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VIEWPOINT

Levelling the playing field of RMD research across Europe to address patients' needs: the emerging EULAR Research Centre

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ABSTRACT

Herein, we describe the Research Centre launched by the European Alliance of Associations for Rheumatology (EULAR) in 2020. The Centre aims to facilitate collaborative research on rheumatic and musculoskeletal diseases (RMD) across Europe. RMDs disable millions of people in Europe and worldwide. Despite progress with improved therapeutics and strategic interventions in several RMDs, there are no cures, and their collective impact remains substantial. Access to RMD-related care, policies prioritizing RMDs, and related research, education, training, and funding differ significantly across European countries. Building a new equipoise in opportunity and capacity across Europe will facilitate optimal understanding of those different factors that influence the epidemiology, pathogenesis, treatment, and outcomes in RMDs. The EULAR Research Centre aims to address the significant barriers to accelerating RMD research across Europe. It provides an RMD research roadmap of unmet needs, expert services, infrastructures, networks, research resources, training, education, and mentoring. It will place RMD research in the ideal position to benefit from forthcoming remarkable advances in digital, biological, and social science anticipated in the coming decades.

CRITICAL NEED TO IMPROVE RHEUMATIC AND MUSCULOSKELETAL DISEASE (RMD) RESEARCH CAPACITY IN EUROPE

RMDs disable millions of people in Europe and worldwide.^{1–3} These debilitating conditions limit the individual, leading to inability to work and enjoy optimal quality of life, significant healthcare expenditures and related societal costs.³ Despite progress in the last two decades with improved therapeutics in several RMDs, there are no cures, and their collective impact remains substantial.

Access to RMD-related care, policies prioritising RMDs and related research, education/training, and funding differ between European countries.^{4–5} For example, Hungary, the Czech Republic, Poland and Bulgaria

have experienced a significant delay in the development of RMD research.^{4–8} A review of scientific congress abstracts submitted to the EULAR between 2012 and 2016 supported these findings. The data demonstrated underrepresentation (<5%), particularly of central European countries such as Croatia, the Czech Republic, Hungary, Poland, Slovakia and Slovenia.⁴ We conducted another review of the last 500 RMD-related articles indexed in PubMed and published by authors in European countries between 21 April 2022 and the previous 1 year. The data showed that the majority of the articles (67.1%) were associated with at least one author from a high-income European country (figure 1). The same search undertaken for the pre-pandemic year of 2019, which served as a control, showed a similar trend (figure 1). (The search strategy is described in online supplemental material 1.) A similar trend has been reported on a global scale: an overwhelming majority of scientific articles in rheumatology has been published by authors from high-income countries worldwide.^{9–10} Additionally, a gender gap for senior authorship positions in rheumatology research articles has been shown, particularly in articles reporting randomised controlled trials and those initiated by industry.¹¹ These discrepancies underscore the need to expand RMD research capacity and inclusivity across Europe.

Only by levelling the playing field of RMD research across European countries will we optimally understand how different factors (eg, geographical regions, environments, health system disparities; and racial, ethnic and genetic backgrounds) influence the epidemiology and outcomes of RMDs. Achieving equity in research will allow us to identify and develop investigators across the



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Year	GDP per capita > 30,000 EUR	GDP per capita 30,000 - 15,000 EUR	GDP per capita < 15,000 EUR
2022	444/662 (67.1%)	151/662 (22.8%)	67/662 (10.1%)
2019	604/1078 (56.0%)	322/1078 (29.9%)	152/1078 (14.1%)

