation is yet described in the literature. Considering the more typical association of pachymeningitis with small vessel vasculitis,[3] our case may reflect variable vessel vasculitis induced by lenalidomide.
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A Novel TNFAIP3 Truncating Variant in a Multigenerational Family with Haploinsufficiency of A20: Expanding the Disease Spectrum from Subclinical Inflammation to Autoimmune Endocrinopathy

Lujain Alahmadi (The Hospital for Sick Children, Toronto); Jason An (Toronto)

Objectives: To describe a three-generation family carrying a novel TNFAIP3 truncating variant (p.Gly440*) and to highlight the wide clinical spectrum of Haploinsufficiency of A20 (HA20).
Methods: We reviewed clinical histories and laboratory findings including genetic testing, in family members across three generations. Gene panel testing was performed by next-generation sequencing at the Hospital for Sick Children and variants were classified as per the American College of Medical Geneticists criteria.
Results: The proband (grandmother), aged 71, was initially referred for unexplained and persistently elevated inflammatory markers (ESR 91mm/h, CRP 58–179mg/L). She had no symptoms of any inflammatory disease. Her son suffered from infant onset recurrent painful orogenital ulcers and arthritis, on a background of granuloma annulare and celiac disease. His inflammatory markers were also elevated (CRP 12–17 mg/L). The proband's daughter was diagnosed in infancy with type 1 diabetes and died from an insulin overdose. Prior to this, she had a son who was also affected by infantile diabetes. Despite having no systemic inflammatory features, he also exhibited elevated CRP (10mg/L). Genetic analysis revealed a heterozygous TNFAIP3 variant, (c.1318G>T, p.Gly440*), in all three individuals. This variant was absent from healthy population databases. It has never been documented in the literature and was bioinformatically predicted to create a premature stop codon leading to an absent or dysfunctional A20 protein. As such, it was classified as Likely Pathogenic. The proband's son was treated initially with colchicine with partial improvement, and later with apremilast, which completely eliminated any further mucocutaneous ulcerations.
Conclusion: We report a novel truncating variant in TNFAIP3 causing HA20 in a multigenerational family. Our case series is in line with the current literature and demonstrates the phenotypic variability of HA20 even within the same family, ranging from silent inflammation to Behçet-like disease to organ-specific autoimmunity. Recognizing the variable expressivity and incomplete penetrance of HA20 is important for early diagnosis, screening of family members, and the use of targeted therapy in affected individuals.

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Cryptic NLRP3 Mosaicism Uncovered by Deep Sequencing in Muckle–wells Syndrome: A Case Report

Lujain Alahmadi (The Hospital for Sick Children, Toronto); Elizabeth Schmitz (Washington

University in St. Louis, St. Louis); Daniela Dominguez (Division of Rheumatology, The Hospital for Sick Children, Toronto); Roberta Berard (Children's Hospital, LHSC, London); Linda Hiraki (Division of Rheumatology, Hospital for Sick Children, Toronto); Megan Cooper (Washington University in St. Louis, St. Louis); Dilan Dissanayake (Division of Rheumatology, The Hospital for Sick Children and University of Toronto, Toronto)

Background: Muckle–Wells syndrome is part of the cryopyrin-associated periodic syndrome (CAPS) family, a group of rare autoinflammatory conditions caused by gain-of-function variants in the NLRP3 gene, leading to uncontrolled activation of the inflammasome and excessive IL-1β release. Although most patients have a detectable genetic change, a small number present with a typical CAPS phenotype but do not carry a known pathogenic variant in NLRP3 on conventional sequencing. In-depth genetic analyses have recently shown that some of these cases are explained by hidden, low-level NLRP3 mosaicism.

Case Report: A 21-year-old male first presented in 2012 at the age of 6 with recurrent episodes of transient, non-pruritic urticarial rash, low-grade fever, fatigue, episodic arthritis of the knees and ankles, and enthesitis predominantly involving the Achilles tendon and dorsal foot insertions. During flares, inflammatory markers were elevated (CRP 12–18 mg/L, ESR 31–38 mm/h, serum amyloid A >160,000 ng/mL), with mild normocytic anemia. Autoimmune serologies and complement levels were normal. In 2013, mild unilateral sensorineural hearing loss was identified and remained stable; MRI of the brain and internal auditory canals was normal. Initial genetic testing with a recurrent fever syndrome panel in 2014 and whole-exome sequencing in 2018 were both reported as negative. Anakinra, initiated in 2014, provided partial improvement but was discontinued due to injection-site reactions. In 2018, with worsening symptoms and elevated inflammation (CRP 47 mg/L, ESR 31 mm/h, SAA 55,264 ng/mL), canakinumab was started, leading to rapid and sustained normalization of inflammatory markers and resolution of clinical symptoms. The patient remained in long-term disease quiescence for approximately 4 years (2018-2022), after which the patient discontinued treatment and was lost to follow-up. In 2025, stored DNA was re-analyzed with high-depth sequencing for a panel of 101 known autoinflammatory genes and identified a NLRP3 variant (p. Arg260Pro, Clinvar classification pathogenic) in approximately 5% of reads. Retrospective analysis of existing whole-exome data did not identify this low-level variant.

Conclusion: Consistent with previous reports of NLRP3 mosaicism as a cause of CAPS, this case demonstrates that negative genetic testing does not exclude cryopyrin-associated periodic syndromes and that somatic mosaicism should be considered when the clinical phenotype is compelling. As sequencing technologies evolve, periodic re-analysis offers a critical second opportunity for diagnosis and targeted treatment.

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An Unusual Case of Infection-Provoked Macrophage Activation Syndrome in Mixed Connective Tissue Disease

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Background: Compared to systemic lupus erythematosus and adult-onset Still’s disease, mixed connective tissue disease (MCTD) is rarely associated with macrophage activation syndrome (MAS). Viruses, including cytomegalovirus (CMV), may potentiate MAS,[1] often in conjunction with an underlying connective tissue disease.[1-3] Despite this, reports of infection-provoked MAS in adults with MCTD remain very rare.[2-3] Here we describe a case of MAS in

a patient with MCTD and concurrent CMV viremia and Clostridioides difficile colitis.
Case Report: A 65-year-old male was diagnosed with MCTD after presenting with pulmonary arterial hypertension, presumed glomerulonephritis, Raynaud's phenomenon, and polyarthritis on a background of coronary artery disease and recent NSTEMI requiring stent placement. Investigation revealed a positive ANA (≥1:640, speckled pattern); high-positive anti-RNP-A, Sm/RNP, Ro60/SSA, Ro52/TRIM21, and SSB; and proteinuria. Right heart catheterization and renal biopsy were deferred given dual-antiplatelet therapy and spontaneous renal recovery. He received methylprednisolone prior to a prednisone taper and initiated mycophenolate mofetil (MMF), hydroxychloroquine, macicentan, and tadalafil. He subsequently presented with watery diarrhea, fever (38.5°C), malaise, weight loss and arthralgia. Infectious work-up revealed CMV viremia (serum viral load >4 million/mL) and C. difficile colitis, for which he initiated ganciclovir and oral vancomycin. He was found to have new bicytopenia (hemoglobin 78 g/L, platelet count 175 X109/L), hyperferritinemia (peak 6751 μg/L), hypertriglyceridemia (3.47 mmol/L), hypofibrinogenemia (nadir 1.0 g/L), and elevated aspartate aminotransferase (101 units/L). His C-reactive protein was 21.0 mg/L (peak) and his complement C3 and C4 were normal. Both hematology and rheumatology were consulted, and the patient was diagnosed with MAS. Bone marrow biopsy was deferred given overwhelming evidence for MAS. His MMF was held for diarrhea, and he was initiated on methylprednisolone (250 mg daily for three consecutive days, followed by taper) and anakinra (100 mg subcutaneously daily, titrated to three-times daily) with clinical and biochemical improvement.
Conclusion: We found only two other published English-language adult cases of MAS in conjunction with MCTD in the context of infection. One case was related to histoplasmosis,[2] and the other to an unspecified infection.[3] It is well known that infections can trigger MAS,[1] and while rare, in the appropriate clinical context, MAS should be considered in patients with MCTD who present with an infection and are not improving with standard treatment and whose biochemical parameters suggest MAS.
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Immune Checkpoint Inhibitors and Hypertension: A Scoping Review
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Objectives: Immune mechanisms are recognized contributors to hypertension, and previous studies have proposed that hypertension may have an autoimmune basis.[1,2] Immune checkpoint inhibitors (ICIs), widely used as immunotherapies across diverse malignancies, have been increasingly reported to cause autoimmune-related adverse effects. In this scoping review, we tested the hypothesis that ICIs may precipitate hypertension through immune-mediated mechanisms.
Methods: A scoping review evaluating the incidence of hypertension in patients receiving ICIs, either as monotherapy or in combination with other anticancer agents, was conducted in accordance with the Joanna Briggs Institute (JBI) methodology and the PRISMA-ScR reporting guidelines. A comprehensive search of PubMed, CINAHL, Embase, and MEDLINE databases was performed for studies published up to June 30, 2025. Eligible studies included adults (≥18 years) with cancer treated with programmed cell death protein-1 (PD-1), programmed death-ligand 1 (PD-L1), or cytotoxic T-lymphocyte–associated protein 4 (CTLA-4) inhibitors, excluding those with pre-existing hypertension. We identified ICI drug classes, combination

regimens, and cancer types that are most frequently associated with hypertension.
Results: A total of 200 studies (n = 226 incidence values) were included in this review. The reported median participant age ranged from 30 to 79 years among patients receiving ICIs in combination with other anticancer agents, and from 54 to 70 years among those treated with ICI monotherapy. The incidence of hypertension demonstrated considerable heterogeneity across studies, with a median of 28.6% (range 0.0–100%) in the combination therapy group (n = 211) and 8.2% (range 0.0–54.3%) in the monotherapy group (n = 15) (Figure 1). Hypertensive events were most reported with PD-1 inhibitors, followed by PD-L1 inhibitors, while CTLA-4 inhibitors demonstrated the lowest reported frequency. Notably, the occurrence of hypertension was more pronounced in combination regimens, particularly those including tyrosine kinase inhibitors (TKIs) or vascular endothelial growth factors (VEGF) inhibitors. Among cancer types, hepatocellular carcinoma and lung cancer were most frequently associated with hypertension in the ICI combination and monotherapy groups, respectively.
Conclusion: Our findings demonstrate that ICIs, especially in combination therapy, increases the occurrence of hypertension in cancer patients, suggesting the importance of immune mechanisms in the development of hypertension. Given the limited number of studies characterizing hypertension arising from ICIs, further research is warranted to elucidate underlying mechanisms, refine risk stratification, and inform evidence-based clinical decision-making.
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Association of Obesity with Higher Disease Activity and Lower Health-Related Quality of Life in Clinical Responders to Psoriatic Arthritis Treatment: Post-Hoc Analysis from the Spirit Studies

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Objectives: To investigate effects of overweight/obesity on health-related quality of life (HR-QoL) and disease activity among patients with psoriatic arthritis (PsA) who achieved American College of Rheumatology criteria (ACR50) or Disease Activity index for Psoriatic Arthritis (DAPSA) low disease activity (LDA).
Methods: This post-hoc, unadjusted, treatment-agnostic analysis included PsA patients from the SPIRIT-P1, -P2, and -H2H studies who were treated with ixekizumab or adalimumab.[1] Patients achieving ACR50 or DAPSA LDA at week 24 (W24) were categorized based on baseline body mass index (BMI): Normal (<25 kg/m2), Overweight (25-<30 kg/m2), and Obesity (≥30 kg/m2). HR-QoL outcomes included Health Assessment Questionnaire-Disability Index (HAQ-DI) and fatigue severity numeric rating scale (NRS). Disease activity was evaluated

using pain visual analogue scale (VAS), swollen joint count (SJC), tender joint count (TJC), patient global assessment of disease activity (PatGA), physician global assessment of disease activity (PGA), and C-reactive protein (CRP). Observed data were presented. Non–parametric (Mann-Whitney U) test was used to account for non-normal distribution of some parameters; overweight or obesity subgroups were compared to the normal BMI subgroup; $p<0.05$ denoted statistical significance. No multiplicity testing adjustment was performed. The analysis was not adjusted for baseline assessments of HR-QoL or disease activity.

Results: Among patients who achieved ACR50 by W24, significant differences were observed between obesity and normal BMI subgroups for HAQ-DI, fatigue severity NRS, pain VAS, and PatGA. CRP levels were significantly elevated for obesity and overweight versus the normal BMI subgroup (Table 1). Among patients who achieved DAPSA LDA by W24, patients with obesity had significantly higher fatigue severity NRS versus normal BMI subgroup. Pain VAS scores were significantly higher for the overweight versus normal BMI groups. Differences in PatGA and CRP were statistically significant between obesity and overweight versus normal BMI subgroup. HAQ-DI differences were not significant across BMI subgroups. No significant differences were observed in PGA, SJC, and TJC across BMI subgroups for patients achieving ACR50 or DAPSA LDA at W24.

Conclusion: In patients with PsA who achieved stringent treatment targets of ACR50 and DAPSA LDA after 24 weeks of treatment, obesity/overweight is associated with some indicators of negative impact on PsA disease activity (pain, PatGA, CRP) and HR-QoL (fatigue, functional disability).These findings suggest that functional ability, HR-QoL, and other health outcomes in patients with PsA and obesity may be further improved by addressing comorbid obesity.

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From Symptoms to Specialist Care in IgG4-Related Ophthalmic Disease: A Retrospective Case Series

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Objectives: IgG4-related ophthalmic disease (IgG4-ROD) is a complex, immune-mediated condition with a broad spectrum of clinical presentations involving the lacrimal glands, orbital tissues, extraocular muscles, and cranial nerves.[1] It is part of the wider spectrum of IgG4-related disease (IgG4-RD), which is characterized by fibroinflammatory lesions, IgG4-positive plasma cell infiltration, storiform fibrosis, and, in many cases, elevated serum IgG4 levels.[1-2] Given the disease's heterogeneity and its overlap with other inflammatory or neoplastic conditions, timely diagnosis and effective management can be challenging. Through a systems-level approach, we examine how patients move through diagnostic and referral pathways within the Canadian healthcare model. By mapping these pathways and identifying delays or gaps in coordination, we aim to inform improvements in care delivery, streamline referral processes, and support earlier diagnosis and intervention. This approach is critical to optimizing outcomes and ensuring equitable access to subspecialty care across a publicly funded system with finite resources.

Methods: In this retrospective, observational case series, we performed a chart review at the University of British Columbia of 180 IgG4-RD patients. Research Ethics Board approval was obtained. Demographic data, IgG4 serum levels, diagnostic and referral pathways, clinical manifestations and pathological findings were retrieved from patients diagnosed with IgG4-ROD between the Jan 1, 2010 - June 1, 2025, all managed under a unified diagnostic and pathological framework. Descriptive analysis was performed on Excel (Microsoft, Redmond, WA).
Results: Eight representative patients with IgG4-ROD were included in this analysis from a cohort of 51 identified cases. Four patients (50%) had acute inflammatory flare-ups preceding the onset of chronic symptoms later attributed to IgG4-ROD. The median time from chronic symptom onset to expert subspecialty assessment was 15.5 months (range 1–23 months). Patients had a median of 6.5 specialist encounters, 1 diagnostic test panel, 2 biopsies, and 2 diagnostic imaging studies before a definitive diagnosis was established.
Conclusion: This study represents the first health-systems analysis of patients with IgG4-ROD in a Canadian context. We observed prolonged intervals before expert care and a high number of specialist encounters along the diagnostic pathway. In a publicly funded system already burdened by long wait times, these findings highlight the need to streamline triage and referral pathways for IgG4-ROD to enable more efficient, coordinated care.
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Developing and Implementing the Mini-Practice Audit Model to Support Rheumatologist Self-Assessment in Clinical Practice

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Objectives: Implementation of new clinical guidelines in routine medical practice is often suboptimal,[1] with rheumatologists facing challenges in self-assessing and identifying care gaps.[2] This pilot project aimed to develop and implement a Mini-Practice Audit Model (mPAM) [3] as a structured, self-directed framework to enhance awareness and uptake of the 2022 Canadian Rheumatology Association (CRA) Rheumatoid Arthritis (RA) guidelines. The mPAM was designed to facilitate guided self-reflection, enabling practitioners to identify knowledge gaps, documentation inconsistencies, and opportunities for improving patient care within a feasible, low-burden audit process.
Methods: An online survey based on the 2022 CRA RA guidelines assessed participants' knowledge, attitudes, and practices, informing the creation of a modified mPAM tool. Participants invited to participate in the pilot project were sampled from current members of the CRA Education and Guidelines Committees. The mPAM guided rheumatologists through a structured mini-audit of their own patient charts, focusing on disease remission rates, medication use, tapering discussions, flare management, and shared decision-making. Each participant received individualized feedback and educational resources, followed by an invitation to complete a re-audit several months later. Quantitative results were analyzed descriptively, and qualitative reflections underwent thematic analysis to identify trends.
Results: Eleven CRA members participated in the pilot; eight completed both the audit and re-audit. In the initial audit, 60% of patients were in remission, predominantly managed with conventional synthetic DMARDs (69%), while biologic or targeted synthetic therapies accounted for 23%. Identified guideline gaps included documentation of tapering (45%), flare discussions

(38%), and shared decision-making (38%). Thematic analysis highlighted inconsistent documentation and limited detail regarding medication and patient communication. Re-audit reflections demonstrated increased awareness of documentation practices, improved incorporation of guideline elements, and reported adoption of strategies such as explicit patient communication on management plans. Participants described the mPAM as relevant, practical, and aligned with Maintenance of Certification (MOC) objectives.
Conclusion: The Mini-Practice Audit Model (mPAM) provides a feasible, effective approach to engage rheumatologists in self-assessment and continuing professional development aligned with disease specific treatment guidelines. By promoting reflective practice through personalized feedback and iterative auditing, the mPAM enhanced participants' awareness of clinical documentation and guideline adherence. The pilot demonstrated potential for broader application across rheumatology and other specialties.
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Sudden Onset Bilateral Carpal Tunnel Syndrome with Progressive Systemic Symptoms in a 57-Year-Old Man with Multiple Sclerosis

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Background: Myopathies in patients with pre-existing neurological disease pose significant diagnostic and management challenges. Distinguishing new musculoskeletal symptoms from manifestations of the underlying neurological disorder requires careful clinical and interdisciplinary assessment. Multiple sclerosis (MS) is primarily an autoimmune demyelinating condition, and its coexistence with autoimmune myopathies is rare. We present a unique case of myofasciitis in a patient with relapsing-remitting MS, highlighting the complexities of evaluation, diagnosis, and treatment in this setting.
Case Report: A 57-year-old man with relapsing-remitting MS on Tecfidera presented with a one-year history of symptoms beginning with sudden-onset bilateral hand numbness, nocturnal heat sensations, plantar fasciitis, and mild foot drop while travelling internationally. Upon returning, nerve conduction studies confirmed bilateral carpal tunnel syndrome, and he underwent right carpal tunnel release without symptomatic improvement. Spinal MRI showed two new MS lesions at C4 and T3, though neither accounted for his symptoms. Over the following months, his musculoskeletal symptoms progressed to weakness, frequent dropping of objects, impaired fine motor control, stiffness in all extremities, and restricted mobility. He also reported a three-month history of constitutional symptoms, including unintentional weight loss of 30 pounds, occasional night sweats, and generalized pruritus. On examination during his initial Rheumatology consultation, he was noted to have positive groove sign over the forearms and calves, lower extremity hyperpigmentation, erythema over the dorsum of the feet, flexor contractures of the fingers with a positive prayer sign, inability to make a fist, diminished bilateral grip strength, and restricted ability to kneel or cross the legs due to fascial tightening. In terms of investigations, comprehensive malignancy screening (pan-CT, PET, colonoscopy, esophagogastroduodenoscopy) was negative. Serologic testing revealed modest CRP elevation and weakly positive anti-Mup44 antibody. Muscle biopsy demonstrated myofasciitis, confirming the diagnosis. The patient provided consent for publication.
Conclusion: The patient was started on prednisone, resulting in prompt symptomatic

improvement. In collaboration with Neurology, rituximab was initiated to manage both myofasciitis and MS concurrently. The weakly positive anti-Mup44 antibody, which is typically associated with inclusion body myositis (IBM), was considered to be clinically insignificant given that the clinical course and rapid response to prednisone were not in keeping with IBM. To our knowledge, this is the first report on a case of myofasciitis in an MS patient. This case highlights the importance of careful physical examination, expedited tissue diagnosis and close interdisciplinary collaboration between neurology and rheumatology for the workup of myopathies in patients with underlying neurological disease.

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Taming the Fire: Lung Sparing MDA-5 DM and MAS Overlap Successfully Treated with Methylprednisolone, Rituximab, IVIG, Anakinra, and Tofacitinib

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Background: Anti-melanoma differentiation-associated protein 5 (MDA5) Dermatomyositis (DM) can be refractory to multiple lines of immunosuppression.[1] Here, we present a case of refractory MDA-5 DM with Macrophage Activation Syndrome (MAS) overlap requiring numerous immunosuppressive courses to achieve stability.

Case Report: A 30-year-old man of East Asian ancestry presents with a 2-month history of heliotrope rash, puffy eyes, periungal erythema, bilateral polyarthritis, as well as muscle weakness progressing to dysphagia and dyspnea. His Initial CK was 993 with a negative ANA, RF, CCP, and a CRP of 12. On his myositis panel, he was positive for anti-MDA-5 (51), anti-Ku positivity (42). His pulmonary function test had decreased DLCO (61%) but increased residual volume (133%), favouring neuromuscular restriction, with only a small non-specific ground glass opacity on CT Chest with no specific ILD signs. He was started on IVIg 2 g/kg as well as methylprednisolone 500 mg 3-day pulse (Figure 1 for full therapeutic course). He also received an initial Rituximab 1g dose 4 days after admission. On day 4, he was planned for discharge, however, his ferritin continued to rise from admission 3,779 ug/L to a peak of 6,412 ug/L on post-admission day 13, with increasing Triglycerides to peak of 2.62 mmol/L, a mid-100s range transaminitis, worsening weakness and therefore there was a concern for macrophage activation syndrome (MAS). Peak H-score was 146, however, no signs of primary HLH was seen on bone marrow biopsy. Soluble CD163 receptor (1467 ng/ml, cutoff was 1217) was positive as well as was sIL2 (360 ng/ml, cutoff was 666)s. He was started on Tofacitinib 11 mg daily and re-pulsed with Methylprednisolone 500 mg for 3 days again. He was also later (see figure 1) given Anakinra 100 mg q8H and pulsed again with Methylprednisolone 500 mg for 3 days and also received a second Rituximab 1g dose and IVIG 2g/kg course. Multiple attempts to taper steroids were unsuccessful with MRI on post-admission day 31 demonstrating thigh hematoma and worsening myositis despite treatment, with the hematoma felt due to myositis which lead to a third course of IVIG (2g/kg) and he improved and MDA-5 level continued to reduce until discharge when it was 17. Ultimately, he was discharged on Anakinra, Prednisone, and Tofacitinib. He remained stable with Prednisone and Anakinra down-taper and was stable at a 6-month follow-up on only Tofacitinib 10 mg BID and Anakinra 100 mg sc on alternating days.

Conclusion: Here we present a novel case of MDA-5 overlap with MAS, in a patient without radiographic ILD, successfully treated by immunosuppression including Tofacitinib and Anakinra. This builds on past work treating MDA-5 with ILD with a triple regimen (Methylprednisolone, Rituximab, Tofacitinib) [2] and further supports the role of Tofacitinib.[3]

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Look Here, Not There! Vasculitic Myopathy and a Tale of Masquerades

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Background: Myalgias and muscle weakness carry a wide differential of etiologies. Rheumatologists will often need to consider diagnoses such as polymyalgia rheumatica (PMR), statin-induced myopathy, and idiopathic inflammatory myopathies (IIM). There are, however, uncommon causes that can also lead to myalgias and weakness. Myopathy of the lower extremities is uncommonly due to small vessel vasculitis involving skeletal muscle in ANCA associated vasculitis (AAV). More rarely, it could be the sole presenting feature of AAV.[1,2,3] We describe a case of muscle weakness that was a diagnostic dilemma with investigations supportive of multiple diagnoses, eventually definitively diagnosed on muscle biopsy.

Case Report: Our patient is a 76-year-old male, presenting with lower limb myalgias, weakness, and elevated inflammatory markers. He was initially treated by his other physicians as PMR with moderate dose prednisone when we met. Despite therapy with moderate dose prednisone, he did not experience significant improvement, and his symptoms were largely proximal lower extremity, with no upper extremity symptoms. He had no skin rash, or other connective tissue disease symptoms. His lower extremity symptoms were not due to inflammatory arthritis in the lower extremity joints. He had no respiratory or renal disease on history or current symptoms. He did endorse a one-year history of chronic nasal congestion, altered taste, reduced appetite, fatigue and night sweats. He was initially on a statin which was discontinued, given a concern for possible statin induced myopathy. Imaging for malignancy was negative. Auto-antibody testing was performed, which eventually identified positive anti-SRP and positive anti-MPO ANCA, as well as elevated rheumatoid factor. While his CK had been found to be within normal limits, serum aldolase levels were found to be elevated. EMG-NCS performed by neuromuscular neurology supported a myopathic process and sensorimotor axonal polyneuropathy likely secondary to his diabetes. Ultimately muscle biopsy confirmed presence of a subacute to chronic destructive vasculitic process involving arterioles and small arteries. With these findings, the unifying diagnosis of ANCA-related small vessel vasculitis involving mainly the lower extremity skeletal muscles was made.

Conclusion: Small vessel vasculitis involving mainly skeletal muscle is an uncommon presentation of ANCA associated vasculitis. The low titre positivity of multiple antibodies supporting entities which can cause similar symptoms contributed to this patient being a diagnostic dilemma. This case serves as an example of the value of consideration for small vessel vasculitis of skeletal muscle as a cause of weakness, and the importance of tissue biopsy to help confirm diagnoses.

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Autoantibodies to the Sodium/potassium Pump Alpha-1 Subunit AT1A1 Identify At-Risk Pregnancies that Will Develop Fetal/congenital Heart Block: Evidence and Translational Plan

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Objectives: Autoimmune congenital heart block (CHB) has been associated with maternal autoimmune disease for a century, particularly in lupus and Sjögren's disease pregnancies. Although 80+% of affected pregnancies are anti-Ro positive, CHB develops in only 1 in 50 such pregnancies, indicating that anti-Ro alone is insufficient. We aimed to identify more predictive maternal autoantibody targets. We hypothesised that the autoantibodies target would be a fetal cardiac protein.

Methods: We assessed sera from pregnancies with CHB outcome compared with anti-Ro–positive pregnancies without CHB. We used solubilized proteins from fetal heart tissue, and from developmentally immature stem cell-derived cardiomyocytes, to characterize the targets of maternal serum antibodies from affected pregnancies, compared to those from unaffected pregnancies. Targets were identified on 2D gels of cardiac proteins exposed to maternal sera and confirmed using single-lane westerns.[1, 2] A targeted 4-peptide ELISA was developed based on the identified cardiac protein epitopes and is being assessed. Additional cohorts from Canada, Germany, Italy, Spain and U.S. are being assessed to refine and validate our assays. (Table 1) In collaboration with EuroImmun AG, we are developing a standardized research assay that can be translated to a laboratory-developed test for clinical care.

Results: Pregnancies with prior CHB were assessed separately (Table 1, Columns 11 to 13). For no prior CHB, sera from 7 affected and 5 unaffected pregnancies identified expanding autoantibody target cardiac proteins (beyond Ro and La) throughout CHB pregnancies, which were absent in unaffected pregnancies. (7/7 versus 0/5; p=0.0013, Fisher Exact Test [FET]) The earliest target was AT1A1 (sodium/potassium pump alpha 1 subunit), and western blots identified these autoantibodies. (7/7 versus 0/5; p=0.0013, FET) A Padua cohort identified the same autoantibody fingerprint, and same AT1A1 reactivity by both western and ELISA. (20/20 versus 0/25; $p<0.00001$, FET). A Toronto (validation) cohort had equivalent results for 2/3 methods. (16/16 versus 0/24; $p<0.00001$, FET). In pregnancies with a prior CHB child, the antibody pattern and anti-AT1A1 ELISA were occasionally positive despite no CHB resulting in a reduced positive predictive value (0.429). Negative predictive value remained at 1.0. Ro-negative autoimmune CHB [3] provided equivalent results. Six additional cohorts are under evaluation.

Conclusion: We have identified AT1A1 as a robust auto-antibody target associated with autoimmune CHB outcome. This marker demonstrates strong discriminatory performance across multiple cohorts. Ongoing multicentre validation and assay development with commercial partner EuroImmun AG will support translation of these findings into a clinical diagnostic test aimed at improving CHB risk prediction.

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Autoantibody Clusters and SIGLEC1 are Predictive of Systemic Lupus Erythematosus Development

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Objectives: Up to one third of patients with suspected SLE progress to definite disease, but reliable predictive markers are lacking. Previously, we developed a Lupus Lymphocyte Activation Score (LLAS) based on key cell subsets (transitional B cells, age-associated B cells, plasmablasts, Tph cells, and Tfh cells) observed in those with or at risk of developing SLE.[1] Here we examined the relationship between autoantibody profiles, blood sialic acid binding Ig like lectin 1 (SIGLEC1, a novel biomarker of macrophage type I interferon), LLAS, and systemic autoimmune rheumatic disease (SARD) development among those with suspected disease.

Methods: Blood samples were collected from 45 patients with new onset (< 5 yrs), positive ANAs, and suspected SLE at Brigham and Women's Hospital Lupus Center. At baseline, none met SLE or other SARD classification criteria. All received prednisone <10mg/day and no immunosuppressants. Using baseline samples, soluble SIGLEC1 was measured by ELISA and a comprehensive autoantibody profile was performed: ANA by indirect immunofluorescence assay on HEp-2 cells and patterns classified according to the International Consensus on ANA Pattern anti-cell (AC) nomenclature, SLE-related autoantibodies, including anti-DFS70 by a fully automated multi-analyte system using particle-based multi-analyte technology, and anti-C1q and anti-phospholipid antibodies by ELISA. To examine patterns of autoantibodies, we used hierarchical clustering and investigated their relationships with disease progression, LLAS (sum of standardized proportions of each of 5 lymphocyte subsets above), and SIGLEC1 levels.

Results: Of 45 patients, 36 had multiple visits with a mean follow-up of 13.6 months. In follow-up, 3 patients were diagnosed with SLE and met 2012 SLICC or 2019 EULAR/ACR criteria; 4 were diagnosed with or suspected of new dermatomyositis or Sjögren disease. We identified 5 clusters of suspected SLE patients based on autoantibody profiles (Figure 1A). Cluster A (AC-4 nuclear speckled with multiple autoantibody reactivity including anti-RNP, -dsDNA, -anti-Ro60/SSA) was more likely to progress or develop a CTD including SLE (OR 1.94, 95%CI 0.42-3.46) than others (Figure 1B), particularly compared to Cluster C (no autoantibodies). Cluster A also had significantly higher SIGLEC1 vs. Cluster E (Figure 1C). There was no difference in LLAS by autoantibody cluster (Figure 1D).

Conclusion: Autoantibody profile characterized by nuclear speckled with multiple autoantibody

reactivity, including anti-RNP, -dsDNA, and -Ro60/SSA, was predictive of SARD development. This cluster also had higher baseline SIGLEC1 vs. those with monospecific DFS70 antibodies or no autoantibodies. Further analyses will assess whether LLAS, SIGLEC1, and autoantibodies are complementary, and when combined, could enhance the prediction of SLE development.
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A Novel TNFRSF1A Gene Variant in a Patient with Recurrent Fevers and Amyloidosis: A Case Report

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Background: TNF Receptor Associated Periodic Syndrome (TRAPS) is a rare autosomal dominant autoinflammatory disorder. It is caused by pathogenic variants in the TNFRSF1A gene which encodes the TNF receptor 1. These mutations impair receptor shedding and disrupt TNFα signaling, leading to uncontrolled inflammation with recurrent fever, serositis, and myalgia [1]. Left untreated, chronic inflammation may result in AA amyloidosis and end-stage renal disease (ESRD). Early recognition and treatment with IL-1 inhibitors can mitigate deterioration and prevent irreversible complications such as amyloidosis. Here we present a case of TRAPS complicated by amyloidosis and associated with a novel variant in TNFRSF1A.

Case Report: A 48-year-old male was referred for early childhood onset, recurrent 3–5-day febrile episodes accompanied by severe abdominal pain, large joint arthralgias and myalgias. He was treated intermittently with corticosteroids and NSAIDs, with incomplete response. At 43 years old he developed chronic kidney disease with renal biopsy compatible with amyloidosis. This eventually progressed to ESRD requiring hemodialysis. Genetic testing was performed when he was 48 years old and revealed a heterozygous missense variant in TNFRSF1A (c.214_215delinsCT, p.Cys72Leu). The mutation resides in exon 3 within the extracellular cysteine-rich domain, and was predicted to disrupt disulfide bond formation, resulting in misfolded receptor protein and defective TNFα signalling. Substitutions at the same residue (Cys72Arg, Cys72Ser) had been previously demonstrated to be causative for TRAPS [2]. His asymptomatic parents did not carry the mutation. As such, this de novo Cys72Leu variant was classified as Likely Pathogenic, and the patient was diagnosed with TRAPS. Anakinra 100 mg SC daily was started which prevented further attacks. However, he remains on hemodialysis and is on the waitlist for renal transplant.

Conclusion: In summary, our case highlights the importance of early recognition of autoinflammatory diseases like TRAPS, in order to initiate targeted treatment and prevent life altering complications such as amyloidosis and ESRD. We report a novel variant in the TNFRSF1A gene, adding to the literature of mutations causing TRAPS. Further studies are needed to functionally characterize the biological impact of Cys72Leu, as well as to elucidate the complex mechanisms between TNF receptor dysfunction and IL-1 signalling.

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Minimal Important Differences (MID) of the Patient Reported Outcomes Measurement Information System (PROMIS) Computerized Adaptive Test (CAT) Measures in a Single Canadian Lupus Cohort

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Objectives: The Patient Reported Outcomes Measurement Information System (PROMIS) has been recognised as a potential tool to harmonize research across diseases in the assessment of physical, mental, and social health. Previous studies have demonstrated reliability, validity and responsiveness evidence for PROMIS CAT in systemic lupus erythematosus (SLE).[1] This study extends this evidence by examining minimal important difference (MID) of PROMIS CAT domains.

Methods: In this longitudinal study, consecutive adult English-speaking SLE patients were invited to participate. Patients completed an assessment using PROMIS CAT's 13 domains (physical function, mobility, pain behaviour, pain interference, ability to participate in social roles, satisfaction with social roles and activities, fatigue, sleep disturbance, sleep-related impairment, applied cognition-abilities, anger, anxiety, and depression) and corresponding legacy instruments at baseline and at 3 and 6 months. The generic anchor question was asked to identify those with symptom severity change. Domain-specific anchor questions were asked at 6 months with responses graded from -7 (greatest worsening) to +7 (greatest improvement), and 0 representing no change. For domain-specific anchors, improvement was defined as >1 and worsening as < -1. Area Under the Curve (AUC) and 95% confidence intervals for each of the 13 domains were calculated and minimal important differences (MID) were derived from the above AUC analysis, also called Anchor-based approach.

Results: 108 patients (90.7% female) were included. MIDs for PROMIS Physical Function were calculated to be -1.84 in patients that improved and -6.17 in patients who worsened over 6 months (Figure 1). MID for Satisfaction with Social Roles and Activities was -4.40 in patients that improved over 6 months (Figure 1). AUC was considered significant (> 0.7) in PROMIS

Physical Function (improved), Satisfaction with Social Roles and Activities (improved), Pain Interference (worsened), fatigue (worsened) and sleep disturbance (worsened).
Conclusion: In summary, MID for PROMIS CAT in SLE cohort varied significantly among categories. Given patients did not demonstrate very significant change over 6 months as expected in the absence of intervention or change in therapy, MID is to be interpreted cautiously in this setting. Physical function and Satisfaction with Social Roles and Activities were domains in which MID could be derived.
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VEXAS Syndrome: A Clinical Case Series from Calgary

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Background: VEXAS (vacuoles, E1 enzyme, X-linked, autoinflammatory, somatic) syndrome was first described in November 2020.[1] It is typically an adult-onset, treatment-refractory autoinflammatory disorder caused by somatic mutations in the UBA1 gene.[1] Canadian data remain limited.[2] We describe a case series of five patients with VEXAS syndrome from Calgary, two of whom underwent allogenic hematopoietic stem cell transplant (alloHSCT) with excellent response.
Case Report: This case series features five male patients (Table 1). The median age at disease onset was 65 (range 50-77) years. The median delay in diagnosis was 18 (range 1-46) months. The median disease duration was 44 (range 20-79) months. All patients had somatic UBA1 variants: p.Met41Val (n=2), p.Met41Thr, p.Met41Leu, and one uncharacterized p.? variant (Table 1). All patients reported constitutional symptoms. Initial working diagnoses included unspecified inflammatory condition, adult-onset Still's disease, relapsing polychondritis (n=2), and atypical polyarteritis nodosa versus undifferentiated connective tissue disease (Table 1). Elevated inflammatory markers were observed in all patients (CRP frequently >100 mg/L). Vacuoles were confirmed on bone marrow biopsy in four patients. Three patients presented with, and one later developed, macrocytic anemia, whereas one patient had intermittent normocytic anemia. Thrombocytopenia and lymphopenia were each observed in three patients. Two patients developed myelodysplastic syndrome following diagnosis of VEXAS. Patients trialed several different therapies including hydroxychloroquine, methotrexate, azathioprine, mycophenolate, rituximab, anakinra, tocilizumab, tofacitinib, ruxolitinib, colchicine and dapsone with limited or no sustained benefit. Corticosteroids were required at moderate-to-high doses in most patients. At present, patient A is maintained on prednisone 35 mg daily. Patient B is taking prednisone 15 mg daily and ruxolitinib 20 mg twice daily. Patient C underwent alloHSCT in April 2025 with resolution of symptoms and discontinuation of prior medications (prednisone and ruxolitinib). Repeat bone marrow biopsy showed <0.5% UBA1. Patient D continues with prednisone 5-6 mg daily and azacitidine. Patient E underwent alloHSCT in August 2023. He developed chronic graft-versus-host disease requiring treatment with prednisone 7 mg daily and belumosudil. There was no evidence of UBA1 mutation on repeat bone marrow biopsy.
Conclusion: In conclusion, this case series highlights the multisystem nature of VEXAS syndrome and the substantial diagnostic delay often encountered in clinical practice. We recommend considering VEXAS syndrome in patients with treatment-resistant autoinflammatory syndrome and cytopenias, especially macrocytic anemia. While conventional immunosuppressive medications have provided limited benefit, allogeneic hematopoietic stem

cell transplant may be promising for select patients.
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HLA Class I Alleles as a Predictor of Retention to Treatment with Il-17 Antagonists in a Cohort of Patients with Psoriatic Arthritis in Newfoundland

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Objectives: The primary aim of the study was to determine whether HLA class I profiles had an association with retention to treatment with the IL-17A inhibitors secukinumab and ixekizumab. A secondary objective was to determine the percentage of patients remaining on IL-17A inhibitors for up to 3 years as well as to assess for HLA class I allele association with predictors of drug retention.

Methods: Data was collected prospectively and analyzed retrospectively from a Newfoundland PsA cohort started in 2007. Patients were indexed on the date they first initiated secukinumab or izekizumab. Retention was assessed at 6, 12, 24, and 36 months using clinical and laboratory data including TJC28, SJC28, health assessment questionnaire (HAQ), patient and physician global assessments, PASI scores, and CRP levels. Serologic HLA class I typing was performed. IBM SPSS v.28.0 was used to calculate Kaplan-Meier survival curves and 2-tailed Spearman correlation coefficients.

Results: 30 patients were included. All were b/tsDMARD experienced. 60% of patients were female. The mean BMI was 31.3 kg/m2 and 33.3% of participants had a smoking history. PsA was diagnosed at a mean age of 42.3 (21-60) years. On index, patients had a mean CRP of 11.5 mg/mL, TJC28 of 6.7, SJC28 of 4.7, and HAQ of 1.5. Overall retention was estimated at 50.3% at 36 months. 23 patients had HLA class I analysis performed. The most common haplotypes were HLA A1 (43.5%), A2 (52.2%), B8 (30.4%), B27 (39.1%), Bw4 (39.1%), and Bw6 (47.8%). HLA Bw4 was negatively associated with retention to IL-17A inhibitors secukinumab and ixekizumab with Spearman correlation coefficient (r) -0.639 (p= 0.025) (Table 2). Although not statistically significant, in those who discontinued IL-17A antagonists before 36 months, HLA A2 and B27 showed tendency for negative association with r -0.418 (p= 0.177) and -0.123 (p= 0.704), respectively. We did not find any definitive association with HLA class I profile and response outcome measures such as CRP or HAQ. There was also no association with discontinuation due to lack of efficacy or side effects. The small nature of the study limited the ability to assess for a difference in response to treatment with either agent.

Conclusion: In patients with psoriatic arthritis, HLA class I type may be associated with various responses to treatment with the IL-17A antagonists secukinumab or ixekizumab. This cohort study is limited by small sample size and has significant potential for error, but further exploration with larger studies is warranted.

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Diagnostic Timelines and Referral Patterns in the Hamilton Health Sciences Systemic Autoinflammatory Disease (HHS SAID) Registry

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Objectives: The study aimed to assess diagnostic timelines and completeness of referrals in the Hamilton Health Sciences Systemic Autoinflammatory Disease (HHS SAID) Registry and identify factors contributing to delays in the referral-to-diagnosis pathway.
Methods: The HHS SAID registry was established to describe and follow patients with systemic autoinflammatory diseases at Hamilton Health Sciences. Patients enrolled in the registry from February 2023 to April 2025 (N=94) were stratified by consultation clinic (Autoinflammatory Clinic [AC] or Pediatric Rheumatology Clinic [PRC]) and by diagnosis (Periodic fever, Aphthous stomatitis, Pharyngitis, and Adenitis [PFAPA]; Syndrome of Undifferentiated Recurrent Fever [SURF]; Familial Mediterranean Fever [FMF]; Other Monogenic Autoinflammatory Syndromes [OMAS]; and systemic Juvenile Idiopathic Arthritis [sJIA]). Descriptive statistics were generated using an available-case approach to summarize demographic, referral, and time-interval data. Group differences were assessed using chi-square or Fisher's exact tests for categorical variables and Mann–Whitney U or Kruskal–Wallis tests with post hoc pairwise comparisons for continuous variables.
Results: Ninety-four participants were included (50 male, 44 female). Sixty pediatric participants were seen through PRC (median age=5.2yr, IQR=6.0yr) and 24 pediatric and adult participants were seen through AC (median=15.4yr, IQR=33.8yr) (p=0.000). Diagnosis stratification amounted to 39 PFAPA (41.5%), 21 FMF (22.3%), 14 OMAS (14.9%), 13 SURF (13.8%), and 7 sJIA (7.5%). Besides sJIA, all other groups had similar referral to consultation times (median range=3.0-4.1mo, p>0.05). From consultation to diagnosis, PFAPA (median=0.0mo) and sJIA (median=0.1mo) showed near-immediate diagnosis, unlike FMF (median=3.0mo, IQR=5.3mo), SURF (median=4.6mo, IQR=14.1mo), and OMAS (median=12.8mo, IQR=33.1mo) (p=0.000). From symptom onset to diagnosis, OMAS (median=47.5mo, IQR=21.7mo, p=0.002), SURF (median=26.2mo, IQR=39.5mo, p=0.001) and PFAPA (median=14.8mo, IQR=18.9mo, p=0.014) had the longest durations (Table 1). Referrals lacked key information in 91.7% (22) of AC and 74.6% (44) of PRC cases. Within the AC, missing information on fever/episode duration (OR=4.5, p=0.003) and symptom onset (OR=3.3, p=0.047) were significantly higher versus the PRC. OMAS was the only group predominantly referred by other specialists (64.3%, p=0.005). All disease groups showed high missing referral information rates on symptom onset, episode duration, and frequency: lowest in PFAPA (61.5%) and >90% in others.
Conclusion: Except for sJIA, all autoinflammatory diseases had long referral, consultation, and diagnostic intervals, most notably SURF and OMAS, reflecting diagnostic uncertainty and referral inefficiencies. High rates of missing referral details may have contributed to these diagnostic delays. Standardized referral templates and clinician education on diverse autoinflammatory presentations may help reduce diagnostic latency and improve timely specialist care.

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Multisystem Sarcoidosis with Extensive Neurologic, Musculoskeletal, Pulmonary, Lymphatic, and Cutaneous Involvement: A Case Report

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Background: Sarcoidosis is a multisystemic inflammatory disorder of unknown etiology characterized by noncaseating granulomas in affected areas, prototypically the lungs and hilar lymph nodes. Clinical presentations are heterogenous, often manifesting with constitutional symptoms.[1] Annual incidence rates in Canada have been estimated at 6 – 7 cases per 100 000, with prevalence of approximately 140 – 150 cases per 100 000.[2] Women are more frequently implicated than men, and those of reported Black or Scandinavian ethnicity are also at increased risk. Neurosarcoidosis can occur in 5-26% of patients with systemic sarcoidosis.[1] Cases of neurosarcoidosis are heterogeneous in and of themselves, dependent on the part of the CNS implicated. Cranial neuropathies, meningitis, dural mass lesions, cerebrovascular disease, peripheral neuropathy, and myopathy are examples of manifestations.
Case Report: This case involves a 30-year-old gentleman with minimal past medical history, who presented at age 25 to an emergency department with a 12-month history of constitutional symptoms, including nearly 100-pound weight loss, fatigue, night sweats, and fevers. This was accompanied by musculoskeletal features such as mid and lower back pain, peripheral edema, and multifocal skin and soft tissue nodules suspected to be in fitting with diffuse lymphadenopathy. After extensive diagnostic workup, it was found that he had extensive fulminant systemic sarcoidosis, proven with excisional biopsy of a mediastinal lymph node. Also present was osseous involvement of the in the hands, feet, pelvic bones, and vertebral bodies of the thoracic and lumbar spine (Figure 1). He experienced rapid improvement with a tapering course of prednisone, which was completed after a total of 14 months of therapy. Recovery was complicated by a generalized tonic-clonic seizure one month after prednisone taper. Investigations yielded neurologic involvement, including parafalcine mass and leptomeningeal sarcoid involvement, as well as involvement of the spinal parenchyma of the thoracic and lumbar spine. Immunosuppression with infliximab and methotrexate (MTX) was initiated. Following 2 years of clinical stability, MTX was discontinued. He continues to experience clinical stability on infliximab infusions every 6 weeks. He had interdisciplinary follow up including with a neuroimmunology clinic. The patient reported feeling back to pre-illness state and is able to function as a caregiver to his young child.
Conclusion: This case illustrates the heterogeneity of systemic sarcoidosis, manifesting in this patient predominantly with both neurosarcoidosis and musculoskeletal manifestations. Systemic immunosuppression can be beneficial for cases with severe/ systemic manifestations. Early recognition and multidisciplinary management are critical for outcomes and to prevent irreversible organ dysfunction.
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Salivary Inflammatory Biomarkers in Chronic Non-Specific Low Back Pain Patients
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Objectives: To determine the expression level of inflammatory mediators in the saliva of

Chronic Non-Specific Low Back Pain (CNSLBP) Patients compared to asymptomatic healthy individuals.
Methods: Twenty-eight patients with CNSLBP and Twenty-eight age and sex-matched asymptomatic participants were selected according to specific inclusion and exclusion criteria. Saliva samples were collected, and total RNA was isolated. Reverse transcription and qPCR were performed using the Quant Studio 3 Real-Time PCR system, ThermoFisher Scientific. Bioinformatics analysis was performed using the STRING database to explore cytokine protein-protein interaction (PPI) and miRNet for miRNA network analysis.
Results: The expression levels of IL-18, TNFα, IL-6, HMGB1, IFNG, IL-2, IL-8, and IL-1β were increased in the saliva of LBP patients compared to the control group. A STRING database analysis of IL-18 protein-protein interactions (PPI) reveals that the PPI enrichment is highly significant, with a p-value < 1.0e-16, and the gene ontology biological process revealed its role in regulating the inflammatory response and other cytokine production. miRNet analysis showed that multiple miRNAs can target more than one cytokine.
Conclusion: The expression levels of inflammatory mediators including IL-18, TNFα, IL-6, HMGB1, IFNG, IL-2, IL-8, and IL-1β were increased in the saliva of CNSLBP patients compared to the control group. A STRING database analysis of IL-18 protein-protein interactions (PPI) reveals that the PPI enrichment is highly significant, with a p-value < 1.0e-16. IL-18 interacts with other cytokines including IL-6, TNF, IL-1B, IFNG, and IL-8. Gene ontology (biological process) revealed its role in regulating the inflammatory response and the production of other cytokines and chemokines. miRNet analysis showed that multiple miRNAs can target both IL-1B and IL-6 including hsa-let-7a-5p, hsa-let-7c-5p, hsa-let-7d-5p, hsa-miR-21-5p, hsa-miR-23a-3p, hsa-miR-25-3p, hsa-miR-26a-5p, and hsa-miR-26b-5p.

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Plasma Proteomics Identifies Pathways and Key Proteins Associated with Postoperative Joint Pain After Total Joint Arthroplasty in Osteoarthritis Patients

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Objectives: To identify molecular pathways and key proteins associated with postoperative joint pain following total joint arthroplasty (TJA) in osteoarthritis (OA) patients using a plasma proteomics approach.
Methods: Primary OA patients who underwent total knee or hip arthroplasty were assessed for their postoperative pain at least one-year after surgery using the WOMAC Likert 3.0 pain subscale. Three pain phenotypes were defined: sustained pain (pain on all five questions), pain while active (pain while walking and taking stairs), and pain at rest (pain while sitting/lying and at night while in bed). Patients reporting no pain were classified as controls. Plasma proteomic profiling was performed using the Olink® Explore HT platform. Associations between postoperative joint pain and protein expression were assessed using logistic regression adjusted for age, sex, and body mass index. Functional enrichment analysis was conducted using KEGG and GO databases. Protein–protein interaction network was constructed using the STRING database and visualized in Cytoscape 3.10.4 to identify hub proteins. Bonferroni correction was applied to control for multiple testing across 5416 proteins and three pain phenotypes ($\alpha=3.08\times10\text{-}6$).

Results: A total of 149 patients were included. The prevalence of sustained pain, pain while active, and pain at rest four years after TJA was 5, 13, and 7%, respectively; 81% reported no pain, thereby served as controls (Figure 1A). No individual protein remained significant after multiple testing correction. However, 246, 332, and 260 proteins were nominally associated ($p<0.05$) with sustained pain, pain while active, and pain at rest, respectively. For sustained pain and pain at rest, the associated proteins were enriched in the MAPK signaling pathway, extracellular matrix, and growth factor activity. Hub proteins included CCL2, ERBB4, SHC1, NCAM1, MMP9, HRAS, FGF3, and NTRK2 for sustained pain, CD86, NCAM1, and ANXA5 for pain at rest (Figure 1B, 1D). Proteins associated with pain while active were enriched in the interleukin 17 signaling pathway, myeloid leukocyte mediated immunity, and cytokine activity. Hub proteins included ITGB2, CASP8, and CCL2 (Figure 1C).
Conclusion: Our data showed distinct molecular signatures for different postoperative pain phenotypes following TJA. While sustained and rest pain shared enrichment in MAPK-related and extracellular matrix pathways, pain while active appeared to involve immune and inflammatory mechanisms. These findings highlight potential protein biomarkers and pathways contributing to heterogeneous postoperative pain experience in OA patients.

