Conclusion: Disrupting specific immune and stromal cell interactions offers novel opportunities for targeted therapeutic intervention in RA and PsA.
Disclosure of Interests: Achilleas Floudas: None declared, Conor Smith: None declared, Orla Tynan: None declared, Nuno Neto: None declared, Vinod Krishna Employee of: Janssen Pharmaceuticals, Sarah Wade: None declared, Megan Hanlon: None declared, Clare Cunningham: None declared, Viviana Marzaioli: None declared, Mary Canavan: None declared, Jean Fletcher: None declared, Suzanne Cole Employee of: Janssen Pharmaceuticals, Ling-Yang Hao Employee of: Janssen Pharmaceuticals, Sunil Nagpal Employee of: Janssen Pharmaceuticals, GSK, Michael Monaghan: None declared, Douglas Veale Consultant of: Janssen, Eli Lilly, Pfizer, Ursula Fearon Consultant of: Janssen, Eli Lilly, Pfizer.
DOI: 10.1136/annrheumdis-2022-eular.1811

OP0069 INCLUSION OF PATIENT RESEARCH PARTNERS IN REMEDY – A RESEARCH CENTER FOR TREATMENT OF RHEUMATIC AND MUSCULOSKELETAL DISEASES

M. Skaar[1], A. T. Tveter[1], H. A. Zangi[1], S. Lillegraven[1], E. Haavardsholm[1], I. Løchting[2], A. Fryxelius[2], I. Kjeken[1]. [1]*Diakonhjemmet Hospital, Division of Rheumatology and Research, Oslo, Norway*; [2]*The Norwegian Rheumatism Association,The Norwegian Rheumatism Association, Oslo, Norway*

Background: Active collaboration between patients and researchers in development and implementation of scientific projects is important to ensure a good match between patient's preferences and the scientific focus in research, contribute to more patient-oriented health research agendas, enhance patient friendly design of research projects, and creating support for implementation (1). Such involvement is strongly advocated by EULAR and is often a prerequisite to receive funding for clinical research projects. At Diakonhjemmet Hospital in Norway, the division of rheumatology and research has for many years worked to involve patient research partners (PRPs) in research. A patient advisory board was established in 2007, led by a person (20% position) who herself has a rheumatic disease. In eight years from 2022, the division will receive funding from the Norwegian Research Council to establish and host a clinical research center for treatment of Rheumatic and Musculoskeletal diseases – the REMEDY center.
Objectives: To describe how involvement of PRPs are organised within the REMEDY center.
Methods: An organisation map was developed as part of the application for funding. The leader of the patient advisory board, together with three senior researchers, were involved in several rounds of discussions on how PRP involvement should be organised in the center, and also in meetings with the larger research group.
Results: The organisation of REMEDY is shown in Figure 1.

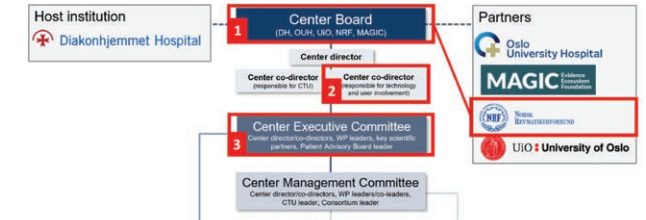

Figure 1. Organisation of REMEDY.

1.All partners, including **The Norwegian Rheumatism Association,** (the largest patient organisastion in the field), are represented at the Center Board. This ensures patient involvement at the strategic level, including setting research agendas and priorities.
2.The center is led by a centre director and two **co-directors**, of which one has a specific responsibility of PRP-involvement
3.The Centre Executive Committee (CEC) consist of the Center Director and co-directors, the WP leaders, **the leader of the patient advisory board**, the key senior scientific staff members of the partner institutions involved in the center and senior staff members deemed appropriate by the Centre Director.
4.**The patient advisory board**, consisting of 10-15 PRPs, is central within the center. Members of the board will be involved in all research projects, collaborating with researchers to improve design, methodology, research outcomes and implementation. The board provides a platform for the members for education, development, and exchange of knowledge and experience.
5.There are seven work packages (WPs) in REMEDY, each approaching the knowledge needs within rheumatic and musculoskeletal diseases (RMDs) treatment from different angles, and with international collaborators. WP7 (Empowering the individual) will provide **a platform for the Patient advisory board**, facilitating input from PRPs to all WPs. The chair of the EULAR study group for collaborative research is an international collaborator in WP7.
The leader of the Patient Advisory board has a 50% position. Additionally, there is funding for board activities, and for PRP involvement in initial project phases, whereas PRP activities are included in applications for external funding.
Conclusion: The REMEDY center is organised to ensure involvement of PRPs at all organisational levels, from individual research trials to the strategic and operational management of the center.
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Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2022-eular.4379