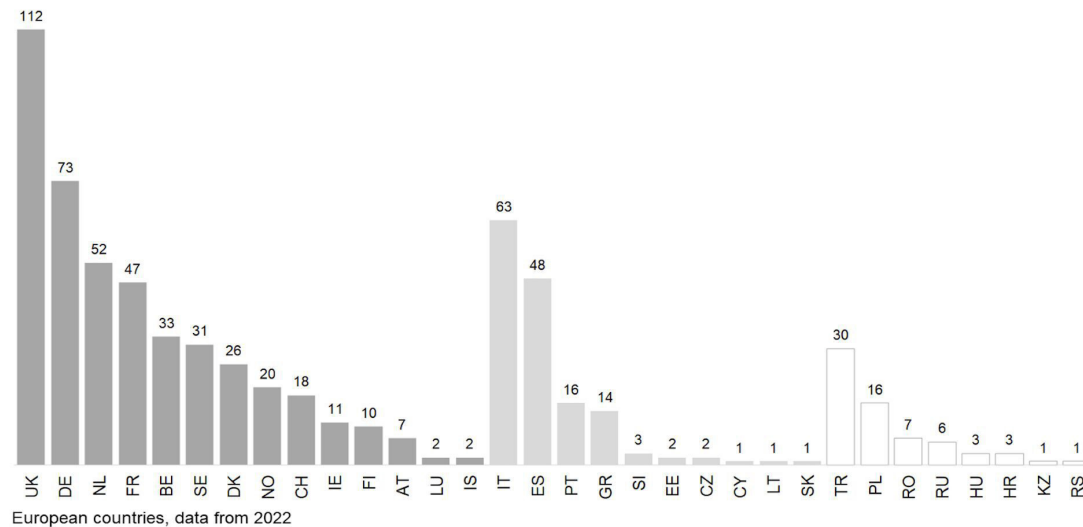


Figure 1 Number of times an RMD-related article was associated with at least one author from a European country. Countries were grouped based on their GDP per capita data from 2020.⁵¹ Data were indexed in PubMed and published in 2022 (analysis group, n=500) and 2019 (control, n=500). For each year, the last 500 papers were analysed, not normalised. GDP, gross domestic product.

continent and maximise opportunities, particularly for early-career investigators. EULAR proposes that equity in RMD research can best be achieved when qualified research teams are based throughout Europe, when they can codevelop research agendas and ideas and access a large portfolio of human and infrastructural resources to address RMD research questions.

EMERGING EULAR RESEARCH CENTRE

In 2019 and 2020, EULAR convened a series of meetings to identify barriers to high-quality, collaborative RMD research across Europe and beyond, recognising the global nature of impactful discovery and clinical research. The workshops brought together basic, translational and clinical research scientists, epidemiologists, public health researchers, presidents of EULAR's Scientific Member Societies for Rheumatology, RMD patient representatives and health professionals. More than 70 participants explored opportunities for research capacity building. Several key themes emerged from the sessions, including the need for improving the quality of RMD research to enhance patient health outcomes; clinical trial support; networking, integration and exchange of information; data and analytical services, capacity building for early-career scientists, equity of access to research across Europe; and optimising funding opportunities and success rates for RMD research, among others.

As a result, in 2020, EULAR launched its Research Centre¹² to facilitate collaborative basic and translational, clinical, epidemiology and public health research across Europe and worldwide to improve the lives of people with RMDs. Similar research capacity-building efforts have been reported in other fields, such as the Cancer

Core Europe,¹³ European Organisation for Research and Treatment of Cancer,¹⁴ European Union (EU)–Canada Joint Infrastructure for Next-Generation Multi-Study Heart Research,¹⁵ Facilitating European Clinical Research project,¹⁶ Innovative Medicines Initiative,¹⁷ European Grid Infrastructure project¹⁸ and the Educational Research Capacity Building in the EU.¹⁹ Yet, no such pan-European effort has focused on fostering RMD research.

The EULAR Research Centre aims to provide an RMD research roadmap of unmet needs, expert services, infrastructures and networks, enabling research resources, training, education and mentoring (figure 2) to foster high-quality, interdisciplinary RMD research among researchers in EULAR-affiliated countries.