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Multi-Omics Identifies Angiogenesis and Lipid Metabolic Pathways were Associated with Early Revision After Total Joint Arthroplasty in Osteoarthritis Patients

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Objectives: To identify molecular pathways and key proteins associated with early revision after total joint arthroplasty (TJA) in osteoarthritis (OA) patients using a multi-omics approach integrating plasma proteomics and metabolomics.
Methods: Primary OA patients who underwent total knee or hip arthroplasty were included. Plasma proteomic profiling was performed using the Olink® Explore HT platform, and plasma metabolomic profiling was conducted using the Biocrates MxP Quant 500 kit. Associations between early revision after TJA and protein expression were evaluated using logistic regression adjusted for age, sex, and body mass index. Functional enrichment analysis was conducted using KEGG and GO databases. Protein–protein interaction network was constructed via the STRING database, visualized in Cytoscape 3.10.4, and hub proteins were identified using the CytoHubba plug-in. Metabolites associated with hub proteins were identified using Spearman correlation analysis. Bonferroni correction was applied for multiple testing ($\alpha=9.23\times10\text{-}6$ for 5,416 proteins; $\alpha=2.70\times10\text{-}5$ for 622 metabolites and 3 hub proteins).
Results: A total of 168 patients were included, with revision data extracted an average of 10.5 years after primary TJA. The early revision rate was 3% (Figure 1A), with a mean time to revision of 2.6 years. No individual protein reached significance after multiple testing correction. However, 337 proteins were nominally associated with early revision ($p<0.05$). These proteins were enriched in complement and coagulation cascades, hematopoietic cell lineage, and regulation of angiogenesis and vasculature development pathways (Figure 1B, 1C). FLT3, IL10, and NRAS were identified as hub proteins (Figure 1D), among which FLT3 and NRAS were negatively associated with early revision TJA, while IL10 was positively associated. Although no metabolite reached multiple-testing corrected significance, 28, 17, and 18 metabolites were

nominally correlated ($p<0.05$) with FLT3, IL10, and NRAS, respectively, predominantly long-chain diglycerides, triglycerides, and phosphatidylcholines.
Conclusion: Multi-omics integration of plasma proteomics and metabolomic data revealed that dysregulation of angiogenesis and lipid metabolic pathways may contribute to the risk of early revision TJA in patients with primary OA. These pathways and their key molecular mediators warrant further validation as potential predictive biomarkers or therapeutic targets.

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Beyond the Outpatient Clinic: The Integral Role of In-Patient Rheumatology Consultation

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Objectives: Rheumatology is considered to be largely an outpatient specialty, however, inpatient consults play a vital role in managing acute patient presentations. This review aims to describe the nature of the inpatient rheumatology consultations that were completed at an academic hospital, Sunnybrook Health Sciences Centre, and demonstrate the impact these consults have towards shaping patient outcomes.
Methods: All inpatient consultations done from March 1, 2024 to February 28, 2025 were summarized. The various categories of data collected included demographic information, consulting services, reason for referral, clinical impact of rheumatology consult, use of joint aspirations/steroid injections, POCUS utilization, urgency of referral, and time followed under the rheumatology service. Findings were also compared to previous 12-month period from June 2011- July 2012 looking at similar data to show changes in the patient population and rheumatology consults over time, significant differences are summarized (Table 1).
Results: A total of 268 consults were completed during the study period, representing a 13% increase since 2012 (n=238). Due to some missing data, the reported figures underestimate the true number of patients and diagnosis seen. Female patients accounted for 58% of all consults compared to 50% in 2012. Referrals were most commonly from general internal medicine (n, 39.6%), cardiology (n, 7.5%), and neurology (n, 8.2%). Patients had a wide variety of rheumatic diseases, but the most common conditions seen were gout (n, 9.7%), osteoarthritis (n, 8.6 %), and systemic lupus erythematous (SLE) (n, 6.3%). Interestingly, the number of consults for SLE and osteoarthritis have increased dramatically compared to 2012 (n, 2.9% and n, 5.9% respectively). Patients were admitted in hospital for an average of 17 days, followed under rheumatology for an average of 5 days, and 54% of all cases were emergent/urgent. Joint aspirations and/or steroid injections were performed in 57 cases, and point-of-care ultrasound was used in 37 cases. Across 268 consultations, rheumatologists helped make the diagnosis in 202 cases (n, 75%) and confirmed diagnosis in 37 (n, 14%) cases (Table 1). Consults also commonly involved suggesting medications (n, 83%) and ordering investigations (n, 79%).
Conclusion: Rheumatology consultations are predominantly urgent/emergent and complex, and rheumatologists play a large role impacting diagnosis, patient management and improving outcomes. As the number of in-patient rheumatology consults increases, access to rheumatology care is vital to treat patients in a timely manner and improve patient's quality of life.

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Alterations in Innate Immune Cells During the Progression of Systemic Autoimmune

Rheumatic Diseases

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Objectives: Systemic autoimmune rheumatic diseases (SARD) exhibit a prolonged pre-clinical phase during which they have anti-nuclear antibodies (ANAs).[1] However, ANAs cannot be reliably used to predict impending disease because a subset of healthy women are ANA+ (~20%) and the majority of these individuals will not progress to SARD.[2] Why some individuals progress while others remain asymptomatic is unknown. Our objective is to evaluate functional alterations in innate immune populations during SARD development.

Methods: CITE-Seq was conducted on innate immune cells from 24 patients including healthy controls (HC, n=5), non-progressor (NP, n=6) IFN high or low, progressors (P, n=5) or SARD (n=8) patients. Differential gene expression analysis was performed to identify genes of interest. Spectral flow cytometry and plasma ELISAs were conducted in an expanded group of patients to validate differences in CITE-Seq genes of interest. A monocyte cell line (THP-1) was used to investigate the kinetics of one gene identified by CITE-Seq to gain a better understanding of potential functional implications.

Results: Non-progressors (NP) exhibited increased gene expression of heat shock proteins (HSPs) like HSP70 and CD52 compared to P (Figure 1A). Both proteins are proposed to promote immune regulation through tolerogenic effects on innate immune cells. Conversely, P exhibited increased gene expression of MHC class II alleles, which are associated with immune activation. Using flow cytometry, we confirmed the differences between groups of surface expression of CD52 and MHC class II on innate immune cells (Figure 1B). Little is known about how HSPs are regulated and expressed. To better understand the kinetics of HSP70, THP-1 cells were heat shocked. Gene expression showed rapid and transient upregulation which was attenuated by 18h, while soluble HSP70 increased steadily following activation of the heat shock response (Figure 1C). Protein HSP70 was decreased at the 12h timepoint using immunofluorescence (Figure 1D), following heat shock, suggesting the release of HSP70. We therefore measured plasma HSP70 in our patient cohort and found that soluble HSP70 was increased in NP compared to P (Figure 1E), in support of our CITE-Seq results. Ongoing experiments are being conducted to evaluate the release of HSP70 by purified innate immune cells from our patient cohort.

Conclusion: Our data shows that NPs exhibit mechanisms of immune suppression that are decreased in P. Importantly, P exhibits immune dysregulation prior to clinical progression. These results will allow us to further investigate the immunological differences in innate cells that may drive or inhibit progression in SARD.

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Anti-TNF-α in Pet Imagery: A Non-Invasive Tool to Personalize Diagnosis and Treatments Against Inflammatory Diseases

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Objectives: Rheumatoid arthritis (RA) is the most prevalent form of immune mediated inflammatory arthritis. It affects close to 1% of Canadian.[1] DMARD therapies are currently guided by a trial-and-error approach to identify the most suitable treatment for each patient. Despite the fast evolution and the high number of available therapy options, the management of rheumatoid symptoms is still challenging. Approximately 30–40% of RA patients do not respond to the first-line treatment.[2] This trial-and-error strategy allows disease progression and may lead to irreversible joint damage due to sustained inflammation. These permanent changes directly affect patients' well-being and autonomy, ultimately increasing healthcare costs for society.

The TNF-α is an inflammation mediator and a key player in inflammatory diseases such as rheumatoid arthritis.[3] TNF-α is found in 50-70 % of RA patients at elevated level in synovial tissues. A phase III clinical trial previously demonstrated that adalimumab, an anti-TNF-α monoclonal antibody, elicited a strong therapeutic response in approximately 60% of RA patients (ACR20).[3]

Based on this observation, we postulate that adalimumab could be used to develop an imagery technique to identify patients with the higher level of TNF-α . This tool could be a game changer to pursue personalized therapy and avoid unnecessary therapeutics.

Methods: In this study we proposed to conjugate a commercial anti-TNF-α antibody (Yuflima, containing adalimumab; Celltrion) with a radiomaker 89 zirconium coupled with a DFO chelator. The 89Zr-DFO-Adalumimab will be used in PET (positron emission tomography) imagery to identify RA patients expressing elevated level of TNf-α in the joint.

Results: We successfully conjugated the radiomarker Zirconium 89 to the Adalumimab antibody. Preliminary results show that the conjugate DFO-Adalumimab is still able to target TNF-α with the same affinity as the commercial adalimumab.

Conclusion: These promising findings will enable us to test 89Zr-DFO-adalimumab in a collagen-induced arthritis (CIA) mouse model (DBA/1 strain) to assess inflammation at the join levels using PET imaging.

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Complement Pathway Heterogeneity in Rheumatoid Arthritis Uncovered Through Longitudinal Serum Proteomics

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Objectives: Rheumatoid arthritis (RA) is a heterogeneous autoimmune disease. Despite established serological classification and advances in therapeutic strategies, around 40% of patients exhibit inadequate responses to first-line DMARDs. Current clinical tools remain limited in their ability to predict treatment response and risk of joint erosion, posing a significant challenge to precision medicine. There is a critical need for novel biomarkers that can reliably forecast disease outcomes and guide therapeutic decisions. Integrating protein signatures with clinical features may enhance risk stratification in rheumatic diseases.[1] In this study, we employed data-independent acquisition mass spectrometry (DIA-MS) to perform a comprehensive longitudinal serum proteomic analysis in RA patients, aiming to identify biomarkers predictive of disease activity and progression.

Methods: This study was conducted on serum samples collected from 107 DMARD- and steroid-free RA patients (48 seronegative, 59 seropositive) enrolled in the EUPA cohort (NCT00512239), between 2005 and 2019, at the CIUSSS de l'Estrie-CHUS, Québec, Canada.[2] Serial sera collected at baseline and at the 12-month follow-up visit were analyzed by DIA-MS. MS data were analyzed using DIA-NN software for peptides/proteins identification and quantification. Statistical analyses were performed using R: Differentially abundant proteins (DAPs) across clusters were identified by Mann–Whitney U test with Bonferroni correction. KEGG enrichment analyses were conducted using the PathfindR R package, with BH correction. Generalized estimating equations (GEE) models were adjusted for age, sex, serology, and symptom duration, with FDR correction using Storey's q-value.

Results: Proteomic profiling quantified 869 serum proteins, of which 368 passed quality control and filtering for downstream statistical analyses. 1-Principal component analysis (PCA) followed by hierarchical clustering of baseline (Figure 1A), and 12-month proteomic data suggested patients could be grouped into two clusters. 2-KEGG pathway analysis of DAPs between patient clusters showed significant enrichment of complement and coagulation cascades pathway. 3-These clusters exhibited distinct serum levels of complement-related proteins (Figure 1B). 4-C68omparison of patient trajectories between baseline and 12-month serum-based clusters (Figure 1C), revealed that transitions between clusters were accompanied by significant modulation of complement-related protein levels (Figure 1D). 5-GEE models identified 29 proteins (q-value ≤0.05) associated with binomial 12-month disease activity, defined as DAS28-CRP ≤2.6 or ≥3.2, which were enriched for KEGG complement and coagulation cascades pathway.

Conclusion: This study highlights the heterogeneity of circulating complement components in early RA patients, suggesting that complement protein profiles may reflect underlying disease

mechanisms beyond general inflammation and could inform future biomarker-driven approaches to RA management.

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Type I Interferons Promote Development of Flares in Systemic Lupus Erythematosus by Enhancing B Cell Activation and Differentiation of Age-Associated B Cells

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Objectives: Systemic lupus erythematosus (SLE) is characterized by unpredictable flares interspersed with periods of disease quiescence. Elevated interferon (IFN) levels increase the likelihood of flares, but the precise immunologic mechanisms by which this occurs are unclear. In mice, IFN exposure expands age-associated B cells (ABCs), a population enriched for autoreactive and ANA-secreting cells. In this study, we examined the role of IFN in the activation and differentiation of B-cell subsets in flaring and quiescent SLE patients.

Methods: A CyTOF panel was developed to quantify IFN-induced proteins (IIPs) across peripheral blood immune populations. A composite IIP score (mean expression of six IIPs) was generated for each cell population as a surrogate for IFN exposure. 15 healthy controls (HCs), 26 quiescent (clinical SLEDAI > 0 for one year with no increase in immunosuppressive treatment, ≤ 10 mg prednisone) and 42 recently flaring (<1 month, change in clinical SLEDAI-2K ≥ 1 requiring escalation of therapy) were analyzed. To assess the direct effects of IFN, naïve B cells from HCs were isolated and stimulated with IFNα, IFNβ, or IFNγ. Cells were cultured under conditions that either promoted or inhibited ABC differentiation, including IL-21, anti-CD40, Fab2, CpG, or IL-4.

Results: CyTOF identified seven B cell subsets, all of which exhibited higher IIP levels and greater activation in flaring versus quiescent patients (Figure1A). ABCs were more abundant in flaring patients, and their frequency correlated with the global IIP signature (Figure1B, C). Expression of activation markers (CD86, TLR7, TLR9, HLA-DR, Ki67) was strongly associated with IIP score, but not disease status, indicating that IFN, rather than flare alone, drives B cell activation (Figure1D). Importantly, the association between activation and IFN exposure was evident even within individual patients, where the top 10% of IFN-experienced B cells had significantly higher activation than the bottom 10%. In vitro, IFNα and IFNβ directly induced expression of activation markers within 18-24 hours. In isolated naïve B cells, all 3 IFNs increased ABC differentiation, even without canonical ABC-inducing signals (Figure1E). Notably, IFN overcame IL-4–mediated suppression of ABC differentiation, in part by reducing IL-4Rα and inducing TLR7 expression. In SLE patients treated with the IFN-blocking therapy Anifrolumab, ABC frequency and IIP signatures decreased (Figure1F).

Conclusion: IFN exposure drives human B-cell activation and promotes differentiation of

ABCs. Our results identify a mechanistic link between IFN signaling and pathogenic B-cell development, and support IFN blockade as a strategy to reduce pathogenic ABCs and prevent SLE flares.

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Genomic Instability in Systemic Sclerosis is Promoted by a PERK/FOXO1-Dependent Axis

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Objectives: Diffuse cutaneous Systemic Sclerosis (dcSSc) is a life-limiting autoimmune disease with minimal treatment options. Autologous hematopoietic stem cell transplantation (ASCT) is a potent disease-modifying therapy in dcSSc; however, its effects on fibroblasts are unknown. We recently showed that dermal fibroblasts (DFs in patients with dcSSc develop a cancer-like phenotype characterized by genomic instability and increased double-stranded DNA breaks (DSBs).[1] However, little is known about the mechanisms promoting DF survival following the accumulation of genomic mutations. We hypothesized that in dcSSc DF genomic instability results in the accumulation of genomic mutations; and that this results in the activation of Protein Kinase R-like ER Kinase (PERK) and transcription of forkhead box1 (FOXO1) promoting resistance-to-apoptosis and fibrosis (Figure 1).

Methods: We used whole exome sequencing (WES) to characterize the mutational frequencies and their associated signatures in dcSSc patients who did not undergo ASCT (dcSSc, N=35) and those who did (post-ASCT, N=9). We also generated DFs from dcSSc, post-AHSCT (or age/sex matched healthy controls (HC), (N=8-10 patients/group), and quantified the frequency of DSBs via γ-H2AX levels (immunoblot (IB)), and DSB nuclear foci (confocal microscopy). We measured the relative ROS levels, mitochondrial membrane potential, and phospho-PERK (active) in DFs to mechanistically link DSB with PERK activation using flow cytometry and/or IB, respectively. We also determined the downstream effects of PERK activation on mitochondria (e.g. mitochondrial dynamics and biogenesis). Then, we measured FOXO1 activation via nuclear translocation, IB, and expression of its downstream mRNA target SOD2. Finally, mitochondrial-dependent resistance-to-apoptosis was determined at baseline, and following treatment with cyclophosphamide, a PERK or a FOXO1-inhibitor using TUNEL and cleaved caspase 9/3 levels (IB).

Results: dcSSc patients' DFs had increased genomic instability and DSBs compared to patients treated with ASCT. dcSSc DFs had increased indicators associated with PERK activation (phospho-PERK, ROS, and mitochondrial membrane potential). This was associated with increased mitochondrial remodelling, mitochondrial biogenesis, and mitochondrial fusion. Importantly, FOXO1 was exclusively activated in dcSSc, but not HC or post-ASCT DFs. Inhibition of PERK or FOXO1 resulted in increased mitochondrial-dependent apoptosis.

Conclusion: Our study highlights a novel mechanism whereby genotoxic signals in dcSSc promote cell survival via a PERK/FOXO1-dependent axis and associated metabolic remodeling (Figure 1). It also provides mechanistic insights related to how changes to the mutational landscape reduce pro-fibrotic signals in DF after ASCT. Future studies targeting this

dysregulated pathway may provide an additional rationale for exploring it therapeutically in patients with dcSSc.

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Impaired DNASE1L3 Activity from a Novel Mutation Identified in Monogenic Systemic Lupus Erythematosus

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Objectives: Monogenic systemic lupus erythematosus (mSLE) is a rare, severe subtype of SLE caused by single-gene mutations that often present in childhood. Although uncommon, mSLE offers valuable insights into lupus pathogenesis and potential therapeutic targets. Over 38 genes have been implicated, including DNASE1L3, which encodes a Ca^{2+}/Mg^{2+}-dependent endonuclease responsible for degrading extracellular nucleic acids and clearing apoptotic debris and neutrophil extracellular traps. DNASE1L3 deficiency has been associated with dysregulation of the type I interferon (IFN-I) pathway. Here, we describe a novel DNASE1L3 variant identified in a family where the pediatric proband presented with hypocomplementemic urticarial vasculitis (HUVS) and lupus nephritis. Our objective was to define the functional and clinical implications of this DNASE1L3 variant (p.T224M).

Methods: Clinical gene panel sequencing (Invitae) identified the variant in the proband. Sanger sequencing confirmed homozygosity in the proband and his asymptomatic younger brother, and heterozygosity in both parents. Three-dimensional protein modelling using PyMol to predict confirmation changes. HEK293T cells overexpressing wild-type and mutant DNASE1L3 constructs were assessed for expression, secretion, and nuclease activity by Western blotting and plasmid/chromatin digestion assays. Single-cell RNA sequencing (scRNA-seq) was performed on PBMCs from both parents, the asymptomatic sibling, and two time points from the patient to explore downstream immune effects.

Results: A homozygous missense variant (c.678C>T; p.T224M) in DNASE1L3 (NM_004944.2) was identified in the affected patient. Structural modelling suggested that the substitution destabilizes the Mg^{2+}-binding site for enzymatic function. Overexpression studies demonstrated that T224M DNASE1L3 is normally expressed and secreted but exhibits markedly reduced nuclease activity compared to wild-type and known pathogenic variants (R206C, W215Gfs*2). Patient sera-based validation studies are underway. Preliminary scRNA-seq analysis revealed elevated expression of IFN-stimulated genes in the patient and mild increases of T, B and NK cell populations in the asymptomatic sibling with the same homozygous variant, suggesting early immune activation and potential predisposition to IFN-I pathway dysregulation.

Conclusion: We have identified a novel homozygous missense mutation in DNASE1L3, encoding an endonuclease previously implicated in mSLE, in a pediatric patient with HVUS and lupus nephritis. We demonstrated that this mutation has normal extracellular secretion but impaired nuclease activity, which implies poor clearance of extracellular nuclear debris likely resulting in type 1 IFN pathway stimulation, and thus leading to autoimmune disease like SLE as

well as highlighting the importance of longitudinal monitoring in at-risk family members.

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Dietary Interventions for Chronic Fatigue in Rheumatic Diseases: An Umbrella Review of Systematic Reviews

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Objectives: Severe fatigue in rheumatic diseases is prevalent, at approximately 50%, and intractable to conventional management in the majority of patients.[1][2] This review explores the impact of dietary interventions on reducing fatigue in patients with rheumatic diseases.

Methods: The search strategy for this umbrella review was developed and executed in collaboration with a medical librarian, using MEDLINE, Embase, CINAHL, and Cochrane Library from inception to August 2025. Quality of included reviews was assessed using AMSTAR 2, and evidence for each intervention was assessed using GRADE methodology.

Results: 2,715 results were retrieved and after removing duplicates, 2,218 unique results remained for title and abstract screening. 270 full-text records were assessed for eligibility, and 49 systematic reviews and meta-analyses were included. Among these, 6 reviews were rated high quality, 22 moderate, 9 low, and 12 critically low. Conditions included are fibromyalgia, systemic lupus erythematosus, rheumatoid arthritis, psoriatic arthritis, spondyloarthritis, Sjögren's disease, and dermatomyositis. The certainty of evidence ranges from very low to moderate (Table).

Conclusion: There is moderate quality evidence to support Vitamin D supplementation, at 1,200 IU/day to 50,000 IU/week, and Fib-19-01 phytotherapy for fatigue management in rheumatic diseases. These interventions offer a new therapeutic opportunity for patients with intractable fatigue or desire to pursue natural therapies. Remaining evidence shows potential, but the low quality highlights a need for further research with rigorous study design. Furthermore, only patients with fibromyalgia and systemic lupus erythematosus are represented within the moderate quality evidence. Although shared pathways underlie fatigue in various rheumatic diseases, supporting generalizability of our findings, it remains important to create a representative evidence base to inform treatment.[3]

References: [1.] Overman C, et al. Clin Rheumatol 2016; 35:409-415. [2.] van Eeden C, et al. Expert Rev Clin Immunol 2022; 18:1049-1070. [3.] Davies K, et al. Nature Rev Rheumatol 2021; 17:651-664.

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A Qualitative Retrospective Review of Rheumatology Referrals to a High-Volume Community Rheumatology Clinic: The Good, the Bad and the Ugly

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Objectives: This study aims to critically examine the quality of incoming referrals in a community rheumatology clinic. By identifying gaps in the information provided and recognizing recurring issues, we seek to reduce inappropriate referrals and improve workflow efficiency, support better communication, streamline referral practices, and enhance patient care.

Methods: This study assessed the quality of 250 consecutive referrals received at Sunnyside Rheumatology Clinic in Kingston Ontario. We defined our audit standards based on the OMA and CPSO referral recommendations, with the standard that referrals meet 100% of the outlined criteria.

Results: While the standard expectation is that referrals meet 100% of the outlined criteria, the analysis of 250 referrals revealed substantial deficiencies in key areas. Notably, 40% of referrals did not include a clearly stated reason for referral, and 60% failed to provide an adequate physical examination. Additionally, 38% of referrals lacked even a description of relevant symptoms. Further gaps included missing personal health history in 10% of referrals, absence of family history in 68%, no allergy documentation in 15%, and missing current or previous medications in 16%. Relevant laboratory work was absent in 26% of referrals, while 34% lacked appropriate imaging. 21% of referrals contained redundant or excessive information. 22% of referrals were returned to the referring physicians with requests for additional information to enable proper triage. Many referrals were rejected outright due to being clearly inappropriate for rheumatology assessment.
Conclusion: This study highlights significant gaps in the quality and completeness of rheumatology referrals, underscoring the need for enhanced collaboration among referring physicians regarding appropriate and acceptable referral practices. In addition to improving adherence to established guidelines, there is a need to educate providers on when it is clinically appropriate to refer patients to rheumatology. By targeting services to patients most likely to benefit and improving the referral process, we can enhance workflow efficiency and ultimately improve patient outcomes and unnecessary burdens on consulting physicians.

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Neonatal Cardiac Function in Offspring Born to Mothers with Systemic Lupus Erythematosus: Insights from the Legacy Cohort

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Objectives: Systemic lupus erythematosus (SLE) increases the risk of placenta-mediated adverse pregnancy outcomes (APO) and may impact offspring cardiovascular health. Transplacental maternal anti-Ro antibodies can affect fetal cardiac function. Speckle tracking echocardiography (STE), a sensitive tool for detecting early cardiac dysfunction, remains underused in neonates. We used STE to assess the influence of maternal anti-Ro antibodies and APO on neonatal myocardial strain.
Methods: Participants were recruited from the Montreal site of the Lupus in prEGnAnCY (LEGACY) cohort, a multicenter prospective cohort enrolling SLE pregnancies at < 17 gestational weeks. APO was evaluated at each trimester and postpartum, and included: 1) gestational hypertension, preeclampsia and/or eclampsia, 2) placental insufficiency,3) placental abruption, and/or 4) small for gestational age (SGA ≤ 5 percentile). Neonatal cardiac function was assessed ≤4 weeks postpartum using STE, with global longitudinal strain (GLS) reported via apical endocardial or apical four-chamber peak longitudinal strain. GLS is expressed as a negative percentage, with more negative values indicating better myocardial contractile function.

We evaluated GLS with univariable and multivariable regression analysis adjusting for neonatal age and birth weight.
Results: This study included 26 pregnant women with SLE, of mean maternal age 35.9± 4.7 years and disease duration 9.9 ± 7.4 years. Most were in Lupus Low Disease Activity State (LLDAS) at baseline (85%), and 65% (15/26) maintained LLDAS throughout pregnancy. Live birth occurred in 89% (23/26), among which APO occurred in 42% (11/26). Out of live births, 3 missed the STE assessment and 4 had suboptimal images preventing GLS estimation. Thus, GLS was assessed in 16 neonates of mean age 11.8 ± 26.2 days at STE (Table 1). HCQ was used by all mothers (16/16), with mean cumulative gestational exposure of 1103.2 ± 294.6 mg x days/kg. Mean GLS was-26.3 ± 4.2%, with term neonates at -26.2 ± 4.3%. Lower mean GLS was observed in neonates born to mothers with APO (-25.2 ± 4.3%) and anti-Ro antibodies (-24.8 ± 4.5) versus their respective counterparts (-27.2 ± 4.1% and -27.9 ± 3.4%). GLS was not significantly associated with APO, or anti-Ro positivity in multivariable models.
Conclusion: We observed lower GLS in neonates born to SLE mothers with anti-Ro antibodies and those with APO. Though not statistically significant, potentially due to small sample size, the trends may reflect subclinical cardiac alterations. These findings support the need for larger studies to clarify the impact of maternal antibodies, APO, and HCQ on fetal cardiac health.

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Outcomes of Transition in Pediatric Rheumatology: Healthcare Utilization and Disease Activity in Juvenile Idiopathic Arthritis Patients Seen at the Young Adults with Rheumatic Disease Clinic in British Columbia

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Objectives: Approximately 50% of patients with juvenile idiopathic arthritis (JIA) require adult rheumatology care.[1] In British Columbia, the Young Adults with Rheumatic Diseases (YARD) clinic provides multidisciplinary care to young adults transitioning from pediatric to adult care. We aimed to describe the disease activity and healthcare utilization of JIA patients seen at BC Children's Hospital who transitioned to the YARD clinic.
Methods: We conducted a retrospective chart review of JIA patients transitioning from pediatric care to the YARD clinic between 2013 and 2023. Inclusion criteria: patients >17 years with ≥ 1 pediatric visit 12 months prior to YARD transfer, ≥1 YARD visit, and one 12-month YARD follow-up (FU). Descriptive statistics assessed demographics, disease activity, medications and healthcare utilization (ED = emergency department, HA = hospital admission) one year pre- and post-transition. For study purposes, "transition" equates to the first YARD visit.
Results: 68 patients (n=47, 69% female) met inclusion criteria: enthesitis-related arthritis (21/68), oligoarticular extended (6/68), oligoarticular persistent (9/68), polyarticular RF-negative (7/68), polyarticular RF-positive (7/68), psoriatic (8/68), systemic (4/68), unclassified (4/68), and rheumatoid arthritis (2/68). The YARD clinic received 122 JIA patient referrals. Median

transition age was 18 years. 13.24% of patients had pre-existing uveitis. Median time from last pediatric visit to first YARD visit was 4.45 months (2.96-6.06). Patients attended an average of 3.54 FU visits 12 months pre-transition and 2.76 visits 12 months post-transition. Median missed rheumatology visits: 0 (0-1) pre- and 0 (0-1) post-transition (Table 1). Median PGA scores were 2 (IQR 0-2, n=64) pre-transition and 0 (0-2, n=53) post-transition. ED visits occurred in 4/68 patients pre- and 3/53 post- transition (Table 1). HA occurred in 3/68 and 1/53 patients pre- and post-transition. Post-transition, 15 patients were discharged <12 months due to repeated missed appointments (3/15), distance/transportation challenges (3/15), refusal of care (2/15), relocation for work/education (2/15), and unspecified reasons (5/15). 7/15 patients were transferred to adult rheumatologists and 5/15 to family physicians.

Conclusion: JIA patients transitioning to the YARD clinic maintained stable rates of ED use and HA in the first year, suggesting minimal acute complications. Missed visit rates remained similar, and clinical disease activity improved. Early discharge was moderately high, primarily due to geographic challenges and patient preferences. These results show that youth with JIA can maintain healthcare engagement and stable outcomes in this model, supporting its efficacy. Further research assessing long-term healthcare utilization and disease control following transfer to adult care is needed.

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Preventable Hospital Admissions in Persons with Gout: A Population-Based Study

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Objectives: Ambulatory care sensitive conditions (ACSCs) are a defined set of diagnoses where appropriate ambulatory care prevents or reduces the need for admission to hospital. Hospitalization rates for ACSCs (inclusive of grand mal seizures, chronic lower respiratory diseases, asthma, diabetes, heart failure and pulmonary edema, hypertension, and angina) are used nationally as indicators for health system quality. We aimed to estimate the rates of ACSC hospitalizations in people with gout compared to matched controls.

Methods: Linked administrative health datasets from the province of Alberta were used to create an incident cohort based on validated ICD codes for gout from years 2002-2023. Controls were selected in a 1:1 ratio matched for age and sex. We used the Canadian Institute for Health Information ACSC ICD-10-CA case definitions to identify hospitalizations from the Discharge Abstract Database as our outcome of interest.[1] We calculated incidence rate ratios (IRR) at 3 and 5 years from the date of the first gout diagnosis using a multivariable regression model adjusting for age, sex, location of residence, and socioeconomic status.

Results: There were 129,378 individuals with incident gout over the study period (66% male, mean age 71 years, 79% urban, 34% with material and social deprivation). Of these, 42.6% (n=55,085) had at least 1 hospital admission for any reason, with a total of 180,696 unique hospitalizations, compared to 31.2% (n=40,373) of controls with 111,102 unique hospitalizations. ACSC hospitalizations accounted for 12% (n=20,889) of all admissions in persons with gout, compared to 10% (n=10,607) of all admissions in controls. This was driven primarily by hospitalizations for heart failure and pulmonary edema in the gout cohort (50.5%) and chronic lower respiratory diseases in the matched cohort (43.4%). After adjusting for age,

sex, location of residence, and socioeconomic status, the IRR for an ACSC hospitalization was increased at 3 years (IRR 1.15, 95%CI 1.09, 1.22) and 5 years (IRR 1.18, 95%CI 1.13, 1.23) in those with gout compared to controls. Among individual ACSCs, the IRR for heart failure and pulmonary edema admissions was increased by 34% at 5 years in those with gout (IRR 1.34, 95%CI 1.23, 1.45) relative to controls.
Conclusion: The risk for potentially preventable hospital admissions is increased in people with gout, primarily driven by heart failure and pulmonary edema. Access to high quality ambulatory care with optimization of comorbidity management is indicated to improve outcomes.
References: [1.] Canadian Institute for Health Information. Available at: https://www.cihi.ca/en/indicators/ambulatory-care-sensitive-conditions-hospitalizations
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Emergency Department Utilization in People with Gout: A 10-Year Population-Based Analysis of Visits in Alberta

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Objectives: The significant increase in gout prevalence in the population is anticipated to have effects on health system use, including acute care visits by patients with gout. Our objective was to analyze trends in ED visits for any reason among patients with gout in Alberta.
Methods: We used linked population-based administrative datasets to retrospectively assess ED use for any reason by persons meeting the case definition for incident gout over a 10-year period (2007/2008-2017/2018). We estimated the annual frequency of ED use and assigned the most responsible diagnosis code to broader diagnostic groupings. We analyzed visit characteristics, acuity at presentation using the Canadian Triage Acuity Scale (CTAS), and disposition using descriptive statistics. All results were additionally stratified by biological sex (male/female) and geographic location of residence (urban/rural).
Results: 646,926 ED visits were made by 88,373 individuals with gout in Alberta. We observed a 69% increase in ED use over the study period by the cohort although the mean number of visits per person per year decreased over the 10-year period, from 1.06 (95% CI 1.03, 1.09) in fiscal year 2008 to 0.79 (95% CI 0.77, 0.80) in fiscal year 2017. The majority of visits for any diagnosis were assessed at CTAS 3 “Urgent” (32.5%) and CTAS 4 “Less urgent” (32.2%). The proportion of visits triaged as ‘Urgent’ increased over the 10-year period, from 25.9% of all visits in 2008, to 37.9% in 2017. Visits specifically for gout accounted for 5.7% of all visits, primarily triaged as CTAS 3 (23.2%) and CTAS 4 (56%). Injuries and infection each accounted for ~11% of all visits. Almost 1 in 5 (17%) visits resulted in admission, although just 1.3% of admissions were for gout flares specifically. About one-fifth (19.6%) of individuals discharged from an initial ED visit had a minimum of one ED return visit within 72 hours. Where the first visit was coded as inflammatory arthritis, 42.2% of return visits were for the same diagnosis. Female patients more frequently required hospital admission (20.4% vs. males 15.7%), and while urban residents had an increased frequency of ED visits (25.6% vs 9.2%), they were less likely to be admitted to hospital than rural residents (11.4% vs. rural 20.0%).

Conclusion: Acute care utilization by persons with gout has increased significantly over time, with lower-acuity presentations dominating gout-related ED visits suggesting unmet ambulatory care needs.

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Evaluation of the Performance of Candidate Enthesitis Ultrasound Scoring Systems for Psoriatic Arthritis Diagnosis – Duet Study

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Objectives: Psoriatic arthritis (PsA) is often diagnosed late, leading to worse outcomes. Enthesitis is a key feature that can aid in early detection, but its clinical assessment is unreliable. Ultrasound (US) offers a more objective method for evaluating enthesitis, yet standardization remains a challenge. The GRAPPA Ultrasound Working Group is developing the Diagnostic Ultrasound Enthesitis Tool (DUET), a PsA-specific sonographic enthesitis scoring system to distinguish PsA from non-inflammatory conditions. While DUET has been derived from a discovery cohort, external validation is needed before its clinical adoption. In this study, we aimed to evaluate the discriminative ability of candidate DUET scores using independent data to inform the selection of a DUET scoring system.

Methods: This retrospective cross-sectional study analyzed US scans from PsA patients and non-psoriatic controls collected in a single centre following standard protocol. All PsA patients met the DUET enrollment criteria including PsA duration <5 years and were not using biologics. Controls had no psoriasis or other autoimmune disease. Enthesis US scans of the quadriceps, proximal and distal patellar tendons, triceps and Achilles were scored by a single reader blinded to the diagnosis for entheseal elementary lesions including hypoechogenicity, thickening, Doppler signal, enthesophytes, calcifications and erosions. We evaluated seven candidate DUET scores, each incorporating different combinations of entheseal sites and elementary lesions. Models were refitted using coefficients estimated in the discovery cohort. Model performance was also stratified by age group.

Results: In our validation cohort of 102 PsA patients and 69 controls, the seven candidate DUET risk scores yielded areas under the curve (AUCs) ranging from 0.660 to 0.764 (Figure 1). Stratifying the risk scores by age with a cutoff of 55 years enhanced AUCs to 0.781 (under 55) and 0.753 (over 55).

Conclusion: The candidate DUET scores demonstrated discriminative ability in an external validation cohort, with additional improvement following age stratification. These findings will guide further refinement of the selected DUET score and inform its integration into clinical and research settings. **Best Abstract on Spondyloarthritis Research Award**

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Bimekizumab Demonstrated Early and Sustained Efficacy Regardless of Baseline Characteristics in Patients with Active Psoriatic Arthritis: Pooled Post Hoc Results Up to 1-Year from Two Phase 3 Studies

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Objectives: To assess the impact of baseline (BL) characteristics on bimekizumab (BKZ) efficacy in patients with psoriatic arthritis (PsA) at Week (Wk)16 vs placebo (PBO) and through 1 year.

Methods: Pooled post hoc analysis was conducted for data from BE OPTIMAL (NCT03895203; biologic DMARD [bDMARD]-naïve) and BE COMPLETE (NCT03896581; TNF inhibitor inadequate response/intolerance [TNFi-IR]). Both studies assessed subcutaneous BKZ 160 mg every 4 wks in patients with PsA and were PBO-controlled to Wk16, then PBO patients switched to BKZ (PBO/BKZ). BE COMPLETE Wk16 completers could enter BE VITAL (NCT04009499; open-label extension), in which all patients received BKZ. Efficacy outcomes are reported by BL patient characteristic subgroups. Efficacy outcomes included ≥50% improvement from BL in ACR response criteria (ACR50), the composite outcome minimal disease activity (MDA), complete resolution of swollen joint count (SJC=0), and 100% improvement from BL in Psoriasis Area and Severity Index (PASI100; in patients with BL psoriasis ≥3% body surface area). Data are reported by randomization group at Wk16; for the BKZ Total group (PBO/BKZ and BKZ-randomized) at Wk52. The association of BKZ-treated vs PBO patients achieving Wk16 response overall and for each subgroup was estimated via odds ratios using logistic regression with factors for treatment, study, region, subgroup, and treatment by subgroup interaction (subgroup and interaction excluded in the overall). All p values are nominal and generated for the treatment by subgroup interaction term; missing data used non-responder imputation.

Results: Of the 1,112 patients randomized to PBO (n=414) or BKZ (n=698), 1,073 (96.5%) completed Wk16 and 1,002 (90.1%) completed Wk52. Overall BL demographics and disease characteristics were generally similar between treatment groups. Achievement of ACR50, MDA, SJC=0, and PASI100 responses were greater with BKZ vs PBO within all patient subgroups at Wk16, with consistent efficacy responses with BKZ treatment for most patient subgroups. Younger patients (<45 years) treated with BKZ were significantly more likely than older patients (≥45 years) to achieve ACR50 (p=0.001), MDA (p=0.006), and SJC=0 (p=0.035) at Wk16. Males were significantly more likely than females to attain ACR50 (p<0.001). Improved efficacy responses with BKZ treatment were sustained or increased from Wk16 to Wk52 across all subgroups (Figure 1); (SJC=0 and PASI100 data not shown).

Conclusion: BKZ demonstrated durable and greater improvements in clinical joint, skin, and composite outcomes measures vs PBO at Wk16, which were sustained to 1 year, regardless of patient demographics and clinical presentation at BL.

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Icotrokinra (ICO), a Novel Targeted Oral Peptide, in Patients (Pts) with Psoriatic Disease: Exploratory Assessments from a Phase 2 Psoriasis (PsO) Study Informing a Phase 3 Clinical Program in Psoriatic Arthritis (PsA)

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Objectives: PsA affects ~20-30% of patients with PsO, causing articular inflammation and impaired quality of life. ICO, a novel targeted oral peptide that binds IL-23 receptor, showed greater clinical response rates vs placebo and a favorable safety profile in moderate-to-severe plaque PsO in the Phase 2 FRONTIER 1&2 studies. We leveraged exploratory serum biomarker, Patient-Reported Outcomes Measurement Information Systems (PROMIS-29), and Psoriasis Area and Severity Index 75% improvement (PASI75) data from a subset of FRONTIER 1 patients with PsO and PsA (PsO+PsA) to support Phase 3 ICONIC-PsA 1 and ICONIC-PsA 2 studies.
Methods: Mean log fold-changes (logFC) in serum β-Defensin-2 (BD-2), IL-22, IL-17A and IL-17F levels were summarized for FRONTIER patients. Improvements ≥5-points in PROMIS-29 domains scores (or ≥2 for pain), and physical/mental component summary (PCS/MCS) scores, are considered clinically meaningful. ICO PsA Phase 3 sample sizes were informed by estimates from model-based analyses, including a meta-analysis that bridged FRONTIER 1 to PASI75 to expected American College of Rheumatology 20% improvement (ACR20) at Week (W)16 and meta-regression modelling that bridged ACR20 to secondary endpoints.
Results: 23/91 (25%) FRONTIER 1 patients had PsO+PsA (ICO, n=20; placebo, n=3). Among patients with biomarker data, mean logFC in serum BD-2, IL-22, IL-17A and IL-17F (data not shown) over time indicated consistent ICO pharmacodynamic effect between patients with PsO only and with PsO+PsA. ICO-treated PsO+PsA patients reported numerically greater mean changes from baseline (BL) at W16 vs placebo across PsA relevant PROMIS-29 domains, i.e. improvements in physical function (7.7 vs 1) and reductions in fatigue (-7.4 vs 2.3 [worsening]), pain interference (-10.7 vs -1.3), and pain intensity (-3.5 vs -1.5). In 20 ICO-treated patients with PsO+PsA, 45% and 70% reported ≥5 point improvement from BL in PROMIS-29 PCS and MCS scores, respectively, vs no patients receiving placebo. ICONIC-PsA 1&2 sample sizes of 540 (5:5:5:3 to ICO Dose 1/2/placebo/active reference arm) and 750 (1:1:1 to ICO Dose 1/2/placebo) (Figure 1) were estimated to provide ≥90% power to detect significant differences between ICO and placebo. Given minorities are often under-recruited in PsA trials, the ICO PsA program aims to assess diverse populations.
Conclusion: Exploratory assessments from FRONTIER 1 showed comparable ICO pharmacodynamic effects between patients with PsO only, and with PsO+PsA. ICO-treated patients with PsO+PsA reported numerically greater improvements in PsA-relevant PROMIS-29 domains vs placebo. Informed by these post-hoc analyses and model-based meta-analyses, the multicenter, double-blind, placebo-controlled ICONIC-PsA 1 and ICONIC-PsA 2 studies will

evaluate ICO in active PsA.

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Bimekizumab Clinical Efficacy Up to 2 Years Across Patients with Psoriatic Arthritis and Varying Baseline Joint Involvement: Results from a Post Hoc Analysis of Two Pooled Phase 3 Studies

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Objectives: To assess bimekizumab (BKZ) efficacy in subgroups of patients with psoriatic arthritis (PsA) with varying baseline (BL) joint involvement over up to 2 years.

Methods: Post hoc analysis assessed subcutaneous BKZ 160mg every 4 weeks (wks; Q4W) in patients with PsA and varying BL joint involvement. Patients were grouped by BL swollen joint count (SJC) based on quartiles: SJC ≤5, 6–≤7, 8–≤12, >12. Due to few patients with BL SJC 3/4, patients with SJC 5 were included in first quartile; quartile sizes vary. Patients were pooled from BE OPTIMAL (NCT03895203; biologic DMARD [bDMARD]-naïve) and BE COMPLETE (NCT03896581; TNF inhibitor inadequate response/intolerance [TNFi-IR]). Unequal trial sizes (BE OPTIMAL 431 BKZ, 281 PBO; BE COMPLETE 267 BKZ, 133 PBO) yielded unequal quartile proportions. Both trials required ≥3 tender and swollen joints and had 16-wk double-blind, placebo (PBO)-controlled periods. Completers of BE OPTIMAL Wk52 or BE COMPLETE Wk16 could enter BE VITAL (NCT04009499; open-label extension), with all patients receiving BKZ. BE OPTIMAL included a reference arm (adalimumab 40mg Q2W); data not reported due to small patient numbers in SJC quartiles. Outcomes reported: ACR ≥50% improvement, Psoriasis Area and Severity Index 100% improvement, minimal disease activity, SJC=0, Pain visual analog scale ≥50/70% improvement from BL, Health Assessment Questionnaire – Disability Index minimal clinically important difference (≥0.35 decrease from BL in patients with BL score ≥0.35). Data were pooled across trials and reported by randomization group at Wk16, Year 1 (Wk52), and Year 2 (Wk104/100 from BE OPTIMAL/BE COMPLETE).

Results: At BL, SJC distributions were: ≤5 (n=370), 6–≤7 (n=215), 8–≤12 (n=275), >12 (n=252). At Wk16, BKZ-treated patients demonstrated numerically greater improvements in joint, skin, composite, and patient-reported outcomes vs PBO, across patients with varying BL joint involvement. For all domains assessed, improvements were sustained to 2 years in BKZ-randomized patients, with robust efficacy across patients with varying BL joint involvement (Figure 1); (patient-reported outcome data not shown). For patients who switched from PBO to BKZ at Wk16, improvements in efficacy similar to BKZ-randomized patients with varying BL joint involvement were reported to Year 1 and sustained to Year 2.

Conclusion: In patients with PsA and varying BL joint involvement, BKZ treatment demonstrated greater improvements vs PBO across disease domains at Wk16, and improvements were sustained to 2 years. Efficacy was robust across all groups of patients with varying BL joint involvement, reflecting the broader range of patients seen in clinical practice.

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Long-Term Safety of Tildrakizumab Through Week 208 in Patients with Psoriatic Arthritis: Results from the Phase 2B Open-Label Extension Study

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Objectives: Tildrakizumab is an anti–IL-23 p19 monoclonal antibody approved for the treatment of adults with moderate-to-severe plaque psoriasis. In a Phase 2b trial in patients with active psoriatic arthritis (PsA; NCT02980692), tildrakizumab treatment significantly improved joint and skin symptoms and was well tolerated for up to 52 weeks.[1] Our objective is to report safety results through Week (W)208 of an open-label long-term extension (LTE) of the trial.

Methods: Patients who completed treatment in the parent study, achieved ACR20 response at W52, and had sufficient clinical benefit per the investigator were eligible for the LTE. Patients received tildrakizumab 200 mg every 4 weeks, 200 mg every 12 weeks (Q12W), or 100 mg Q12W until parent study database lock (≥52 weeks of treatment), after which all patients received tildrakizumab 100 mg Q12W through W208. Safety was assessed in all patients who entered the LTE and received ≥1 dose of tildrakizumab based on frequency and severity of adverse events (AEs); frequency of serious AEs (SAEs), AEs of special interest (AESIs) and clinical interest (AECIs); and presence of antidrug antibodies (ADAs) to tildrakizumab. Analyses were based on the treatment received.

Results: Of 281 patients who entered the LTE, 205 completed treatments through W208. Any AEs, treatment-related AEs (TRAEs), SAEs, and treatment-related SAEs occurred in 224/281 (79.7%), 55/281 (19.6%), 40/281 (14.2%), and 2/281 (0.7%) patients, respectively (Table). The most common TRAEs were upper respiratory tract infection (3.2%) and nasopharyngitis (2.5%). Overall, 17/281 (6.0%) and 7/281 (2.5%) patients discontinued the study due to AEs and TRAEs, respectively, chiefly infections and infestations. AESIs were reported in 13/281 (4.6%) patients and included infections and infestations (1.8%); cardiac disorders (1.1%; not treatment related); malignancies (n = 2; 0.7%); respiratory, thoracic, and mediastinal disorders (n = 2; 0.7%); and vascular disorders (n = 1; 0.4%). Only 1 AECI occurred during the LTE. Two patients died due to AEs (1 aortic dissection and 1 metastatic adenocarcinoma, neither treatment related). Non–treatment-emergent (TE) and TE ADAs were detected in 2.8% and 1.1% and non-TE and TE neutralizing ADAs in 0.7% and 0.4% of patients, respectively. Patients' ADA status was not associated with AEs of hypersensitivity or injection-site reactions, AESIs, or AECIs.

Conclusion: The safety profile of tildrakizumab was maintained through extension W208 in

patients with PsA. These data support continued development of tildrakizumab to treat patients with active PsA.

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Mindfulness Matters: Early Insights from the Making Mindfulness Matter© in Children with Juvenile Idiopathic Arthritis Study

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Objectives: Poor mental health (MH) in the pediatric rheumatology population has been shown to affect quality of life, educational attainment, and disease-related outcomes, such as medication adherence, healthcare utilization, and transition to adult care. Although patients with juvenile idiopathic arthritis (JIA) represent the single largest disease group in pediatric rheumatology practice, there are gaps in our understanding of the co-morbid mental health effects in JIA, and in research on interventions to optimize MH for these patients. Preventive, skills-based approaches may strengthen coping and resilience, addressing the scarcity of pediatric MH resources. The Making Mindfulness Matter JIA (M3©-JIA) trial evaluates the feasibility, acceptability, and preliminary impact of an online mindfulness-based intervention in children with JIA and their caregivers.

Methods: M3©-JIA is a three-site, parallel, randomized controlled trial recruiting caregiver–child dyads (ages 4–12) into either an 8-week M3© intervention or wait-list control. Weekly online sessions are led by trained facilitators, with caregivers and children attending separate groups. The M3© program incorporates neuropsychology, social-emotional learning and positive psychology. Quantitative data includes demographics, attendance, and pre-/post-intervention questionnaires assessing mindfulness and parenting practices; qualitative feedback was collected through open-text responses.

Results: Of 67 dyads screened to date, 22 (33%) were randomized (11 intervention, 11 control). Most caregivers were mothers (86%), mean age 40.6 ± 6.5 years. Children were predominantly female (82%) with a mean age at enrolment of 9.3 ± 2.7 years and disease duration of 5.3 ± 3.1 years. Attendance was higher among caregivers than children (≥80% session attendance: 75% vs. 50%), with strong engagement in both groups (camera on ≥85% of session: 75% vs. 88%). Post-intervention, children reported greater awareness and use of mindfulness skills—for example, knowledge of “breathing breaks” increased from 42% to 100%, and understanding emotional regulation from 50% to 95%. Caregivers showed improvements in mindfulness and parenting confidence (e.g., practicing mindfulness regularly: 31% to 63%; confidence in helping their child calm down: 69% to 90%) (Table 1). Qualitative feedback highlighted enjoyment, connection, and the value of creative, hands-on activities.

Conclusion: Preliminary findings demonstrate that M3© is feasible, engaging, and positively received by children with JIA and their caregivers. Early data suggest improvements in mindfulness awareness and parenting practices. While primarily scheduling challenges limited randomization rates, strong adherence and satisfaction support the promise of M3© as a scalable mental health support strategy within JIA care.

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Paint Me a Picture: Illustrating the Psychosocial Impact of Different Juvenile Idiopathic Arthritis Categories. Results from the Capri Registry

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Objectives: Our study aims to build on the emerging knowledge of the psychosocial challenges of living with juvenile idiopathic arthritis (JIA), by examining differences across the 7 JIA categories and identifying associated factors.

Methods: We included 1072 patients (0-18 years old) enrolled within 3 months of diagnosis in the Canadian Alliance of Pediatric Rheumatology Investigators (CAPRI) Registry. The treating rheumatologist assigned JIA categories using ILAR classification criteria. Descriptive statistics summarized patient characteristics at baseline and at one year. Psychosocial impact was measured utilizing the psychosocial domain (22 items) within the Juvenile Arthritis Quality of Life Questionnaire (JAQQ). Boxplots visualized changes in JAQQ-psychosocial median scores over time, and Wilcoxon ranked-sum tests highlighted significant differences for JIA categories. Hierarchical clustering of patients using the standardized scores (Z-scores) of 22 JAQQ-psychosocial items produced heatmaps for JIA categories (baseline and one year), as well as a heatmap for JIA patients at enrollment (Figure 1). Spearman correlations investigated factors associated with psychosocial impact, and univariate and multivariate regressions quantified the relationship between factors and psychosocial impact. Analyses were conducted using STATA 15 and Python 3.13.

Results: Results: Descriptive statistics showed oligoarthritis was the most frequent category (45.4% of patients) and polyarthritis RF-positive was the less frequent (3.8%). Significant improvements in JAQQ-psychosocial scores from enrollment to one year were observed for polyarthritis RF-negative, polyarthritis RF-positive, psoriatic, and systemic arthritis ($p<0.05$). Hierarchical clustering of JIA patients at enrollment (n=1072) revealed four patient clusters by psychosocial impact: minimal (51.0%), mild (30.6%), moderate (9.3%), and severe (9.0%). JAQQ-psychosocial items clustered into externalizing behaviours, internalizing behaviours, and school-related problems (Figure 1). Heatmaps at enrollment across JIA categories (excluding undifferentiated) showed polyarthritis RF-positive with the highest percentage of patients with severe psychosocial impact (12.5%, mean Z-score 2.24). Oligoarthritis patients exhibited a continuum of psychosocial impact, while psoriatic arthritis patients clustered at minimal or severe extremes. Spearman correlations showed moderate associations between psychosocial impact and functional disability, fatigue, pain, and other JAQQ domains at baseline and at one year (correlations=0.4-0.6). CHAQ disability index, fatigue, and pain interference were significant predictors of psychosocial impact in multivariate regression.

Conclusion: Conclusion: Our findings suggest that patients diagnosed with certain JIA categories are at higher risk for greater psychosocial impact, especially polyarthritis RF-positive. Exploring the category-specific psychosocial burdens is vital for targeted, tailored psychosocial interventions to complement medical treatment for JIA.

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Anifrolumab for Refractory Juvenile Dermatomyositis: A Multicenter Pediatric Case Series

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Objectives: Refractory juvenile dermatomyositis (JDM) and idiopathic inflammatory myopathies pose significant therapeutic challenges, with a subset of patients failing to respond to the standard therapy of corticosteroids and immunosuppressants. Anifrolumab, a monoclonal antibody targeting the type I interferon receptor, has demonstrated effectiveness in treatment-resistant pediatric myositis, yet evidence is limited to a recent few case reports.[1] We aimed to detail the efficacy and safety of anifrolumab in treating four pediatric cases with refractory inflammatory myositis.