OP0070 INTERVENTION WITH METHOTREXATE IN ARTHRALGIA AT RISK FOR RHEUMATOID ARTHRITIS TO REDUCE THE DEVELOPMENT OF PERSISTENT ARTHRITIS AND ITS DISEASE BURDEN (TREAT EARLIER): A DOUBLE-BLIND, RANDOMISED, PLACEBO-CONTROLLED TRIAL

D. Krijbolder[1], M. Verstappen[1], B. van Dijk[1], Y. Dakkak[1], L. Burgers[1], A. Boer[1], Y. Jung Park[1], M. De Witt[2], K. Visser[3], M. R. Kok[4], E. Molenaar[5], P. de Jong[6], S. Böhringer[7], T. Huizinga[1], C. Allaart[1], E. Niemantsverdriet[1], A. van der Helm-van Mil[1,6]. [1]*Leiden University Medical Center (LUMC), Rheumatology, Leiden, Netherlands*; [2]*Reinier de Graaf Gasthuis, Rheumatology, Delft, Netherlands*; [3]*Haga Hospital (Leyweg), Rheumatology, Den Haag, Netherlands*; [4]*Maasstad Hospital, Rheumatology, Rotterdam, Netherlands*; [5]*Groene Hart Hospital, Rheumatology, Gouda, Netherlands*; [6]*Erasmus MC, Rheumatology, Rotterdam, Netherlands*; [7]*Leiden University Medical Center (LUMC), Biomedical Data Sciences, Leiden, Netherlands*

Background: Rheumatoid arthritis (RA) is the most common autoimmune disease, and requires long-term treatment to suppress inflammation. Currently, methotrexate is initiated as first-line treatment when arthritis becomes clinically apparent with joint swelling. However, disease processes begin long before and become clinically recognizable when patients develop symptoms. We hypothesized that the 'at risk phase' of symptoms and subclinical joint-inflammation is a therapeutic window to permanently modify the disease course.
Objectives: We studied if intervention in the pre-arthritis phase of arthralgia and subclinical joint inflammation prevents the development of clinical arthritis or reduces the burden of disease.
Methods: In this randomised, double-blind, 2-year proof-of-concept trial, adults with arthralgia clinically suspected of progressing to RA and MRI-detected subclinical joint-inflammation, recruited from all rheumatology outpatient-clinics in the south-west-Netherlands, were randomly assigned (1:1) to a single intramuscular glucocorticoid injection (120mg) and a one-year course of oral methotrexate (up to 25mg/week), or placebo injection and placebo tablets. Subsequently, participants were followed for another year without study medication. The primary endpoint was the development of clinically detectable arthritis (fulfilling the 2010 RA-criteria or involving ≥2 joints) that persisted for at least 2 weeks. Patient reported physical functioning, along with symptoms and workability, were key secondary endpoints and measured 4-monthly. Additionally, the course of MRI-detected inflammation was studied (the sum of tenosynovitis, synovitis, osteitis, scored with the RA-MRI Scoring (RAMRIS) method). All participants entered the intention-to-treat analysis. We performed two prespecified subgroup analyses. Firstly, analyses were restricted in participants with high risk of clinical arthritis development (PPV ≥70%). Secondly, analyses were stratified for ACPA-status. The trial is registered with the Netherlands Trials Registry (NTR4853 trial NL4599).
Results: From April 16th, 2015 to September 11th, 2019, we randomly assigned 236 participants to treatment (n=119) or placebo (n=117). After 24 months, arthritis free survival was similar in both groups (80% versus 82%, HR 0.81 (95%CI 0.45, 1.48)). Physical functioning improved more in the treatment-group during the first months and remained better (mean between-group difference over two-years HAQ -0·1(-0·2,-0·03;p=0·004). Similarly, pain (-9 on scale 0-100: (95%CI -12,-4; p<0·001), morning stiffness (-12 (95%CI -16,-8;p<0·001), presenteeism (-8% (95%CI -13%,-3%;p=0·001) showed sustained improvement compared to placebo. MRI-detected joint-inflammation was also persistently improved (mean difference over 2 years -1·4 points (95%CI -2·0,-0.9;p<0·001). High-risk participants in the treatment group showed a delay in clinical arthritis development: they developed the endpoint less often during treatment, but frequencies became similar at 24 months (67% in both groups). A similar delaying effect was observed in ACPA-positive participants, where 48% and 52% had developed persistent clinical arthritis at 24 months. The number of serious adverse events was equal between the groups; adverse events were as expected from methotrexate.

