REMEDY 2023

ANNUAL REPORT

REMEDY
CENTER FOR TREATMENT OF RHEUMATIC AND MUSCULOSKELETAL DISEASES

REMEDY – Center for treatment of Rheumatic and Musculoskeletal Diseases is a “Centre for Clinical Treatment Research”. It was established in 2022 with funding from the Research Council of Norway (128 million NOK) as a targeted, long-term investment to strengthen and further develop outstanding research and innovation environments to improve treatment. In addition, REMEDY is supported by a generous grant from the Olav Thon Foundation (32 million NOK).

Our aim is to evolve patient care in the field of rheumatology and musculoskeletal diseases, with significant impact on individuals and society. We seek to develop novel therapies and excellent treatment strategies by adopting a comprehensive research approach to the field. We strive to conduct clinical studies that have the potential to change clinical practice.

The Research Council of Norway

OLAV THON FOUNDATION

CONTENT

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Introduction

Rheumatic and musculoskeletal diseases affect one in four people and are associated with morbidity, reduced quality of life, increased mortality, and severe long-term pain and disability. The large individual and societal impact of these conditions underlines the need for comprehensive and coordinated actions to improve patient outcomes.

Directors' comments

We are proud to present the second annual report of REMEDY – Center for Treatment of Rheumatic and Musculoskeletal Diseases. The establishment of REMEDY was made possible by large grants from the Research Council of Norway and the Olav Thon Foundation.

After completing the first full year of operations, we can fully see the impact of how these generous contributions lay the foundation for research that can change outcomes for individual patients. With the completion of our second year, we feel that it is timely to reflect on some of the milestones and advancements in 2023.

In the past year, REMEDY has solidified its position as a leading academic center for rheumatic and musculoskeletal research. We are especially pleased to have welcomed two renowned international guest professors, enriching our academic environment with scientific excellence, extensive experience, and diverse perspectives, contributing to increased collaborations across borders.

A central achievement of this year is the establishment of the Clinical Trial Unit. This facility equips us with the resources and infrastructure needed to support and facilitate practice-changing clinical trials, providing support for clinically relevant advancements in the treatment of rheumatic and musculoskeletal disorders. Additionally, this year we can look back on a successful annual research seminar and large research grants that fund new initiatives.

We are proud to report on the initiation of several new clinical trials, collaborating with both national and international partners. These partnerships underscore our commitment to a collaborative and multidisciplinary approach, with leading roles in innovative research on a global scale.

The hard work of the researchers within the center is reflected in the numerous publications in prestigious medical journals. These publications are important in the dissemination of knowledge with implications for international patient care and treatment strategies.

Our heartfelt thanks extend to everyone who has contributed to the success of REMEDY. We express our gratitude to our partners, researchers, patient research partners, clinical personnel, patients, and the funding bodies that have supported our projects.

In closing, REMEDY remains committed to advancing groundbreaking clinical research, fostering collaborations, and ensuring that our discoveries translate into improved patient outcomes. We look forward to your continued support as we embark on the next phase of our journey.

Sincerely,

"REMEDY remains committed to advancing groundbreaking clinical research, fostering collaborations, and ensuring that our discoveries translate into improved patient outcomes"

Espen A. Haavardsholm
Professor, MD PhD
Centre Director

Siri Lillegraven
Senior Researcher, MD PhD MPH
Vice Director

Anne Therese Tveter
Professor, PT PhD
Vice Director

Vision and goals

Research area

REMEDY is a Norwegian Centre for Clinical Treatment Research focusing on rheumatic and musculoskeletal diseases. These diseases constitute a heterogeneous group of diseases associated with significant morbidity, reduced quality of life, and increased mortality. The conditions have major consequences for society and the individual.

Aims of the center

The overarching aim of the REMEDY center is to improve treatment of rheumatic and musculoskeletal diseases by randomized clinical trials assessing novel treatment and treatment strategies, in combination with research and innovation to untangle the causes and characteristics of these diseases. The seven work packages approach the knowledge gaps within the field from different angles, ensuring that the research results will benefit patients in all stages of the diseases.

Vision

Our vision is to be a world-leading center developing state-of-the-art treatment and management strategies across rheumatic and musculoskeletal diseases, to benefit the individual and society.

Impact of the REMEDY center

Ground-breaking research that will change national and international treatment recommendations

For patients

- Increased quality of life
- Work participation
- Improved physical function
- Personalized treatment strategies
- User involvement in research
- Patient empowerment

For healthcare systems

- Improved treatment
- Fast-track from research to implementation
- Decision support tools and digitalization
- Remote healthcare
- Education of highly qualified researchers and healthcare personnel

For industry

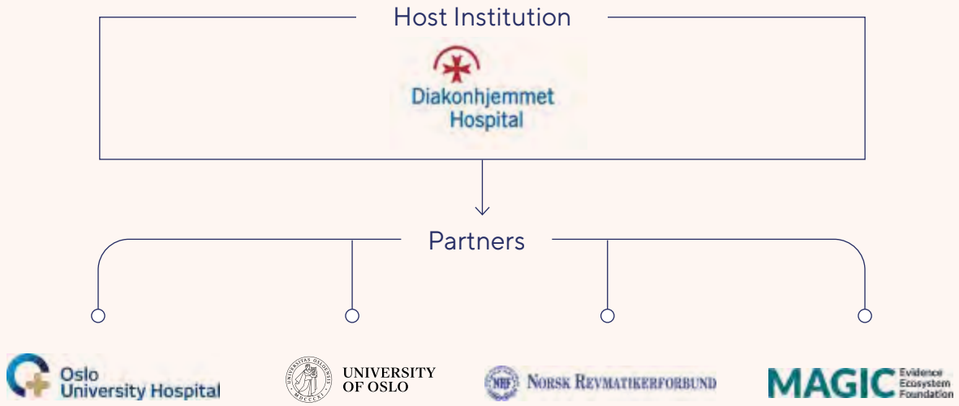
- Implementation of digital platforms
- One-stop shop for pharmaceutical trials
- Innovative technologies
- Performing phase II-IV trials
- Collaboration

For society

- Considerable gains for large patient groups
- Rapid implementation of results
- Sustainable healthcare
- Utilization of registry data
- Translational value for other chronic diseases

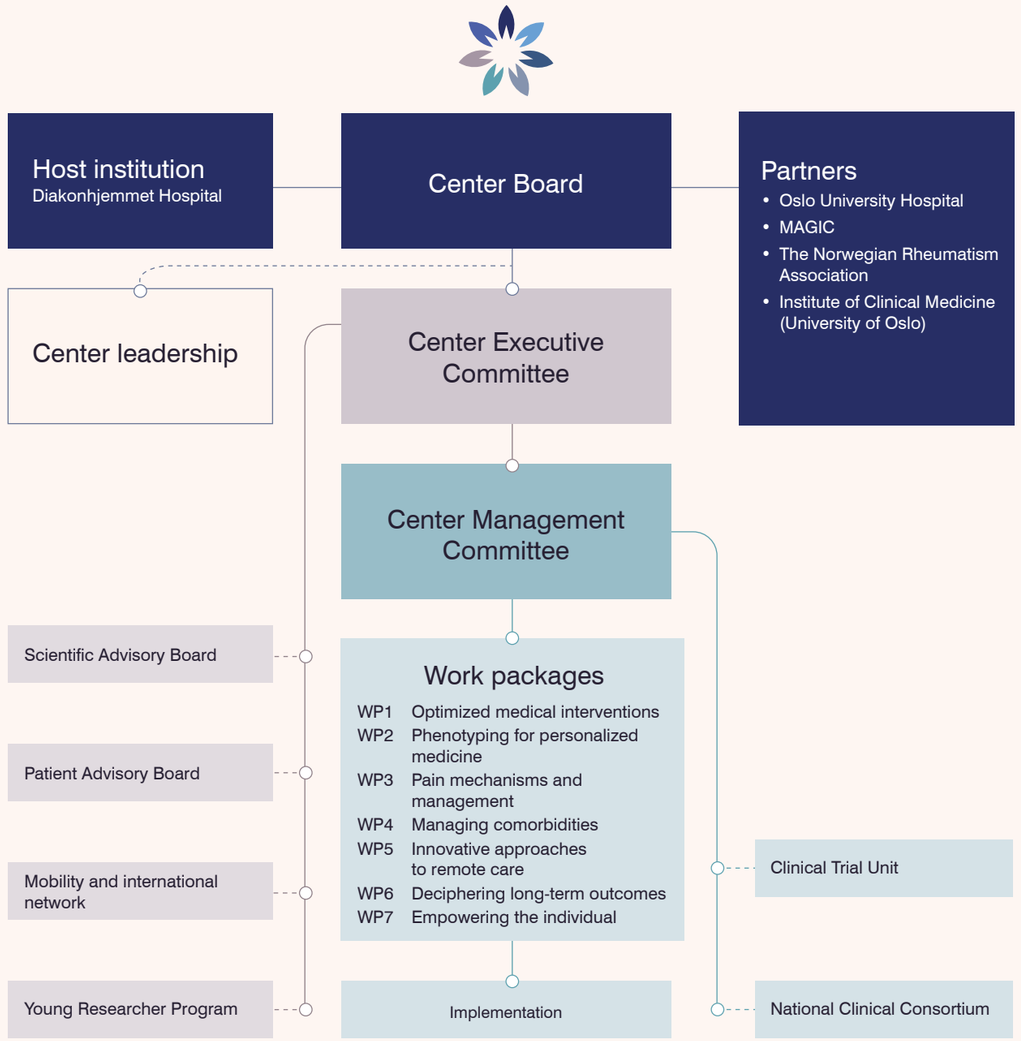
Organization

Diakonhjemmet Hospital is the host institution for REMEDY, in partnership with Oslo University Hospital, the Institute of Clinical Medicine at the University of Oslo, the MAGIC Evidence Eco-system Foundation and the Norwegian Rheumatism Association.



Organization structure

The center is organized to have a clear governance and advisory structure, with active involvement from the host institution, the partner institutions, international collaborators, and users, to ensure oversight and optimal performance of the center.



Center Board

The Center Board consists of one member from each of the partnering institutions and is led by the chief executive officer (CEO) at Diakonhjemmet Hospital. The board will assist the center directors in overseeing the operations of the center in an advisory capacity. The board is responsible for the approval of the annual work plan, financial year-end statements, and the annual report. The board held two meetings in 2023.

Center leadership

The REMEDY center is led by Professor Espen A. Haavardsholm (MD, PhD) together with the two vice directors, senior researcher Siri Lillegraven (MD, MPH, PhD) and Professor Anne Therese Tveter (physiotherapist, PhD), and administrative manager Eline Lundgaard. The center leadership is responsible for overseeing and coordinating activities in the center and the center committees, as well as reporting to the Research Council of Norway. The center leadership meet weekly.

Center Executive Committee

The Center Executive Committee (CEC) consists of the center directors, the work package leaders, the leader of the Patient Advisory Board, the leaders of the Young Researcher Program and key senior scientific staff members from all the partnering institutions. The CEC is responsible for the development and maintenance of the long-term strategic plan for the center. The CEC held five meetings in 2023.

Center Management Committee

The Center Management Committee (CMC) consists of the center directors, the leaders and co-leaders of the individual work packages, the leaders of the National Clinical Consortium and the leader of the Clinical Trial Unit. The CMC is responsible for the ongoing day-to-day implementation of the long-term center strategy. The CMC had 11 meetings in 2023.

Center Board

Jan Frich
Chair of the Board,
CEO of Diakonhjemmet Hospital

Kjetil Bergsmark
Board member,
Head of Division of
Rheumatology and Research,
Diakonhjemmet Hospital

John-Anker Zwart
Board member,
Head of Research,
Division of Clinical Neurology,
Oslo University Hospital

Shuo-Wang Qiao
Board member,
Deputy Head, Institute
of Clinical Medicine,
The University of Oslo

Bo Gleditsch
Board member,
General secretary, The Norwegian
Rheumatism Association

Per Olav Vandvik
Board member,
CEO, MAGIC Evidence
Ecosystem Foundation

Center leadership

Espen A. Haavardsholm
Center director,
Professor, MD, PhD

Siri Lillegraven
Vice Director,
Senior Researcher,
MD, MPH, PhD

Anne Therese Tveter
Vice Director,
Professor,
Physiotherapist, PhD

Eline Lundgaard
Administrative manager

REMEDY partners

In this section, we present insights into the main collaborations with the partner institutions, showcasing the competencies within REMEDY. All partnering institutions actively engage in the organization, management and research activities conducted within the framework of the center, as well as dissemination and implementation both nationally and internationally.

INTRODUCTION CENTER HIGLIGHTS WORK PACKAGES OTHER ACTIVITIES RESEARCH PROJECTS OUTREACH AND PUBLICATIONS

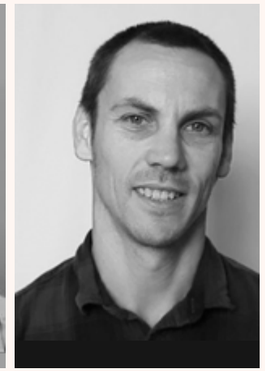
MAGIC Evidence Ecosystem Foundation

The MAGIC team involved in REMEDY:

Per Olav Vandvik
CEO

Leticia Kawano-Dourado
Researcher

Siri Seterelv
Researcher



Stjin Van de Velde
Senior researcher

MAGIC Evidence Ecosystem Foundation (MAGIC/www.magicevidence.org) is a Norwegian non-profit organization committed to increasing value and reducing waste, through a digital and trustworthy evidence ecosystem. At the core of this evidence ecosystem is MAGICapp (www.magicapp.org) that facilitates the authoring, publication and dynamic updating of trustworthy guidelines, available on all devices open access for clinicians and their patients worldwide. MAGIC has experienced a breakthrough for living guidelines through the COVID-19 pandemic.

MAGIC is involved in REMEDY supporting the translation of research findings into trustworthy guidelines, through their flagship project The BMJ Rapid Recommendations. Following practice-changing trials from REMEDY, MAGIC convenes an international panel of unconflicted experts and patient partners and creates trustworthy clinical practice guidelines. These are supported by linked systematic reviews and published both in MAGICapp and in the BMJ. The first topic focus on the use of proactive therapeutic drug monitoring (TDM) of biologic drugs in immune-mediated inflammatory diseases, triggered by the NOR-DRUM trial from REMEDY. The BMJ Rapid Recommendation will be published spring 2024, coordinated with an adapted and translated version of this guideline through the Norwegian Society of Rheumatology. MAGIC will study the implementation of this guideline across all hospitals in Norway through another research project ("Enhancing the Evidence Ecosystem"). This gives REMEDY the opportunity to understand how we better can close the loop from new trials to increased value in health care, here through the implementation of TDM, with clear benefit for patients.

Oslo University Hospital – FORMI

The Musculoskeletal Health Research and Communication Unit (FORMI) is a research unit under the Department of Research and Innovation, Division of Clinical Neuroscience, Oslo University Hospital. FORMI aims to elevate the level of knowledge regarding musculoskeletal injuries, diseases, and disorders, as well as neuroscience in collaboration with patient and public involvement (PPI). The unit conducts clinical, epidemiological, genetic, health economic, and basic research projects in the field of musculoskeletal health. These projects have both local, national, and international significance.

Patient and Public Involvement

In addition to a high level of research, the unit is actively engaged in several Patient in Public Initiatives. The FORMI PPI network consists of engaged and trained patient representatives representing various patient organizations to ensure the quality of user involvement in musculoskeletal health research in the future. PPI involvement initiatives involves various implementation methods throughout the research processes, fig. (“the Research Arrow”).

Collaboration

FORMI and REMEDY have collaborated over the past year arranging two courses in user involvement in research for both researchers and patient representatives together. The purpose of the course is to increase knowledge about PPI throughout the research process for both researchers and individuals with experiential expertise. The course provides examples of how user involvement in research can be organized in the various phases of the research process. There is a focus on collaboration, how to enhance each other’s abilities, facilitate common language, and mutual understanding.

Video information about PPI: Brukermedvirkning forklart av FORMI (youtube.com).

↑ A fine selection of researchers from the rheumatology research groups at OUS united at the 2023 REMEDY seminar.

Oslo University Hospital – Rikshospitalet, Department of Rheumatology

Our three research groups; *Fibrotic Inflammatory Rheumatic Diseases (NorFIORD)*, *Epidemiology and Outcomes in Rheumatic Diseases,* and *Paediatric Rheumatology Research Group* conducts clinical and translational research focusing on patient groups who have systemic inflammatory conditions and receive clinical care from the Dept. of Rheumatology, OUH Rikshospitalet. As partner in REMEDY since 2022, we have excellent opportunities to further develop our clinical treatment research portfolio. Clinical treatment research is a key priority for OUH, hence our partnership in REMEDY is of major relevance.

Summarized, our long-term ambitions are to design, fund, and conduct research projects that: address important, unmet clinical needs in patients with systemic inflammatory conditions and immune-dysregulation and provide results that are robust and have potential to change clinical practice.

We have set up three specific aims for our research:

- Improve our understanding of epidemiology, gene-environment interactions, spectre of clinical phenotypes and disease trajectories of major systemic inflammatory conditions through prospective, multi-disciplinary observational studies of population-based patient cohorts.
- Provide new insights on target organ dysfunction and failure in systemic inflammatory conditions by high-resolution studies of pattern, extent, severity, and progression rates of major target organ afflictions, focusing on heart, lungs, joints, and the gastro-intestinal tract.
- By randomized, controlled trials, determine safety and efficacy of new therapeutic approaches in patient cohorts with well-characterized systemic inflammatory conditions.

In 2023, one of our research groups was awarded grants from the Research Council of Norway and South-Eastern Norway Regional Health Authority, to “The MOVE JIA-trial” – *MOVing towards Evidence based treatment strategies for children with Juvenile Idiopathic Arthritis in sustained remission*, which will be part of the project portfolio of the REMEDY center.

Photo: Lars Petter Devik

↑ Postdoctoral researcher Johanna Elin Gehin working in the laboratorium.