Methods: We retrospectively and prospectively reviewed the medical records of patients with childhood-onset inflammatory myositis who experienced persistent disease activity and were treated with anifrolumab. This study involved two tertiary medical centers: Hospital Sant Joan de Déu in Barcelona and the Hospital for Sick Children in Toronto. Data on demographics, disease manifestations and severity, laboratory findings, treatment details, and responses to therapy were collected.

Results: Four patients, three females and one male, aged 3.5 to 10 years at the time of diagnosis, were identified (Table 1). The median time from diagnosis to starting anifrolumab was 12 months (IQR 7.8 to 31). All presented with muscle weakness and cutaneous features, and patient 1 also had ulcerative skin disease, bowel perforation, and pulmonary infections. Patients 1 and 4 were positive for anti-NXP2 antibody, while patients 2 and 3 had positive anti-p155. Prior to commencing on anifrolumab infusions, all patients received prednisone, methylprednisolone pulses, and intravenous immunoglobulins (IVIG), along with two or more of methotrexate, tacrolimus, mycophenolate mofetil (MMF), and cyclophosphamide. Patient 1 also needed three surgeries due to bowel perforation. Clinical responses were evaluated after six anifrolumab infusions (5mg/kg q4 weeks) for patient 1, three infusions for patients 2 and 4, and two infusions for patient 3. All four patients demonstrated clinically meaningful improvement in their skin

involvement and overall disease activity. Patient 4 experienced a halt in the progression of the calcinosis lesion, while patient 1 also saw significant improvement in muscle strength and no recurrence of gastrointestinal involvement. The prednisone dosage was substantially reduced in patients 2 and 3, while it was discontinued in case 1. No anifrolumab-related adverse effects were observed.
Conclusion: This study highlights the promising efficacy of anifrolumab in the management of refractory JDM, with clinically meaningful improvement in cutaneous and other involvement, along with a favorable safety profile. These findings provide additional support for the systemic inhibition of type I interferon in managing the disease and emphasize the need for prospective studies.
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Response to Hydroxychloroquine in Immune Thrombocytopenia in Childhood-Onset Systemic Lupus Erythematosus

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Objectives: The management of immune thrombocytopenia in childhood-onset systemic lupus erythematosus (cSLE) is not standardized. We examined the efficacy and safety of hydroxychloroquine (HCQ) as monotherapy for thrombocytopenia in cSLE.[1]
Methods: We retrospectively reviewed the medical records of patients who developed thrombocytopenia (platelet count < 100 ×109/L) and were diagnosed with cSLE and followed in the rheumatology clinic at The Hospital for Sick Children (SickKids) between January 2005 and December 2024. In this clinic, structured data, including disease activity (assessed by the Systemic Lupus Erythematosus Disease Activity Index (SLEDAI)), are prospectively collected at every visit. Definite cSLE was defined by the 2019 EULAR/ACR classification criteria, while patients with incipient cSLE had clinical features of evolving SLE but achieved a EULAR/ACR score below 10. A complete response was defined as a platelet count >100 ×109/L with no bleeding. Partial response was defined as a platelet count >30 ×109/L with at least a 2-fold increase from the lowest count and no bleeding. Descriptive statistics were used to characterize the study groups and outcomes.
Results: Of the 798 patient records reviewed, 207 (26%) of patients had thrombocytopenia. One hundred sixty-one patients (78% female) with a median age of 12.7 years (IQR 10.1-14.5) and a median platelet count of 22 ×109/L (IQR 7-59) at the time of thrombocytopenia diagnosis were included.[1] The median lowest platelet count was 11 ×109/L (IQR 2-41). 131 patients (81%)

had definite, and 30 (19%) had incipient cSLE (Table 1). One hundred and nine (67%) of patients were treated with corticosteroids, and 80 (50%) of them received IVIG prior to commencing on HCQ (Table 2). Seventy-three (45%) patients achieved complete or partial responses before initiating HCQ. 147 (91%) patients were treated with HCQ, initiated at a median of 6 months (IQR 2.7 - 12.2) after thrombocytopenia diagnosis, at a median platelet count of 77 × 10^9/L (IQR 32.5-198.0). Of those, thirty-five (24%) patients were treated with HCQ monotherapy (Table 3). All 35 responded; 30 had complete responses after a median follow-up of 52 months (IQR 33-75). Of the 147 patients who received HCQ during their disease course, 11 experienced side effects, and 7 of them had to discontinue the treatment due to these effects.

Conclusion: While most patients initially required additional treatments, HCQ monotherapy effectively maintained a partial or complete response in thrombocytopenia for over 4 years in approximately 1 in 5 cSLE patients.

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A Novel Approach to Monitoring Calcinosis in Juvenile Dermatomyositis: Serial Low-Dose Whole-Body CT

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Objectives: Evaluating the overall impact of calcinosis and response to therapy in juvenile dermatomyositis (JDM) remains challenging, primarily relying on physician assessments or plain X-rays.[1] We aimed to explore the use of an ultra-low-dose protocol for whole-body CT imaging as a novel approach to monitor the distribution and burden of calcinosis in a cohort of patients with JDM.

Methods: The study focused on patients diagnosed with probable or definite JDM as per the Bohan and Peter criteria, followed at the Hospital for Sick Children during the years January 2000 to September 2025, who developed calcinosis based on physical examination or previous imaging studies. Eligible patients who have undergone at least two serial non-contrast, ultra-low-dose whole-body CT scans during their follow-up were included in the study. Imaging data analysis was conducted to detect the regional distribution and volume of calcinosis, assess changes over time, and compare serial CT scans performed for each included patient.

Results: Out of the 256 patients with JDM, 54 (21%) developed calcinosis during follow-up. Among these, three patients with a median age of 7.8 years (IQR 7.2-9.9) at JDM diagnosis underwent two serial non-contrast, ultra-low-dose whole-body CT scans each to assess their calcinosis during their follow-up. Two of the cases were positive for anti-NXP2, while case 2 had negative myositis-specific antibody serology. The median duration of disease at the development of calcinosis was 17 months (IQR 8.5-22). The median duration between the first

and second CT scans was 12 months (IQR 9.5-13). In all three cases, follow-up CT scans revealed an increase in the size and distribution of previously observed deposits, along with the appearance of new calcification clusters (Figures 1). Furthermore, the 3D reconstruction of confluent calcinosis revealed a distinct structure and distribution of certain densities compared to earlier evaluations conducted through X-ray and physical examination. This resulted in an intensification of treatment in each of the three cases. The median effective dose for a low-dose CT scan used was significantly lower than the standard protocol, about 10 times less than in adults.

Conclusion: An ultra-low-dose protocol for whole-body CT can serve as a safe and objective, valuable tool for monitoring changes in calcinosis, thereby contributing to improved patient care and outcomes.

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High-Sensitivity C-Reactive Protein as a Biomarker of Disease Activity in Psoriatic Arthritis

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Objectives: C-reactive protein (CRP) is commonly used to assess disease activity in psoriatic arthritis (PsA), yet, fewer than 50% of patients with active PsA have elevated CRP levels. High-sensitivity C-reactive protein (hsCRP) assays detect lower concentrations missed by conventional methods but their role as biomarkers of PsA disease activity remains uncertain. We aimed to evaluate the association between hsCRP levels and clinical and sonographic measures of PsA activity.

Methods: We analyzed data from the Gladman-Krembil cohort that included patients with PsA followed from January 2016 to April 2025 ("clinical cohort"). Patients in this cohort are followed at 3–12-month intervals with standardized collection of medication use, PsA disease activity measures, patient-reported outcomes, and laboratory tests. The following measures of disease activity were assessed: Disease Activity measures included disease activity in Psoriatic Arthritis (DAPSA), clinical DAPSA (cDAPSA), Minimal Disease Activity (MDA), tender and swollen joint count (TJC, SJC), Psoriasis Area and Severity Index (PASI), enthesitis and dactylitis counts, patient pain, global assessment, and function, classifying patients as remission/low (DAPSA < 14) or moderate/high disease activity (≥14). HsCRP levels were measured using standardized high-sensitivity assays. A smaller subset underwent a comprehensive ultrasound of their joints/entheses before and 3 months following initiation of advanced therapy ("US cohort"). Total inflammatory sonographic scores, including synovitis, paratenonitis, tenosynovitis, and enthesitis, were calculated. Associations between hsCRP and clinical and sonographic measures of disease activity were analyzed using GEE multivariable regression models, which were

adjusted for age, sex, and body mass index (BMI).
Results: A total of 1263 patients (10568 visits) from the clinical cohort and 144 patients (222 visits) from the US cohort were analyzed. Baseline mean hsCRP levels were 6.3±15.1mg/L and 8±12.4 mg/L in the clinical and US cohorts, respectively. Higher hsCRP was independently associated with higher DAPSA, TJC, SJC, dactylitis count, PASI (clinical cohort), and with patient-reported outcomes such as pain, global assessment of disease activity, and physical dyfunction (Table 1). Higher hsCRP levels were also significantly associated with reduced odds of achieving DAPSA-LDA, cDAPSA-LDA, and MDA. HsCRP was associated with SPARCC enthesitis score in the US cohort but not in the clinical cohort and with synovitis, paratenonitis, and tenosynovitis scores. HsCRP was associated with sonographic enthesitis count but not with the total enthesitis score.
Conclusion: HsCRP is associated with both clinical and sonographic measures of inflammation in PsA. These findings support its utility as a simple, objective biomarker for monitoring both clinical and subclinical disease activity in PsA.

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Comparative Outcomes in Pregnant Patients with Rheumatoid Arthritis Treated with and Without Tumour Necrosis Factor Inhibitors: A Systematic Review and Meta-Analysis

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Objectives: Pregnant patients with higher rheumatoid arthritis (RA) disease activity are at increased risk of perinatal complications.[1] There is a paucity of safety data for continuation of tumour necrosis factor inhibitors (TNFi) in pregnancy.[2] A knowledge gap exists as to whether pregnant patients with RA who use TNFi experience different rates of perinatal outcomes compared to those who do not use TNFi. The objective was to identify differences in outcomes amongst patients with RA who are treated with and without TNFi during pregnancy.
Methods: Using a protocol prospectively registered on PROSPERO, systematic review of MEDLINE, EMBASE, Web of Science, Scopus, CENTRAL, and Google Scholar was performed according to PRISMA guidelines. Studies reporting outcomes comparing patients with RA who did and did not receive TNFi during pregnancy were included. Collected outcomes included: 3rd trimester DAS28-CRP, congenital anomalies, pregnancy loss, small for gestation age (SGA), preterm birth, and serious maternal and neonatal infections. Using RevMan version 5.4 with fixed effects modelling if I2 <25%, binary outcomes were analyzed using Mantel-Haenszel risk ratio and continuous outcomes were calculated using inverse variance method as mean difference.
Results: Outcome data from 9 patient populations were included. There were no significant differences between patients who did and did not use TNFi with regard to congenital anomalies (RR = 1.13; 95% CI = 0.62-2.08, p = 0.69), SGA (RR = 0.89; 95% CI = 0.56-1.41, p = 0.61), and preterm birth (RR = 0.99; 95% CI = 0.76-1.31, p = 0.97) (Figure 1). Among outcomes with 3 or fewer studies reporting, there were no significant differences in 3rd trimester DAS28-CRP scores (mean difference = 0.08; 95% CI -0.11-0.26, p = 0.41), pregnancy loss (RR = 1.03; 95% CI 0.26-4.19 p = 0.96), serious maternal infection (RR = 0.94; 95% CI 0.32-2.76, p = 0.91), and serious neonatal/infant infection (RR = 1.02; 95% CI = 0.35-3.00, p = 0.97).
Conclusion: To our knowledge, this is the first meta-analysis evaluating outcomes in pregnant women with RA only, treated with or without anti-TNF inhibitors. Amongst patients with RA, TNFi use in pregnancy does not appear to be associated with congenital anomalies, SGA, or

preterm birth. This could help inform patient counselling around the continuation of TNFi in the prenatal period in this particular patient population. Additional original research is required to determine whether the similarities in disease activity are confounded by low sample size, selection bias, additional medication use, and timing of TNFi discontinuation.
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Rheumatoid Arthritis Associated Interstitial Lung Disease in a Single Centre Cohort: Be Vigilant in Older Male Smokers Who Are Seropositive and Have a Low DLCO at Baseline

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Objectives: To characterize serologic, inflammatory, and pulmonary function profiles of patients with rheumatoid arthritis–associated interstitial lung disease (RA-ILD) in a tertiary Canadian cohort, and to identify early markers of physiologic decline following ILD diagnosis.

Methods: This retrospective case series included 98 patients with confirmed RA-ILD followed in Hamilton, Ontario. Demographics, including sex, smoking history, autoantibody titers, inflammatory biomarkers, and pulmonary function test (PFT) results were abstracted from clinical records. Clinically meaningful progression was defined as ≥10% absolute decline in forced vital capacity (FVC %) or diffusing capacity for carbon monoxide (DLCO %) predicted. Patients with ≥2 PFTs within two years of ILD diagnosis (n = 54) were assessed, of whom 14 (26%) exhibited >10% functional change.

Results: Of 98 patients, 82 had pulmonary data and 54 had serial PFTs within two years; 14 (25.9%) demonstrated >10% change in FVC and/or DLCO, indicating progression. Of the progressors, 9 were male (64%), suggesting greater susceptibility to functional decline among men. Compared with the broader cohort, the progression group showed higher autoantibody titers (mean RF 280 IU/mL vs 164 IU/mL; anti-CCP 147 vs 131 U/mL) and greater smoking exposure (mean 48.4 vs 38.3 pack-years). Despite greater physiologic decline, they exhibited lower inflammatory markers (CRP 11.5 vs 15.6 mg/L; ESR 21.4 vs 31.8 mm/hr), necessitating further analysis to determine whether decline occurs independently of systemic inflammation. Functionally, the progression group had higher FVC (82.9% vs 75.9%) but lower DLCO (46.9% vs 50.7%), potentially suggesting disproportionate impairment in gas transfer and early fibrotic or microvascular injury. Radiographically, 11 of 16 patients with available HRCT follow-up demonstrated disease progression, 8 of whom exhibited a usual interstitial pneumonia (UIP) pattern, consistent with previously described aggressive fibrosing phenotypes.[2] The rate and pattern of progression are comparable to those reported in previous RA-ILD studies,[3] reinforcing the established link between seropositivity, smoking, and pulmonary decline.[1]

Conclusion: Approximately one in four RA-ILD patients experienced clinically significant pulmonary function decline within two years of diagnosis. Progression occurred predominantly among male patients, who were highly seropositive, heavily smoking-exposed, and more likely to exhibit a UIP pattern with reduced DLCO, even in the absence of elevated systemic inflammation. These findings delineate a distinct high-risk RA-ILD phenotype that warrants early, proactive monitoring and timely therapeutic intervention, including consideration of

antifibrotic or immunomodulatory strategies, to prevent irreversible pulmonary decline and respiratory failure [1-3].
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Effects of Pharmacotherapy on Fibromyalgia Symptoms and Functional Outcomes in Systemic Lupus Erythematosus: A Moderation Analysis on a Multicenter Canadian Study

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Objectives: Fibromyalgia (FM) symptoms are a common comorbidity in systemic lupus erythematosus (SLE), contributing to increased pain, fatigue, and insomnia. These symptoms can significantly impair physical and cognitive function, making it harder to perform daily activities, exercise, and tasks requiring concentration. This study examines the effect of FM symptoms on function and explores how various treatment approaches can moderate these effects through a multicenter cross-sectional analysis of SLE patients from seven Canadian clinics.

Methods: Data on disease burden metrics (FM symptoms, pain areas, disease activity, and irreversible damage), medication use (antimalarials, corticosteroids, immunosuppressants, biologics and narcotics), and sociodemographic factors were collected. Linear mixed-effects models evaluated the effect of FM symptoms and other disease burden variables on five functional outcomes: fatigue severity (FSS), cognitive dysfunction (PDQ), disability (WHODAS), depression (BDI), and work role functioning (WRF). Moderation models were used to assess if SLE treatments ameliorated the effect of these variables on function, while correcting for multiple testing.

Results: The models established that a higher number of reported fibromyalgia symptoms was the strongest predictor of functional impairment, being significantly associated with increased fatigue ($\beta = 1.06$, $p < 0.001$), cognitive dysfunction ($\beta = 1.21$, $p < 0.001$), and higher disability ($\beta = 0.68$, $p < 0.001$), and depression scores ($\beta = 0.73$, $p < 0.001$). Conversely, irreversible damage scores were uniquely linked to worsened work role functioning ($\beta = -4.41$, $p = 0.020$). Building on these models, moderation analyses revealed that certain treatments lowered the effect of the

disease burden metrics on various function metrics (Figure 1). Immunosuppressants moderated the impact of organ damage on disability from $\beta = 2.62$ to $\beta = 0.45$ ($p = 0.022$) and perceived deficits from 2.28 to -0.84 ($p = 0.041$). Corticosteroids attenuated the association between FM symptoms and cognitive dysfunction falling from $\beta = 1.42$ to $\beta = 0.14$ in users ($p = .024$).
Conclusion: This study demonstrates that the reported number of fibromyalgia symptoms is the dominant factor driving functional burden across nearly all measured domains in SLE, surpassing the impact of disease activity. Most significantly, we provide evidence that certain SLE treatments act as functional shields: corticosteroids protecting cognition from FM effects and immunosuppressants mitigating disability linked to damage. These moderation effects strongly support tailoring treatment not only to disease activity but also to the patient's functional risk profile, moving clinical practice closer to truly personalized medicine. **Supported by a CIORA grant**

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Assessing the Southend GCA Probability Score in Patients Referred to a University Rheumatology Practice for Suspected Giant Cell Arteritis (GCA)

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Objectives: The Southend GCA Probability Score (GCAPS) is a simple tool that can be used in clinic to assess the pre-test probability of giant cell arteritis (GCA), to guide decisions for testing and/or initiation of prednisone.[1] We aimed to retrospectively assess its validity in patients referred to the University of Alberta for suspected GCA.
Methods: Electronic medical records of patients referred to University of Alberta Rheumatology for query GCA between January 2022 and January 2024 were retrospectively reviewed. Patients with relapsing GCA, or those whose charts lacked sufficient data to calculate a GCAPS were excluded. Data was extracted from the first rheumatology visit and inputted into the Southend GCAPS Calculator. The sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of a High, Intermediate or Low risk GCAPS score were calculated using both 1) the clinical diagnosis of GCA at 3 months follow up, and 2) confirmed diagnosis of GCA by testing [either temporal artery biopsy, ultrasound, or PET/CT], as gold standard. Receiver operator characteristic (ROC) curves were plotted using numerical GCAPS scores.
Results: 81 referrals for new onset, suspected GCA were identified, of which 62 contained all data to calculate a GCAPS score. Ultimately, GCA was diagnosed in 39 patients (27 patients confirmed by test, 12 diagnosed clinically) and excluded in 23. Of 62 patients, 31 (50%) had a High risk GCAPS, 23 (37.7%) had Intermediate risk and 8 (12.9%) had Low risk GCAPs. See distribution of results (Table 1). Using the clinical diagnosis at 3 months as gold standard, the sensitivity of having either Intermediate/or High risk GCAPS was very high at 97.4%, with specificity of 30%, PPV of 70.4% and NPV 87.5%. The sensitivity of High risk GCAPS alone was lower at 66.7%, but with higher specificity of 78.3%, PPV=83.9%, NPV=58.1%. Using only confirmed diagnosis of GCA as gold standard, the sensitivity of Intermediate/or High risk GCAPs was 100%, with specificity of 30%, PPV of 62.8% and NPV 100%. The GCAPS ROC AUC was good at 0.805 (95% CI 0.697-0.913). At the previously determined optimal cut-point of 9.5, the sensitivity was 97.4% but specificity was low at 34.8%.
Conclusion: In our population, an Intermediate or High risk GCAPS score was highly sensitive for the final diagnosis of GCA, suggesting that for those with Low-risk scores, GCA is unlikely and other diagnosis should be strongly considered.

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Providers' Perspectives on Diagnostic Testing for Giant Cell Arteritis

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Objectives: Suspected giant cell arteritis (GCA) is a rheumatologic emergency, but there is no standard pathway for diagnosis at our centre. We aimed to improve our understanding of physicians' experiences with diagnostic testing for GCA and to identify barriers/strategies for improved access.

Methods: Specialist providers involved in the diagnosis or treatment of patients with suspected GCA in Edmonton, AB, were invited by email to complete an anonymous survey regarding their experiences requesting and/or performing temporal artery biopsy (TAB), PET/CT, and temporal artery ultrasound (U/S). Descriptive statistics and one-way ANOVAs were used to analyze the data.

Results: In total, 31 physicians from 5 specialties completed the survey. See physician demographics (Table 1). Of the 3 tests, urgent access to TAB was deemed the most essential for diagnosing GCA (with mean score 4.3 +/-0.86 on 1-5 point scale; 1=not important, 5=essential) as compared to U/S (mean score 3.9 +/-0.79) and PET/CT (mean score 3.40 +/0.82),p=0.004. TAB was most difficult to access, however (mean score 3.8 +/-0.52; 1=easy to access, 5=cannot access) as compared to U/S or PET/CT (mean 2.6 +/-1.1 and 3.1 +/- 0.91, respectively, p<0.001.) Administrative burden was also greatest for TAB (mean score 4.2 +/-0.62) vs. U/S (2.95+/- 1.2) or PET/CT (2.95 +/-0.89), p<0.001. Overall,15/20 (75%) rheumatologists/neurologists reported that they either cannot access or find it very challenging to access TAB urgently, particularly for patients without visual involvement. Among 8 surgeons who completed the survey, 6 performed an average of 6-10 TABs/each last year, and 2 did not perform TABs. Scheduling of urgent biopsies, focused scope of practice/lack of capacity, and lack of exposure to procedure in training were cited as surgical barriers. Nuclear medicine physicians read between 21-30 PET/CT scans/each for query GCA last year. The limited number of PET/CT scanners and inability to flag untreated, suspected GCA cases for urgent booking were identified as nuclear medicine barriers. The main reported barrier to TA U/S was that it is currently offered by a single provider only. Overall, 62% (18/29) of all respondents reported being very/somewhat unsatisfied with the process for diagnosing GCA, and only 4/20 (20%) rheumatologists/neurologists reported feeling very confident about their current ability to diagnose/exclude GCA.

Conclusion: Providers across multiple specialties were generally unsatisfied with diagnostic testing for GCA, and perceived confidence in ability to accurately diagnose is low (20%.) Increasing the availability of TA U/S may help offset the need for TAB and improve care.

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Co-Development and Evaluation of a Flare Action Plan for Rheumatoid Arthritis

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Objectives: To co-develop and evaluate a flare action plan for people living with rheumatoid arthritis (RA).
Methods: As part of a patient-initiated follow-up model (called Appointments by Choice or ABC) [1], a multi-method, phased approach was utilized to co-develop and evaluate the flare action plan (Figure 1). Following an environmental scan of patient-facing materials for RA flare self-management [2], the action plan was iteratively co-developed with the research team (including rheumatologist, physiotherapy, and knowledge mobilization expertise), a design team, and patient partners. The evaluation phase was completed post-ABC implementation to ascertain the real-world value of the action plan. This evaluation included Patient Education Materials Assessment Tool (PEMAT)[3] ratings completed by patient partners (n=4) to capture the understandability and actionability of the action plan, and qualitative interviews with ABC patients (n=15). PEMAT scores were analyzed with descriptive statistics and interviews were analyzed using thematic analysis.
Results: The iterative co-development phase included multiple steps: 1) content development with research team expertise, 2) incorporation of patient partner feedback, 3) visual design with a design team, and 4) research team and patient partner feedback on both content and design. During evaluation, averaged patient partner PEMAT scores were 88.3% for understandability and 90% for actionability. Among the 15 participants who were interviewed, the median age was 61 years (IQR = 9) and participants had lived with RA for a median of 11.5 years (IQR = 4.8). 60% identified as female, and 60% identified as White/European. Three key themes emerged from interview data. 1) “This isn’t new… but it’s good to read it again” - participants described how the flare management strategies presented in the action plan were a good reminder for those who have been living with RA for many years, and a valuable resource for newly diagnosed individuals. 2) “It’s inviting” – participants had positive reactions to the design and visual aspects of the action plan, describing clear organization and layout, and inviting colours and visuals. 3) “It’ll be in my corner” - participants described how the action plan could be valuable for future reference.
Conclusion: The flare action plan was developed for people with RA to support evidence-based self-management. It has demonstrated value for patients on the ABC pathway, as shown by PEMAT ratings and qualitative data, and could be targeted towards newly diagnosed individuals. Furthermore, this patient-facing material could be disseminated more broadly across Canada and adapted for other chronic conditions.
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Implementation of the Appointments by Choice Model for Rheumatoid Arthritis: A Patient-Initiated Follow-Up Pilot Study

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Objectives: This study aimed to understand the barriers and facilitators to implementing the "Appointments By Choice" (ABC) patient-initiated follow-up model of care in rheumatoid arthritis (RA).[1] Objectives were to evaluate preliminary data on reach, adoption, and implementation of ABC.

Methods: The 1-arm non-randomized ABC implementation pilot study began in January 2024 at a multipractice rheumatology clinic in Alberta. People with (1) established RA, (2) well-controlled disease, (3) no major medication changes, and (4) no other active complex conditions were invited to participate in ABC1. Primary implementation outcomes, informed by the RE-AIM framework,[2] included reach, adoption, and implementation. Secondary outcomes were safety and effectiveness. Quantitative data from surveys and chart reviews were summarized using descriptive statistics. Qualitative data from weekly meetings and interviews were analyzed using thematic analysis, with mapping to CFIR,[3] domains within each RE-AIM category (Table 1).

Results: Reach: Over 18 months, 76/140 (54.3%) of eligible individuals consented to participate in ABC. The most common reason for declining was a "preference for usual care" (14/64, 21.9%). Participant altruistic motivation to free-up physician time for those in-need was a facilitator, whereas lack of physician time to discuss ABC was a barrier. Adoption: 5/7 rheumatologists approached participated in ABC, representing over 1/3 of the clinic. The phased rollout of ABC and tension for change were adoption facilitators. Meanwhile, limited early leadership support was a barrier. Implementation: Facilitators included adapting recruitment workflows to rheumatologist preferences, improved integration of ABC processes in the EMR, and clear contact lists for clinical and research teams. Barriers included limited ABC understanding among clinic staff, incomplete transfer of care communication, and participant confusion about ABC due to inconsistent information provided at baseline. Safety/Effectiveness: 68/76 (89.5%) ABC participants remained on ABC, with 2 withdrawing and 6 returning to usual care due to flares, infection and medication change. 31 participants contacted the flare clinic (0.4 calls/week) for support with flares, lab tests, imaging results, and other minor concerns. Overall,

1,520 minutes of rheumatologist time was saved due to reduced appointment frequency, equivalent to 38 new patient consults. Safety and effectiveness facilitators included limited flares and positive participant experiences with flare clinic support. Barriers were mixed rheumatologist perspectives on the value of ABC and limited usefulness of the self-report flare questionnaire.
Conclusion: Early insights show promise of ABC for improving the efficiency and patient-centeredness in rheumatology care. For expanded implementation, adaptations are required to address barriers faced during our pilot study.
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The Cost-Effectiveness of Early Versus Delayed Disease-Modifying Antirheumatic Drugs for Psoriatic Arthritis

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Objectives: Disease-modifying anti-rheumatic drugs (DMARDs) are the standard first-line therapy for psoriatic arthritis (PsA), effectively improving clinical symptoms and health-related quality of life. While conventional synthetic DMARDs (csDMARDs) are typically prescribed initially, targeted synthetic (tsDMARDs) and biologic DMARDs (bDMARDs) have demonstrated efficacy in improving joint and skin outcomes, achieving minimal disease activity (MDA), and preventing radiographic progression.[1] Emerging evidence suggests that delayed DMARD initiation is associated with worse functional outcomes, lower MDA achievement rates, and greater irreversible joint damage.[2] This cost-utility analysis evaluates the economic and health-related impacts of early versus delayed DMARD initiation for DMARD-naive adult PsA patients, comparing direct medical costs and quality-adjusted life-years (QALYs).
Methods: A Markov model simulated disease progression over five years using monthly cycles from a U.S. payer perspective. Transition probabilities, EQ-5D utilities, and healthcare resource utilization were derived from a targeted literature review. Patients began in a pre-treatment state and transitioned monthly among four health states following DMARD initiation: complete response (sustained MDA), partial response (non-sustained MDA), non-response (did not meet MDA), or death. Modelled therapies included methotrexate (csDMARD), tofacitinib or apremilast (tsDMARDs), and biologic DMARDs (bDMARDs). Early initiation was defined as ≤1 year after PsA diagnosis and delayed initiation occurred >1 year after diagnosis. The mean time from diagnosis to DMARD initiation was 0.2 years in the early group and 8.6 years in the delayed group. Cost differences between exposure groups were modelled using a regression equation linking Health Assessment Questionnaire Disability Index (HAQ-DI) scores to direct

medical costs, where higher HAQ-DI scores were associated with higher costs.[3]
Results: Early DMARD initiation resulted in a gain of 0.33 QALYs and a cost savings of USD$7,473.52 per patient relative to delayed initiation, producing a dominant incremental cost-effectiveness ratio of –USD$22,479.24/QALY (Figure 1). The model was most sensitive to changes in direct medical costs (range: –USD$206,875.18/QALY to USD$161,915.70/QALY) and MDA rates (range: –USD$437,673.70/QALY to –USD$14,947.59/QALY).
Conclusion: This study demonstrates that early DMARD initiation in DMARD-naive patients with PsA provides superior clinical and economic outcomes compared to delayed initiation, making it the dominant strategy. The substantial economic value of early initiation is largely driven by achieving early disease control, preventing irreversible joint damage, and improving long-term functional outcomes. These benefits translate into reduced healthcare costs and greater patient outcomes, reinforcing the importance of early therapeutic intervention and advocating for the reconsideration of reimbursement frameworks to allow timely access to effective treatment.
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Responsiveness of Patient-Reported Outcomes by Disease Trajectory in Systemic Lupus Erythematosus

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Objectives: Systemic lupus erythematosus (SLE) is a life-threatening autoimmune disease with heterogeneous manifestations that cause substantial morbidity and premature mortality. Beyond organ damage, patients experience persistent symptoms such as fatigue, pain, and functional limitation, which profoundly impair quality of life and are often under-recognised by physician-assessed indices.[1] Patient-reported outcomes (PROs) are essential for capturing treatment benefit, yet their responsiveness and alignment with clinical activity across disease trajectories remain incompletely defined.
Methods: We pooled patient-level data from four phase III belimumab trials in adults with active SLE (n=1065). Patients were stratified into four previously defined disease trajectory classes according to baseline disease activity (high vs. moderate) and treatment response (responder vs. non-responder).[2] PROs included Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F), 36-Item Short Form physical (PCS) and mental (MCS) component summaries, EuroQol 5-Dimension (EQ-5D), and EuroQoL Visual Analog Scale (EQ-VAS). Responsiveness was assessed with standardised response means (SRMs) across timepoints and classes. Correlations with SLEDAI-2K, BILAG, and Physician's Global Assessment (PGA) were examined using Spearman's coefficients and compared with Steiger's Z (α=0.05). Sensitivity analyses were performed using complete-case datasets at each timepoint.
Results: FACIT-F and SF-36 PCS were the most responsive PROs and showed the strongest correlations with clinical indices (Table 1). FACIT-F was most responsive early (up to week 20), particularly among non-responders and moderately active responders, while SF-36 PCS was most responsive later (weeks 20-52), especially among responders. EQ-5D consistently demonstrated the lowest responsiveness (peak SRM 0.54) and weakest correlations. PGA correlated most strongly with PRO changes; SLEDAI-2K correlations were weak and

inconsistent. Data completeness declined modestly from 95% at baseline to 82% at week 52. Analyses restricted to patients with complete 52-week follow-up yielded results consistent with the main findings, with FACIT-F and SF-36 PCS remaining the most responsive instruments and EQ-5D showing minimal change detection.
Conclusion: This is the first study to longitudinally evaluate PRO performance by disease trajectory in SLE using pooled patient-level data from belimumab trials. We show that PRO performance is dynamic, trajectory-dependent, and domain-specific. FACIT-F and SF-36 PCS consistently outperformed EQ-5D in capturing clinically meaningful change and aligning with physician assessments. The consistently poor responsiveness of EQ-5D underscore limitations of generic preference-based measures in SLE. These findings emphasize the importance of selecting sensitive, patient-centred instruments in clinical trials, routine care, and health technology assessments. Failure to do so risks underestimating the true value of therapies in a complex, symptom-driven disease such as SLE.
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Patient Perspectives of the Barriers and Facilitators to Participating in Appointments by Choice: A Qualitative Study of a Patient-Initiated Follow-Up Implementation Pilot Using the Consolidated Framework for Implementation Research

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Objectives: We explored the barriers and facilitators of participating in the patient-initiated follow-up strategy Appointments By Choice (ABC) from the perspectives of participating patients with rheumatoid arthritis (RA).
Methods: Patients enrolled in the ABC pilot were invited via email to participate in semi-structured qualitative interviews. Patients were selected from two different time points: mid-study (6 months) and end-of-study (12 months), post-enrolment. Demographic information was collected at study enrolment through an online survey hosted on Qualtrics. Interviews were conducted using Zoom Videoconferencing and were one hour in length. Interview transcripts were independently analyzed thematically and in duplicate using the Consolidated Framework for Implementation Research (CFIR) to identify barriers and facilitators to ABC participation.[1] Coders met regularly to address additional themes as they emerged from the transcripts, to discuss and modify codes, and reconcile differences. Interviews ceased once saturation was met. Ten CFIR codes representing key domains (Implementation process, individual, inner setting, innovation, and innovation outcomes) were applied deductively, and five additional codes were

introduced inductively to capture emergent themes.
Results: Ten participants (5 mid-study, 5 end-of-study) were interviewed. The median age was 61 years (IQR = 13.75), and participants had lived with RA for a median of 11.5 years (IQR = 13). Four out of the ten participants identified as White/European, and six out of the ten participants identified as female. Reported barriers included uncertainty about whom to contact in the event of a flare or other rheumatologic concern, and challenges maintaining regular lab testing when in-person follow-up reminders were absent. Other barriers included missing the physician/patient relationship and the social visit aspect of the rheumatology clinic appointment. Facilitators included shared decision-making with rheumatologists, the availability of a flare action plan promoting self-management,[2] and the use of a self-reported flare questionnaire,[3] as ongoing "check-ins". Patients valued the flexibility of the ABC model, particularly those living at a distance, and highlighted the responsiveness of the flare clinic and pharmacist support in medication adjustments. An unexpected facilitator was patients' altruistic motivation, awareness of clinic workload and willingness to defer appointments to allow others with greater needs to be seen sooner. Select domains and patient quotes are displayed (Table 1).
Conclusion: People with RA described ABC as a feasible and acceptable model of care, with minimal barriers identified. Addressing clarity around flare management and lab testing will improve patient experience and willingness to participate in this patient-initiated follow-up model.
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Parent Psychological Distress Moderates the Association Between Child Psychopathology and Disease Activity in Children with Juvenile Idiopathic Arthritis

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Objectives: Parents of children with juvenile idiopathic arthritis (JIA) commonly experience mental health problems that negatively affect their well-being and quality of life. Among parents of children with JIA, both their child's mental health and disease activity have been linked to higher levels of parent burden and stress.[1] Despite this, whether parent distress relates to children's disease outcomes remains unknown. We investigated whether parent psychological distress moderates the association between child mental health and disease activity in children with JIA.
Methods: Parents and their children (10-16 years) with JIA were recruited from clinics at McMaster and Alberta Children's Hospitals. At enrolment, we measured child mental health using the parent-reported Emotional Behavioural Scales (EBS), and the child-reported EBS (CEBS). Parent psychological distress was measured using the Kessler 6 (K6), and Parent Stress Scale (PSS). Disease activity was measured by self-perceived impact of JIA based on a single

question within the Patient Global Assessment (PtGA). Descriptive statistics were determined for all variables of interest. Multiple regression analyses using product-term interactions estimated whether parent psychological distress moderated the association between child mental health, categorized as internalizing and externalizing psychopathology and disease activity. Covariates included parent and child age and sex, household income, and parent education.
Results: Baseline characteristics for parent–youth dyads (n=132) are shown (Table 1). There were significant ($p<.05$) moderating effects of both measures of parent psychological distress (PSS and K6 modelled independently) on the association between disease activity and internalizing psychopathology. Significant interaction effects were observed for child-reported internalizing × PSS ($\beta=-.248$, $p=.005$) and × K6 ($\beta=-.753$, $p<.05$), as well as parent-reported internalizing × PSS ($\beta=-.218$, $p=.005$), and × K6 ($\beta=-.671$, $p<.05$). No moderating effects were found for the association between externalizing psychopathology and disease activity.
Conclusion: Overall, parent stress/distress was a significant moderator of the relationship between child mental health and disease activity, with more distress associated with worse disease activity. This study will continue to assess child mental health outcomes for up to 18 months. Findings will inform early prevention of parental stress and subsequent mental health problems in children with JIA. Understanding the psychosocial impact of JIA will support the development of individualized mental health services and support.
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Patient Appointment Reminders Are Associated with Lower Clinic Non-Attendance Rates for Outpatient Rheumatology Clinic

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Objectives: Outpatient clinic non-attendance for chronic disease management leads to poor outcomes for the patient unable to attend, in addition to longer wait times for other patients waiting for evaluation.[1] Studies of non-attendance in other settings and subspecialties have identified appointment reminders as a useful tool to improve appointment attendance.[2] The value of appointment reminders was explored at Kingston Health Sciences Centre outpatient Rheumatology clinics. The non-attendance rate of clinics utilizing appointment reminders (phone calls or emails) were compared to a clinic not employing appointment reminders.
Methods: Three out of five Rheumatology clinics at the Kingston Health Sciences Centre employ phone call appointment reminders, a fourth clinic employed phone call or email reminders, while the fifth clinic did not employ any reminders. Our primary outcome measure was the non-attendance rate in the reminder group (clinics 1-4) compared to the no reminder group (clinic 5). Secondary outcomes of interest included the correlation between confirmation of attendance and non-attendance rate across clinics, and whether email reminders were comparable to phone call reminders in reducing the non-attendance rate.
Results: The non-attendance rate was lower in clinics utilizing any appointment reminder method (6.9% 95%CI:6.0-7.8) as compared to no reminders (10.0% 95%CI:8.1-12.0) (Chi-square (1,N=3917) 9.73, $p=.002$). The administrative time cost was the balancing measure for the study and ranged from 28 to 50 hours of administrative time over a 6-month period in the clinics that performed appointment reminders. Appointment confirmation rate correlated with lower non-attendance rate (Pearson $r(2) = -0.91$, $p = .04$) at a cost of administrative time if reminders were given by phone call. However, email reminders were a method of increasing

confirmation rate with less added time cost and had comparable beneficial influence on non-attendance rate to phone call reminders 5.9% vs 6.9% respectively, (Chi-square (1,N=3346) 0.45, p=.83).
Conclusion: Appointment reminders significantly lowered the non-attendance rate for outpatient rheumatology clinics. This was at a cost of 28 to 50 hours of administrative work over a 6-month period. Confirming appointments at the time of reminders also lowered the non-attendance rate but required extra time to do so if done by telephone. Both reminder calls and reminder emails were comparably effective, and email reminders with the added function of confirming appointments could be a method of improving the confirmation rate at a time savings. Utilizing email reminders for those patients who are able to adopt it may be the more efficient method overall.
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Rates of Neonatal Lupus Erythematosus in Neonates of Anti-Ro/SSA Positive Mothers Treated with or Without Hydroxychloroquine

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Objectives: 1. Evaluate the risk of neonatal lupus erythematosus (NLE), including congenital heart block (CHB), in neonates born to mothers with anti-Ro/SSA antibodies (anti-Ro60/SSA, anti-LA/SSB, and anti-Ro52), who were treated with or without Hydroxychloroquine (HCQ) during pregnancy, which has evidence for safety. [1]
2. Compare patient characteristics, including anti-Ro/SSA titers, and their relationship on rates of NLE.
Methods: Prospective cohort study of pregnant adults aged ≥18 years with positive anti-Ro/SSA antibodies, with or without a systemic autoimmune or rheumatic disease (SARD), who were followed in the Obstetrical Rheumatology Clinic at The Ottawa Hospital until three months postpartum. Clinical data was extracted independently by two reviewers through standardized chart review. The relationship between maternal HCQ use and neonatal outcomes was analyzed descriptively.
Results: 31 pregnant women with anti-Ro/SSA positivity were included. Mean age was 34 ± 5. The majority (61.3%) had a SARD, while 38.7% had no diagnosis. 35.5% had isolated anti-Ro60/SSA antibodies, 19.4% had dual positivity, and 38.7% had triple antibody positivity. 74.2% were treated with HCQ, with 78.2% started pre-conception or first trimester and until delivery. Dose of 400mg (39.1%) or 5mg/kg/day (43.5%). NLE occurred in 3 cases overall (10%), each treated with HCQ, and none reported in the non-HCQ group. 2 NLE cases presented with cutaneous NLE and CHB (8.7%), while the other was limited to cutaneous NLE (4.3%). One case of CHB was treated since pre-conception (type 1) and the other (type III) treated only in third trimester. Both diagnosed between 18-24 weeks gestation, with 87.1% screened for CHB between 16-26 weeks. Each case of NLE occurred with triple positive high titer anti-Ro60, anti-Ro52, and anti-La (Figure 1), with high titer anti-LA/SSB showing a statistically significant difference (p=0.004). Only 10% of patients had anti-La/SSB >1,375, yet this accounted for 66.7% of NLE cases.
Conclusion: This is the first study to evaluate the rates of NLE in neonates of anti-Ro/SSA positive mothers treated with HCQ. The results are skewed by a patient with type III CHB prior to starting HCQ late in pregnancy. Accounting for this, rates of NLE with HCQ (8.6%)

compared to without (12.5%) are more aligned with prior data. Additionally, the few cases of NLE in this study occurred only with triple positive high titer Ro/La antibodies. This may suggest that patients with low titer antibodies do not require the same rigorous screening, or that treatment with HCQ is more effective in this subset of patients in preventing NLE.
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Rapid Onset Neutropenia After Mycophenolate Mofetil Initiation: Two Cases

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Background: Mycophenolate mofetil (MMF) is widely used as an immunosuppressive therapy for autoimmune diseases. Although leukopenia and neutropenia are recognized adverse effects, these typically develop subacutely. To date, rapidly developing cytopenias within days of treatment onset have not been documented. We report two cases of neutropenia occurring within 4 days of exposure to MMF, both of which recurred upon re-challenge, suggesting a likely hypersensitivity phenomenon.

Case Report: Case 1 involves a 46-year-old man with newly diagnosed idiopathic inflammatory myositis who was treated with MMF 500mg daily along with glucocorticoids and IVIG. Within 3 days he developed neutropenia with neutrophils nadiring at 0.4 x 10^9/L on day 6 after MMF initiation. His neutropenia resolved with cessation of MMF and administration of filgastrin. However, re-challenge with MMF at 250mg daily led to recurrence of neutropenia within one day so MMF was permanently discontinued, after which his neutrophil count quickly rebounded. Case 2 involves a 73-year-old woman with a new diagnosis of limited cutaneous systemic sclerosis and scleroderma renal crisis, who was initiated on MMF 500mg twice daily. Within four days her neutrophils dropped from 11.1 x 10^9/L to 2.4 x 10^9/L. Accordingly, the MMF was held for a day, after which her neutrophil count normalized, so MMF was re-initiated at a lower dose of 500mg daily. Within four days neutropenia had recurred, so MMF was discontinued and the neutropenia resolved within two days.

Conclusion: Bone marrow suppression is a well-established side-effect of MMF, with leukopenia and neutropenia occurring in as many as 25% of patients.[1] Onset, however, is generally subacute, occurring >100 days after initiation of MMF.[1, 2] Prior to our cases, we found no reports of neutropenia or leukopenia developing within a matter of several days of MMF initiation without other obvious causal factors. A complex array of enzymes is responsible for metabolism and defects of any of these can lead to supratherapeutic drug or metabolite levels. Pharmacokinetic studies of MRP2/ABCC2 variants in renal transplant patients have identified both high expressor and low expressor phenotypes that can lead to either sub therapeutic or supratherapeutic MMF levels at standard dosing.[3] However, there is not yet a body of study investigating whether the pharmacokinetic differences seen in MRP2/ABCC2 variants translate into adverse events such as MMF-related neutropenia. The confirmation of such a link would offer a potential target for genetic screening, which could help to prevent hypersensitivity events in patients treated with MMF.

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Confirming the Validity of the New EULAR/ACR Classification Criteria for Pediatric Chronic Nonbacterial Osteomyelitis

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Objectives: We aimed to investigate the performance characteristics of the new European Alliance of Associations for Rheumatology (EULAR) / American College of Rheumatology (ACR) classification criteria for pediatric CNO, in a distinct real-world clinical setting and compare it to the performance characteristics of the existing Jansson and Bristol diagnostic criteria.

Methods: Single-center cross-sectional study including children ≤18 years, diagnosed with CNO, acute infectious osteomyelitis (AOM) and bone malignancy from June 1, 2018 to May 31, 2024. Patients with other mimicking conditions, immunodeficiency, sickle cell disease, or those previously included in the original development cohort were excluded. Patients were divided into two groups: a CNO group and a non-CNO group (AOM and bone malignancy), from the latter a representative, random, sample was selected (www.random.org). Demographic, clinical, laboratory, imaging and pathology data were collected at disease onset. EULAR/ACR criteria were retrospectively applied to the entire cohort, independently from the initial diagnosis. Patients with an aggregate score ≥ 55 points were classified as having CNO. A secondary analysis was conducted excluding patients with missing data. Classification results using the new criteria were compared with the final clinical diagnosis based on physician assessment (criterion standard). The same analysis was applied to Jansson and Bristol criteria. Sensitivity and specificity, positive likelihood ratio (LR+) and post-test probability (PTP) (pre-test probability: 20%, based on CNO prevalence in our center) were calculated.

Results: Of 164 children included, 82 had CNO, 41 were randomly selected from 274 cases of AOM, and 41 from 849 cases of bone malignancy. The median age was 10 years (IQR 3–16), with 62% girls and 37% boys, 33% had a bone biopsy. Overall, 40% scored ≥ 55 and 60% did not, with 19 false positive and 3 false negative. The EULAR/ACR criteria demonstrated 77% sensitivity and 96% specificity, with a LR+ of 19.25 and PTP of 83%. In our secondary analysis

excluding patients with incomplete data, results remained consistent (sensitivity 79%, specificity 96%, LR+ 19.75, PTP 83.2%). In comparison, the Jansson criteria showed 78% sensitivity, 67% specificity, LR+ of 2.36, and PTP of 37%. The Bristol criteria yielded 89% sensitivity, 70% specificity, LR+ of 2.97, and PTP of 43%.
Conclusion: Based on its favorable sensitivity and specificity, especially in comparison to existing criteria, the new EULAR/ACR criteria appeared to be more effective in distinguishing CNO from AOM and bone malignancy at disease onset, results consistent with findings from the original validation cohort. **Best Abstract by a Rheumatology Post- Graduate Research Trainee Award**

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Addressing Symptoms of Burnout Amongst Pediatric Rheumatology Fellows: a Quality Improvement Project

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Objectives: To report the results of a quality improvement initiative aimed at reducing burnout symptoms among pediatric rheumatology fellows in a tertiary academic hospital as measured by the Maslach Burnout Inventory (MBI) by 20% over 6 months.
Methods: Baseline MBI was completed by pediatric rheumatology fellows as a screen of burnout symptoms. All fellows were enrolled in 2023-2024 academic year. The MBI reports scores in three categories: emotional exhaustion (EE), depersonalization (DP), and personal accomplishment (PA), with higher scores equating to higher risk of burnout. A stakeholder group was formed, including 8 pediatric rheumatology fellows, and engaged colleagues including allied health team members and staff physicians within the Division of Rheumatology. The workgroup identified key and modifiable contributors to burnout within the workplace. Processes were implemented and modified using multiple plans, do, study, act (PDSA) cycles. Wellness sessions were run by the study leads (fellows and faculty) and implemented with attendance and post-session feedback obtained as process measures to guide subsequent PDSA cycles. The MBI was followed at the 0, 3-, and 6-month mark to assess success of these strategies.
Results: A baseline MBI was completed by 3/12 pediatric rheumatology fellows as an audit. Average scores were EE = 15.7/36 (moderate), DP = 10.0/20 (moderate), and PA = 13.0/32 (low). Each wellness session represented a new PDSA cycle. Five PDSA cycles were completed from January to June 2024. The initial cycle highlighted that there was no process in place to address symptoms of burnout. Implementation strategies included "Treats and Talks" focused sessions during protected educational time, social events among fellows and external events that included the fellows' families. Eight fellows completed the six-month follow-up MBI. Six-month MBI scores showed improvement in all MBI domains with EE = 10.8/36 (low), DP = 4.6/12 (low), and PA = 8.8/32 (low), a decrease of 31%, 54%, and 32% respectively. Average session attendance was 7/12 fellows, and average benefit score was 6.1/10.

Conclusion: Our study has revealed a baseline risk of burnout amongst pediatric rheumatology fellows at our tertiary academic hospital. With a quality improvement-based approach we have implemented change strategies that show reduced risk of burnout, as measured by the MBI at 6 months. Ongoing change ideas will be focused on the sustainability of these changes.

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Factors Contributing to Low Quality of Life Scores in Patients with Systemic Lupus Erythematosus.

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Objectives: The LupusQoL is a validated, disease-specific instrument for assessing health-related quality of life (HRQoL) in patients with systemic lupus erythematosus (SLE). Identifying factors influencing HRQoL is essential for optimizing patient-centered care. This study aimed to determine the clinical, psychosocial, and treatment-related predictors of impaired HRQoL, as measured by the LupusQoL.

Methods: In this cross-sectional study, consecutive SLE patients fulfilling the 2019 EULAR/ACR classification criteria were recruited with informed consent under institutional ethics approval. Demographics, social determinants of health, and LupusQoL scores were collected via standardized questionnaires. Clinical data, including SLEDAI-2K, ACR Damage Index, healthcare utilization, and medication use, were abstracted from medical records. Low QoL was defined as a score below the 50th percentile. Between-group comparisons were performed using t-tests, chi-square, or Mann–Whitney U tests.

Results: Among 207 patients (mean age 53.1 ± 14.2 years; 88.4% female), 39 (18.8%) had low HRQoL and 168 (81.2%) had high HRQoL. Across all eight LupusQoL domains, patients with high HRQoL scored significantly better (all $p < 0.001$). The greatest differences were observed in the Physical, Planning and Burden domains. The low HRQoL group had higher ACR Damage Index scores (1.89 ± 1.87 vs. 1.21 ± 1.75; $p = 0.022$), while mean SLEDAI-2K scores were similar (2.12 ± 2.66 vs. 2.00 ± 2.31; $p = 0.777$). Depression/anxiety was more prevalent among patients with low HRQoL (48.0% vs. 25.2%; $\chi^2 = 8.6$, $p = 0.004$). Fibromyalgia was more frequent among patients with low HRQoL compared to those with high HRQoL (21% vs. 5.5%; $\chi^2 = 10.2$, $p = 0.001$), indicating a strong association between comorbid fibromyalgia and impaired quality of life. Prednisone use was also associated with lower HRQoL scores (41% vs. 26%; $\chi^2 = 3.8$, $p = 0.05$). No statistically significant differences were observed in age, ethnicity, marital status, income, or primary care access.

Conclusion: In this SLE cohort depression, anxiety, fibromyalgia, corticosteroid use, and greater cumulative organ damage were the strongest predictors of poor HRQoL, outweighing demographic or disease activity measures. Marked impairments across physical, planning, and burden domains highlight the multifactorial nature of HRQoL in SLE and underscore the need for integrated mental health care, steroid-sparing strategies, and prevention of organ damage to enhance quality of life.

