

Supplementary Figure S1. Magnitudes of the associations between cytokines and KOA outcomes stratified by Knee Osteoarthritis Inflammatory Phenotypes (**KOIP**). The boxplot shows the absolute value of the correlation-like measurements used for assess the associations between the cytokines evaluated in the study and baseline clinical (KOOS pain, functional disability and symptoms), ultrasound (effusion and synovial tissue thickness), radiographic severity (Kellgren-Lawrence, osteophytes and joint space narrowing), and progression at two years of follow-up according to the same radiographic criteria. Correlation-like measurements were: Spearman correlations (continuous or ordinal outcomes) and Glass rank biserial correlations (binary outcomes). Kellgren-Lawrence staging and joint space marrowing at baseline were treated as ordinal in these analyses. Differences between each KOIP and the whole dataset (*All*) were statistically significant according to a Wilcoxon test (all p-values < 1.30e-16). **KOIP:** Knee Osteoarthritis Inflammatory Phenotype.

Supplementary Figures S2-S33. Association of synovial and plasma **cytokines** with **clinical severity and radiographic progression** within each Knee Osteoarthritis Inflammatory Phenotype (**KOIP**). In each graphic, the panels show scatter plots, the Spearman correlation coefficient and its corresponding asymptotic 95% confidence interval (between brackets) and p-value (baseline pain, functional disability and joint effusion); or boxplots, stripcharts, group medians, Fold-Change (**FC**) between groups, their corresponding 95% confidence interval and the p-value derived from a Mann-Whitney test (radiographic progression). A positive FC indicates higher average levels of Irisin in progressors while negative FCs represent higher Irisin levels in stable patients. Cytokine's values are represented in a transformed scale according to a Tukey's ladder of powers, to symmetrize their distribution and make them more suitable for graphical representation (see Supplementary Table S2); axis value labels are shown in the original scale. **Corr.:** Correlation; **FC:** Fold-Change; **pv:** p-value; **KOOS:** Knee injury and Osteoarthritis Outcome Scores (reversed scores); **KL:** Kellgren-Lawrence; **JSN:** Joint Space Narrowing; **KOIP:** Knee Osteoarthritis Inflammatory Phenotype.

KOOS functional disability

- [S2: synovial Omentin](#)
- [S3: plasma Interleukin-6](#)

KOOS pain

- [S4: synovial Osteopontin](#)
- [S5: plasma Interleukin-6](#)

KL radiographic progression

- [S6: synovial Resistin](#)
- [S7: synovial C-reactive protein](#)
- [S8: plasma Omentin](#)

Osteophytes radiographic progression

- [S9: synovial Irisin](#)
- [S10: synovial Leptin](#)
- [S11: synovial Adiponectin](#)
- [S12: synovial Omentin](#)
- [S13: synovial Osteopontin](#)
- [S14: synovial Calprotectin](#)
- [S15: plasma Irisin](#)
- [S16: plasma Leptin](#)
- [S17: plasma Omentin](#)
- [S18: plasma Osteopontin](#)
- [S19: plasma Interleukin-8](#)

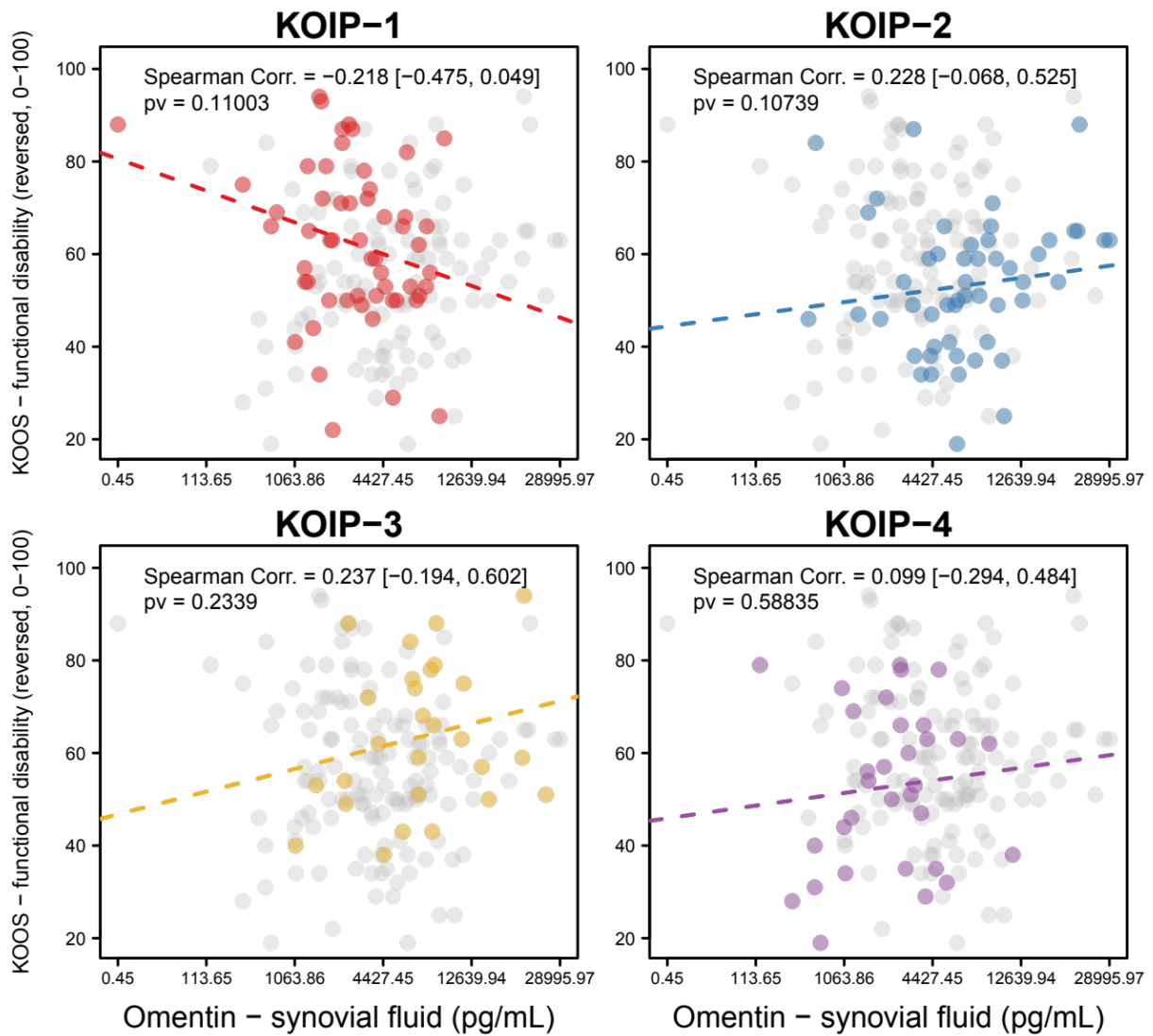
JSN radiographic progression

- [S20: synovial Irisin](#)
- [S21: synovial Leptin](#)
- [S22: synovial Omentin](#)
- [S23: synovial Osteopontin](#)
- [S24: plasma Irisin](#)
- [S25: plasma Leptin](#)

Ultrasound Joint Effusion

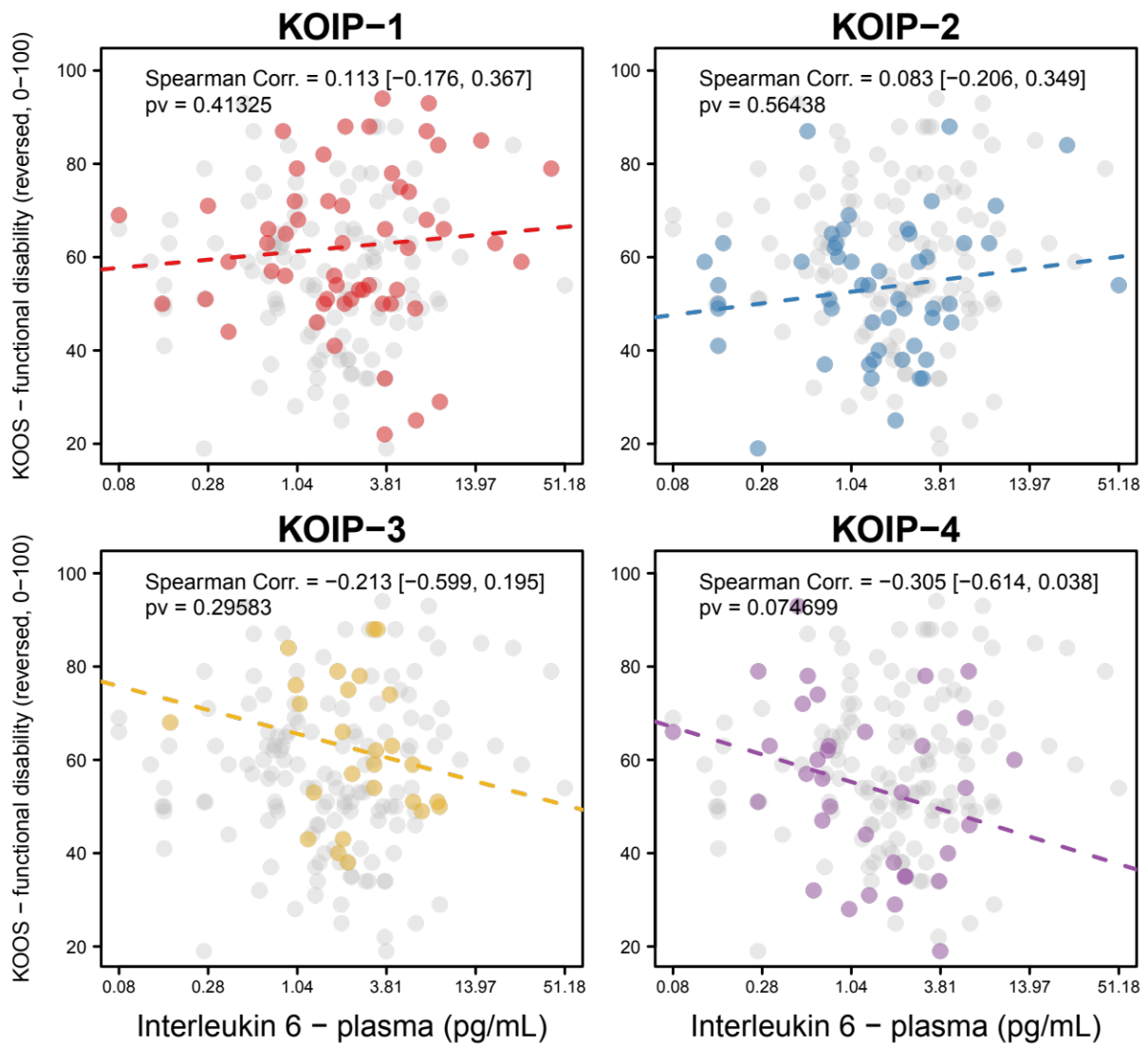
- [S26: synovial Irisin](#)
- [S27: synovial Leptin](#)
- [S28: synovial Omentin](#)
- [S29: synovial C-reactive protein](#)
- [S30: plasma Leptin](#)
- [S31: plasma Calprotectin](#)
- [S32: plasma Interleukin-6](#)
- [S33: plasma C-reactive protein](#)

S2: KOOS functional disability - synovial Omentin



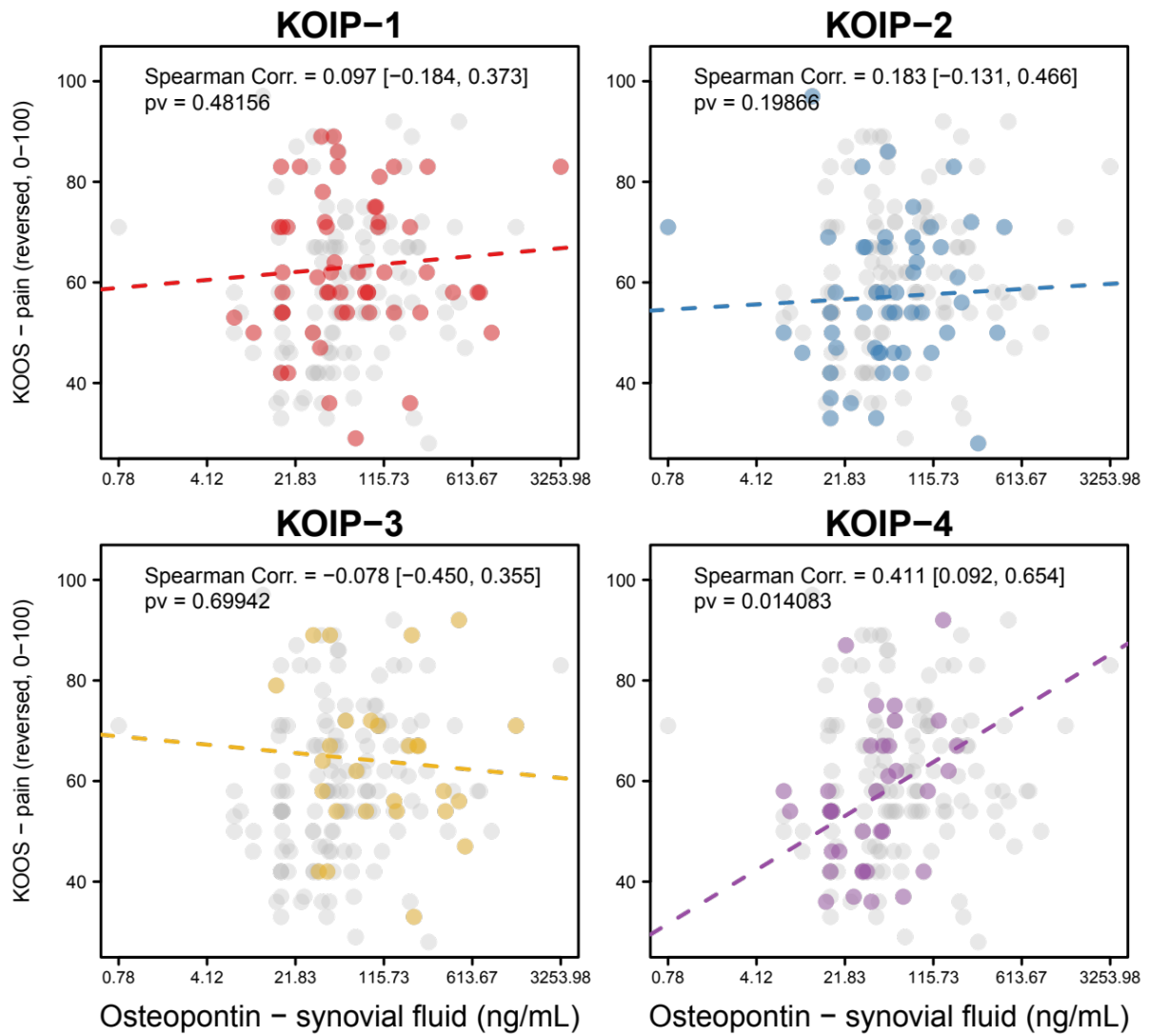
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S3: KOOS functional disability - plasma Interleukin-6