The Department of Medical Biochemistry at Oslo University Hospital, Radiumhospitalet

The Department of Medical Biochemistry at Oslo University Hospital, Radiumhospitalet, has a long tradition for developing in-house immunoassay.

In the last decade, a broad range of assays for measuring biologic drugs and patient anti-drug antibodies in patient samples has been established. These assays enable therapeutic monitoring of biologic drugs, and are currently used both in routine patient care and in research.

Established collaboration

Several collaborative projects using biobank samples and data from REMEDY, i.e. from the NOR-DMARD, ULRABIT and NOR-VEAC trials, have advanced our understanding of the relationship between serum drug levels, patient anti-drug antibodies and clinical outcome in patients treated with biologic drugs. In addition, the analytical service provided by the laboratory at Oslo University Hospital was important to both the NOR-SWITCH and the NOR-DRUM trials.

SQUEEZE

The Department of Medical Biochemistry at Oslo University Hospital is a partner in the SQUEEZE consortium. The main focus in 2023 has been to increase our knowledge on the therapeutic ranges of TNF inhibitors administered subcutaneously (by the patients themselves), in order to include these drugs in the planned European RA-DRUM trial within SQUEEZE. For this project, we use samples and data from the NORD-STAR trial, but also have access to data from industry trials.

FACTS

Nils Bolstad, MD PhD,
group leader, consultant

Department of Medical Biochemistry

Oslo University Hospital,
Radiumhospitalet

- Immunoassay development
- Tumor marker assays
- Assays for 20 biologic drugs
- Partner SQUEEZE

The Norwegian Rheumatism Association

About us

The Norwegian Rheumatism Association (NRF), founded in 1951, is a nationwide non-profit organization committed to supporting individuals with rheumatic and musculoskeletal diseases. Dedicated to influencing health and social policies, NRF offers courses, guidance services, and social activities, including holiday stays and day trips, across its 18 county branches and 215 local branches.

With around 30,000 members as of 2023, NRF collaborates closely with researchers at the REMEDY center, and actively supports research initiatives. Emphasizing a holistic approach to well-being, the association plays a crucial role in promoting the health and quality of life for people with rheumatic and musculoskeletal diseases.

Dialogue Seminar

Diakonhjemmet Hospital/REMEDY, the National Advisory Unit on Rehabilitation in Rheumatology (NKRR), and the Norwegian Rheumatism Association invited researchers, clinicians, and patients to the annual Dialogue Seminar to get updates on research on rheumatic diseases. The main theme for 2023 was personalized treatment.

EULAR

Several employees and the Chairman of the Norwegian Rheumatism Association, Bo Gleditsch, were present at EULAR. Anna Fryxelius, from the Norwegian Rheumatism Association, presented the project “Sykt Aktiv”, which shows that a user-supported intervention organized by a patient organization has the potential to help people with chronic pain and rheumatic conditions return to work and live healthy and active lives.

Webinar

Senior consultant Dr. Guro Løvik Goll (Diakonhjemmet Hospital) participated in a webinar in collaboration with the Norwegian Rheumatism Association to discuss the results of the Nor-vaC study. The findings show that people with rheumatic diseases who are on immunosuppressive treatment may need more vaccine doses to get the same effect as others have significant importance for our members.

Podcast

Physiotherapist Camilla Fongen and Professor Ingvild Kjeken (Diakonhjemmet Hospital) have been guests on RevmaPodden to discuss how people with rheumatic diseases can cope with everyday life when it is really cold. Anna Fryxelius participated at the American College of Rheumatology (ACR) Congress, where she, together with senior consultant Guro Løvik Goll, discussed new and exciting research in RevmaPodden that will be of great benefit to people with rheumatic disease.

↑ The new board of the Norwegian Rheumatism Association, led by Marleen Rotnes. From left: May-Liz Lindsetmo Bestvold, Are Jacob Opdal, Marleen Rotnes, Jørn Flagtvedt Meinertz, Stine Wasenius Dahl, Hege Backstrøm Sandblost, Ann Kristin Bakke, Eva Rønningen. Photo: Camilla Stabell.

FACTS

The Norwegian Rheumatism Association’s focus on healthy living:

- Discussions with experienced patient advisers (peer-to-peer service)
- Exercise in a gym or warm water
- Support groups about life with chronic illness
- Pain management support groups
- Fatigue management support groups

University of Oslo – Department of Medical Genetics: Genetics of autoimmunity

The IMMGEN group: From left Fatima Heinicke, Martine Mesel, Marte Viken, Siri Flåm, Marte Heimli, Benedicte Lie. In front, from left: Anne Rydland, Maria Vigeland, Hanne Hjorthaug. Photo: Line Mygland, OUS

Our research goals

The IMMGEN research group focuses on understanding the molecular and cellular mechanisms for development of rheumatoid arthritis and juvenile idiopathic arthritis, as well as for treatment response. We also aim to understand the underlying autoimmune break of immunological self-tolerance.

Omics and single cell

To achieve our goals, we utilize several layers of biological information for studying immune cells down to a single cell level before we identify the spatial location of the disease relevant cells. Such deep molecular data from blood, synovial fluid and tissue is combined with clinical characteristics to achieve insight into the pathogenesis at a cellular level. Furthermore, we investigate extracellular vesicles and their proteins to understand the communication between cells during an inflammation.

Long standing collaboration

The IMMGEN group has for two decades collaborated with the Division of Rheumatology and Research at Diakonhjemmet, which has enabled us to perform biological studies of basic disease mechanisms combined with patient phenotypes from clinical studies.

Øyvind Bakke started as a PhD student in the group this year. He is working on the MinJIA project in close collaboration with Department of Rheumatology, OUH. Photo: Øystein Horgmo, UiO

The IMMGEN group:

- Led by Professor Benedicte Lie
- A multidisciplinary team: Senior researcher, 2 Staff engineers, 1 postdoc, 5 PhD students, 2 Master students, and 1 Associate Member
- Heavily involved in WP2
- REMEDY partner at the University of Oslo
- Located at Department of Medical Genetics, Oslo University Hospital
- Main international collaborative groups: Sarah Teichmann (University of Cambridge); Pierre Antoine Gourraud (University of Nantes); Tom Huizinga (University of Leiden)
- Funding mainly from the Norwegian Research Council, South-Eastern Norway Regional Health Authority and The Norwegian Rheumatism Association

We generate single cell suspensions of cells from blood, synovial fluid, synovial tissue or other affected organs in order to characterize their molecular activities and identify the cells which deviates due to disease. Photo: Hanne Hjorthaug, OUS

Hanne Hjorthaug makes sure that the patient samples are stored correctly. Photo: Bård Gudim

Single cell technologies

REMEDY researchers are employing the novel and powerful multimodular single cell and spatial technologies. These methods have revolutionized the understanding of cellular heterogeneity, the location of cells in tissues and the cellular functions and interactions in health and disease.

Each cell undergoes high-throughput sequencing. Siri Flåm is operating the instrument. Photo: nyebilder.no

Deep sequencing

The single cells obtained from patients, e.g. from synovial tissue, synovial fluid or blood, are undergoing high-throughput sequencing to obtain cell specific information about the gene activity (RNAseq), gene regulation (ATACseq, ChIPseq) and protein markers (CITEseq), in addition to immune receptor usage (TCR and BCR seq).

Precision medicine

The holistic view of each cell provided by these technologies offers us a precise and comprehensive characterization of cells involved in the disease processes. Understanding disease mechanisms and treatment responses at such a detailed molecular level aids the advancement of precision medicine, where the goal is to bring information about each patients underlying biology into clinical practice to assist diagnostic processes and treatment decisions.

FACTS

- Several REMEDY projects utilizes single cell technologies
- Important technology for WP2 regarding precision medicine
- State-of-the-art instrumentation is located at REMEDY's partner at Department of Medical Genetics, University of Oslo
- We are part of the Human Cell Atlas network aiming to map every cell in the human body

User involvement in research

Leader
Marianne Skaar
Advisor in user involvement in research

Diakonhjemmet Hospital has a long tradition with user involvement in research in scientific projects and effort has been put on further development of this collaboration in 2023, focusing on four main priorities (panel on p. 25).

Together with FORMI at OUH, which is a partner in REMEDY, two courses in user involvement in research have been conducted for researchers, PhD candidates and patient research partners. To further build on this course, REMEDY collaborate in the development of a credit-awarding course in user involvement in research for PhD candidates and patient research partners together with the University of Bergen and the other Centers for clinical treatment research; Neuro-SysMed, NorHEAD and MATRIX. NorCrin, FORMI and the Norwegian Health Association are also partners in this collaboration. The first course is planned in April 2024. The advisor in user involvement in research in REMEDY is part of the program committee and have attended several meetings in 2023. The advisor has additionally taken an initiative to establish a network for advisors in user involvement in research from different institutions and organizations, and this group have had two meetings in 2023.

The advisor has also been actively disseminating the experiences from user involvement in research in different settings such as lectures for master students and PhD candidates, as well as different seminars and webinars. To increase competence on user involvement in research in REMEDY, the advisor has also provided guidance to researchers and PhD candidates within the center. To increase awareness on user involvement in research, the Director and one of the Vice directors of the REMEDY center have written an editorial in The Journal of the Norwegian Medical Association, highlighting the importance of user involvement in enhancing relevance and quality of research.

An important part of the user involvement in REMEDY is the Patient Advisory Board, now comprising more than 20 members that all have attended courses in user involvement in research. In 2023, five member meetings have been organized, providing opportunities for the members of the board to actively engage with external stakeholders. These meetings have also served as a platform for members to share their valuable experiences from collaborating in the various research projects in REMEDY.

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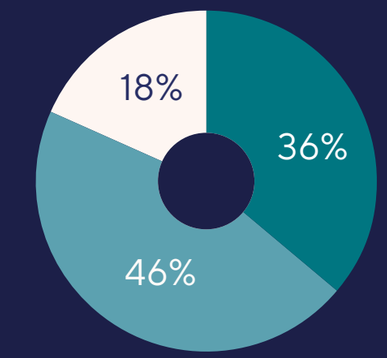
Four main priorities for user involvement in research in 2023:

- Early involvement of patient research partners in all work packages
- Conducting courses in user involvement in research for researchers, PhD candidates and patient research partners
- Guidance of PhD candidates in user involvement in research
- Active engagement with external stakeholders

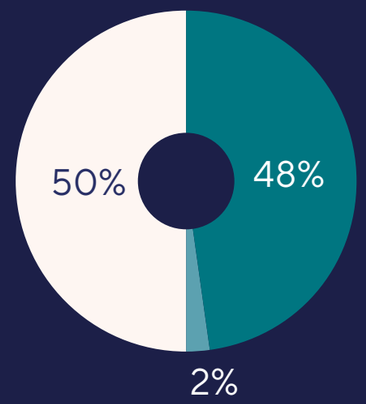
Facts and figures

71,4 million NOK



- Own financing
- Other financing
- RCN grant (Research Council of Norway)

55,3 million NOK



- South-Eastern Norway Regional Health Authority
- Other international funding
- Other national funding

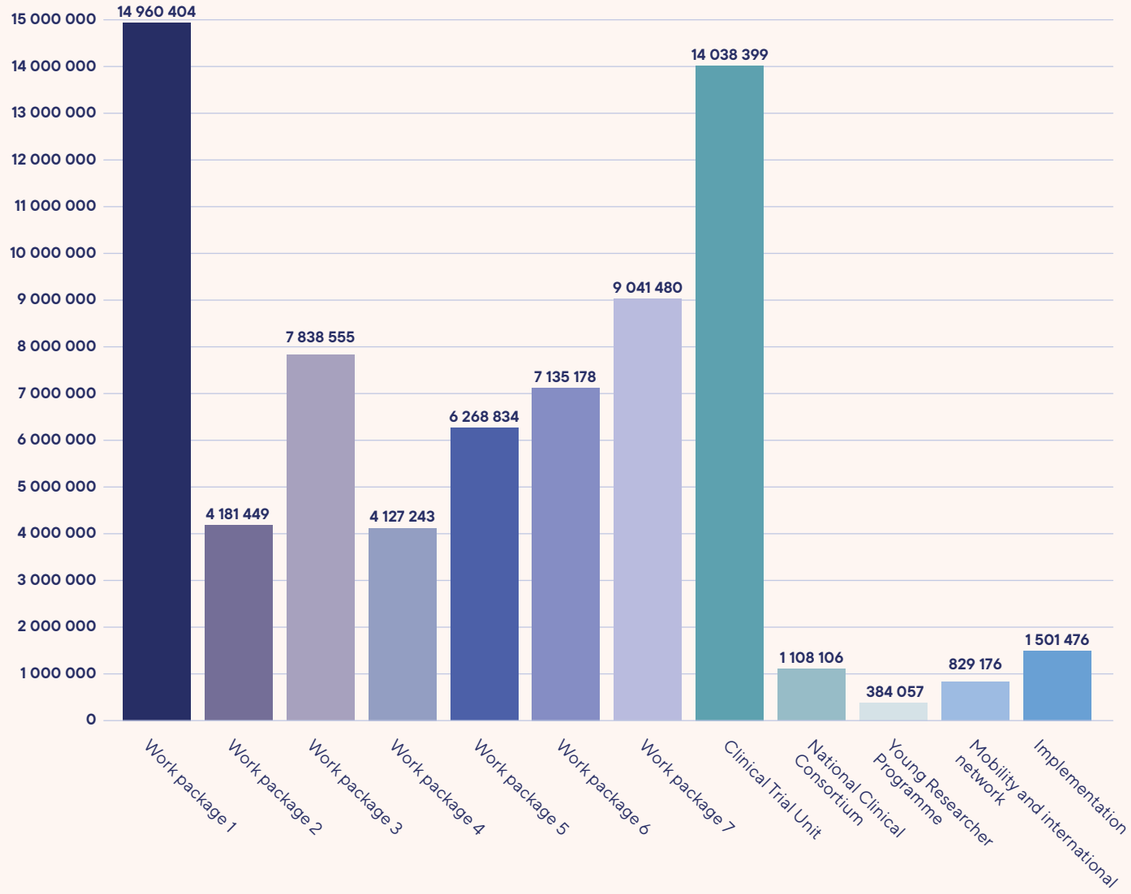
REMEDY funding 2023

This figure shows the total costs for 2023 and how these costs are funded. Total costs for 2023 are 71,4 MNOK. Own financing includes funds provided by the host institution and partners. Other financing includes financing secured before 2022 from public funding schemes, mainly from the regional health authorities, interregional authorities, the DAM Foundation and other publically available grants.

Obtained grants in 2023

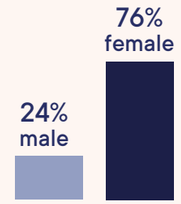
REMEDY researchers have obtained a number of grants during 2023 for projects in the coming years. The total amount obtained is 55,3 MNOK. This is mainly financing from the South-Eastern Norway Regional Health Authority, as well as other national grants such as the DAM Foundation and the Research Council of Norway.

REMEDY activitites (cost in NOK)



REMEDY human resources

92
individuals performed work in the center



46,6
Mean age (years)

REMEDY: Climate and sustainability

Human-induced climate change and nature destruction threaten to undermine decades of progress in global health. The healthcare sector is a substantial contributor to greenhouse gas emissions. REMEDY is committed to contribute to a transition towards sustainable research and clinical practice.

The healthcare sector is responsible for approximately 5 % of global greenhouse gas emissions. This is more than aviation and shipping combined. Also scientific research has a significant carbon footprint.

REMEDY takes action to mitigate climate change. We aim to decrease the carbon footprint of our research-related activity, and also to conduct studies with potential to shift clinical practice towards low-carbon solutions.

In June 2023, REMEDY was co-organizers of Green congress ("Grønn kongress"), an annual national conference targeting the Norwegian rheumatology community. The conference summarizes and disseminates current international research and knowledge in our field. The aim of the event is to reduce carbon emissions associated with the extensive travelling to international congresses and at the same time communicate international research results to as many as possible. Furthermore, we aim to increase awareness among healthcare personnel and researchers about the harms of nature- and climate change and possible solutions to address them. Each year we invite a climate scientist to give a state-of-the-art lecture. Speaker in 2023 was senior researcher at CICERO, Bjørn Samset.

We actively work to minimize the carbon footprint of Green congress itself, reducing emissions where possible. In 2022 and 2023 the arrangement received the certificate of an environmental approved event from Foundation for Environmental Education.

The onsite and virtual event was a success. Around 430 people attended the conference and their feedback was excellent. We were invited to talk about the event at a course for health leaders arranged by the University of Oslo in November 2023.

In June 2023 we published a commentary in Lancet Rheumatology, discussing the substantial carbon footprint associated with international conferences, proposing virtual and hybrid formats as more sustainable alternatives. The commentary also addresses the financial and social barriers to on-site attendance, particularly for individuals from low income and middle income countries and under-represented groups.

During 2023 REMEDY has started implementing environmental endpoints in our clinical trials. We will perform lifecycle assessments to quantify and compare the carbon footprint of the study interventions. This can inform decision makers, developing clinical practice at the lowest possible environmental burden. Additionally, our innovative remote care projects aim to reduce the carbon emissions associated with patients travelling to hospital visits.

Grønn kongress

Climate scientist Bjørn Samset talked about climat changes and global warming

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02

Center highlights

Highlights 2023

The REMEDY center has had an eventful second year. In this section, we present some of our highlights during 2023, including awards, national and international collaboration, obtained funding and center/network activities. We also showcase the career development of some of our young researchers, and provide more in-depth coverage of a selection of the projects in REMEDY, the newly funded research network on decentralized clinical studies (RECONNECT), and the 2023 Annual Research Retreat.

JANUARY

Dissertation

PhD candidate Helene Lindtvedt Valaas defended her thesis “Rehabilitation trajectories for individuals with rheumatic and musculoskeletal diseases. Goal attainment, adherence to self-management, and follow-up care”.

FEBRUARY

Inven2

Diakonhjemmet Hospital entered into an agreement with Inven2 to manage contracts, negotiations, and financial aspects for industry-funded clinical trials.

FEBRUARY

Visiting professor

Daniel H. Solomon, Professor at Harvard Medical School becomes visiting professor at REMEDY.