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Evaluating Frailty in Systemic Lupus Erythematosus: A Scoping Review

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Objectives: There is growing interest in using frailty to better understand the heterogeneous

health outcomes observed among people living with systemic lupus erythematosus (SLE). This scoping review aimed to 1) Identify and describe the tools and measures used to characterize frailty in SLE; 2) Describe the associations of frailty with cross-sectional and longitudinal outcomes in SLE; and 3) Compare the estimated prevalence of frailty in SLE across studies.
Methods: This study was performed following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR). A comprehensive search was conducted in Ovid MEDLINE, Embase, Cochrane Library and Scopus from inception to July 14th, 2025. The search strategy used keywords and Medical Subject Headings for "systemic lupus erythematosus" and "frailty". Included articles were English language full-length original research articles of any study design that described the use of a frailty measure/tool in patients with SLE. Data were extracted using a standardised form by two independent reviewers. Risk of bias assessment was done using the NHLBI Quality Assessment Tool for Observational Cohorts and Cross-Sectional Studies.
Results: The search yielded 797 articles for title/abstract screening, of which 83 underwent full text review. Twenty-four articles were included (14 cohort studies, 10 cross-sectional studies). All included studies received an overall rating of "fair" or "good" in the risk of bias assessment. Frailty was assessed using six different measures. One specifically constructed for use in SLE, the Systemic Lupus International Collaborating Clinics Frailty Index (SLICC-FI), was the most frequently used (15 studies), followed by the Fried phenotype (5 studies) and FRAIL scale (5 studies) (Table 1). The prevalence of frailty was reported by all 24 studies, ranging from 6.2% to 80.9%. Older age was positively associated with frailty in 8 of 13 studies. In univariable analyses, regardless of the measure used, frailty was associated with an increased risk of adverse outcomes during follow-up, including damage accrual, hospitalizations, and mortality, as well as worsening disability, quality of life and cognitive impairment.
Conclusion: Several different tools are used to measure frailty among people living with SLE. Regardless of whether it is measured using the phenotypic approach or the deficit accumulation approach, frailty is consistently associated with an increased risk of adverse health outcomes in SLE. The optimal approach for measuring frailty in this population may vary across different clinical and research contexts.

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Multicentric Reticulohistiocytosis Presenting as Seronegative Erosive Inflammatory Arthritis: A Diagnostic Challenge in Rheumatology

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Background: To describe a rare case of multicentric reticulohistiocytosis (MRH) presenting with seronegative erosive inflammatory arthritis mimicking rheumatoid arthritis, highlighting the diagnostic challenge and importance of dermatologic evaluation in rheumatologic disorders.
Case Report: A 36-year-old Hispanic female presented with a one-year history of progressive bilateral small and large joint arthralgias involving the MCPs, PIPs, wrists, and knees. Laboratory investigations revealed negative rheumatoid factor, anti-cyclic citrullinated peptide antibody, antinuclear antibody, and HLA-B27. C-reactive protein was mildly elevated (11 mg/L), and baseline imaging was normal. The patient received sequential therapy with methotrexate, leflunomide, and biologics agents including adalimumab and JAK inhibitors (tofacitinib, upadacitinib, baricitinib) with only partial or transient responses. Over a six-year disease course, the patient developed new erosions on serial hand radiographs and violaceous periungual macules with nodular lesions over the digits. Infectious causes were excluded. An

urgent dermatology consultation was requested. Skin biopsy revealed multinucleated histiocytes and giant cells with eosinophilic, ground-glass cytoplasm—findings diagnostic of multicentric reticulohistiocytosis.[1] Given persistent disease activity, intravenous tocilizumab was initiated alongside a tapering course of prednisone, resulting in stabilization of joint symptoms and improvement in skin lesions.
Conclusion: Multicentric reticulohistiocytosis is a rare systemic granulomatous disorder that may mimic seronegative erosive arthritis, often leading to diagnostic delay. Recognition of characteristic cutaneous findings and histopathologic confirmation are essential for diagnosis.[2] Reported treatments include corticosteroids, methotrexate, cyclophosphamide, and TNF inhibitors with variable benefit. Although data remain limited, biologic therapies—particularly IL-6 inhibition—appear promising for refractory disease.[3] Early dermatologic collaboration and multidisciplinary management are key to optimizing outcomes.
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Gaps in Care for Hydroxychloroquine-Related Retinopathy Screening in British Columbia: A Population-Based Cohort Study

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Objectives: To describe rates of adherence to current guidelines for hydroxychloroquine-related retinopathy (HCQ-R) screenings among long-term (≥1 year) HCQ-users in British Columbia (BC) and to identify associated healthcare-system and patient-level predictors.[1]
Methods: We conducted a longitudinal retrospective-cohort (Jan 1, 1997–Dec 31, 2023) using BC administrative health data (capturing all provincially funded services including outpatient and hospital visits, dispensed medications, and demographics). We identified all adults with systemic lupus erythematosus (SLE) or rheumatoid arthritis (RA) who started HCQ after diagnosis and remained on HCQ for ≥1 year. We followed this cohort for HCQ-R screening from HCQ initiation assessing for baseline and subsequent annual screenings until HCQ discontinuation, loss-to-follow-up, death or administrative end of study. Outcome: A valid screening (guideline-concordant): 1) ICD-9 code (362.XX or V67.51) by an ophthalmologist/optometrist and 2) an optical coherence tomography (OCT) (22067) or/and visual-field (02043) fee item billed by an ophthalmologist/optometrist. We defined "no screening" as the absence of both retinal-exam ICD9-code and OCT/visual-field fee-items. Statistical analyses: We estimated the rates of valid screening at baseline and annually among those remaining on HCQ (risk set). Multivariable generalized-estimating-equations assessed association of valid annual screening with predictors including physician-care pattern (continuous-rheumatologist-care (Rheum-care), family-physician-only-care (FP-only), intermittent rheumatologist-care with gaps of family-physician-only-care (Int-Rheum-FP-only) or started by rheumatologist-care then hands-off to family-physician-only-care (Start-Rheum-then-FP-only)), regional healthcare authority, baseline screening, years since HCQ initiation, demographics, and comorbidity.
Results: Among 22,572 HCQ initiators (75.26% female; mean age 53.64±15.06 years; SLE

8.52%; mean HCQ-exposure 6.40±5.34 years), only 4,400 (19.5%) had a valid baseline screening and 11,676 (51.7%) had no screening. From year 2 to 25, risk set decreased from 21,634 to 809 with valid annual screening ranged from 17.9% to 22.5%. Rates of no screening remained almost constant (~63%). Relative to Rheum-care, odds of having valid annual screening (adjusted-OR, 95% CI) were lower (P-value<0.0001) for FP-only (0.67, 0.62–0.72), Int-Rheum-FP-only (0.71, 0.68–0.75), and Start-Rheum-then-FP-only (0.64, 0.58–0.71). Compared to Vancouver-Coastal health, odds were lower (P-value<0.0001) in Interior (0.84, 0.79–0.90), Fraser (0.76, 0.71–0.81), Northern (0.71, 0.66–0.76), and Island (0.34, 0.31–0.39) health authorities. Table 1 presents adjusted-ORs for valid baseline screening, years since HCQ initiation, and patient-level predictors (Table 1).

Conclusion: In this real-world longitudinal study, about 50% of HCQ initiators and 63% of long-term HCQ users did not receive guideline-concordant HCQ-R screenings. Baseline screening and continuous rheumatologist care had strong association with ongoing guideline-concordant annual screenings. Strengthening guideline-oriented practices and addressing regional gaps may improve screening and reduce preventable vision loss.

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Interim Analysis of the Retinal Toxicity and Hydroxychloroquine Therapy (Intact): A Prospective Population-Based Cohort Study

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Objectives: To estimate the risk of Hydroxychloroquine-related Retinopathy (HCQ-R) among long-term HCQ users (≥5 years) in British Columbia (BC).

Methods: We conducted a prospective cohort study in BC, using a standardized retina-screening protocol for HCQ-R through a network of 20 ophthalmologic/retina clinics all-over BC, starting in October 2022. Sample: we included patients with rheumatoid arthritis (RA) or systemic lupus erythematosus (SLE) who were on HCQ at enrollment and have been using it for ≥5 years. Over 40 rheumatology practices in BC were engaged to identify eligible participants through their electronic medical record (EMR) system, which were flagged in EMRs. Then, informed consent by their rheumatologist was obtained to be referred to an ophthalmologic/retina clinic closer to them for annual HCQ-R screening using macular Spectral-Domain Optical Coherence Tomography (SD-OCT). Normal scans were booked for the next year's annual screening. Outcome: We assessed HCQ-R events defined as equivocal or abnormal scans based on the eye specialist diagnosis, which then were uploaded to a secure cloud platform for independent, masked review and staging by two retina specialists, with discrepancies resolved through consensus. For quality control, 30% of normal scans were also randomly selected for review. Statistical analyses: We estimated risk of HCQ-R using the cumulative incidence function (CIF), accounting for right censoring and competing risk of death.

Results: There were about 3,000 of eligible participants detected and flagged in the EMRs of BC rheumatologists. From October 1, 2022, to September 31, 2025, 1,300 referrals (~40% of flagged) were received; 952 participants completed a first visit, 254 a second, and 54 a third. Participants were predominantly female (84.3%) with mean age of 58.2±15.0 years, and 43.5%

had SLE (Table 1). Sixteen HCQ-R events (early or moderate) were confirmed; 13 equivocal cases remain under review pending confirmatory testing. CIF estimates (risk (95% CI) at X years since HCQ initiation) were as following: 0 at 5 years; 0.36% (0.10–1.00) at 10 years; 0.72% (0.07–1.60) at 15 years; 1.25% (0.53–2.55) at 20 years; 4.23% (2.04–7.65) at 25 years; and 6.54% (3.17–11.58) at 30 years. There was no adequate risk set to estimate CIF beyond 30 years.

Conclusion: In this interim analysis of the INTACT study, we identified that cumulative risk of pre-clinical HCQ-R detected through screening using SD-OCT roughly doubled across 5-year intervals from 10–20 years, then tripled from 20–25 years. Next, we will expand enrollment and link pharmacy claims to capture time-varying dose for dose-stratified risk estimates.

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Risk of Retinopathy Associated with Long-Term Use of Hydroxychloroquine in Patients with Rheumatic Diseases: A Systematic Review and Meta-Analysis

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Objectives: To determine risk (prevalence and cumulative incidence) and risk factors of Hydroxychloroquine-related Retinopathy (HCQ-R) among long-term HCQ users with rheumatic diseases screened using Spectral-Domain Optical Coherence Tomography (SD-OCT) through a systematic review and meta-analysis of observational studies.

Methods: A systematic search of PubMed, Scopus, Ovid, Embase, and WHO databases (inception–December 31, 2024) identified observational studies meeting: (1) adults with rheumatic diseases on HCQ ≥1 year; (2) SD-OCT for HCQ-R screening; (3) reported or data to calculate HCQ-R prevalence or cumulative incidence; (4) risk factors reported as hazard ratios (HRs) or odds ratios (ORs) with 95% CIs or calculable data; and (5) English full-text. Study quality was assessed using Newcastle–Ottawa Scale. Random-effects meta-analysis estimated pooled prevalence, cumulative incidence, and risk-factor associations. We assessed heterogeneity with the Q-test and I^2, then explored sources of variability via subgroup analyses across cohort type, study quality, publication year, and follow-up length. To address confounding effects, we fit multivariate meta-regression on logit-transformed prevalence/cumulative-incidence to quantify each factor's independent contribution to between-study heterogeneity. Publication bias was assessed with funnel plots and Egger's test.

Results: We screened 775 records; 19 met inclusion criteria (18 cohort, 1 case-control). Pooled HCQ-R prevalence (2008–2023) was 5.1% (95%CI: 3.9–6.5) (Figure 1). Pooled HCQ-R cumulative incidence was 0.1% (0.0–0.5) at 5 years, 2.6% (1.6–4.1) at 10 years, and 5.6% (3.2–9.6) at 15 years. Risk factors (HR, 95%CI) were daily dose >5 mg/kg of actual body weight (4.32, 2.80–6.65); chronic kidney disease (CKD) (1.94,1.27–2.96); female sex (3.78, 1.90–7.48) and Asian vs White ethnicity (1.67, 1.07–2.62). There was substantial heterogeneity between studies that reported period prevalence ($Q=197.44$, $p<0.0001$; $I^2=94.4\%$). Subgroup analysis revealed cohort type (retrospective vs. prospective) as the only variable which explained part of heterogeneity ($p<0.001$) (Figure 1). In multivariable meta-regression, retrospective cohorts still showed higher prevalence after adjustment for follow-up length ($\beta=1.72$, 95% CI 1.04–2.40; $p<0.001$) or publication year ($\beta=1.69$, 95% CI 0.52–2.85; $p<0.01$). Heterogeneity among cumulative incidence studies was non-significant (≤5 years ($Q=6.47$), 5–10 years ($Q=6.85$), and

10–15 years (Q=3.94); p>0.05). Prevalence studies showed mild small-study funnel asymmetry, but Egger's test was non-significant (p>0.05). Cumulative-incidence studies showed a symmetric funnel with non-significant Egger's test.
Conclusion: Pooled prevalence of 5.1% reflects the overall burden of HCQ-R from 2008 to 2023. HCQ-R risk increases with duration of HCQ use and is dose-dependent, reaching 5.5% by 15 years. Findings support dose optimization with intensified screening for higher-risk patients including CKD, female and Asian patients.

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Team-Based Outpatient Rheumatology Care: A Scoping Review of Terminology, Team Composition, and Impact on Advancing the Quintuple Aim

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Objectives: Team-based models of rheumatology care, in which rheumatologists and interdisciplinary healthcare professionals (IHPs) collaborate in care delivery, are increasingly recognised to improve outcomes across all domains of the Quintuple Aim (population health, patient experience, value, provider well-being, and health equity). To systematically map existing evidence across all domains of the Quintuple Aim, we conducted a scoping review of studies evaluating outpatient team-based rheumatology care.
Methods: This scoping review followed Joanna Briggs Institute methodology and adhered to the PRISMA-ScR checklist. We searched MEDLINE, EMBASE, Web of Science, Cochrane CENTRAL, and CINAHL from inception to May 2024. We included peer-reviewed studies that evaluated outpatient team-based rheumatology care involving at least one rheumatologist and one IHP, compared with any other outpatient care model. Terminology describing care models was examined in relation to reported team composition, and outcomes were mapped to the Quintuple Aim targets.
Results: The search identified 6,139 unique records, of which 76 reports representing 67 studies met inclusion criteria. Most included studies were published within the past 15 years, indicating a recent surge in research on team-based rheumatology care (Figure 1). A wide range of team-based care models was evaluated across different rheumatic diseases and clinical contexts, ranging from smaller teams comprising a rheumatologist and one IHP to large, comprehensive care teams involving multiple health professionals and physicians from other specialties. Terminology used to describe care models was inconsistent, with terms (e.g., multidisciplinary/interdisciplinary) often used interchangeably. In addition, most studies lacked sufficient description of the care model to enable replication. Population/patient health was the most frequently examined Quintuple Aim domain (n = 52, 78%), with outcomes largely centred on disease activity, physical function, and quality of life. Thirty-nine studies (58%) assessed patient experience outcomes (e.g., satisfaction, self-efficacy). Cost outcomes were evaluated in 15 studies (22%), and provider-focused outcomes in 8 studies (12%). Equity was addressed in only one study, and none investigated the impact of team-based care on provider mental health or

burnout. Most evaluations showed positive impacts, but were short-term, with observation periods limited to ≤12 months.
Conclusion: This review highlights a rapidly expanding yet heterogeneous evidence base on team-based care models in rheumatology. Most studies focused on short-term evaluations of health outcomes and patient experience, with few addressing cost-effectiveness, provider well-being, and equity. Future research should adopt standardized terminology, improve reporting of team structures and processes, and include longer-term evaluations to capture impacts across the full Quintuple Aim.

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Novel Indicators for Monitoring Rheumatoid Arthritis Care Quality: A Delphi Consensus Process to Determine Rheumatoid Arthritis-Specific Ambulatory Care Sensitive Conditions

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Objectives: Ambulatory care sensitive conditions (ACSCs) constitute a set of medical conditions where access to high quality outpatient healthcare services prevents or reduces costly acute care interactions for exacerbations of these diseases. Hospitalizations for ACSCs serve as indicators of access, quality, and performance of the health system.[1] However, the ACSCs in use are largely based on general populations. This study aimed to determine rheumatoid arthritis (RA)-specific ACSCs that may reflect opportunities to prevent possibly avoidable hospitalizations for persons with RA.
Methods: A modified e-Delphi process was utilized to build consensus on the preventability and importance of various hospitalization diagnoses occurring in persons living with RA identified from a systematic literature review. Clinical panelists were Canadian and US healthcare providers (rheumatologists, internists, pharmacists, occupational therapists, and physiotherapists) with expertise in the care of persons with RA. Consumer panelists were Canadians living with physician-diagnosed RA. Clinical panelists completed 2 rounds of anonymous voting, with an asynchronous discussion board hosted between rounds. Consumer panelists completed the same process considering the remaining candidate items where consensus had not yet been reached. An interactive webinar preceded a final combined panel round of voting. Consensus criteria were guided by the RAND/UCLA Appropriateness Method.[2, 3]
Results: Twenty-two clinical and 8 consumer panelists provided expert opinion. There were 46 initial conditions for consideration with 1 condition added by the clinical panel and 2 by the consumer panel. At the conclusion of the 5 voting rounds, 12 conditions were identified as RA-specific ACSCs: those specific to RA disease activity (RA disease flare, vasculitis), RA-related associations and complications (osteoarthritis, osteoporotic fracture, cervical spine instability, anemia/pancytopenia) and acute (upper respiratory infection, septic arthritis) and opportunistic (pneumonia/pneumocystis jirovecii, herpes zoster, tuberculosis reactivation, and other general opportunistic) infections.
Conclusion: This study identified 12 potential RA-specific ACSCs. Next steps include monitoring these conditions in a health context to understand their performance as possible RA-specific ACSCs.

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Impact of Unmet Workplace Accommodation Needs on Work Productivity in Those with Systemic Sclerosis Gastrointestinal Involvement

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Objectives: Systemic sclerosis (SSc) is a systemic autoimmune rheumatic disease with gastrointestinal manifestations that may restrict participation in the workplace. Our objectives were to study work factors, unmet workplace accommodations and association with work productivity between those with and without SSc-associated gastrointestinal symptoms.

Methods: A cross-sectional study was conducted in individuals 16 years or older with SSc, who were employed or had been employed in the last five years. Demographics, disease manifestations including patient reported outcomes, frequency of disease flares, specific limitations at work, and the need, availability and use of various workplace supports were collected. Regression models were used to evaluate the unadjusted and adjusted relationship between unmet accommodation needs and workplace outcomes (absenteeism, job disruption and presenteeism; respectively) between participants with and without SSc-associated GI involvement. A p-value of <0.05 was considered statistically significant.

Results: We report 217 participants (175 (80.6%) women, 42 (19.4%) men) where 129 (59.4%) had gastrointestinal symptoms and 88 (40.6%) did not have any GI symptoms related to SSc. Those with GI involvement scored lower on self-related health outcomes ($p<0.0001$), have greater amounts of pain ($p<0.0003$) and fatigue ($p<0.0001$), have worse patient-reported health overall ($p<0.0001$), more health variability ($p<0.0001$), and more disease flares ($p<0.0004$). Participants with SSc-associated GI symptoms needed more workplace accommodations than those without GI symptoms, including flexible hours or flex time (65.9% versus 46.6%), extended health benefits (84.1% versus 68.2%), breaks and rest periods (58.7% versus 33.3%), special equipment (62.1% versus 44.8%), modified job duties (48.8% versus 26.1%), altered work schedule (54.9% versus 33.3%), and the need to work from home on occasion (56.4% versus 37.4%) (Table 1). Participants with SSc-GI manifestations were 3.68 times more likely to have unmet workplace accommodations than those without GI manifestations; this did not change when the subjects disclosed their diagnosis to their supervisors. Those with GI involvement had higher job disruption scores (on average, 1.2 scores higher) and reported greater disease-related impairment in job productivity (on average, 2.3 scores higher) than those without GI involvement; this is also true when adjusted for biological sex and age.

Conclusion: The presence of GI symptoms poses a significant burden on productive employment in individuals with SSc. This study lays the groundwork for where SSc- specific efforts in workplace policies and practices should be directed.

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The Impact of Medication Adherence on Peripartum Outcomes in Women with SLE: A Population Level Analysis

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Objectives: Pregnancy outcomes of women with SLE are worse compared to those without immune-mediated inflammatory diseases (IMID). Factors contributing to higher risk may include concomitant corticosteroid or other medication use and active disease in the peripartum period. Despite international recommendations, the uptake of SLE treatments such as antimalarials during pregnancy remain suboptimal. We examined medication use and maternal/neonatal outcomes in a contemporary, population-level, pregnancy-birth cohort

Methods: The study population included all singleton pregnancies with ≥22 weeks of gestation, between July 2008 and December 2024 in Alberta, Canada. Previously validated algorithms based on ICD-10 codes were used to identify women with SLE and no IMID. We compared maternal characteristics, comorbidities and neonatal outcomes between no IMID and SLE groups. Dispensation of SLE-related medications was evaluated in two time periods (2008-2016; 2017-2024). Proportion of days covered (PDC) during pregnancy for each medication was calculated to estimate adherence. Logistic regression was used to calculate the odds of developing preterm labour when exposed to SLE-related medications after adjusting for maternal factors

Results: Among 787,346 pregnancies of 474,197 women, 994 pregnancies were by women with SLE and 786,352 had no IMID. Pregnant women with SLE were more likely to have renal disease (No IMID 5% vs SLE 10.4%), pre-existing hypertension (No IMID 7.6% vs SLE 23.5%), pre-eclampsia/eclampsia (No IMID 4% vs SLE 9.9%) while neonates in mothers with SLE had more congenital anomalies (No IMID 9.8% vs SLE 13%), were smaller for gestational age (No IMID 12.5% vs SLE 16.1%) and had more NICU admissions (No IMID 9.6% vs SLE 20.2%). SLE prescription dispensations included corticosteroids 21%, NSAIDs 5.5%, antimalarials 46.6%, and pregnancy safe DMARDs 9.5%. Mean PDC for anti-malarials increased from 60.6 (SD 30.3) to 72.2 (SD 27.4) between 2008-2016 and 2017-2024. Preterm delivery was more common in women with SLE (17.4%) versus no IMID (7.0%). In multivariable models, factors that were significantly associated with higher risk of preterm delivery in women with SLE included: low PDC (< 40%) of anti-malarials (compared to high PDC (> 80%)); high PDC of corticosteroids (compared to no use); active disease, being married and pre-eclampsia/eclampsia (Table 1).

Conclusion: Pregnancy-safe medication use has increased over time but peripartum outcomes remain poor for SLE women. Despite use in SLE flares, corticosteroid use may increase risk of preterm labour. Adherence to anti-malarial use during pregnancy may improve outcomes through reduction of flares. Further patient education and close disease monitoring in the peripartum period is recommended. **Supported by a CIORA grant**

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High Cardiovascular Burden from Glucocorticoid Exposure in Giant Cell Arteritis: A

Retrospective Cohort Analysis

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Objectives: Giant Cell Arteritis (GCA) is the most common type of vasculitis in adults, with high morbidity including cardiovascular disease (CVD).[1] Although tocilizumab and upadacitinib are approved for use in GCA, many patients remain dependent on high cumulative glucocorticoid doses, exposing them to the risk of cardiovascular toxicity.[2] Population-based data on glucocorticoid-associated CVD risk in GCA is scarce. We aimed to assess the association between glucocorticoid exposure and the risk of CVD in patients with GCA at the population level.

Methods: We used administrative data from British Columbia (BC), including all outpatient and hospital visits, all dispensed medications, vital statistics, demographics, and cancer registry. We assembled a population-based retrospective cohort of GCA with incident glucocorticoid use. Sample: all newly diagnosed GCA patients receiving healthcare between January 1997-December 2023 with no glucocorticoid exposure and no CVD events prior to GCA onset. GCA was defined by ≥1 code for GCA by a rheumatologist or hospital (ICD-9-CM 446.5; ICD-10 M31.5), or two ICD-9-CM codes for GCA between ≥2 months-2 years apart by a non-rheumatologist physician. Exposure: glucocorticoid dosing was calculated using Pharmanet data. Exposure was categorized as current use (Yes/No), current dose (mg/day), total past cumulative dose (grams), and total cumulative duration of use(months). Outcomes: We identified CVD outcomes using inpatient and outpatient ICD-9 billing codes, including myocardial infarction (MI) (ICD-9 410), stroke (434), and venous thromboembolism (VTE: DVT and PE) (453, 415.1, 673.2, 639.6). Associations between glucocorticoid exposure and CVD were estimated using a Cox proportional hazard model, adjusted for relevant confounders as in our previous studies.

Results: 4,681 patients with newly diagnosed GCA were identified with incident glucocorticoid use and no prevalent CVD (mean age 70.4, 68.9% female), with a mean Charlson comorbidity score of 0.94 (SD 1.58). During follow-up, we identified 969 CVD events (439 MI, 645 stroke, 134 VTE). Compared to non-users, glucocorticoid use was associated with a 113% increase in risk of CVD (Table 1). Moreover, current daily dose (15% per each 5 mg) and cumulative glucocorticoid dose (78% per each gram accumulated in the past) were associated with an increased risk of CVD. Cumulative duration of glucocorticoid use was also associated with a 23% increased risk of CVD per each month of use.

Conclusion: Among patients with GCA, glucocorticoid use, daily dose, cumulative dose, and cumulative duration were significantly associated with increased risk of CVD. New strategies with newer therapies should target minimizing glucocorticoid use in patients with GCA.

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Identifying a Gap in Antiphospholipid Antibody Syndrome Testing in Young Patients with Thrombotic and Obstetric Events

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Objectives: Antiphospholipid antibody syndrome (APS) is an autoimmune disease characterized by thrombosis and/or certain obstetric complications in the presence of persistent antiphospholipid antibodies (aPL). In previous studies, 17% of patients <50 years old who experienced any cerebrovascular event tested positive for aPL (lupus anticoagulant (LAC), anticardiolipin (aCL), or anti-β2 Glycoprotein I (aβ2GP1)).[1] Current guidelines recommend that patients <50 with unprovoked venous thromboembolism, stroke, arterial thrombosis, or pregnancy morbidity be tested for aPL.[2] Here, we describe rates of aPL testing in young patients with thrombotic events (TE) (myocardial infarction (MI), stroke, deep vein thrombosis (DVT), pulmonary embolism (PE)) and obstetric events (OE) (stillbirth, preeclampsia) at the population level.
Methods: We assembled a retrospective cohort study using administrative data from British Columbia (BC). Our data includes outpatient and hospital visits, all dispensed medications, vital statistics, demographics, and cancer registry. Sample: We identified all patients <50 years of age with an initial MI (ICD-9 410), stroke (434), DVT (453), PE (415.1, 673.2, 639.6), stillbirth (779.9), or preeclampsia (642) between January 1997-December 2023. Outcomes: We identified all outpatient aPL testing ordered for this cohort during the study period for these patients using fee codes (LAC (90377), aCL IgG and IgM antibodies (91145, 91146), aβ2GP1 (90046, 90047)). We report the rates and mean time to outpatient testing for aPL after initial event.
Results: Among 112,622 patients who developed the outcomes of interest, we report 25,010 TEs, 77,725 stillbirths, and 9,847 cases of pre-eclampsia in patients <50. Of these, a minority of patients – 4.4% of MI, 28.9% of stroke, 34.2% of DVT, 36.8% of PE, 4.3% of stillbirths, and 9.6% of preeclampsia – were tested for ≥1 aPL, with median time elapsed between the event and first testing described in Table 1. Among those tested for ≥1 aPL, 21.1% of MI, 12.9% of stroke, 13.0% of DVT, 12.0% of PE, 17.7% of stillbirth, and 14.7% of preeclampsia cases were diagnosed with a systemic autoimmune rheumatic disease within ±90 days of testing; repeat TEs and OEs were also common (Table 1).
Conclusion: We found low levels (<10%) and delays in aPL testing following initial thrombotic/obstetric events. A late APS diagnosis may fail to prevent subsequent recurrences of APS-associated events.
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Low Dose, High Impact: Acetylsalicylic Acid and Preterm Pre-Eclampsia Prevention in Rheumatic Disease

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Objectives: Pre-eclampsia (PE) is an important cause of maternal and neonatal morbidity and mortality, particularly when onset is preterm (<37 weeks gestational age). PE occurs in 1.6-2.6% of all Canadian pregnancies.[1] Patients with certain rheumatic diseases are at higher risk for PE,

most notably SLE which confers a threefold increase in risk.[2] Other risk factors include nulliparity and metabolic conditions like hypertension and diabetes. Prophylactic low-dose acetylsalicylic acid (ASA) (81 or 162 mg daily) for high-risk pregnancies has been shown to reduce risk of preterm PE by 62%.[3] There are limited data on ASA use in pregnant patients with rheumatic diseases. We describe the baseline characteristics and incidence of preterm PE in patients with rheumatic diseases receiving ASA compared to those not receiving ASA.
Methods: Patients at two specialized Canadian clinics for pregnancy in rheumatic diseases were recruited to the Canadian Pregnancy and Rheumatic Diseases registry (CaPRIS) between July 2020-October 2025. Participants were 18 or older, pregnant or planning pregnancy, and had one or more rheumatic diseases. Preeclampsia risk was assessed and ASA was started by the treating rheumatologist or obstetrical provider, either 81mg or 162mg daily starting before 14 weeks gestational age (GA) until 36 weeks GA. Baseline characteristics and pregnancy outcomes were compared with Fisher's exact test and Student's t-test.
Results: We included 110 pregnancies and their baseline characteristics and outcomes (Table 1). Seventy-five patients (68%) received ASA; 35 patients (32%) did not. Patients on ASA were more likely to have SLE ($p < 0.01$); 4 of 21 patients (19%) with SLE in our cohort developed pre-eclampsia. Patients not treated with ASA were more likely to have axial spondyloarthritis ($p < 0.01$). Ten patients (13%) on ASA developed preterm PE while 3 patients (9%) not on ASA developed preterm PE ($p=0.55$). There was no difference in GA at delivery or fetal weight between the groups.
Conclusion: Guidelines recommend low-dose ASA for prevention of preeclampsia in pregnant patients at increased risk. 68% of patients with rheumatic diseases in our clinics met these criteria. Rates of PE and preterm PE were higher in this cohort than national averages. However, we did not observe a significant difference in rate of preterm PE for high-risk patients treated with ASA compared to low-risk patients. These data suggest that ASA is effective in mitigating risk of preterm PE in high-risk patients with rheumatic diseases and should be considered routinely in such patients.
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Epidemiology and Clinical Features of Anti-Neutrophil Cytoplasmic Antibody-Associated Vasculitis in a Multiethnic Tertiary Care Centre Cohort

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Objectives: At our centre, ANCA-associated vasculitis (AAV) is seen with increasing frequency. We have a multiethnic population for whom less information is known about AAV,[1,2] and sought to describe the demographic characteristics, diagnostic settings, and mortality of patients diagnosed with AAV at a single tertiary care centre.
Methods: Records of all patients with AAV were abstracted from 2015-2025 from the electronic medical record at a single tertiary care centre. Demographic data, including ethnicity by self-report, diagnostic setting, ANCA subtype (granulomatosis with polyangiitis [GPA], microscopic polyangiitis [MPA], and eosinophilic granulomatosis with polyangiitis [eGPA]), and vital status at last follow-up were included. Descriptive statistics were used to characterize the cohort and compare patients from different ethnic backgrounds and ANCA subtypes. Survival was compared using Cox proportional hazard models.

Results: A total of 334 patients were identified; 192 (58%) were female. Mean age at diagnosis was 53 years ±18; mean disease duration was 10 years ±7. 61% (n=202) of patients were White, 30% (n=101) Indigenous, 8% (n=26) Asian, and 1.5% other (n=5). 49% of patients were diagnosed in a hospital ward, 36% in ambulatory care, 9% in intensive care and unknown in 6%. GPA was diagnosed in 50% (n=167), MPA in 38% (n=128), and EGPA in 11 %. Males were more frequently diagnosed with EGPA (61%, 39% in females; p=0.12) and were older at diagnosis (56±17 years, females 51±19 years; p-0.011). Sixty-two patients (19%) died during the study period. Mean age at death was 61 ±19 years. Indigenous patients were younger at diagnosis (46±18 years; White = 56±18 years; Asian = 55±18 years; p<0.001). Indigenous patients were more often diagnosed with MPA (50%), compared to 34% of white patients and 30% of Asian patients (p = 0.029). More Indigenous patients had died by the end of the follow-up period (28%; White 14%, Asian 19%; p=0.028). Adjusted hazard ratio for mortality was 4.5 (95%CI 2.5-8.3, p<0.001) for Indigenous patients compared to White patients (Figure 1).
Conclusion: On initial exploratory analysis of a large single centre cohort, AAV appears to affect all ethnicities proportionally. We found differences in onset age and AAV subtype between ethnicities, with Indigenous patients diagnosed at a younger age and more often with MPA. Mortality was overall high at 19% during the follow-up period, with adjusted mortality particularly high in Indigenous patients. More studies are needed to determine factors contributing to poor outcomes and differences between ethnic groups.
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Exploring Facilitators and Barriers to Physiotherapists' Delivery of a Falls Prevention Program with Brief Action Planning Counselling in Community-Dwelling Older Adults with a History of Falls

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Objectives: Falls are a leading cause of injury and hospitalization among older adults, including those with rheumatic conditions that can increase falls risk.[1] The Otago Exercise Program (OEP) can reduce falls by 35%,[2] but sustained participation remains challenging. Structured self-management approaches can improve adherence, yet little is known about physiotherapists' experiences delivering these approaches in community-based falls prevention. This qualitative study explored facilitators and barriers influencing physiotherapists' delivery of OEP+ (home-based OEP with Brief Action Planning [BAP] and a Fitbit-compatible app) in community-dwelling older adults with a history of falls.

Methods: A qualitative study using directed content analysis guided by the Theoretical Domains Framework (TDF),[3] was conducted. Semi-structured Zoom interviews (30–60 minutes) were completed with 13 physiotherapists purposively sampled after delivering OEP+ to community-dwelling older adults for 12 months. OEP+ combined OEP with BAP, a structured approach to support self-management which involves goal setting, action planning, and feedback, plus a Fitbit-compatible app. Interviews were audio-recorded, transcribed verbatim, and analyzed using the TDF, which integrates constructs from behaviour change theories to identify factors influencing implementation. Three researchers (CP, ST, EW) independently coded transcripts and reached consensus.
Results: Thirteen physiotherapists participated (7 private, 6 public), aged 20–64 years (31% aged 20–34, 54% aged 35–49, 15% aged 50–64), with a median of 15 years of experience (IQR=6–22). Two had prior exposure to using OEP in practice, and seven had home-care experience. Facilitators and barriers to delivery were categorized using the TDF (Table 1). Facilitators included prior knowledge of OEP components, structured session planning, use of BAP support materials, context-sensitive application of BAP, ability to adapt exercises for home environments, and prior home care experience. External support (e.g., patient family involvement, app-based cues) reinforced program delivery, while minimal equipment needs enhanced accessibility. Barriers included time gaps between training and delivery, rigidity of BAP structure, difficulty recalling exercise progressions, scripted follow-up calls limiting conversation flow, unclear communication about time expectations, scheduling and workload challenges, time-intensive home visits, and technical app issues. Some physiotherapists reported low confidence delivering follow-up phone visits and frustration with scheduling delays, though several planned to continue applying BAP skills in future practice. These factors collectively influenced physiotherapists' ability to integrate OEP+ effectively into community practice.
Conclusion: Modifiable factors, including practical supports and program design, shape physiotherapists' ability to deliver OEP+ effectively in community falls prevention. Findings can support development of theory-informed strategies to enhance uptake, engagement, and sustainability of community falls prevention.
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Health Service Use, Access, and Challenges for 2S/LGBTQIA+ Individuals with Rheumatic Conditions

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Objectives: Rheumatic conditions require multidisciplinary care to optimize health and quality of life. 2S/LGBTQIA+ communities (Two-Spirit, lesbian, gay, bisexual, transgender, queer or questioning, intersex, asexual, and additional sexual and gender-expansive identities) experience higher rates of rheumatic conditions,[1,2] yet remain underrepresented in rheumatology research.[3] This study examined healthcare use, access, and barriers among 2S/LGBTQIA+ individuals with rheumatic conditions.
Methods: We analyzed data from the Community-Based Research Centre's Our Health 2022 Canada-wide survey. This cross-sectional, multilingual (English, French, Spanish) survey was

conducted April–September 2022 and recruited 2S/LGBTQIA+ participants aged ≥15 years through social media, community agencies, and paid advertisements. Respondents self-completed an anonymous online questionnaire capturing sociodemographics, healthcare use, access gaps, and sources of support. Those who self-reported a formal diagnosis of ≥1 rheumatic condition(s) were included. Descriptive statistics summarized outcomes.
Results: Among 4,037 respondents, 497 (12%) reported ≥1 rheumatic conditions. Reported diagnosed conditions included fibromyalgia (n=169), osteoarthritis (n=152), psoriasis or psoriatic arthritis (n=105), Raynaud's syndrome (n=88), rheumatoid arthritis (n=55), gout (n=36), ankylosing spondylitis (n=32), lupus (n=11), and Sjögren's syndrome (n=8). Median age was 40 years; 66% were assigned female at birth, 36% identified as trans, 27% as non-binary, and 2% as intersex. Indigenous participants comprised 9% of the sample, of whom 66% identified as Two-Spirit. Among those who reported needing specific health services to manage their chronic health condition(s), unmet need was most frequent for personal home support (68%), foot care (60%), gender-affirming surgery (48%), home nursing (44%), alternative therapies (40%), gender-affirming care (38%), and physical therapy (34%) (Table 1). Common barriers included wait times (75%), difficulty obtaining appointments (70%), referral challenges (46%), service unavailability (45%), cost (40%), transportation (32%), and lack of gender- or sexuality-affirming providers (15%). Nearly half (49%) stopped, reduced, or delayed filling medications because they could not afford them, and 39% reported experiencing discrimination in healthcare. Despite these challenges, participants described drawing strength and support from friends, family/chosen family, pets, partners, social media communities and, among Indigenous respondents, Elders or Knowledge Keepers. Participants also reported positive impacts of living with a chronic condition, including building community connections, finding pride in their identity/experience, and engaging in activism.
Conclusion: Reported challenges reflect entrenched inequities in healthcare that disproportionately affect 2S/LGBTQIA+ communities. Addressing these inequities requires structural change, integrating affirming, inclusive, and community-informed approaches into clinical practice and service delivery. Centering health justice principles in models of care can help ensure 2S/LGBTQIA+ communities receive equitable and affirming rheumatology care.
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Patient Perspectives on the Environmental Impact of their Advanced Therapy Injection Device

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Objectives: Data demonstrates there is a significant environmental impact using medications requiring injection, including the injecting device and needle. Rheumatology patient perspectives on this impact have not been previously explored. As part of a larger study, we aim to report individual behaviours and perspectives on disposal of rheumatology advanced therapy devices.
Methods: In the first half of 2025, a survey on patient perceptions about patient support programs was made available in the waiting room at 3 rheumatology centres in Edmonton, Alberta, and was also electronically shared with those using a patient portal at one centre. A portion of the survey focused on how patients dispose of their syringe/autoinjector, and their interest in recycling their device if that option were available to them.
Results: Results: Of 580 respondents, 265 currently using an injecting device provided

responses about their preferences on this topic. 172 dispose of their device in a sharp's container, 66 return it to their pharmacy, and 27 dispose in their garbage at home. Men more often than women disposed of their devices in the garbage at home, with no differences noted based on age, income, or whether they lived in an urban or rural community. 332 responded with their preferences to recycle their device: 17% definitely would, 27% probably would, 21% might, 27% probably would not, and 8% definitely would not. Patients older than 65 were less likely to be in favour of recycling compared to those younger than 65. How individuals disposed of their devices was not statistically associated with their opinions on recycling.
Conclusion: Conclusions: The majority of rheumatology patients using an advanced therapy are disposing of their injecting device appropriately, although there appears to be room for improved education for some. As a majority of those surveyed would be interested in recycling their device as an alternative option, this may present a unique opportunity for the healthcare industry to invest in this service for patients, simultaneously lessening the environmental impact of these devices.

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The Cost-Effectiveness of Early Versus Delayed Belimumab Treatment for Systemic Lupus Erythematosus

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Objectives: Belimumab is an approved biologic therapy for active, autoantibody-positive SLE that has been shown to reduce disease activity, flare frequency, and glucocorticoid use, thereby preventing organ damage.[1] It is typically reserved for refractory disease but emerging evidence suggests earlier initiation of belimumab may lead to higher response rates, greater achievement of remission or low disease activity, and further reduction in glucocortoid use.[2] This cost-utility analysis evaluates the economic and health impacts of early versus delayed belimumab initiation for biologic-naive adult patients with clinically active SLE, comparing direct medical costs and quality-adjusted life-years (QALYs).
Methods: A Markov model was developed to simulate disease progression over 5 years with monthly cycles from the U.S. payer perspective. Costs included drug acquisition, hospitalizations, outpatient care, and emergency visits, updated to 2024 USD. Transition probabilities, Euro-QoL-5D utility values, and healthcare resource utilization were derived from a targeted literature review. Patients began in a pre-treatment state and transitioned monthly between four health states: complete response (assessed by SLE Responder Index-4; SRI-4), partial response, non-response (did not meet SRI-4 and experienced a flare or treatment-emergent adverse event), and death. Patients in the early group had higher disease activity (3-point higher SLEDAI-2K) and higher glucocorticoid use (10mg/day more prednisone) at baseline relative to the delayed group. Early belimumab was defined as initiation within 2 years of diagnosis and delayed initiation followed failure of standard immunosuppressants.
Results: Early belimumab initiation provided an additional 0.09 QALYs at a cost savings of USD$8,639.48 per patient relative to delayed belimumab, yielding a favourable incremental cost-effectiveness ratio (ICER) of –USD$93,092.98/QALY, making it the dominant strategy. Sensitivity analyses identified utility values, flare rates, and SRI-4 response rates as key drivers (Figure 1). Early belimumab retained dominance across most parameter variations, though cost-

effectiveness was attenuated in parameter extremes favouring delayed initiation.
Conclusion: Early initiation of belimumab in biologic-naive adults with clinically active SLE is both clinically and economically advantageous, offering greater health benefits at a lower cost compared to delayed initiation. These findings support timely adoption of belimumab in appropriate patients and highlight the need to reform reimbursement policies that delay access. As mounting evidence across immune-mediated diseases supports early biologic intervention as disease-modifying, frameworks must evolve to recognize treatment timing as a critical driver of long-term outcomes.[3] This model highlights the potential of early belimumab to reduce morbidity, mitigate irreversible organ damage, and generate sustained value for patients and health systems.
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Building Consensus on Key Strategies for the Implementation of Interdisciplinary Team-Based Rheumatology Care in Canada

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Objectives: While interdisciplinary team-based models of rheumatology care have the potential to transform rheumatology service delivery, there is no collective understanding on how best to implement them. This study aimed to identify and prioritise implementation strategies for optimal team-based models of rheumatology care based on the consensus of Canadian rheumatology health professionals.
Methods: We conducted a modified Delphi study with Canadian rheumatologists and interdisciplinary health professionals (IHPs) with experience working in interdisciplinary rheumatology care teams. We developed an initial list of implementation strategies from a case study evaluation,[1] aligned with the Expert Recommendations for Implementing Change taxonomy.[2] In Round 1, participants rated 33 implementation strategies for their usefulness in optimally implementing interdisciplinary team-based rheumatology care (from 1 [not at all useful] to 9 [extremely useful]), nominated additional strategies, and provided feedback on wording. Consensus was achieved for "useful" strategies when ≥70% of participants in both groups rated the implementation strategy as 7-9 after Round 1. Round 2 (ongoing) involves re-rating statements not achieving consensus (after reviewing group medians and quartiles) and rating strategies added. Analyses were completed overall and stratified by rheumatologists and IHPs.
Results: Fifty-five rheumatology health professionals (26 rheumatologists, 29 IHPs) participated

in Round 1. Rheumatologists were from Ontario (65%), the Prairies (19%), British Columbia (8%), Quebec (4%), and the Atlantic (4%); most practised for 10-19 years (39%) in a fee-for-service model (55%). IHPs consisted of physiotherapists, occupational therapists, nurses, pharmacists, physician assistants, and chiropractors from Ontario (76%), the Prairies (14%), the Atlantic (7%), and British Columbia (4%); most practised for ≥20 years (59%) and were salaried (90%). After Round 1, consensus was achieved for 25 implementation strategies (76%) (Table 1), with five additional strategies proposed by participants for subsequent rating. The highest rated implementation strategies reaching consensus were in the categories: support clinicians (constructing IHP roles, shared communication mechanisms, identifying champions), clinic space (shared electronic medical record), external needs (funding for implementation and sustainment), and training (by rheumatologists, mentorship).
Conclusion: Twenty-five implementation strategies reached consensus after Round 1. Canadian rheumatology health professionals agreed that support and training for clinicians, shared team communication mechanisms, and access to sustainable funding were the most useful implementation strategies for optimal team-based rheumatology care. Results of this study will be used in a future co-design study with patients, clinicians, researchers, and organisation/policy representatives to operationalise core and adaptable implementation strategies, including feasibility and contextual considerations, to develop an overall implementation approach.
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Characteristics of a Pilot Rheumatology Rapid Access Clinic in Toronto, Canada

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Objectives: Rapid Access Clinics (RACs) are designed to provide timely access to specialist care for patients with conditions requiring semi-urgent intervention and have been well described in other disciplines.[1][2] This descriptive analysis aimed to describe the care provided by a Rheumatology Rapid Access Clinic (RRAC) in Toronto Ontario, specifically the referral patterns, wait times, diagnostic outcomes, and patient dispositions.
Methods: RRAC was established at St. Michael’s Hospital (SMH) in September 2022 to provide care for patients with semi-urgent conditions referred from the SMH Emergency Department, family practice units and subspecialty clinics. Referral criteria included patients with inflammatory arthritis (acute mono/polyarthritis, crystalline arthropathies), systemic autoimmune rheumatic diseases, vasculitis, polymyalgia rheumatica, and acute non-inflammatory conditions. Long-term rheumatology care was not provided in the RRAC. A retrospective chart review was conducted for all new patient referrals to the RRAC from September 2022 through October 2024. Extracted data included demographics, referral source, diagnosis, time from referral to consultation date provided, number of RRAC follow-up visits, and final patient disposition. Descriptive statistics summarized patient characteristics.
Results: The RRAC database included 334 patient referrals, of which 305 (92%) were seen in consultation and 26 (8%) who did not attend. The mean age of patients seen was 57 years (range 20–98) with 56% being female (184). The most common referral sources were family health teams (31.1%), specialty clinics (22.8%), and the emergency department (20.1%). Median wait time from referral to consultation date was 10.2 days (mean 7.5), with 33 patients (11.1%) seen on the same day. Inflammatory conditions were diagnosed in 61% of referred patients, with detailed diagnostic outcomes summarized (Table 1). Follow-up in the RRAC was deemed

necessary for 180 patients (59%), with a mean of 1.54 visits per patient. Final disposition included referral to long-term rheumatology care (43%), discharge to family health teams (27%), referral to specialty care (16%), and inpatient admission (0.99%).
Conclusion: Implementation of the RRAC at SMH improved timely access for semi-urgent patients, with wait times to consultation date well below Canadian Rheumatology Association benchmarks.[3] The RRAC successfully prioritized patients with inflammatory conditions, ensuring early diagnosis and treatment initiation. By focusing on triage, assessment, and short-term follow-up, the clinic preserved long-term rheumatology capacity. These findings support RRACs as a scalable strategy to address access gaps in rheumatology care. Future studies should evaluate patient-reported outcomes and cost-effectiveness to inform integration of RRACs into broader healthcare frameworks.
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How Often does Follow up 18F-FDG PET/ct Improve or Become Inactive in Patients with Active Large Vessel-Giant Cell Arteritis (LV-GCA) After Escalating Treatment: A Systematic Review
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Objectives: Biomarkers that correlate with clinical disease activity are greatly needed in giant cell arteritis (GCA), particularly for patients with large vessel vasculitis (LVV) and those receiving tocilizumab (TCZ.). We performed an updated systematic review to determine 1) how often does vascular uptake on FDG PET/CT improve or 2) become inactive in patients with large vessel GCA (LV-GCA) who clinically improve after escalating treatment.
Methods: MEDLINE, EMBASE, CINAHL, Scopus, and Cochrane Library were searched from inception through February 29, 2024. Full text longitudinal studies were included if they: described a minimum of 2 patients with active LV-GCA on baseline PET, and the results of follow up PET scan done >= 3 months after escalating immunosuppression, along with an assessment of clinical disease activity. Two reviewers independently performed screening, full text review and data collection, and assessment of study quality using the Quality Assessment of Diagnostic Studies-2 (QUADAS-2).[1]
Results: 3131 unique references were screened, of which 25 studies were included (7 prospective, 18 retrospective), describing 377 patients with GCA. Mean patient age was 70.2 years (+/-5.4 yrs) and 72% were women. In 24 (96%) studies, patients received glucocorticoids, and in 10 studies (40%) tocilizumab was added. Patients underwent an average of 2.3 PET scans, at mean 9.2 +/-5 months apart. An assessment of both clinical disease activity and follow up PET in comparison to baseline results (improved/not improved) was available for 158 LV-GCA patients. Overall, vascular FDG uptake improved on follow up PET in 122/149 (82%) patients who clinically improved with treatment. In the 62 patients who received TCZ, follow up PET improved in 100%. In the 9 patients without clinical improvement, none (0%) had radiographic improvement on repeat PET. In 283 patients with LV-GCA, baseline and follow up PET scans were reported as either still active or inactive. Ultimately, follow up PET became inactive in 119

of 254 patients (47%) who entered clinical remission on treatment. Among the 29 patients who remained clinically active, PET became inactive in 3 (10%). In the TCZ-treated patients, follow up PET became inactive in 76/112 patients (68%) in clinical remission, and remained radiographically active in 6/6 (100%) who remained clinically active.
Conclusion: Vascular FDG uptake on follow up PET improved in most (>80%) patients with LV- GCA patients who clinically improved on treatment but ultimately became radiographically-inactive in fewer than half (47%.) Follow up scans improved (100%) and became inactive (68%) more often in TCZ-treated patients.
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Retention in Rheumatology Care Across the Juvenile Idiopathic Arthritis Care Pathway: From Diagnosis Through Transition

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Objectives: Juvenile idiopathic arthritis (JIA) comprises a heterogeneous group of childhood-onset arthritides, many of whom require continuous pediatric rheumatology care and transition to adult rheumatologists. We examined retention in pediatric rheumatology care from childhood through adulthood and transition times between pediatric and adult rheumatology care.
Methods: This was a population-based longitudinal study following an inception cohort of children/adolescents with JIA diagnosed between 2010 and 2018, and followed until January 2024. JIA patients were defined as those with at least three diagnosis codes for inflammatory arthritis (ICD 714, 720, 721) over two years, with at least one by a pediatric rheumatologist before their 16th birthday. Patients were followed from their first pediatric rheumatologist visit until the earliest of their first adult rheumatologist visit, 23rd birthday, death, out-migration or study end date. For each follow-up year, we classified patients as engaged in care (at least one pediatric rheumatologist visit), out of care (no visits that year), lost to follow-up (after three-year gap), re-engaged in care (after gap year(s)), or transferred to adult rheumatology care, and assessed for longitudinal transitions between care states. For JIA patients transitioning to adult rheumatology care, we described the interval between their last pediatric rheumatologist visit prior to their first adult rheumatologist visit.
Results: Among 2,919 patients with JIA, the median (IQR) age at diagnosis was 11 (6-14) years and 63% were female. By five years of follow-up, only 42% of patients were engaged in pediatric rheumatology care, with 31% lost to follow-up (Figure). Among 923 patients who successfully transitioned to adult rheumatologists, 601 (65%) where seen by adult rheumatology within 6 months of their last pediatric rheumatology visit (throughout the entire study period), and the mean (SD) interval between the last pediatric and first adult visit decreased from 584 (891) days at the start of the observation period to 150 (289) by end of the study period.

Conclusion: This study found that nearly half of JIA patients do not remain continuously engaged in pediatric rheumatology care through to transition to adult rheumatology care. However, transition times from pediatric to adult rheumatology care improved over calendar time. Given the limitations of health administrative data with few diagnosis codes to identify all JIA subtypes (some of whom do not require transition), further research requires more detailed clinical data to identify which JIA patients are experiencing gaps in care and further strengthen retention and successful transitions to adult care.

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Creation of a Transition Clinic and Registry for Young Adults with Juvenile Idiopathic Arthritis: The Women's College Hospital Experience

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Objectives: Transfer from pediatric to adult healthcare for young adults with rheumatic conditions occurs during a period of significant change. Preparedness and self-management skills influence follow-up care—up to 50% may be lost to follow-up at time of transfer, risking poor health outcomes. Transition clinics can provide coordinated, developmentally appropriate continuity of care, where young adults are seen jointly by pediatric and adult rheumatologists during these vulnerable years. Our aim is to report on the creation of a young adult clinic dedicated to supporting the transition of individuals diagnosed with juvenile idiopathic arthritis (JIA), as well as a registry to enable research and quality improvement.