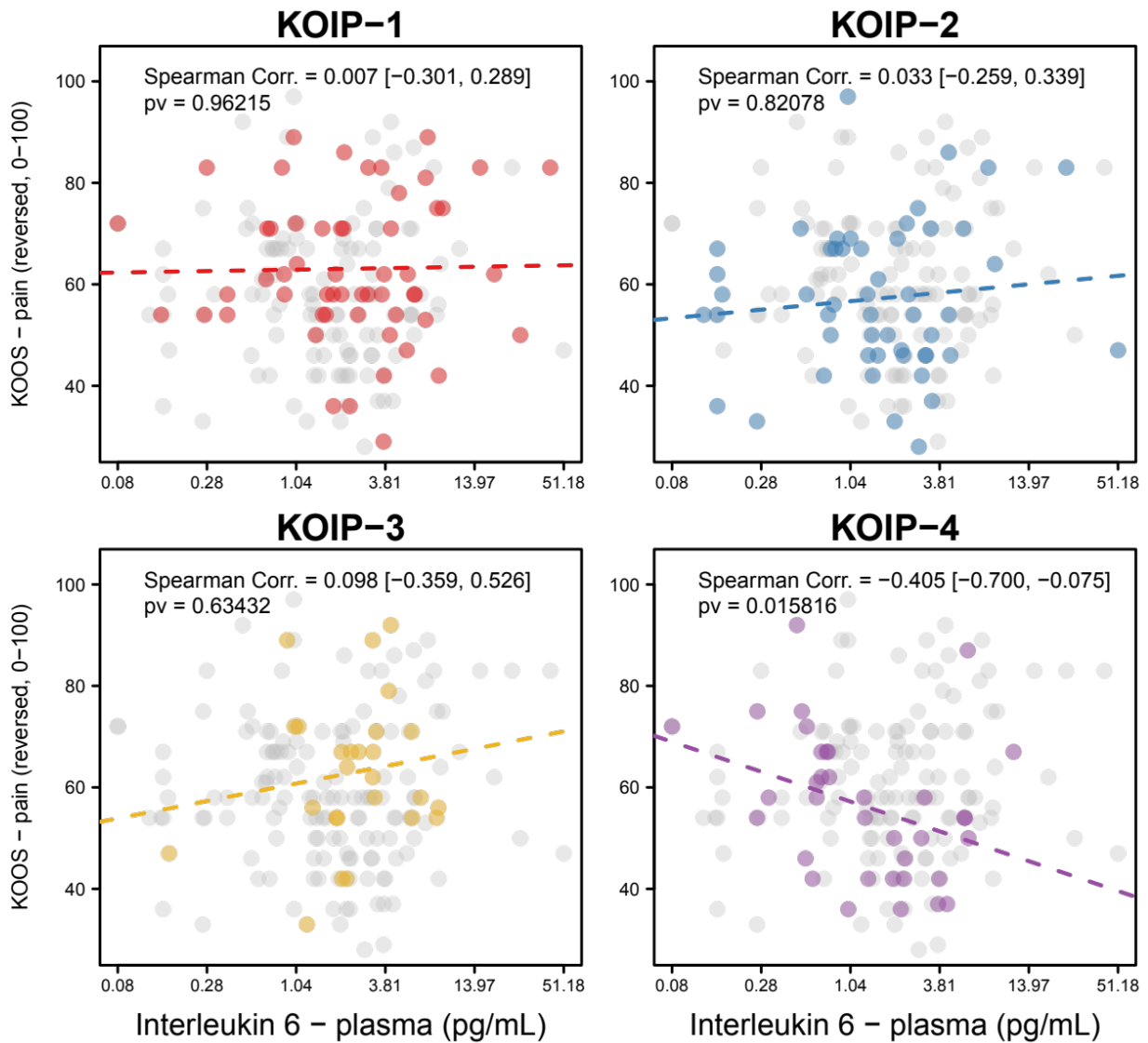
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S4: KOOS pain - synovial Osteopontin



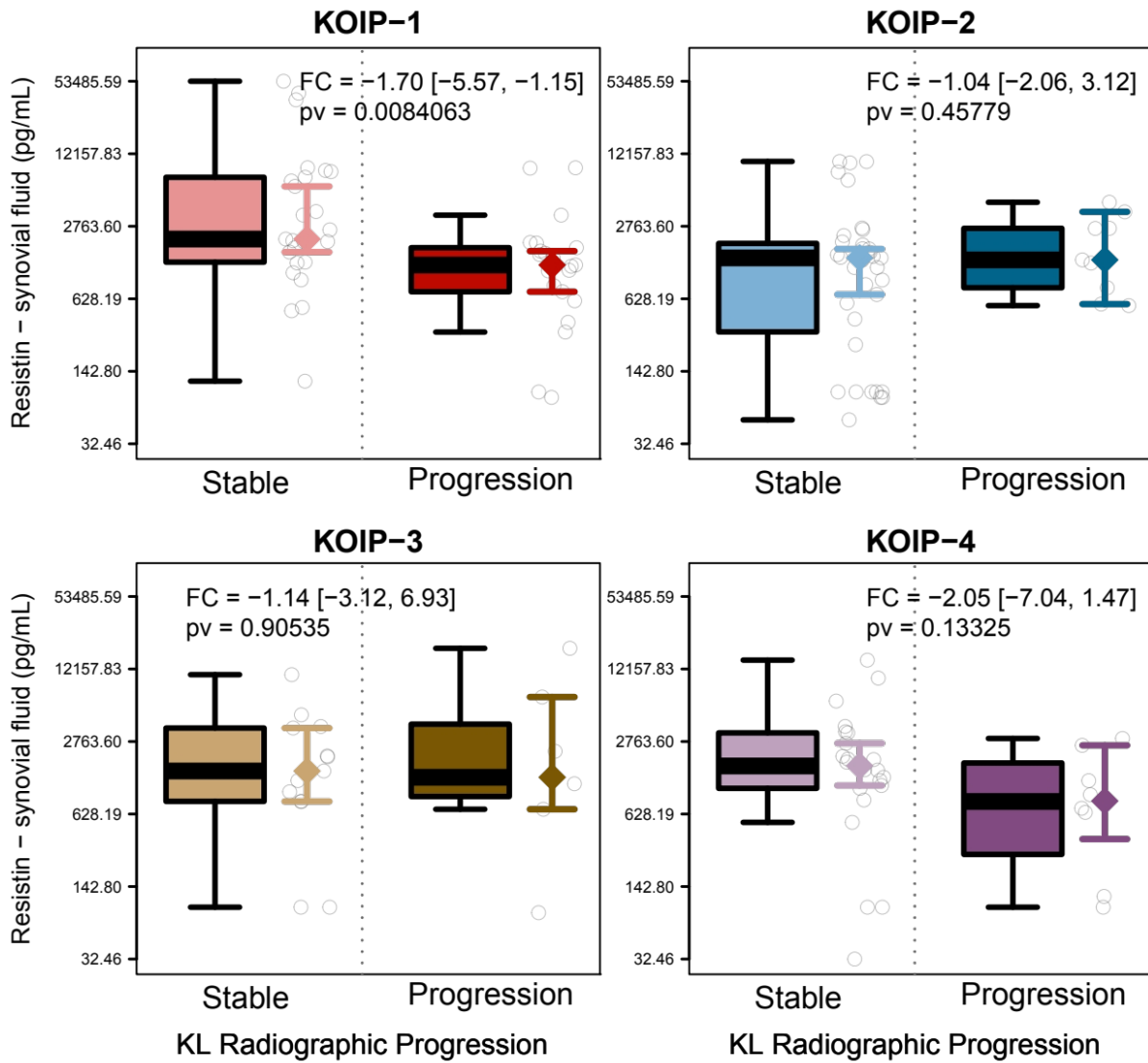
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S5: KOOS pain - plasma Interleukin-6



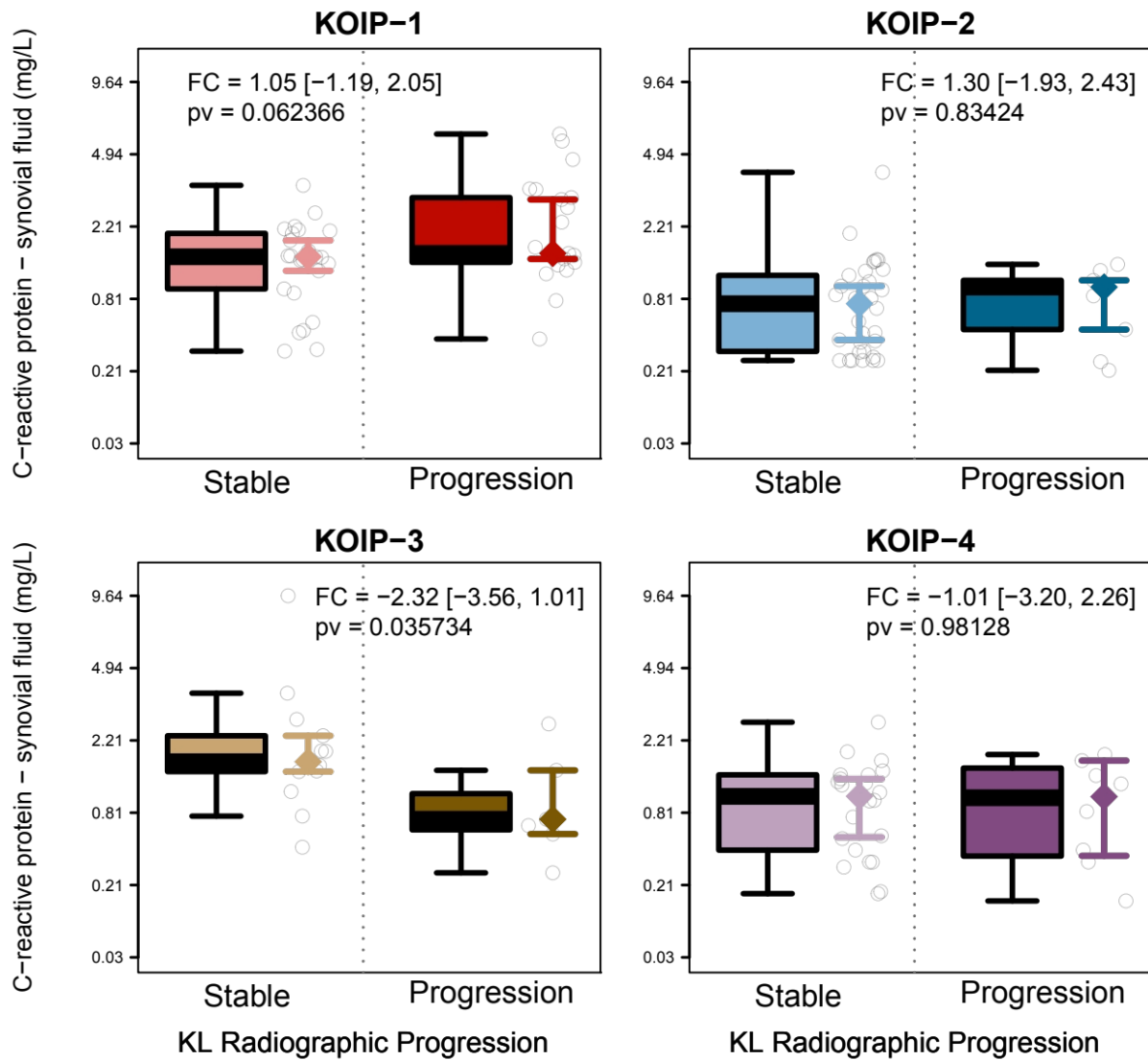
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S6: KL radiographic progression - synovial Resistin



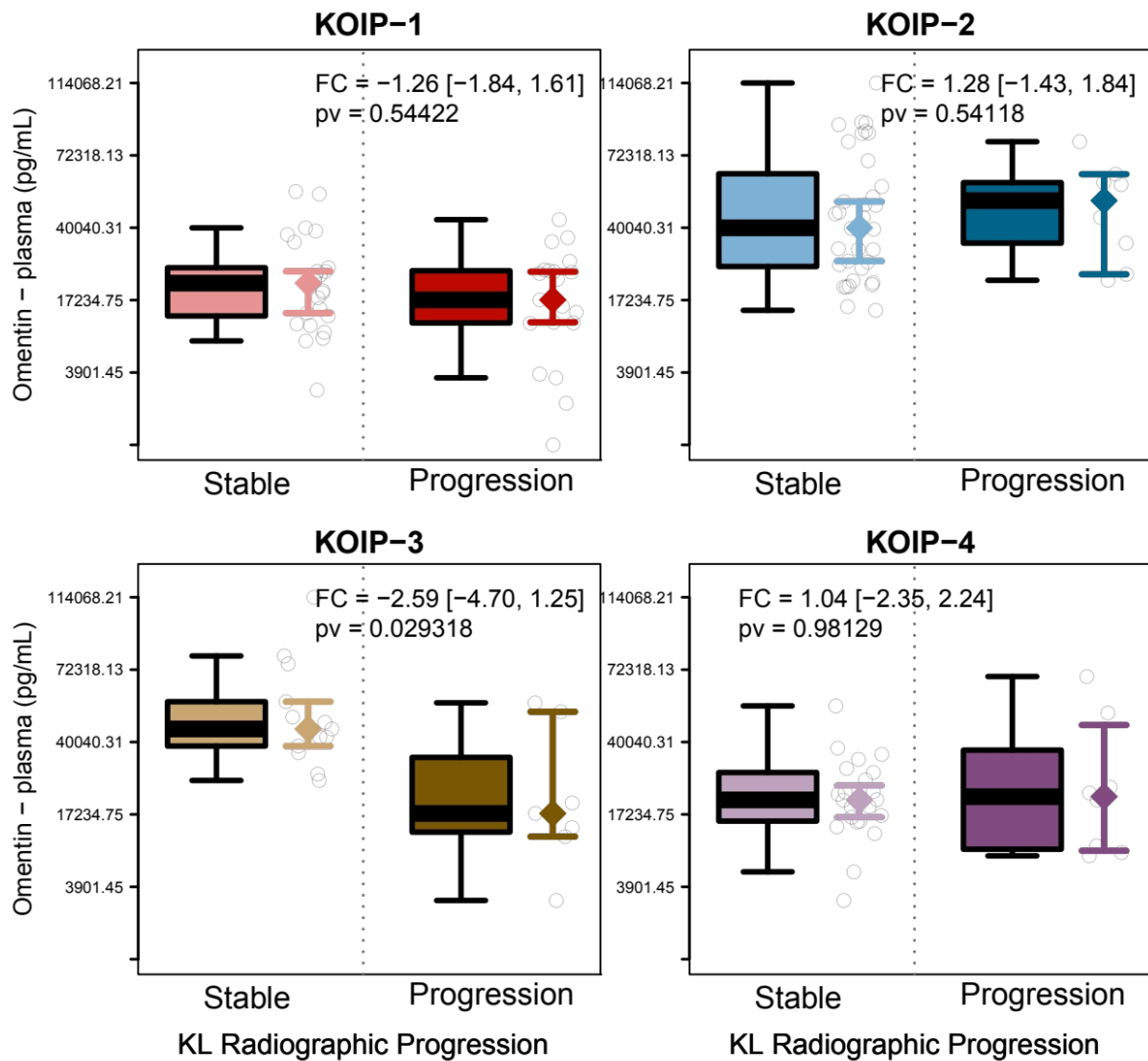
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S7: KL radiographic progression - synovial C-reactive protein