Research expert consultations

One early feature of the EULAR Research Centre is the Research Consultation Service (figure 2). It matches RMD investigators with research experts across various areas, for example, study design, data analysis planning and execution, patient involvement, reporting of research findings and EU grant writing. Not all junior and mid-level faculty members have access to peer or senior researchers who have the expertise to advise them on aspects of grant writing, planning specific projects and career decisions. The service addresses this gap. Previous reports have described consultation services as successful tools to support different types of research, for example, community-based research²⁰ and special populations research.²¹

The Consultation Service was piloted in November 2020 and—throughout the pilot period—is available at

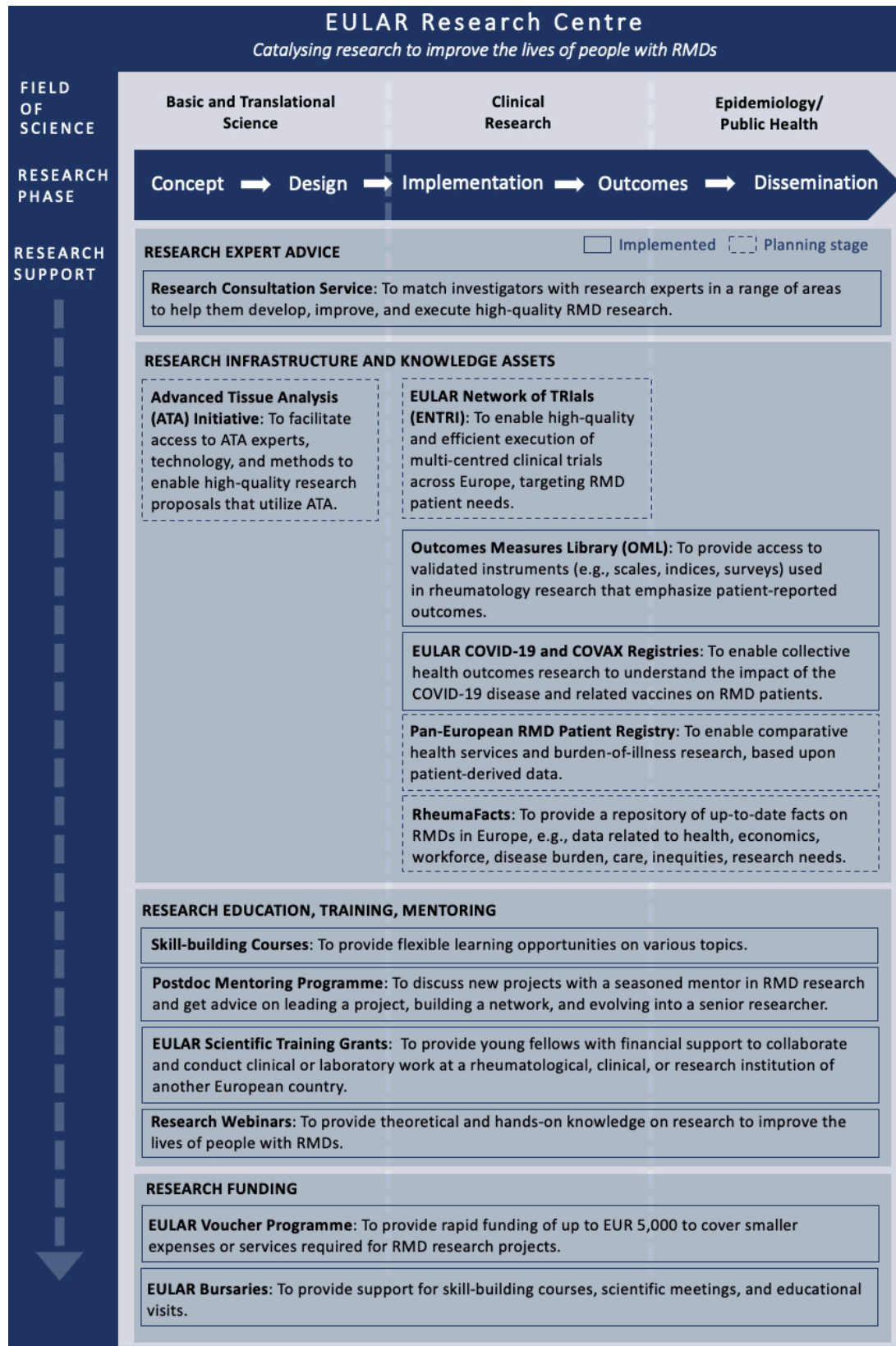


Figure 2 EULAR Research Centre support areas. RMD, rheumatic and musculoskeletal disease.

no cost to RMD investigators in EULAR-affiliated countries. More than 80 consultants (including clinical and translational researchers, epidemiologists, health professionals and patient engagement experts) were selected

based on their research and content expertise from successful RMD investigators in EULAR-affiliated countries. During the pilot, 19 consultants have supported 16 research projects in 12 European countries (figure 3).