JANUARY

Course in user involvement in research

Researchers, PhD fellows and Patient Research Partners convened for the sessions. The course was held two times in 2023 in collaboration with FORMI at Oslo University Hospital.

MARCH

Annual Research Retreat

The Annual Retreat was arranged at Sanner Hotel with more than 100 researchers, clinicians and patient research partners present.

APRIL

Clinical Trial Unit

The Clinical Trial Unit was established, with Line Melå Jacobsen as head.

MAY

TRACTION workshop

The first TRACTION workshop focusing on non-pharmacological clinical trials was arranged in Lisbon, Portugal, in collaboration with REMEDY.

JUNE

EULAR Honorary Award

Professor Espen A. Haavardsholm was appointed EULAR Honorary Member for outstanding service in accomplishing the objectives of EULAR.

MAY

Dissertation

PhD-candidate Alexander Fraser defended his thesis “Reverse total shoulder arthroplasty in the operative treatment of displaced proximal humeral fractures”.

JUNE

FOREUM Abstract Award

Professor Sella Provan received the FOREUM Abstract Award in the Clinical Research category with the abstract “ Interstitial lung diseas in patients with rheumatoid pr psoriatic arthritis starting bDMARDs: Incidence vs general population, and the role of methotraxate co-medication.

JUNE

Green congress

The environmentally certified Green congress was held on June 16th, summarizing key points from the 2023 EULAR congress. The event attracted over 430 attendees, both in person and virtually. A keynote speech by Intergovernmental Panel on Climate Change member, Bjørn Samset, highlighted the urgent issues of climate change.

AUGUST

Scandinavian Rheumatology Research Foundation

Associate professsor Guro Løvik Goll received the Norwegian award at the Scandinavian Rheumatology Congress (SCR).

AUGUST

Visiting professor

Désirée van der Heijde, Professor at Leiden University Medical Center, was appointed as visiting professor at the REMEDY center.

SEPTEMBER

Dissertation

PhD-candidate Kenth-Louis H. Joseph defended his thesis “Exploring physical function, activity, and sustainable delivery of first-line treatment for patients with osteoarthritis”.

SEPTEMBER

MOVE-JIA

The project was allocated 11 million NOK from the Research Council of Norway’s women’s health initiative.

SEPTEMBER

WP2 seminar

The seminar was arranged with international state-of-the-art lectures by professors Tom Huizinga and Costantino Pitzalis.

OCTOBER

Dialogue seminar

Co-organized with the Norwegian Rheumatism Association to present the most recent research to patients with rheumatic and musculoskeletal diseases.

OCTOBER

EMA approval PICASSO

First clinical study involving medicinal product submitted and approved through EMAs new portal CTIS with CTU support.

OCTOBER

DAM Foundation supports three REMEDY projects

Anna-Birgitte Aga, Ida Kristin Haugen and Nina Østerås were each awarded three million NOK from DAM Foundation to support new research projects, in collaboration with the Norwegian Rheumatism Association.

NOVEMBER

Board meeting with new Chair

Professor and CEO of Diakonhjemmet Hospital, Jan Frich.

NOVEMBER

Funding to establish Research Lab at Diakonhjemmet Hospital

Allocation from the hospital fund for equipment procurement.

NOVEMBER

Recruitment completed for two major randomized controlled trials

A total of 386 participants were recruited for the Happy Hand project, and 242 for the ReMonit trial.

DECEMBER

New professor

Anne Therese Tveter was appointed professor in Health and rehabilitation at OsloMet.

DECEMBER

Funding from South-Eastern Norway Regional Health Authority

Anna-Birgitte Aga, Karen Minde Fagerli, Lene Bugge Nordberg and Nina Paulshus Sundlisæter were awarded project funding while Tuva Moseng received funding for a regional research network.

CAREER DEVELOPMENT
– going from PhD to postdoc

Aims to improve the well-being of patients with juvenile arthritis

Juvenile idiopathic arthritis (JIA), the predominant chronic rheumatic condition among children and adolescents, currently lacks controlled studies and guidelines regarding maintenance treatment and medication withdrawal for patients in stable remission.

Siri Opsahl Hetlevik

Consultant Physician,
PhD and Postdoctoral Researcher
at Oslo University Hospital

Left untreated, juvenile idiopathic arthritis (JIA) causes joint inflammation, risking damage and loss of function. While modern treatment strategies enable many patients with JIA to achieve inactive disaese without signs or symptoms of the disease, little is known about optimal mainteinance strategies for patients in remission.

Evidence-based treatment recommendations

Consultant physician Siri Opsahl Hetlevik at Oslo University Hospital has received startup funds from Young Researcher Program in REMEDY to plan a randomized trial to assess adjustment of medication for JIA patients in stable remission. Her work contributes to the national MOVE-JIA study.

– I chose this area of research because I want to contribute to better and more targeted treatments for a vulnerable patient group. The research is important because it can fill a critical knowledge gap. We hope to improve patients' quality of life by reducing medication side effects while maintaining remission, Hetlevik says.

The initial funding from REMEDY covered salaries during the study's planning phase, protocol development, and establishing partnerships.

– This was crucial for drafting successful applications, leading to additional research grants from the Research Council of Norway and the South-Eastern NorwayRegional Health Authority. In addition, I have received funding for my postdoctoral position from the Norwegian Women's Public Health Association, she says.

Studying the effects of drug tapering

The MOVE-JIA study aims to compare the outcomes of reducing methotrexate versus scaling back biological medications, so-called TNFi (tumor necrosis factor inhibitors) and will evaluate if using TNFi or methotrexate alone is as effective as their combined treatment.

Hetlevik explains that patients are split into three groups to track disease flare-ups over a year: one stops TNFi, another stops methotrexate, and the third continues both treatments.

Researching within REMEDY

She combines a 50 percent postdoctoral position in MOVE-JIA with a clinical position and work in the National quality and competence network for pediatric and adolescent rheumatology.

– Our collaboration with REMEDY has been extremely valuable so far. Not just because of the financial support in the initial phase of the project, but also because of the supportive environment. We have greatly benefited from assistance with application writing, inspirational and useful discussions through REMEDY seminars and meetings, emphasizes Siri Opsahl.

CAREER DEVELOPMENT
– going from PhD to postdoc

The immune system can modulate the effects of drugs

For her doctoral thesis, Ingrid Jyssum conducted research on how the immune systems of patients with inflammatory joint diseases respond to drugs such as COVID-19 vaccines and biological drugs.

Ingrid Jyssum

MD and PhD fellow at
Diakonhjemmet Hospital

– We discovered that patients with inflammatory joint diseases, who were treated with immunosuppressive drugs, needed an additional vaccine dose to achieve the same level of protection against COVID-19 as healthy individuals. Some biological drugs resulted in a poor vaccine response in the patients, even after repeated vaccinations. These findings were important as we were in the midst of the COVID-19 pandemic. The results contributed to deciding on a vaccination strategy for patients with such diseases, Jyssum says.

Antibodies reduced the effect of the world's most widely used biological drug

– In a different study, we found that 10 percent of the patients using the biological drug adalimumab developed antibodies against the drug, reducing its effectiveness. Adalimumab, the most commonly used biological drug worldwide, is currently dosed the same for everyone.

– When we looked at this drug, we also found that the level of adalimumab in the blood was relevant for the treatment's effectiveness. More knowledge about how to tailor the medication to the individual is crucial for improving treatment, she emphasizes.

Funding and further research

To conduct her PhD research, she received support from South-Eastern Norway Regional Health Authority. Additionally, parts of the vaccine research was funded by Coalition for Epidemic Preparedness Innovations (CEPI). She is now awaiting feedback on her thesis before her doctoral dissertation. She has already planned to continue as a postdoctoral fellow in the EU project SQUEEZE, where she will be the national coordinating investigator in the RA-DRUM study, a multicenter, multinational study to be managed from Diakonhjemmet Hospital.

– In this study, we will examine the effect of therapeutic drug monitoring (TDM), a treatment strategy where we adjust the dosage of the drug based on regular assessments of drug levels and antibodies against the drug in the blood. We will compare a group receiving TDM to a group receiving standard treatment. We aim to see if personalized treatment with TDM leads to less disease flares, Jyssum explains.

– It's fantastic to be a PhD candidate in REMEDY. There are so many exciting projects and talented, inspiring researchers working here. I enjoy being part of REMEDY because I have good research groups around me with people I like to collaborate with, and because I get the opportunity to participate in projects I find academically stimulating. Further research has been a topic of discussion several times during my PhD, and there has been great support and assistance from the community to continue with research as a postdoctoral fellow, says Jyssum enthusiastically.

CAREER DEVELOPMENT
– going from PhD to postdoc

Improving shoulder fracture care: DelPhi study findings

Elderly patients quite often suffer serious fractures that impact shoulder function. Orthopaedic surgeon Alexander Nilsskog Fraser's PhD project revealed notable differences in operative treatment outcomes.

Alexander Nilsskog Fraser

Orthopaedic surgeon, PhD, Consultant Physician and Postdoctoral Researcher at Diakonhjemmet Hospital

Fraser's PhD project was based on the DelPhi study, a randomized controlled trial conducted at seven Norwegian hospitals including Diakonhjemmet Hospital. The study showed that reverse shoulder prostheses outperform plate fixation.

Published in the American Journal of Bone and Joint Surgery (JBJS), the study gained widespread national and international attention.

Funding

Sophies Minde Orthopedics funded a 20% research position over two years, and the Diakonhjemmet Internal Research Fund, in conjunction with the REMEDY Young Researcher Programme, jointly provided funding for a 50% research sabbatical from the clinic during a transitional period.

– This played a vital role in the completion of my PhD and paved the way for my postdoctoral position, including authoring the five-year article for the DelPhi study. This also served as excellent preparation for my doctoral dissertation in May 2023, Fraser notes.

More research

Fraser points out the need for high-quality studies in the field. The DelPhi study answered some important questions regarding operative treatment of severe shoulder fractures.

– We are now eagerly awaiting the results of another large trial, Nordic DeltaCon, where reverse arthroplasty is compared with non-operative treatment.

Currently, alongside his clinical work, Fraser holds a 50% postdoctoral position funded by REMEDY, continuing his research in shoulder surgery.

Fraser is highly enthusiastic about researching within REMEDY, praising the project's meticulous planning and execution, the professional and committed management, and the supportive work environment. He also commends the organization's ability to host significant events and courses.

Follow the link to read a summary of his doctoral work at the University of Oslo:

https://www.med.uio.no/klinmed/english/research/news-and-events/events/disputations/2023/fraser-alexander-nilsskog.html

CAREER DEVELOPMENT
– going from PhD to postdoc

Customized medicine for inflammatory joint diseases

Inflammatory joint diseases are often treated with biological medicines. To keep patients as symptom-free as possible, with minimal side effects, the correct dosage is crucial. Consultant Physician Johanna Elin Gehin (PhD) at Department of Medical Biochemistry Oslo University Hospital (OUH) wanted to contribute to better control of dosing in individuals.

Johanna Elin Gehin

Consultant Physician. PhD and Postdoctoral Researcher at Oslo University Hospital

– I chose this because it was an exciting research collaboration between OUH and Diakonhjemmet Hospital, within my field of interest. I had started as a laboratory physician after a few years of clinical rheumatology. The innovative analyses at OUH, combined with unique material from the registry studies NORDMARD and ULRABIT at Diakonhjemmet Hospital, made the project possible, Gehin explains.

Personalized treatment

Her PhD thesis, finished in 2022, focused on how we can make treatment with biological medicines, such as TNF inhibitors, more precise for people with inflammatory joint diseases. The funds she received from the REMEDY Young Researcher Programme in 2022 allowed her to expand her research to include more biological medicines for rheumatoid arthritis as part of her postdoctoral project.

– The research contributes to a better understanding of how we can measure and interpret blood levels of medications commonly prescribed to this patient group. When we know exactly how much medicine is needed to be effective, we can customize the treatment with therapeutic drug monitoring (TDM), she explains.

Medicine concentration in the blood

Gehin says that this requires knowledge of the optimal level of medicines in the blood. The researchers therefore looked at the relationship between the drug concentrations in the blood and its effect. They found ideal levels for the TNF inhibitors certolizumab pegol and golimumab. For etanercept, they did not find a clear pattern. Monitoring the level of this medicine thus seemed to be less important.

Postdoctoral in EU project

After her doctoral degree, she continued her research as a postdoctoral researcher in the EU project, SQUEEZE.

– This has given us the opportunity to delve deeper into how we can improve treatment with TNF inhibitors, she says.

The project includes studies to identify therapeutic ranges, as well as a large multi-center clinical randomized trial to examine the effect of TDM, in the study RA-DRUM.

– Researching within REMEDY has been incredibly rewarding, especially because of the academic seminars and the opportunity to meet and discuss with other researchers, emphasizes Johanna Elin Gehin. During the course, she had the opportunity to be part of the team behind the NOR-DRUM trial, which demonstrated the clinical effect of TDM. – It was extremely rewarding, she adds.

CAREER DEVELOPMENT
– going from PhD to postdoc

Pain associated with hand osteoarthritis

Photo: Nicolas Tourrenc, Diakonhjemmet sykehus

Many people with hand osteoarthritis experience severe pain, but the pain severity does not always correlate with the structural changes. In her PhD, Gløersen explored other factors that may contribute to symptoms in these patients.

Marthe Gløersen

MD, PhD, Postdoctoral Researcher at Diakonhjemmet Hospital

Gløersen started as a research assistant in the Nor-Hand study during her medical studies in 2016, with data collection at Diakonhjemmet Hospital. She began her PhD full-time in 2019, funded by Eckbos Legat, and delivered her thesis in 2023. Her work involved data analysis, writing of papers and the thesis, as well as postdoctoral preparations.

– Seeing many patients suffering from pain that cannot be explained solely by radiographic findings sparked my curiosity, she says.

Higher BMI, more pain

She emphasizes the need to study and understand the pain mechanisms in these patients to improve treatment strategies and their quality of life. Using data from 300 participants with hand osteoarthritis in the Nor-Hand study, they found that individuals with higher BMI reported more pain.

– This was found not only in load-bearing joints, such as knees, but also in the hands, explains Gløersen.

Pain sensitization

This led them to investigate whether factors produced by adipose tissue, which can cause a low-grade inflammation, played a role. The analyses indicated that the hormone leptin could partially explain the increased hand pain in people with a higher BMI.

– Higher BMI was also linked to greater pain sensitization, i.e., increased pain sensitivity. Further, greater pain sensitization was related to symptoms like more painful joints in the hands and in the rest of the body and reduced physical function, she reports.

The research indicates that obesity and increased pain sensitivity could affect hand osteoarthritis symptoms. Pain sensitization may explain why some patients have pain and functional impairment, despite limited structural changes. Further studies are needed to assess if preventing or treating obesity can reduce hand pain.

Postdoctor

Gløersen is now continuing as a postdoctoral researcher in the PICASSO study, which is a large, randomized controlled multicenter trial originating from Diakonhjemmet Hospital. Data collection is ongoing at six hospitals in Norway. Recruitment of patients began in November 2023, aiming to include 354 patients to compare the effects of corticosteroid injections, saline injections, and an occupational therapy intervention for osteoarthritis in the thumb base joint.

Gløersen values working at REMEDY, appreciating the collaborative spirit, support from statisticians and advisors, and the support from the community in the transition to a postdoctoral researcher. She credits her supervisor, Ida K. BosHaugen, and colleagues at Diakonhjemmet Hospital for their pivotal roles in study planning and protocol development in the PICASSO trial.

Associations of Body Mass Index With Pain and the Mediating Role of Inflammatory Biomarkers in People With Hand Osteoarthritis.

Associations of pain sensitisation with tender and painful joint counts in people with hand osteoarthritis: results from the Nor-Hand study.

Associations between pain sensitization and measures of physical function in people with hand osteoarthritis: Results from the Nor-Hand study.

CAREER DEVELOPMENT
– going from PhD to postdoc

Biological mechanisms of chronic low back pain

Photo: Øystein Horgmo

Most cases of chronic low back pain have unknown etiology. The patients are typically viewed through a biopsycosocial model, although the biological mechanisms involved remain poorly understood. In her thesis, Maria Dehli Vigeland investigated the molecular mechanisms underlying the course of thedisease and its treatment.

Maria Dehli Vigeland

MD, PhD, Oslo University Hospital

– We found correlations between MRI images of patients' backs and expression of inflammatory genes measured in blood. Furthermore, the patients' self-reported pain levels were also reflected in their gene expression. Interestingly, the second article revealed that different genes were involved in men and women, she says.

These studies underscored the significance of biological elements in conditions often perceived as predominantly lifestyle-related or driven by psychosocial factors. Furthermore, the findings emphasized the importance of considering gender differences in pain research.

Long-term antibiotics treatment

Due to the limited understanding of the causes for these patients' pain, treatment strategies with a weak evidence base, such as long-term antibiotic use, have become prevalent.

– Our research demonstrated that 100 days of antibiotic treatment led to persistent changes in gene expression and DNA methylation in blood. Given that the implications of these modifications remain uncertain, we advocate for a cautious approach in prescribing long-term antibiotic therapy, Vigeland says.

Funding and further research

Vigeland's PhD research was conducted within the framework of the AIM study, a comprehensive project focused on patients with chronic low back pain, which received funding from South-Eastern Norway Regional Health Authority. Furthermore, her thesis writing was supported by additional funding from the Young Researcher Program within REMEDY.

– Being part of REMEDY has been incredibly inspiring," she emphasizes, "as it unites all the relevant disciplines for my research. It also simplifies the process of seeking advice or collaboration as a PhD student. In a few months, I hope to begin my role as a postdoctoral researcher with Professor Benedicte Lie, continuing my involvement within REMEDY, she adds.