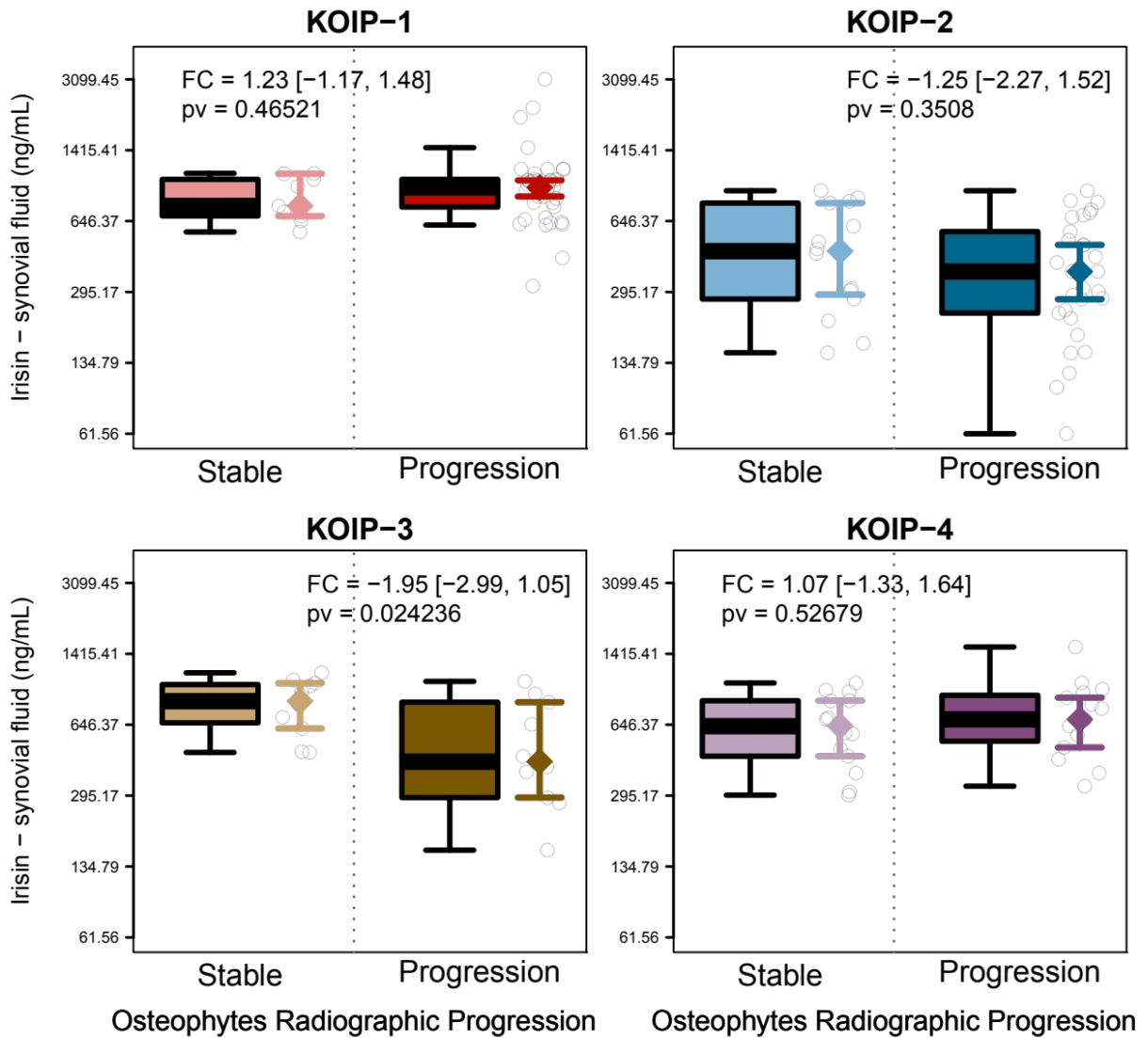
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S8: KL radiographic progression - plasma Omentin



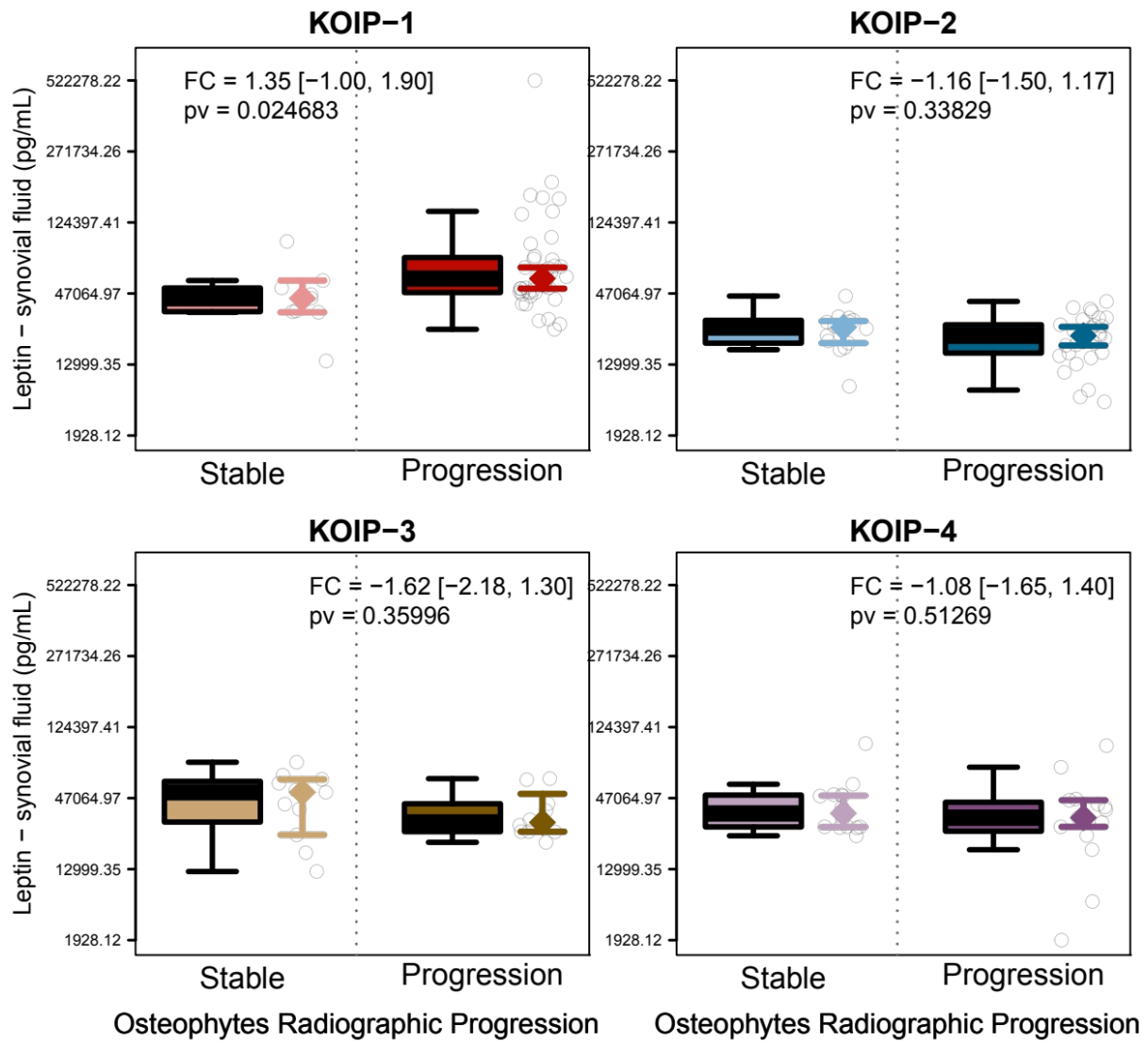
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S9: Osteophytes radiographic progression - synovial Irisin



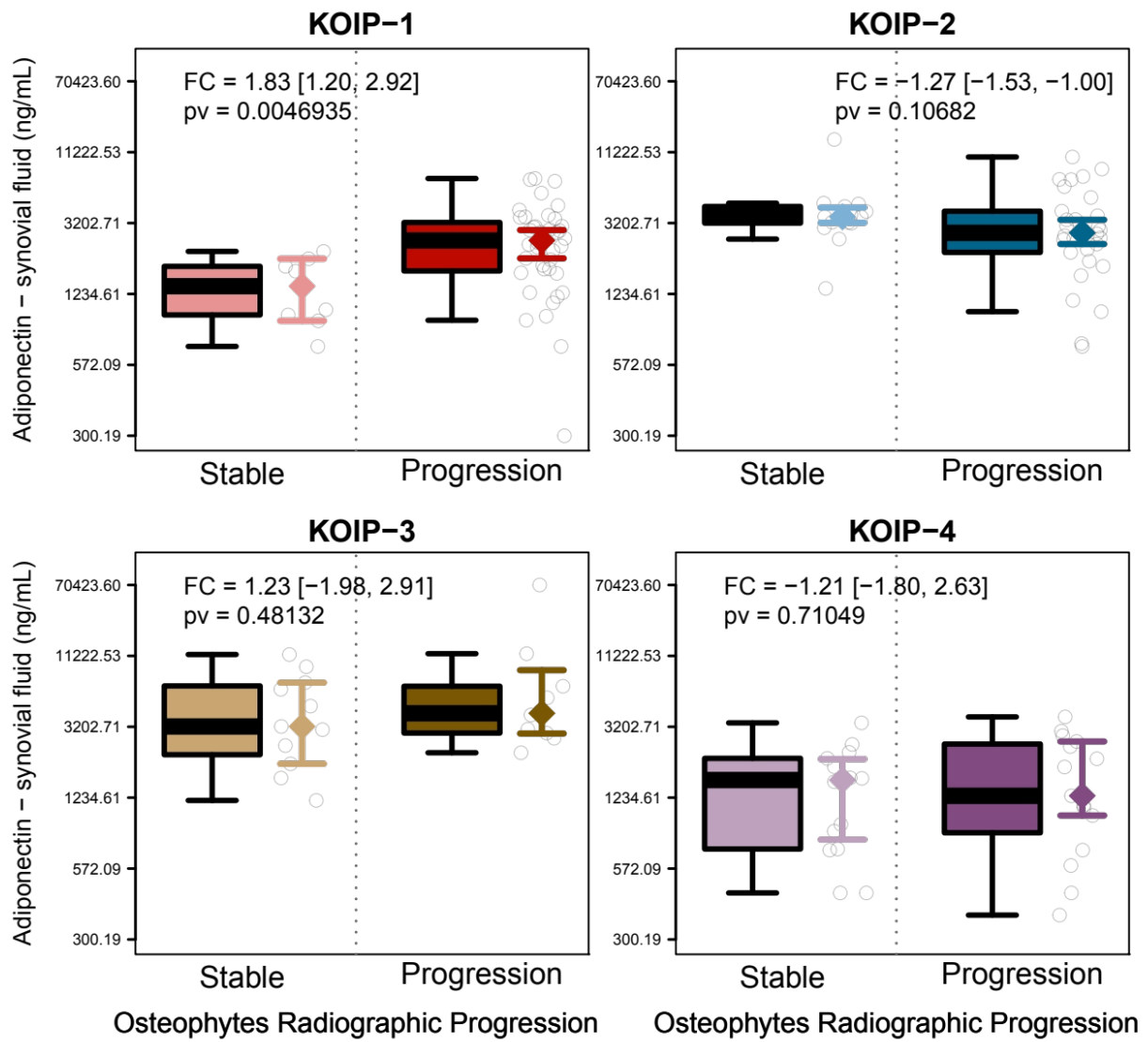
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S10: Osteophytes radiographic progression - synovial Leptin



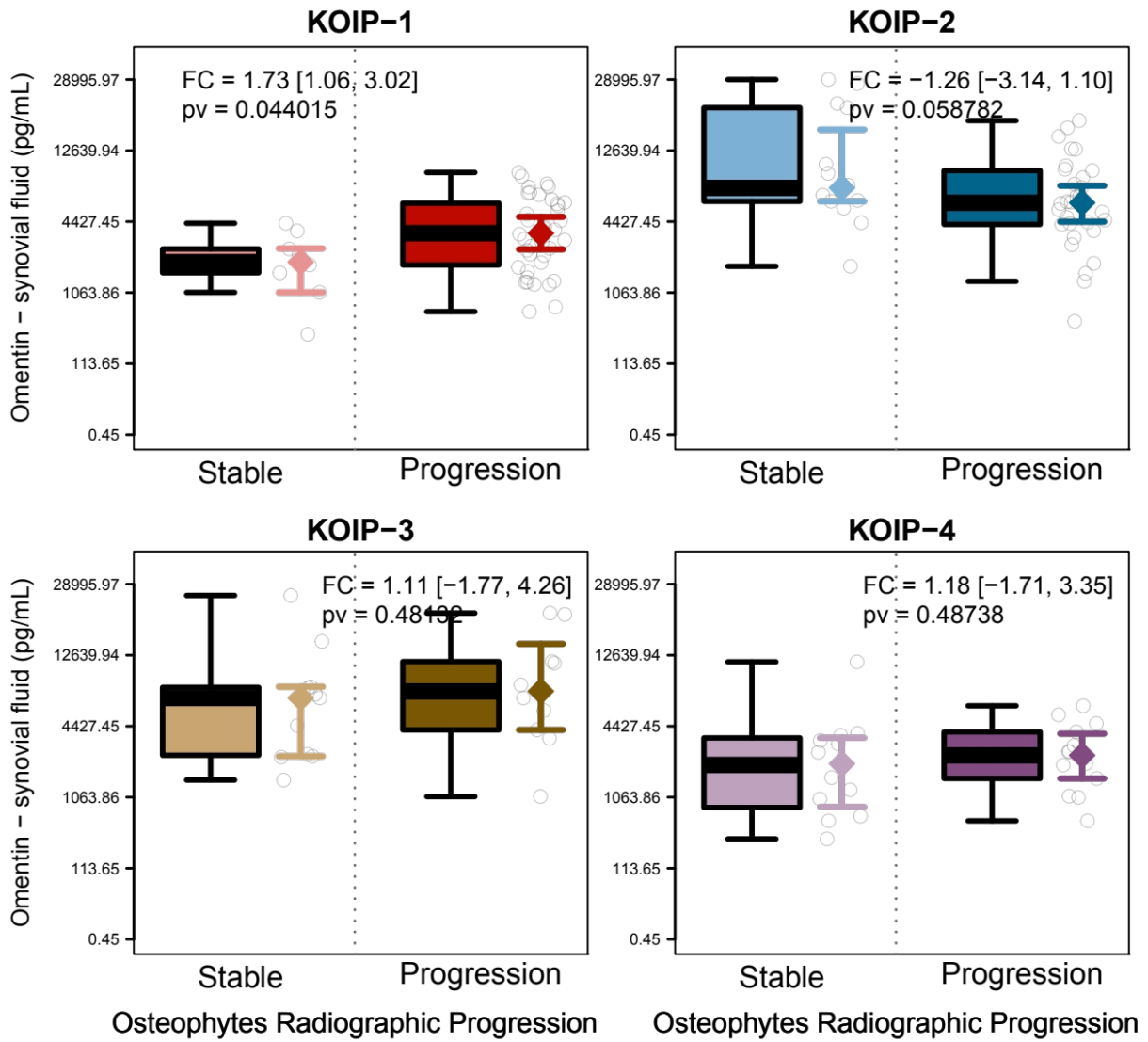
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S11: Osteophytes radiographic progression - synovial Adiponectin



