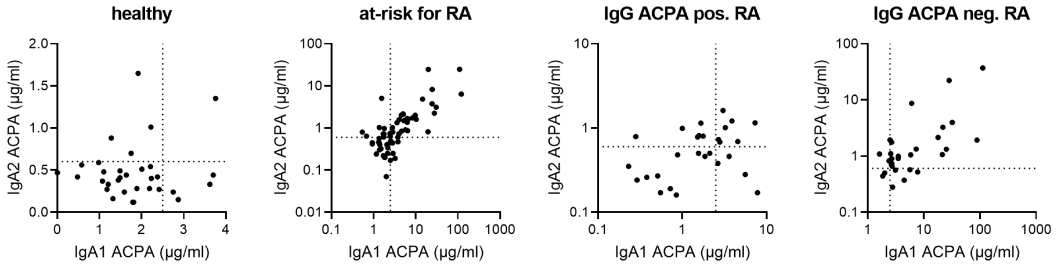
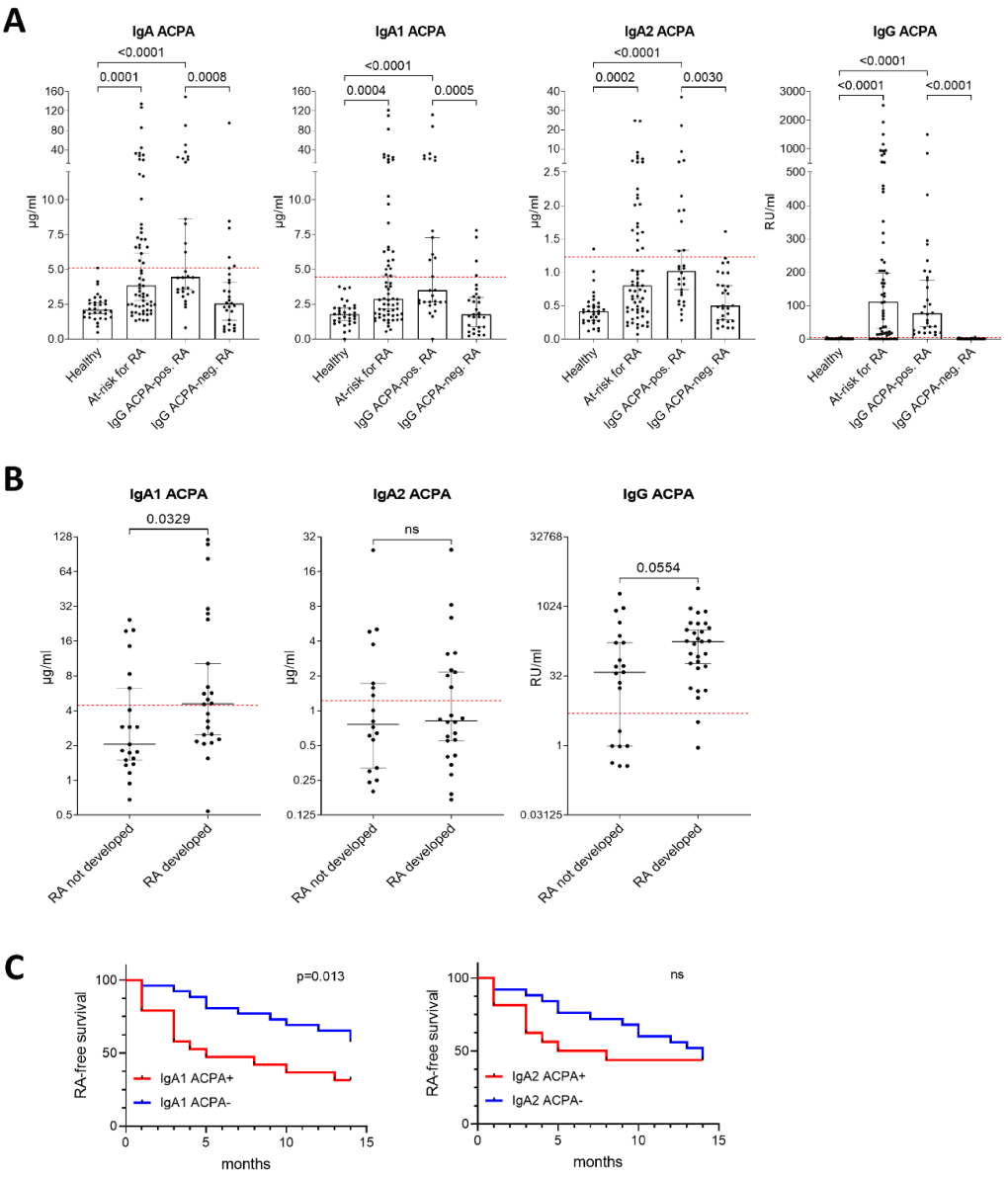
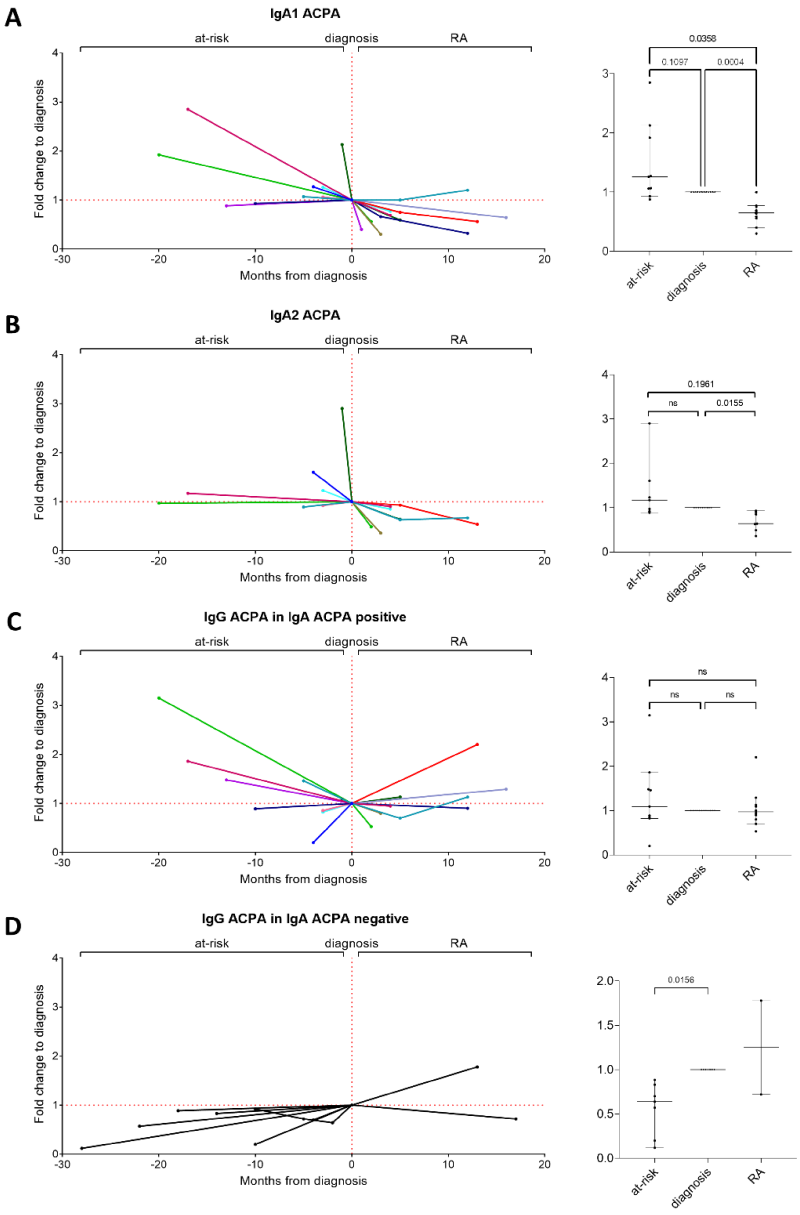