Vigeland MD, Flåm ST, Vigeland MD, Espeland A, Kristoffersen PM, Vetti N, Wigemyr M, Bråten LCH, Gjefsen E, Schistad EI, Haugen AJ, Froholdt A, Skouen JS, Zwart JA, Storheim K, Pedersen LM, Lie BA; AIM Study Group Correlation between gene expression and MRI STIR signals in patients with chronic low back pain and Modic changes indicates immune involvement *Scientific Reports. 2022 Jan 7;12(1):215.*

Vigeland MD, Flåm ST, Vigeland MD, Espeland A, Zucknick M, Wigemyr M, Bråten LCH, Gjefsen E, Zwart JA, Storheim K, Pedersen LM, Selmer K, Lie BA, Gervin K, The Aim Study Group Long-Term Use of Amoxicillin Is Associated with Changes in Gene Expression and DNA Methylation in Patients with Low Back Pain and Modic Changes *Antibiotics (Basel). 2023 Jul 21;12(7):1217.*

Omtale i Morgenbladet

Can patients with rheumatoid arthritis taper treatment after reaching sustained remission?

The ARCTIC REWIND trial

ARCTIC REWIND

A majority of patients diagnosed with rheumatoid arthritis today can reach remission, a state with no or very little symptoms of disease activity. It has been uncertain whether these patients have to continue the same treatment level to maintain remission. In the ARCTIC REWIND trials, we have examined if these patients can taper and withdraw treatment.

Modern treatment

– Untreated, rheumatoid arthritis can have major impact on the life of the patient, with pain, loss of physical function and joint damage, says rheumatologist and postdoc Nina Paulshus Sundlisæter.

– In the last two decades, introduction of new therapeutic agents and structured treatment strategies have changed the outcome of the disease significantly, and a majority of patients now reach remission, a disease state with no or very little signs and symptoms of inflammatory disease activity.

– However, rheumatoid arthritis is a chronic disease, and many patients live with the disease for decades. When the patient is feeling really well, a common question has become whether he or she needs to remain on the same amount of medication that was necessary to reach remission, says Paulshus Sundlisæter.

ARCTIC REWIND

In the ARCTIC REWIND project, two separate randomized clinical trials were performed to examine the effects of tapering and withdrawal of rheumatoid arthritis medication in patients who had been in remissiom for at least a year. The first trial assessed methotrexate and other conventional synthetic disease-modifying antirheumatic drugs (csDMARDs). The second trial assessed tapering to withdrawal of tumor necrosis factor inhibitors (TNFi), a group of biologic drugs.

Both studies were performed as large national collaborations, and involved a majority of Norwegian rheumatology departments.

Novel results

Data from both trials have been published in 2023. This includes publications in JAMA and the leading rheumatology journal. The results show that patients more often have disease activity flares when tapering both medication types, but individual considerations are important and the data should inform shared decision making. The results have also been highlighted by the Annals of Internal Medicine in their journal club section, and a late breaking abstract was mentioned as one of ten highlights at the American rheumatology congress.

– When talking to clinicians in Norway and internationally, they say that they use the results from ARCTIC REWIND in their everyday conversations with patients, says principal investigator Siri Lillegraven.

– We are very happy to have achieved our aim of providing clinically important results which might contribute to improved care for this patient group.

Funding

From 2012-2023, ARCTIC REWIND has received grants from the Research Council of Norway (8 mill NOK) and The South-Eastern Norway Regional Health Authority (several grants, for a total of approximately 24 million NOK).

↑ Some of the core researchers involved in the ARCTIC REWIND trials.

FACTS

- ARCTIC REWIND investigates tapering of disease-modifying antirheumatic drugs in patients with rheumatoid arthritis in sustained remission
- The project contains two separate randomized clinical trials assessing different medications
- The studies were made possible by extensive collaboration across Norwegian rheumatology departments

IMPORTANT PUBLICATIONS

Lillegraven, S. et al. "Discontinuation of Conventional Synthetic Disease-Modifying Antirheumatic Drugs in Patients with Rheumatoid Arthritis and Excellent Disease Control." *JAMA 329, no. 12 (Mar 28 2023): 1024-26.*

Lillegraven, S. et al. "Effect of Tapered Versus Stable Treatment with Tumour Necrosis Factor Inhibitors on Disease Flares in Patients with Rheumatoid Arthritis in Remission: A Randomised, Open Label, Non-Inferiority Trial." *Ann Rheum Dis 2023 Nov;82(11):1394-1403).*

Lillegraven, S. et al. "Effect of Half-Dose Vs Stable-Dose Conventional Synthetic Disease-Modifying Antirheumatic Drugs on Disease Flares in Patients with Rheumatoid Arthritis in Remission: The Arctic Rewind Randomized Clinical Trial." *JAMA 325 (17): 1755-64.*

Important treatment progress in gout

Gout is a major problem for those affected. It leads to painful episodes with inflammation in joints and tendons. Despite effective and easily available drugs to treat gout by lowering urate in the blood, the disease is often not well treated. In consequence, patients experience deposition of uric acid crystals in the tissue, with subsequent flares and functional impairment. All this can be avoided applying a targeted treatment strategy.

What was studied?

In the NOR-Gout study, we investigated whether reduced levels of uric acid in the blood through targeted treatment prevents new attacks of gout and reduces the deposition of crystals in the tissue.

For this purpose, we established a cohort of gout patients who came to the rheumatology outpatient clinic after an acute attack of arthritis and having increased levels of urate in the blood. Altogether, 211 patients were treated with a targeted intervention with an interview by a study nurse at the rheumatology outpatient clinic including information about uric acid-lowering medication.

Follow-up with a nurse was done, if necessary, every month until the treatment goal of low uric acid level was reached. Follow-up with a doctor at fixed time intervals (3 and 6 months, as well as after 1, 2 and 5 years) included a comprehensive ultrasound examination of urate crystal depositions. Furthermore, an X-ray examination with dual energy computed tomography to detect depositions was carried out annually for the first two years. The 5 years with follow-up allowed us to study the long-term course of adherence to medication in addition to questionnaires examining health-related quality of life as well as work productivity.

What were the results?

After one year of intensive treatment 85% of patients achieved the target of urate levels, and there was in addition a major reduction in urate crystal deposition. This reduction in deposition continued during maintenance of treatment through year 2 to 5. In other words, the body was gradually emptied for damaging urate depositions in joints and tendons.

During the second year of the study the frequency of flares in gout was clearly reduced and only experienced in one of four patients. Patients had further achieved a better understanding of the necessity to take their medication.

We also found that fluctuation in serum urate over time was related to a higher chance of flare, and that there was a relationship between inflammatory markers in the blood and deposition of urate crystals.

In general, the situation was much improved once patients had been followed with intensive treatment during the first year. Most patients could continue work. Lifestyle with reduced body mass index or waist circumference as well as lower blood lipids at the start of the study were related to achieving good gout outcomes with no flares and achievement of low serum urate levels.

Importance of the study

This study is the first to include such a high number of gout patients followed for a number of years with extensive imaging and clinical examinations, and demonstrated that optimal medication of gout patients can easily be improved through tight control of patients using a clear treatment target. This resulted in significant reduction of urate crystal depositions and thus less disease burden as well as an improved quality of life. Cooperation between a physician and a nurse are a key to optimal treatment, as is contribution from other specialists – cardiologists and radiologists – which contributed to make this study globally unique.

PUBLICATIONS IN 2023

Uhlig T, Karoliussen LF, Sexton J, Provan SA, Kvien TK, Haavardsholm EA, Hammer HB. "Course and predictors of work productivity in gout – results from the NOR-Gout longitudinal 2-year treat-to-target study." *Rheumatology (Oxford). 2023;62:3886-92.*

Uhlig T, Karoliussen LF, Sexton J, Kvien TK, Haavardsholm EA, Hammer HB. "Lifestyle factors predict gout outcomes – results from the NOR-Gout longitudinal 2-year treat-to-target study." *RMD Open 2023;9:e003600.*

Uhlig T, Karoliussen LF, Sexton J, Kvien TK, Haavardsholm EA, Taylor WJ, Hammer HB. "Beliefs about medicines in gout patients: results from the NOR-Gout 2-year study." *Scand J Rheumatol. 2023;52:664-72 .*

An e-self-management program for people with hand osteoarthritis

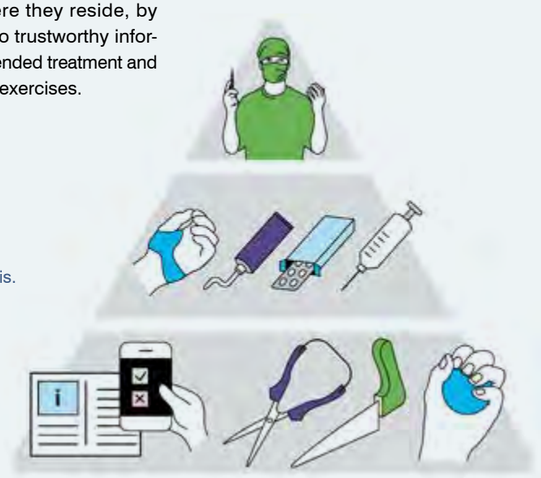
Happy Hands

Hand osteoarthritis affects nearly half of all women and a quarter of all men and is a major cause of pain and impaired hand function. There is no cure, but international recommendations state that information, hand exercises, and use of assistive devices are effective measures to reduce pain and improve function. The quality of care is in general sub-optimal for this patient group and people with hand osteoarthritis have poor access to recommended treatment both in primary and specialist care.

Strategic documents highlight the use of eHealth in self-management and better exploitation of healthcare resources. Based on funding from the Dam Foundation, project managers Anne Therese Tveter and Ingvild Kjeken developed the Happy Hands app together with a project group comprising patient research partners, clinicians, researchers, IT-personnel, a film photographer and an animator. The overarching goal of the Happy Hands app is to deliver a standalone intervention that supports and empowers people with hand osteoarthritis to self-manage their disease, regardless of where they reside, by providing access to trustworthy information on recommended treatment and guidance on hand exercises.

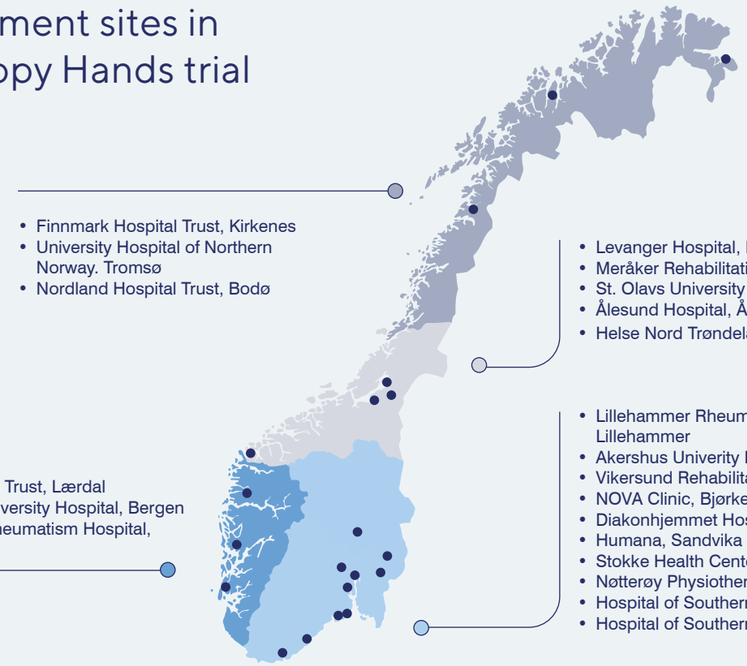
Results from a feasibility study comprising 70 patients with hand osteoarthritis showed that the patients considered the app to be highly usable and useful. The results further indicated that the app may improve quality of care, grip strength, activity performance, pain and stiffness.

A large multicenter randomized controlled trial with 386 participants recruited from all over Norway is now ongoing. Preliminary results from this trial are very promising and indicate that patients benefit from this app. The next step is to work together with Inven2 on strategies for making the app available for people with hand osteoarthritis.



→ Current treatment recommendations for hand osteoarthritis.

Recruitment sites in the Happy Hands trial



- Finnmark Hospital Trust, Kirkenes
- University Hospital of Northern Norway. Tromsø
- Nordland Hospital Trust, Bodø

- Førde Hospital Trust, Lærdal
- Haukeland University Hospital, Bergen
- Haugesund Rheumatism Hospital, Haugesund

- Levanger Hospital, Levanger
- Meråker Rehabilitation Center, Meråker
- St. Olavs University Hospital
- Ålesund Hospital, Ålesund
- Helse Nord Trøndelag

- Lillehammer Rheumatism Hospital, Lillehammer
- Akershus Univerity Hospital, Kongsvinger
- Vikersund Rehabilitation Center, Vikersund
- NOVA Clinic, Bjørkelangen
- Diakonhjemmet Hospital, Oslo
- Humana, Sandvika
- Stokke Health Center, Tønsberg
- Nøtterøy Physiotherapy Clinic, Tønsberg
- Hospital of Southern Norway, Arendal
- Hospital of Southern Norway, Kristiansand

The app is designed to guide the participants through a series of questionnaires, informative videos, exercise videos, quizzes, and customized feedback messages over 12 weeks.

MOVing towards pErsonalized medicine
for children and adolescents with Juvenile
Idiopathic Arthritis in sustained remission.
A comparison of three treatment strategies:

The MOVE-JIA trial

The Section of Pediatric Rheumatology at Oslo University Hospital as partner of the REMEDY center want to assess two different withdrawal treatment strategies, compared with continuing methotrexate and tumor necrosis factor inhibitor, on the risk of flares in patients with juvenile idiopathic arthritis in sustained remission.

In this randomized controlled trial, the research team aim to optimize the management of patients with juvenile idiopathic arthritis (JIA) who are in stable disease remission. Balancing the risk of JIA flare with the long-term burden of medications and their side effects is a crucial concern for patients, parents, and caregivers.

JIA is the most common chronic rheumatic condition in children and adolescents, predominantly affecting girls. The disease causes joint inflammation and can lead to joint damage and disability. Fortunately, due to modern medications and treatment strategies, many JIA patients can achieve “sustained remission” – with no symptoms of the disease.

But there is a question that lingers: how best to manage JIA patients once they are in remission? The answer is not clear as there are no controlled studies to guide us, and there are no recommendations on whether to reduce or withdraw the treatment.

Introducing the “MOVE-JIA” trial: a national study that will include 150 JIA patients in sustained remission treated with tumor necrosis factor-inhibitor (TNFi) and methotrexate. They will be randomly divided into three groups: A) Gradual TNFi withdrawal, B) Gradual methotrexate withdrawal, or C) Continued stable treatment with both TNFi and methotrexate. The primary goal is to measure how many patients experience a disease flare within a year.

The MOVE-JIA trial will be the first study to investigate if reducing methotrexate is less likely to cause disease flares compared to reducing TNFi in JIA patients.

↑ Irene Urnes Tjernlund, Merete Lindén Dahle, Anna-Birgitte Aga, Pernille Bøyesen and Siri Opsahl Hetlevik will be responsible and coordinate the multicenter MOVE-JIA trial.

The study will also assess whether single treatment with either TNFi or methotrexate is as effective as combination of both treatments.

The research project is led by Anna-Birgitte Aga rheumatologist and senior researcher, together with senior consultants and postdocs Siri Opsahl Hetlevik and Pernille Bøyesen, all from Section of Pediatric Rheumatology at Oslo University Hospital.

The MOVE-JIA trial is a collaborative national effort, including all pediatric rheumatology units in Norway and active patient participation, ensuring the swift application of the results into clinical practice. The findings will provide much-needed insights on how to best manage children and adolescents with JIA who are in remission.

FACTS

Participating centers:

- Oslo University Hospital (OUH)
- Haukeland University Hospital, Bergen
- Stavanger University Hospital, Stavanger
- St. Olavs hospital, Trondheim University Hospital
- University Hospital of North Norway, Tromsø
- Vestre Viken Hospital Trust, Drammen
- Sorlandet Hospital Trust, Kristiansand

RECONNECT

Professor Anne Therese Tveter, Associate professor Tuva Moseng and Professor Nina Østerås are part of the management team in RECONNECT.

The Regional Research Network on Decentralized Clinical Studies (RECONNECT) was allocated 6 mill NOK by the South-Eastern Norway Regional Health Authority (Helse Sør-Øst RHF) in December 2023. The network aims to contribute to the improvement of knowledge and collaboration in clinical studies using decentralized elements. It is a perfect match for WP5 in REMEDY.

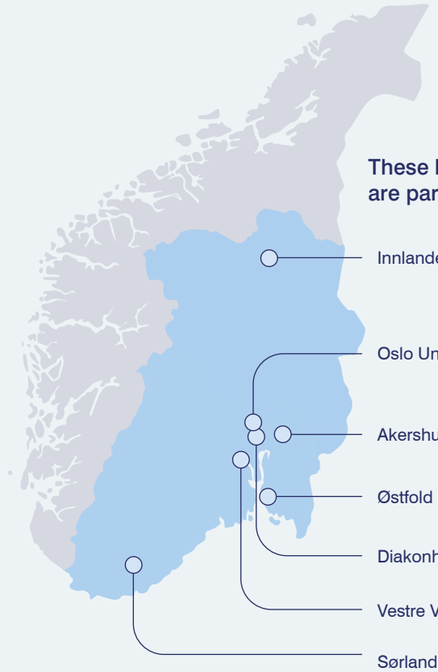
Associate Professor and Postdoctoral Research Fellow, Tuva Moseng, will lead the network along with Professors Anne Therese Tveter and Nina Østerås from Diakonhjemmet Hospital, as well as Martha Colban, a Special Advisor at Oslo University Hospital. They are also joined by Kim Fangen, a user representative in research from Sørlandet Hospital Trust.

The National Action Plan for Clinical Studies 2021-2025 emphasizes the need to double the number of studies. The goal is that five percent of all patients should participate in clinical trials by 2025.

One way of reaching this goal is to conduct more decentralized studies. This can contribute to more representative results and better health outcomes across the population. Decentralization of clinical studies can also reduce costs and carbon footprint, as more patients participating in clinical studies can contribute with their data and experiences from home.

The network has three specific areas which includes digital data collection, issues regarding medical equipment, and drug management in decentralized clinical studies. Additionally, knowledge sharing is a central aspect.