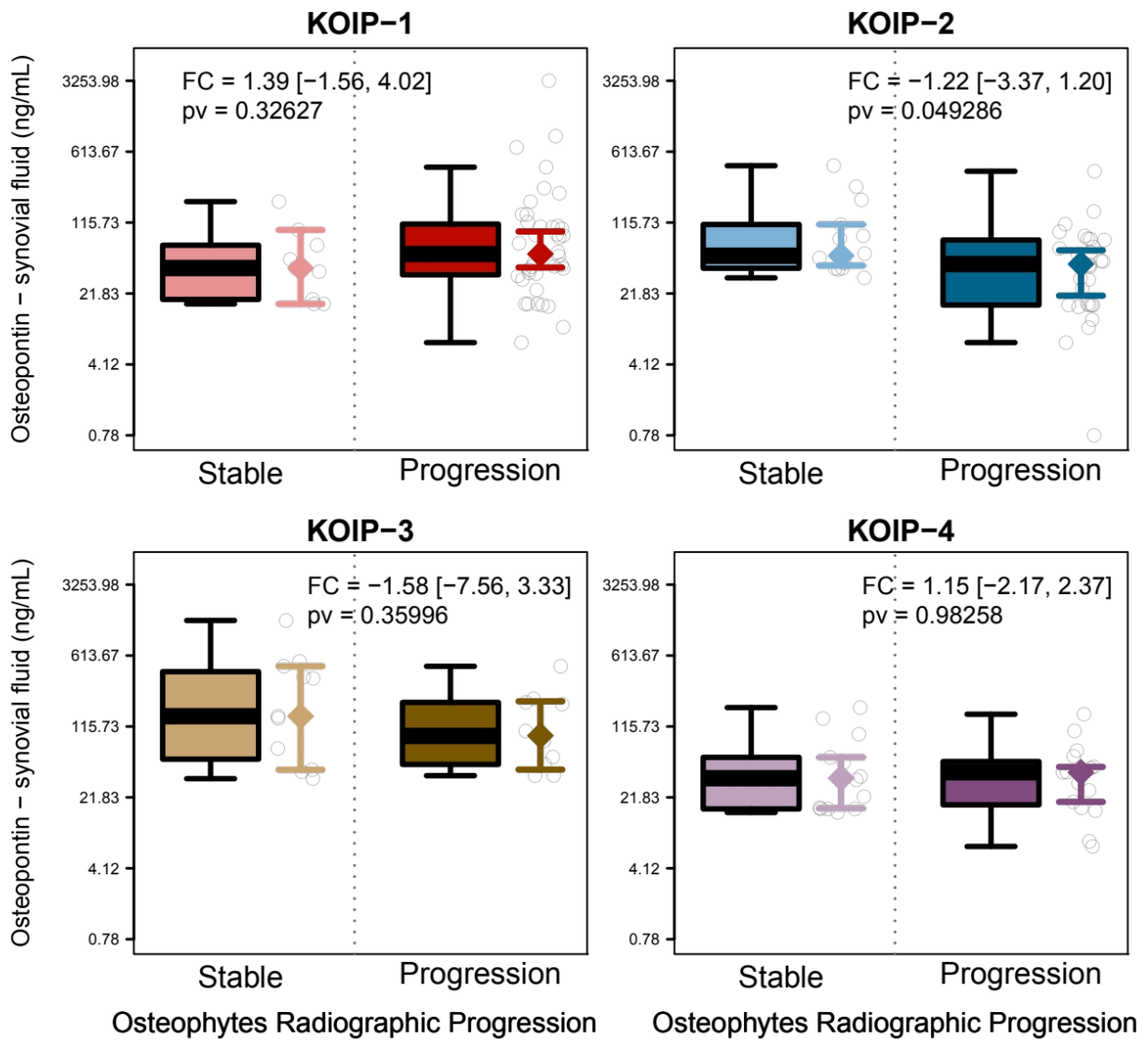
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S12: Osteophytes radiographic progression - synovial Omentin



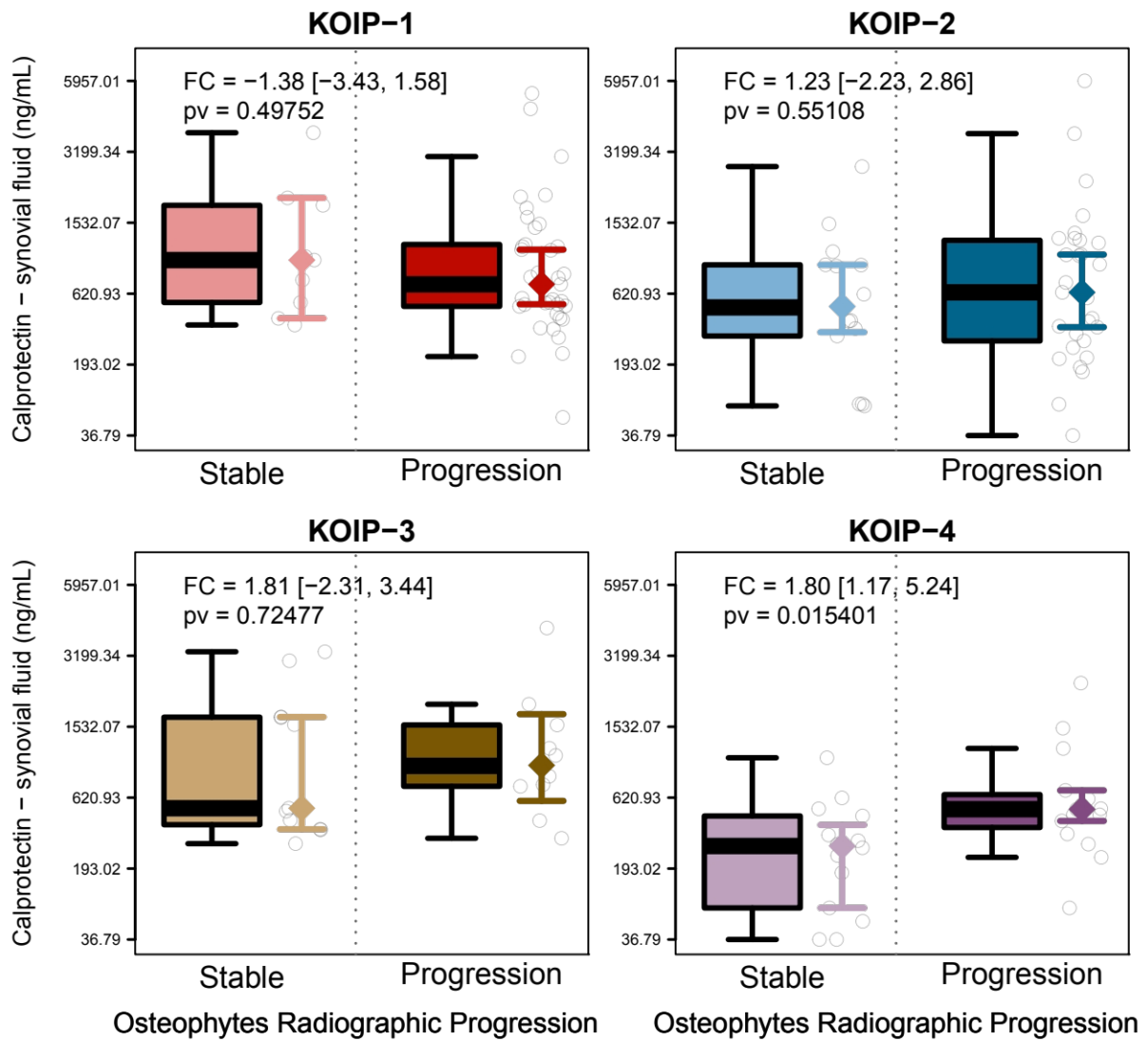
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S13: Osteophytes radiographic progression - synovial Osteopontin



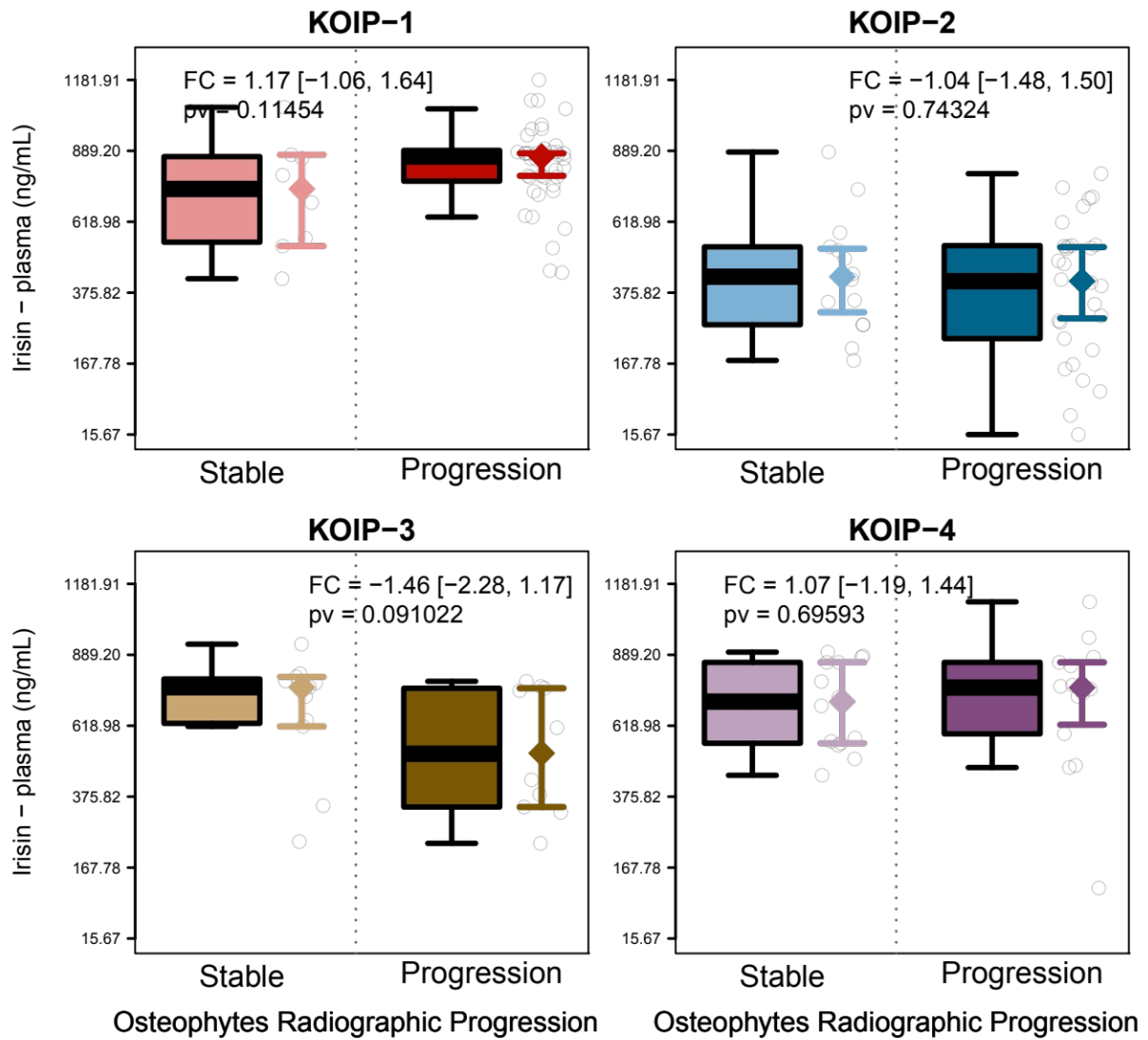
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S14: Osteophytes radiographic progression - synovial Calprotectin



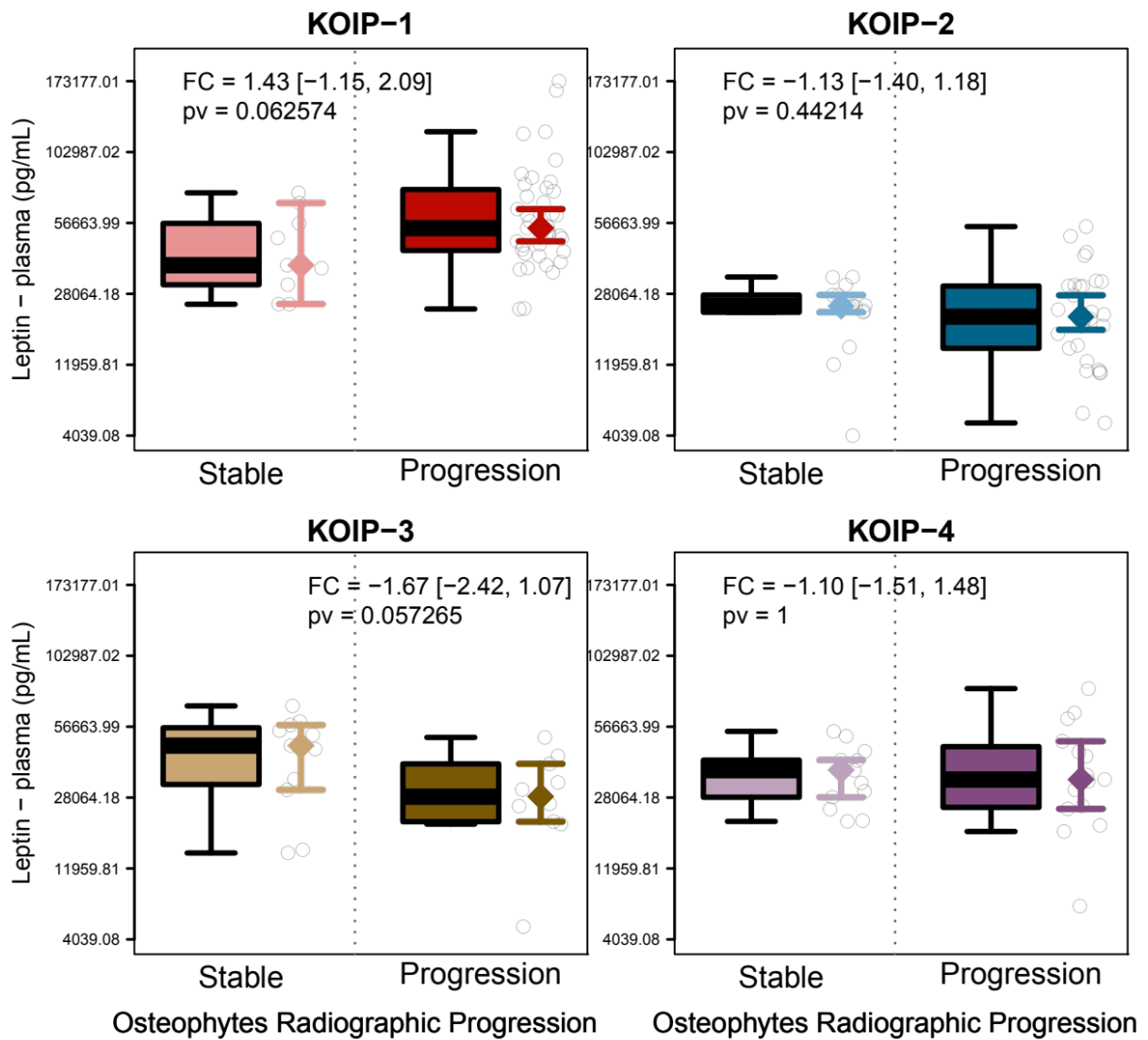
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S15: Osteophytes radiographic progression - plasma Irisin