Conclusion: Methotrexate, the cornerstone treatment of RA, initiated at the pre-arthritis stage of joint symptoms and subclinical inflammation, did not prevent the development of clinical arthritis, but modified the disease course as measured by sustained improvement in MRI-detected inflammation, related symptoms and impairments. These findings of sustained disease modification may open up a new treatment landscape in a pre-arthritis phase of RA, where limitations can be just as severe as at the onset of clinical arthritis.

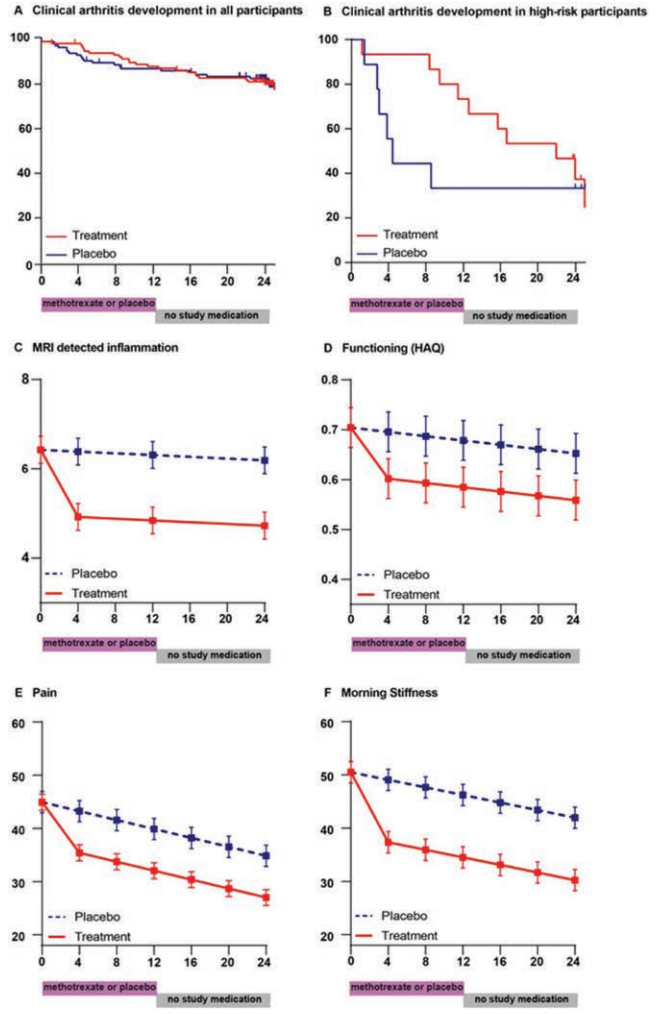


Figure 1.

Acknowledgements: We thank Prof. dr. R. ten Cate, prof. dr. S. le Cessie and dr. A.M.J. Langers for their role in the Data Safety and Monitoring Board. We thank all participants, and all rheumatologist of the following hospitals: Albert Schweitzer Hospital, Alrijne Hospital, Erasmus Medical Center, Haven-policlinic Rotterdam, IJselland Hospital, Ikazia Hospital, Franciscus Gasthuis & Vlietland Hospital, Groene Hart Hospital, Haaglanden Medical Center (all locations), Haga Hospital, Langeland Hospital, Meander Medical Center, Maasstad, Hospital, Reinier de Graaf Gasthuis, Reumazorg Zuid-West Nederland and Spaarne Gasthuis. We acknowledge the team of treating rheumatologists and research nurses of the LUMC, in particular Dr F.J. van der Giesen. Our gratitude also goes to the PhD students who scored MRIs for trial screening, in particular dr. H.W. van Steenbergen, dr. W. Nieuwenhuis, dr. R.M. ten Brink, dr. D.M. Boeters, dr. L. Mangnus, X.M.E. Matthijssen and F. Wouters. We thank dr. M. Reijnierse, prof. dr. S.C. Cannegieter and prof. dr. D. van der Heijde for their advice, and dr. J. Schoones for his help with the systematic literature search. We acknowledge the funder of the study: NWO ZonMW grant (program 'translationeel onderzoek', project number 95104004).
Disclosure of Interests: None declared.
DOI: 10.1136/annrheumdis-2022-eular.264