The RECONNECT network will facilitate increased collaboration between medical disciplines, technological expertise, and patient groups. The RECONNECT network also provides a model where user representatives contribute their experiences with the use of decentralized elements providing valuable insights for increased research quality.



The seven hospitals in the network represent different diagnostic groups and have experience with different decentralized elements in various types of clinical studies.

Annual Retreat

A highly successful research seminar was held at Sanner Hotel on March 22–24, 2023, with more than 100 participants from REMEDY. Our guest professor from Harvard University and Brigham and Women's Hospital, Professor Daniel H. Solomon, gave several interesting presentations, including how to develop excellent research environments and tips on how to write and review a manuscript.

On the first day, four state-of-the-art lectures were given, followed by discussions in thematic workshops. Professor Daniel H. Solomon presented on how to design clinical trials with clinical impact, while Professor John Torgils Vaage from Oslo University Hospital lectured on immunological analyses in a clinical trial setting. Professor George Metsios from the University of Thessaly in Greece highlighted the role of exercise in rheumatic and musculoskeletal diseases, and Professor Merete Hetland from Rikshospitalet Glostrup/University of Copenhagen presented on the use of registers to understand long-term outcomes of diseases. The day was concluded with presentations from recipients of the Young Researcher Program's grant before the participants were engaged in a social treasure hunt across the venue.

The theme of the research seminar was "Developing excellent research projects," and the second day began with a presentation by Professor Espen A. Haavardsholm on how to decipher a grant call – and obtain an excellent score from the reviewer panel. The rest of the day was dedicated to project discussions, where new project ideas were presented and discussed. These project discussions have been a tradition in our research environment for several years, and many of the project ideas discussed in workshops like this have later received substantial funding. The final day of the retreat was reserved for Young Researchers. Professor Daniel H. Solomon presented on how to be a good mentor and successful trainee. Practical tips for successful grant writing were provided by Siri Lillegraven. Furthermore, lectures were given on how to collaborate across internal departments, how to apply novel technologies, and the young researchers gained insights into opportunities for traveling abroad as PhD or postdoctoral candidates.

Pictures from the Annual retreat at Sanner Hotel.

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03

Work Packages

The seven work packages in REMEDY have a broad interdisciplinary focus on all aspects of rheumatic and musculoskeletal diseases – from epidemiology, pathogenesis and disease mechanisms to factors that promote health and wellbeing.

Work packages

The overarching aim of the REMEDY center is to improve treatment of rheumatic and musculoskeletal diseases (RMDs) by randomized clinical trials assessing novel treatment and treatment strategies, in combination with research and innovation to untangle the causes and characteristics of RMDs.

The seven work packages approach the knowledge needs within RMD treatment from different angles, ensuring that the research results will benefit patients in all stages of the diseases. This multifaceted construct will result in high quality in all aspects of comprehensive treatment courses. We will conduct clinical trials to test new therapies and treatment strategies.Translational research activities will improve understanding of disease mechanisms and identify potential novel targets for treatment of diseases and pain. Development of precision medicine means that the patient will receive the correct treatment earlier in the disease course, optimizing the chance of treatment response and reducing irreversible damage. Increased knowledge about how to identify and treat comorbid conditions is expected to have direct consequences for mortality and morbidity. Use of remote monitoring, supported by artificial intelligence (e.g., through machine learning), will provide more flexible care for the patients, while detecting important changes of disease activity with less use of healthcare resources. Health registries are national assets, giving a unique opportunity for real world data and linkage of health information, and may be used to improve long-term outcomes in patients with RMDs. The development of empowerment-oriented self-management interventions may contribute to reduce variability and ensure health equity for people with RMDs.

INTRODUCTION CENTER HIGLIGHTS WORK PACKAGES OTHER ACTIVITIES RESEARCH PROJECTS OUTREACH AND PUBLICATIONS

WP1

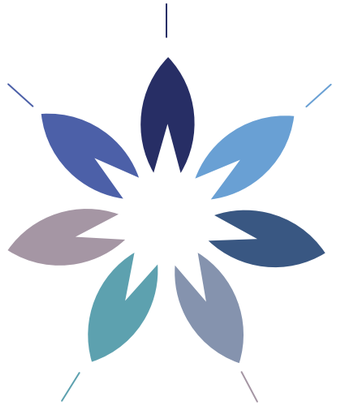
To develop, assess and implement innovative interventions and treatment strategies to optimize patient outcomes in RMDs.

WP7

To empower patients and enhance their ability and self-efficacy to deal with medical, role and emotional management.

WP2

To improve precise diagnosis, characterize and stratify RMDs into clinically relevant subgroups and to develop the necessary tools to offer personalized treatment.



WP6

To disentangle the longitudinal disease course of RMDs in order to understand the disease and treatment associated outcomes, including work ability and health economics.

WP3

To better understand underlying pain mechanisms in order to optimize pain management.

WP5

To develop, assess and implement feasible, effective and cost-effective approaches to remote monitoring and follow-up, tailored to the individual patient.

WP4

To reduce the burden of comorbidities in people with RMDs with a special focus on cardiovascular diseases.

Work package 1

Optimized medical interventions

Leader

Siri Lillegraven, senior researcher, MD MPH PhD

Co-leader

Silje W. Syversen, associate professor, MD PhD

Viewpoint

Evidence based medicine is a cornerstone in modern medicine, and requires high-quality knowledge generated by randomized clinical trials. Randomized clinical trials have also become a stated focus area for the Norwegian health care system, through multiple initiatives.

In REMEDY, randomized clinical trials assess interventions such as drugs, surgical techniques, approaches to organization of health care, diet, physical exercise and decision support tools for treatment allocation. Examples of the latter include imaging-informed treatment algorithms and algorithms based on therapeutic drug monitoring,

In 2023, several large new randomized clinical trials have been under planning and initiation, after securing funding the previous year. These projects illustrate the broad focus of the center, as they include large randomized clinical trials assessing surgery for hip fractures, osteoarthritis treatment, optimizing of biological treatment of rheumatoid arthritis, diet for patients with inflammatory joint diseases, and tapering of treatment for juvenile idiopathic arthritis.

These randomized clinical trials are made possible through a continuous partnership between clinicians, researchers, and patient partners, and by collaboration across partner institutions and study centers in multicenter trials. This collaboration is also key to ensure that novel knowledge is disseminated to clinical personnel and patients in an effective manner.

The work package arranges half-yearly seminars with programs focusing on topics of interest across diseases and projects. We also work closely with the clinical trial unit to expand knowledge-sharing across studies, e.g. regarding the new CTIS system for European approval of clinical trials.

We were especially happy that the MOVE-JIA trial, assessing treatment strategies in juvenile idiopathic arthritis with Oslo University Hospital as sponsor, secured two large grants. We are also proud that several publications from the work package presented novel results from our trials, and gained recognition for potential clinical importance. This included publications in JAMA, Journal of Internal Medicine and all major rheumatology journals.

Highlights of the year

Start of new study: The large PICASSO trial started recruitment at all four study centers.

Patient recruitment: Several studies continued patient recruitment, including the large NOR-SPRINT study with participating centers across Norway.

Funding: The MOVE-JIA trial obtained two large grants. Additional funding was secured for studies such as ARCTIC-FORWARD, ARCTIC REWIND and NOR-SPRINT.

International attention: Data from the NORD-STAR and ARCTIC REWIND trials were presented at congresses in addition to publications in major journals, and gained significant international attention.

Key publications

Lillegraven, S. et al. "Discontinuation of Conventional Synthetic Disease-Modifying Antirheumatic Drugs in Patients with Rheumatoid Arthritis and Excellent Disease Control." *JAMA, 2023 Mar;329(12): 1024-26*.

Østergaard, M. et al. "Certolizumab Pegol, Abatacept, Tocilizumab or Active Conventional Treatment in Early Rheumatoid Arthritis: 48-Week Clinical and Radiographic Results of the Investigator-Initiated Randomised Controlled Nord-Star Trial." *J Intern Med, 2023 May;293(5): 648-55*.

Lillegraven, S. et al. "Effect of Tapered Versus Stable Treatment with Tumour Necrosis Factor Inhibitors on Disease Flares in Patients with Rheumatoid Arthritis in Remission: A Randomised, Open Label, Non-Inferiority Trial." *Ann Rheum Dis 2023 Nov;82(11):1394-1403.*

Aim

The main aim of work package 1 is to develop, assess and implement innovative interventions to optimize patient outcomes in rheumatic and musculoskeletal diseases. This includes investigation of personalized treatment strategies, novel drugs, surgical procedures, imaging guided interventions, and non-pharmacological therapies.

Work package 2

Phenotyping for personalized medicine

Leader

Hilde Berner Hammer, professor, MD PhD

Co-leader

Guro Løvik Goll, associate professor, MD PhD

Viewpoint

The collaboration between clinicians, clinical scientists and laboratory researchers within this work package facilitates the exchange of results and ideas between translational science and clinicians that benefit all of REMEDY.

REMEDY has currently assembled extensive biobanks from well-characterized patients (full blood, serum, plasma). Such samples provide a unique material for addressing key questions within rheumatic and musculoskeletal diseases, as exemplified by projects tailoring the dose of biologic drugs to the individual patient. We have in 2023 continued our long-standing work to lead the field studying how the clinician may tailor treatment based on serum drug measurements.

The Nor-vaC study, assessing vaccine response to Covid-19 vaccines in patients using immunosuppressive medication, has gained international recognition. The data provided by the project has been instrumental in the development of updated vaccination advice for this patient group.

In 2023, further advances have been made to plan biobanks of leucocytes (PBMC and joint fluid) and biopsies from synovial tissue. The BIKE study was successfully completed, using ultrasound to guide biopsies of knee joint synovitis in patients with rheumatoid arthritis or osteoarthritis. Biopsies from joint synovitis are central to several planned collaborations the next few years and give us the opportunity to study personalized treatment regimens and new treatment targets.

We have also planned for a ground-breaking study: Early STratification of patients with acute ARThritis (START) with the primary aim to build a platform for identification of markers in early inflammatory arthritis to ensure timely diagnosis and correct initial treatment. The study will include a broad assessment of laboratory variables and genetics in addition to exploration of potential markers in joint fluid and biopsies.

The NOR-Gout study includes a high number of gout patients followed for five years by clinical, ultrasound and laboratory assessments. We have finalized the follow-up, and the results are exciting by showing a gradual reduction of crystal depositions during medical treatment, indicating a potential to cure this disease by personalized optimization of medication.

WP2 organised a fall seminar with international leaders in the field of personalized medicine, resulting in extended participation in international studies. The contact between basic-, translational- and clinical researchers has thus been proven valuable and resulted in several new emerging projects in 2023.

Highlights of the year

Seminar: Internationally renowned professors Costantino Pitzalis (London) and Tom Huizinga (Leiden) gave excellent talks at a well-attended meeting. They also participated in project discussions, initiating several new collaborative projects within personalized medicine.

Technical development: Collaboration with expert sites including a study visit in March to Queen Mary University London, has enabled us to establish new tissue sampling techniques.

Early arthritis: Projects to characterize and stratify very early arthritis have received external funding, with a dedicated PhD student now added to the study group.

Key publications

Bjørlykke KH et al. “Four SARS-CoV-2 vaccine doses or hybrid immunity in patients on immunosuppressive therapies: a Norwegian cohort study.” *Lancet Rheumatol. 2023*.

Brun, M. K. et al. “HLA-DQ2 Is Associated with Anti-Drug Antibody Formation to Infliximab in Patients with Immune-Mediated Inflammatory Diseases.” *J Intern Med, 2023 May;293(5): 648-55*.

Jyssum I et al. “Adalimumab serum levels and anti-drug antibodies: associations to treatment response and drug survival in inflammatory joint diseases.” *Rheumatology (Oxford). 2023*.

Aim

The main aim of work package 2 is to identify novel biomarkers, genetic- and epigenetic markers for disease severity and treatment responses, which can be used for characterization and stratification of early rheumatic and musculoskeletal disease, as well as for improvement of treatment response.

Work package 3

Pain mechanisms and management

Leader

Ida K. Haugen, senior researcher, MD, PhD

Co-leader

Kaja Selmer, senior researcher, MD, PhD

Viewpoint

Better understanding of the pain etiology is needed for personalized pain management and better care for patients with chronic pain. We want to identify factors outside the joint that clinicians should have in mind when treating patients with pain due to musculoskeletal and rheumatic diseases. Identifying important biopsychosocial factors, such as altered pain modulation in the central nervous system, emotional factors, cognitive functioning and genetic factors, that contribute to pain is of importance. Additionally, the work package will focus on classification of people into different pain phenotypes and endotypes, as these may require different management.

Four studies are affiliated to the work package, including the large ongoing randomized controlled MERINO trial and three large cohort studies (Nor-Hand study, RehabNytte and NOR-DMARD study).

In 2023, we continued our work looking at factors outside the joint that could explain part of the pain experience in people with hand osteoarthritis. We published two papers from the Nor-Hand study focusing on pain sensitization, and its association with comorbidities and physical function. A new PhD student started in June 2023 and will focus on the associations between pain, sleep and fatigue in people with hand osteoarthritis using the the rich data collection in the Nor-Hand study. Preliminary analyses have shown strong associations between pain and sleep. Furthermore, we identified different subgroups of patents with hand osteoarthritis with different levels of pain sensitization, cognitive factors such as pain catastrophizing, psychological factors such as symptoms of anxiety and depression, degree of osteoarthritis, education, age and sex. Interestingly, the patients who were characterized with most severe sensitization and psychological symptoms displayed the most severe pain, despite little degree of hand osteoarthritis. Results from the Nor-Hand study gained much interest at international conferences in osteoarthritis with oral abstract presentation.

In 2023, external funding was received for a PhD starting a new study within the Nor-DMARD register, where we will investigate how cognitive functioning will affect patient outcomes after initiating biological therapies in patients with rheumatoid arthritis and other systemic inflammatory joint diseases.

Lastly, in the fall 2023, we hired a postdoc who will work with molecular endophenotyping in pain. She will first analyze genetic and epigenetic data from patients from the GeNeup study to investigate whether molecular signatures are associated with pain phenotypes. Later, she will also analyze molecular data from the Nor-Hand study. The postdoc will start in January 2024.

Highlights of the year

New insight: Analyses of the follow-up data of the Nor-Hand study continued, focusing on the consequences and potential risk factors for pain and pain sensitization in people with hand osteoarthritis.

New funding: Physiotherapist Daniel Huseby Bordvik started his PhD on pain, fatigue and sleep problems in people with hand osteoarthritis with funding from the Norwegian Women's Public Health Association Haugesund research fund. He will use data from the Nor-Hand study and started in June 2023.

Outreach: Elisabeth Mulrooney gave an oral presentation at the international osteoarthritis conference (OARSI) about how pain differs in its intensity and evolution across subgroups of patients with different clinical characteristics such as central pain modulation and psychological factors.

Key publications

Mulrooney, E., et al. "Comorbidities in people with hand OA and their associations with pain severity and sensitization: Data from the longitudinal Nor-Hand study." *Osteoarth Cartil Open 2023;5:100367*.

Gloersen, M., et al. "Associations between pain sensitization and measures of physical function in people with hand osteoarthritis: Results from the Nor-Hand study." *Osteoarthritis Cartilage 2023;31:1388-95*.

Aim

The primary aim of work package 3 is to increase the understanding of the complexity of pain and the variety of different factors that can contribute to pain. Additionally, we aim to identify subgroups of patients with similar characteristics and clinical outcomes.

Work package 4

Managing comorbidities

Leader

Anne Grete Semb, senior researcher, MD PhD

Co-leader

Eirik Ikdahl, postdoc researcher MD PhD

Viewpoint

Patients with rheumatic diseases have an increased risk of comorbidities, especially cardiovascular diseases. The impact of improved preventive medicine is incontestable, and the superiority of preventive medicine over curative medicine with regards to resource utilisation is indisputable. Accordingly, strategies that have positive effects on comorbidities in this patient group may also entail substantial health economic benefits.

A main focus area for the work package is cardiovascular diseases and improved cardiovascular prevention in relation to ischemic stroke, exercise related health, heart-friendly diet, lipid lowering medication and antihypertensive treatment. An example is the randomized controlled ExeHeart trial, assessing the effect of 12-week high-intensity exercise intervention on cardiorespiratory fitness and cardiovascular risk factors in patients with inflammatory rheumatic disease.

The Norwegian Cardio-Rheuma (NCR) register includes data from the last decade on the total Norwegian population above 18 years (approx. 4.6 mill individuals) by linkage of several of the national health registries. In 2023, data from this newly established national register were used to describe the risk of pulmonary embolism in patients with inflammatory joint diseases in Norway, and how use of non-steroidal anti-inflammatory drugs affect this risk.

The work package is involved in several collaborative networks, such as the Diet Study, a Scandinavian research collaboration on a randomized controlled trial comparing brief and extended information on heartfriendly diets effect on lipids, change in diet and carbon footprint. The SURF-SLE and APS project is a broad international clinical consortium for systematic recording of cardiovascular risk factors, examining cardiovascular preventive treatment in 3401 SLE patients across 27 centers in 24 countries.

Projects within the work package will also address other important comorbidities such as lung disease, kidney disease, diabetes mellitus, infections, malignancies, osteoporosis, gastrointestinal disease, and depression. Several new projects are under development within these research areas such as the establishment of a broad, clinic based comorbidity research register.

Highlights of the year

Register establishment: The Norwegian national Cardio-Rheuma register (NCR) was established and several evaluations related to cardiovascular mortality and morbidity in patients with rheumatic joint diseases has been published.

Large-scale international study: The SURF-SLE and APS project is a unique collaboration across 24 countries. It is the world´s largest registry of cardiovascular risk factors in patients with SLE and antiphospholipid syndrome.

Completed study inclusion: 1) All articles in the EXE-Heart trial have been published. 2) The last patient inclusion in the audit SURF-SLE and APS was in Q1 2023. The main manuscript has been submitted to an international peer-reviewed journal.