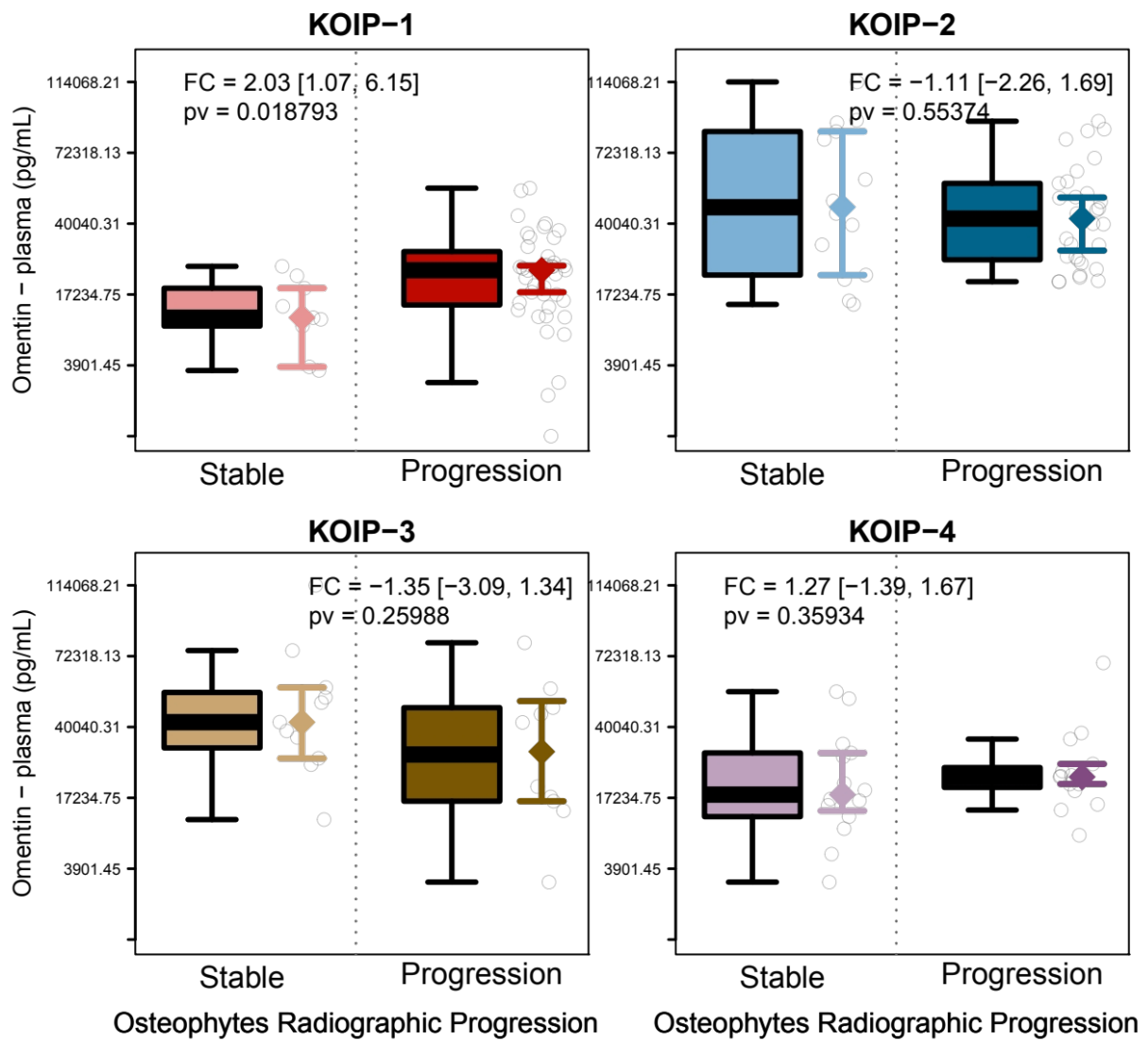
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S16: Osteophytes radiographic progression - plasma Leptin



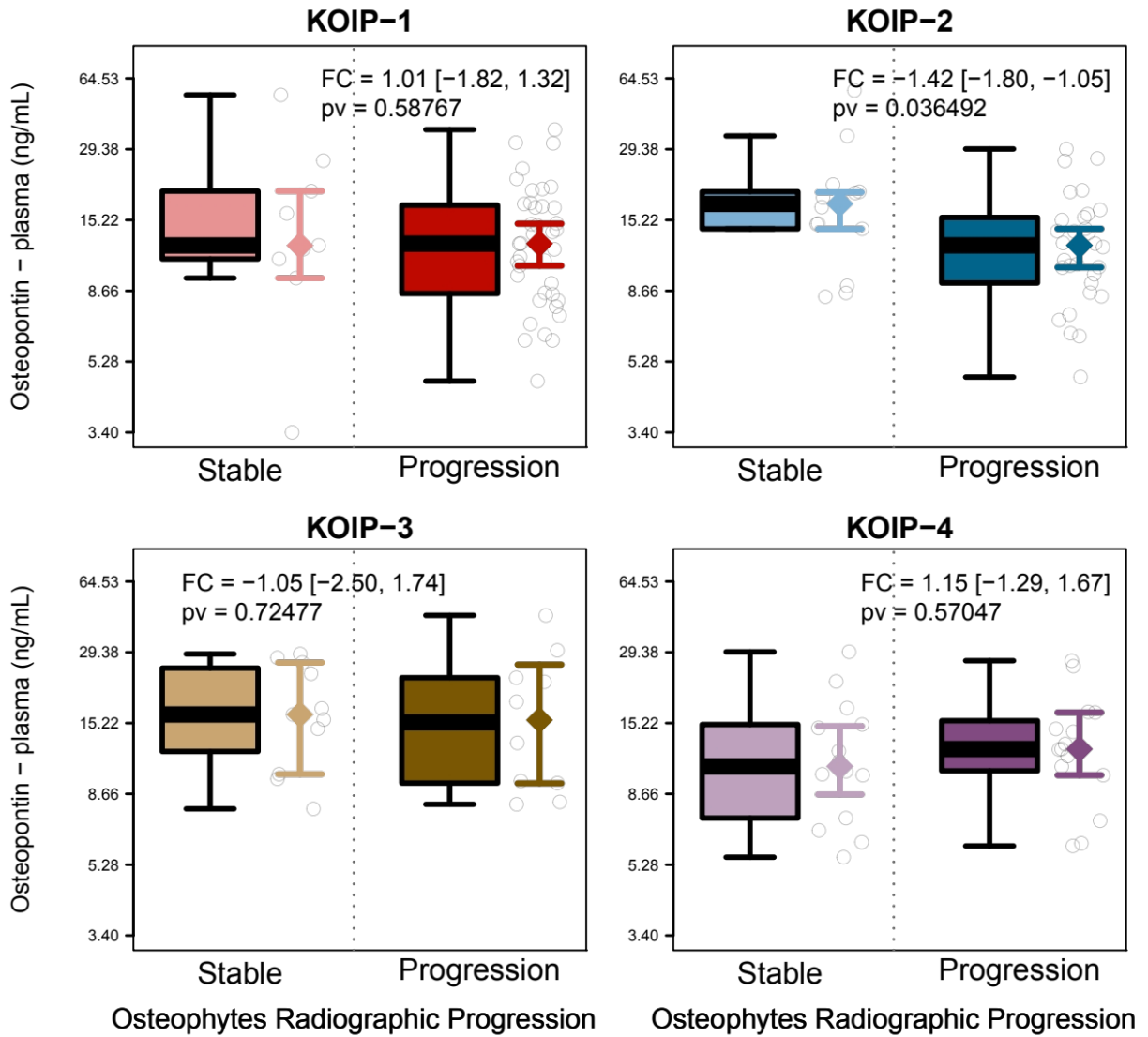
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S17: Osteophytes radiographic progression - plasma Omentin



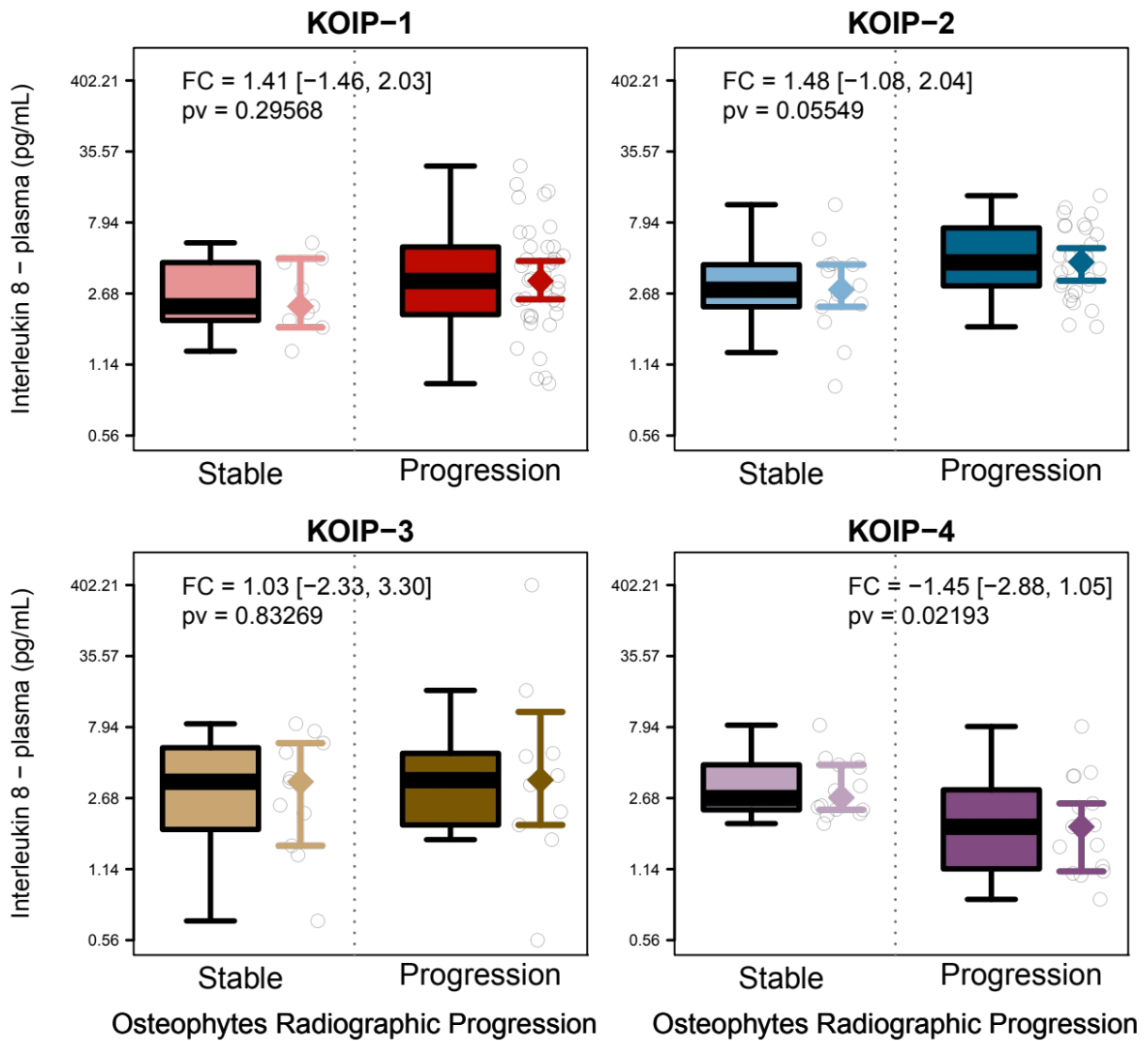
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S18: Osteophytes radiographic progression - plasma Osteopontin



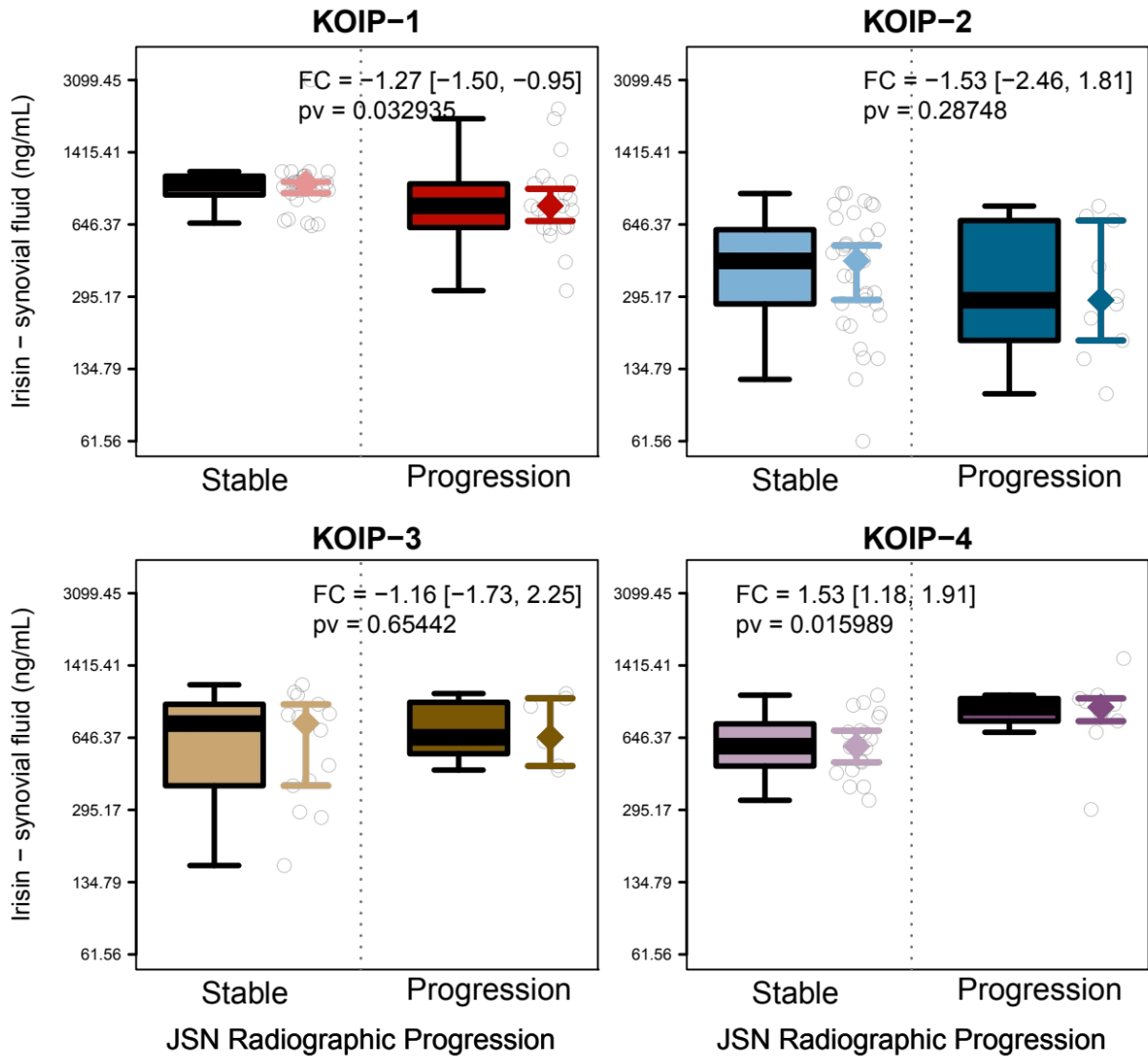
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S19: Osteophytes radiographic progression - plasma Interleukin-8



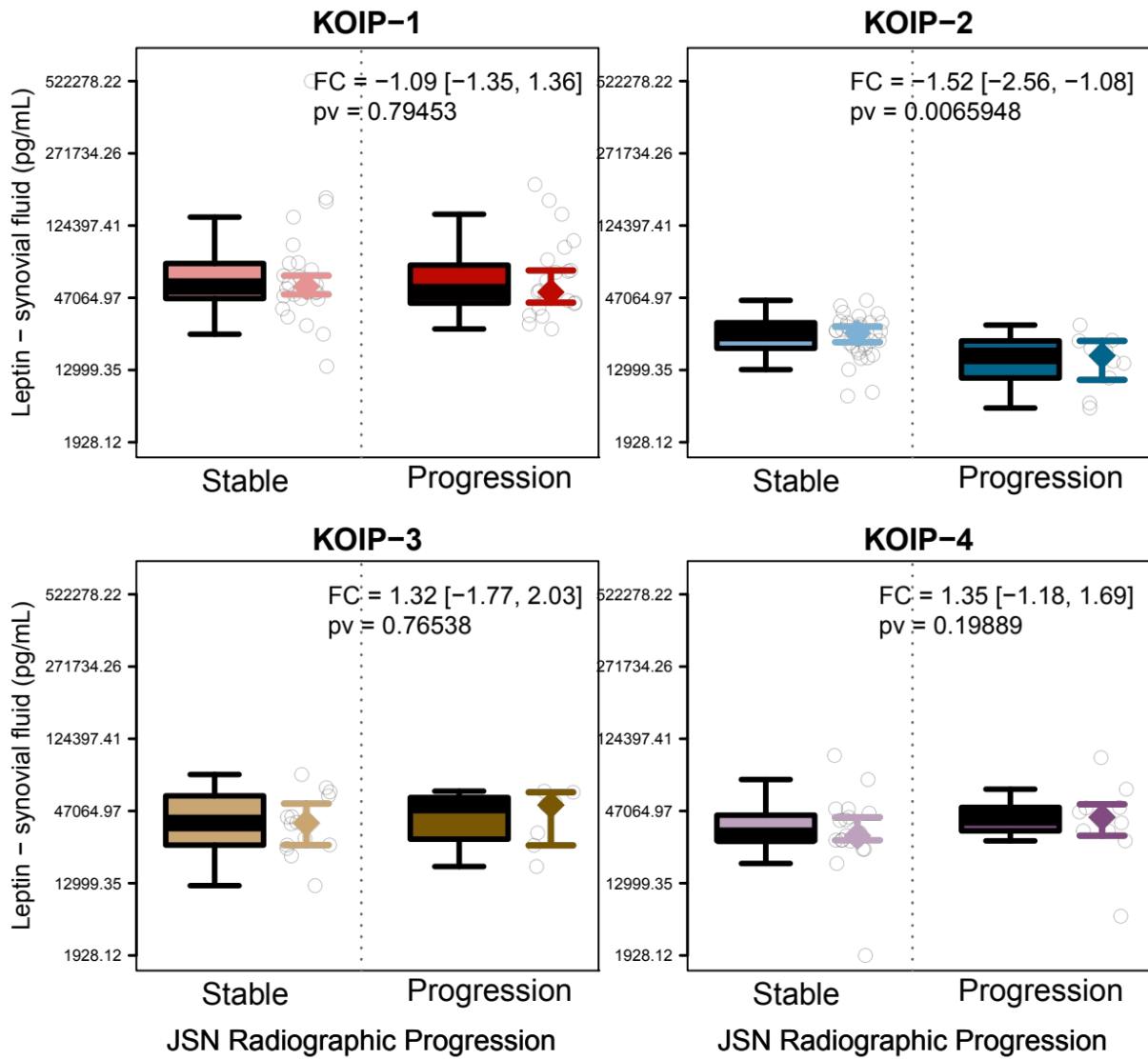
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S20: JSN radiographic progression - synovial Irisin