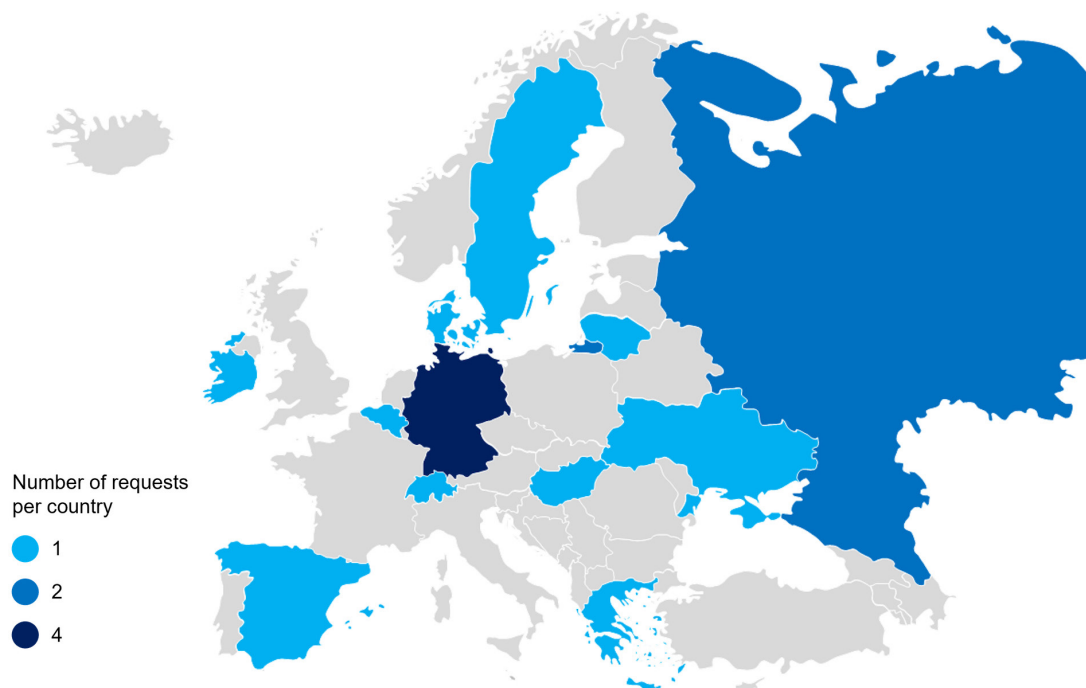


Figure 3 Distribution of EULAR's Research Consultation Service requests (n=16) by European countries received between December 2020 and March 2022.

EULAR rejected 18 requests from investigators in non-eligible countries outside Europe, such as India, Japan and Algeria. In the future, as the programme develops, it is hoped that this initiative can be extended beyond EULAR-affiliated countries, where unmet needs are demonstrably present, to support the global development of high-quality RMD research. Thus far, among the outcomes of the research support provided during the pilot period are two publications from investigators in Lithuania²² and Belgium,²³ three abstract presentations at international conferences as well as two subsequent grants in the amount of €442.000 (€435.000 and €7.000).

During the pilot, EULAR further sought feedback from both the service users and consultants using postconsultation surveys, interviews and annual progress reports, which were generally highly positive. Several challenges that affected users and consultants were also reported. Users mentioned discomfort to share early-stage scientific ideas and express additional consultation needs that might have arisen because of the consultation, for example, help with conducting a calculation. Consultants, on the other hand, noted a lack of clarity regarding the scope of the service (eg, providing advice on a study protocol vs writing a study protocol) and language barriers in some cases when service users' first language was not English. To address these barriers, EULAR followed up with users and consultants individually to facilitate user–consultant team calls. EULAR also developed information resources (frequently asked questions and infographic) and offered information sessions via webinars and the EULAR Congress.