Key publications

Ikdahl E, Rollefstad S, Kazemi A, Provan SA, Larsen TL, Semb AG. "Non-steroidal anti-inflammatory drugs and risk of pulmonary embolism in patients with inflammatory joint disease-results from the nationwide Norwegian Cardio-rheuma registry" *Eur Heart J Cardiovasc Pharmacother. 2024 Jan 5;10(1):27-34*.

Nordén KR, Dagfinrud H, Semb AG, Hisdal J, Metsios GS, Sexton J, Fongen C, Bakke EA, Tveter AT. "Criterion Validity and Responsiveness of Estimated Cardiorespiratory Fitness Models in Patients with Inflammatory Joint Disease" *J Clin Med. 2023 Oct 25;12(21):6753*.

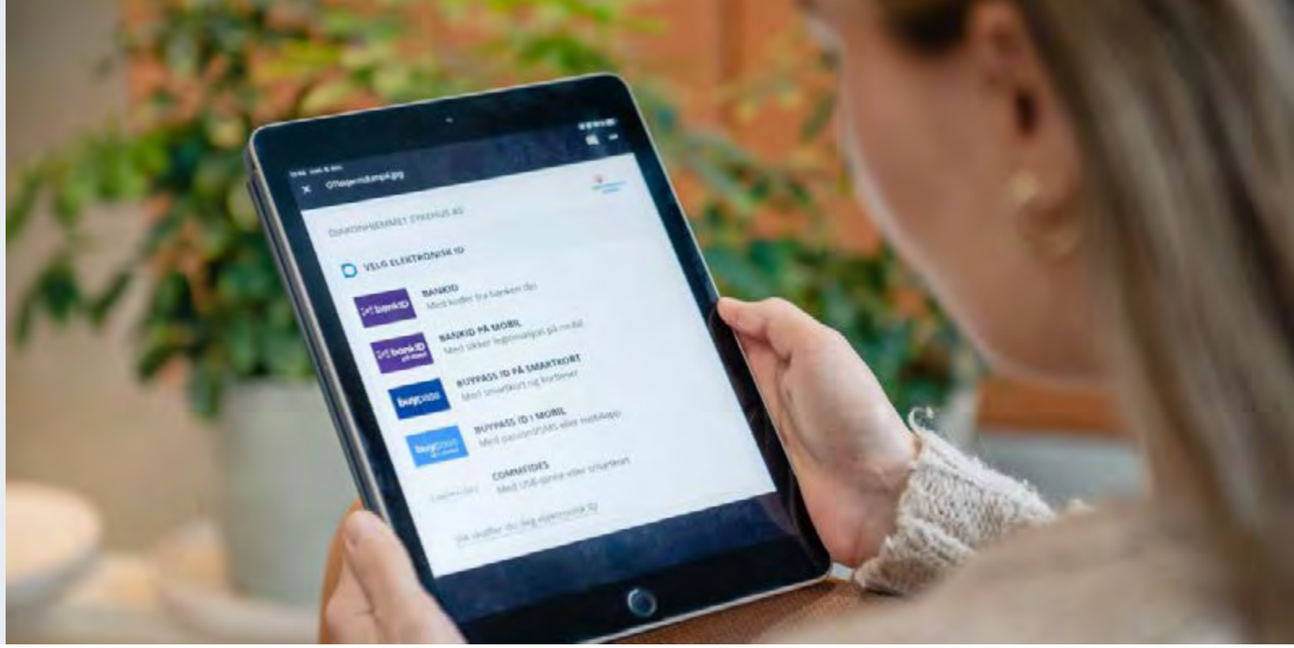
Nordén KR, Semb AG, Dagfinrud H, Hisdal J, Ødegård S, Sexton J, Fongen C, Skandsen J, Blanck T, Metsios GS, Tveter AT. "Associations between cardiovascular risk factors, disease activity and cardiorespiratory fitness in patients with inflammatory joint disease: a cross-sectional analysis." *BMC Sports Sci Med Rehabil. 2023 Apr 21;15(1):63*.

Aim

The main aim of work package 4 is to develop and evaluate strategies for optimal management of comorbidities in patients with rheumatic- and musculoskeletal diseases, including prevention of cardiovascular disease and the identification and management of other important comorbidities such as lung diseases and diabetes mellitus.

Work package 5

Innovative approaches to remote care



Leader

Nina Østerås, professor, physiotherapist, PhD

Co-leader

Anne Therese Tveter, professor, physiotherapist, PhD

Viewpoint

The demographic changes and the future lack off health personnel require the healthcare sector to rethink current work procedures and develop strategies to work "smarter". Digitalization, technology and remote care is nominated a strategic priority for the healthcare services for achieving a sustainable healthcare sector. The Regional Health Thrusts signal to the Specialist healthcare services that they should implement remote care strategies to identify and deliver personalized patient follow-up according to the patients' need. However, evidence on the efficacy and safety of remote care strategies in rheumatic and musculoskeletal diseases is limited, and more research is needed. The goal of the work package is to contribute in testing and implementing digital solutions that can contribute to sustainable healthcare services.

There are five studies that are primarily affiliated with the work package, and an additional three studies that are associated. In 2023, the data collection in the ReMonit trial with 18-months follow-up of 242 patients was completed. The recruitment of patients in the NOR-Flare trial was progressed reaching 226 of the required 260. Both trials assess the effect and cost-effectiveness of remote care in patients with rheumatic diseases. A post doc candidate in the RemoteUX study has interviewed patients in the ReMonit study about their experiences and views on remote care. Additional funding was secured for a post doctor in the ReMonit Gout study testing a self-management application for patients with gout and for developing a regional research network for desentralized clinical studies (RECONNECT).

In addition to the ongoing studies, the activities in the work package have focused on building knowledge about software applications categorized as medical devices, the EU regulation for medical devices, and the formal application process for clinical studies on software applications as a medical device. Members of the work package have participated at the initial meeting for a national research network for remote care and has also started developing an international network on remote care. Group members in the work package have been responsible for the update of recommendations for the core treatment of hip and knee osteoarthritis.

Highlights of the year

New funding: The ReMonit Gout clinical trial received additional funding for one post doctor from the DAM Foundation (3 million NOK). Funding for a regional research network on desentralized clinical studies was received from the South-Eastern Norway Regional Health Authority (6 million NOK).

New software applications: The Urika application for the ReMonit Gout and the Genus application for the OA-AID have been developed and are subject to intensive rounds of testing and iterations.

New achievement: Senior researcher Anne Therese Tveter was appointed professor in health and rehabilitation at Oslo Metropolitan University.

Completed data collection: The ReMonit trial completed the data collection with 18-months follow-up.

Key publications

Berg IJ, et al. "Follow-Up of Patients With Axial Spondyloarthritis in Specialist Health Care With Remote Monitoring and Self-Monitoring Compared With Regular Face-to-Face Follow-Up Visits (the ReMonit Study): Protocol for a Randomized, Controlled Open-Label Noninferiority Trial." *JMIR Res Protoc. 2023 Dec 27;12:e52872*.

Thomassen EEK, Berg IJ, Kristianslund EK, Tveter AT, Østerås N. "Willingness, perceived facilitators and barriers to use remote care among healthcare professionals – a cross-sectional study." *BMC Health Serv Res. 2023 Nov 27;23(1):1307*.

Moseng T, et al. "EULAR recommendations for the non-pharmacological core management of hip and knee osteoarthritis: 2023 update" *Ann Rheum Dis. 2024 Jan 11:ard-2023-225041*.

Aim

The main aim of work package 5 is to determine the feasibility, efficacy, safety, user-satisfaction, and costeffectiveness of remote care.

Work package 6

Deciphering long-term outcomes

Leader
Till Uhlig, professor, MD, PhD

Co-leader
Sella Provan, professor, MD, PhD

Viewpoint

To merge and utilize granular data from a variety of sources, such as observational studies, databases and national registers is a main objective for studies that are developed by members of this research group. Established studies that provide information on different diagnoses and situations such as gout or rehabilitation are managed by group members and provide longitudinal data. Merging these studies with similar studies in other countries and linkage to data registers provide enriched data. One specific goal of these linkages is to provide information on less frequent manifestations of diseases or treatments, such as comorbidities and adverse events. Combining data from several studies enhances the statistical power to determine trends of disease outcomes.

The work package includes five studies that are primarily affiliated to REMEDY (NOR-DMARD, NOR-Gout, RehabNytte, SPACE, and NOECON). In NOR-DMARD we have continued to share data with Nordic and European registers and have also explored new opportunities to exploit our rich registry data in the GDPR-era. Three PhD students are currently working on NOR-DMARD data.

In RehabNytte, a PhD student examines worker productivity in response to rehabilitation in a national perspective and will also compare productivity and welfare benefit expenditure with a matched Norwegian population drawn from the National Welfare Agency (NAV) register.

The work package aspires to build up competence within health economy throughout and around REMEDY. We have employed an experienced health economist who will strengthen competence in health economy in our group and two master-students health-economic studies at the department of health-management and health economics at the University of Oslo are writing their thesis on data from this work-package. The group also works on data from the wider REMEDY group including NOR-ECON, performing health economic analyses in RCTs. In collaboration with professor Eline Aas, University of Oslo, we started to arrange a school in health economic analyses with participants from both Diakonhjemmet Hospital and partnering institutions in REMEDY. Increased competence in health economy will allow further evaluation and analysis in a number of research projects within the research center.

Highlights of the year

Registry linkage: Collaboration with both Nordic and European registers have resulted in new publications, including also data from the national vaccine register.

New findings: In the observational study on gout, work productivity, psychological beliefs and lifestyle factor have been linked to clinical outcome in gout such as achievement of the treatment target and disease flares. First results on work ability and rehabilitation are published from RehabNytte.

Completed study: The NOR-Gout trial has completed 5-year follow-up of 163 patients.

Employment: Our new health economist, postdoc Gunhild Hagen, was employed and will strengthen competence in the field of health economy in REMDEY.

Key publications

Skinnes M, et al. “Work ability Work ability in the year after rehabilitation – results from the RehabNytte cohort on fehalf of the RehabNytte Consortium.” *J Clin Med. 2023;12:7391*.

Uhlig T, et al. “Course and predictors of work productivity in gout – results from the NOR-Gout longitudinal 2-year treat-to-target study.” *Rheumatology (Oxford) 2023;62:3886-3892*.

Uhlig T, et al. “Lifestyle factors predict gout outcomes – results from the NOR-Gout longitudinal 2-year treat-to-target study.” *RMD Open 2023;9:e003600*.

Michelsen B, et al. “Differences and similarities between the EULAR/ASAS-EULAR and national recommendations for treatment of patients with psoriatic arthritis and axial spondyloarthritis across Europe” *RMD Open 2023;33:10070*.

Aim

The primary aim of work package 6 is to explore long-term efficacy, safety, and health-economic consequences of novel treatment alternatives through linkage of longitudinal registries.

Work package 7

Empowering the individual

Leader

Ingvild Kjeken, professor, occupational therapist, PhD

Co-leader

Anne Therese Tveter, professor, physiotherapist, PhD

Viewpoint

Empowerment and self-management is rooted in an understanding that the origins of good health are not necessarily the same as the origins of poor health. Effective health promoting interventions need to build on patients' strengths and resources and be adapted to their level of self-efficacy and health literacy, and their social, economic, and cultural context.

The REMEDY Patient advisory board is coordinated by and have their base in work package 7, and was established to ensure that patient research partners are involved in all new projects, from the initial phase when research questions are developed, to the implementation of results and interventions in clinical practice.

A total of 10 studies are primarily affiliated to this work package, among them four studies aiming to develop effective interventions for people with osteoarthritis, two studies focusing on improved quality and coordination in rehabilitation, and one exploring involvement of patients in the development and delivery of healthcare services. Development of innovative eHealth interventions such as apps and web-based programmes is a common focus across studies. With a steadily increasing immigrant population, we also have a particular focus on how to improve communication between immigrant patients with rheumatic diseases, health professionals and employees in the Norwegian Labour and Welfare Service, with the aim of improving treatment outcomes for these patient groups. Through these efforts, we build important expertise to meet future needs for flexible, sustainable, and cost-effective interventions.

Highlights of the year

Thesis completed: PhD student Helene Lindtvedt Valaas defended her thesis "Rehabilitation trajectories for individuals with rheumatic and musculoskeletal diseases. Goal attainment, adherence to self-management, and follow-up care".

New funding: The SPARK-study received funding from HSØ for a PhD-student.

Patient involvement in research: Arranged two courses for researchers and patient research partners.

Innovation: Recruitment of 382 participants in the Happy Hand randomized controlled trial was completed.

Key publications

Tveter, A. T., et al. "Is multimodal occupational therapy in addition to usual care cost-effective in people with thumb carpometacarpal osteoarthritis? A cost-utility analysis of a randomised controlled trial – PubMed (nih.gov)" *BMJ Open. 2023;13(6):e063103*.

Sagen, J., et al. "Patient engagement in the development and delivery of healthcare services: a systematic scoping review – PubMed (nih.gov)" *BMJ Open Qual. 2023;12(2)*.

Berdal, G., et al. "Bridging gaps across levels of care in rehabilitation of patients with rheumatic and musculoskeletal diseases: Results from a stepped-wedge cluster randomized controlled trial – PubMed (nih.gov)" *Clin Rehabil. 2023;37(9):1153-77*.

Aim

The primary aim of work package 7 is to empower patients and enhance their ability and self-efficacy to deal with medical, role and emotional management of their disease.

BACK TO CONTENTS

04
Other Activities

Clinical Trial Unit

Leader

Line M Jacobsen, PhD

Background in pain research and passionate about clinical studies and pharmacological interventions after having spent almost a decade in the global pharma industry.

Viewpoint

Clinical Trials Units (CTUs) are specialist units that provide expert methodological advice and coordination required to undertake successful clinical trials, both investigator-ini-tiated and industry-funded trials.

The establishment of the CTU as a separate unit at Diakonhjemmet Hospital was a major milestone in 2023 to secure research support for clinical trials. Specialized personnel with research and clinical trial experience have been recruited and onboarded, and the team now consists of a research advisor, research coordinators, statisticians, informaticians, study nurses and biobank personnel.

Ensuring well prepared procedures and necessary research infrastructure in place is key for the conduction of high quality clinical trials. One of the tasks of the CTU is to ensure that randomized clinical trials involving investigational medicinal products is per-formed in compliance with the EU Directive for Clinical Trials and International Conference on Harmonisation (ICH) good clinical practice (GCP). In 2023, major effort has been made by the CTU to secure our first trials to enter the new Clinical Trials Information System (CTIS) implemented by the European Medicines Agency (EMA) and receive approval from EMA.

Translational research is important for multiple trials in REMEDY. Developing biobank infrastructure fit for this purpose has been a focus area for CTU, substantial efforts have been made to ensure biobank- and research lab facilities at Diakonhjemmet will be optimized for research and remain relevant also for future research purposes.

High-level statistical knowledge is vital for the interpretation of clinical trials. CTU has throughout 2023 contributed to statistical design and analysis plans of multiple clinical trials in addition to structuring, managing and analyzing clinical data in various projects. Providing statistical guidance to researchers is another important contribution from CTU to further develop research capabilities in the hospital environment.

The CTU collaborates with the Regional Clinical Trial Unit of South-Eastern Norway Regional Health Authority, NorTrials, Inven2 and the NorCRIN network with regards to external monitoring, participation in industry-funded clinical trials and multiple network activities to increase knowledge and quality.

Highlights of the year

Organization: The Clinical Trial Unit was established as a separate unit at Diakonhjemmet Hospital.

Hiring processes: Highly specialized staff members with research and clinical trial experience have been recruited to the unit.

Biobank: Restructuring and planning of new biobank premises, research lab and technical solutions.

RECRUITMENTS IN 2023:

Julie Røkke Osen, MSc
Biobank Coordinator

Background in biochemistry and cell biology. Experience includes years in immunology research and biobanking of biological materials used for research.

Lene Maria Sundbakk, PhD, MSc
Research Statistician

Background in statistics and pharmacoepidemiology, and motivated by the opportunity to contribute to improving patient outcomes through rigorous statistical analysis.

Camilla Schanke Mørstad, MSc
Research Coordinator

Background as a research nurse working with a variety of clinical trials. Passionate about research support and quality assurance when working with clinical trials.

Heidi Sletten, MSc
Research Coordinator

Radiographer with master in biomedicine with a background in nuclear medicine including years with PET/CT experience. Highly motivated to contribute in clinical studies to help improve patient care.

Eli Sollerud, MSc
Research Coordinator and Clinical Dietitian

Background includes research on nutrition and metabolism in cancer, and clinical practice in overweight and obesity, cancer and gastro. Interested in preventive medicine and lifestyle changes.

Line Gaundal, PhD, MSc
Research Coordinator

Background includes research on diet, microbiota and metabolic regulation. Motivated by clinical research leading to health improvements.

Aim

To provide the support necessary to design, conduct, analyze and publish clinical trials in an efficient manner.

The National Clinical Consortium

Leader rheumatology

Marte Schrumpf Heiberg, senior researcher, MD, PhD

Leader rehabilitation

Rikke Helene Moe, senior researcher, physiotherapist, PhD

Viewpoint

Over the past years, cross-regional collaboration within rheumatic and musculoskeletal disease research has been strengthened. With REMEDY, the national collaboration has been extended and formalized by the establishment of a national clinical consortium. All rheumatology hospital departments as well as rheumatologists in private practice and several rehabilitation institutions are represented in the consortium. The infrastructure of REMEDY is available for the consortium members.

Our digital communication platform (Induct.net), enables consortium members to identify potential research partners, exchange project ideas and share information about future and ongoing research, meetings, and webinars.

The “Green congress” was arranged in Oslo on the 16th of June, reviewing the latest news within international rheumatic and musculoskeletal disease research. This annual congress has a green profile and a strong focus on climate and sustainability. The Green congress in 2023 was a great success with more than 430 on-site and virtual attendees.