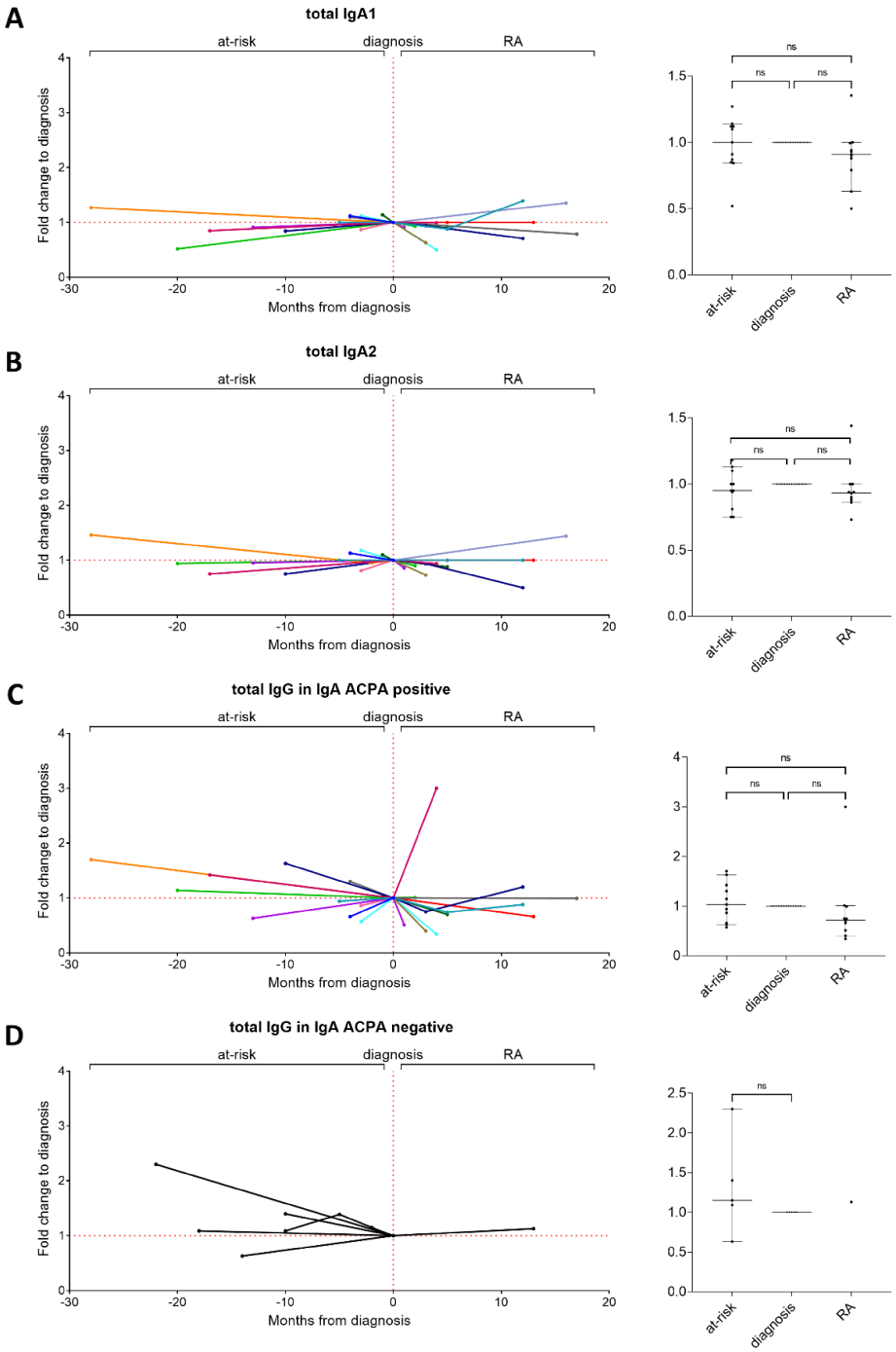
Supplementary Figure 1 Serum concentrations of IgA1 ACPA compared to IgA2 ACPA in healthy controls (n=32), individuals at-risk for RA (n=63), IgG ACPA-positive (n=30) and IgG ACPA-negative (n=29) RA patients. Dotted lines show the cut-offs for positivity.