Research infrastructure and knowledge assets

The lack of high-quality RMD research infrastructure across European countries poses another practical barrier to levelling the playing field. Resource needs may vary by location, including specialised research equipment; space; resources to collect, analyse and store specimens and data; medical record systems; skilled staff, among others. Limitations in these areas can affect the feasibility, quality, efficiency and equity of research. Long-term, the EULAR Research Centre aims to provide solutions to address these types of structural barriers to pan-European RMD research, either directly or by leveraging other funding resources as they arise. To get started, EULAR launched several research support initiatives that address mutual pan-European research infrastructure priorities (figure 2).

1. With the *Advanced Tissue Analysis (ATA) Initiative*, EULAR will support researchers interested in using advanced biological sample and tissue analysis technologies (eg, multiplex testing of cytokines and proteins, autoantibody profiling, genomic analysis, proteomics, miRNA analysis, metabolomics, single-cell methodologies and spatial transcriptomics) to answer innovative RMD research questions. While biological agents have improved the treatment of RMDs such as rheumatoid arthritis (RA), health outcomes in patients with RA are still poorer than in the general population. It remains difficult to predict which drug will be effective for a given patient.²⁴ To overcome the challenges of current, 'lottery-like'²⁵ therapeutic approaches, there is a need for novel biomarkers tailored to patients' expected therapeutic responsiveness. Synovial tissue

research, for example, has become widely developed, but large discrepancies exist in the way synovial tissue is handled, and how data pertaining to biopsy procedure, quality check and experimental results are reported in the literature. This heterogeneity hampers the progress of research.²⁶ Through EULAR's ATA Initiative, investigators can request advice on research proposals from a network of experts in the field who will promote the accurate application of ATA technologies and methods. Importantly, they will also be able to leverage the necessary expertise and technology resources available at these institutions to strengthen the competitiveness of their research proposals. By enabling investigators across Europe to use these new ATA technologies, EULAR hopes to increase the chances of improving RMD patient outcomes and achieving success, as seen in oncology, using precision medicine-guided therapeutics.

2. The EULAR Research Centre has developed several knowledge assets available to investigators:
 - The *EULAR COVID-19 Registry*^{27 28} was developed in collaboration with the Paediatric Rheumatology European Society and working with the Global Rheumatology Alliance (GRA) to collect health outcome data of paediatric and adult patients with RMD in Europe who have been infected with SARS-CoV-2. Since its launch in March 2020, the GRA and the COVID-19 registry combined included more than 21 000 clinician-reported cases. Rheumatology clinicians from Europe and other EULAR-affiliated countries were invited to report COVID-19 cases in their patients with RMDs across the entire severity spectrum—from asymptomatic patients to less severe or mild cases and the most severe ones. Anonymised data were regularly shared with the international registry and made available to investigators. Among the first registry-supported outcomes are several papers providing important evidence. One study, for example, showed that children and young people with arthritis are not at high risk of severe COVID-19.^{29 30} Another analysis demonstrated that COVID-19-related deaths among people with rheumatic diseases were associated with known general factors (older age, male sex and specific comorbidities) and disease-specific factors (disease activity and specific medications, including rituximab and corticosteroids), highlighting an association with moderate/high disease activity.^{31 32}
 - The *EULAR COVAX Registry*³³ was developed to collect health outcome data from patients with RMDs after their first or second injection of the COVID-19 vaccine. The COVID-19 vaccines have raised many questions for RMD patients, especially those with inflammatory RMDs and patients treated with drugs that may influence their immune system. Rheumatologists in Europe and other EULAR-affiliated countries are invited to add to the more than 7000 clinical-reported cases already in the registry. The

data are available to investigators and have already enabled successful research projects. One of these studies indicated that most patients tolerated their vaccination well, with rare reports of flares and sporadic reports of serious adverse events.³⁴