Methods: Discussions and needs assessment were conducted prior to establishing the clinic to determine its aims, patient population, capacity, infrastructure, workforce planning, location, and feasibility. The clinic was modeled after the Young Adult with Rheumatic Diseases clinic at BC Children's Hospital as a shared-care clinic with pediatric and adult providers. To evaluate the clinic's impact, a registry was created to collect data on attendees' engagement and health outcomes. The registry was developed in collaboration with pediatric and adult teams.

Results: The Women's College Hospital Young Adult Clinic opened in 2019, staffed by a pediatric and adult rheumatologist and an advanced-practice physiotherapy practitioner. From

2019-2025, the clinic has followed 225 patients. The JIA Young Adult Clinic Helping Transition (JIA YACHT) registry was created and modelled after the Canadian Arthritis Network Disease Impact and Outcomes (CANDIO) registry at The Hospital for Sick Children. Recruitment began in May 2025, and since inception, 65 participants have been enrolled. Of these, 52/65 (80%) were female, 63/65 (97%) were on medications, with a median swollen joint count of 0 (range: 0-14), median physician global assessment score of 3 (range: 1-8), median patient global assessment score of 2 (range: 1-8), and median pain score of 3 (range: 1-9). The median time from referral to first clinic visit for registry participants was 134 days. The registry has proven to be an effective tool for monitoring important health outcomes post transfer such as uveitis status.
Conclusion: The creation of a dedicated transition clinic and registry has provided a strategic approach to transferring young adults with JIA from pediatric to adult care. This first-in-Canada transition registry enables standardized, systematic monitoring and evaluation of post-transfer care processes, identification of practice gaps, and tracking of patient outcomes. These insights will inform best practices and support ongoing improvements in transitional care.

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A Qualitative Exploration of Mental Health Needs Among Youth Living with Juvenile Spondyloarthritis: Perspectives of Youth and their Caregivers

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Objectives: To explore the mental health impact and care needs of youth living with Juvenile Spondyloarthritis (JSpA) from the perspective of patients and caregivers.
Methods: Participants aged 12-18 years with a JSpA diagnosis and their caregivers were recruited in person through the JSpA Clinic at The Hospital for Sick Children using purposive sampling prioritizing those screening positive for anxiety and/or depression. Nine semi-structured interviews were completed with youth living with JSpA (n=4) and their caregivers (n=6). Youth participants included three males and one female, with a mean age of 17 years. Caregiver participants included two fathers and four mothers, with one interview completed jointly by both parents. Interviews were virtually conducted by a social worker experienced in qualitative mental health research, audio-recorded, transcribed verbatim, de-identified, and imported into Dedoose Software for qualitative analysis. Data was analyzed using Braun and Clarke's thematic analysis.
Results: Preliminary analysis identified five interconnected themes illustrating the mental health impact in youth with JSpA. 1) Families were the primary source of emotional and practical support, as youth commonly relied on parents for reassurance, encouragement and help coping with symptoms. 2) Youth demonstrated resilience by maintaining a positive outlook, focusing on tasks they could still participate in and showing determination to continue meaningful activities despite pain, fatigue, or fear of treatment procedures. 3) They described varied coping strategies to manage emotional and physical challenges, including engaging in sports and hobbies when

able, resting during pain flares or low-energy periods, and seeking comfort through enjoyable activities and family. 4) Symptom burden significantly disrupted school, social life, and recreation, particularly before effective disease management. Although improved control of arthritis enhanced daily functioning for many youths, ongoing pain and fatigue continued to limit participation and require adaptations, demonstrating that challenges persist even with inactive disease. 5) Symptoms and aspects of medical care often trigger distressing emotions, including frustration when symptoms persisted, worry about future flares, and stress or fear associated with procedures such as MRIs and injections.
Conclusion: Youth with JSpA experience disruptions to daily life and emotional distress, particularly early in their disease course, and some continue to face challenges despite disease management and inactive disease. Although many show resilience and benefit from strong family support and adaptive coping strategies, these findings underscore the need for integrated mental health resources within pediatric rheumatology to better support youth wellbeing and reduce stress on families.

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Patient Perspectives on Industry Sponsored Patient Support Programs for Advanced Therapy in Rheumatology

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Objectives: Industry sponsored rheumatology patient support programs (PSPs) for advanced therapies (ATs) are commonplace. While there is limited data to demonstrate their effectiveness in patient care, patient perspectives are even more lacking. This study aims to report patient views on PSPs.
Methods: In the first half of 2025, a survey on patient perceptions about PSPs was made available in the waiting room at 3 rheumatology centres in Edmonton, Alberta, while also electronically shared with those using ATs with access to a patient portal at one centre. The survey asked patients about their experiences with PSPs, perceived value, and understanding of the programs.
Results: 580 individuals started the survey, with 63% completing it in its entirety. Respondents reported using 36 ATs (17 biosimilars); 43% were on their first AT and 23% had used 3+, with 66% having been on treatment for 4+ years. Only 43.1% knew they were enrolled in a PSP, while 27.4% were not sure. More than 45% of these respondents did not know the name of their PSP, 57% did not know the name of their PSP contact, and 60% did not know where their PSP was located. One-third of patients did not recall the last time they were contacted by their PSP, while another third indicated it was annually or less. At least 36% indicated they had experienced challenges with their PSP. 36.2% of respondents were not told or unsure if their rheumatologist told them they would be enrolled in a PSP, and 49% did not know PSPs were funded by pharmaceutical companies. Those with less education and rural living were more likely to be unaware of this funding model, while those with higher incomes were more likely to be aware. Over 50% were unsure or did not think it was right that PSPs are funded by pharmaceutical companies. Despite this, 73.3% of patients were generally satisfied with PSP support, with just under 80% felt there was at least some value to PSPs, and 63.3% felt it likely improved their overall treatment experience.
Conclusion: While it appears, most patients have some appreciation of PSPs, improved communication from healthcare providers and PSPs is likely necessary for patients to better understand basic information about their PSP, including how PSPs are funded. Further data

about patients perceived program values and challenges would likely help to further improve the structure of these programs.

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Patient Perspectives on the Use of their Home Pharmacies for Advanced Therapy Prescriptions in Rheumatology

Steven Katz (Queen's University, Kingston); Jill Hall (University of Alberta, Edmonton)

Objectives: While prior studies suggest patient outcomes and safety are improved when all patient medication prescriptions are filled by one pharmacy coordinating this component of care (their 'home pharmacy'), rheumatology patients on advanced therapies (b/tsDMARD) are provided alternate options by industry sponsored support programs (PSPs) for dispensing these specific medications. This study aims to describe where individuals on advanced therapies fill these prescriptions and their perceptions on the available options.

Methods: In the first half of 2025, a survey on patient perceptions about PSPs was made available in the waiting room at 3 rheumatology centres in Edmonton, Alberta; the survey was also electronically shared with all patients using b/tsDMARDs signed up to a patient portal at one site. A portion of the survey focused on, in addition to collecting demographic data, where patients fill their b/tsDMARD, and how important it was to them to fill the prescription at their home pharmacy. Data were analyzed descriptively.

Results: Of 580 respondents, 244 provided responses about which pharmacy dispenses their advanced therapy. While 51% are able to access their b/tsDMARD at their home pharmacy, 23% use a pharmacy as instructed by their PSP, and 15% receive it delivered to their home. 56% of all patients preferred to fill prescriptions at their home pharmacy, 35% indicated it did not matter, while 9% were not sure. Of those who fill at their own pharmacy, 84% preferred this option, 10% indicated it did not matter, while 6% were not sure. Of those who did not fill at their home pharmacy, 32% would prefer to use their home pharmacy. There was no difference in patient preferences based on age, gender, income, education, type(s) of insurance, or if they lived in an urban vs rural community.

Conclusion: Individuals on advanced therapies generally prefer to fill their prescriptions at their home pharmacy. In order to best accommodate patient preferences, as well optimize overall patient outcomes and safety, patient support programs should be encouraged to transparently work with their clients to ensure their medications are filled in a manner that is most preferred by them.

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Hamilton Centralized Access to Rheumatology Evaluation (H-Care): A Central Triage Model

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Objectives: Patients referred to rheumatology in Hamilton have faced prolonged wait times due to inefficiencies in the historic referral system, where each rheumatologist independently processed and triaged incoming referrals.[1] The objective of the Hamilton Centralized Access to Rheumatology Evaluation (H-CARE) initiative was to develop and implement a central triage (CT) system for rheumatology referrals. This system aimed to establish a data-driven framework to monitor referral flow, reduce wait times, and minimize administrative inefficiencies.

Methods: H-CARE was developed using the OSCARPro EMR and launched on January 27, 2025. It is staffed by two part-time administrative coordinators, an Advanced Clinician

Practitioner in Arthritis Care (ACPAC), and staff rheumatologists who review referrals on a rotating weekly basis. Standard operating procedures were established to standardize referral intake, urgency categorization, and assignment to appropriate physicians. H-CARE operates under a CT Quality Improvement Subcommittee comprising senior rheumatologist investigators, a rheumatology fellow primary investigator, methodologists, and CT administrators. A cross-sectional descriptive analysis was conducted for the first six months. Metrics analyzed included the number of referrals per week, distribution by differential diagnosis, urgency category, proportion of redirected or rejected referrals, and time required for triaging.
Results: In the first 6 months, a total of 1,095 referrals were processed, with 229 direct referrals to specific providers (Table 1). The most common referral diagnoses were inflammatory arthritis (IA) (226, 21%), rheumatoid arthritis (RA) (129, 12%), osteoporosis (OP) (88, 8%), vasculitis (67, 6%), and polymyalgia rheumatica (58, 5%). IA, RA, and OP accounted for over 40% of all referrals. Wait-time distribution showed 72% of referrals were triaged and booked to be seen within three months, with 4.7% booked within one week, 6.9% within two weeks, and 23.5% within one month. With H-CARE, 100% of referrals sent to individual rheumatologist's office were booked within the time frame recommended on triage. Additionally, 100% of referrals were acknowledged within the 14-day period mandated by the College of Physicians and Surgeons of Ontario (CPSO. A total of 60 (5.5%) referrals were rejected and 144 (13.2%) were redirected to another service such as neurology, physiatry, or pain specialists.
Conclusion: H-CARE has been a successful pilot, generating valuable data to inform rheumatology service demand. All referrals were assigned to rheumatologists with availability and booking within triage-designated time frames. By centralizing referral intake, H-CARE provides a scalable foundation for innovations such as integrating ACPACs and future consideration of artificial intelligence (AI)–assisted triaging within rheumatology across the region.
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Mixed-Methods Feasibility Study to Test Implementation of Quality Indicator Toolkits for Total Hip and Knee Replacement Rehabilitation: Impact on Clinician Behaviour, Patient Outcomes and Experiences

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Objectives: We developed evidence-based, consensus-generated quality indicators (QIs) to address care gaps in total hip (THR) and knee replacement (TKR) rehabilitation.[1] This paper describes the effects of implementing the QIs using clinician (QUICK-TJR) and patient (EQUIP-TJR) targeted online toolkits on clinician behaviour (QI adherence), patient-reported outcomes, and patient experience and satisfaction with rehabilitation.
Methods: We conducted a mixed methods feasibility study in two outpatient settings. Following 3 months of usual care, clinicians completed an online questionnaire to capture baseline QI adherence.[2] With help from 'clinical champions', we introduced the QUICK toolkit and 6 weeks later the EQUIP toolkit. After a 3-month transition phase, the clinics entered a maintenance phase with continued access to toolkit resources (video, checklist, infographic, QUICK guides). We collected QI adherence data continuously over 9 months (chart audits and patient questionnaires) and pre-post study (clinician questionnaires). We performed descriptive

analyses for participant demographics and QI adherence. For effectiveness data (HOOS/KOOS-4 subscales), we explored relationships between QI adherence, outcomes and experience using SAS (V9.4, Cary, NC).
Results: We consented 46 THR/TKR patients: mean age 71.7 (7.2) years, mostly female (63%), retired (76%), living with ≥1 family member (79%) and ≥1 comorbidity (50%). All agreed to have their charts audited using a standardized REDCap form and 31 complete questionnaires. Fifteen physiotherapists and one rehabilitation assistant gave consent and 14 completed pre/post QI questionnaires. Clinicians were 50% female, and 63% were ≥40 years and had >10 years THR/TKR treatment experience. Mean (SD) baseline QI adherence was THR 12% (8.4%) and TKR 8.1% (11.1%) (chart audit) and 55.0% (12.9%) and 42.9% (27.3%) (patient questionnaire). During the maintenance phase, mean QI adherence was not significantly different for THR and TKR by either data source. Mean clinician-reported pre/post QI data was THR 17.3% (12.8%) and 28.2% (24.8%) (p=0.06) and TKR 18.0% (13.2%) and 26.7% (25.7%) (p=0.09). In univariate analyses, there were no notable differences in HOOS/KOOS subscale values between baseline and maintenances phases. Overall, 73% of patients rated their rehabilitation experience as excellent and 47% were very satisfied with their outcomes. Patient reported QI adherence was strongly associated with overall satisfaction (p=0.004) and positively associated with overall experience (p=0.10).
Conclusion: Overall, adherence to 10 THR/TKR rehabilitation QIs was low, regardless of data source, with minimal improvement after introduction of QI toolkits and resources. Positive associations between QI adherence and patient experience and satisfaction are promising. Implementation issues need to be addressed before conducting a definitive implementation trial.
References: [1.] Westby MD. Osteoarthritis Cartilage 2018;26:370-82. [2.] Westby MD. Physiother Can 2025;77:28-41.

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Mixed-Methods Feasibility Study to Test Uptake of Quality Indicator Resources for Rehabilitation After Total Hip and Knee Replacement: Feasibility Outcomes

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Objectives: We developed evidence-based quality indicators (QIs) to address care gaps in total hip (THR) and knee replacement (TKR) rehabilitation.[1] A feasibility study was designed to test methods (recruitment, consent, retention, engagement) for a stepped-wedge cluster randomized trial to implement ten post-acute QIs using online toolkits.
Methods: We conducted a 9-month mixed methods, pragmatic feasibility study at two outpatient settings. Following 3 months of providing usual rehabilitation care, we led site-specific focus groups with clinicians to identify barriers and facilitators to QI implementation. With help of clinical champions, we then provided a 45-minute training webinar, introduced the clinician toolkit (QUICK-TJR) and 6 weeks later, the patient toolkit (EQUIP-TJR). This transition phase was followed by a 3-month maintenance phase with ongoing toolkit access. Clinical champions identified potentially eligible patients at time of discharge and provided contact information to a research coordinator. After confirming eligibility, we asked consenting patients to complete a REDCap online questionnaire and audited their chart using a standardized form. We collected QI adherence data continuously (chart audits, patient questionnaires) and pre-post study (clinician questionnaire). We analyzed feasibility data descriptively.

Results: Sixteen clinicians (100%) at a private clinic and hospital outpatient department consented; 14(88%) participated in baseline focus groups/interviews; 100% completed the initial clinician QI questionnaire and 15(94%) participated in or viewed the webinar. Post-webinar, 93% said they intended to access the toolkit within the next week and 100% agreed the resources would positively impact their care of THR/TKR patients. Initially, 14 accessed the online toolkit; this decreased to 7/14(50%) in the maintenance phase. Clinician retention was good with 88% completing the final questionnaire and 100% end of study discussions. In total, 46 patients following primary THR (n=10) or TKR (n=36) participated; well below anticipated levels during the Mar.-Nov. 2024 study period. There were 66 patients deemed eligible by clinicians; we screened 59(89%) and 7(11%) did not respond to calls; 49(83%) were confirmed eligible and 46(94%) provided consent. All had their chart audited and 31(67%) completed the QI questionnaire. Of the 22 patients who had access to the EQUIP toolkit in the later phases, 5(23%) accessed it and 4(80%) agreed it helped them engage in their own care.
Conclusion: Study feasibility was confirmed with the high rates of recruitment, consent and retention by both clinicians and patients. Despite good initial clinician engagement, there was limited uptake of QI resources among clinicians and patients overall. This will be addressed prior to the planned trial.
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Delivery Matters: A Cluster Randomized Trial of a Brief Action Planning-Based Physiotherapy Intervention with Digital Support to Improve Adherence to a Fall Prevention Exercise Program in Older Adults at Risk of Falls

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Objectives: Older adults with arthritis are at increased risk of falls. The Otago Exercise Program (OEP), implemented worldwide, reduces falls by 35% in high-risk populations. While OEP is cost-effective for older adults with arthritis, participation and adherence remain low. This study assessed whether training physiotherapists in behaviour change techniques improved participant adherence to prescribed exercises.
Methods: Physiotherapists working in the Greater Vancouver Area were randomly assigned to receive OEP training either alone (OEP group) or with Brief Action Planning (BAP) training and use of an exercise tracking app (OEP+ group; NCT04851405). BAP is a structured coaching approach involving goal setting, action planning, and monitoring/feedback. Following training, physiotherapists were matched with older adults with a recent history of falls recruited through the Vancouver Falls Prevention Clinic. They delivered the program through five home visits over six months, followed by monthly phone calls for six months. Older adults were instructed to perform lower-body exercises (>3x/week) and short walks (2x/week). OEP adherence (primary

outcome) was self-reported by monthly calendar over 12 months. Secondary outcomes included prospective fall count, Short Physical Performance Battery (SPPB), daily step count, and EuroQol-5D-5L assessed at baseline, 6 months, and 12 months. Exercise and walking adherence were calculated separately as: (sessions completed/sessions expected) x100. Analyses followed an intention-to-treat approach using Generalized Linear Mixed-effect Models for longitudinal outcomes adjusting for age and sex. Fall counts were analyzed using quasi-Poisson regressions with robust sandwich standard errors to address potential overdispersion. Missing data was handled using multiple imputations.

Results: Thirty-five physiotherapists visited 128 older adults (OEP+: n=58, 81.0% female; OEP: n=70, 68.6% female). Both groups were similar in age [OEP+: 80.9 years (SD 6.1); OEP: 82.0 years (SD 6.8)]. 61.7% reported arthritis and 37.5% participated during the COVID-19 pandemic. The adjusted mean difference in exercise adherence was 11.4% (95%CI: 0.4, 22.4), favouring OEP+ (Table 1). Multiple imputation analyses showed a similar magnitude of difference in exercise adherence; 8.0% (95%CI: 1.6%, 14.3%). Walking adherence was similar between groups. The adjusted mean difference from baseline to 12 months for SPPB was 0.83 (95%CI: 0.14, 1.52). Fall rates were lower in OEP+ (incident rate ratio: 0.63; 95%CI 0.48-0.82).

Conclusion: Delivery of the OEP by physiotherapists trained in BAP and supported by an exercise tracking app improved exercise adherence, physical performance, and fall counts over 12 months in older adults at risk of falls. This research may inform the delivery of fall prevention interventions among older adults with arthritis.

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Bridging the Gap Between Complexity and Care: Translating Network Meta-Analysis into a Meaningful Tool for Patients with Rheumatoid Arthritis

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Objectives: To develop and evaluate a patient-centered decision aid that translates network meta-analysis (NMA) data into clear, accessible information supporting shared decision-making for patients with rheumatoid arthritis (RA) experiencing an inadequate response to TNF inhibitors (TNF-IR).

Methods: A two-page decision aid was designed to compare treatment efficacy data for patient switching therapies after TNF-IR. Relative treatment effects for ACR50 response for second-line biologic and targeted synthetic DMARDs were derived from an NMA of clinical trials.[1] These effects were converted into real-world outcome probabilities using data from a Canadian observational study of outcomes after TNF-IR.[2] We explored various data presentation formats to understand preferences among patients and rheumatologists, testing variation in how treatment benefits were scaled, grouped, and displayed.[3] Feedback was collected through semi-structured interviews with patients and a survey of the Canadian Rheumatology Association Guidelines panels.

Results: Six semi-structured interviews with patients living with RA provided multiple diverse perspectives on treatment decision-making. Thematic analysis highlighted a strong need for more comprehensive and accessible information than what patients typically receive from health care

providers. Patients explained the emotional and cognitive challenges of switching treatment and expressed that more comprehensive information could reduce uncertainty. They value resources that improve understanding and confidence in choosing treatments. They also valued time to review treatment options before appointments, allowing them to prepare questions and engage more confidently with their rheumatologist. A key theme was information gaps; this caused an increase in patients' reliance on clinicians. Many patients explained how limited knowledge and confidence led them to defer to their rheumatologist's judgment when making decisions. Patients responded positively to the prototype decision aid, appreciating its clarity, relevance, and inclusion of Canadian scaled data. Percentages were preferred over point estimates, and responders valued content reflecting real-world clinical experiences. Physician survey responses (n=7) reinforced the value of decision aids in clinical care and overall aligned with patient feedback (Table 1).

Conclusion: Implementing a patient-centered decision aid that provides accessible, localized information can enhance understanding, confidence, and engagement in treatment planning for patients with RA. Improving how data is presented supports informed treatment choices and strengthens shared decision making in RA care and beyond. By bridging the gap between complex evidence and patient experience, this approach supports evidence-informed and value-based care. This could be used to implement similar tools across chronic disease contexts and strengthen shared decision making overall.

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Identifying and Supporting At-Risk Vasculitis Patients: Integrating Targeted Mental Health Screening and Psychology Referral into Rheumatology Care

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Objectives: Mental health concerns are common, yet underrecognized in patients with vasculitis.[1]This pilot study aimed to identify mental health needs by developing a screening tool and referral pathway to improve access to care and quality of life.

Methods: Forty-two vasculitis patients consented to participate, 21 completed screening using the Patient Health Questionnaire-2 and -9 (PHQ-2, PHQ-9), Generalized Anxiety Disorder-7 (GAD-7), Multidimensional Fatigue Inventory (MFI), Pittsburgh Sleep Quality Index (PSQI), Herth Hope Index (HHI), AAV-PRO, SF-36 and Alcohol Use Disorders Identification Test-Consumption (AUD-C). Disease severity was measured using the Birmingham Vasculitis Activity Score (BVAS) and Vasculitis Damage Index (VDI). Three voluntary sessions with a clinical psychologist were offered. Patient-reported outcomes were assessed at baseline and post-psychologist sessions.

Results: Thirteen patients (62%) attended psychology sessions. Five attended three sessions, one attended two, and seven attended one. Post-sessions, the AAV-PRO indicated improvements in

systemic symptoms (mean 38.0 to 26.9), treatment side effects (33.1 to 22.3), social/emotional impact (28.2 to 21.1), and future concerns (30.7 to 22.7). SF-36 scores improved in energy/fatigue (38% to 50%) and sleep quality (PSQI 7.8 to 6.6). PHQ-9 and GAD-7 scores showed minor improvements (PHQ-9: 5.8 to 5.5; GAD-7: 4.15 to 4.38). AUD-C scores decreased from 3.0 to 2.38. Overall, 54% reported improved well-being, 70% perceived mental health benefits and satisfaction with care (mean 9.15/10).
Conclusion: Integrating mental health screening and referral is feasible and may improve patient-outcomes. Future research should refine and validate a comprehensive screening tool with interpretation guidance and establish clear referral guidelines.
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Number Needed to Screen for Axial Spondyloarthritis: Preliminary Results from the Fastrax Cohort

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Objectives: Prevalence estimates for axial spondyloarthritis (axSpA) is 1% [1], suggesting the number needed to screen (NNS) to identify one patient with axSpA is 100, assuming perfect sensitivity of the screening mechanism. FASTRAX is a model of care designed to screen patients with chronic low back pain for axSpA and utilizes Advanced Clinician Practitioner in Arthritis Care (ACPAC)-trained extended scope providers and rheumatology fellows as screeners. The aim of this study is to determine the NNS to diagnose one patient with axSpA through the FASTRAX model at its three Ontario sites (Toronto, Thunder Bay and Ottawa).
Methods: Adults (≥18 years) with low back pain >3 months duration, onset age <45 years were referred by their primary care provider, specialist (e.g. ophthalmologist, gastroenterologist) or provincial low back pain program (https://lowbackrac.ca) for axSpA screening. Screeners performed standard of care assessment (i.e. history, physical exam, imaging and laboratory investigations). Screened patients were reviewed by the attending rheumatologist with expertise in spondyloarthritis. Screeners indicated risk of axSpA on a 11-point scale (-5, high confidence not axSpA to +5, high confidence axSpA). Risk assignment was dichotomized to negative or positive risk of axSpA. The rheumatologist provided final diagnosis for all patients. Prevalence of axSpA was calculated as the number of axSpA diagnoses/total number of patients screened. Sensitivity and specificity were calculated for the screener's assignment of risk against the rheumatologist's diagnosis (gold standard). Number needed to screen was calculated as 1/ (prevalence of axSpA in the screening model * sensitivity of the screener).
Results: In total, 269 patients completed the screening process: mean (SD) age of 39.6 (10.5) years; 38 % were male; mean (SD) duration of back pain was 11.5 (11.1) years. Referral sources varied by site. 36 patients were diagnosed with axSpA, for a prevalence of 13.4%. Overall sensitivity and specificity of the screener's assignment of axSpA risk were 91.7% (95%CI 87.4% to 95.9%) and 75.0% (95%CI 68.3% to 81.7%), respectively, with 100% sensitivity at Thunder

Bay and Toronto sites. NNS was 9 people with chronic back pain to identify one patient with axSpA and ranged from 5 to 19, depending on site (see Table 1).
Conclusion: The FASTRAX model for axSpA screening demonstrates the NNS for one patient diagnosed with axSpA is 9, ranging from 5 to 19 depending on screening site in Ontario. This is far fewer NNS based on current population prevalence estimates and demonstrates a valid and efficient pathway to identify patients with axSpA.
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Unusual 18F-FDG PET/CT Images in Pediatric Systemic Lupus Erythematosus

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Background: Systemic Lupus Erythematous (SLE) is a complex autoimmune disease that can affect multiple organs. Uncommon presentations may delay diagnosis and introduction of proper therapies. We report a case of SLE in 15-year-old girl with extensive fascia involvement detected by 18F-FDG PET/CT imaging. To our knowledge, this finding has not previously been reported in SLE.
Case Report: We present the case of a 15-year-old Haitian girl with no significant past medical history who presented with a 6-month history of progressive fatigue, arthralgias and myalgias. Clinical examination was notable for polyarthritis, painful subcutaneous nodules on the upper and lower extremities, hemorrhagic bullous lesions on the toes and absence of muscle weakness. Investigations revealed bicytopenia (Hb 68 g/L; lymphocytes 0.8x109/L), elevated inflammatory markers (C protein reactive 45 mg/L and serum erythrocyte sedimentation rate 60 mm/h), low levels of complement C3 (0.39 g/L) and C4 (0.06 g/L), elevated serum immunoglobulin G (23.57 g/L), normal muscular enzyme levels (CK 68 U/L), proteinuria (urine protein/creatinine ratio 0.39 g/mmol) and mild microscopic hematuria. Autoantibodies tests were significantly positive for anti-nuclear (1/640 homogenous pattern), anti-double-stranded DNA (139.9 UI/mL, normal < 100 UI/mL) but negative for anti-extractable nuclear antigen. While awaiting for specific autoantibody results, 18F-FDG PET/CT was performed to better understand the underlying process and help in the differential diagnoses. The study demonstrated increased FDG uptake/avidity in (a) fascias of bilateral upper and lower extremities (Figure 1), a feature that, to our knowledge, has not previously been reported in SLE; (b) the muscles predominantly in the upper limbs; (c) the basal ganglia; (d) both kidneys and (e) multiple lymph nodes. Renal biopsy revealed a diffuse segmental lupus nephritis (class IV-S). The patient was started on immunomodulatory therapy (intravenous steroids pulses, intravenous belimumab, mycophenolate mofetil and hydroxychloroquine), resulting in progressive symptoms resolution including relief from upper and lower limb pain, which were not only related to myositis but also to inflammatory fasciitis.
Conclusion: This is the first SLE patient reported with extensive fascia uptake on 18F-FDG PET/CT. In patients with SLE, typical 18F-FDG PET/CT findings include cerebral metabolism modifications and increased metabolic activity in lymph nodes, the spleen and bone marrow.[1] This unique case highlights the importance of recognizing SLE in patients presenting with inflammatory fasciitis or when extensive fascia uptake is seen on 18F-FDG PET/CT.

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IgG4-Related Skin Disease in a 9-Year-Old Patient: Remission Under Mycophenolate Mofetil After Rituximab Failure

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Background: IgG4 related disease (IgG4-RD) is a systemic immune-mediated disease characterized by inflammation and fibrosis of nearly any organ.[1] This condition is rarely reported in children and especially with cutaneous involvement. We report the case of IgG4 related disease in a young girl with an initial orbital presentation, which evolved with an isolated multicentric skin presentation. Remission was not achieved with rituximab therapy, but patient remains disease free after two years of mycophenolate mofetil (MMF) monotherapy.

Case Report: A nine-year-old girl was referred to our Tertiary Center for painless unilateral swollen upper eyelids, progressing for 5 months. Personal history was negative. Imagery confirmed a well-defined heterogeneous mass of the upper orbit. Initial workup showed elevated inflammatory markers, normal IgG4, absence of antinuclear and slightly positive p-ANCA antibodies (MPO). Histopathological examination of the orbital biopsy revealed IgG4-positive plasma cell infiltration, confirming the diagnosis of IgG4-RD. Remission was rapidly achieved with oral steroids (initially 1 mg/kg/day) with a 5 month-tapering. Few months later, the patient presented with subcutaneous asymptomatic lesions on her left thigh, initially diagnosed as post-traumatic hematoma. Persistence and the emergence of a second lesion on the thorax raise the suspicion of infiltrative tumor. On 18F-FDG PET/CT, two other lesions on the right thigh and the right buttock were revealed. Skin biopsy confirmed IgG4-RD relapse. Complementary workup showed serological positivity of IgG4 (3.15 g/L). Rituximab was started with initial remission during the first year. Relapses occurred with recurrent skin infiltration following each viral episode, even with a second cure of rituximab. Given the lack of response to rituximab, treatment was switched to MMF (2000 mg/m²/day) with a complete remission (and negative PET/CT).

Conclusion: This case highlights the importance of considering atypical forms of IgG4-RD, especially in pediatric populations, which can lead to misdiagnosis. As far as we know, this case is the fifth one describing cutaneous involvement in pediatric patients. The treatment remains challenging. Corticosteroids and B cell-targeted therapies are the cornerstones of treatment.[1] Rituximab has been considered a first-line therapy in IgG4-RD, particularly for patients with severe or refractory disease. However, for some patients, alternative therapies are sometimes needed.[2] MMF is an alternative effective steroid sparing agent with more positive evidence for the latter.[3]

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Cardiac Involvement in Systemic Sclerosis Beyond the Right Heart: Novel and Conventional Cardiac Magnetic Resonance Phenomics Based Evaluation

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Objectives: Systemic sclerosis (SSc) patients can experience a broad range of cardiovascular complications – with cardiomyopathy development posing risks of future major cardiovascular events. We comprehensively investigated cardiovascular phenotypes of SSc patients referred for CMR and compared them to healthy volunteers (HV) using conventional CMR metrics and advanced 4D modelling.
Methods: 100 SSc patients and 100 HV were studied from the Cardiovascular Imaging Registry of Calgary. All patients underwent CMR imaging inclusive of cine and late gadolinium enhancement (LGE). Conventional analyses were performed using cvi42 software. A comparison of conventional CMR markers between SSc patients and HV were utilized to identify SSc patients with a cardiomyopathy, defined as an abnormal left ventricular ejection fraction [LVEF] < 55% or LGE presence. SSc cardiomyopathic individuals were processed using 4Deep and age- and sex-matched compared against HV to characterize SSc cardiomyopathy phenotype. 4Deep is a locally developed deep learning-based 4D modelling pipeline which automatically segments cines to deliver spatially registered bi-layer 4D LV meshes, providing regional 3D wall thickness, mass, and principal strain. Patients were followed for a composite outcome of death, heart failure admission, or sustained ventricular tachycardia.
Results: Clinical and CMR characteristics of the SSc (median age 57 years old, 67% female) and HV patients (median age of 46 years old, 54% female) are summarized (Table 1). Conventional CMR analysis revealed 30% of SSc patients with a cardiomyopathy (21% abnormal LVEF, 18% abnormal LGE) and 20% with an abnormal right ventricular (RV) EF. 4Deep analysis of 24 age- and sex-matched SSc patients with LV cardiomyopathy to HV revealed SSc patients experienced significant reductions of 14.7% LVEF, 18.8% mean max. principal strain, and increases of 1.3 mm in LV wall thickness and 3.1% mean min. principal strain in comparison to HV. SSc patients with a cardiomyopathy experienced significantly reduced minimum principal strain deformation in septal and apical segments of the heart. Over a median follow-up of 4.1 years, 32% of SSc patients developed a composite primary outcome. In the full cohort, a multivariable model including age, sex, LVEF, LGE fibrosis burden, and RVEF showed RVEF as the only independent predictor (HR 0.95 [0.91–0.99], p=0.006).
Conclusion: In this large cohort of SSc patients referred for CMR, one third demonstrated LV cardiomyopathy with 38% showing LV or RV abnormality. LV disease localized to the septal and apical segments. Larger studies are needed to determine the incremental prognostic value of these features beyond RVEF.

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Management of Pre Existing Inflammatory Arthritis During Immune Checkpoint Inhibitor Therapy for Metastatic Renal Cell Cancer with a TNF-Inhibitor for over 6 Years: A Case Report

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Background: The use of immune checkpoint inhibitors (ICIs) has transformed cancer care by using the body's own immune system to target malignant cells. ICIs can cause unintended off-target effects, termed immune related adverse events (irAEs), which can be de novo or related to preexisting autoimmune diseases (PADs). Patients with PADs require close monitoring as they are at higher risk of developing de novo irAEs as well as PAD flares, which occur in over a third of patients.[1] Optimal management strategies for PAD flares, to control symptoms without negatively impacting cancer outcomes, remains unknown. Data on the long-term use of biologic disease modifying anti-rheumatic drugs (bDMARDs) such as TNF-inhibitors (TNFi) in patients on ICI is lacking. This case describes concomitant treatment with both an ICI and a TNFi in a patient experiencing a flare of preexisting inflammatory arthritis (P-IA).
Case Report: A 57-year-old man with rheumatoid arthritis was in remission on methotrexate and a TNFi when he was diagnosed with metastatic renal cell carcinoma (RCC) and both immunosuppressives were discontinued. After failing 3 lines of therapy, he was initiated on ICI (nivolumab). Following 3 cycles of ICI he experienced a P-IA flare, which failed to respond to intraarticular glucocorticoids and methotrexate. Given the significant impact on his quality of life (QOL), a TNFi was re-initiated, his P-IA went into remission and no further irAEs developed. After a total of 78 cycles (6.5 years) of nivolumab, and palliative radiation to the bone, the patient had progression of his RCC, and the decision was made to discontinue ICI.
Conclusion: This case outlines a man with metastatic RCC and P-IA who received concurrent treatment with an ICI and TNFi for over 6-years with control of his and P-IA and no other irAEs. Current guidelines for management of P-IA prior to ICI initiation recommend reducing immunosuppression to the lowest required amount or stopping it completely.[2] The optimal management of P-IA flares during ICI is less clear. Despite attempts to minimize immunosuppression, some patients will require treatment with a bDMARD to facilitate ongoing ICI and maximize QOL. A recent phase 1 clinical trial suggested that concomitant use of a TNFi and ICI may increase ICI efficacy while also preventing irAEs.[3] We hypothesize that use of the TNFi in our patients may have ameliorated the risk of developing other irAEs. Further research is needed into the safety of long-term bDMARDs use in patients receiving ICI.
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Effect of Guselkumab and IL-17 Inhibitors on Work Productivity and Activity Impairment in Psoriatic Arthritis: 6-Month Results of the PsABIOnd Observational Study

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Objectives: Work impairment is a key issue in PsA. Biologic treatments can improve work status in patients with PsA; however, there is lack of comparative real-world data for different classes, e.g. IL-23 and IL-17 inhibitors(i). The current analysis aimed to assess PsA patient-reported outcomes (PRO), specifically work productivity, activity impairment, and disease impact after 6 months of treatment with guselkumab (GUS) and IL-17i.

Methods: PsABIOnd (NCT05049798) is a global observational study in PsA patients starting GUS or IL-17i as 1st-to-4th line of biologic therapy per standard of care.[1] Here, the full population of the PsABIOnd study was analyzed over the first 6 months of follow-up. Work productivity and activity impairment were assessed via the Work Productivity and Activity Impairment Questionnaire (WPAI; 0-100).[2] Patient-reported disease impact was assessed using the PsA Impact of Disease-12 (PsAID-12; 0-10),[3] including the mean total score and proportions of pts achieving minimal clinically important improvement (MCII); improvement by ≥1.4; among pts with BL PsAID-12 score ≥1.4). All analyses were performed according to initial treatment group allocation, and treatment comparison was based on 95% confidence intervals (CI).

Results: 1134 patients were analyzed; 555 and 579 received GUS or IL-17i, respectively, as their initial treatment. Mean age (53.2/53.5 yrs), sex (60.4%/59.2% female), and prior exposure to a targeted drug (63.4%/62.3%) were comparable for GUS/IL-17i. Mean overall baseline work productivity loss (42.3%/44.5% for GUS/IL17i groups), absenteeism (14.3%/12.9%), presenteeism (39.2%/42.1%), activity impairment (48.5%/50.6%), and mean baseline PsAID-12 total score (5.1/5.1) were also similar between groups. At the 6-month visit, comparable improvements were observed in all WPAI outcomes with GUS and IL-17i. Mean (95% CI) improvements in GUS/IL-17i were: overall work productivity loss (-13.1 [-16.5, -9.7]/-13.8 [-17.5, -10.1]%), absenteeism (-6.4 [-10.4, -2.4]/-2.5 [-5.1, 0.2]%), presenteeism (-12.5 [-15.7, -9.3]/-14.0 [-17.5, -10.5]%), activity impairment (-13.1 [-15.4, -10.8]/-15.7 [-18.2, -13.1]%); (Figure 1). Mean PsAID-12 total scores also improved significantly (-1.6 [-1.7, -1.4]/-1.8 [-2.0, -1.6]) reaching levels (3.5/3.3) indicative of symptom impact below the patient acceptable symptom state threshold (≤ 4.0) in both groups. Rates of pts achieving PsAID-12 MCII at 6 months were also comparable (54.7%/55.9%).

Conclusion: By 6 months of treatment in real-world, improvements in work productivity and ability to perform daily activities were observed with both GUS and IL-17i, paralleled with clinically meaningful improvements in patient-reported multidomain disease impact. Based on overlapping CIs, improvements in PROs were comparable between the two classes. These results may be useful for reimbursement decisions and healthcare provider/patient shared treatment decision-making.

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Persistence and Effectiveness Across PsA Patient Subgroups with Guselkumab and IL-17 Inhibitors: 6-Month Results of the Psabiond Observational Study

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Objectives: Randomized controlled trials demonstrated the efficacy of IL-23 inhibitors (i) and IL-17i in PsA; however, real-world data on their effectiveness in heterogeneous patient subgroups are limited. Some subgroups, such as older, obese, or biologic-experienced patients, are of particular interest as they report worse outcomes.[1] The objective was to assess the 6-month persistence and effectiveness of guselkumab (GUS) and IL-17i across these subgroups of interest.

Methods: PsABIOnd (NCT05049798) is a global observational study in patients with PsA starting GUS or IL-17i as 1st-to-4th line of biologic therapy per their standard of care.2The full population of the PsABIOnd study over 6 months of follow up was analyzed. Analyses were performed according to initial treatment group allocation in the overall population and in specific subgroups defined by baseline (BL) age, sex, BMI categories, and prior biologic use. Persistence on treatment (i.e., no stop/switch) over 6 months was assessed via the Kaplan-Meier estimator function. Propensity score (PS) analysis was used to evaluate hazard ratio (HR) of GUS vs IL-17i stop/switch prior to the 6-month visit, adjusting for BL variable imbalances across cohorts. Effectiveness was descriptively assessed using rates and means at BL and 6 months of the following measures: swollen and tender joint counts, clinical Disease Activity Index for PsA - based low disease activity /remission, the Leeds Enthesitis Index, psoriasis body surface area, Dermatology Life Quality Index and number of nails affected by psoriatic disease. Dactylitis was not assessed due to the low prevalence of dactylitis at BL.

Results: Of the 1134 pts analyzed, 555 and 579 pts received GUS or IL-17i, respectively, as their initial treatment. At BL, the GUS/IL-17i cohorts were generally well balanced across subgroups of interest: 83.4%/81.3% were <65 years of age; 60.4%/59.2% were female; 48.0%/43.4% had BMI≥30 kg/m2; and 63.4%/62.3% had previously received ≥1 targeted therapy. Persistence on treatment was high in both cohorts, with 526/555 (94.8%) GUS and 539/579 (93.1%) IL-17i pts remaining on their initial treatment at the 6-month visit (PS-adjusted HR of GUS vs IL-17i stop/switch [95% confidence interval]: 0.93 [0.75-1.16]); (Figure 1). Across patient subgroups of interest, similar improvements in joint symptoms enthesitis skin involvement, and psoriatic nail disease were observed with GUS and IL-17i at the 6-month visit.

Conclusion: Treatment with GUS or IL-17i resulted in comparable treatment persistence and effectiveness, regardless of age, sex, BMI, or treatment history, through 6 months. These results support the real-world effectiveness of GUS and IL-17i across PsA subpopulations.

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Durable Inhibition of Structural Damage Progression and Improvements in Joint Disease

Activity with Guselkumab in Active and Erosive Psoriatic Arthritis: Week 48 Results from Apex

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Objectives: APEX (NCT04882098) evaluates guselkumab (GUS), a fully-human mAb able to bind CD64 and selectively inhibit the IL-23p19-subunit, in participants (pts) with active and erosive PsA. At Week(W)24, GUS demonstrated significantly higher ACR20 rates (primary endpoint) and radiographic progression inhibition vs placebo (PBO; major secondary endpoint). Here we report W48 findings.

Methods: APEX enrolled adults with active PsA (≥3 tender, ≥3 swollen joints; CRP ≥0.3 mg/dL) and ≥2 erosive joints on radiographs of hands/feet, despite previous non-biologic therapy. The modified full analysis set comprised 1020 randomized pts (273 GUS 100mg Q4W; 371 GUS 100mg at W0/W4 then Q8W; 376 PBO-to-GUS Q4W at W24). Key endpoints through W48 included ACR20/ACR50 rates and least squares mean (LSM) change in PsA-modified van der Heijde-Sharp (vdH-S) score per reading session 2 (W0/24/48 radiographs). Exposure-adjusted incidence rates of adverse events (AEs) per 100 pt-years (100PY) [95% CI] are reported through W48.

Results: GUS Q4W/Q8W ACR20 rates increased from W24 (67%/68% vs 47% PBO; both $p<0.001$) to W48 (71%/74%). GUS ACR50 rates increased from W24 (41%/42% vs 20% PBO; both nominal-$p<0.001$) to W48 (51%/56%). At W48, 71% and 48% of PBO-to-GUS Q4W pts achieved ACR20 and ACR50, respectively. Reading session 2 results indicated continued suppression of radiographic progression with GUS Q4W/Q8W from W0-24 (LSM changes in PsA-modified vdH-S score: 0.36/0.46) throughout W24-48 (0.24/0.32). Radiographic progression in the PBO group from W0-24 (0.96) was curtailed by GUS W24-48 (0.41). Through W24, AE incidence rates with GUS Q4W/Q8W (168[146-191]/163[145-183]) and PBO (174[155-195]) were similar. Incidence rates did not increase with continued GUS (W0-48: 147 [132-163]/148 [136-162]), or after PBO-to-GUS transition (W24-48: 156 [138-176]).

Conclusion: In biologic-naïve adults with active and erosive PsA, inhibition of radiographic progression and joint disease activity improvements with GUS were durable through W48 without increased AE incidence, further substantiating GUS benefit for preserving joint health.

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Natural History of Concomitant Immune-Mediated Inflammatory Diseases: Psoriatic Disease and Inflammatory Bowel Disease Regarding Disease Course and Healthcare Utilization – A JANL-HIP Study

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Objectives: The coexistence of multiple immune-mediated diseases (IMIDs) presents substantial challenges in healthcare management. This study investigates the timing of onset for psoriatic disease (PsD) and inflammatory bowel disease (IBD) and assesses how the sequence of diagnosis impacts mortality and hospitalization costs in patients with these concurrent conditions.
Methods: We conducted a retrospective analysis using data from the Newfoundland and Labrador Centre for Health Information (NLCHI) spanning 2009 to 2019. Patients diagnosed with PsD were identified using the ICD-9 code 696 and matched with 75,500 controls without PsD. From this cohort of approximately 100,000 patients, individuals with IBD were identified using ICD-9 codes 555 for Crohn's disease (CD) and 556 for ulcerative colitis (UC). The study recorded the sequence of IMID occurrences, mortality rates, and total hospitalization costs.
Results: The analysis identified 15,100 patients with PsD and 2,800 with IBD. Among these, 14,368 had only PsD, 2,068 had only IBD, and 732 had both conditions, indicating that 4.8% of PsD patients also had IBD, including 525 with CD and 207 with UC. Notably, 65% of patients with both PsD and IBD were diagnosed with IBD first. This trend was consistent for both CD and UC, where 65% of patients developed CD or UC prior to PsD. For those diagnosed with PsD first, CD appeared an average of 7.58 years later, while PsD developed 9.76 years later when CD was diagnosed first ($p = 0.004$). In the case of UC, it followed PsD by 6.88 years, whereas PsD followed UC by 7.41 years ($p = 0.13$). The average age at death for patients diagnosed with CD before PsD was 67.6 years, compared to 70.7 years for those diagnosed with PsD first ($p = 0.06$). For patients diagnosed with UC before PsD, the average age at death was 66.5 years, compared to 78.3 years for those diagnosed with PsD first ($p = 0.0001$). No significant differences in total hospitalization costs were observed among the groups.
Conclusion: The sequence of diagnosis in patients with multiple IMIDs significantly influences the timing of the onset of the second disease and may have implications for mortality. These findings highlight the necessity for effective management strategies for patients with concurrent IMIDs and underscore the potential impact of the order of diagnosis on patient outcomes.
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Immune Checkpoint Inhibitor Associated Large Vessel Vasculitis: A Case Series from the Canadian Research Group of Rheumatology in Immuno-Oncology

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Objectives: The use of immune checkpoint inhibitors (ICI) for cancer treatment continues to increase as indications expand, both in the palliative and adjuvant setting. Immune related adverse events (irAE) can affect any organ due to immune system stimulation. ICI associated large vessel vasculitis (ICI-LVV) is a rare irAE, with descriptions limited to small case series

and reports. We aimed to identify and characterize the manifestations, management and outcomes of ICI-LVV in a national multi-center cohort.
Methods: We searched the Canadian Research Group of Rheumatology in Immuno-Oncology (CanRIO) retrospective and prospective cohorts for cases of de novo ICI-LVV. Cases of pre-existing LVV were excluded. Demographic, clinical and laboratory data were extracted from the study databases.
Results: We identified 13 patients who developed LVV after ICI exposure, most commonly for melanoma (n=5) and non-small cell lung cancer (n=3). Most patients received single agent ICI (69%). The median time from ICI exposure to symptom onset was 4.0 months (IQR 1.5-15). Isolated large vessel (n=5) or isolated cranial involvement (n=5) were the most common presentations. In those with cranial involvement (n=8), headache (n=8), jaw claudication (n=6) and scalp tenderness (n=6) were the most common symptoms. In those with confirmed large vessel involvement, (n=8), the most common radiographic finding was hypermetabolism on PET scan (n=6), often found incidentally without associated symptoms. There was one case of stenosis, and no aneurysms identified on imaging. Six patients had temporal artery biopsy and 2 were consistent with LVV, without clear histopathologic differences from idiopathic giant cell arteritis. Eleven patients were treated with glucocorticoids: Two relapsed during taper, one required additional immunosuppression (methotrexate and tocilizumab). Two patients with normal inflammatory markers and isolated large vessel involvement (hypermetabolism on PET) had remission without treatment. Only 2 patients continued ICI after ICI-LVV diagnosis, both without vasculitis recurrence/progression. There was no vision loss or death attributable to ICI-LVV.
Conclusion: Isolated cranial or large vessel involvement were the most common presentations of ICI-LVV. Like idiopathic GCA, headache was the most common clinical manifestation in those with cranial involvement. In contrast, isolated large vessel involvement was commonly found on PET, incidentally and without clinical symptoms. Careful clinical correlation is required in cases of isolated large vessel involvement, as not all may require treatment. This has important implications given the potential impact of immunosuppression on ICI and tumour outcomes. Further studies are needed into the clinical presentation, underlying pathological mechanisms and optimal management of ICI-LVV.
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Atypical Pediatric Lyme Arthritis Mimicking Juvenile Arthritis: Three Cases
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Background: Lyme disease incidence is rising in Canada.[1] While Lyme arthritis typically presents as monoarthritis of a large joint, most often the knee, it can also mimic juvenile idiopathic arthritis (JIA) in pattern and chronicity.[2] We describe three children whose initial

presentations resembled JIA but were ultimately diagnosed with Lyme arthritis.
Case Report: We reviewed the charts of three pediatric patients referred for suspected JIA and later diagnosed with Lyme arthritis. We describe the demographics, exposure history, symptoms and physical examination findings, investigations, treatment, and outcomes. Case 1: An 11-year-old boy from rural Norfolk County, Ontario, developed chronic right-knee arthritis with a large Baker's cyst and significantly limited range of motion. He reported a suspected tick bite one year earlier. He was initially thought to have oligoarticular JIA with MRI confirming active synovitis and a larger Baker's cyst. However, Lyme serology was positive. After eight weeks of doxycycline and naproxen, he achieved complete clinical resolution of arthritis and Baker's cyst that has been sustained for the past four years. Case 2: A 13-year-old boy from Mount Pleasant, Ontario with subacute left-knee swelling accompanied by fever and highly elevated CRP of 163 was admitted due to suspected septic arthritis. Synovial fluid was markedly neutrophilic but culture-negative, and he later developed contralateral knee and right wrist effusions, prompting consideration of JIA. A detailed history revealed a febrile illness with erythema-migrans-like rash the prior summer. Lyme serology was positive and Lyme PCR in synovial fluid later returned positive. He completed one week of IV ceftriaxone, eight weeks of doxycycline, and a subsequent four-week course of IV ceftriaxone for persistent mild arthritis with full recovery. There has been no recurrence at one year of follow-up. Case 3: A 13-year-old girl from Oakville, Ontario, developed right-knee arthritis and left TMJ pain with visible swelling, tenderness, and limited range of motion. She had been camping extensively in Nova Scotia, PEI, and Maine eight months earlier. While she was initially suspected to have oligoarticular JIA because of TMJ involvement, Lyme disease was suspected due to the mismatch between arthritis affecting only two joints and elevated inflammatory markers (CRP 68, ESR 45). Her Lyme serology was positive. After eight weeks of doxycycline and naproxen, she was asymptomatic with no recurrence over the past five years.
Conclusion: These cases highlight the importance of maintaining a high index of suspicion for Lyme arthritis in children and adolescents with inflammatory joint disease, including presentations that suggest JIA. Recognizing the variable presentations of Lyme arthritis and incorporating appropriate testing can ensure timely, targeted therapy and prevent unnecessary immunosuppression.
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Exploring Decisional Factors to Include Approaches in a Patient Decision Aid for Juvenile Idiopathic Arthritis Symptom Management

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Objectives: Youth with juvenile idiopathic arthritis (JIA) experience physical and mental health symptoms that negatively impact their participation in daily life activities. The JIA Option Map is a web-based patient decision aid (PDA) created to facilitate decision-making for JIA symptom management. While PDAs should include evidence-based information, the literature does not specify how to decide on the symptom management approaches to include. We aimed to explore factors considered by patient partners and health care providers (HCPs) when choosing new approaches to update the JIA Option Map.

Methods: Our research team included patient partners and a wide range of HCPs and researchers with expertise in JIA and shared decision making. We conducted individual virtual consultations with research team members to present recent evidence on approaches to managing JIA-related pain, fatigue, and mental health symptoms. Approaches were identified through a scoping review. For each approach, we presented evidence from clinical practice guidelines (CPGs), systematic reviews and clinical trials, along with assessments of their methodological quality. Team members were asked whether each approach should be added to the JIA Option Map, and to rate the level of recommendation based on evidence and expert recommendations (i.e., usually, sometimes or not recommended).