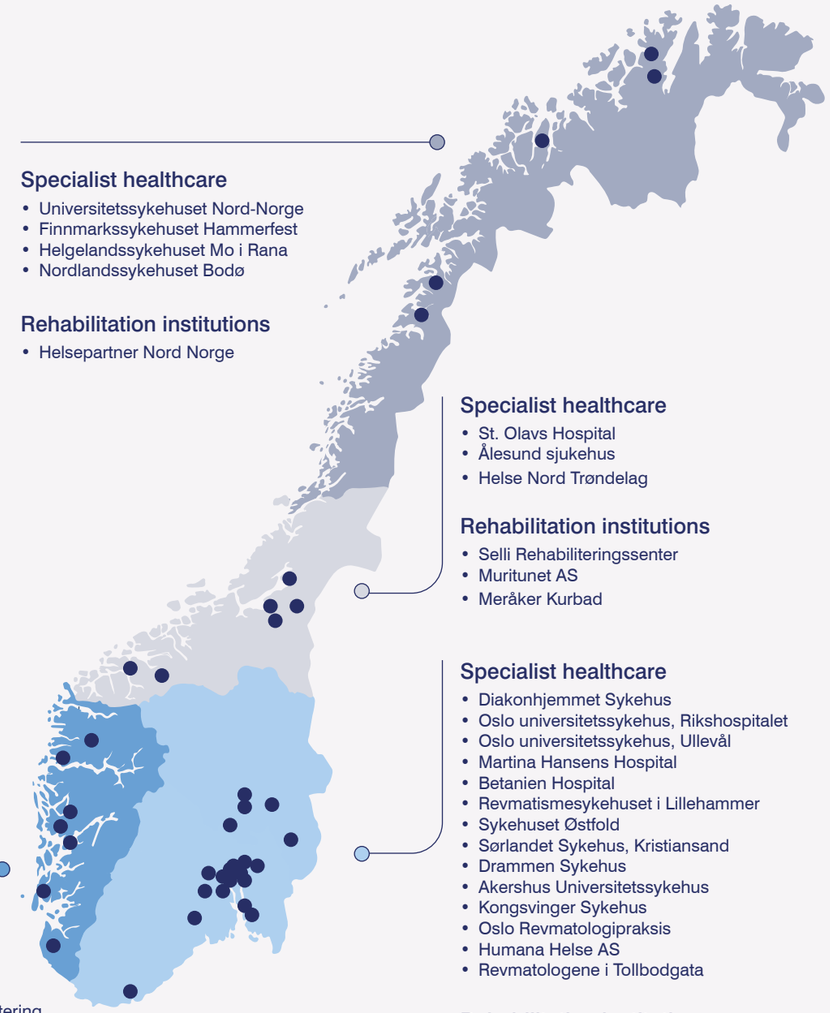
A digital consortium meeting was held on the 30th of November. The newly established clinical trial unit was presented as well as new research projects, inviting consortium members to participate in planned multicenter studies.

Aim

The aim of the National clinical consortium is to promote and facilitate national multicenter trials, thereby securing equal opportunities for healthcare providers and patients in Norway to participate in clinical trials.

Highlights of the year

- Green congress was arranged 16th of June.
- Thet annual meeting in the the National Clinical Consortium was held the 30th of November.
- Results from several multi-centre clinical trials conducted within the National Clinical Consortium was presented at major congresses, along with publications in major medical journals (NOR-DRUM, ARCTIC REWIND, NORD-STAR).



Young Researcher Program

Leader

Karen Minde Fagerli, Postdoc, MD PhD

Co-leader

Alexander Mathiessen, Postdoc, MD PhD

Co-leader

Tuva Moseng Postdoc, PT PhD

Viewpoint

REMEDY has launched an ambitious career development and training program targeting early career researchers. In March of 2023, the first seminar of the program was successfully arranged with 60 participants. The seminar included sessions on mentorship, collaborative research, and foreign exchange by guest professor Daniel H. Solomon and senior REMEDY researchers. These sessions provided insights into the latest research methodologies and fostered a collaborative environment, encouraging participants to engage in interdisciplinary dialogues and network building.

We have introduced a novel mentoring program for early-career researchers. In this initiative, three candidates were selected through an application process and carefully paired with external mentors. These mentors are distinguished academics, outside the candidate's collaborative sphere, but with expertise highly relevant to their work. This pairing does not only facilitate personalized guidance and support but also provides the researchers with a unique opportunity to benefit from the mentors' extensive professional network and experience.

Aim

To provide excellent training and support for early career researchers within REMEDY.

Our commitment to fund young researchers at critical stages of their careers continues. Following our October 2023 call for proposals, we awarded three research projects with grants of 167.000 NOK each. This funding is aimed at fostering innovative and impactful research that can contribute significantly to their respective fields.

Furthermore, we have also seen the success of recipients of the 2022 research grants, including new funding secured for a large study on juvenile idiopathic arthritis. Their success confirms that our initiatives are not only advancing scientific exploration but also contributes to the development of the next generation of research leaders.

GRANT RECIPIENTS

Marthe Mæhlen

Awarded a grant for research into the effects of a specific immunosuppressant treatment on interstitial lung disease in myositis patients. Interstitial lung disease is a severe complication of myositis, but not well studied due to the rarity of the disease. The grant will support the candidate for three months to finalize the data collection and pursue further postdoctoral funding.

Fatima Heineke

Received funding for her innovative approach to understanding rheumatoid arthritis. The research aims to enhance the understanding of the complex molecular dynamics the disease and involves cutting-edge genetic analysis of single immune cells, comparing active disease flare-ups with remission periods and healthy individuals. The grant will cover the costs of this novel analysis method.

Eirik Ikdahl

Grant awarded to initiate a project exploring the value of ultrasound to detect interstitial lung disease in patients with rheumatoid arthritis. This serious complication is currently assessed by CT-scanning, and ultrasound assessment would allow for easier, safer and less costly screening. The funding will cover ultrasound equipment as well as CT examinations for patients in the initiation of the project.

International collaboration

REMEDY is involved in numerous large international collaborations. A few central projects are highlighted in the next paragraphs.

Senior researcher Rikke H. Moe presenting at the TRACTION workshop.

The TRACTION consortium

The TRACTION project (Trials foR heAlth Care inTerventIONs) was established in September 2022, and in 2023 a website was launched. This network aims to facilitate specialization training, providing educational materials and mentoring regarding non-pharmacological clinical trials. REMEDY is an active partner, and participated actively in the first workshop in Lisbon on May 25th and 26th 2023.

SQUEEZE

The SQUEEZE project has received funding from the European Union's Horizon Europe research and innovation programme. The project addresses the identified unmet needs in three areas of clinical relevance in rheumatoid arthritis treatment: (a) lack of guidance on choosing the right drug; (b) insufficient dose or route while on a specific drug; and (c) lack of a care setting and digital support tools that allow full exploitation of drug benefits.

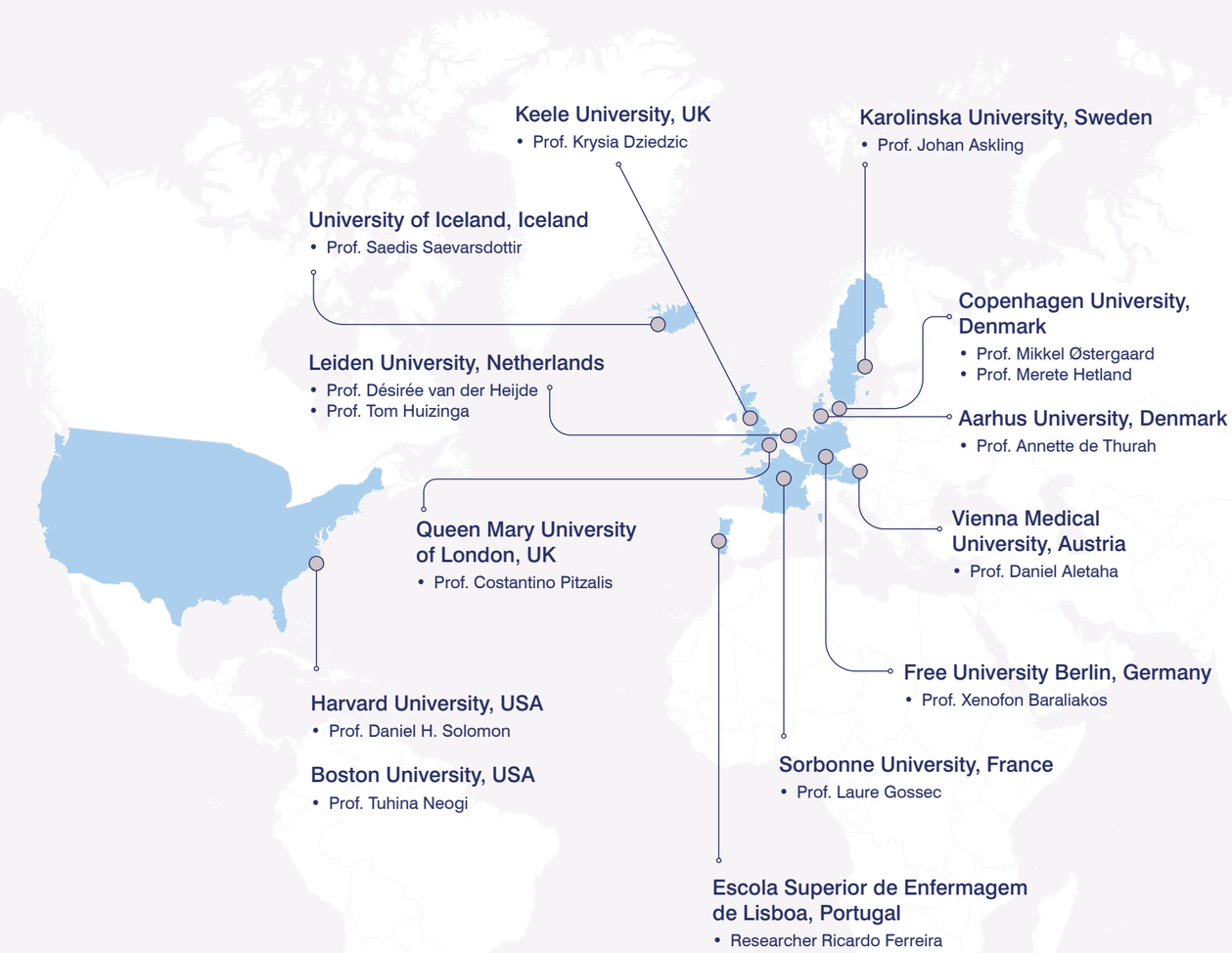
The overall conceptual approach of SQUEEZE is underpinned by a complementary methodological approach utilizing large-scale data analysis and clinical trials to predict patients likely to respond to drugs. This include translational studies and technologies to validate innovative biomarker platforms, and embracing behavioral studies including design thinking to fuel real-life translation. REMEDY is an active partner in SQUEEZE, and participate in all clinical trials within the project, as well as a number of other inititiatives.

ScandRA

ScandRA is European Research Area PerMed partnership that builds on previous successful international collaborations between academia, health care, patients, industry and SMEs in biomarker technologies, data interoperability and e-health. In the Scandinavian countries, the partners (including REMEDY) have collected enormous amounts of information on patients with rheumatoid arthritis in multiple longitudinal prospective registers and biobanks. ScandRA has unique cohorts with detailed clinical data on rheumatoid arthritis disease activity, treatment, and life-style, in combination with novel genomic- and biomarker-data from blood samples from the same cohorts, and to facilitate the emergent results into clinical practice.

Main international collaborators

The main international collaborators in the map below represent major institutions across the globe that significantly strengthen the research conducted in the REMEDY center:



Visiting professors at REMEDY

In 2023, REMEDY officially appointed two visiting professors, both internationally leading scientists. Professor Daniel H. Solomon and professor Désirée van der Heijde are formally engaged by the Institute of Clinical Medicine at the University of Oslo. Having such international capacities as part of our environment offers unique opportunities to discuss new projects and results. We have collaborated with Daniel H. Solomon and Désirée van der Heijde for many years and are pleased that these collaborations are now being further developed.

Professor Désirée van der Heijde

Désirée van der Heijde, MD, PhD, is a Professor of Rheumatology, in particular outcome research in rheumatic diseases, at Leiden University Medical Center.

Her major research interest is in the methodology of outcomes assessment and its application in clinical research. Specific areas of interest are radiographic scoring methods in rheumatoid arthritis, psoriatic arthritis, and spondyloarthritis, as well as scoring of magnetic resonance imaging in spondyloarthritis. She has developed several disease activity and other outcome measures. Prof. van der Heijde has received several prizes and honourable appointments, and she has published more than 1050 papers in the international literature, as well as multiple chapters in leading rheumatology textbooks. She is associate editor of the Annals of Rheumatic Diseases and member of the editorial board of RMD Open and the Journal of Rheumatology.

Professor Daniel H. Solomon

Daniel H. Solomon, MD, MPH, is a Professor of Medicine at Harvard Medical School and holds the Matthew H. Liang Distinguished Chair in Arthritis and Population Health at the Brigham and Women's Hospital in Boston, MA, USA.

Prof. Solomon has published over 450 original articles and over 100 editorials and book chapters. His articles have been cited over 100,000 times. He has been continuously funded for over 25 years on numerous NIH, foundation, and industry-supported grants.

He is the current Editor in Chief of Arthritis & Rheumatology, the premier rheumatology journal in the United States.

He is the Principal Investigator of numerous studies, as well as a project that aims to improve clinical research in rheumatology. He has mentored over 40 trainees and been recognized with mentoring awards from the American College of Rheumatology, Harvard Medical School and Brigham and Women's Hospital.

FACTS

The Visiting Professor Program

The Visiting Professor Program at the Faculty of Medicine, University of Oslo, ensures that internationally leading foreign academics stay at the faculty for 1–2 years. The stay can be for a single period or multiple shorter periods. Visiting professors are expected to contribute academically, intellectually, and culturally to the academic communities. The visiting professor is engaged for one year, and if successful, further engagement is offered for one more year.

Implementation

Leader

Per Olav Vandvik, Professor, MD PhD

Co-leader

Leticia Kawano-Dourado, Senior researcher, MD PhD

Co-leader

Eirik Klami Kristianslund, Postdoc researcher, MD PhD

Aim

To translate new research findings to clinical practice through BMJ Rapid Recommendations, including adaption for national use and implementation.

Furthermore, we see the current BMJ Rapid Recommendation as an opportunity to provide a global audience with trustworthy, accessible, and timely recommendations within the field of personalized medicine.

Viewpoint

REMEDY is dedicated to contributing to the implementation of the findings from our clinical research program. Partners Diakonhjemmet Hospital, Norwegian Rheumatism Association and MAGIC develop treatment recommendations originating from the high-quality clinical trials of the research center, in collaboration with the BMJ. A total of four BMJ Rapid Recommendations are planned, using advanced standards and methods to create trustworthy guidelines. These recommendations are triggered by potential practice-changing results from randomized controlled trials. Further implementation in Norwegian clinical practice guidelines will be ensured with a collaboration with the Norwegian Society of Rheumatology.

The development of the first REMEDY BMJ Rapid Recommendation, guiding proactive therapeutic drug monitoring of biologic drugs in inflammatory diseases, was initiated in 2022, triggered by two randomized controlled trials (NOR-DRUM A and B) originating from Diakonhjemmet Hospital and published in the medical journal JAMA in 2021. This guideline process was completed at the end of 2023, and results will be published in 2024, hopefully contributing to implementation of a personalized medicine approach to treatment with biologic drugs.

REMEDY researchers have had key roles in the development of the recommendations of EULAR, the European rheumatology associations, for the treatment of hip and knee osteoarthritis, an effort which reached the head pages of Norway's largest newspaper in addition to the impact it will have among clinicians treating these patients.

We have also contributed to other recommendations from EULAR, such as the 2023 the recommendations on management of rheumatoid arthritis. On the national arena, we have been active involved in a range of national recommendations from the Norwegian Society of Rheumatology, including management of psoriatic arthritis and recommendations on vaccination, follow-up of medication and COVID-19 and rheumatic disease.

Work package 5 of REMEDY focuses on the remote care of rheumatic and musculoskeletal diseases, in effect testing ways to implement treatment follow-up. Several projects involve digitally implementing treatment approaches already established in clinical practice with traditional patient follow-up. One example is the ReMonit Gout study, which investigates remote follow-up of urate-lowering treatment of gout. The approach that is digitally implemented in this study has already been tested in a previous study from our group – NOR-GOUT – and is in use in the clinic at Diakonhjemmet.

In preparation for the implementation of clinical research, it is necessary to identify relevant barriers and facilitators for the introduction of the new measure. In 2023, REMEDY has contributed to research on barriers and facilitators for the introduction of two key interventions from our research – remote follow-up and therapeutic drug monitoring.

The future of research implementation may include evidence-based decision support integrated in digital patient system, including the electronic health records. This is an aim of MAGIC. REMEDY also works with external partners moving towards this aim. A new project involves SINTEF and commercial partner DiaGraphIT with a goal of implementing AI-powered decision support in clinical data systems, such as DiaGraphIT's GoTreatIt, which is used for follow-up of patients in most rheumatology departments in Norway.