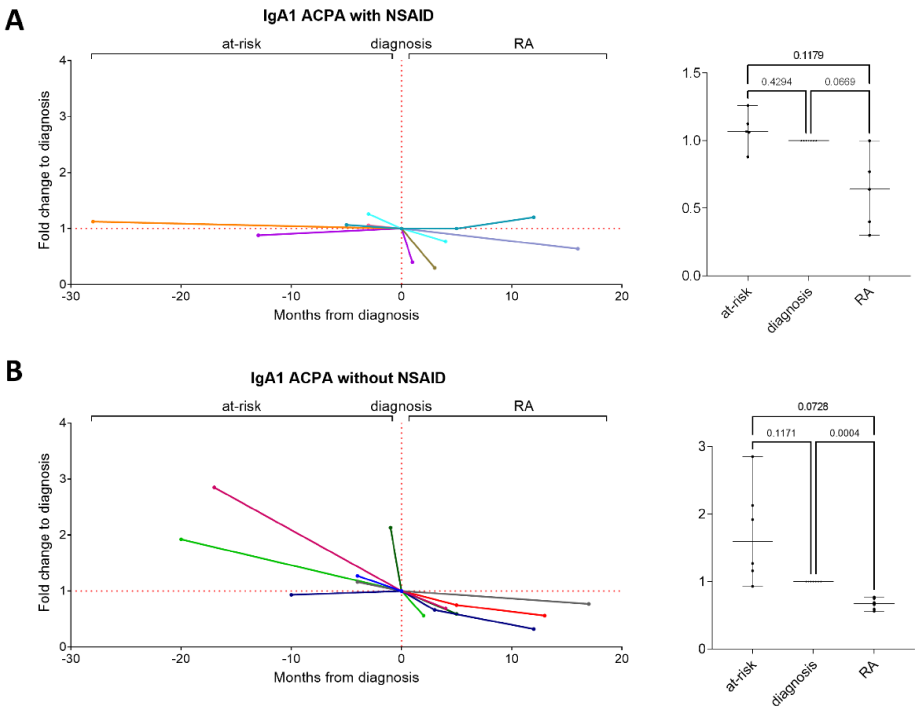
Supplementary Figure 2 (A) Serum concentrations (median with 95% confidence interval) and prevalence of IgA, IgA1, IgA2 and IgG ACPA in healthy controls (n=32), individuals at-risk for RA (n=63), IgG ACPA-positive (n=30) and IgG ACPA-negative (n=29) RA patients. Dotted lines show conservative cut-offs for positivity (mean + 3 SD of healthy group). Significances were tested with Kruskal-Wallis test with Dunn's multiple comparisons correction. (B) Serum concentrations (median with 95% confidence interval) of IgA1, IgA2 and IgG ACPA in RA-at risk individuals who did (n=24) or did not (n=21 for IgA1 and IgG ACPA / n=18 for IgA2 ACPA) develop RA in a 14-months period. Three patients were excluded from the IgA2 ACPA analysis due to high differences between technical replicates. Significances were tested with Mann-Whitney test. (C) Progression-free survival curves of IgA1 and IgA2 ACPA-positive (= IgA1/IgA2 ACPA+) and negative (= IgA1/IgA2 ACPA-) RA at-risk individuals with follow-up of 14 months after serum collection. Significances were tested with Log-Rank (Mantel-Cox) test. ns – not significant.