OP0071

ASSOCIATION BETWEEN LONG-TERM EXPOSURE TO AIR POLLUTION AND IMMUNE-MEDIATED DISEASES: A POPULATION-BASED COHORT STUDY

G. Adami[1], M. Pontalti[1], C. Benini[1], A. Fassio[1], E. Bertoldo[1], D. Gatti[1], M. Rossini[1]. [1]*University of Verona, Rheumatology Unit, Verona, Italy*

Background: Environmental air pollution has been associated with disruption of the immune system at a molecular level.
Objectives: The primary aim of the present study is to describe the association between long-term exposure to air pollution and risk of developing immune-mediated conditions.
Methods: We conducted a retrospective observational study on a nation-wide dataset of women and men. Diagnoses of various immune-mediated diseases were retrieved. Data on the monitoring of PM10 and PM2.5 concentrations were retrieved from the Italian institute of environment protection and research (ISPRA). The long-term average PMs concentrations were the exposure of interest. Every study subject was linked to a PMs exposure value, which resulted from the average concentration of urban, rural and near-traffic stations of the subject residency from January 2013 to November 2020. Patients were linked to the nearest air quality station through ZIP code centroids. Generalized linear models were employed to determine the relationship between autoimmune diseases prevalence and PM. The fully adjusted model included age, body mass index (BMI), menopause, glucocorticoid treatment, treatment with adjuvant hormone therapy for breast or prostate cancer, specialty of the physician that entered the data and macro-area of residency (stratified as a categorical variable: northern Italy, central Italy and southern Italy.
Results: 81,363 subjects were included in the study. We found a positive association between PM10 and the risk of autoimmune diseases (ρ +0.007, p 0.014). Every 10 µg/m3 increase in PM10 concentration was associated with an incremental 7% risk of having autoimmune disease. Exposure to PM10 above 30 µg/m3 and PM2.5 above 20 µg/m3 was associated with a 12% and 13% higher risk of autoimmune disease pooled together, respectively (aOR 1.12, 95% CI 1.05-1.20 and aOR 1.13, 95% CI 1.06-1.20). Exposure to PM10 was associated with an increased risk of rheumatoid arthritis (aOR 1.408, 95% CI 1.271-1.560) but no other autoimmune diseases, whereas exposure to high levels of PM2.5 were associated with an increased risk of rheumatoid arthritis (aOR 1.559, 95% CI 1.401-1.734), CTDs (aOR 1.147, 95% CI 1.024-1.286) and IBDs (1.206, 95% CI 1.028-1.415) but no other autoimmune diseases.
Conclusion: Long-term exposure to air pollution was associated with higher risk of developing autoimmune diseases, in particular rheumatoid arthritis, CTDs and IBD. Chronic exposure to levels above the threshold for human protection was associated with a 10% higher risk of developing immune-mediated diseases.

Figure 1. A. Prevalence of auto-immune diseases across Italy in the DeFRA database; B. Long-term exposure to particulate matter (PM) of less than 10 µm in Italy (2013-2019 average concentration µg/m3)

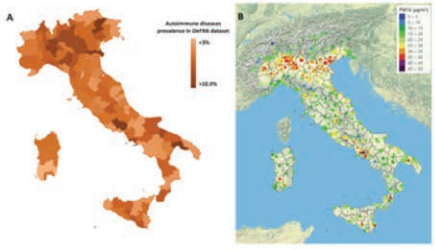


Figure 2. Risk of immune-mediated conditions at chronic exposure to PM10 ≥30 µg/m³

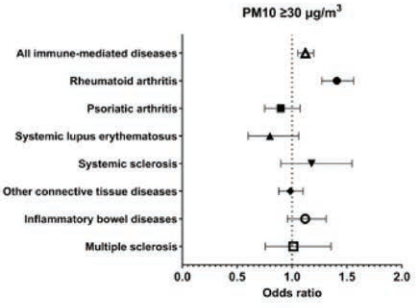
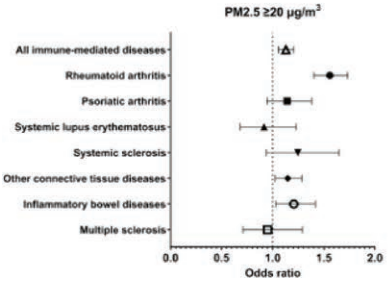


Figure 3. Risk of immune-mediated conditions at chronic exposure to PM2.5 ≥20 µg/m³



Disclosure of Interests: Giovanni Adami Shareholder of: Galapagos, Theramex, Marco Pontalti: None declared, Camilla Benini: None declared, Angelo Fassio: None declared, Eugenia Bertoldo: None declared, Davide Gatti: None