3. The *EULAR Outcomes Measures Library (OML)*³⁵ offers investigators a comprehensive database of validated instruments (eg, indices, surveys and scales) used in rheumatology that emphasise patient-reported outcomes (PROs). PROs, such as symptoms, health-related quality of life or patient-perceived health status, are reported directly by the patient and are essential tools to inform patients, clinicians and policymakers about disease-related morbidity and patient suffering, especially in chronic diseases. The OML offers the necessary data to help RMD investigators choose those research instruments with the highest level of validation.
4. Two additional EULAR data initiatives are under way. EULAR is developing a *Pan-European RMD Patient Registry* to collect longitudinal patient-generated health data. The goal is to enable comparative health services research and burden-of-disease research. The data will be obtained exclusively from patients with RMDs. Anonymised data will be available for research and include a range of variables, such as sociodemographic data, employment situation, disease activity, drug therapy, quality of life, healthcare, unmet medical needs and patient-reported research priorities. Interested patients with RMDs will be able to sign up without any clinician intervention. Special consideration will be taken to ensure the representation of patients with RMDs from under-represented and minority groups.
5. A *'RheumaFacts' Data Repository* project is also under way to provide up-to-date RMD-related data from across European countries to highlight the disease burden of RMDs, healthcare gaps and inequalities. The data will be available to researchers as well as to other groups such as funding agencies, decision-makers and policymakers who can advance population health at a European level.
6. Finally, the new *EULAR Network of Trials (ENTRI)* will address critical roadblocks in RMD-related clinical trials, initiated by investigators or industry. The network will consist of clinical centres with experience in clinical trials and access to cohorts of patients with RMDs. Collaboratively, they will enable high-quality and efficient multicentre clinical trials across Europe, targeting patient populations from across a wide range of RMDs. Investigators will be able to get advice on their clinical trial protocols via the EULAR Consultation Service and use ENTRI as a mechanism for the rapid and efficient roll-out of multicentre clinical trials. As part of this process, investigators will have access to clinical trial tools, such as toolkits, standard operating procedures, electronic case report forms database templates and best-practice study manuals to share across centres. Additional features of the network will include (1) a web-based portal that lists members of

the network, highlighting areas of expertise, patient populations, and active or in-setup studies; (2) adoption of novel trial designs such as pragmatic trials that address clinically relevant questions; (3) targeting a wide range of patients and at-risk populations across the RMD spectrum, including rare and complex diseases; (4) the potential for novel approaches including virtual trials, light-touch, web-based recruitment, randomisation, data capture and monitoring; and (5) establishing a curriculum with the EULAR School for training a new cadre of clinical trialists (see further).

The financial support for the establishment and maintenance of these initiatives, services and databases during the next few years is exclusively provided by EULAR.

Research education, training and mentoring

Significant investment in rheumatology workforce development is needed to enhance RMD research across Europe.³⁶ Several barriers exist including the varying number of rheumatology providers across European countries, insufficient local research training opportunities, disparate incentivisation of research across institutions, and precedence of clinical care duties over research and mentoring.³⁷ Early-career investigators might have problems in finding research mentors and collaborators. Consequently, the generalisability of current research and evidence is questionable, as it is being dominated by investigators in a few high-income countries, as shown in figure 1.

In close collaboration with the EULAR School of Rheumatology,^{38 39} the EULAR Research Centre aims to advance rheumatology workforce development (eg, physicians, health professionals and researchers in rheumatology, and patients with RMDs) through standardised training and evaluation. Those interested can choose from a range of *courses and online modules*, covering topics such as immunology,⁴⁰ epidemiology,⁴¹ evidence-based practice⁴² and health economics in rheumatology,⁴³ among others.