Results: Thirteen team members participated in the consultations (5 patient partners and 8 HCPs), during which we presented evidence on seven approaches. Most team members agreed that the approaches should be added to the JIA Option Map, with most rated as "sometimes" or "usually" recommended. These included massage for youth and parent anxiety and youth stress, and self-management programs for parent stress and child self-esteem. Three members did not agree to add the following approaches until more information on safety and accessibility was gathered: laser therapy for fatigue and pain, Watsu (Water-Shiatsu) for pain, and video game-based task-oriented activity for pain. Both HCPs and patient partners indicated that they based their decisions primarily on CPG recommendations, personal experience, and evidence on effectiveness, safety and accessibility.

Conclusion: Overall, most HCPs and patient partners supported adding the proposed approaches to the JIA Option Map based on available evidence. They considered similar factors when making decisions and found accessibility of some approaches to be a limiting factor. Next steps will include gathering additional information on certain approaches to reach consensus on their inclusion and recommendation levels. These findings provide insight into the decision-making process for integrating symptom management approaches into a complex patient decision

aid. **Supported by a CIORA grant**

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A Systematic Review of Approaches to Manage Mental Health Symptoms Among Children and Youth with Juvenile Idiopathic Arthritis to Inform the JIA Option Map

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Objectives: Children and youth with juvenile idiopathic arthritis (JIA) often experience mental health symptoms such as anxiety, stress, depression, and low self-esteem, which can significantly affect their daily lives. These symptoms are frequently underrecognized. In this systematic review (SR), we aimed to identify evidence on approaches to manage mental health symptoms in JIA to inform updates of our team's web-based patient decision aid (JIA Option Map).

Methods: We searched MEDLINE, Embase, PsycINFO, CINAHL, and CENTRAL from inception to September 2024. We included randomized controlled trials (RCTs), systematic reviews (SRs) and clinical practice guidelines (CPGs) evaluating approaches to manage mental health symptoms compared to any control group in children and youth 0–21 years with JIA. Two reviewers independently screened studies, extracted data, and assessed risk of bias using Cochrane RoB 2.0 (RCTs), AMSTAR 2 (SRs with meta-analyses) and AGREE II (CPGs). Certainty of evidence was appraised using GRADE. Findings were summarized descriptively, and standardized mean differences or risk ratios were calculated where applicable. Reporting followed PRISMA guidelines.

Results: We included 11 RCTs, one SR and two CPGs. The RCTs evaluated educational and self-management programs, cognitive behavioral therapy, exercises, massage and relaxation. One SR on eHealth and mHealth interventions reported on the RCTs already included without conducting a meta-analysis. One CPG recommended Pilates, and another recommended early psychological care. Overall, RCTs were rated as having moderate to high risk of bias, resulting in low to moderate certainty of evidence. Most studies did not show statistically significant

effects on mental health outcomes, except for four RCTs that showed positive results. One showed, with moderate certainty, that Pilates improved psychosocial health-related quality of life compared with conventional exercises. Another showed, with moderate certainty, that healthy sleep improved youth mood compared with restricted sleep. Another showed, with low certainty, that a web-based self-management program for parents reduced parent stress and improved child self-esteem compared with usual care. The last showed, with low certainty, that parent-delivered massage reduced youth and parent anxiety and youth stress compared with relaxation. No adverse events were reported in these trials.
Conclusion: Few studies have evaluated approaches to managing mental health symptoms in JIA. Pilates, healthy sleep, parent web-based self-management programs and massage may be beneficial, but the certainty of evidence is limited, and adverse events were often not reported. These findings may assist patients' and providers' decision making and will inform updates to the JIA Option Map. **Supported by a CIORA grant**

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A Systematic Review of Approaches to Manage Fatigue Among Children and Youth with Juvenile Idiopathic Arthritis

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Objectives: Children and youth with juvenile idiopathic arthritis (JIA) frequently experience fatigue, which adversely affects daily functioning. Fatigue is a common yet under-researched symptom in JIA. There is a need for evidence-based information on how to manage fatigue and to present this information in the JIA Option Map, a web-based patient decision aid for JIA symptoms. This systematic review (SR) aimed to determine the benefits and harms of approaches to manage fatigue for children and youth with JIA.
Methods: We conducted a comprehensive search of five major databases (MEDLINE, Embase, PsycINFO, CINAHL, and CENTRAL) from inception to September 2024. We included

randomized controlled trials (RCTs), SRs and clinical practice guidelines (CPGs) evaluating approaches to manage fatigue compared to any control group in children and youth 0–21 years with JIA. Two reviewers independently screened studies, extracted data, and assessed risk of bias using Cochrane RoB 2.0 (for RCTs), AMSTAR 2 (for SRs with a meta-analysis) and AGREE II (for CPGs). Certainty of evidence was appraised using GRADE. Evidence was summarized descriptively, and standardized mean differences and risk ratios were calculated where applicable. Reporting follows PRISMA guidelines.
Results: We included four RCTs and two SRs. The RCTs assessed laser therapy, exercises and self-management strategies. The SRs summarized existing evidence on physical activity and self-management approaches but did not conduct meta-analyses. No CPGs were included in this SR as they did not report recommendations specific to fatigue. Overall, RCTs were rated as having moderate to high risk of bias, resulting in low to moderate certainty of evidence. RCTs did not demonstrate statistically significant effects, except for one RCT, which showed with moderate certainty that adding low-level laser therapy to an exercise program reduced fatigue compared with exercise alone. No adverse events were reported.
Conclusion: We included four RCTs and two SRs. The RCTs assessed laser therapy, exercises and self-management strategies. The SRs summarized existing evidence on physical activity and self-management approaches but did not conduct meta-analyses. No CPGs were included in this SR as they did not report recommendations specific to fatigue. Overall, RCTs were rated as having moderate to high risk of bias, resulting in low to moderate certainty of evidence. RCTs did not demonstrate statistically significant effects, except for one RCT, which showed with moderate certainty that adding low-level laser therapy to an exercise program reduced fatigue compared with exercise alone. No adverse events were reported. This SR highlights the limited number of studies assessing interventions to manage fatigue in JIA. A low-level laser added to an exercise program RCT may improve fatigue; however, the certainty of the evidence was suboptimal, and adverse events were not reported. These findings will inform updates to the JIA Option Map to help support families' and clinicians' decision-making and will orient future research priorities. **Supported by a CIORA grant**.

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The Road to Readiness: Transition Trajectories of Youth with Juvenile Idiopathic Arthritis and Juvenile-Onset Systemic Lupus Erythematosus.

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Objectives: For youth with Juvenile Idiopathic Arthritis (JIA) and juvenile-onset Systemic Lupus Erythematosus (jSLE), the time leading up to the transfer from pediatric to adult care is especially vulnerable. During this period, it is essential to optimize skill development, independence and confidence in managing their own health. Few studies have explored how transition readiness changes over time in youth prior to transferring to adult care, or the role that sex and age may play in this trajectory of change.
Methods: Patients 14-17 years with JIA or jSLE were recruited from the multidisciplinary McMaster Rheumatology Transition Clinic and asked to complete the 14-item Transition-Q (max 100) at each visit to assess transition readiness. After each patient completed the Transition-Q, a member of the healthcare team would discuss their responses with them and set

goals for the next appointment. Descriptive statistics summarized patient demographics. Generalized estimating equations examined the predictive value of sex, number of visits, age at enrollment and age at diagnosis on changes in transition readiness while accounting for time.
Results: Analyses included 384 observations from 94 participants. Number of clinic visits per participant ranged from 1 to 8, with varying time between visits. Age at diagnosis was not a significant predictor of changes in Transition-Q score ($p=0.551$). More visits ($\beta=8.02$, $p=<0.001$), female sex ($\beta=6.87$, $p=0.031$), and older age at enrollment ($\beta=3.94$, $p<0.001$) were significant positive predictors of improvements in Transition-Q score (Figure.). There was no significant interaction between sex and number of visits ($p=0.17$) indicating that the association between visit number and Transition-Q score did not differ meaningfully between males and females.
Conclusion: Our study demonstrated improvements in transition readiness with females, older age and longer follow-up predicting larger improvements. This suggests that males and those who are younger may require additional supports to optimize transition readiness prior to the transfer to adult care. It also suggests that these males and those who had fewer visits in pediatric care prior to the transfer may require more supports upon arrival in adult care.

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Use of Hypnosis for Intra-Articular Steroid Injections in Children with Juvenile Idiopathic Arthritis

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Objectives: Intra-articular steroid (IAS) injections are a common treatment for Juvenile Idiopathic Arthritis (JIA) but can cause anxiety in children, particularly due to needle fear. To facilitate cooperation, general anesthesia is often used for younger children or those requiring multiple injections. Older children undergoing one or two joint injections may stay awake, sometimes with optional midazolam sedation which requires post-procedure monitoring. Hypnosis offers a non-pharmacological alternative to reduce anxiety and distress.[1] By inducing a natural altered state of consciousness, characterized by focused attention and reduced peripheral awareness, hypnosis enables children to focus inward and ignore external stimuli.[2] Unlike sedation, hypnosis does not require post-procedure monitoring, allowing for quicker recovery and discharge.
We report our experience using hypnosis to manage pain and anxiety during IAS injections in a tertiary care rheumatology clinic.
Methods: Since March 2020, a nurse trained in hypnosis has offered this technique to children undergoing IAS injections. To evaluate its impact, children provided feedback using visual analogue scales (VAS) and personal reflections.[3] Procedure difficulty score was rated from 0 (no difficulty) to 10 (maximum difficulty), and perceived benefit score from 0 (no benefit) to 10 (maximum benefit). During the same period, children receiving IAS injections with other supportive strategies completed the same scales and shared reflections. Feedback was collected post-procedure by the same nurse who supported each child using their chosen method.
Results: Data was collected on 80 procedures in 62 children: 55 procedures with hypnosis, 25 using other strategies (phone distraction (7), music (4), conversation (4), midazolam (2), breathing techniques (4) or no specific intervention (4)). Groups were comparable for age, gender and joint injected (Table 1). All children successfully completed the procedure. Children in the hypnosis group reported lower procedure difficulty and higher perceived benefit compared to those with other methods. Overall, children voiced that hypnosis helped them focus on their

chosen experience and not on the procedure, while children using other methods expressed more physical sensations. Clinicians observed a calming effect with hypnosis contributing to better procedural tolerance.
Conclusion: Children consistently report hypnosis as helpful. Hypnosis provides a compassionate way to accompany children in a challenging moment. It helps them stay engaged, feel capable, and actively participate in their own care.
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Systemic JIA with Macrophage Activation Syndrome Complicated by Drug-Induced Liver Injury

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Background: Systemic juvenile idiopathic arthritis (sJIA) is an autoinflammatory condition that presents diagnostic and therapeutic challenges, especially when complicated by macrophage activation syndrome (MAS) - a life-threatening hyperinflammatory syndrome. Standard therapies for MAS secondary to sJIA include interleukin-1 (IL-1) inhibitors anakinra and canakinumab.[1] Reversible drug induced liver injury from anakinra and canakinumab has been reported, occurring in up to 10% of patients.[2] Specifically, with canakinumab, elevations in hepatic enzymes have been reported in up to 5% but rarely severe.[3] This case highlights the challenges of diagnosis and management for MAS in sJIA with concurrent drug-induced liver injury.
Case Report: A 16-year-old male, diagnosed with sJIA at age 13, initially presented with quotidian fever, evanescent rash, hepatosplenomegaly and polyarthritis, with no MAS... Initial treatment included prednisone, naproxen and tocilizumab. Due to persistent rash and arthritis, his therapy was changed to anakinra 100mg daily. One year later, he developed pharyngitis and fevers, progressing over 2 weeks into fulminant MAS with unremitting fevers, and supportive labs (Figure 1). His hepatic enzymes remained normal throughout. He stabilized with pulsed methylprednisolone and increasing anakinra to 200mg (3mg/kg). One month later, he developed significant liver injury, with transaminitis and mildly elevated unconjugated bilirubin. Workup revealed no concurrent infection, fever/sJIA flare, or other etiology. His presentation was most consistent with drug-induced liver injury, and anakinra was discontinued. Canakinumab started at 300 mg every 4 weeks. This allowed for prednisone tapering to 10mg over 3 months. However, a progressive transaminitis recurred, spiking 2-3 weeks following each canakinumab administration. During treatment, the patient had no symptoms of sJIA with normal CRP and cell counts. After three doses of canakinumab, he developed jaundice, elevated INR and elevated conjugated bilirubin with a peak ALT of 3000 U/L. Liver biopsy demonstrated features of drug-induced liver injury and hemophagocytosis, suggesting a possible mixed presentation with underlying sJIA disease activity and residual MAS. However, he remained afebrile with no signs of sJIA disease activity. Canakinumab was discontinued and 1 month later he started tofacitinib for breakthrough arthritis while on 10mg of prednisone. Two months later, he remains asymptomatic from sJIA and his liver injury has been resolved. His CRP is only mildly elevated on tofacitinib monotherapy.
Conclusion: This case represents the first detailed description of reversible severe liver injury

associated with canakinumab in sJIA complicated with MAS. On tofacitinib, the patient was able to effectively recover from the liver injury and taper off corticosteroid.
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Moverx: Digital Exercise Prescriptions for Kids with Juvenile Idiopathic Arthritis

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Objectives: Juvenile idiopathic arthritis (JIA) patients require regular rehabilitation exercises to improve and maintain joint range of motion (ROM).[1] Access to therapy may be limited for some patients, most community clinics lack allied health team members, and poor adherence arises from brief in-person instruction with or without written details and reminders given subsequently.

To address this problem, a multidisciplinary team at Montreal Children's Hospital (MCH) have developed an extensive library of exercise videos to be prescribed by Paediatric Rheumatology Care Providers (PRCPs) as indicated by their individual patients' needs. Previous work has demonstrated: (1) satisfaction with the video content by PRCPs [2]; (2) patient preference for videos over written handouts [3]; and (3) improved exercise technique accuracy in follow-up encounters with prescription of these videos.

To date, there has been a significant barrier to dissemination of the video library to PRCPs outside MCH in a secure manner. This project leveraged a novel online platform housed at the Hospital for Sick Children (SickKids) in Toronto, namely the UCAN CAN DU research network to prescribe ROM exercise videos to patients with Rheumatological diagnoses.

Methods: A nonrandomized, prospective, interrupted time series quality improvement project guided by the Model for Improvement framework was initiated in April 2025 and is ongoing. Encounters within scope were in-person visits with established Rheumatology patients aged 2-17 years who had an indication for ROM exercise prescription.

Results: To date, 25 ROM exercise video links have been shared with patients/patient families. Initial PDSA cycles focused on several technical challenges, such as creating a unique URL link of source videos to patients. Subsequent focus has been on promoting access at home and securing feedback from patients/families. Preliminary survey response was 20%; however, informal feedback from >90% of those who did access the videos at home illustrated high satisfaction and self-efficacy (Figure 1). Prescribers found the process easy, though logistical barriers such as password protected access during busy clinics reduced satisfaction.

Conclusion: Preliminary results suggest success in leveraging this novel online platform to prescribe ROM exercise videos to patients with Rheumatological diagnoses in a secure and user-friendly manner. Future directions will centre on dissemination of platform access to sites across Canada and entail a large-scale study that closely tracks any technical issues and incentivizes patient/family feedback. We anticipate that successfully and appropriately spreading access to

this platform will address the unmet needs of PRCPs, especially those without access to allied health.

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Integrating Routine Mental Health Screening and Follow-Up in Pediatric Rheumatology Clinic: A Quality Improvement Initiative

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Objectives: Youth with Juvenile Idiopathic Arthritis (JIA) experience higher rates of anxiety and depression compared to the general population, which can worsen physical symptoms and reduce treatment adherence.[1] Despite this, there is a lack of primary prevention in pediatric subspecialty clinics, leaving many youth undiagnosed and untreated. This quality improvement initiative sought to increase (i) mental health screening rates from 0% to at least 75% and (ii) structured follow-up of screenings from 0% to at least 75%.

Methods: This 2-phase initiative was conducted at McMaster Children's Hospital Rheumatology clinic, serving >800 youth with JIA annually. Eligible patients were 12–18 years old attending in-person clinics. We employed driver diagrams, fishbone analysis, and workflow mapping to identify barriers and refine processes. In Phase 1, clinicians administered the Patient Health Questionnaire (PHQ-4) verbally upon arrival, and documented results in the electronic health record (EHR) using standardized templates. During Phase 2, a structured algorithm, co-created by a multidisciplinary team, was implemented to ensure follow-up was tailored to the patient's score, with options including education and resource provision, referral to allied health professionals, connection to community support, or urgent safety assessment. Follow-up action was recorded in the EHR. Process, outcome, and balancing measures were tracked.

Results: Between May 2024 and February 2025, screening rates increased from 0% to >75% and were sustained (Figure 1). Phase 2, implemented May to August 2025, saw >75% of positive screens have documented follow-up actions in the EHR, consistent with the care algorithm. Of 266 patients screened, 221 (83%) scored in the normal range (0–2), 33 (12%) mild (3–5), 7 (3%) moderate (6–8), and 5 (2%) severe (9–12) on the PHQ-4. Balancing measures indicated that screening was acceptable to both patients and clinicians, as assessed through in-house questionnaires. Across both phases, key enablers included iterative education and reminders to sustain engagement, workflow modifications to address time constraints, and integration of EHR tools and feedback charts to support adherence and provider buy-in. Weekly performance feedback, statistical process control charts, and targeted staff training further facilitated implementation and sustainment.

Conclusion: This QI initiative demonstrates that integrating routine PHQ-4 screening into pediatric rheumatology care is both feasible and sustainable, improving identification of at-risk youth and standardizing follow-up. Lessons learned provide a scalable model for other pediatric subspecialty clinics.

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Publicly Funded Formulary Coverage of Biologic and Synthetic Disease Modifying Anti-Rheumatic Drugs for Children with Chronic Arthritis in Canada: Are We Doing Enough?

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Objectives: Biologic and synthetic disease modifying anti-rheumatic drugs (bDMARD, sDMARD) have transformed the management of inflammatory arthritis, yet paediatric access remains variable across Canada, often requiring special authorization. We aimed to characterize trends and disparities in access to these therapies through publicly funded provincial programs and Non-insured Health Benefits (NIHB) for First Nations/Inuit. We also examined differences in coverage compared to Health Canada (HC) indications.

Methods: We reviewed all provincial formularies and NIHB program to determine bDMAARD/sDMARD coverage for paediatric and adult inflammatory arthritis relative to HC indications and compared our data to previously published findings from 2012.[1] We surveyed and interviewed 1 academic paediatric rheumatologist from each province to determine ease of access to these drugs.

Results: More HC indications exist for bDMARD/sDMARD in adults compared to children. In adults, 9x more drugs are listed for ankylosing spondylitis and 6x more for psoriatic arthritis compared to juvenile idiopathic arthritis (JIA) subtypes (Table 1). There are 2x more drugs with HC indications for rheumatoid arthritis than polyarticular JIA. Even when these drugs have a federally approved paediatric indication, NIHB, intended to promote equitable access for disadvantaged populations, only covers half of them (Table 1). NIHB demonstrated greater accessibility overall, with faster approval times and longer renewal periods compared to the provinces. The total number of distinct adult and paediatric bDMARD/sDMARD for inflammatory arthritis indications covered by NIHB and provincial public plans doubled since 2010. However, significant paediatric interprovincial variability is observed, with 7 bDMARDs in Ontario, and 67% of the remaining provinces funding 4 or less drugs (Table 1). The success observed in Ontario reflects strong advocacy efforts and physician-led submissions. All provincial formularies included anti-IL-6 treatment for systemic JIA whereas the Maritimes and Ontario notably also covered anti–IL-1 drugs. Paediatric rheumatologists reported differences in

ease of accessing bDMARDs, with approval times under 1 week in Manitoba and Saskatchewan and 1-4 weeks in all provinces except Quebec, which averaged 3-6 months. Renewal intervals were 3 months in Alberta, 6 months then annually in all provinces except Ontario, which reported 1-3 years. Denials occurred in all provinces because of restrictive formularies and nonstandard indications.
Conclusion: While bDMARDs have significantly improved JIA outcomes,[2] access to these drugs remains limited compared with adults despite advances since 2010. Substantial interprovincial disparities and inequities were reported in the approval and renewal processes.
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Social Barriers and Stigma in Youth with Juvenile Idiopathic Arthritis: A Systematic Review

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Objectives: The objective of this study was to better understand the social experiences of youth with juvenile idiopathic arthritis (JIA). JIA may significantly impact the physical, social, and emotional well-being of affected youth, due to experiences such as school absences, restricted participation in activities, and social isolation.[1] In addition, youth with JIA may also face stigma, discrimination, and misunderstanding from peers, teachers, and even healthcare professionals.[1]
Methods: Four scientific literature databases were searched for qualitative studies published in peer-reviewed journals from 2014 to 2024 that explored social or stigma experiences of youth with JIA (aged <25 years). A total of 1471 articles were retrieved from the search. After removing duplicates, 697 unique titles and abstracts were screened for eligibility, leading to 32 articles for full text review. and 18 studies were included for data extraction. Two reviewers conducted a meta-synthesis following the three-stage method outlined by Thomas and Harden.[2]
Results: Six key themes emerged: (1) Physical Barriers to Social Interaction (absences, limited participation, and pushing beyond limits); (2) Lack of Understanding from Others (lack of factual information, invisible disease, ability to relate, and over/under-estimated); (3) Enacted Stigma (not believes of accused of lying or exaggerating, trivialization, social isolation, verbal harassment or bullying, and discrimination), (4) Anticipated Stigma (anticipation of a negative reaction, anticipation of discrimination, and concealment); (5) Internalized Stigma (wanting to be normal or feeling different, personal identity, perceived burden to others, and social-emotional impact); and (6) Social Strengths and Supports (self-disclosure, supportive others, supportive accommodation, peers with JIA, social media, and positive outlook).
Conclusion: The review findings suggest that increasing public awareness, fostering peer support, enhancing self-advocacy skills, and implementing stigma-reduction strategies better support the social functioning of youth with JIA. Future research should explore the long-term effects of stigma and evaluate targeted interventions to improve social experiences and quality of life for this population.
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Assessment of Needs, Transition Readiness, and Satisfaction at the Young Adult with Rheumatic Diseases (Yard) Transition Clinic in British Columbia: A 2025 Updated Survey

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Objectives: Between 25% and 75% of youth with rheumatic diseases experience gaps in transition care.[1] The Pediatric Rheumatology Division at British Columbia Children's Hospital (BCCH) established the Young Adult Rheumatic Disease (YARD) Clinic almost 40 years ago ,[2] to address these challenges.

This study aims to evaluate the perceived needs, transition readiness, and overall satisfaction of patients currently attending the YARD Clinic, seven years after the initial survey by Jessa et al., [3] to ensure the clinic continues to meet the evolving needs of its patients.

Methods: We conducted a cross-sectional descriptive study using a self-administered questionnaire including both closed- and open-ended questions. Eligible participants were all active YARD patients as of September 1st, 2025, who had attended at least one clinic visit. Recruitment was done via email and in person. Participants completed an anonymous 15-minute survey electronically (REDCap) or on paper. Quantitative data were analyzed using descriptive statistics, while qualitative responses underwent thematic analysis.

Results: Of the 59 active YARD patients, 26 surveys (including 3 partial) were completed between September 1st and October 30th, 2025. The mean age was 19.15 ± 1.17 years; 69.2% (n=18) were female and diagnosed primarily with JIA (57.7%, n=15) or SLE (19.2%, n=5). Disease duration ranged from 1–5 years in 38.5% (n=10) to >10 years in 26.9% (n=7). Time as a YARD patient varied from < 6 months (26.9%, n=7) to > 24 months (38.5%, n=10). Most participants learned about YARD during their final year at BCCH (76.9%, n=20), mainly from their pediatric rheumatologist (96.2%, n=25). Overall satisfaction with care in the YARD clinic was high: 80.8% (n=21) were satisfied and 19.2% (n=5) were neutral. Participants felt comfortable discussing their conditions, contacting the team between visits, and reported receiving sufficient information about their disease and mental health resources. They also noted that YARD helped them gain independence and understand how their illness might affect their future. Suggested areas for improvement included access to multidisciplinary providers, communication around scheduling, and more information on reproductive health, substance use, and insurance. Responses to transition readiness questions (Table 1), were variable.

Conclusion: Seven years after the previous evaluation, the YARD Clinic continues to provide effective, patient-centered transition care. Self-reported readiness was variable, reinforcing the need for structured support during transition. High satisfaction and perceived support highlight its valuable role in bridging pediatric and adult care. Addressing identified gaps through targeted quality improvement may further strengthen patients' transition readiness and long-term outcomes.

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Exploring Training Needs to Facilitate Shared Decision Making in Juvenile Idiopathic Arthritis Symptom Management and the Use of the JIA Option Map

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Objectives: Our team developed the JIA Option Map, a web-based patient decision aid (PDA) designed to support shared decision-making (SDM) for juvenile idiopathic arthritis (JIA) symptom management. Since training for health care providers (HCP) can enhance SDM and the use of PDAs, we aimed to explore training needs to support SDM in JIA symptom management and the implementation of the JIA Option Map.

Methods: We used a qualitative descriptive study design and conducted virtual semi-structured interviews with young people aged 10 years and older with JIA, their caregivers, and HCPs (target: up to 15 per group). Interview guides, informed by the Interprofessional SDM (IP-SDM) model, explored participants’ experiences with SDM, as well as perceived barriers, facilitators, and training needs for HCPs to use SDM and the JIA Option Map. Interviews were video-recorded, transcribed verbatim, and analyzed using inductive and deductive content analysis guided by the IP-SDM model.

Results: To date, HCPs described providing varying levels of information about treatment

options and their benefits and risks, depending on their team roles (e.g., treatment vs. referral), but they rarely mentioned scientific evidence. While some HCPs reported considering patients' values and preferences, young people felt that final decisions were often left to them without enough guidance to reflect on their values. They expressed a desire for HCPs to better explain available options and clarify what matters most to patients. Reported barriers to SDM included limited time, power imbalances between HCPs and young people, and limited access to evidence-based information tools. Facilitators included access to tools such as the JIA Option Map and training in decision coaching to help HCPs support patients in a non-directive way. Participants recommended virtual, self-paced training modules featuring real-world clinical cases to demonstrate SDM and integration of the JIA Option Map. They also suggested that all HCPs at a given site receive SDM training to support interprofessional SDM.
Conclusion: Preliminary findings highlight the need for HCPs to provide evidence-based information on JIA symptom management options to help patients articulate their values and preferences. Participants identified a need for practical SDM training, including guidance on using the JIA Option Map. Additional interviews will further clarify training needs to facilitate SDM in JIA symptom management. **Supported by a CIORA grant**

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Effectiveness of Upadacitinib in Refractory Skin and Rapidly Progressive Lung Manifestations of Myositis

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Background: Limited data is available on the use of Upadacitinib in idiopathic inflammatory myositis, as most available studies have focused on tofacitinib as a therapeutic option to target the interferon pathway. Here, we report two cases demonstrating the use of Upadacitinib in different disease domains of idiopathic inflammatory myositis including severe lung and skin involvement.
Case Report: The first patient is a 35-year-old man presented with MDA5 positive rapidly progressive interstitial lung disease ILD, mediastinal mass and ulceration of the dorsum of the fingers. He experienced two hospital admissions for lung flares prior to full diagnosis. He was treated with mycophenolate mofetil and prednisone but attempts to taper prednisone resulted in worsening pulmonary symptoms. He then developed a spontaneous pneumothorax and ILD flare and was admitted for addition of rituximab (1g on day 0 and day14) along with IVIG. Despite treatment, he remained oxygen-dependent and was placed on the lung-transplant waiting list. Upadacitinib was initiated 3 months later, replacing mycophenolate mofetil. A follow-up CT chest after approximately one month of upadacitinib demonstrated resolution of dense inflammatory opacites with residual fibrosis, and he successfully waned off supplemental oxygen. He currently does not require urgent consideration for transplant. The second patient is a 54-year-old with dermatomyositis presented with severe cutaneous manifestations including Gottron's papules, heliotrope rash, and mechanic's hands. She had previously received multiple therapies: methotrexate, azathioprine, mycophenolate mofetil, hydroxychloroquine, IVIG (discontinued due to migraines), and abatacept with persistent disease activity and difficulty tapering prednisone. Upadacitinib was initiated, leading to marked improvement of her skin lesions and successful discontinuation of Prednisone. She remained in remission for approximately three years before developing mild cutaneous recurrence suggesting a disease flare. Discussion:
Conclusion: Addition of Upadacitinib may represent a promising therapeutic option for

idiopathic inflammatory myositis, demonstrating efficacy in the different disease domains of lung and skin in patient's refractory to standard therapy, potentially by targeting the interferon pathway.

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Case Report: Knuckle Pads - A Mimic of Gottron's Papules Not to Miss!

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Background: Gottron's papules are a hallmark cutaneous finding of adult and juvenile dermatomyositis (DM), and their presence should suggest these diagnoses. In some cases, skin involvement can precede muscle disease or maybe the sole disease manifestation (amyopathic DM), making a correct diagnosis particularly important. Knuckle pads are a benign fibrotic condition that can look very similar to Gottron's papules, appearing as erythematous or flesh-coloured plaques over the dorsa of the interphalangeal (IP) joints. Primary knuckle pads are usually idiopathic but may be inherited as part of a genetic syndrome. Secondary forms (pseudo-knuckle pads) are caused by repetitive trauma.[1] This case illustrates the importance of distinguishing knuckle pads from Gottron's papules to prevent unnecessary patient/parental concern and costly investigations.

Case Report: A 7-year-old boy was assessed for suspected juvenile DM, with a two-month history of raised erythematous lesions over the proximal and distal IP joints of both hands suggestive of Gottron's papules. The rash was not painful or pruritic. He was otherwise asymptomatic with a negative review of systems, and no history of traumatic injury. Past medical and family history were non-contributory. A topical steroid had no effect on the rash. On examination, he appeared well, with pink papular and nodular lesions over proximal IP joints 1-5 and distal IP joints 2-5 bilaterally (Figure 1). Joint examination and muscle strength were normal; there were no nailfold abnormalities or other rashes. Laboratory investigations, including creatine phosphokinase, alanine transaminase, aspartate aminotransferase, lactate dehydrogenase and erythrocyte sedimentation rate were normal. Myositis-specific antibodies were negative; antinuclear antibody testing was positive for anti-RNP (low-titer). MRI of the pelvic girdle showed no evidence of myositis. The differential diagnosis of Gottron's papules was reconsidered, and a diagnosis of knuckle pads was made based on their characteristic appearance. Skin findings more suggestive of knuckle pads rather than Gottron's papules included their firm, smooth, and mobile nature and the well-demarcated, dome-shaped appearance of many of the lesions. No treatment was given and the lesions resolved spontaneously, as is commonly seen in children.

Conclusion: Our case highlights the importance of recognizing knuckle pads as a mimic of Gottron's papules. This will prevent misdiagnosis and allow rheumatologists to avoid unnecessary and expensive investigations. After inherited and secondary forms are excluded, patients can be reassured of the benign nature of this disorder.

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Isolated Neck Extensor Myositis and Chest Wall Skin Thickening: Case Report of a Rare Initial Presentation of Systemic Sclerosis and Overlap Myositis

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Background: Systemic sclerosis is a multisystemic connective tissue characterized by immune dysregulation, fibrosis and vasculopathy. Skin thickening, a cardinal feature of this disease process, characteristically progresses in a centripetal pattern.[1] Overlap disease with idiopathic inflammatory myositis can be seen, classically involving weakness of the proximal muscle groups of the upper and lower limbs.[2]

Case Report: We report the case of a 46-year-old female referred for assessment of possible systemic sclerosis with a several month history of neck extensor weakness, Raynaud's phenomenon, moderate skin thickening isolated to the chest, positive ANA 1:640 nucleolar, and elevated CK of 436. Over the next few months, she developed rapidly progressive and severe skin thickening of the proximal and distal extremities, face and hands with associated sclerodactyly. Advanced serological testing was negative for myositis or systemic sclerosis associated with autoantibodies. Baseline investigations including echocardiogram, pulmonary function test and high-resolution CT scan of the lungs were normal. MRI of the extremities and neck demonstrated mild edema to the posterior neck paraspinal muscles, EMG of the neck extensors was positive for irritable myopathy, and subsequent muscle biopsy of the cervical paraspinal muscles demonstrated marked fibrosis with end-stage muscle atrophy in keeping with partially treated myositis. Punch biopsies of the skin demonstrated sclerosing dermatitis. A diagnosis of diffuse cutaneous systemic sclerosis with overlap myositis was made. She was treated initially with methotrexate followed by mycophenolate, however due to rapidly progressive cutaneous disease she underwent autologous hematopoietic stem cell transplant approximately 8 months after initial presentation. With ongoing follow-up 6 months post-transplant, the patients' skin thickening had significantly improved, her myositis and Raynaud's phenomenon had resolved, and she remained in remission off all immunosuppressive therapies.

Conclusion: Isolated neck extensor myositis and initial skin thickening of the chest is a rare presentation of early diffuse cutaneous systemic sclerosis. This case highlights the importance of close follow up of patients with atypical disease manifestations and seeking histopathological correlation to assist in making a definitive diagnosis.

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Unpacking the Comparator: Mapping 'Usual Care' in Non-Surgical Knee OA Trials

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Objectives: "Usual care" is a common comparator in randomized trials (RCTs) evaluating

interventions for knee osteoarthritis (OA), but it lacks a standardized definition. This scoping review aimed to systematically map how usual care has been defined and reported in knee OA RCTs, with attention to the terminology, components, and adherence to reporting standards.
Methods: We searched MEDLINE, EMBASE, CENTRAL, CINAHL, and the ClinicalTrials.gov registry from inception to May 2025 for trials involving adults with knee OA that compared a non-surgical intervention to usual care (or similar terms). Paired reviewers independently screened citations and extracted study characteristics, terminology used to describe and components of usual care, care setting, OA severity and diagnosis, intervention type, and references to external guidelines. We summarized findings and assessed reporting quality using the Template for Intervention Description and Replication (TIDieR) and Consensus on Exercise Reporting Template (CERT) checklists, where applicable.
Results: Of 11804 citations screened, we identified 154 RCTs across 33 countries. “Usual care” was the most frequently used descriptor term (53.9%), with definitions that varied considerably. While 68.2% of trials provided detailed descriptions, nearly one-third offered only vague or minimal information. Only 22.7% referenced external guidelines. Usual care content ranged from minimal care to complex multimodal packages, with substantial variation by intervention type. Reporting quality was suboptimal: trials addressed, on average, just over half of TIDieR and approximately two thirds of CERT checklist items. Usual care often lacked transparency, standardization, and reference to best practice recommendations.
Conclusion: One in three knee OA trials using usual care as a comparator did not provide a clear, detailed definition of “usual care.” Variability in usual care definitions and reporting compromise trial validity, limit evidence synthesis, and hinder clinical translation. There is an urgent need for standardized and detailed reporting of usual care interventions in knee OA trials.

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Sex Disparities in Clinical Need, Willingness, and Surgeon Recommendations for Total Knee Arthroplasty

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Objectives: Sex disparities exist in the receipt of total knee arthroplasty (TKA) for osteoarthritis (OA), with females disproportionately less likely to undergo surgery. Understanding the reasons for this gap is critical for equitable health care delivery. Lower willingness to undergo TKA, a strong predictor of future surgery, may explain lower rates of TKA referral among females versus males. However, it is unknown whether surgeons’ recommendations for TKA differ by patient sex among those who express TKA willingness at orthopedic consultation. We examined the inter-relationships of patient sex and TKA willingness on surgeon’s TKA recommendations.
Methods: This cross-sectional study included individuals with knee OA referred for TKA to two centralized hip/knee centres in Alberta, Canada. A pre-consultation questionnaire assessed patients’ TKA need, readiness, willingness, importance of various TKA outcomes, health status and contextual factors. Using multivariable logistic regression, we examined the determinants of TKA “definite willingness” (yes/no) in females and males, separately, and in a combined model, the odds of a female versus a male being “definitely willing”, adjusting for these factors. Using multivariable log Poisson regression adjusting for clustering by surgeon and potential confounders, we examined the adjusted risk ratios (RRs) for receipt of a TKA recommendation

associated with patient sex and willingness.
Results: Of 2,064 participants, 58.6% were female with mean age (SD) 65.7 (9.2) years. Compared with males, females had worse knee symptoms, were more likely to report their symptoms as unacceptable and to have received non-surgical therapies. In both sexes, definite TKA willingness was associated with greater knee pain, unacceptable symptoms, and expectations for TKA regarding pain relief and activities. Adjusting for these factors, females were less likely than males to be "definitely willing" (adjusted OR 0.61, 95% CI 0.46, 0.82). The risk ratio for receiving a TKA recommendation for those "definitely willing" was 1.26 (95% CI 1.14, 1.38) for females and 1.90 (95% CI 1.48, 2.43) for males.
Conclusion: Among individuals with knee OA referred for TKA consultation with an orthopaedic surgeon, females had greater clinical need but were less likely than males to indicate willingness to undergo surgery if offered. Among patients who were "definitely willing" to consider TKA, surgeons were more likely to recommend surgery to males than females, indicating sex disparities in TKA recommendations at the point of surgeon consultation.

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Determinants of Six-Minute Walk Test Performance in Individuals with Knee Osteoarthritis

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Objectives: Knee osteoarthritis (OA) is a leading cause of physical disability worldwide. Assessing physical function is important to guide treatment. The six-minute walk test (6MWT), recommended by the Osteoarthritis Research Society International (OARSI) as a performance-based measure of physical function,[1] was originally developed to assess submaximal aerobic fitness in people with cardiovascular and respiratory disease. In knee OA, evidence regarding its association with other measures of OA-related function is inconsistent,[2,3] raising uncertainty about the degree to which 6WMT performance reflects knee OA severity versus other patient-related factors. In individuals with symptomatic knee OA scheduled for primary total knee arthroplasty (TKA), this study assessed the contributions of OA-related and non-OA-related patient factors to 6MWT distance.
Methods: In this cross-sectional study within the Alberta BEST-Knee cohort, participants with symptomatic knee OA scheduled for primary TKA completed a standardized questionnaire assessing sociodemographic factors (age, sex, level of education), patient-reported knee OA symptoms (WOMAC pain, KOOS-PS), comorbidities (number of symptomatic lower extremity joints, lower back pain, number of non-MSK comorbidities, BMI), and psychosocial factors (PHQ-8 depressive symptoms, arthritis coping). A subset of participants additionally completed the 6MWT prior to surgery. The characteristics of those who completed the 6MWT were compared by tertiles of 6MWT distance. Multivariable linear regression modelling was used to assess the contribution of OA-related and non-OA patient factors to 6MWT distance.
Results: Among 278 participants (mean age 67 years, 65% female), individuals in the lowest tertile of 6MWT distance were more likely to be older, female, not have post-secondary education, report more comorbidities, have higher BMI, more depressive symptoms, poorer arthritis coping, greater perceived difficulty walking, higher WOMAC pain, worse KOOS-PS, and were more likely to be using a gait aid than those in the middle and uppermost tertiles. In multivariable analysis, lower scores for knee pain and disability, younger age, male sex, lower

BMI, fewer non-musculoskeletal comorbidities, post-secondary education, and greater perceived arthritis coping were associated with greater 6MWT distance (Table 1). Low back pain, number of other troublesome joints, or depressive symptoms were not independently associated with 6MWT distance.
Conclusion: While 6MWT distance declines with greater knee OA symptom severity, other biomedical and psychosocial factors also significantly influence 6MWT performance. These factors should be considered when using and interpreting the 6MWT in this population.
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Plasma Proteomics Identifies LEP and FABP4 as Key Mediators of Obesity-Related Knee Osteoarthritis

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Objectives: To identify and validate molecular markers for obesity-related knee osteoarthritis (OB^+OA^+) by integrating proteomic and genetic data.
Methods: Plasma samples from 171 primary knee OA patients, including 86 OB+OA+ and 85 OB-OA+ patients, with age, sex, and comorbidities matched between the two groups, were analyzed using the Olink Explore HT platform, quantifying 5,416 proteins. Logistic regression models were utilized to identify significant proteins. Genetic variants located within the corresponding genes of the identified proteins were retrieved from the available genome-wide genotype data, and their associations with the identified protein expressions were examined.
Results: Proteomic analysis revealed leptin (LEP) and fatty acid-binding protein 4 (FABP4) as significantly associated with the OB+OA+ group ($p < 9.23\times10^{-6}$) after adjusting for age, sex, hypertension, hyperlipidemia, other cardiovascular diseases, and diabetes, and controlling for multiple testing across 5,416 proteins (Figure 1A). Genetic analysis identified SNPs rs141614112 (G>A) in LEP ($p < 0.04$) and rs33998908 (delT) in FABP4 ($p < 0.02$) as variants associated with their respective protein concentrations (Figure 1B and C). However, neither variant demonstrated a significant association with OB+OA+ phenotype. Validation of the findings in four groups including OB+OA+, OB-OA+, OB+OA-, and OB-OA- with a large sample size is underway.
Conclusion: Our data demonstrated LEP and FABP4 as key protein biomarkers for OB+OA+. While genetic variants influenced circulating protein levels, their lack of direct association with the clinical phenotype suggests that environmental and metabolic factors may play a greater role in the manifestation of obesity-related knee OA.

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Atypical Femoral Fractures over the Decades: Bisphosphonates Still Dominate the Landscape

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Objectives: Despite strong evidence supporting their effectiveness in preventing fragility fractures, fewer than 20% of patients receive anti-osteoporotic therapy after a fracture. This gap is partly due to rare adverse events, including atypical femoral fractures (AFFs) linked to bisphosphonate (BP) use. The impact of denosumab on AFF risk remains uncertain. This study aimed to determine whether bisphosphonates remain the predominant treatment associated with AFFs, or whether denosumab also contributes.
Methods: A retrospective analysis identified cases coded as "closed fracture of the femoral shaft" from January 2008 to October 2025 (N = 686). Among 372 patients aged >40 years, and after excluding traumatic and polytrauma cases, AFFs were confirmed radiologically. Eighty patients presented AFFs (sometimes bilateral), mean age 75.2 years: 40 during 2008 - 2015 (early cohort) and 40 during 2016 - 2025 (recent cohort). Cohorts were comparable for age and biochemical parameters (creatinine, phosphate, ionized calcium, vitamin D, CTX). Treatment data were missing for 8 patients, and duration for 18. Among patients with data (n = 62), all had received bisphosphonates- ongoing or within one year- or had transitioned to denosumab (≥2 doses; mean ± SD 11.25 ± 7.7 years).
Results: In the early cohort (n = 35), 33 patients were on bisphosphonates at AFF, two on denosumab after 5 and 9 years of prior BP therapy (2 and 4 doses). In the recent cohort (n = 38), all patients were on antiresorptives and had prior BP exposure (10.35 ± 6.5 years). Eleven were on denosumab (mean 5 ± 4 years), all with prior BP (9 ± 5.5 years). One had 13 years of denosumab, six had 5–9 years- equal to or exceeding prior BP duration in five cases. The remaining four had 2–4 doses of denosumab after long-term BP (10–20 years orally or several years IV). Comparing labs within one-month post-AFF (denosumab >5 years, n = 5, compared with others in the recent cohort, n = 9), serum creatinine and CTX were significantly lower ($p < 0.01$).
Conclusion: Bisphosphonates remain the main treatment associated with AFFs despite increased denosumab use. Most AFFs under denosumab occurred after prior BP exposure, but some followed minimal BP treatment, suggesting a potential long-term contribution of denosumab. Extended denosumab therapy (>5 years) accounted for 15% of AFFs, half after brief BP exposure. Further analyses are needed to identify risk factors and better define cumulative risk from long-term antiresorptive therapy.

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Sustained Efficacy, Safety and Immunogenicity Following Single Switch from Reference Product Denosumab to FKS518 Proposed Biosimilar in Postmenopausal Women with Osteoporosis (Results from the Pivotal Lumiade 3 Study)

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Objectives: There is considerable interest in transitioning patients to biosimilars to provide highly effective therapies while controlling costs. FKS518 is a denosumab biosimilar approved for use in patients with osteoporosis, with proven therapeutic efficacy to the reference product.

Efficacy, safety and immunogenicity results after single treatment transition in the phase three study (LUMIADE-3, NCT04934072) are reported here.
Methods: Postmenopausal osteoporotic women aged 55-85 with lumbar spine bone mineral density (LS-BMD) T-score ≤ -2.5 and ≥ -4.0 were recruited for this randomized, double-blind, parallel-group trial. Patients were randomized 1:1 for three 60mg administrations of reference denosumab or FKS518, stratified by age and prior bisphosphonate use. At week 52 (W52), those on reference denosumab were re-randomized 1:1 to continue or switch to FKS518. Those on FKS518 continued their treatment. Efficacy and safety endpoints W52 to W78 included LS-BMD, BMD at femoral neck and total hip, occurrence of adverse events (AE), serious AEs, local tolerability and immunogenicity. Repeated measures analysis of percent change from baseline (%CfB) was performed. Safety parameters were reported descriptively for the three post-switch groups.
Results: Patients were randomized to FKS518 (n=276) or reference denosumab (277). Clinically relevant increases in LS-BMD, femoral neck BMD, and total hip BMD were seen at W52 in both treatment groups. %CfB in LS-BMD, femoral neck BMD and total hip BMD were also similar between those who continued on reference denosumab (125) and those who switched to FKS518 (124) (Figure 1), with repeated measures analysis consistently showing the 95% CI for the difference between groups were narrowed around zero. No clinically meaningful differences in safety, tolerability or immunogenicity were observed after switching from reference denosumab to FKS518 compared to patients who continued with either treatment. The most frequently reported TEAEs were Nasopharyngitis and Upper respiratory tract infection (W52 to W78). Only 5 patients experienced injection site reactions during the 78-week study, none were serious, and no differences between treatments were seen. The number of patients with anti-drug antibodies was low.
Conclusion: This study demonstrated therapeutic equivalence between FKS518 and reference denosumab and showed sustained efficacy after transitioning to FKS518, with no impact on safety or immunogenicity.

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A Rapid Scoping Review of Recommendations for Deprescribing Bisphosphonates to Inform Clinical Decision Support

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Objectives: Bisphosphonates are central to osteoporosis management, but prolonged use may not be needed in some individuals, and/or increase the risk of rare adverse events. [1] Deprescribing guidance could support safe discontinuation decisions, including for individuals initiated on bisphosphonates to prevent glucocorticoid-induced osteoporosis (GIOP). This rapid scoping review examined deprescribing, drug holiday, and treatment duration recommendations within osteoporosis guidelines to inform decision support for rheumatologists and other clinicians.
Methods: We conducted a rapid scoping review searching PubMed, Embase, MEDLINE, and grey literature. Leveraging a prior systematic review of guidelines published 2012–2022,[2] we updated the search to June 10, 2025, and expanded the scope to include GIOP and other secondary osteoporosis. Eligible guidelines contained ≥1 deprescribing recommendation for adults receiving bisphosphonates. One reviewer screened all records, with independent

verification of selected records by a second reviewer. We extracted deprescribing criteria, considerations for monitoring and re-prescribing, and evidence grading.
Results: We identified 291 records, reviewed 104 in full, and included 41 guidance documents from 23 countries (7 new, 34 retained from the original review.[2] Two thirds (66%, n=27) relied on expert consensus without structured evidence grading, while 34% (n=14) used formal evidence appraisal methods including the GRADE framework (17%, n=7). All recommendations focused on deprescribing in individuals with initial indications for therapy. Most (93%, n=38) framed deprescribing as a drug holiday and generally recommended consideration after ≥5 years of oral or ≥3 years of intravenous bisphosphonate exposure in individuals without high fracture risk (34%, n=14), without prior or incident fractures on treatment (34%, n = 14), and/or with bone mineral density (BMD) T-score > -2.5 (29%, n=12). Three (7%) recommended deprescribing in other settings, including after glucocorticoid withdrawal in the setting of low fracture risk (n=1). Few incorporated individualized factors including life expectancy (5%, n=2), overall health (3%, n=1), or patient preferences (18%, n = 7). The majority (73%, n = 30) outlined when deprescribing should be avoided. Suggested drug holiday durations ranged 1–5 years. About half (44%, n = 18) advised BMD or fracture monitoring after deprescribing, and 29% (n = 12) recommended restarting therapy if BMD declined or a new fracture occurred.
Conclusion: Most guidelines framed bisphosphonate deprescribing as drug holidays in postmenopausal osteoporosis, implying that future re-prescribing will be necessary. Recommendations were largely consensus-based. Practical guidance regarding deprescribing in patients who started bisphosphonates to prevent GIOP was scarce. Our results can inform decision support to guide safe deprescribing.
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Use of the Il-1 Inhibitor (Anakinra) for the Treatment of Acute Myocarditis in Pediatric Patients: a Single-Center Experience

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Objectives: Myocarditis is an acute inflammatory process of the myocardium characterized by impaired contractile function. The incidence is 1–2 cases/100,000 children, but it has increased since 2020 due to Pediatric Multisystem Inflammatory Syndrome (MIS-C). The pathogenesis involves an inflammatory process mediated by IL-1. Treatment remains heterogeneous: in addition to hemodynamic support, IVIG and corticosteroids (CS) are well-established treatments, although modalities are not standardized.
Anakinra, an IL-1 receptor antagonist, could be useful in modulating the inflammatory response and improving cardiac function in the acute phase. To describe the clinical course and treatment in pediatric patients with acute myocarditis, isolated or associated with MIS-C, admitted to our Hospital (Ospedale Maggiore Policlinico, Milan IT) between 2020 and July 2025.
Methods: A single-center, retrospective, observational study. Inclusion criteria: age <18 years, diagnosis of myocarditis according to ESC guidelines. Exclusion criteria: chronic or pre-existing

heart diseases. Patients were divided into 2 groups based on the therapy implemented, comparing clinical characteristics and cardiac function outcome (ejection fraction and time to normalization): Group A: patients treated with maximal therapy (high-dose steroid+IVIG+Anakinra). Group B: patients treated with IVIG +/- systemic steroid.
Results: 24 patients (median age 10; IQR 7.3-13.3) were identified, presenting with global myocarditis (13/24) or focal myocarditis (11/24), 8 females. 13 patients had MIS-C, and 11 had isolated myocarditis. - 3 patients with focal myocarditis did not receive anti-inflammatory therapy. - 9/21 Group A. In these patients, the median Ejection Fraction (EF) at the start of treatment was 45%, with normalization achieved in 5.3 days. 2/9 (22%) had a preserved EF at the start of treatment, with high inflammatory markers. - 12/21 Group B: 9/12 received IVIG + CS, 2/12 IVIG only, and 1/12 CS only. The median EF at the start of treatment was 50% (normal in 6/12), normalizing in 6.6 days. The death of an 11-day-old neonate (weight 3.3 kg), with viral myocarditis without associated comorbidities and treated with IVIG only, was recorded in this group.
Conclusion: Despite the limitations related to the sample size and the retrospective nature of the study, the data suggest that early and more aggressive immunomodulatory treatment may contribute to a faster recovery of contractile function and improve outcomes. Treatment with Anakinra could represent a valid therapeutic option for optimizing anti-inflammatory therapy in the acute phase. No adverse events were observed in patients treated with IV Anakinra (5–10 mg/kg/day). Further controlled prospective studies will be necessary to confirm the observed data
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Understanding Lyme Disease Information for Children, Youth, and Parents: A Content and Thematic Analysis of Publicly Available Websites

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Objectives: Lyme disease (LD) is the most common tick-borne disease in Canada.[1] While early symptoms of LD (e.g. bulls-eye rash) are relatively well-known to the lay public, awareness of other presentations may be less appreciated. Our previous research found that parents of children with LA were fearful about a LD diagnosis and were not aware that arthritis could be a manifestation of LD.[2] The accessibility and scope of publicly available information may contribute to this finding. Our objectives were to identify prominent online sources of LD information and determine (1) the webpage readability (2) the availability of LA, parent, and pediatric-specific information, and (3) overall messaging about LD.
Methods: An incognito Google search was performed using relevant search terms pertaining to LD and LA (top 20 sites from each search were reviewed, duplicates removed). Flesch-Kincaid Grade Level (FKGL) and Flesch-Kincaid Reading Ease Scores (FRES) (score 60-70 = grade 8-9) were assessed for each site. A content analysis of the government and hospital-based (GH) websites was conducted to evaluate the availability of information on LA, focusing on information tailored to parents and children. The remaining websites (e.g. non-profit foundations, for-profit organizations, etc.) were assessed to identify alignment with the reference

standard of the Public Health Agency of Canada, and where non-alignment occurred (conflicting with or absent from PHAC), qualitative analysis was performed to identify themes in the information presented.
Results: 82 websites were reviewed. 22% had a FKGL < grade 8, 29% grade 8-12, and 49% > grade 12. One-third (32%) had a FRES ≥ 60. Among 49 GH websites, 17 (35%) specified which joints may become painful in LD. Of these 17, only 8 (47%) specifically used the term LA as a manifestation of LD, and only 4 websites contained information on the clinical course and outcomes of LA. 21/49 (43%) websites had parent-specific information, while only 2/49 (4%) had pediatric-targeted information. Qualitative analysis of the remaining 33 websites included focus on broad symptomology related to LD, negative outcomes, long term symptoms, and uncertainty surrounding LD testing.
Conclusion: The reading level of online information may hinder public comprehension. There are gaps in specific information presented about LA overall and in information catering to children, youth, and parents. This information will guide the development of evidence-based knowledge translation tools, as well as inform healthcare providers of the scope of online information their patients may encounter.
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Rheuminating About Alcohol and Drugs? Assessing the Informational Needs of Adolescents and Young Adults with Chronic Rheumatic Disease

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Objectives: Providing information to adolescents and young adults (AYA) with rheumatic diseases about the use of alcohol, recreational drugs, and reproductive health and their impact on disease and medications is critical to ensuring they can make educated decisions about their health and behaviours. We aimed to understand the informational needs of AYAs and their preferences for how (e.g., websites, pamphlets, etc.), when (e.g., starting age) and how frequently (e.g., every visit, annually) they would like to receive this information.
Methods: A questionnaire co-developed with patient partners was circulated to 16-22 year olds in rheumatology clinics and by social media. Participants rated how informed they were on alcohol and recreational drug consumption, and reproductive health, as it related to their disease and medications. Responses were summarized using descriptive statistics. Respondents were then invited to participate in a virtual focus group facilitated by a Child Life Specialist and patient partner. Focus group scripts were analysed using inductive thematic analyses.
Results: Of 93 survey responses, 67 completed the entire questionnaire. Most respondents were female (80.6%), 16-18 years old (55.9%) and diagnosed with JIA (67.7%). The majority felt poorly informed on how to manage symptoms after drug/alcohol consumption (68%/58%), how different types of recreational drugs/alcohol interact with medications (67%/54%), and considerations when becoming a parent (47.8%). Fewer respondents felt poorly informed about short- (37.7%/24.4%) and long- (36.2%/23.1%) term effects of recreational drug/alcohol consumption. Participants preferred informational resources were, in order, websites (70.2%), healthcare team (49.7%), pamphlets/brochures (39.2%), podcasts (27.6%) and parent/caregiver

(18.5%). Focus group participants (8 females, 3 males) generally felt uninformed about how recreational drug and alcohol consumption, and reproductive health interacts with their medications and rheumatic disease (Table 1). Females preferred to receive information through social media/websites and males wanted an online collection of resources to rate and provide comments, while both valued learning from lived experiences. When asked which topics should be prioritized in educational materials, the top three were effects of alcohol on medications, effects of medications on reproductive health, and limits of consuming alcohol on medication and with rheumatic disease. Their preference of when and how often they wanted to receive information was age 14-16 years, with discussions occurring at every clinic visit.
Conclusion: The majority of AYA felt poorly informed about potentially harmful activities and expressed desire for more education. Preferred educational resources included social media, resource databases, and stories of lived experiences.