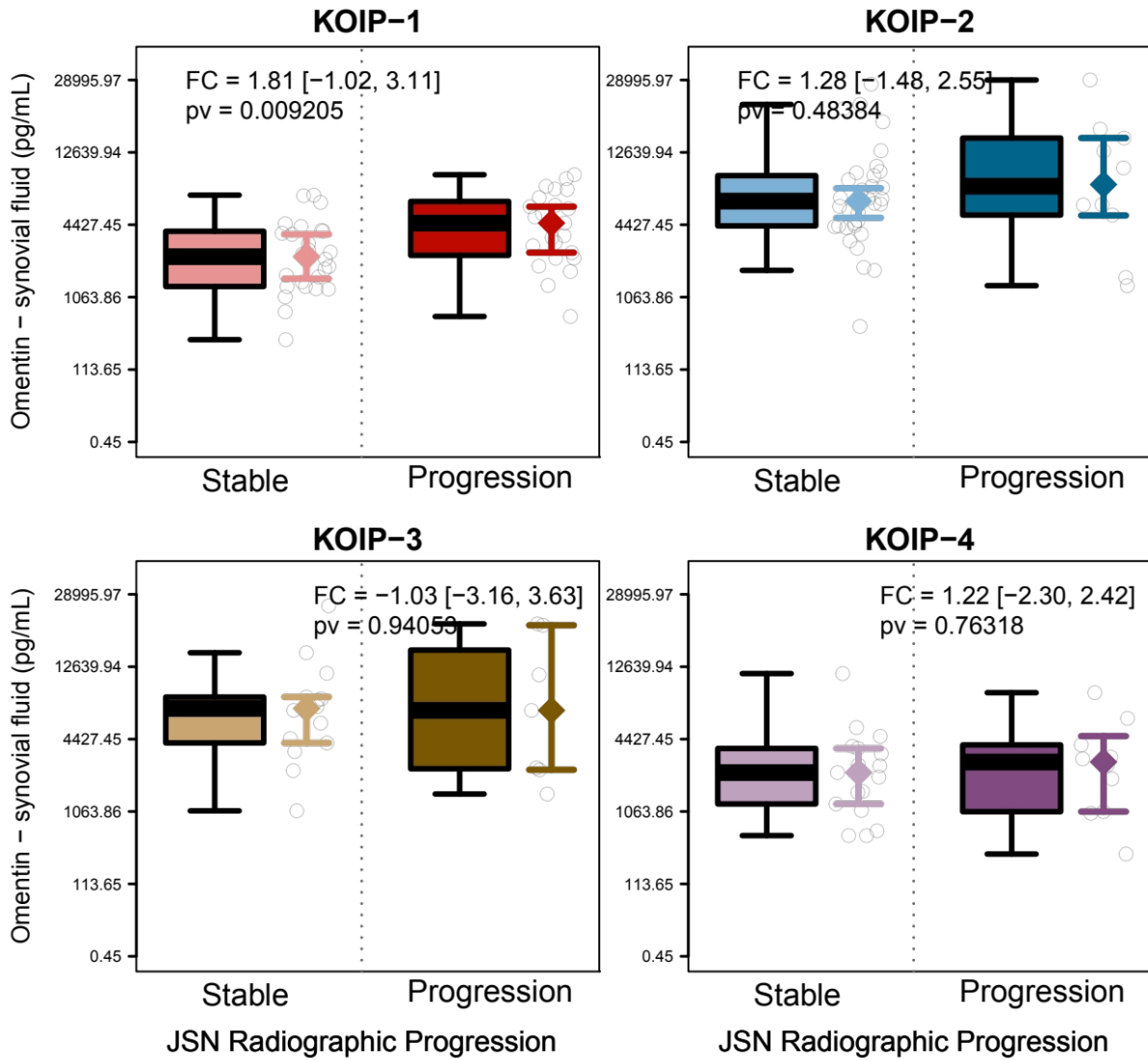
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S21: JSN radiographic progression - synovial Leptin



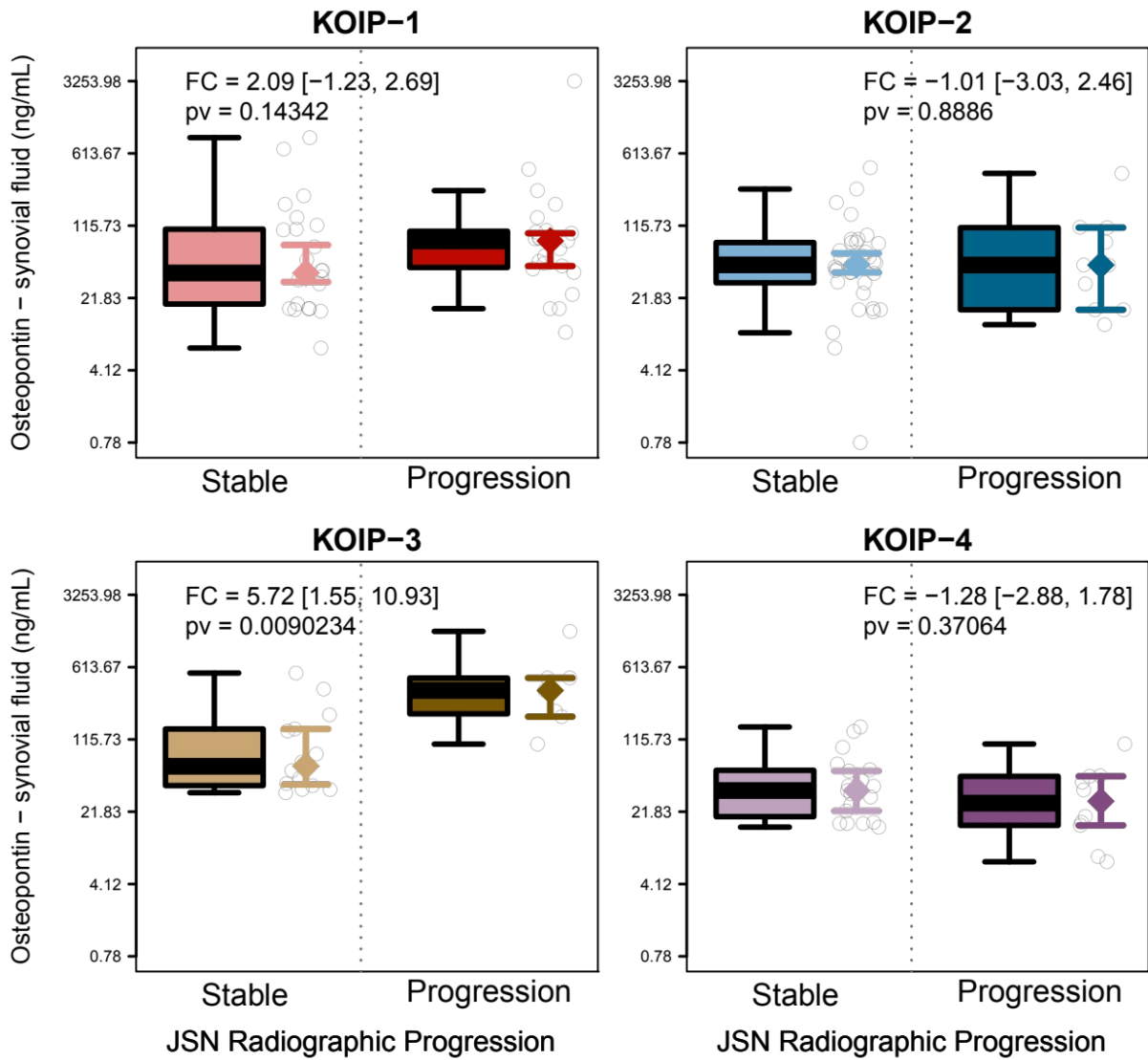
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S22: JSN radiographic progression - synovial Omentin



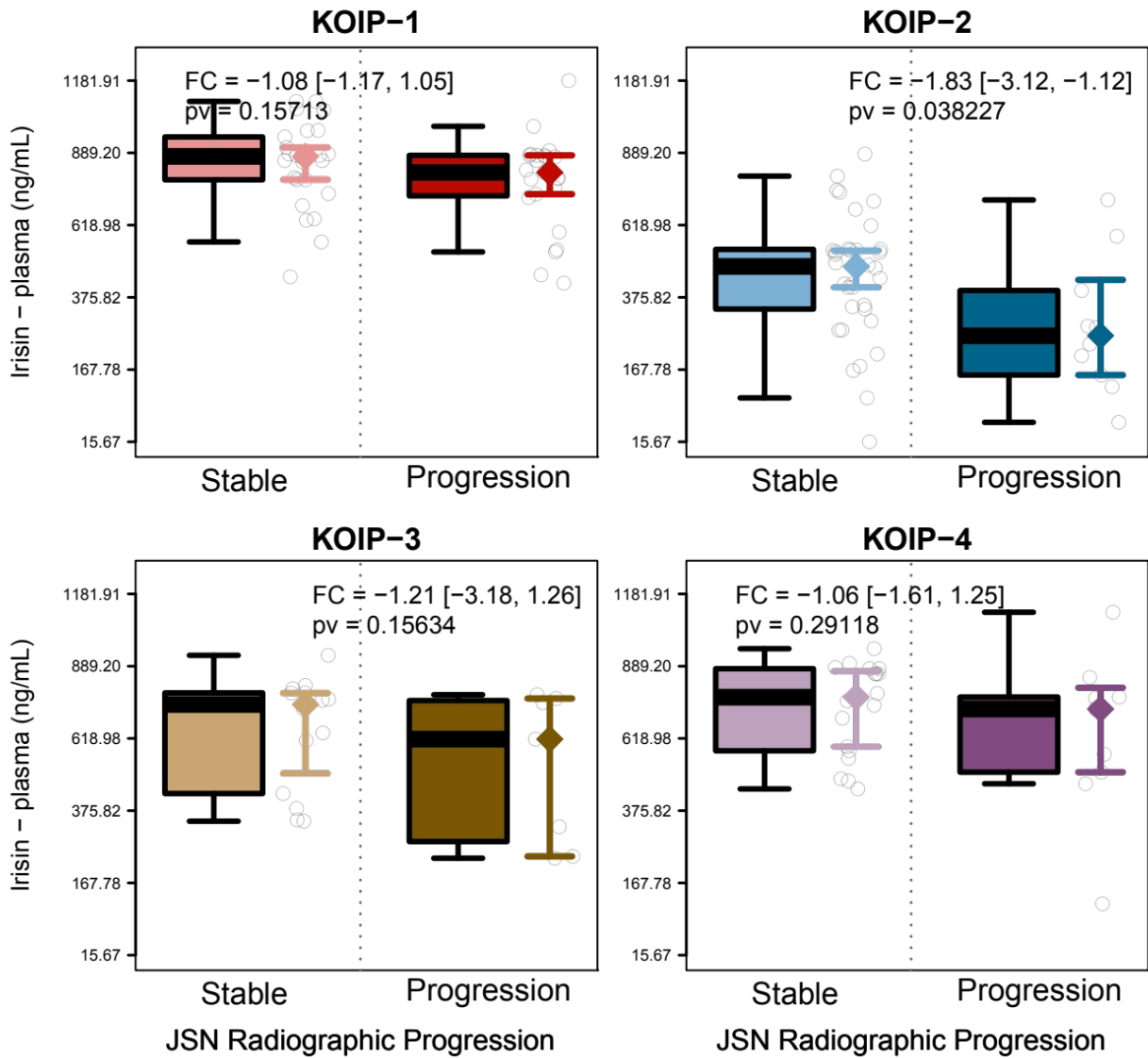
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S23: JSN radiographic progression - synovial Osteopontin



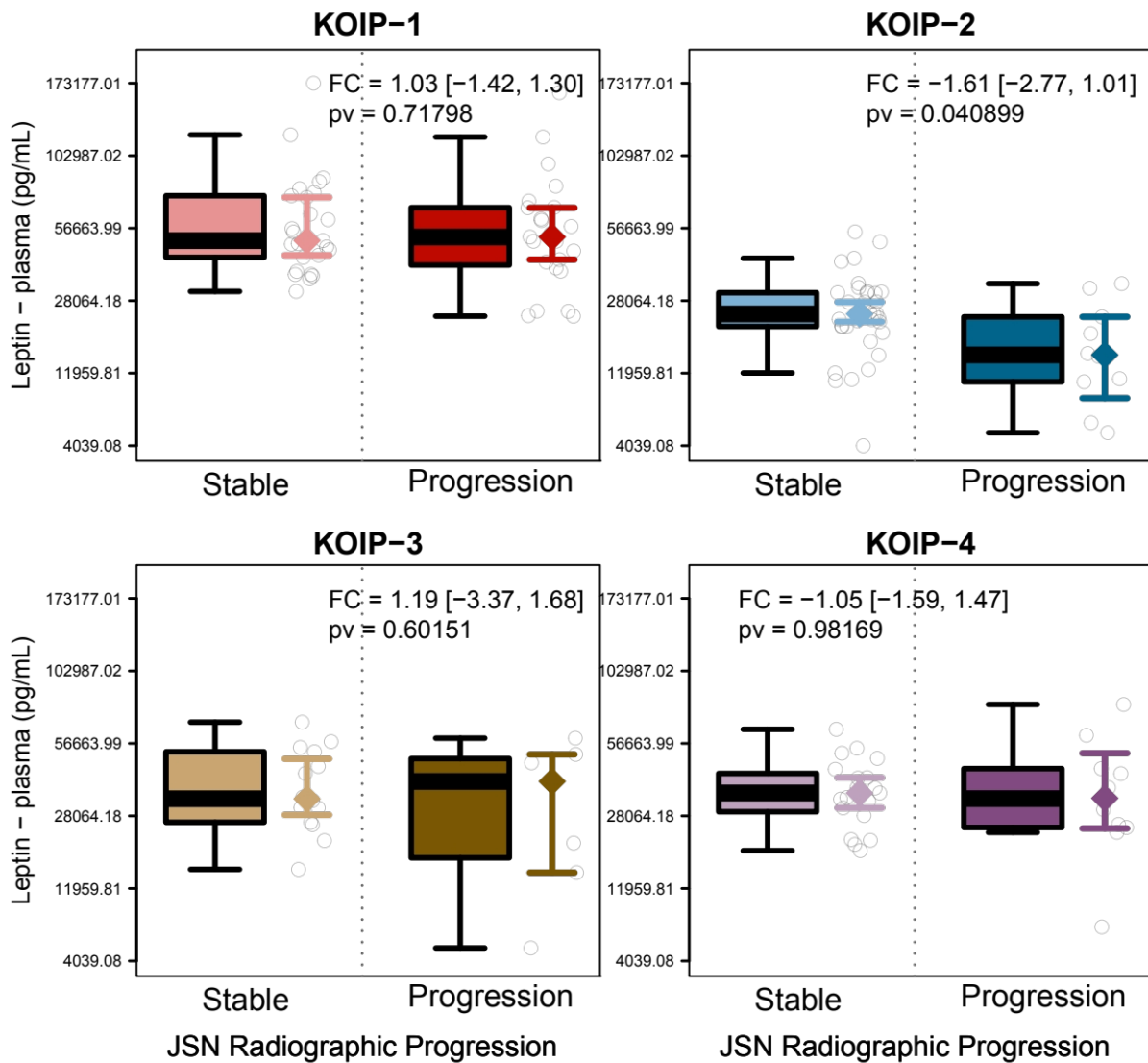
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S24: JSN radiographic progression - plasma Irisin



