aged ≥ 18 with an enrollment SU measurement. We used Cox proportional hazards regression models to estimate sex-specific mortality risk relative to a referent SU 5-6 mg/dL, adjusting for NHANES cycle, age, race, body mass index (BMI), education, alcohol use, smoking, hypertension, total cholesterol, estimated glomerular filtration rate (GFR), and competing risks, using age as a time scale for survival analysis.

Results: Among 19,954 men and 21,853 women, there were 5,714 male deaths and 4,901 female deaths (median follow-up 14.2 ± 6.9 years). Among men, there was a 33% increased all-cause mortality risk at SU < 4 mg/dL (HR 1.33, 95% CI 1.17-1.51) and 52% increased all-cause mortality risk at SU > 8 mg/dL (HR 1.52, 95% CI 1.37-1.69) compared to subjects with SU 5-6 mg/dL, driven by cause-specific mortality from diabetes at low SU and chronic lower respiratory diseases and cardiovascular disease at high SU (Table). In women, there was no increased mortality risk at low SU and a 45% increased all-cause mortality risk at SU > 7 mg/dL (HR 1.45, CI 1.31-1.61) compared to subjects with SU 5-6 mg/dL, driven by cause-specific mortality from diabetes. Mortality from Alzheimer's disease was lower at high SU among men (HR 0.23, 95% CI 0.05-0.99) and women (HR 0.54, 95% CI 0.25-1.15).

Conclusion: In large cohorts representative of the US population, there was a U-shaped relationship between SU and all-cause mortality in men but not women. In men with low SU, mortality was driven primarily by diabetes, which may be explained by the uricosuric effect of uncontrolled hyperglycemia in diabetes patients. The lower mortality from Alzheimer's disease at high SU agrees with previously shown inverse associations between gout and Alzheimer's disease. Further studies are needed to determine the presence of causality underlying these associations.

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OP0016

GUT MICROBIOTA DYSBIOSIS IN THE HIGH-RISK INDIVIDUAL FOR RA TRIGGERS THE MUCOSAL IMMUNITY PERTURBATION AND PROMOTES RHEUMATOID ARTHRITIS DEVELOPMENT

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Background: The early treatment of rheumatoid arthritis (RA) is associated with better outcomes. In recent years, studies in our understanding of the preclinical events in RA help to define the "at-risk" populations who might go on to develop RA. Emerging evidence indicate that initiating events may occur at mucosal surfaces including oral cavity, lung and gut influenced by the local microbiome. Therefore, identifying the microbiome characteristics in prospective cohorts of at-risk individuals enables risk prediction or prevention of RA.

Objectives: Here, we undertook this study to clarify the intestinal microbiota changes in individuals at high risk for RA. Meanwhile, we performed fecal transplantation study to investigate whereby the intestinal dysbiosis in the pre-RA population contributes to RA initiation and development, and provide a new prevention strategy for the treatment of this disease.

Methods: 42 high-risk for RA individuals (Pre-RA), who were defined as having a positive serum antibody for anti-cyclic citrullinated peptide (CCP), 31 RA patients and 38 healthy individuals (HC) were recruited in this study. The V3-V4 region of 16S ribosomal RNA of fecal samples from these individuals were sequenced. We evaluated the gut permeability and the gut barrier dysfunction using HE staining and RT-PCR in mice receiving fecal transplantation (FMT). Flow cytometry was applied to measure the proportions of T cell subsets in immune organs. The disease severity of collagen-induced arthritis (CIA) was also evaluated after the mice receiving FMT.

Results: Alpha diversity analysis showed a comparable community richness and a lower community diversity of the intestinal microbiota in Pre-RA compared to HC (Fig 1A). At the family level, the abundance of *Bacteroidaceae* gradually decreased from HC to Pre-RA individuals and to RA patients (Fig 1B). On the contrary, the enriched abundances of *Streptococcaceae*, *Lactobacillus*, *Lactococcus*, *Weissella* and *unclassified_o_Lactobacillales* were observed in RA patients (Fig 1B). There was different intestinal microbiota construction between groups based on principal coordinate analysis (PCoA). The intestinal microbiota communities dynamically shifted from HC to Pre-RA and to RA patients (Fig 1C). Fecal transplantation study showed that gut microbiota from Pre-RA group (P) significantly increased the fluorescence intensity (Fig 2A), accompanied with a significantly decreased ZO-1 gene expression (Fig 2B), and injured epithelial microvilli of the small intestine (Fig 2C). Moreover, the percentages of Th17 cells in the mesenteric lymph nodes (mLN) and Peyer patches (PP) were also significantly increased in P and R groups (Fig 2D, E). Importantly, in CIA models, the joints redness and swelling in the mice receiving Pre-RA faeces occurred earlier and were more severe compared to HC-transplanted mice (Fig 2F, G and H).