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Long-Term Outcomes of Postnatal Immunosuppressive Therapy in Children with Cardiac Neonatal Lupus Erythematosus

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Objectives: Neonatal lupus erythematosus (NLE) is a passively acquired autoimmune condition. The antibody-mediated neonatal heart disease of NLE is associated with a high risk of mortality and adverse health outcomes. Prenatal treatment can slow progression to complete heart block and improve neonatal survival, but the impacts of postnatal immunosuppressant treatment have not been described. This study describes the outcomes of children with antibody-mediated cardiac NLE treated with postnatal therapy.
Methods: We reviewed patients consented from the NLE clinic in a tertiary pediatric center born between January 1, 1997 – June 10, 2024. We identified patients with cardiac manifestations who received postnatal immunosuppressants. The protocol typically included 1 dose of intravenous immunoglobulin (IVIG) 2g/kg, pulse corticosteroid of 30 mg/kg/day for 3 days, followed by 2 mg/kg/day for 4 weeks with tapering guided by troponin levels. We reviewed medical records with long-term outcomes supplemented by patient/parent questionnaires. We report the prevalence of features and outcomes using summary statistics.
Results: We reviewed 33 patients with cardiac manifestations of NLE and postnatal therapy. Of the total cohort, 28 (85%) mothers received prenatal immunosuppressive therapy with dexamethasone, IVIG and/or a beta agonist. The median duration of follow-up was 6.04 years (IQR: 2.47 – 11.36 years). The majority (70%) of patients presented with heart block at birth (first-degree/second-degree atrioventricular block [n=7], complete heart block [n=16]). The remaining 10 patients had extranodal manifestations of cardiac inflammation, including echogenic endocardium and valvular regurgitation. Of the 7 patients with first or second-degree block at birth, 4 progressed to complete heart block within an average of 11 months. One patient with first-degree block had complete reversal to normal sinus rhythm. Of the 18 (70%) patients

that required a permanent pacemaker, 83% were paced within the first year of life. Of all patients that developed complete heart block in their lifetime, 2 never required pacing (age at last follow-up 17.38 and 19.25 years). No patients required a heart transplant. Three patients developed device-associated or sternal wound infections an average of 1.1 months after birth. Mortality in the cohort was 9% with cause of death attributed to circulatory shock due to sepsis and an unrelated genetic syndrome.

Conclusion: We report on the outcomes of a large series of children with cardiac NLE who received postnatal immunosuppressive therapy. The vast majority of patients had good outcomes. Postnatal immunosuppressive therapy may be responsible for improved cardiovascular outcomes in children with antibody-mediated neonatal heart disease.

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Identifying Clinically-Based Patient Clusters for People with Systemic Inflammatory Disease Using Unsupervised Machine Learning

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Objectives: Systemic inflammatory diseases (SIDs) are characterized by non-infectious multisystem inflammation. Genetic panels diagnose only 25% of suspected SID patients, due to SIDs' clinical and genetic heterogeneity. We hypothesize that unsupervised machine learning and multifactorial data integration of clinical and laboratory data will improve the diagnosis and management of SIDs by identifying clinically-based patient phenotypes.

Methods: We included pediatric genetically undiagnosed SID patients (symptom onset <18 years old) with clinical, laboratory, and whole-exome sequencing data. Genetic ancestry was inferred using principal components and PEDDY with 1K Genomes as a referent. Disease manifestations were divided into clinical and laboratory data sets, weighted by missingness and the data set size, then input into similarity network fusion (SNF) to identify patient clusters. Fisher's exact test (Bonferroni corrected $P<0.0004$) identified variables with different distributions between clusters. Clusters

were validated with 1000 independent simulated SNFs (simSNF). In each simSNF, we randomly used 70% of the cohort, thereafter the results across all iterations were aggregated. We tested autosomes (n=17443) and chromosome X (n=737) gene-level associations between SNF-clusters, adjusted for sex and ancestry, using SKAT-O (SAIGEv1.4.5). We completed gene set enrichment pathway analysis aggregated with SKAT-O genetic associations across all Biological Process Gene Ontology pathways. We estimated the effective number of independent pathways (Galwey method, P<4.9x10-5; 0.05/3571 independent pathways).
Results: We included 104 patients with undifferentiated SID (Figure 1A). SNF revealed 2 clusters. The median age of symptom onset in cluster 1 (n=72) was 5.7 years (Q1-Q3: 3.3-11.2) and cluster 2 (n=32), 6 years (Q1-Q3: 1-13.6). Cluster 2 included patients with consistently higher prevalence (>946/1000 simSNFs) of elevated levels of IgG antibodies (according to each laboratory's reference standard), transaminitis, anti-nuclear antibodies, anemia, and macrophage activation syndrome compared to patients in cluster 1 (P<4.9x10-5; Figure 1B). Laboratory manifestations predominantly characterized the clusters. Sensitivity analysis demonstrated that 89% of patients consistently clustered together over 1000 simSNFs. Individually, none of the tested genes were associated with cluster membership (P>2.5x10-6). Pathway analysis demonstrated a significant association between "flavonoid metabolic process" GO:0009812 and cluster membership (NES=1.94; P=3.7x10-6). This metabolic process is a known anti-inflammatory pathway responsible for arachidonic acid metabolism, inhibiting NF-κB and MAPK signaling, and suppressing dendritic and mast cell activation.
Conclusion: We identified 2 robust patient clusters from clinical and laboratory manifestations in a heterogeneous SID cohort with SNF. Cluster differences were primarily influenced by laboratory manifestations. Future work will use imputed gene expression to determine the role of flavonoid metabolism on SID pathogenesis.

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Identifying Clinical Endophenotypes in Childhood-Onset Systemic Lupus Erythematosus Using Unsupervised Machine Learning

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Objectives: Childhood-onset systemic lupus erythematosus (cSLE) is a clinically heterogeneous autoimmune disease. We hypothesize that unsupervised machine learning may identify clinically homogeneous patient subtypes with distinct genetics.
Methods: We included cSLE patients diagnosed and followed at a tertiary care pediatric lupus clinic between 1992–2023 and genotyped using Illumina multiethnic arrays, imputed with TopMed. We extracted SLE manifestations, date of manifestation onset, and demographic characteristics from dedicated Lupus databases. Genetic ancestry was inferred using principal components and ADMIXTURE with 1K Genomes as a referent. We used the

presence/absence and time to each SLE manifestation onset from SLE diagnosis to identify patient clusters with similarity network fusion (SNF). SNF clusters were validated with simulation-based sensitivity analysis. We ran 1000 independent simulated SNFs (simSNF). In each simSNF, we randomly used 70% of the cohort, and then the results across all iterations were aggregated. Kaplan-Meier and Cox models compared time to manifestation onset between clusters. Cluster differences in demographic and manifestation prevalences were tested using χ^2 or Fisher's exact test. We tested autosomes (n= 17448) and chromosome X (n=713) gene-level associations between SNF-clusters, adjusted for sex and ancestry, using SKAT-O (SAIGEv1.4.5). We completed gene set enrichment pathway analysis aggregated with SKAT-O genetic associations across 'Immune system process' Gene Ontology pathway (GO:0002376) and its decedents. We estimated the effective number of independent immune-related pathways (Galwey method, P<7x10-5; 0.05/664 independent pathways).

Results: In a cohort of 442 cSLE patients (83% female, median diagnosis age 14.2 years), SNF identified 2 clusters. Cluster 1 (n=205) were predominantly of European ancestry (41%), while cluster 2 (n=237) was mainly composed of patients of East Asian (30%) and South Asian (22%) ancestry (P=3×10-9) (Figure 1A). Cluster 2 patients had higher prevalence and earlier onset of 9 cSLE manifestations (e.g. lupus nephritis III/IV, anemia, anti-dsDNA) in >900/1000 simSNFs (HR>1.8; P<6×10-5) (Figure 1B). Simulation-based sensitivity analysis demonstrated that 95% of patients consistently clustered together over 1000 simulations. Individually, none of the tested genes were associated with cluster membership (P>5.8x10-8). None of the tested immunology related GO pathways were significantly associated with cluster membership.

Conclusion: In a large multiethnic cSLE cohort, SNF identified 2 robust clusters. The cluster with more severe disease and earlier onset was enriched for patients of East and South Asian ancestry. We did not find an association between genes or immunologic gene pathways and cluster membership.

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Disease Burden and Comorbidities in Patients with Psoriatic Arthritis and Concomitant Obesity - A Pooled Analysis of Three Clinical Trials

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Objectives: The relationship between psoriatic arthritis (PsA) and obesity is complex and may be bidirectional. Obesity can increase the risk of developing PsA, and weight loss interventions in patients with PsA may lead to reducing disease activity. This analysis pooled data from SPIRIT-P1, SPIRIT-P2, and SPIRIT-H2H clinical trials with biologic-naive and biologic-experienced adult patients with active PsA.

Methods: Patient characteristics, disease burden, and comorbidities at baseline (BL) were analyzed across the following body mass index (BMI, kg/m2) groups: <25 (normal), ≥25 to <30 (overweight), and ≥30 (obesity). The non-parametric Mann-Whitney U test was used to statistically compare differences between obesity or overweight groups to the normal group, with

p-value ≤0.05 signaling statistical differences.
Results: Among 1284 patients, 42.6% had a BMI of ≥30 (obesity). Patients with obesity had higher mean (standard deviation) tender joint counts (23.0 [14.7]), swollen joint counts (12.1 [9.2]), Disease Activity index in PsA (49.1 [23.0]), Disease Activity Score 28-CRP (5.1 [1.0]), fatigue numeric rating scale score (6.2 [2.3]), Health Assessment Questionnaire-Disability Index score (1.3 [0.6]), and 36-Item Short Form Health Survey (SF-36) Physical Component Summary score (34.0 [9.0]) compared to the normal group, with statistical significance (p≤0.05). Similar numerical trends were observed for overweight groups compared to normal group at BL, but without statistical significance (Table 1). SF-36 Mental Component Summary scores were statistically significant for obesity (46.2 [12.3]) and overweight (47.0 [11.8]) groups compared to normal group. Current enthesitis diagnosis was higher in obesity (66.2%) and overweight (58.1%) groups compared to the normal group (54.4%). Patients with higher BMI showed a greater prevalence of comorbidities at BL: cardiovascular disease (obesity 55.4%, overweight 36.0%, normal 18.1%), hypertension (obesity 51.9%, overweight 30.8%, normal 11.4%), hyperlipidemia (obesity 5.5%, overweight 5.0%, normal 1.7%), diabetes (obesity 19.4%, overweight 12.8%, normal 3.4%), and metabolic dysfunction-associated liver disease (obesity 1.5%, overweight 0.7%, normal 0.7%).
Conclusion: Active PsA patients enrolled in the SPIRIT program with obesity or overweight experienced higher BL cardiometabolic burdens like hypertension, hyperlipidemia, diabetes, cardiovascular disease, and metabolic dysfunction-associated liver disease, along with higher disease burden as evident by disease activity and patient-reported outcome measures. These underscore the broader unmet healthcare needs in PsA patients with increased BMI. With new options to manage both active PsA and comorbidities, there may be an opportunity for rheumatologists to intervene to provide holistic care, shifting from disease management to health improvement.

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Dietary Interventions in Psoriatic Arthritis: A Randomized Controlled Clinical Trial

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Objectives: The Dietary Interventions in Psoriatic Arthritis (DIPSA) study is a multicentre randomized controlled trial (RCT) designed to evaluate the efficacy of two personalized dietary interventions in improving clinical outcomes in patients with active psoriatic arthritis (PsA), compared to standard of care.
Methods: Adults with moderately active PsA (Disease Activity index for PsA (DAPSA) >10), BMI 25-40, and stable therapy were recruited from 3 centres. Participants were randomized to one of 3 arms: (1) Mediterranean (Med) diet focused on healthy food composition; (2) Low-calorie Dietary Approaches to Stop Hypertension (DASH-LC) diet targeting weight reduction; or (3) Standard-of-care control arm receiving general, non-personalized dietary advice.

Interventions were delivered by registered dietitians through 2 in-person consultations and 7 structured telephone sessions. Clinical evaluations were performed at baseline, 12, and 24 weeks. Patient-reported outcomes were collected from weeks 0 to 24. The primary outcome was change in DAPSA. Secondary outcomes included changes in pain, PROMIS fatigue, Psoriatic Arthritis Impact of Disease (PsAID), tender/swollen joint counts, anthropometric measures, and inflammatory markers. Hierarchical mixed effect regression models were used for the change in responses from baseline and to assess differences between arms.
Results: Of 92 randomized patients (Med: n=31, DASH-LC: n=30, Control: n=31), 80 provided complete data on responses. Mean age was 55±13 (70% women) and mean BMI was 33±4.3. All groups experienced modest and statistically significant weight loss by week 12 (Med: -1.36 kg; DASH-LC: -2.47 kg; Control: -1.88 kg) (Figure 1A), with small additional reductions by week 24. No significant differences in weight loss were observed between arms. At week 12, significant reductions in DAPSA were observed in the DASH-LC (-4.93) and control (-4.25) groups; by week 24 all groups showed improvement (Med: -4.87; DASH-LC: -5.42; Control: -6.53) (Figure 1B) with no significant differences between-groups. Minimal Disease Activity (MDA) was achieved at week 12 by 38% in DASH-LC and 29% in Med versus 16% in control ($p=0.23$ and $p=0.06$, respectively) (Figure 1C), though week 24 rates were similar across groups. Improvements in pain, fatigue, PsAID, and tender joint counts were observed across all arms. The magnitude of weight loss was significantly associated with improvement in clinical outcomes, including DAPSA, pain, and tender joint count, independent of treatment group (Figure 1D-1E).
Conclusion: Both personalized dietary interventions and standard dietary advice led to modest weight loss and improvements in PsA disease activity. The amount of weight lost was positively associated with the reduction in symptoms.

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The Development and Validation of a Diagnostic Ultrasound Enthesitis Score (Duet) for Psoriatic Arthritis

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Objectives: Enthesitis is a key lesion in psoriatic arthritis (PsA). The Diagnostic Ultrasound

Enthesitis Tool (DUET) study aimed to develop and validate a novel sonographic scoring system for enthesitis to aid PsA diagnosis.
Methods: We prospectively enrolled patients with early PsA, psoriasis alone, and people with non-inflammatory musculoskeletal symptoms as controls, across 17 centers. Participants underwent ultrasound assessments of 16 entheseal sites in the upper and lower extremities, performed by local sonographers. Images were centrally reviewed by 3 readers to derive a consensus score for inflammatory lesions (hypoechogenicity [0-1], thickening [0-1], power Doppler [PD, 0-3]) and structural lesions (calcification [0-3], enthesophyte [0-3], erosion [0-1]). Using a stepwise approach with logistic regression models stratified by age, we identified optimal combinations of lesions and their weighting, and entheseal sites that maximized the ability to distinguish PsA from controls. Data from the discovery cohort, supplemented by an existing validation dataset, were used to determine cut-off points that optimize sensitivity while maintaining specificity above 70%. We further evaluated the association between the DUET score and PsA disease activity measures.
Results: We analyzed 213 patients with PsA (mean duration 1.9±3.4 yrs), 100 with psoriasis and 106 controls. The mean age was 49.9±14.6 and 53.7% were females. Tenderness at ≥1 entheseal site was observed in 70% of PsA patients, 49% of controls and 33% of psoriasis. Initial evaluation of 4 inflammatory and 5 structural sub-scores across 16 entheseal sites yielded 48 candidate scores. Stratification by age improved discriminative performance. The best performing score (DUET score), comprising inflammatory (hypoechogenicity+thickening+2×PD) and structural (enthesophyte+3×erosion) (Figure 1A), sub-scores at the Achilles, patellar tendon insertion, and triceps tendon, achieved an overall AUC of 0.65. Age-specific cut-offs (at age 55) yielded specificity of 73-74% and sensitivity of 47-49% (Figure 1B). In the validation cohort (101 PsA, 69 controls), specificity improved to 74-100% with comparable sensitivity (49-52%). Sensitivity increased up to 63% in patients with tender entheseal sites (Figure 1C). The mean DUET score was significantly higher in PsA compared with controls and psoriasis (9.07 vs. 5.48 and 6.38, respectively; $p<0.01$) (Figure 1D). Scores were elevated among obese patients, those with tender entheses, and those about to escalate PsA therapy.
Conclusion: DUET is a newly developed sonographic tool that may assist in the diagnosis of PsA, particularly among individuals with tender entheseal sites. The findings suggest that large joint enthesitis is a universal feature of early PsA.

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Differential Impact of Body Mass Index on Minimal Disease Activity Across Therapies in Psoriatic Arthritis

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Objectives: Overweight and obesity are associated with reduced odds of achieving minimal disease activity (MDA). Whether this effect is mediated by direct inflammation or psychosocial

factors remains unclear. This study aimed to assess a) the influence of body mass index (BMI) on MDA and its components, b) study this association across drug classes.
Methods: Patients with available body mass index (BMI) values were selected from a large longitudinally assessed PsA cohort followed from 1978. These patients are followed every six months with comprehensive documentation of demographic data, clinical and patient-reported outcomes, and treatment details. Generalized estimating equations (GEE) were used to assess the association of BMI with MDA and its subcomponents, adjusting for age, sex, anxiety, depression, fibromyalgia, smoking, radiographic damage (modified Steinbrocker score), osteoarthritis, use of TNFi and PDE4i. We also evaluated the association between BMI at drug initiation and longitudinally assessed BMI (to incorporate effects of drugs on BMI) with MDA across six drug classes (TNFi, IL-17i, IL-23i, IL-12/23i, JAKi, PDE4i) using univariable and multivariable GEE. The multivariable model was adjusted for age, sex, anxiety, depression, fibromyalgia, smoking, radiographic damage (modified Steinbrocker score), osteoarthritis, and line of treatment.
Results: Of 1291 patients included, the mean age was 44.7 (SD 13) years, and 44% were males. The mean BMI was 28.8 (SD 6.36) kg/m2. 582 patients received b- and/or tsDMARDs (80 patients - infliximab, 353 - other TNFis, 166 - IL17i, 64 - IL12/23i, 71 - IL23i, 32 - JAKi, and 57 - PDE4i). Higher BMI was significantly associated with lower odds of MDA [OR 0.97; 95% CI 0.94-0.99], and worse outcomes across multiple MDA subcomponents, including enthesitis, tender joint count, PASI, patient pain, global assessments, and HAQ, but not swollen joint count in the multivariable model (Figure 1A). In multivariable models for drug stratified analyses, both BMI at drug initiation [0.95 (0.93-0.98)] and longitudinally assessed BMI [0.95 (0.92-0.97)] were significantly associated with reduced MDA in the TNFi group. BMI did not impact the response across infliximab and other drug groups (Figure 1B and 1C).
Conclusion: BMI is independently associated with reduced odds of being in MDA, largely driven by subjective and skin domains. The impact appears most pronounced among patients treated with TNFis, but not infliximab or other drug classes. This highlights the need for tailored therapeutic strategies in obese PsA patients and the potential importance of addressing psychosocial factors and weight management in clinical care.

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Clinical Relevance of Pelvic and Heel Enthesophytes in Psoriatic Arthritis

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Objectives: Enthesitis is a hallmark feature of psoriatic arthritis (PsA), but its clinical assessment can be confounded by subjective assessment and overlapping fibromyalgia. We aimed to investigate the clinical and functional associations of radiographic enthesophytes in a large longitudinal PsA cohort.
Methods: Data from 1,602 prospectively enrolled PsA patients with available radiographs were analyzed. Clinical assessments are conducted every six months for recording disease activity, patient-reported outcomes (Health Assessment Questionnaire [HAQ] and Short Form 36 physical

function [SF-36 PF]), and treatment details, with radiographs obtained biennially. Radiographic pelvic enthesophytes and calcaneal spurs (Achilles/plantar) are systematically recorded. Associations of enthesophytes (all, pelvic, and heel) with demographic, clinical, and functional measures were evaluated using generalized estimating equations.
Results: 1,176 patients of 1,602 (73%) had enthesophytes over the follow-up period; 763 (48%) had pelvic enthesophytes and 1,017 (63%) had calcaneal spurs. Pelvic enthesophytes were associated with older age (OR 1.04, 95% CI 1.03-1.05), male sex (2.08, 1.74-2.49), and lower tender joint counts (0.99, 0.97-1.00). Calcaneal spurs were associated with lower swollen joint counts (0.98, 0.96-1.00). Both pelvic and calcaneal enthesophytes were associated with higher body mass index (BMI), osteoarthritis, concomitant presence of diffuse idiopathic skeletal hyperostosis (DISH), diabetes mellitus, psoriasis area and severity index (PASI) scores, axial disease, and higher modified Steinbrocker scores. No association was observed with clinical enthesitis. Functionally, calcaneal spurs were linked to worse HAQ (OR 1.24, 95% CI 1.04-1.47) and worse SF36 physical function scores (0.99, 0.99-1.00), whereas pelvic enthesophytes had minimal impact on function. There was no association observed with patient global assessment (Figure 1).
Conclusion: Pelvic and calcaneal radiographic enthesophytes are common in PsA and associate with PsA-related (PASI, axial involvement, greater peripheral damage) and comorbid factors (higher BMI, diabetes, OA/DISH, and for pelvic subtype, male sex and older age). Calcaneal spurs adversely affect functional indices, unlike pelvic enthesophytes. These findings emphasize the relevance of radiographic enthesophytes beyond clinical enthesitis assessment.

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Real-World Performance of GRAPPA and EULAR Definitions of Difficult-To-Treat (D2T) Psoriatic Arthritis: Insights from the Orchestra Cohort

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Objectives: Psoriatic arthritis (PsA) is a complex inflammatory disease with significant musculoskeletal, dermatological, and comorbidity burden. Despite therapeutic advances, many patients remain difficult to treat. Conventional definitions often overlook distinctions between inflammatory and non-inflammatory drivers, risking inappropriate treatment escalation. Two consensus frameworks—the Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA) and the European Alliance of Associations for Rheumatology (EULAR)—have recently been proposed to better capture this complexity and differentiate true inflammatory refractoriness from non-inflammatory causes.[1,2] In this study, we aim to evaluate the applicability, overlap, and clinical utility of GRAPPA and EULAR definitions for complex/difficult-to-manage (C2M/D2M) and treatment-refractory PsA (TrPsA) in a real-world cohort.
Methods: We applied GRAPPA and EULAR frameworks to 76 PsA patients from the Ottawa Rheumatology CompreHEnSive TReatment and Assessment (ORCHESTRA) cohort, which includes patients with inflammatory arthritis initiating a new advanced therapy. Patients were categorized into broader groups, C2M-PsA (GRAPPA) and D2M-PsA (EULAR), and narrower

inflammation-based subsets, TrPsA under GRAPPA and EULAR. Disease characteristics and Minimal Disease Activity (MDA) outcomes were assessed at 3 and 6 months.
Results: GRAPPA identified more patients as C2M-PsA (38/76; 50%) than EULAR's D2M-PsA (17/76; 22.4%), reflecting broader inclusion. All D2M cases were encompassed within C2M, while GRAPPA uniquely identified 21 patients (Table). TrPsA classification showed near-perfect agreement ($\kappa = 0.917$). No significant MDA differences were observed across definitions, though within GRAPPA, inflammatory TrPsA showed numerically higher MDA rates. Non-articular domains (dactylitis, nail/skin psoriasis) were more frequently captured in the broader C2M/D2M than in the inflammatory subsets.
Conclusion: Applying EULAR and GRAPPA definitions in a real-world PsA cohort revealed complementary strengths: GRAPPA's inclusiveness versus EULAR's selectivity. Evaluating both across real-world and research settings will aid harmonization and validation of D2T-PsA frameworks. Integrating imaging-based models such as Persistent Inflammatory PsA (PiPsA) and Non-Inflammatory PsA (NiPsA) may further refine precision and clinical relevance.
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Defining Difficult-To-Treat Rheumatoid Arthritis in Routine Care: Comparative Performance of Published Criteria and Description of Early and Late D2T-RA Phenotypes

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Objectives: Despite advances in treat-to-target strategies, a subset of rheumatoid arthritis (RA) patients remains refractory to therapy, described as difficult-to-treat RA (D2T-RA). The European Alliance of Associations for Rheumatology (EULAR) has proposed formal criteria for D2T RA. Yet, their application in real-world settings varies, leading to inconsistent prevalence and limited comparability across studies.[1,2] Moreover, the timing of refractoriness—whether patients become D2T early or later in their course—remains largely unexplored. This study compared several published D2T-RA definitions within a real-world cohort and introduced a temporal framework distinguishing early and late D2T-RA.
Methods: Using data from the Ontario Best Practices Research Initiative (OBRI), a real-world RA registry, we evaluated four adapted versions of the EULAR D2T-RA definition among patients who initiated their first advanced therapy after enrollment. These adaptations differed by the timeframe allowed for treatment failure and the disease activity measures applied. We

compared their prevalence, overlap, and agreement, and explored temporal anchors to identify balanced thresholds for distinguishing early versus late D2T-RA.
Results: Among 1121 eligible patients, 215 (19%) met D2T-RA criteria according to ≥1 definition (Table). Their mean (±SD) age was 54.8 ± 11.5 years, and most were female (85.1%). The mean disease duration was 7.7 ± 8.6 years. The prevalence of D2T-RA ranged from 5.5% (definition 4) to 12.7% (definition 2). Definitions 1 and 2, which incorporated multiple disease activity indicators, identified the largest proportion of patients, whereas definition 4—based solely on initiation of a third b/tsDMARD without timeframe restriction—was most restrictive. Agreement between definitions ranged widely (κ = –0.67 to 0.87), with the highest concordance between definitions 1 and 2 (κ = 0.87). Temporal analyses across multiple anchors showed that defining D2T onset from the initiation of the first advanced therapy yielded the most balanced early-to-late distribution, approximately 45% versus 55%—when applying a two-year threshold, compared with more skewed ratios (>70% late) observed with other temporal anchors.
Conclusion: Our findings highlight substantial heterogeneity across adapted D2T-RA definitions, indicating they are not interchangeable. More inclusive definitions identify broader groups of patients with active disease and incorporate clinical and patient-reported measures, whereas more restrictive definitions—focused mainly on the number of advanced therapies—may underestimate disease impact. A two-year threshold from the first advanced therapy offers a balanced distinction between early and late D2T-RA. These findings emphasize the need for harmonized multidimensional definitions and temporal stratification to improve comparability and guide clinical decision-making.
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Baseline Predictors of Difficult-To-Treat Rheumatoid Arthritis Across Adapted Definitions: Insights from the OBRI-RA Registry

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Objectives: In the first phase of this study, four adapted definitions of difficult-to-treat rheumatoid arthritis (D2T-RA) were evaluated within the Ontario Best Practices Research Initiative (OBRI), differing by criteria for treatment failure, active or symptomatic disease, and clinician perception (Figure). These definitions showed heterogeneity in prevalence, with broader definitions capturing patients with higher disease activity and worse function. Building

on those findings, this analysis examined baseline clinical and demographic characteristics associated with D2T-RA and assessed whether similar predictors emerged across the four definitions.
Methods: Data were derived from the Ontario Best Practices Research Initiative (OBRI), a longitudinal, real-world registry of patients with rheumatoid arthritis (RA). Multivariable logistic regression analyses were conducted among participants with established RA who initiated their first advanced therapy (biologic or targeted synthetic DMARD) after enrollment. Candidate predictors were identified a priori based on existing literature encompassing demographic, clinical, serologic, and treatment-related variables. Separate regression models were developed for each of the four adapted definitions of D2T-RA.
Results: A total of 507 patients were included in the complete case analysis. The mean (SD) age was 56.9 (12.2) years, the mean disease duration was 7.6 (9.1) years, and 80.3% were female. The prevalence of difficult-to-treat RA (D2T-RA) ranged from 5.7% (Definition 4) to 14.4% (Definition 2). In multivariable models, female sex independently predicted D2T-RA under Definitions 2 (OR 2.46, 95% CI 1.10–5.49) and 3 (OR 3.42, 95% CI 1.11–10.5), and higher HAQ-pain scores were consistently associated with D2T-RA across inclusive definitions (OR 1.60–2.00, $p < 0.05$). Radiographic erosions were significant only under Definition 3 (OR 2.03, 95% CI 1.02–4.03). No predictors reached significance for the restrictive Definition 4 aside from borderline methotrexate use ($p = 0.053$). Disease duration, seropositivity, smoking, obesity, and baseline disease activity were not independently associated with D2T-RA. Model performance was fair across definitions (AUC 0.68–0.74) (Figure).
Conclusion: Female sex and higher pain-related functional impairment consistently predicted D2T-RA across the more inclusive definitions, suggesting that sex/gender considerations and pain perception are important factors to consider in treatment refractoriness. In contrast, restrictive definitions based solely on treatment count demonstrated limited discriminative value. These findings suggest that adapted D2T-RA definitions capture different facets of the disease spectrum, and their use should be guided by the specific clinical or research context—whether the goal is to identify persistent refractory inflammatory disease or to characterize the broader, multidimensional burden encountered in real-world practice.

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Clinical Joint Tenderness in First-Nations First-Degree Relatives of Rheumatoid Arthritis Patients: Examining Factors Associated with Functional Disability and Progression to RA

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Objectives: Rheumatoid arthritis (RA) is a systemic autoimmune disease affecting synovial joints. Prior to the clinical onset of arthritis, autoantibodies and non-specific joint symptoms often appear in the absence of joint swelling. We previously found that functional disability correlates with anti-citrullinated protein antibodies (ACPA) and future RA development. Here, we examine the role of joint tenderness on physical exam in a cohort of First Nations first-degree relatives (FDRs) of RA patients in Manitoba.[1,2]
Methods: Tender joint counts from a 66-joint assessment were obtained at the inception visit through clinical examination. Serologic data (RF and ACPA) and patient-reported measures of function, pain, and overall wellness were also collected.
Results: 624 FDR baseline joint tenderness assessments and questionnaires were analyzed. Among these, 211 FDR (33.8%) had at least one tender joint on physical exam. Clinical joint

tenderness was more common in females (p=0.04), individuals with diabetes (Figure 1A), (p=0.03), those living in urban areas (p<0.0001, compared to rural) and participants reporting ≥30 minutes of morning stiffness (p=0.003). Self-reported joint tenderness in the hands was significantly higher in those who reported hand pain (Figure 1B), ($p < 0.0001$). Joint tenderness was also higher in individuals who reported functional disability based on the health assessment questionnaire (Figure 1C), ($p < 0.0001$). Clinical joint tenderness correlated with self-reported fatigue ($r = 0.28$, $p < 0.0001$), pain ($r = 0.33$, $p < 0.0001$), overall wellness ($r = 0.25$, $p < 0.0001$) scores. The presence of ACPA was not associated with joint tenderness ($p = 0.82$). In contrast, RF titers demonstrated a positive correlation with the total number of tender joints ($r = 0.11$, $p = 0.005$) and there was a trend towards increased joint tenderness on examination in RF positive individuals (p=0.15). During follow-up, 20 participants progressed to clinical RA, as previously reported, progressors were younger (p=0.004) and had higher baseline ACPA titers (Figure1D), (p=0.02). 63.2% of progressors exhibited clinically significant tenderness in at least one hand joint however, no individual joints demonstrated a statistically significant difference in tenderness between progressors and non-progressors.

Conclusion: Joint tenderness is common among First Nations FDRs of RA patients and is linked to worse functional and wellness outcomes, particularly in women, diabetics, and urban residents. These findings underscore the need for early identification and monitoring in high-risk groups. A better understanding of how self-reported symptoms and exam findings relate to future RA risk may improve risk stratification and early intervention.

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Giant Cell Arteritis with Scalp and Tongue Necrosis: A Rare Case of Extensive Mucocutaneous Ischemia

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Background: Giant Cell Arteritis (GCA) is a primary large-vessel vasculitis that typically affects individuals over the age of 50.[1] It is characterized by granulomatous inflammation involving all three layers of the vessel wall, primarily affecting the major branches of the aorta, including the extracranial branches of the carotid arteries.[1-3] Typical disease presentations involve polymyalgia rheumatica (PMR), weight loss, jaw claudication, headaches, temporal tenderness, and vision loss (partial or complete).[3]

Case Report: We reviewed the clinical course, diagnostic workup, and management of a 76-year-old Caucasian man with a 60-pack-year smoking history and comorbid hypertension, who developed severe scalp and tongue necrosis from GCA. Clinical data were mainly obtained from dental and rheumatology office visits in addition to pathology reports. Pertinent investigations included CT brain and angiography, laboratory testing (ESR, CRP), oral biopsy, and temporal artery biopsy. Relevant imaging and histopathology findings were incorporated. The patient provided informed consent for publication. The patient experienced several weeks of evolving symptoms, including jaw claudication, bilateral headaches, transient diplopia, and eventually

developed scalp tenderness with necrosis, and a painful tongue ulcer (Figure 1A & B). Initial dental and neurologic evaluations were unrevealing, contributing to a delayed diagnosis. Laboratory studies showed mildly elevated inflammatory markers (ESR 24 mm/hr, CRP 29 mg/L). Temporal artery biopsy confirmed severe active arteritis with multinucleated giant cells and partial luminal occlusion. High-dose prednisone (50 mg daily) was initiated, followed by tocilizumab 162 mg subcutaneously weekly as a steroid-sparing agent. The patient demonstrated rapid clinical improvement, with near-complete resolution of scalp and tongue necrosis within two months (Figure 1C & D) and no recurrence of visual symptoms during follow-up.
Conclusion: This case highlights the importance of promptly recognizing atypical GCA presentations, such as scalp and tongue necrosis, which are linked to delayed diagnosis and increased morbidity. Early initiation of corticosteroids with adjunctive tocilizumab led to rapid recovery and prevention of complications in our patient. Notably, his 60-pack-year smoking history raises the possibility that heavy, long-term smoking may predispose to more severe or necrotizing forms of GCA. Future studies are needed to clarify the role of smoking as a risk factor and potential disease modifier in GCA, which may help guide earlier diagnosis and tailored treatment strategies.
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Higher Anxiety at 3 Months Predicts Escalation to Biologics/JAKi by 12 and 24 Months in Early RA: Results from the Canadian Early Arthritis Cohort (CATCH)

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Objectives: Pain, fatigue, anxiety and depression are common in new RA and may predict worse outcomes. We compared the likelihood of biologics/JAKi use by 12 and 24 months by pain, fatigue, anxiety, and depression status at diagnosis and after 3 months of MTX.
Methods: We evaluated new RA patients in the Canadian Early Arthritis Cohort (CATCH) between 1/17-8/22 with active disease and on MTX. Participants underwent assessments and completed PROMIS-29 at 0 and 3 months. Anxiety, depression, fatigue, and pain interference were defined as PROMIS ≥55. Multivariable logistic regression and ROC curves at baseline and 3 months were adjusted for CDAI, age, sex, race, education, smoking, obesity, comorbidities, serology, and symptom duration.
Results: 255 adults had a mean (SD) age of 56(14), and were mostly women (69%), White (78%) with a CDAI of 30(14) at diagnosis. All started MTX monotherapy [55%] or with csDMARDs [45%]. At 3 months, mean CDAI improved substantially; 41% were classified as

anxious (Table). Mean Pain, Fatigue, Anxiety and Depression scores were 8-15 points higher in anxious vs. non-anxious patients. By 12 months, >2X as many patients who were anxious at 3 months were on advanced therapies (15% vs. 7%); a similar trend was observed at 24 months (18% vs. 10%). However, the proportion of patients on advanced therapies was similar by pain interference, fatigue, or depression status at 3 months. The optimal multivariable model for predicting advanced therapy use by 12 months included Anxiety status and CDAI at 3 months after adjustment for covariates (ROC=0.84). Patients who were anxious at 3 months had 5.1 the odds (95% CI 1.4, 18.2) of being on advanced therapy at 1 year, with a similar trend at 24 months (OR 3.0; 95% CI 1.1, 8.2). In contrast, Depression, Pain, and Fatigue status at 3 months was not associated with a greater likelihood of advanced therapy use by 12 and 24 months.
Conclusion: In CATCH, 41% reported anxiety at 3 months even after a robust response to treatment. A novel finding is that Anxiety at 3 months (but not pain, fatigue, or depression) predicted worse CDAI, PROs and 3-5 times greater odds of advanced therapy use by 12 and 24 months. Anxious patients may be more likely to advocate for a treatment change; anxiety may also reflect a greater impact of social determinants of health. Better understanding of anxiety in early RA may help improve QOL and support treatment decision making.

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Granuloma Annulare as a Mimic for Rheumatoid Nodules: A Diagnostic Challenge

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Background: We present a case of juxta-articular pseudorheumatoid nodules from atypical granuloma annulare as a mimic for true rheumatoid nodules.
Case Report: An 86-year-old male was sent to our rheumatology clinic for evaluation of rheumatoid arthritis. His past medical history was relevant for localized squamous cell carcinoma of the penis, chronic kidney disease, type 2 diabetes mellitus, COPD, provoked pulmonary embolism, and peripheral arterial disease. He was initially sent to a plastic surgeon for multiple painless, skin-colored nodules on his hands and forearms. He had two nodules excised and sent for pathology. On both occasions, palisaded granulomatous inflammation with histiocytes and necrobiosis was seen, consistent with rheumatoid nodules (Figure 1A and 1B). However, on clinical assessment there was no suggestion of previous or current inflammatory arthritis on history or physical exam. There was no history of methotrexate use suggesting methotrexate nodulosis. CT scan of the chest, abdomen and pelvis was negative for active malignancies. Infectious disease consultation did not reveal any other infectious causes, including syphillis. Rheumatoid factor, anti-cyclic citrullinated peptide antibodies (ACPA) and anti-nuclear antibody (ANA) testing were negative. Acid-Fast Bacilli, Grocott Methenamine Silver, Periodic Acid Schiff special stains on the excised nodules were negative for mycobacterial and fungal organisms. Alcian Blue stain was also not prominent (Figure 1C). Given the inconsistency between the clinical context and histologic findings, this case was re-reviewed by two dermatopathologists. It was determined that the most likely diagnosis was a rare, variant of nodular granuloma annulare known as a “juxta-articular pseudorheumatoid nodule”, which can have identical or near identical histology to a rheumatoid nodule. The patient is now followed by dermatology, with a plan of observation and surgical excision as needed.
Conclusion: Rheumatologists, dermatologists, and pathologists should be aware of this rare entity, to avoid confusion and misdiagnosis of rheumatoid arthritis. This phenomenon is uncommon in adults; documentation is limited to case series and its etiology and natural history

in adults are not well documented.[1-3] Distinction on histology from a rheumatoid nodule cannot be made with certainty, but it is possible that pseudorheumatoid nodules can have more histiocytes, mucin, and less stromal fibrosis.[1] Ultimately clinical correlation is important to distinguish from rheumatoid nodules.[1-3] Surgical excision is the most common treatment, although many non-surgical options have been described with limited efficacy and evidence.[2,3]

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Clinical Practice Audit of Hydroxychloroquine Prescription and Monitoring in Rheumatology Practice

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Objectives: Hydroxychloroquine (HCQ) is widely used for autoimmune conditions but carries retinal toxicity risk. Guidelines recommend weight-based dosing (≤5 mg/kg of body weight/day) and regular ophthalmological monitoring, yet clinical adherence varies. This study audits HCQ prescribing practices and monitoring adherence in a community-based rheumatology practice.

Methods: We conducted a retrospective audit examining HCQ prescribing and monitoring patterns from two rheumatologists sharing an electronic medical record (EMR) system. All patients with HCQ exposure between 1999 and May 2025 were included. Data collected included patient demographics, weight, height, rheumatological diagnoses, prescribed doses, treatment duration, and ophthalmological examinations. We identified patients discontinuing HCQ per eye specialist recommendations and collected detailed information on suspected or confirmed retinopathy cases.

Results: Among 1,073 patients prescribed HCQ, 86% were female with mean age 61 years and mean weight 71.5 kg. Mean treatment duration was 116.2 months. Primary diagnoses included rheumatoid arthritis (51.6%), systemic lupus erythematosus (30.4%), and mixed connective tissue disease (6.7%). Fifty patients (4.7%) had missing data that precluded accurate dose calculations. These missing data categories included patient weight, HCQ start/end date, initial dosage, or a combination of all categories. Among patients with complete data, 60.5% received doses ≤5 mg/kg of body weight/day, while 35.9% exceeded this threshold. Regarding monitoring, only 37.5% had documented ophthalmological visits within 5 years of starting HCQ, and 15.7% had visits after 5 years; 46.8% lacked any visit documentation. Twenty-four patients (2.2%) discontinued HCQ per eye specialist advice, with 11 having confirmed HCQ-induced retinopathy. Among these 11 patients, the mean dose was 4.93 mg/kg/day (median 4.71 mg/kg/day). More details regarding these results can be found in (Table 1).

Conclusion: This audit revealed significant gaps in HCQ prescribing and monitoring practices. Over one-third of patients received excessive weight-based doses, and documentation of ophthalmological monitoring was inadequate in nearly half of patients. Key improvements needed include improved documentation of patient weight for accurate dosing calculations, systematic recording of treatment duration and ophthalmological examinations, and clearer

documentation of discontinuation reasons. Implementing standardized protocols and regular audit cycles could enhance patient safety and optimize outcomes while minimizing retinal toxicity risk.

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Perspectives on Clinical Trial Participation for Novel Advanced Therapies: A Focus Group Study in Systemic Lupus Erythematosus

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Objectives: To identify barriers and facilitators perceived by people with SLE regarding participation in clinical trials for novel/advanced agents, such as cellular therapies.

Methods: Adults from our SLE research cohort were invited to participate in 1-hour virtual focus groups concerning their perspectives on clinical trials for novel/advanced SLE therapies. Sessions, facilitated by trained moderators using standardized questions, were recorded and transcribed. An inductive thematic analysis approach was used to code the data and generate themes/sub-themes.

Results: Nineteen patients participated in four focus groups (two in English, two in French). The mean age (range) was 50.0 (21-77) years, and mean disease duration was 21.4 years. Most (90%) of participants were female and 79% (15/19) were White, with the remainder being Black, Asian, and Hispanic. Six major themes emerged: two barriers and four facilitators to trial participation. The first barrier was time and logistical constraints, such as employment and travel. The second was risk aversion, including subthemes of concerns of SLE flare, drug side effects and early-phase trials. Facilitators included receiving clear, detailed clinical trial information. Disease instability was another driver, making patients increasingly willing to accept elevated health risks, time commitment and/or logistical challenges. Desire to support the lupus community was also an important factor. Finally, access in clinical trials to mental health counsellors, peer support, and close medical follow-up were strong facilitators of participation.

Conclusion: We identified potential barriers and facilitators/driving factors for SLE patients regarding clinical trial participation, which are particularly relevant for novel/advanced agents like cellular therapies.

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Artificial Intelligence-Based Online Symptom Assessment Tools for Systemic Lupus Erythematosus Diagnosis: Patient Perspectives

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Objectives: To identify perceptions of SLE patients regarding artificial intelligence (AI)-based online symptom assessment tools, regarding their potential to address diagnostic barriers.
Methods: Adults from our SLE research cohort were invited to participate in 60-90 minute virtual focus groups concerning their experiences obtaining an SLE diagnosis and perspectives on patient-facing online symptom assessment tools to assist/expedite diagnosis. Sessions were facilitated by trained moderators using standardized questions and included a demonstration of an AI-based symptom checker application. An inductive thematic data analysis was used to code the transcripts and generate themes/sub-themes.
Results: Twenty-four patients participated in four focus groups (two in English, two in French). The mean age (standard deviation) was 50.4 (9.7) years and the mean duration (standard deviation) since SLE diagnosis was 19.1 (8.8) years. Most (92%) of participants were female and 50% were White, with the remainder being Asian, Black, Hispanic or Indigenous. Themes concerned the following: 1) diagnostic journeys including barriers to timely SLE diagnosis, 2) familiarity with online health tools, 3) perceived benefits and 4) concerns regarding AI symptom assessment tools. The most prominent benefits identified were symptom awareness and validation, encouragement to seek care, and facilitation of healthcare discussions. Numerous concerns were expressed including narrow usefulness given SLE complexity, structural limitations relating to healthcare access and provider receptiveness, the possibility of misinformation, and minor issues of data privacy.
Conclusion: This paper provides SLE patient perspectives on the benefits and limitations of AI-based online symptom assessment tools in addressing diagnostic delays of a complex diagnostic condition.

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Temporal Trends in the Incidence of Systemic Lupus Erythematosus in the United States: Holding Steady?

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Objectives: Systemic lupus erythematosus (SLE) is associated with significant morbidity and healthcare burden. Estimates of SLE incidence help inform research and public health initiatives, including rheumatology workforce planning. SLE incidence estimates may be affected by health care access or care-seeking behaviour (impacted by COVID-19 pandemic years, 2020-2022) and/or by environmental factors (e.g. viral triggers, climate change). We estimated annual SLE incidence rates over time, using real-world US data.

Methods: Using the Merative™ MarketScan® Commercial (+/-Medicare Supplemental) databases, we identified adults (18+) with >2 years of continuous enrollment and no SLE diagnoses during those 2 years between Jan. 2016-Dec. 2022. Among these, a 20% random sample was selected for analysis. Time zero was first qualifying date for cohort entry. Incident SLE was defined by International Classification of Diseases diagnostic codes, based on ≥2 physician visits ≥8 weeks apart within two years and/or ≥1 hospitalization. Individuals were followed from time zero until earliest SLE diagnosis, health plan disenrollment, or end of follow-up. Annual SLE incidence rates were calculated with 95% confidence intervals (CI). We report incidence overall and stratified by sex. Female-specific rates were further stratified according to whether person-time was contributed during reproductive age (age < 52). We assessed age (continuous) and sex in a multivariate hazard regression predicting SLE onset, controlling for calendar year.
Results: We analyzed 4.6 million individuals followed an average of 2.8 years (standard deviation, SD 2.2); 52.6% were female, mean age at time zero was 43.1 years (SD 14.8). During this period, 1,593 new SLE cases (89.2% female) were identified across 12.9 million person-years (12.3 events per 100,000 person-years). No clear difference in incidence comparing 2020-2022 (12.6 events /100,000 person-years) versus 2016-2019 (12.2 events/100,000 person-years). In any given calendar year, incidence was much greater among females, with a higher incidence during reproductive years (23.3 events/100,000 person-years; 95% CI 21.9-24.9) versus later (16.8 events/100,000 person-years; 95% CI 15.3-18.5) (Table 1). In multivariate models, hazard ratios (HR) for female sex was 7.47 (95% CI 6.38-8.75) and for age (continuous),1.00 (95% CI 1.00, 1.01).
Conclusion: These clinically relevant real-world data suggest SLE incidence in the US is holding steady, during the period 2016-2022. Limitations of our analyses include selection bias (all individuals had private insurance), short average follow-up time, and possible outcome misclassification (e.g. prevalent SLE cases mischaracterized as incident). Ongoing analyses will consider other factors, such as urban-versus-rural residence, race/ethnicity, and environmental exposures over longer periods.

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Ozone and Fine Particulate Matter Components of Air Pollution Are Associated with Systemic Lupus Erythematosus Risk

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Objectives: Concerns are growing regarding the relationship of air pollution (especially fine particulate matter, PM2.5) in diseases like systemic lupus erythematosus (SLE). It is unclear which chemical components of ambient PM2.5 may be most harmful, and whether other air pollutants play additional roles. We aimed to evaluate the association between the mixture of PM2.5 components and SLE onset, quantifying their relative contributions to SLE risk, and potential effect modification by ambient ozone levels.

Methods: Using MarketScan® administrative health data, we assembled an urban open cohort of all enrollees ≥18-year-old (without prior SLE) with residential core-based statistical area (CBSA) information. Each year after 2013, eligible individuals entered the cohort and were followed until SLE onset, death, insurance disenrollment, or study end (Dec. 2023). SLE incident cases were identified by ≥1 hospitalization or ≥2 physician billing diagnostic codes. From the cohort, all SLE cases and a 20% random baseline sub-cohort were combined into a case-cohort sample. Concentrations of PM2.5 components (ammonium, black carbon, mineral dust, sulfate, nitrate, organic matter, sea salt) and ambient ozone for two years before cohort entry were estimated by satellite- and ground-based models and assigned based on CBSAs at cohort entry. Extended quantile g-computation models assessed potential associations of SLE onset with the mixture of PM2.5components, ozone and their interaction, adjusting for sex, age, baseline chronic obstructive pulmonary disease (as a proxy for smoking), geographic region, and year of cohort entry. Index weights estimated by quantile g-computation models quantified the relative contributions of individual PM2.5 components to SLE risk.
Results: Our case-cohort sample numbered 8,345,067 individuals including 21,485 new SLE cases. At the median ozone referent level (i.e., 36.1 parts per billion), the adjusted hazard ratio for SLE onset was 1.142 (95% confidence interval, CI 1.107-1.179) per every quartile increase in all PM2.5 components (Table 1). Ozone was also associated with increased risk of SLE (HR 1.009, 95% CI 1.001-1.017). There was effect modification such that the HR for PM2.5 was highest when ozone level was lowest (Table 1). Similar results were seen in sub-groups stratified by sex or age. Mineral dust consistently had the largest index weight across different sub-groups and ozone levels.
Conclusion: PM2.5 and ozone were associated with SLE onset; mineral dust was an important contributor. Mineral dust triggers pulmonary inflammation and is a plausible trigger of autoimmunity and SLE onset. Addressing sources of ambient mineral dust (road traffic, construction, farming) may help reduce SLE incidence.