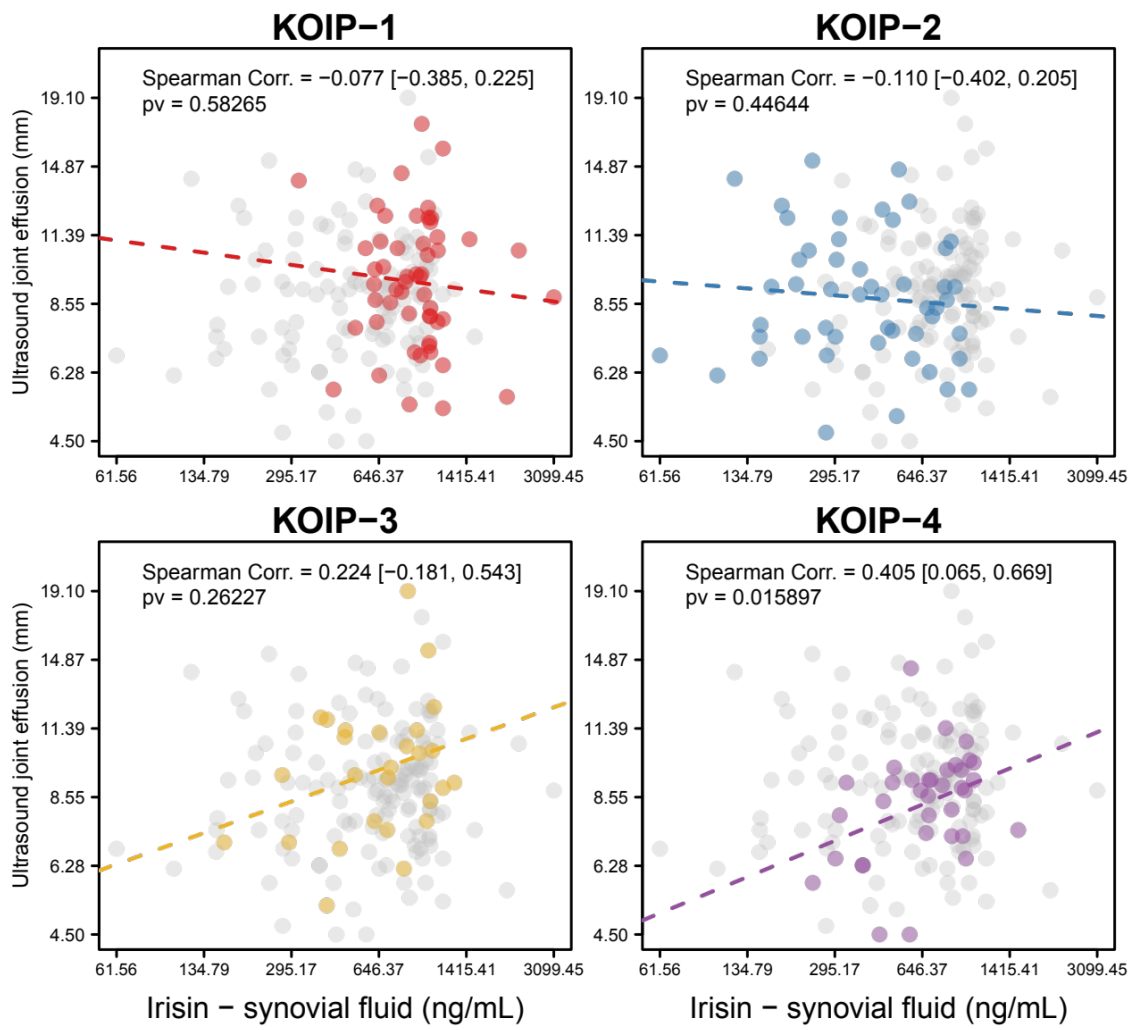
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S25: JSN radiographic progression - plasma Leptin



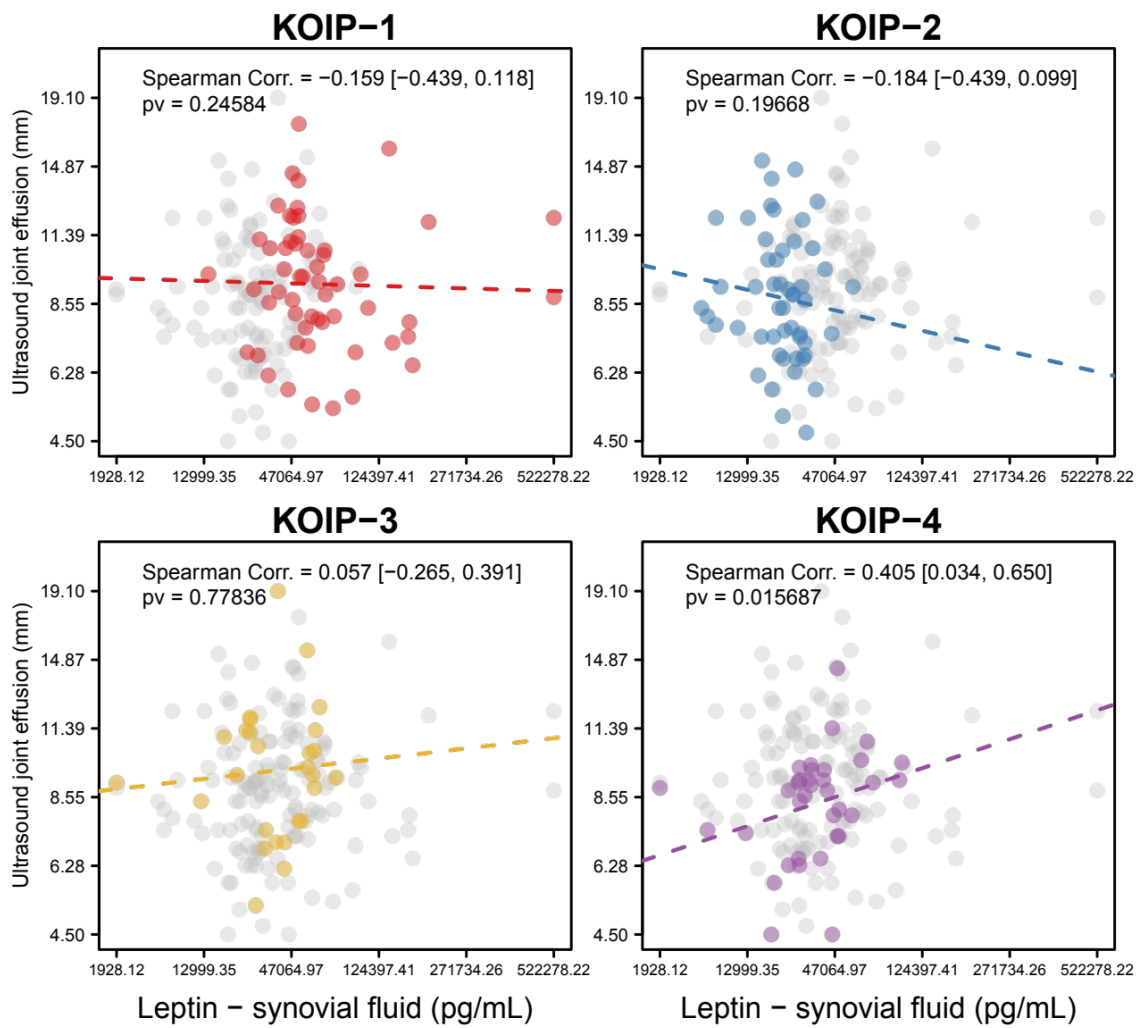
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S26: Ultrasound Joint Effusion - synovial Irisin



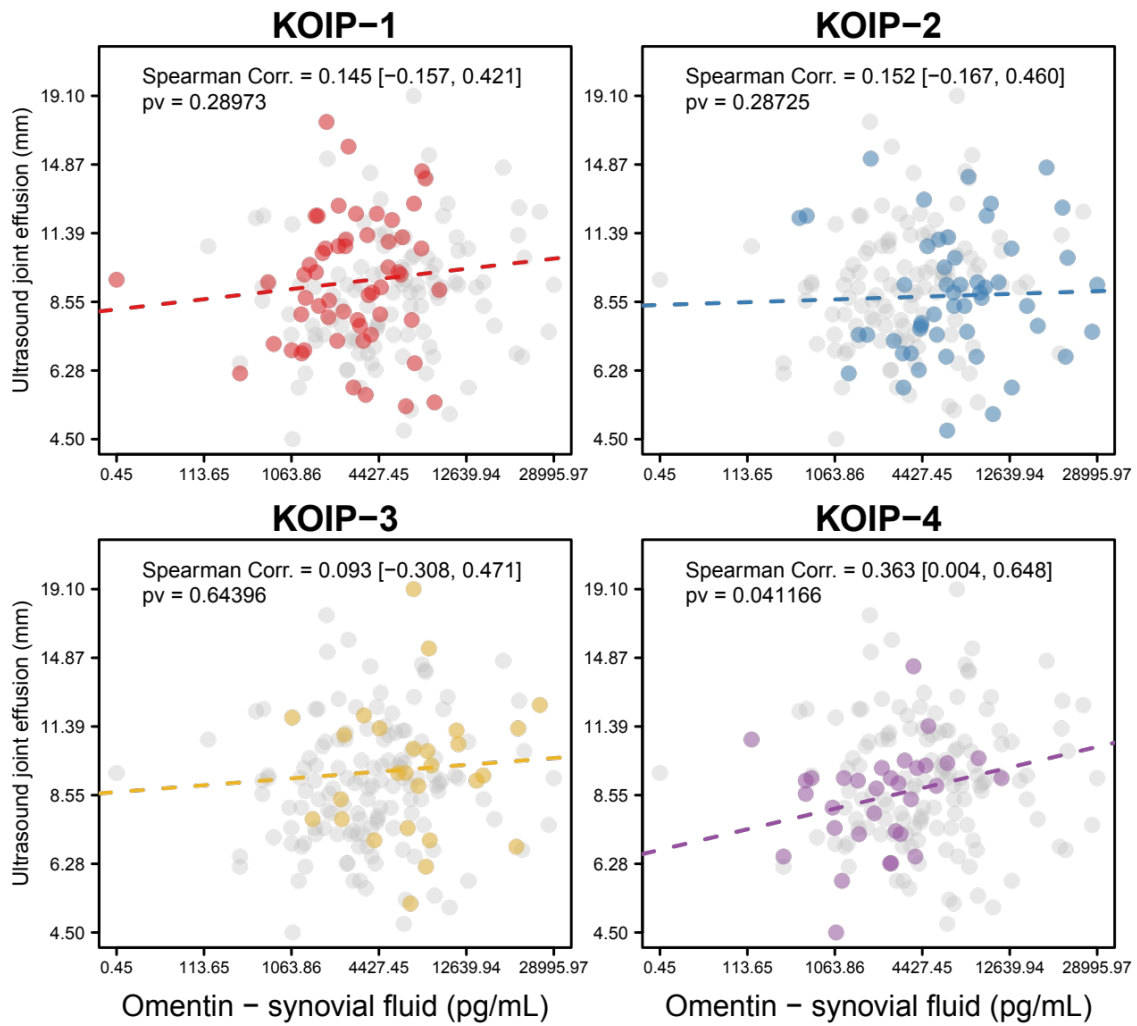
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S27: Ultrasound Joint Effusion - synovial Leptin



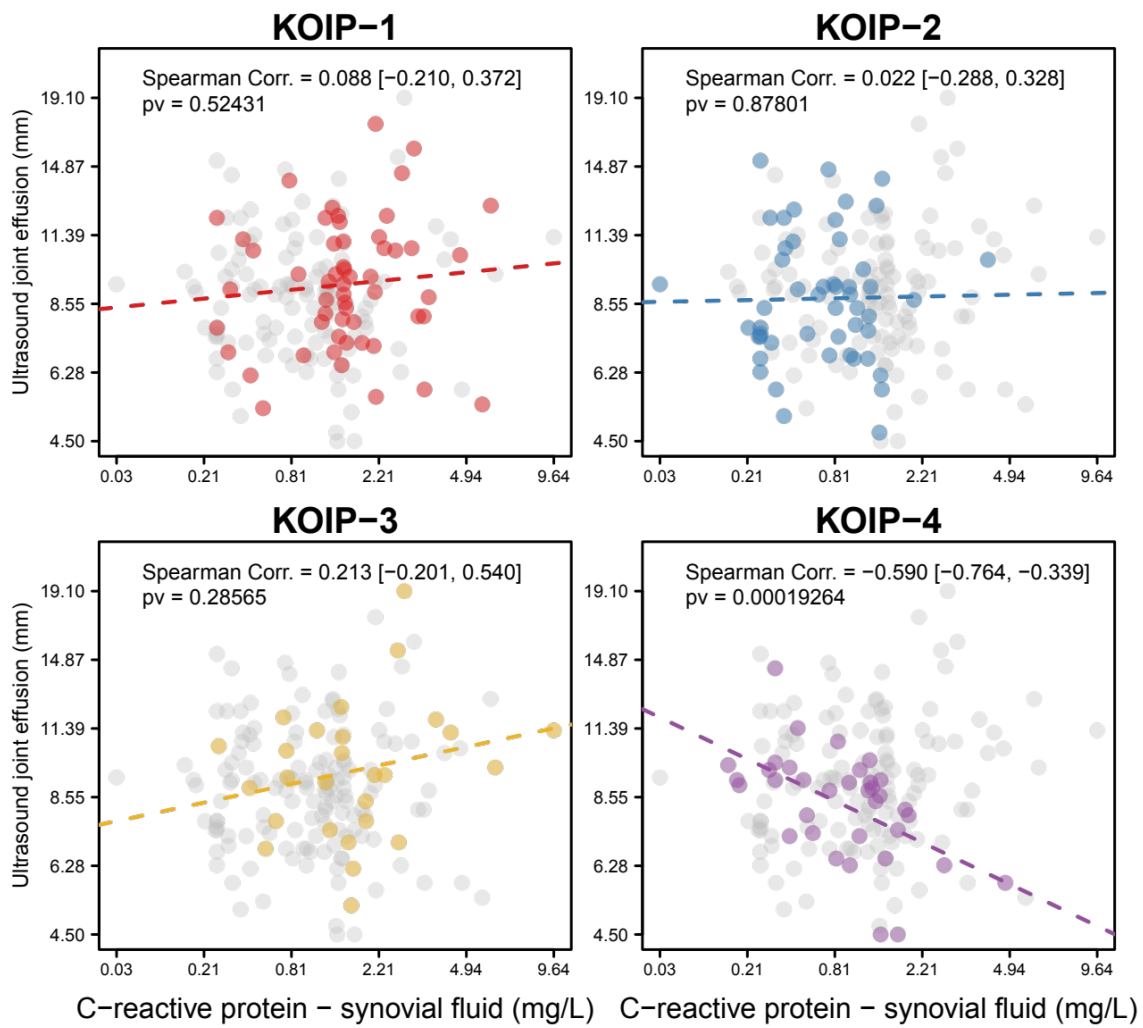
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S28: Ultrasound Joint Effusion - synovial Omentin