Additionally, dedicated mentoring opportunities, for example, the *Postdoc Mentoring Programme*, are offered through the EULAR Network of Young Rheumatologists. Awardees will have the possibility of discussing new projects with a seasoned mentor in RMD research and get advice on leading a project, building a network and establishing themselves as senior researchers.⁴⁴ Training grants and bursaries also provide opportunities for research training (see further). Finally, regular informational *research webinars* highlight diverse topics to provide theoretical and hands-on knowledge on research to improve the lives of people with RMDs.⁴⁵

Research funding

The EULAR Research Centre intends to support capacity building by helping investigators address smaller, ad hoc research funding gaps that may prevent them from continuing or closing out an RMD research project. For example, the new *Research Voucher Programme*,⁴⁶ offered by

EULAR's Research Centre, provides rapid funding of up to €5000 to cover smaller expenses or services required for RMD research projects. Investigators can use the funds in various ways: (1) to purchase core services, technology and equipment for their RMD research projects; (2) to cover professional grant writing support to apply for EU grants; and (3) to support RMD-related articles in high-quality peer-review journals. In the first quarter of 2022, EULAR awarded four research vouchers to support RMD investigators in Italy, Spain and Switzerland, allowing them to purchase metagenomic, next-generation sequencing and proteomic analyses.

Short- (1–3 weeks) and longer-term (1–6 months) *scientific training grants*^{47 48} allow young fellows from European countries to collaborate and conduct clinical or laboratory work at a rheumatological, clinical or research institution of another European country. The awards are designed to help improve the standard of research and care across Europe.

EULAR bursaries support a range of skill-building opportunities, for example, courses and scientific meetings in rheumatology,⁴⁹ such as the European Workshop for Rheumatology Research, and educational visits to health professionals other than physicians working in the field of rheumatology.⁵⁰

The EULAR Research Centre provides smaller funding to support training and proof-of-concept studies, aiming to result in more extensive support for an RMD research project. A couple of years ago, EULAR also founded a dedicated, established research funding agency, the EULAR Foundation for Research in Rheumatology (FOREUM),⁴⁵ which has been registered as a separate legal entity in 2014.⁴⁵ FOREUM grants funding for highly competitive, multicentre RMD research projects and individual career grants, primarily driven by scientific excellence, innovation and impact. An important goal for FOREUM and the EULAR Research Centre is to work collaboratively and synergistically, providing support for RMD research projects across the research life cycle and fostering promising RMD research across Europe. To receive financial support for research projects, investigators are encouraged to apply for FOREUM funding.

Evaluation

With the inception of the Research Centre, EULAR has renewed its commitment to research evaluation and implemented an evaluation programme. EULAR will collect a set of outcomes to assess the performance of its Centre and the impact of the provided research support (eg, number of investigators supported, subsequent publications and other forms of dissemination, other research outputs such as datasets or software code, awards or recognitions, patents, start-ups, the amount of subsequent research funding). The collected data will ensure the Centre's accountability, identify usage gaps and barriers, and inform the planning for future directions.

CONCLUSIONS AND OUTLOOK

European RMD research has been at the forefront globally in the last decade when the impact of research has been remarkable in the RMD field. New pathogenesis understanding, diagnostics and therapeutic strategies abound. Large registries and the application of public health approaches have substantially improved our understanding of the impact of RMDs and the positive effects of interventions at individual, family and societal levels. As laid out in this viewpoint, we must recognise that significant barriers to accelerating RMD research still need to be addressed. EULAR has created the Research Centre to serve as a transformational catalyst to address these unmet needs. Our evolution as a research community seeks to be inclusive—we will welcome advice and feedback on how we can optimally design the Centre and its strategic efforts going forward.* The era of artificial intelligence, big data, molecular biosciences and social media will place at our disposal the most remarkable tools to change the lives of people with RMDs—we must not miss this unparalleled opportunity.

*For any questions and to receive news from the EULAR Research Centre, please visit the EULAR.org website or reach out to research@eular.org.

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Competing interests Since 2019, KR has served as a scientific advisor to EULAR and, as such, is affiliated with EULAR. Due to her more than 10 years of experience with virtual research centres and research networks, KR was actively invited to help develop a virtual EULAR research centre, which evolved into the EULAR

Research Centre described in this paper. She received compensation from EULAR for her work as a scientific advisor and consultant on EULAR projects, including her time effort spent on this paper. Her current academic home is the SUNY Upstate Medical University in the USA.

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