The digital and trusthworty Evidence Ecosystem

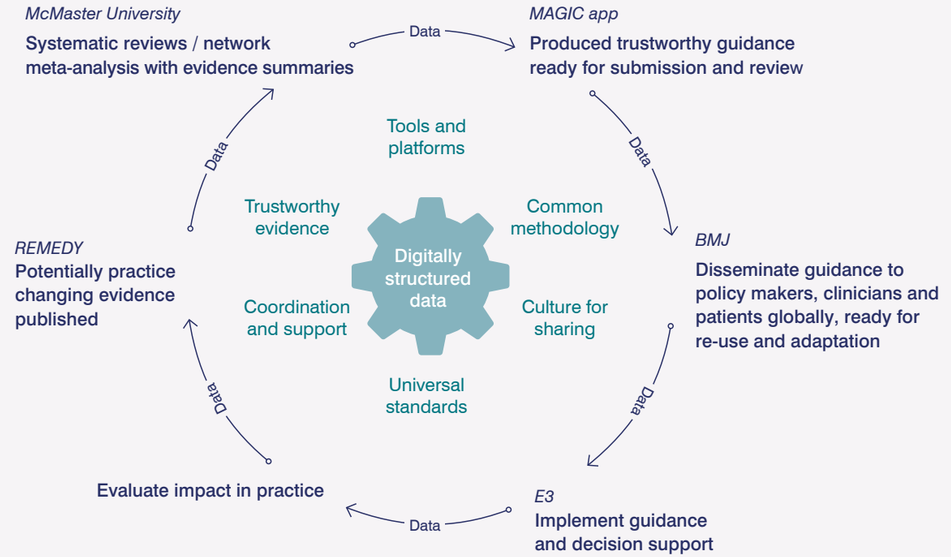


Figure 1: *The figure illustrates the Digital and Trustworthy Evidence Ecosystem, where the ultimate goal is to increase value and reduce waste in healthcare and research by facilitating the flow (arrows) from producing, synthesizing, disseminating and implementing evidence into practice.*

Highlights of the year

- The REMEDY BMJ Rapid Recommendation on TDM of biologic drugs for inflammatory diseases completed four panel meetings and agreed on a recommendation
- REMEDY researchers first and last author of EULAR's recommendations for management of hip and knee osteoarthritis
- MAGIC's E3 project connected to REMEDY – will study the implementation of the first REMEDY RapidRec

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05
Research projects

Overview of research projects

The REMEDY project portefolio represents the broad approach to assessment of rheumatic and musculoskeletal disease treatment. More information about the specific projects can be found at remedy-senter.no

INTRODUCTION CENTER HIGLIGHTS WORK PACKAGES OTHER ACTIVITIES RESEARCH PROJECTS OUTREACH AND PUBLICATIONS

ALERT

Health literacy in immigrants with inflammatory joint disease

A qualitative study exploring health literacy in immigrants with inflammatory joint disease

ARCTIC

Remission in patients with rheumatoid arthritis

A randomized controlled trial investigating the use of ultrasound in clinical follow-up

ARCTIC FORWARD

10-year follow-up of patients with rheumatoid arthritis receiving early treat-to-target treatment

The project aims to explore the long-term consequences of current recommended treatment

ARCTIC REWIND

Treatment strategies in rheumatoid arthritis after achieving long-term disease control

A randomized controlled trial comparing tapering /discontinuation of disease-modifying drugs to stable treatment

BackToBasic

Infliximab in chronic low back pain and modic changes

A multicenter, randomized, double-blind, placebo-controlled trial assessing the efficacy of intravenous infusions of TNF-inhibitors

BIKE

Biopsies of synovitis from the knee joint of RA or OA patients

A study aiming to establish good methods for ultrasound-guided biopsies of synovitis in joints

BioTest

Experimental precision medicine

Observational study investigating whether biopsies from joints can help predict who will benefit from which treatment

BRIDGE

Continuity and quality in the rehabilitation of patients with musculoskeletal diseases

A multicenter randomized controlled trial to improve continuity and quality in rehabilitation of people with rheumatic and musculoskeletal diseases

Care pathway

Development of a treatment pathway for patients with hand osteoarthritis

A randomized controlled trial and a qualitative study assessing the effect and experience with task shifting in hand osteoarthritis

DietStudy

Effect of brief versus individually tailored dietary advice

A randomized controlled trial in patients with inflammatory joint disease

DigiOA

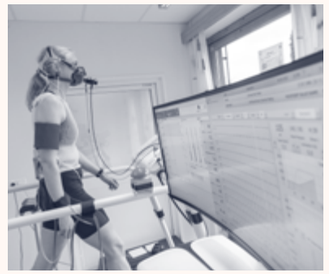
Digital osteoarthritis treatment

A randomized controlled trial comparing an exercise program provided through an app with regular follow-up with a physiotherapist in patients with hip or knee osteoarthritis

EULAR rec hip knee OA

EULAR recommendations for treatment of hip and knee osteoarthritis

A EULAR task force aiming to update of the EULAR recommendations for non-pharmacological core management of hip and knee osteoarthritis



ExeHeart

Improved Cardiovascular Health for Patients with Inflammatory Joint Disease

A randomized controlled trial investigateing whether 12-week high-intensity training improve cardiovascular health and provide better risk factor control than current practice

Happy Hands

An app for digital self-management of hand osteoarthritis

A multicenter randomized controlled trial assessing the effecacy, cost-effectiveness and experiences with use of the Happy Hands app

HIFSAT

Hip fracture surgical approach trial

A randomized controlled trial comparing two different surgical procedures in patients with hip fracture

Hip fracture database

Diakonhjemmet hip fracture database

A database with over 7000 hip fracture patients collected since 2006

MERINO

Methotrexate in the treatment of erosive hand osteoarthritis

Randomized controlled trial on the efficacy of methotrexate on pain in people with hand osteoarthritis

MethMax

Maximixing treatment effect

A clinical trial assessing if providing methotrexate subcutaneously is more effective than tablets in patients with rheumatoid arthritis

MOVE-JIA

Best management of juvenile ideopathic arthritis

Randomized controlled trial assessing optimal management of patients with juvenile idiopathic arthritis

MyJIA

Strategies towards personalised treatment in juvenile ideopathic arthritis (JIA)

A multicenter randomized controlled trial investigating different treatments in patients with juvenile ideopathic arthritis

NCR

The Norwegian Cardio-Rheuma register

A register on the incidence, prevalence and mortality of cardiovascular disease in patients with inflammatory joint disease

NOECON

Health economics in the treatment of patients with inflammatory joint disease

A register study assessing the health economics of treat-to-target treatment in patients with inflammatory joint disease

NOR-CACTUS

Comparison of treatment strategies for carpal tunnel syndrom

A multicenter randomized controlled trial comparing injection treatment and surgery in patients with carpal tunnel syndrom

NOR-DMARD

The Norwegian Antirheumatic Drug Register

An observational study of patients with inflammatory joint disease treated with biological drugs in clinical practice

NOR-DRUM

The Norwegian therapeutic drug monitoring study

A randomized controlled trial investigating the effectiveness of therapeutic drug monitoring in achieving remission in patients receiving infliximab treatment

NORD-STAR

The Nordic rheumatic disease strategy trials and registries study

A multicenter randomized trial in the Nordic countries investigating the effect of active conventional treatment compared three different biologic drugs in early rheumatoid arthritis

NOR-Flare

Remote monitoring of patients with rheumatoid arthritis

A randomized controlled trial comparing remote monitoring to standard follow-up at the hospital in patients with rheumatoid arthritis

NOR-Gout

Gout in Norway

A cohort study investigating outcomes after intensive treatment with the objective to lower serum urate in gout patients

Nor-Hand

Longitudinal observational study of people with hand osteoarthritis

An observational study of people with hand osteoarthritis aiming for increased understanding of pain

NOR-SPRINT

Follow-up of newly diagnosed patients with psoriatic arthritis with and without imaging

A randomized controlled trial assessing whether structured imaging contributes to significantly improved disease control in patients with psoriatic arthritis

Nor-vaC

Immunological response to COVID-19 vaccine in patients on immunosuppressive therapy

A large cohort study ealuating the immunological response to COVID-19 vaccines in people on immunosuppressive treatment due to chronic gastrointestial or inflammatory joint disease

PICASSO

Painful inflammatory carpometacarpal-1 osteoarthritis treatment with intraarticular steroids, saline or occupational therapy

A three-armed randomized controlled trial assessing the effect of cortisone injections, saline injections and non-pharmacological treatment

OA-AID

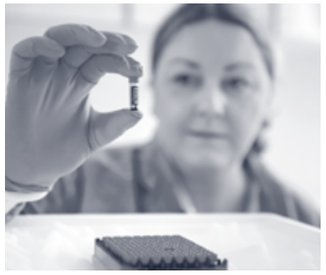
Decision aids and remote monitoring to support shared decision-making

A randomized controlled trial evaluating a self-management app to increase knowledge and facilitate shared decision making in patients with knee osteoarthritis

QI-HOA

Quality indicators for hand osteoarthritis

Development and testing of a questionnaire to assess patient-reported quality of hand OA care



RA-DRUM

Therapeutic drug monitoring in RA

A clinical trial assessing whether therapeutic drug monitoring improves efficacy of biological treatment in RA

RehabNytte

Specialised rehabilitation in patients with musculoskeletal diseases

A longitudinal multicenter study aiming at better and more efficient rehabilitation services

ReMonit

Follow-up of patients with spondyloarthritis

A randomized controlled trial comparing two new remote follow-up strategies with standard follow-up at the hospital

ReMonit Gout

Remote monitoring and self-management of gout

A randomized controlled trial investigating a self-management app for patients with gout starting medical treatment to lower their serum uric acid level

RemoteUX

User experience with remote monitoring for patients with inflammatory joint diseases

A qualitative study assessing patients' and health professionals' experiences with remote care from the ReMonit trial and the NOR-Flare trial

RIMRA

Rheumatic immune-related adverse events in patients treated with immunotherapy

A study aiming to describe the clinical presentation and disease course of rheumatic immune-related adverse events in patients treated with immunotherapy

SPACE

Spondyloarthritis caught early

A study examining outcomes of spondylarthritis from early disease onset

SPARK

Spondyloarthritis kondis

Development and evaluation of a personalised digital exercise intervention in patients with spondyloarthritis in a randomized controlled trial

SQUEEZE

Maximising impact of prescription drugs in rheumatoid arthritis

A large European consortium comprising several projects addressing different approaches to rheumatoid arthrtitis treatment

START

Stratification of acute inflammatory arthritis

An observational study of patients with new-onset arthritis with the aim of identifying markers for rapid diagnosis and personalised treatment

SURF-PsA

Survey of risk factors in spondyloarthritis

Survey of cardiovascular disease and risk factor management in patients with spondyloarthritis across world regions

Tankegods

Understanding and coping with chronic illness

A study aiming at increased knowledge and improved communication among patients and health professionals

ULRABIT

Longitudinal ultrasound study of patients with rheumatoid arthritis

An observational clinical study including patients initiating biologic DMARD treatment

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06

Outreach and publications

Public outreach

97
Scientific publications

3
Master theses

3
PhD theses

62
Public communication

140
Conference proceedings

68
Mass media total

January

DAGENS MEDISIN, FRONT PAGE

Adults with juvenile arthritis benefit significantly from medications

Dagens Medisin highlighted a significant study by Imane Bardan. This research demonstrates that adults with juvenile arthritis experience substantial benefits from medications commonly used to treat rheumatoid arthritis.

January

VG, FRONT PAGE

How elite athletes alleviate rheumatic pain through training

Three elite athletes, including wrestler Felix Baldauf and skier Sjur Røthe, revealed their rheumatic pain management involving medication and high-intensity interval training (HIIT). This approach, also effective for soccer star Sigurd Rosted, aligns with professor Hanne Dagfinrud's research, demonstrating that HIIT reduces disease activity, pain, and fatigue in ankylosing spondylitis patients, while improving cardiovascular health.

February

VG, FRONT PAGE

Two out of three will become symptom-free

Professor Espen A. Haavardsholm on rheumatoid arthritis treatment: Two out of three could reach remission and become symptom-free. Early diagnosis and proper treatment mean that the majority of those diagnosed with rheumatoid arthritis today may reach this treatment goal, with no signs and symptoms of active disease. However, failure to adequately treat the condition not only damages the joints, but also increases the risk of serious comorbidities.

March

VG, FRONT PAGE

How your weight can influence osteoarthritis

The link between obesity and knee osteoarthritis has previously been established, and research finds that excess body fat also plays a role in arthritis in other joints. A recent Norwegian study highlights a connection between hand osteoarthritis and the level of pain experienced. Professor Nina Østerås, Senior researcher Ida K. Bos-Haugen, and dietician Sissel Urke Olsen are cited.

April

DAGENS MEDISIN

Some patients may manage without medication

The team behind Norway's ARCTIC REWIND study reports promising results for rheumatoid arthritis patients. Physician and researcher Siri Lillegraven notes, "The findings indicate that patients in prolonged remission could potentially cease medication." The ARCTIC REWIND study is a randomized, multicenter trial on reducing disease-modifying drugs in arthritis patients.

October

DAGBLADET

New medication for backaches

Bimekizumab (Bimzelx) was approved for adults with axial spondyloarthritis and ankylosing spondylitis who haven't benefited from other treatments. Administered monthly by specialists, this biologic drug shows promise in studies. Rheumatologist Inger Jorid Berg highlights its value in expanding treatment options.

October

DAGBLADET , FRONT PAGE

How to receive the right treatment for gout

Gout typically begins with a painful big toe and leads to attacks with joint pain. Affecting around 10% of men over 70-75, it's often undertreated. Both genders can develop gout, but men are more prone. Proper treatment is essential to prevent complications like crystal build up in joints and chronic dysfunction, notes professor, Till Uhlig, an internationally renowned expert in this disease.

October

VG, FRONT PAGE

A rescue for people with rheumatism

Physiotherapist Kristine Røren Nordén, working on her PhD within the ExeHeart study. This study investigates how physical fitness affects cardiovascular disease risk in patients with inflammatory joint diseases, considering factors like inflammation, high blood pressure, and cholesterol.

October

DAGBLADET

New treatment for hand osteoarthritis

Physician and researcher Ida Kristin Bos-Haugen shares insights on the PICASSO study, which explores various treatment methods, and the MERINO study, aimed at evaluating whether methotrexate can alleviate pain, improve joint function, and limit joint damage in hand osteoarthritis. Initial recommendations for hand osteoarthritis include exercise and other aids to enhance function and relieve symptoms.

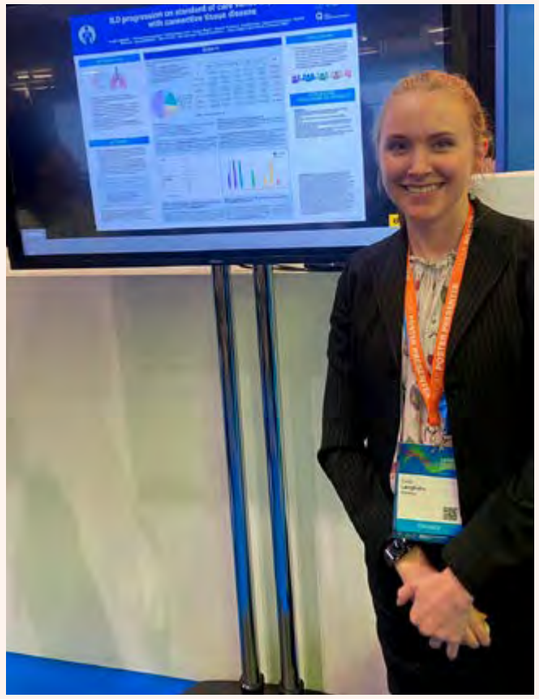
Posters and presentations

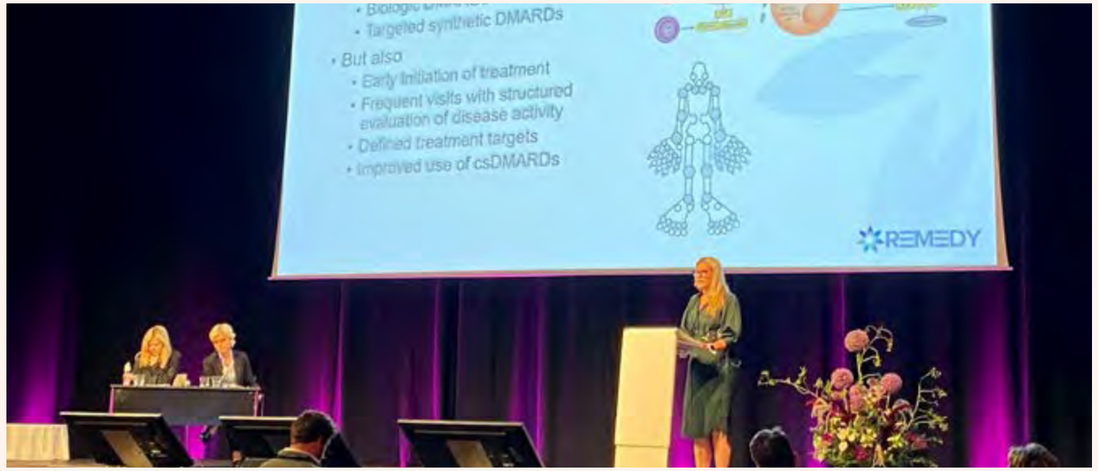
MUSS

The national research conference on musculoskeletal health (MUSS) was held at Gardermoen, Norway, from 16th to 17th of November 2023. This is an interdisciplinary conference that covers research related to musculoskeletal health and serves as a meeting point for researchers, healthcare professionals and user representatives.

EULAR

The European Congress of Rheumatology (EULAR) was held in Milan, Italy, from 31st of May to 3rd of June 2023. 12719 delegates attended the congress either “on-site” or virtually. REMEDY was highly present at the congress with more than 30 oral presentations and posters.



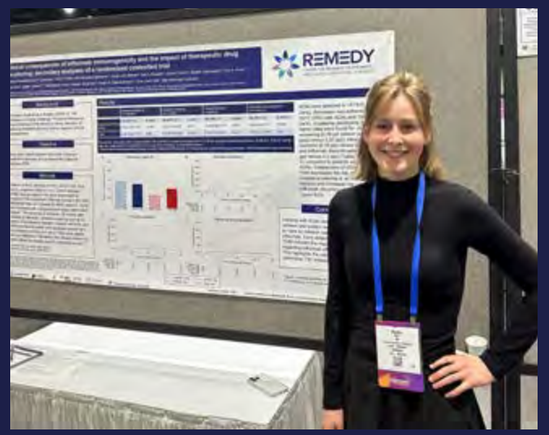


SCR

The 39th Scandinavian Congress of Rheumatology (SCR) was held in Copenhagen, Denmark, from 23rd to 26th of August 2023. The congress is an inspiring event, where clinicians and scientists can exchange knowledge, experience, and ideas to promote collaboration.

ACR

The American College of Rheumatology (ACR) Convergence 2023 was held in San Diego, USA, from 10th to 15th of November 2023. The congress gathered 9000 international delegates “on-site” while 4300 attended virtually.



Publications:

A

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