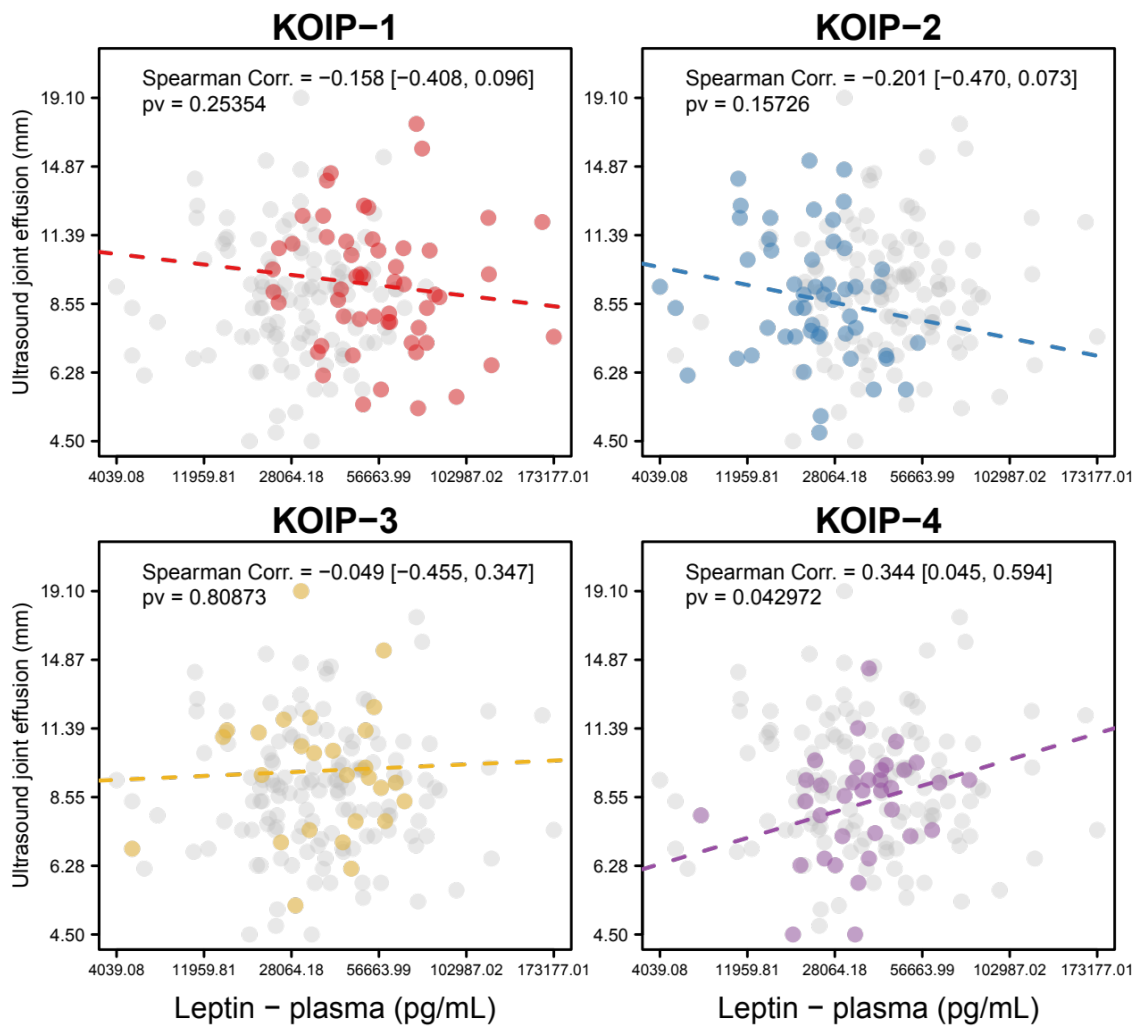
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S29: Ultrasound Joint Effusion - synovial C-Reactive Protein



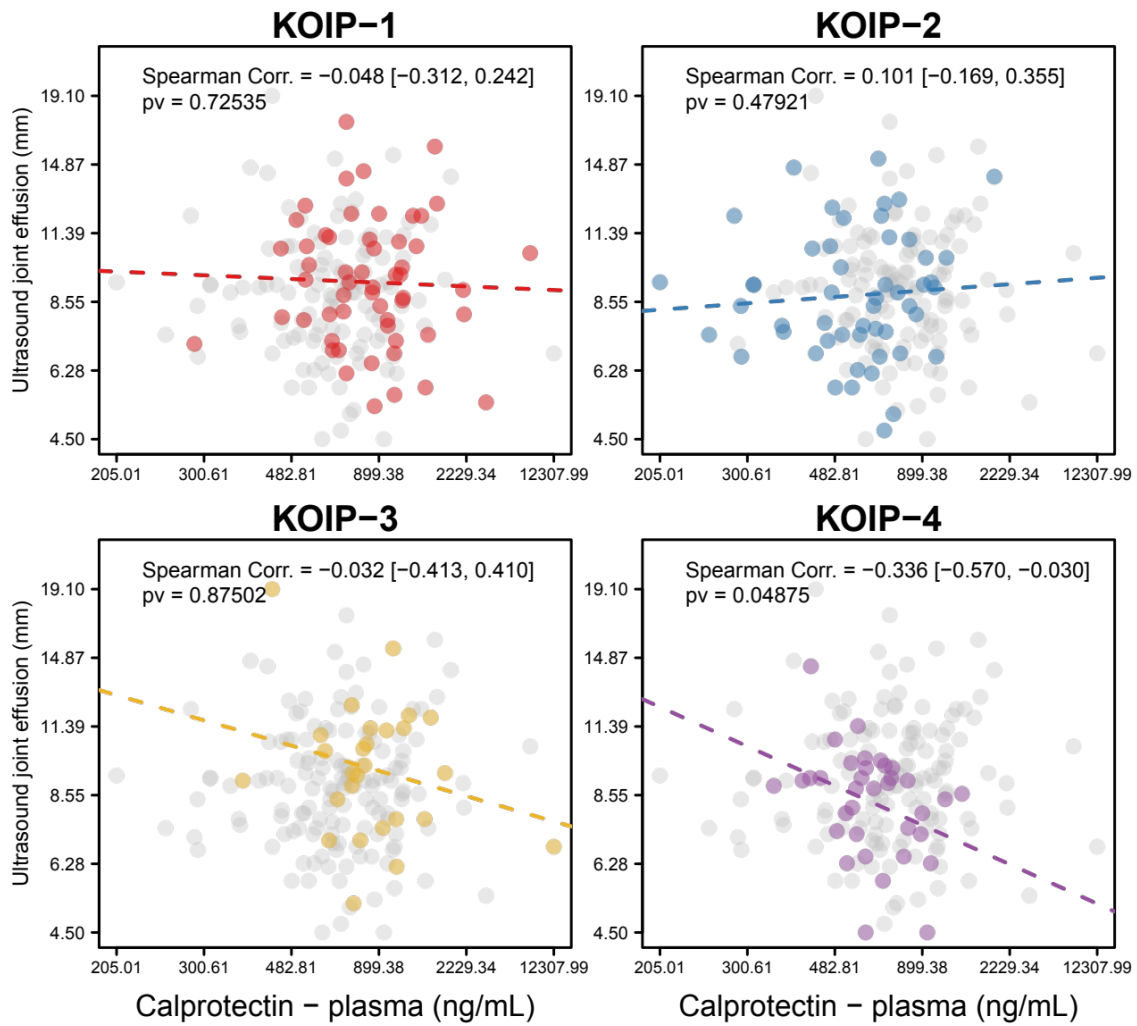
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S30: Ultrasound Joint Effusion - plasma Leptin



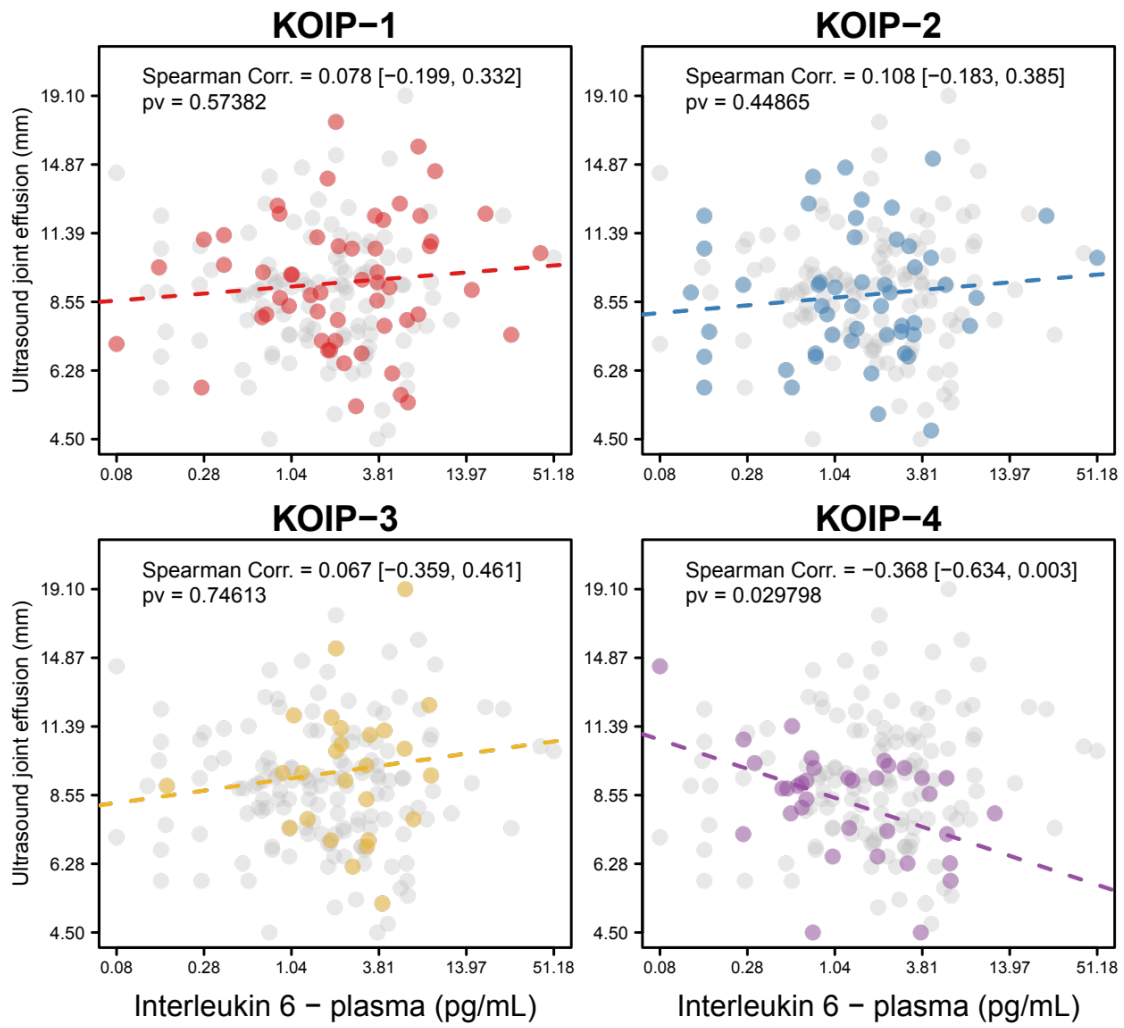
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S31: Ultrasound Joint Effusion - plasma Calprotectin



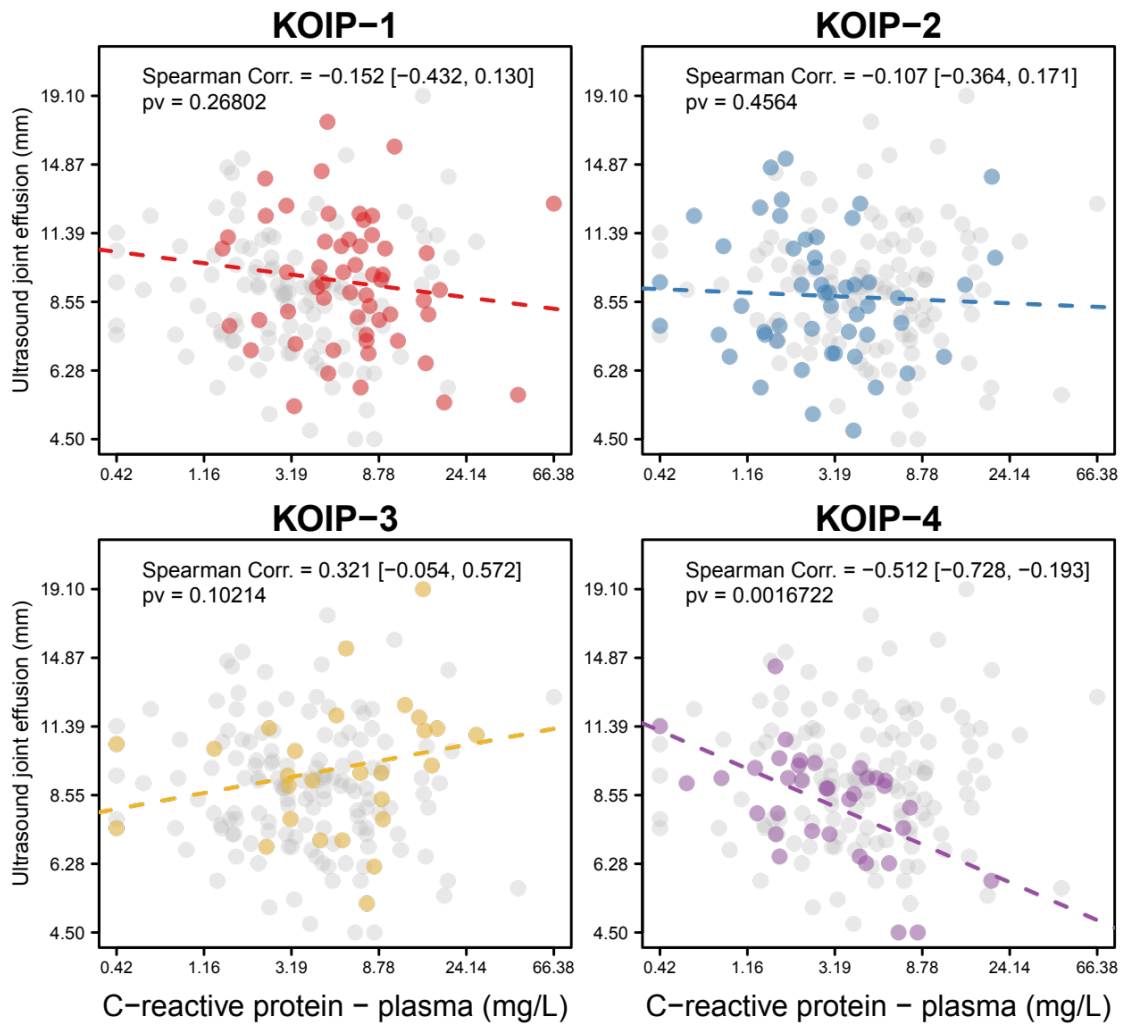
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S32: Ultrasound Joint Effusion - plasma Interleukin-6



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S33: Ultrasound Joint Effusion - plasma C-reactive protein



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