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Chondrodysplasia Punctata in an Infant Suspected Secondary to Maternal Systemic Lupus Erythematosus

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Background: Systemic lupus erythematosus (SLE) may cause maternal and/or fetal complications in pregnancy. Fetal complications such as miscarriage and neonatal lupus/congenital heart block are well-described, but there are a small number of case reports in the literature of skeletal dysplasia suspected secondary to maternal SLE.[1] We report here a case of chondrodysplasia punctata suspected secondary to maternal SLE.
Case Report: A 31-year-old female was diagnosed with SLE 6 years prior to pregnancy. Manifestations had included arthritis, oral ulcers, Raynaud's phenomenon, pleuritis, myositis, neutrophilic urticaria, cytopenias, and hypocomplementemia. Serologic testing revealed positivity for ANA, SSA, and anti-Smith antibodies. At the time of pregnancy, she was being treated with hydroxychloroquine, anakinra, IVIG, and low-dose prednisone. She had previously been treated with azathioprine, methotrexate, mycophenolate mofetil, tacrolimus, rituximab, upadacitinib, and anifrolumab but had not received any of these immediately preceding or during pregnancy. The patient became pregnant unexpectedly and started on routine care for SLE with SSA antibodies in pregnancy. This included hydroxychloroquine 400mg daily, low-dose ASA for pre-eclampsia prophylaxis, weekly fetal heart rate monitoring between weeks 16-26, and

echocardiogram at week 20. On detailed anatomic ultrasound at 20 weeks a flattened nasal profile was noted, suspicious for midface hypoplasia. Additionally, there were at least 2 vertebral segmental anomalies. This prompted referral to Medical Genetics for evaluation of a potential skeletal dysplasia, in particular chondrodysplasia punctata. Subsequent ultrasounds confirmed findings. Fetal genetic testing via amniocentesis was negative for any causal mutations. There were no exposures to teratogens or infections associated with chondrodysplasia punctata. Chondrodysplasia punctata has been occasionally reported associated with maternal autoimmune disease. Therefore, it was suspected that the infant's presentation was secondary to maternal SLE. The infant was born at 39 weeks and was small for gestational age. On subsequent examination, features of midface hypoplasia were confirmed and X-rays of the spine revealed multilevel vertebral segmentation anomalies. The infant is pending further evaluation by pediatric orthopedic surgery.
Conclusion: SLE has numerous well-described effects on mother and fetus in pregnancy. However, fetal malformations are only rarely described. We report a case of chondrodysplasia punctata in an infant born to a mother with SLE in which all other known causes of chondrodysplasia punctata (genetic, medication, infections) were excluded. This adds to a growing number of reports suggesting a possible association between SLE and chondrodysplasia punctata.
References: [1.] Chitayat D et al. Am J Med Genet A 2008;146A:3038-53.

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Systemic Lupus Erythematosus Disease Activity and Clinical Outcomes After Kidney Transplantation for Lupus Nephritis: A Single-Centre Study

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Objectives: Systemic lupus erythematosus (SLE) is frequently complicated by lupus nephritis (LN), a major cause of morbidity and renal failure.[1] Kidney transplantation improves survival and is the preferred treatment for end-stage renal disease secondary to LN.[2] While transplant-related outcomes such as graft survival are well characterized, few studies have examined the broader post-transplant course of SLE. We aimed to characterize post-transplant lupus disease activity, flare frequency, and the prevalence of major comorbidities and adverse events.
Methods: A retrospective chart review was conducted for patients with SLE followed at The Ottawa Hospital who underwent kidney transplantation for LN between 2006 and 2023. Demographic, clinical, and serologic data were extracted from electronic medical records. Post-transplant disease activity was assessed using the SLE Disease Activity Index (SLEDAI-2k) and cumulative damage using SLICC/ACR Damage Index (SDI). Adverse outcomes, including graft rejection, cardiovascular events, infections, metabolic complications, osteoporotic fractures, avascular necrosis, and malignancy, were recorded. Data were summarized descriptively.
Results: 13 female patients were identified in our cohort (13/400), with a mean age of 44.8 ± 6.2 years at transplantation and mean follow-up of 8.4 ± 5.1 years. Time spent on dialysis prior to transplantation ranged from 3 months to 13 years. Ethnic distribution of patients was 54% White, 15% Black, 15% East Asian, 8% Indigenous, and 8% Middle Eastern. Deceased kidney donor (54%) was slightly more common than living donor (46%). Most patients received prednisone (92%) and calcineurin inhibitors (85%) as part of maintenance post-transplant immunosuppression. Mean cumulative SDI was elevated at 6.2 ± 2.0 (range 3–10). SLEDAI-2k scores (n=9) ranged from 0–6 (mean 1.2 ± 2.0); most maintained remission or low disease

activity, and only one patient experienced a lupus flare requiring treatment escalation. Post-transplant adverse outcomes included cardiovascular events (15%), new-onset diabetes (15%), and major infections (38%). Additional complications included cataracts (15%), osteoporotic fractures (15%), and avascular necrosis (8%). One patient experienced biopsy-proven graft rejection, but no malignancies or deaths were observed during the post-transplant period.
Conclusion: Lupus activity following kidney transplantation for LN remained quiescent, with few flares observed; however, treatment-related complications were more common. While these interim findings are based on a limited cohort, they suggest that post-transplant SLE patients tend to maintain disease control, but they demonstrate the need for ongoing monitoring of complications and organ damage from chronic prednisone use. Continued patient recruitment and longitudinal follow-up are in progress.
References: [1.] Hanly J. Rheumatology 2016;55;252-262. [2.] Brilland B. Kidney Int Rep 2025;10;1163-74.

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Characterizing Systemic Lupus Erythematosus in Males: A Retrospective Chart Review Study from the Ottawa Hospital Lupus Clinic

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Objectives: Male systemic lupus erythematosus (SLE) remains uncommon but is often linked with more severe organ involvement, particularly lupus nephritis. Limited Canadian data describe the clinical characteristics and treatment patterns of this population. This study aimed to characterize male SLE patients at a tertiary lupus clinic, focusing on disease features, retinal toxicity outcomes, and lupus nephritis prevalence.
Methods: A retrospective chart review was conducted on 37 male SLE patients followed at the Ottawa Hospital Lupus Clinic. Demographic, serologic, and clinical data were collected using a standardized form. Disease activity was assessed by SLEDAI-2K, and classification was based on EULAR/ACR 2019 criteria. Medication exposure, comorbidities, and organ system-specific complications were analyzed descriptively.
Results: We identified 37 males in the current lupus cohort of 410 patients. The mean age at diagnosis was 38.9 ± 17.4 years, and the current mean age was 54.4 ± 14.8 years. Ethnicity was primarily Caucasian (76%). The mean BMI was 26.1 ± 5.0 kg/m². Most patients (62%) were nonsmokers and 46% reported alcohol use. Common comorbidities included hypertension (41%), chronic kidney disease (24%), and diabetes (19%). The median EULAR/ACR score at diagnosis was 20 [IQR 16–26], with renal (46%) and mucocutaneous (43%) domains most frequently affected. Mean SLEDAI-2K at last visit was 1.3 ± 1.7, indicating current low disease activity. Hydroxychloroquine (HCQ) was prescribed in 23 of 37 patients (62%), with a mean daily dose of 396 mg. An additional 8 patients (22%) discontinued HCQ due to retinal toxicity or drug intolerance. HCQ- associated retinal toxicity (as confirmed by optical coherence tomography or electroretinography) occurred in 6 patients (16.2%), after a mean exposure dose exposure of 350mg/day for 14 years. Two of these patients (33%) had prior chloroquine treatment on average for 16.5 years. Lupus nephritis (LN) was documented in 18 (49%) patients, most commonly Class IV (46%) and Class V (46%), with two cases of IV/V LN (16%). Neuropsychiatric and cardiopulmonary involvement each occurred in 13.5%, while hematologic manifestations were rare (2.7%). One death was reported in the cohort related to heart failure.
Conclusion: Male SLE patients in this cohort demonstrated a high prevalence of renal disease and a notable incidence of Plaquenil-related retinal toxicity. These findings emphasize the

importance of long-term ocular and renal monitoring in male SLE management. Further work comparing the female cohort to the male cohort will help highlight key sex-differences in manifestations, outcomes and prognosis.

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Anifrolumab use in Jaccoud Arthropathy, Chilblains and Refractory SLE - A Case Report and Literature Review

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Background: Anifrolumab, an anti-interferon I receptor monoclonal antibody, is the second biologic molecule to be recognized for treatment of active systemic lupus erythematosus (SLE). Jaccoud's arthropathy (JA) a reducible, non-erosive subtype of musculoskeletal involvement in SLE patients, and Chilblain Lupus Erythematosus (CHLE), a subtype of cutaneous involvement presenting as a spectrum of acral cold-induced lesions that can progress to painful ulcerations, are two rare manifestations of SLE with treatment guidelines mostly relying on clinical cases and experts' opinion.

Case Report: We report a case of a patient diagnosed with coexisting SLE, CHLE requiring amputation and mutilating JA. Clinical response on all aspects remained suboptimal after multiple lines of treatment including Hydroxychloroquine, high dose Prednisone, Mycophenolate mofetil, Ustekinumab, Azathioprine, Belimumab. She showed positive clinical response to Anifrolumab, with significant reduction of arthralgia and complete resolution of chilblains lesions. This was maintained at 1 year post introduction of Anifrolumab with only complication attributable to this treatment being a cutaneous abscess treated with topical and systemic antibiotics. Following this improvement, we decided to proceed to a narrative review of literature regarding management of both CHLE and JA. Guidelines did not recommend Anifrolumab directly for any of those two subtypes of SLE. The line of treatment after Belimumab in the most up to date Cases of both presentations were compiled, with specific interest in patients reported to have received Anifrolumab as part of their treatment regimen. We collected ten cases of CHLE treated with Anifrolumab. We also found one case of JA that demonstrated improvement of arthralgia on Anifrolumab. Most of the patients had also failed to respond to multiple lines of treatment including trial of Belimumab and/or Rituximab. All cases responded completely to Anifrolumab within 8 to 20 weeks. We did not find reports of cases followed for longer intervals.

Conclusion: With our case, we are participating in the growing weight of evidence that Anifrolumab is a safe and potent treatment option that should be considered in refractory cutaneous lupus, including CHLE, and potentially in refractory arthralgia, even in JA subtypes.

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Risk of Impaired Ovarian Reserve in Women Exposed to Fludarabine-Based Conditioning Prior to Cell Therapies

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Objectives: Cell-based therapies, including chimeric antigen receptor T-cell, are emerging as promising treatments for refractory systemic autoimmune diseases such as systemic lupus

erythematosus (SLE). These therapies require lymphodepletion, a conditioning regimen typically consisting of fludarabine and cyclophosphamide, to induce immunosuppression and enhance cell expansion. While cyclophosphamide's gonadotoxicity has been described in other settings, the effects of fludarabine-based conditioning remain poorly characterized. This is particularly important for women with SLE, who are often of reproductive age and may have non-gonadotoxic alternatives. Therefore, we conducted a systematic review to synthesize available evidence regarding the effect of fludarabine-based conditioning on ovarian function in women receiving cell therapies.

Methods: We systematically searched PubMed, Embase, and Web of Science from January 1997 to October 2025 for keywords related to fludarabine, fertility, ovarian reserve, and cell therapies [i.e. hematopoietic stem cell transplantation (HSCT), mesenchymal stem/stromal cell, or adoptive cell therapy]. Data were extracted by two independent reviewers for relevant subgroups or individual patients, including reproductive biomarkers, menstrual status, and pregnancies at last follow-up. Risk of bias was assessed using the Newcastle–Ottawa Scale. The review was conducted in accordance with PRISMA guidelines.

Results: Of 253 records, nine met inclusion criteria, reporting reproductive outcomes in adult women treated with fludarabine ± cyclophosphamide ± total body irradiation (TBI) without other alkylating agents. Included studies comprised four case reports, four case series, and one cohort study. Collectively, 50 women were analyzed, 32 of whom were exposed to fludarabine and cyclophosphamide without TBI. Only four did not receive cyclophosphamide. One study described patients with autoimmune disease (n=5), all of whom had SLE. Cumulative doses of fludarabine and cyclophosphamide ranged from 75-200 mg/m2 and 50-160 mg/kg respectively. Many patients (43-100%) exhibited premature ovarian insufficiency at last follow-up (3-60 months), with AMH levels generally below 0.5 ng/mL (Table 1). Amenorrhea was common, occurring in 58%. However, longitudinal data from several reports suggested delayed recovery of ovarian function. Six pregnancies occurred overall, all after fludarabine + cyclophosphamide ± TBI, including two via assisted reproductive technologies.

Conclusion: Available evidence suggests that exposure to fludarabine ± cyclophosphamide ± TBI is associated with reduced ovarian function, although partial or complete recovery may occur over time. However, the independent effect of fludarabine remains difficult to assess due to concurrent exposures in most regimens. Our findings underscore the need for comprehensive study of women with autoimmune diseases to better define gonadotoxicity related to fludarabine-based conditioning in cell therapy.

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Kardia Mobile 6-Lead Applicability for Hydroxychloroquine Baseline ECG Testing and Monitoring in Systemic Lupus Erythematosus

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Objectives: Hydroxychloroquine is the first line treatment for systemic lupus erythematosus and is used to treat several other autoimmune conditions. One potential side effect is the prolongation of the QT interval, which can be monitored with a 12-lead ECG.[1] However, there are several barriers to obtaining ECGs and most patients do not receive one, despite the recognized risk.[2] An emerging solution is the use of mobile devices. The objective of this study is to evaluate and compare the accuracy and clinical utility of the 6-Lead KardiaMobile ECG device to the standard 12-lead ECG for monitoring QT interval in patients on hydroxychloroquine.

Methods: 6-L KardiaMobile ECG readings were obtained from patients on hydroxychloroquine at the Ottawa Hospital Rheumatology Clinic, which involves a 30 second reading, holding the device with two thumbs on the left leg. 12-lead ECGs were recorded within a year of the KardiaMobile reading. A chart review was conducted for patients, and we extracted data related to age, sex, indication, dose and duration of use, concomitant QT-prolonging drug use, smoking, and QT interval length. Bland-Altman, paired t-tests, and Pearson correlation were performed using R.
Results: KardiaMobile readings were obtained from 34 patients, of which 13 patients had corresponding ECGs. Mean QTcF measured using the KardiaMobile device was 12.2 ± 16.4 ms lower than the 12-Lead ECG. Bland–Altman analysis showed 95% limits of agreement from −44.3 ms to +19.8 ms, with no evidence of proportional bias across the QTcF range. QTcF values from both methods were moderately correlated ($r = 0.69$, $p = 0.009$). 69% of patients were taking at least one other QT-prolonging medication. The most common classes were proton pump inhibitors (34%) and antidepressants (26%). Variances between groups were analyzed, including dose, number of QT-prolonging medications, and time on hydroxychloroquine; no trends were identified. QTcF was moderately correlated with age ($r = 0.50$, $p = 0.007$).
Conclusion: The KardiaMobile device shows mild underestimation of the QTcF interval in real world practice, however this discrepancy is small and unlikely to affect clinical decision-making. The difference was within the expected range of inter-method variability reported in previous validation studies. Additionally, the device was easy and feasible for patients to use. These findings suggest that mobile ECGs may provide a clinically acceptable alternative for QTcF monitoring in patients on HCQ, particularly in resource-limited settings, while considering its limitations in high-risk patients. However, more data is needed and patient recruitment is ongoing.
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Macrophage Activation Syndrome in Mixed Connective Tissue Disease: A Case of Multisystem Crisis and Recovery

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Background: Objective: To describe a life-threatening presentation of macrophage activation syndrome (MAS) in a young adult with mixed connective tissue disease (MCTD) with predominant features of SLE, highlighting diagnostic challenges, therapeutic escalation, and the multidisciplinary coordination required for recovery.
Case Report: Objectives: Methods: A 28-year-old female with MCTD and Systemic Lupus Erythematosus (SLE) features (managed by Rheumatology in the community), presented to the ER with 3 days of febrile illness, headache and diplopia, chest pain, diarrhea, and profound myalgias. She had been off treatment for several months due to intolerance to Azathioprine and self-discontinuation of Hydroxychloroquine and was recently started on Rinvoq by Dermatology for her only active symptom of inflammatory dermatosis. In the hospital, initial labs revealed bi cytopenia (hemoglobin 111, platelets 128), elevated ferritin (10,827 µg/L), CK (490 U/L), troponin (75 ng/L), and BNP (2497 ng/L). Imaging confirmed myocarditis and MRI brain showed cytotoxic lesion of the corpus callosum (CLOCC). MAS was suspected based on fever, cytopenia's, hyperferritinemia, and systemic inflammation. Initial treatment included pulse IV methylprednisolone (1 gm daily for three days), Anakinra 100 mg SC BID, and continuation of

Rinvoq. The patient initially improved but suffered a pulseless electrical activity (PEA) arrest on day four, requiring 10 minutes of CPR and ICU transfer. Anakinra was escalated, and Emapalumab access was urgently pursued. Results: Following Emapalumab initiation and intensified immunosuppression, the patient stabilized. She was extubated on day five post-arrest and transitioned back to the medical unit. Rituximab was added, and hydroxychloroquine was reintroduced. Laboratory markers improved: ferritin decreased to 982 µg/L over two weeks, CK and liver enzymes improved, and inflammatory markers resolved. Post ICU stay was complicated by ongoing diplopia and headache, digital gangrene, new proteinuria, and persistent oral ulcerations. Multispecialty involvement included Cardiology, Neurology, Nephrology, Dermatology, and Hematology.

Conclusion: MAS in MCTD can present subtly before rapid deterioration. Early recognition of hyperferritinemia and cytopenia's is critical. This case underscores the importance of clinical suspicion, therapeutic escalation, including biologics like anakinra and Emapalumab, and highlights the logistical challenges of accessing rare therapies. Multisystem involvement demands coordinated care, and even with clinical improvement, vigilance is essential due to the risk of delayed complications. We recognize the importance of reporting this case and advocating for the use of these limited access medications that are pivotal for this life-threatening condition.

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Sociodemographic and Clinical Predictors of Cognitive Performance in Lupus

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Objectives: To identify sociodemographic, biological, and clinical determinants influencing longitudinal cognitive performance in systemic lupus erythematosus (SLE), evaluated globally and across distinct cognitive domains.

Methods: Adults with systemic lupus erythematosus (2019 EULAR/ACR criteria) at a tertiary lupus clinic completed repeated neuropsychological assessments using the American College of Rheumatology (ACR) Neuropsychological Battery. Test-level outcomes were standardized to z-scores and analyzed to retain domain-specific detail. Candidate predictors included sociodemographic, disease-related, and treatment variables such as age, sex, education, disease duration, depression (BDI-II), anxiety (BAI), and current use of glucocorticoids, antimalarials, immunosuppressants, or biologics. Multilevel Bayesian models with random effects for patient and domain/test accounted for repeated measures and test hierarchy. A conventional model was compared with a prespecified model applying selective shrinkage for weak associations, and model fit was evaluated using leave-one-out cross-validation (LOOIC) to assess predictive performance.

Results: The dataset included 245 patients contributing 8465 visits with repeated cognitive assessments over 4 years. The selective shrinkage model showed superior predictive performance and is presented here. Overall cognitive performance improved modestly over time

(+0.10 z-score units; 95% CrI 0.06–0.14). Higher anxiety was associated with worse cognition (−0.010 per BAI point; 95% CrI −0.015 to −0.005). Increasing age related to poorer performance (−0.011 per year; 95% CrI −0.020 to −0.002), while longer disease duration showed a slight positive trend (0.019 per year; 95% CrI 0.006–0.030). Higher education corresponded to better scores (0.20; 95% CrI −0.01–0.50). Medication classes and SDI were not consistently associated with outcomes (Figure 1). Domain- and test-level effects revealed variability across and within domains, highlighting heterogeneous cognitive functioning in lupus.
Conclusion: In this longitudinal SLE cohort, anxiety, age, and disease duration were the most consistent correlates of cognitive performance, independent of damage and medication class. Clinically, identifying and managing anxiety may yield greater benefits for cognitive health than medication adjustments alone. Modeling performance at the test level revealed differences both between domains and within tasks, indicating that cognitive function in lupus is not uniform. These findings highlight the need for individualized, domain-specific assessment and targeted interventions to address specific cognitive challenges in lupus.

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Balancing Cohesion and Diversity in Competence Committees: Insights from Internal Medicine and Rheumatology

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Objectives: In 2019, Rheumatology in Canada transitioned to competency-based medical education (CBME), mandating the development of competence committees (CCs). CCs interpret aggregated assessment data about residents to inform decisions about learner progress and achievement. In the psychology literature, groups are generally thought to make better decisions than individuals by generating more ideas, drawing on broader perspectives, and reducing errors. Evidence suggests that heterogeneous groups—when supported by robust rules and procedures—are more likely than homogeneous groups to consider a broader range of options leading to higher-quality decisions.[1] While equity, diversity, and inclusion (EDI) are increasingly emphasized, little is known about how CCs in internal medicine and its subspecialties consider and enact diversity in their membership and deliberations.
Methods: We conducted a qualitative study using semi-structured interviews with 18 CC members and chairs from six Canadian universities. All participants were drawn from internal medicine or its subspecialties, including two from Rheumatology. Interviews explored perspectives on diversity, committee composition, decision-making rules, and fairness. Data were transcribed, coded in NVivo™, and analyzed thematically, with reflexive dialogue across a multidisciplinary research team informing interpretation.
Results: Five themes emerged. (1) Diversity beyond demographics: Ethnicity was rarely considered; instead, committees emphasized variation in academic rank, practice site, life stage, or assessment philosophy. (2) High agreement and collegiality limited structured decision-making: Consensus was easily reached, though participants acknowledged risks of groupthink. (3) Integrating context and diversity considerations: Committees valued contextual and anecdotal data, particularly regarding international medical graduates and equity-deserving residents. (4) Awareness sparked by reflection, but training absent: Few had received CC-specific EDI

training; interviews prompted recognition of this gap. (5) CBME as aspirational but burdensome: CC responsibilities were widely viewed as resource intensive.
Conclusion: Cultural diversity was rarely prioritized, reflecting both structural limitations and resource constraints. CCs valued multiple forms of diversity and recognized the risks of excessive cohesion. Decision-making was typically consensus-driven and collegial but concerns about groupthink and lack of formal decision rules persisted. Efforts to incorporate contextual information aimed to promote fairness but lacked consistent safeguards against bias. As CBME continues to evolve, CCs must balance cohesion with diversity, efficiency with deliberation, and objectivity with contextual fairness. Achieving this will require local innovations—such as bias training, deliberate diversification, and explicit decision rules—alongside broader systemic reform to ensure fair, defensible, and developmentally oriented assessment for all learners.
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Moving Equity into Practice: Evaluation of an Online Asynchronous Continuing Medical Education Program for Rheumatology Care

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Objectives: Persistent health inequities exist in the diagnosis, treatment, and outcomes of rheumatologic diseases among at-risk populations in Canada. Prior research identified barriers and facilitators experienced by at-risk populations in Canada when accessing rheumatology care along with proposed multi-level equity solutions to improve equity in RA care delivery.[1, 2] This knowledge informed the development of a 10-part, 3-module asynchronous online continuing medical education (CME) program that employed evidence-based teaching strategies and best practices for online learning that was deployed nationally to rheumatology clinicians. We evaluated the engagement and acceptability of the e-learning strategy, received feedback on areas for enhancement, and gained insight on the effectiveness of the program by documenting intended changes in provider practice behaviours reported after completing the program.
Methods: Participants were recruited through e-blasts and promotion by the Canadian Rheumatology Association. Participants could elect to complete the entire course, or only modules pertaining to their needs and interests. Module 1 was an introductory chapter focused on basic knowledge related to equity. Module 2 included 7 specific sections addressing the realities and challenges faced by each of the at-risk communities. Module 3 concluded the course with recommendations for equity-oriented practices and policy changes. We evaluated domains of engagement, overall satisfaction with the program, content completeness, the quality of materials, program length, and relevance to practice using descriptive statistics. Free text boxes were provided for comments on program effectiveness and suggestions for individual module and overall program improvement. At program completion, participants were asked to submit

Commitment-to-Change Statements which were analyzed using a phenomenological thematic analysis model for exploring how healthcare providers would incorporate equitable care into their RA practice.
Results: Forty-six participants enrolled (n=43 English and n=3 French language versions) and engaged with the program, with 37% completing all 10 sections. Overall participant satisfaction was high, with 87% indicating increased awareness and an enhanced ability to support equity in practice. Intended changes (Figure 1) included enhancing accessibility to care, implementing trauma-informed and culturally safe practices, and delivering equitable clinical care. One theme highlighted the importance of ongoing professional development and collaboration with local health and social service networks. Recommended improvements were to provide downloadable one-page summaries for each module and supply more case-based learning experiences.
Conclusion: The Equity in Rheumatology Care CME program was acceptable and effective. Four domains for practice change offer concrete strategies to reduce disparities in care among underserved populations.
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Brentuximab Vedotin in Severe Systemic Sclerosis: Data on Long-Term Follow-Up and Retreatment

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Objectives: We previously reported skin and forced vital capacity (FVC) improvements in an open-label clinical trial exploring the use of brentuximab vedotin (BV) in patients with severe diffuse cutaneous systemic sclerosis (dcSSc).[1] Long-term outcomes after therapy was discontinued, and retreatment experience remain unknown.
Methods: Observational study including the participants completing the original Brentuximab vedotin case series. Retreatment was authorized by Health Canada if the modified Rodnan skin score (mRSS) increased ≥6 or immunosuppression failure. Three of 10 patients received a new course of BV. The mRSS and pulmonary function tests were assessed at baseline, end of treatment (week 52), and during follow-up (as per usual clinical practice) until last visit or death.
Results: Ten patients were included (Table 1). Six were female (60%), with a median age at the end of the initial study of 62 (SD 14.1) years. Disease duration at the time of the first BV cycle was 4.7 years (SD 3.4). The mean change in mRSS after the original BV treatment (week 0 to 52) was -11.3 (5.8 SD). Patients were followed for up to week 192 (last follow up visit or death). At week 104, 5 patients had mRSS worsening (≥6 points) and 5 remained relatively stable. Three patients were retreated intravenous BV 0.6mg/Kg every 3 weeks: patient #5 had skin progression 3 years after finishing the original trial despite background immunosuppression, mRSS improved from 30 to 24; patient #10 had skin progression at week 108 with lack of

response to initial BV treatment, her mRSS started at 29 and increased to 34; and patient #11 due to skin contracture progression while on standard immunosuppression, his mRSS progressed from 29 to 48 at week 104, dying and he died from scleroderma renal crisis (SRC) during retreatment. By week 156, 4 out of 10 patients had died due to SSc complications. One patient (who dropped out early due to PAH progression) received a lung transplant. Another one developed new onset PAH. For the remaining patients, 3 had a stable mRSS compared to week 52 over follow-up; and 3 worsened. Most received concomitant immune suppression.
Conclusion: Half of the patients treated with BV experienced scleroderma skin progression within the first year after the last infusion, despite standard of care immunosuppression. Retreatment with BV might be beneficial but data are heterogeneous, and the timing of retreatment is unknown.
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Physical Rehabilitation Interventions for Hand Function in People with Systemic Sclerosis. A Scoping Review

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Objectives: To synthesize current evidence for physical rehabilitation interventions to improve hand function in people with systemic sclerosis (SSc).
Methods: Medline and Pubmed were searched to identify studies of rehabilitation interventions for hand function in SSc. Articles were included based on reporting of participants aged 18 years or older with SSc; physical therapy, occupational therapy or rehabilitation interventions; any aspect of hand function as an outcome, and English language. The study was conducted according to the PRISMA Extension for Scoping Reviews.
Results: Eighteen studies involving 1,205 participants were included. Study designs included 13 randomized controlled trials, 2 pretest-posttest studies, 1 controlled trial, 1 quasi-experimental study, and 1 pilot study. Small sample sizes were common, with 9 studies including fewer than 40 participants. Interventions included combination of manual therapy and prescribed exercises (Table 1); self-administered exercise protocol, virtual treatment platform or telerehabilitation program; paraffin wax; manual lymphatic drainage; and dynamic splinting.
Conclusion: Evidence supports supervised exercises and manual therapy to improve hand function in people with SSc. Despite consensus recommendations advocating for physical rehabilitation and hand-stretching as part of standard care in SSc, high-quality research remains limited.

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Systemic Sclerosis Induced by Immune Checkpoint Inhibitors from the Canadian Research Group of Rheumatology in Immuno-Oncology (Canrio): A Case Series

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Objectives: Immune checkpoint inhibitors (ICIs) have revolutionized cancer therapy, improving outcomes in multiple advanced malignancies. Their use is often limited by immune-related

adverse events (irAEs), including rare rheumatic irAEs, such as ICI-induced systemic sclerosis (ICI-SSc). Compared to idiopathic SSc, ICI-SSc typically presents with fewer extra-cutaneous manifestations and negative serologies, but data remains limited.[1] This case series describes the clinical presentation, management, and outcomes of patients with ICI-SSc to guide clinicians in balancing autoimmune toxicities with cancer control.

Methods: A retrospective chart review was conducted on 7 adults diagnosed with systemic sclerosis following ICI exposure between March 2021 and August 2025. All patients were referred to a Canadian academic rheumatology clinic specializing in Immuno-Oncology during ICI therapy. Clinical data was abstracted from medical records, including patient demographics, malignancy type and stage, ICI type and duration, clinical features, serologies, treatment, and outcomes.

Results: Of the 7 patients identified, 5 (71.4%) were female and 2 (28.6%) were male, with a mean age (SD) of 63 (10.9) years. Malignancies included: metastatic melanoma (n=4), metastatic squamous cell carcinoma (n=1), breast cancer Stage IIA/IIB (n=1), and metastatic endometrial adenocarcinoma (n=1). ICIs used included: pembrolizumab (n=2), nivolumab (n=1), cemiplimab (n=1), and ipilimumab/nivolumab combination followed by nivolumab monotherapy (n=2), which were discontinued due to SSc symptoms within 1–13 months of initiation. Serologies showed ANA positivity in 4 patients (57.1%), with SSc-specific antibodies (anti-Scl-70) detected in 1 patient. Other antibodies detected included anti-RP-11, anti-RP-155, anti-Ro-52, anti-chromatin, and anti-OJ. 2 patients had negative serologies, 1 with elevated inflammatory markers. All patients had scleordactyl (diffuse 57.1%, limited 42.9%) and extra-cutaneous features, most commonly Raynaud's phenomenon (71.4%). Other manifestations included inflammatory arthritis (42.9%), nailfold capillary changes (42.9%), esophageal dysmotility (28.6%), telangiectasia (14.3%), and sicca symptoms (14.3%). No patients developed interstitial lung disease, pulmonary arterial hypertension, or scleroderma renal crisis. Management included ICI cessation for all patients, prednisone (85.7%), disease-modifying antirheumatic drugs (mycophenolate mofetil 57.1%, methotrexate 28.6%, hydroxychloroquine 28.6%), infliximab and intravenous immunoglobulins, and vasodilatory therapies. All malignancies were stable at 6-months post-ICI therapy.

Conclusion: ICI-SSc is a significant irAE primarily characterized by cutaneous manifestations but, in contrast to previous reports, this case series demonstrates that extra-cutaneous manifestations and seropositivity can occur. Along with ICI-cessation, immunosuppressive therapy was effective in symptom control without compromising cancer stability. This work may assist those involved in caring of patients with ICI-SSc to initiate immunosuppressive therapy and minimize the risk of end-organ complications.

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Identification of Clinical and Radiologic Markers of Disease Presentation in Patients with Scleroderma Related Interstitial Lung Disease (SSc-ILD) in a Cohort from Ontario, Canada

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Objectives: Systemic sclerosis (SSc) is a multisystem autoimmune disease characterized by vasculopathy, inflammation and fibrosis of multiple organs including the skin, lungs, heart, and GI tract.[1] Lung involvement, characterized by interstitial lung disease (SSc-ILD) and

pulmonary hypertension, occurs in 50-70% of individuals and represents the leading cause of death for patients with SSc.[1,2] Prior studies have identified risk factors for development of SSc-ILD, including older age, male sex, the presence of diffuse disease, those with anti-Scl-70/anti-topoisomerase I antibody, and the absence of anti-centromere antibody.[1-3] In this study, we examined the clinical risk factors that predict incident ILD in patients with SSc. We also examined two quality improvement measures: 1) whether patients with evidence of fibrosis on chest x-ray undergo high-resolution computed tomography (HRCT), and 2) whether patients with evidence of pulmonary hypertension on echocardiogram undergo right heart catherization (RHC).

Methods: We analyzed data from 162 patients with SSc in Hamilton, Ontario who are registered in the Canadian Scleroderma Research Group registry, a national longitudinal registry of adult SSc patients. We summarized clinical risk factors between patients who do versus do not develop ILD during the follow-up period of the CSRG and compared them using logistic regression modelling. We also determined the proportion of patients with abnormal chest x-rays who did and did not receive HRCT, as well as the proportion of patients with pulmonary hypertension on echocardiogram who did and did not undergo RHC.

Results: In this cohort of SSc patients, the presence of interstitial lung disease was associated with the diffuse cutaneous subtype of the disease ($p = 0.01$), anti-topoisomerase I antibody positivity ($p < 0.01$), lower baseline DLCO ($p < 0.01$), lower baseline FVC ($p < 0.01$), and elevated RVSP (> 40mmHg) on echocardiogram ($p < 0.01$). Among patients with abnormal chest X-rays, 84.6% underwent HRCT, whereas only 40% of patients with elevated RVSP underwent RHC.

Conclusion: These findings further validate clinical predictors of SSc-ILD, highlight potential new ones, and document practice patterns on the assessment of key pulmonary complications associated with SSc. These findings underscore the need for both early recognition and improved quality of care in this population.

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Are We Putting the ‘cart’ Before the Horse in Systemic Sclerosis? A Review of the Car-T Studies in Scleroderma

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Objectives: Chimeric antigen receptor T-cell (CAR-T) therapy is emerging as a novel approach for systemic sclerosis (SSc). We reviewed the current trial landscape—including study design, therapeutic targets, comparative arms—and integrated these findings with the most recent SSc case series.

Methods: On August 20, 2026, we searched ClinicalTrials.gov and ClinicalTrialsRegister.eu using “scleroderma” OR “systemic sclerosis” AND “CAR-T,” and screened references from published studies; identifying 29 actively recruiting trials; extracted prespecified data, including trial identifiers, targets, eligibility criteria, SSc participant details, interstitial lung disease (ILD) rules, product source, immunosuppression protocols, hospitalization requirements, comparators, sponsors, and study designs.

Results: Most targeted CD19: 27/29 trials (11 CD19-only; 16 multi-target constructs, i.e. CD19 plus BCMA). One study each targeted CD20 or BCMA alone. Products were autologous in 20/29 and allogeneic ("off-the-shelf") in 9/29. Only two trials were randomized, and just one used an active comparator (rituximab). Mostly early diffuse cutaneous SSc (dcSSc) were eligible for inclusion. SSc enrollment was often within broader autoimmune "basket" trials; or SSc-specific studies (n=12). ILD eligibility criteria were inconsistently reported in trial registration: unspecified in 22/29, permitted in 5/29 (with limitations) and required in 1/29. Most protocols mandated immunosuppression washouts and lymphodepletion (Table 1). Three reports demonstrated feasibility and early clinical benefit in SSc. The BREAKFREE-1 update described a multicenter CD19 CAR-T with acceptable safety and encouraging signals in five SSc patients.[1] Another reported deep B-cell depletion and clinical responses in two patients with dcSSc.[2] Schett et al. presented the largest series to date: six patients with dcSSc showed improvements in skin and lung disease with manageable safety (low-grade cytokine release, no major neurotoxicity).[3]
Conclusion: The SSc CAR-T landscape is promising but fragmented—dominated by early-phase, non-comparative designs with several targets and treatment regimens. Progress could be accelerated by: (1) harmonized eligibility and outcome measures across CD19, CD20, and BCMA programs; (2) fewer and larger multicenter trials; (3) inclusion of comparators or delayed-start designs; and (4) transparent reporting of subsets of SSc and SSc-ILD patients to learn whether it is 'too late' for some patients to have optimal benefit. Early clinical signals support further development, but the high cost and risk of inequitable access demand parallel strategies for affordability and global access of CAR-T benefits.
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Mesenchymal Stromal Cells in Systemic Sclerosis Have a Profibrotic and Senescent Transcriptomic Profile

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Objectives: Mesenchymal stromal cells (MSCs) are non-hematopoietic multipotent cells with immunomodulatory, proangiogenic, and antifibrotic properties.[1] The three pathogenic axes in systemic sclerosis (SSc) are autoimmunity, vasculopathy, and fibrosis.[2] Considering that donor characteristics impact MSCs' functional properties,[3] we hypothesized that adipose-derived MSCs in SSc are dysfunctional. We aimed to characterize MSC's phenotype from healthy donors and SSc patients.
Methods: MSCs were isolated from adipose tissue contained in two 4 mm forearm punch biopsies performed on eight SSc patients and eight age- and sex-matched healthy controls (Ctrl). MSCs were characterized according to the International Society for Cell and Gene Therapy (ISCT) minimal criteria. Bulk RNA sequencing was done and differentially expressed genes (DEGs) were defined as a fold change >2 or <−2, and a Benjamini–Hochberg adjusted p-value <0.05. Unsupervised hierarchical clustering and gene set enrichment analysis (GSEA) were conducted to identify enriched biological processes and signaling pathways.
Results: Results: SSc and Ctrl MSCs met ISCT criteria (i.e., adhered to plastic, differentiated

into three lineages, and exhibited specific surface markers). Compared to Ctrl, SSc MSCs had 151 upregulated and 16 downregulated genes (Figure 1A). GSEA documented the enrichment of profibrotic and senescence pathways in SSc MSCs (Figure 1B-C) which depicted a myofibroblast-like phenotype, characterized by increased ACTA2 expression.
Conclusion: SSc MSCs have a distinct transcriptomic profile with enrichment of profibrotic and senescence pathways which may contribute to disease pathogenesis. Future studies will explore the effects of MSC modulation on mitigating SSc severity.
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Successful Treatment of Resistant Orbital Eye Disease in Granulomatosis with Polyangiitis with the Addition of Methotrexate to Standard of Care

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Background: Granulomatosis with polyangiitis (GPA) is an antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis involving small to medium-sized vessels and characterized by multisystem involvement. The standard induction treatment for organ or life-threatening GPA includes pulse steroids with rituximab or cyclophosphamide.[1] We present a patient with systemic GPA with sinusitis, otomastoiditis, pachymeningitis, pulmonary nodules, splenic involvement, and positive PR3. Despite undergoing standard induction therapy, the patient developed persistent orbital disease, which responded to the addition of methotrexate.
Case Report: A previously healthy 44-year-old female presented with several months of fatigue, myalgias, weight loss, and right-sided headaches. Examination revealed binocular diplopia, right-sided cranial nerve V, VI, and VII neuropathies, and bilateral positive Babinski reflex. C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) were elevated at 154mg/L (<1mg/L) and 120mm/h (<20mm/h), respectively, with PR3 positivity of 148RU/mL (<20RU/mL). Imaging showed right sided pachymeningeal thickening, pulmonary nodules, paraspinal soft tissue masses, and splenic lesions. Splenic biopsy confirmed a diagnosis of GPA. She received pulse steroids and IV cyclophosphamide for induction therapy. Four months later, the patient developed right eye swelling and proptosis, causing significant difficulty with eye opening. Inflammatory markers and PR3 levels remained elevated. There was persistent pachymeningeal thickening with new right orbital involvement on repeat imaging. Conjunctival biopsy showed neutrophilic and granulomatous inflammation. Induction treatment was switched to rituximab, but response was limited despite four doses. Repeat conjunctival biopsy confirmed persistent GPA with perivascular neutrophils and eosinophils with focal areas of necrosis and granulomatous inflammation despite undetectable PR3 level. Surgical debulking and addition of oral cyclophosphamide provided limited improvement. Given her persistent ocular symptoms, oral methotrexate at 15mg was added to rituximab maintenance and 15 mg of prednisone after a multidisciplinary review. The patient showed a good response, with CRP decreasing to 16.5mg/L and prednisone successfully tapered to 5mg, with significant improvement in her orbital symptoms.
Conclusion: Orbital involvement, particularly orbital mass, in GPA can be associated with refractory disease. Emerging evidence supports the use of combined rituximab and methotrexate therapy to prevent irreversible damage.[2-3] This case demonstrates successful treatment of

resistant orbital GPA with combination therapy, without major complications or infections. In severe GPA with orbital eye disease, early consideration of rituximab and methotrexate combination therapy may improve outcomes and prevent damage.
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Beyond the Bone Marrow: Aortic Inflammation in Waldenström's Macroglobulinemia

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Background: Peri-aortitis is defined by inflammation of the adventitia layer of the aortic wall that can extend into the connective tissue surrounding the aorta. Primary peri-aortitis refers to IgG4-related or primary inflammatory diseases, whereas secondary causes can be non-inflammatory in nature. The differential diagnosis of peri-aortitis typically includes large vessel vasculitis, small vessel vasculitis, IgG4-RD, systemic connective tissue disease, Erdheim-Chester, infections and malignancy.[1] We present a case of presumed amyloid peri-aortitis secondary to Waldenström's macroglobulinemia.

Case Report: A 79-year-old man with a history of monoclonal gammopathy of undetermined significance (MGUS) underwent CT imaging of the chest, abdomen, and pelvis to evaluate a presentation of weakness, intermittent cognitive changes, facial purpura, elevated inflammatory markers, and an episode of syncope. Imaging revealed circumferential mural thickening of the thoracic and abdominal aorta with perivascular fat stranding, consistent with peri-aortitis. He underwent initial evaluation which revealed leukocytosis, elevated erythrocyte sedimentation rate and elevated kappa:lambda ratio with monoclonal protein spike on serum protein electrophoresis. Otherwise, his lab work was negative for anti-neutrophil cytoplasmic antibodies (ANCA), antinuclear antibodies (ANA), rheumatoid factor, complements, c-reactive protein and infectious work up. He was started on prednisone due to concern for large vessel vasculitis without any change in symptoms. During his evaluation he was also found to have nephrotic-range proteinuria and peripheral edema. A kidney biopsy was consistent with AL amyloidosis. A bone marrow biopsy was consistent with Waldenström's macroglobulinemia (WM). The vascular findings were reinterpreted as amyloid aortitis secondary to WM. The patient's corticosteroids were tapered without change in clinical status, and he transitioned to treatment with bendamustine-rituximab chemotherapy with stability of his aorta on repeat imaging.

Conclusion: This case demonstrates an unusual cause for periaortitis and demonstrates the need for a comprehensive workup for individuals presenting with this condition including assessment for hematologic malignancies.

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Takayasu Arteritis Presenting with Kidney Infarction, Cranial Nerve Palsy, and Osteomyelitis

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Background: Takayasu arteritis (TA) is a large-vessel vasculitis that primarily affects the aorta and its branches, increasing the risk of vascular complications like aneurysms and ischemic events. In the settings of aortic root involvement, aortic valve replacement can be prompted. However, the presence of a prosthetic valve poses risks of thromboembolism, infective

endocarditis, and hemolytic anemia. The diagnosis and management of these conditions in the settings of coexisting TA can be challenging and prompt a multidisciplinary approach.
Case Report: We present a case report of an African American female in her mid-30s with Takayasu arteritis, a prior Bentall procedure with mechanical aortic valve replacement, and coronary artery aneurysm bypass surgery. She presented with acute right-sided flank pain, right submandibular pain, and dysphagia. A month prior, she saw her primary care physician for a sore throat and right submandibular swelling with difficulty swallowing. She received several courses of antibiotics, with some improvement on levofloxacin. An ENT specialist noted paralysis of the right soft palate and right-sided tongue deviation. A head and neck CT scan was ordered, however, the patient presented to the ED before it could be performed. In the ED, she was diagnosed with right kidney infarction and an aneurysm of the right external carotid artery, causing partial paralysis of cranial nerve XII. Additional findings included C6-C7 osteomyelitis/discitis and ischemic infarctions in the left temporal and occipital lobes. Blood cultures grew Enterococcus faecalis, raising suspicion for septic emboli, prompting further evaluation for infectious endocarditis and mycotic aneurysm. Transthoracic echocardiography and transesophageal echocardiography performed at the primary facility did not reveal signs of infective endocarditis. However, given the high suspicion for mechanical valve endocarditis, further evaluation was pursued. The patient was transferred to a tertiary center, where reoperation of the prior aortic valve replacement revealed a perivalvular abscess. Intraoperative cultures grew Enterococcus faecalis. The carotid artery aneurysm was successfully repaired, leading to improvement in her neurologic symptoms. Pathology showed vessel wall fibrosis and thrombus formation.
Conclusion: This case highlights the challenges of managing TA complicated by prosthetic valve infectious endocarditis with embolic phenomena. The unusual presentation required a multidisciplinary approach to balance medical and surgical interventions. Early recognition and individualized care are essential to optimize outcomes in complex cases.

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Distinct Clinical and Laboratory Profiles of Biopsy-Positive and Biopsy-Negative Giant Cell Arteritis: A Meta Analysis

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Objectives: Although temporal artery biopsy (TAB) remains the diagnostic reference for giant cell arteritis (GCA) in resource-restricted settings that lack access to imaging, up to half of clinically diagnosed patients have negative biopsy results.[1,2] This study aimed to describe the characteristics of biopsy-negative (TAB^{-}) compared to biopsy-positive (TAB+) GCA.
Methods: We systematically searched Scopus, PubMed, Ovid MEDLINE, and the Cochrane Library to identify studies comparing demographic, clinical, and laboratory characteristics of TAB^{+} and TAB^{-} patients with GCA. Two independent reviewers screened a total of 4,452 records using predefined inclusion and exclusion criteria; 85 full-text articles were reviewed, and 11 met the criteria for inclusion. Extracted variables included study design, demographics, clinical features, laboratory investigations, and disease-related complications. A random-effects meta-analysis was performed, reporting mean differences (MDs) for continuous outcomes and odds ratios (ORs) for dichotomous outcomes, each with corresponding 95% confidence intervals (CIs). Heterogeneity across studies was evaluated using the I^2 statistic.
Results: Results: A total of 11 studies (10 retrospective and 1 prospective) were included in the

analysis, representing a broad geographic distribution. The majority originated from Europe (54.5%), followed by studies from Asia (27.2%) and North America (18.1%). The median sample size across studies was 114 patients, with a range from 42 to 715 patients. The mean follow-up duration is 13.45 ± SD 4.80 years [6-21 years]. TAB+ patients were slightly older than TAB– patients (MD = +4.36 years; 95% CI 1.62–7.09; I^2 = 68%). Inflammatory markers were significantly higher in the TAB+ group: erythrocyte sedimentation rate (MD = +14.06 mm/h; 95% CI 6.35–21.77; I^2 = 76%) and C-reactive protein levels (MD = +12.36 mg/L; 95% CI 0.44–24.29; I^2 = 63%). Jaw claudication was more frequent in TAB+ patients (OR = 3.07; 95% CI 1.79–5.26; $p < 0.001$; I^2 = 51%). Visual symptoms (OR = 1.62; 95% CI 0.66–3.96; I^2 = 65%), headache (OR = 1.22; 95% CI 0.70–2.14; I^2 = 61%) and polymyalgia rheumatica symptoms (OR = 1.06; 95% CI 0.69–1.61; I^2 = 7%) did not differ significantly between the two groups.
Conclusion: Conclusions: TAB+ GCA patients exhibit a distinct clinical and laboratory phenotype characterized by older age, higher acute phase reactants, and a greater likelihood of jaw calculation. These differences underscore the heterogeneity of GCA and highlight the importance of multi-modal diagnostic approaches. Recognizing these phenotypic patterns may also support more timely and effective management decisions.
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Chronic Nonbacterial Osteomyelitis (CNO) and Takayasu Arteritis - Three Cases in a Tertiary Pediatric Hospital and a Literature Review

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Objectives: Chronic nonbacterial osteomyelitis (CNO) and Takayasu arteritis (TAK) are distinct inflammatory disorders traditionally considered unrelated.[1,2] Fewer than 10 cases of co-occurrence have been reported, including 5 pediatric patients,[3] suggesting a possible overlap within the autoinflammatory spectrum. We describe three pediatric cases of CNO who developed TAK-like large-vessel vasculitis.
Methods: We conducted a retrospective review of three pediatric patients diagnosed with CNO at The Hospital for Sick Children (Toronto, Canada) who later developed large-vessel vasculitis. Patients were identified through a review of the Childhood Arthritis and Rheumatic Diseases (CARD) Biobank, which was conducted under institutional Research Ethics Board (REB) approval (#1000046337).
Results: Case Presentations: Case 1: A 12-year-old White-European female with CNO involving the clavicle, thoracic spine, and sacrum developed isolated pulmonary artery vasculitis at age 15, presenting with chest pain and systemic inflammation. She responded to corticosteroids and infliximab; Case 2: A 5-year-old male of Guyanese ethnicity, diagnosed with CNO involving mandible and long bones; At the age of 15 he had persistent unexplained elevated inflammatory markers; imaging revealed extensive abdominal aortic and branch vessel vasculitis as well as

renal arteries, despite being asymptomatic. He required corticosteroids, infliximab, and leflunomide, with flares (new onset hypertension with imaging suggestive of SMA and renal arteries inflammation) linked to non-adherence; Case 3: An 8-year-old South Asian female with congenital anomalies (intestinal malrotation, bicornuate uterus, poly-splenia) and Failure to Thrive (FTT) at infancy was diagnosed with cervical spine CNO and developed medium/large vessel vasculitis at age 11 involving thoracic and abdominal aorta and femoral arteries, with work-up following presentation of erythema-nodosum-like lesions. She was managed with corticosteroids, infliximab and methotrexate (Table 1), (CNO and TAK - cases summary).
Conclusion: This series highlights a rare but clinically relevant association between CNO and TAK-like-vasculitis. Vigilance for vascular involvement in patients with CNO is essential for timely diagnosis and management. These observations may provide clues toward understanding shared pathogenic mechanisms.
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Recurrent Lymphocytic Pleural Effusions as an Atypical Presentation of VEXAS Syndrome: A Case Report

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Background: VEXAS (Vacuoles, E1 enzyme, X-linked, Autoinflammatory, Somatic) syndrome is a recently described adult-onset autoinflammatory disorder caused by somatic mutations in the UBA1 gene. The condition predominantly affects men over 50 years of age and manifests with heterogeneous rheumatologic, dermatologic, hematologic, and systemic inflammatory features. Pulmonary manifestations occur in over half of patients, but pleural effusions are relatively uncommon.[1] Given its clinical heterogeneity and overlap with autoimmune, infectious, and hematologic diseases, diagnosis remains challenging and relies on genetic confirmation of UBA1 mutations.
Case Report: A 60-year-old man presented with a one-year history of non-productive cough, dyspnea, pleuritic chest pain, fatigue, night sweats, and 10 kg unintentional weight loss. He reported intermittent left ankle swelling, bilateral stiffness, and two episodes of unilateral periorbital edema responsive to short prednisone courses. Laboratory investigations revealed mild macrocytic anemia (hemoglobin 121 g/L, MCV 97.6 fL) and elevated C-reactive protein (38.7 mg/L). Autoimmune and infectious workup, including ANA, ANCA, rheumatoid factor, and extensive infectious serologies, were negative. Imaging demonstrated recurrent right-sided pleural effusions without evidence of malignancy. Thoracentesis yielded a lymphocyte-predominant exudative effusion (80% lymphocytes), with negative cultures and cytology. A subsequent contralateral pleural effusion showed similar findings. Flow cytometry identified a minor B-cell population without definitive lymphoproliferative disorder. Bone marrow biopsy revealed hypercellular marrow with trilineage hematopoiesis, megakaryocytic dysplasia, and mild fibrosis, but no lymphoma. Next-generation sequencing identified a somatic UBA1 p.Met41Thr (c.122T>C) mutation (variant allele fraction 76.6%), confirming VEXAS syndrome, along with a concurrent DNMT3A frameshift mutation (VAF 39.7%) consistent with clonal

hematopoiesis. The patient was treated with oral prednisone 30–40 mg daily, resulting in complete resolution of inflammatory arthritis, improvement of constitutional symptoms, and normalization of inflammatory markers after four weeks. He was subsequently referred for initiation of ruxolitinib as a steroid-sparing agent.[2]

Conclusion: This case highlights VEXAS syndrome as a diagnostic consideration in older men with persistent systemic inflammation, recurrent lymphocytic pleural effusions, episodic arthritis, and periorbital edema in the absence of infection, malignancy, or autoimmune disease. Pleural effusions, although uncommon, may be the primary pulmonary manifestation. Comprehensive evaluation, including next-generation sequencing for UBA1 mutations, is essential for accurate diagnosis and facilitates targeted management with glucocorticoids and steroid-sparing agents. Early recognition improves outcomes and underscores the need for multidisciplinary care.

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