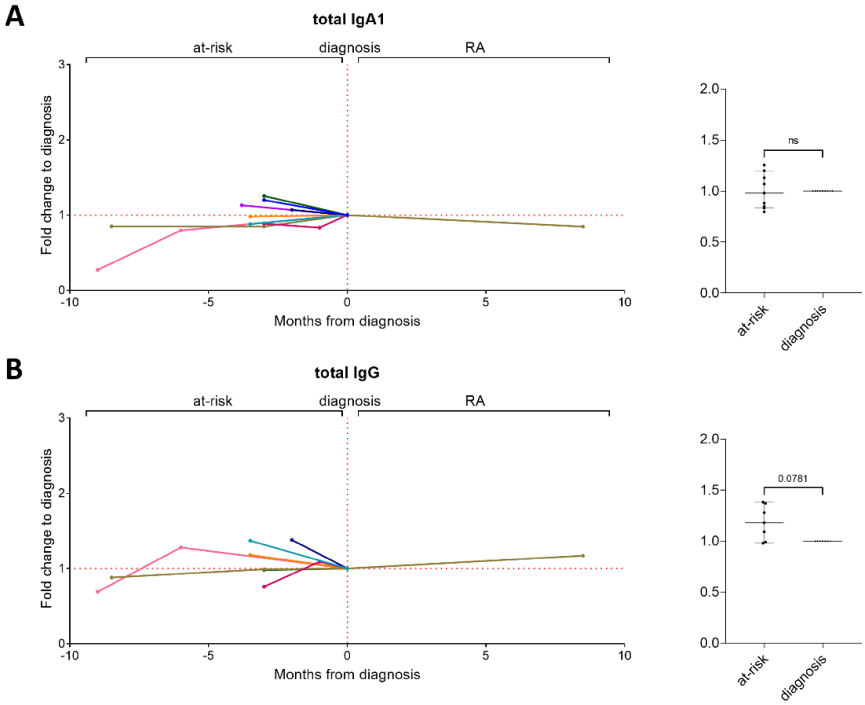
Supplementary Figure 3 Dynamic changes in serum ACPA levels in RA at-risk individuals during transition from the at-risk state to RA. Only at-risk individuals positive for IgA ACPA according to the conservative cutoff (mean + 3 SD of healthy group) were used for the analysis. Shown are fold changes of (A) IgA1 ACPA (n=12), (B) IgA2 ACPA (n=9) and IgG ACPA in (C) IgA ACPA-positive individuals (n=12) and (D) IgA ACPA-negative individuals (n=7) compared to the levels at RA onset (set as 1). Each line represents one at-risk individual (same color represents the same individual). Significances were tested with mixed effects model (modified ANOVA) with Tukey's multiple comparisons correction. ns – not significant.



Supplementary Figure 4 Dynamic changes in total serum antibody levels in RA at-risk individuals during transition from the at-risk state to RA. Shown are fold changes of (A) IgA1 (n=14), (B) IgA2 (n=13) and IgG in (C) IgA ACPA-positive individuals (n=14) and (D) IgA ACPA-negative individuals (n=5) compared to the levels at RA onset (set as 1). Each line represents one at-risk individual (same color represents the same individual). Significances were tested with mixed effects model (modified ANOVA) with Tukey's multiple comparisons correction. ns – not significant.



Supplementary Figure 5 Dynamic changes in serum IgA1 ACPA levels in RA at-risk individuals taking (A) NSAIDs (N=7) or (B) not (N=7) during transition from the at-risk state to RA. Shown are fold changes compared to the levels at RA onset (set as 1). Each line represents one at-risk individual (same color represents the same individual). Significances were tested with mixed effects model (modified ANOVA) with Tukey's multiple comparisons correction. ns – not significant.



Supplementary Figure 6 Dynamic changes in total serum antibody levels in individuals from the confirmatory cohort from the Medical University of Vienna during transition from the at-risk state to RA. Shown are fold changes of (A) total IgA1 (n=9) and (B) total IgG (n=6) compared to the levels at RA onset (set as 1). Each line represents one individual (same color represents the same individual). Significances were tested with Wilcoxon test. ns – not significant.