Figure 1.

Figure 2.

Conclusion: The intestinal microbiota changed gradually during disease progression of human rheumatoid arthritis. The gut microbiota from Pre-RA individuals can trigger the gut barrier dysfunction and intestinal mucosal immunity imbalance, which may further contribute to the arthritis initiation and development.

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OP0017

THERAPEUTIC DRUG MONITORING COMPARED TO STANDARD TREATMENT OF PATIENTS STARTING INFLIXIMAB THERAPY: RESULTS FROM A MULTICENTRE RANDOMISED TRIAL OF 400 PATIENTS

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Background: A lack or loss of response to TNF α inhibitors (TNFi) has been associated with low serum drug levels and formation of anti-drug antibodies (ADAb). Therapeutic drug monitoring (TDM), an individualised treatment strategy based on regular assessments of serum drug levels, has been suggested to optimise efficacy of TNFi. It is still unclear if TDM improves clinical outcomes, and the value of TDM has recently been included in the research agenda across different specialties. This first randomised controlled trial on the effectiveness of TDM in a range of immune mediated inflammatory diseases including rheumatic diseases, the NORwegian DRUG Monitoring trial part A (NOR-DRUM (A)) focus on the induction period of infliximab (INX) treatment.

Objectives: To assess if TDM is superior to standard treatment in order to achieve remission in patients starting INX.

Methods: In the investigator-initiated, randomised, open-label, multicentre NOR-DRUM (A) study, adult patients with rheumatoid arthritis (RA), psoriatic arthritis (PsA), spondyloarthritis (SpA), ulcerative colitis (UC), Crohn's disease (CD) and psoriasis (Ps) starting INX therapy were randomly assigned to administration of INX according to a treatment strategy based on TDM (TDM arm) or to standard administration of INX without TDM (control arm). Study visits were conducted at each infusion. The primary endpoint was remission at week 30. In the TDM arm, the dose and interval were adjusted according to INX trough levels to reach the therapeutic range (Figure 1). If the patient developed significant levels of ADAb, INX was terminated. To guide the investigators, the TDM strategy was integrated in an interactive eCRF. The primary endpoint was analysed by mixed effect logistic regression in the full analyses set (FAS), adjusting for diagnoses. Infections and infusion reactions were specified as adverse events (AEs) of special interest. Clinical trial.gov: NCT03074656

Results: We enrolled 411 patients at 21 study centres between January 2017 and December 2018. 398 patients (RA 80, PsA 42, SpA 117, UC 80, CD 57, Ps 22) received the allocated strategy and were included in the FAS population. Demographic and baseline characteristics were comparable in both arms. TDM was not found to be superior to standard treatment with regard to the primary outcome. Remission at week 30 was reached in 100 (53%) and 106 (54%) of the patients in the TDM and control arm, respectively (adjusted difference, 1.5%; 95% confidence interval (CI), -8.2 to 11.1, $p=0.78$) (Figure 2). Consistent results were shown for all the secondary endpoints (Figure 3) and in the sensitivity analyses. Twenty patients (10%) in the TDM arm and 30 patients (15%) in the control arm developed significant levels of ADAb. The number of adverse events (AE) was similar in both groups, however infusion reactions were less frequent (5 patients (2.5%) vs 16 patients (8.0%)) in the TDM arm (difference 5.5% (95% CI 1.1, 9.8%)).

Conclusion: NOR-DRUM (A) is the first randomised trial to address effectiveness of TDM in the induction period of TNFi treatment, and the first trial to address TDM in rheumatic diseases. In this study, TDM was not superior to standard treatment in order to achieve remission. Although improved safety is indicated by a reduction in infusion reactions, implementation of TDM as a general strategy in the induction period of INX is not supported by the NOR-DRUM (A) study.

Figure 1 Treatment strategy in the TDM arm

Figure 2. Difference in remission rate, overall and by disease

Figure 3. Generic (A-F) and disease specific (G-L) composite measures over study period.

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LB0001

EFFICACY AND SAFETY OF UPADACITINIB VERSUS PLACEBO AND ADALIMUMAB IN PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS AND INADEQUATE RESPONSE TO NON-BIOLOGIC DISEASE-MODIFYING ANTI-RHEUMATIC DRUGS (SELECT-PSA-1): A DOUBLE-BLIND, RANDOMIZED CONTROLLED PHASE 3 TRIAL

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