



DELIVERABLE 2.4 PUBLIC FINAL REPORT

ERN-EuroBloodNet

European Reference Network on Rare Hematological Diseases

EUROPEAN REFERENCE NETWORKS
FOR RARE, LOW PREVALENCE AND COMPLEX DISEASES

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Short Description

Public report including all the activities implemented and results achieved by ERN-EuroBloodNet for their dissemination to RHDs target groups

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ERN-EUROBLOODNET 5 YEARS OF IMPLEMENTATION

Haematological diseases involve abnormalities of blood and bone marrow cells, lymphoid organs and coagulation factors, and almost all of them are defined as rare with a prevalence less than 1 in 2000 individuals. As for other rare diseases, diagnosis of rare hematological diseases (RHDs) is often delayed, and treatment is suboptimal. In addition, they require extensive knowledge and experience, as well as costly diagnostic and therapeutic infrastructures. The European Reference Network on Rare Hematological Disorders ([ERN-EuroBloodNet](#)) was officially established by the European Commission in 2017 with the aim of improving the healthcare and overall quality of life of patients with a RHD by facilitating best practice sharing for safe and high-quality cross-border healthcare while gathering evidence for cost-effective treatments development. In order to achieve the general objective, five specific objectives were established: 1) Improve equal access to highly specialised healthcare delivery for RHDs across Europe, 2) Promote best practice in prevention, diagnosis and clinical care across EU, 3) Disseminate cutting-edge knowledge and facilitate continuing medical education in the field of RHDs, 4) Provide inter-professional consultation by sharing of expertise and safe exchange of clinical information, and 5) Foster European cooperation in highly specialised procedures for diagnosis, innovative treatments and research. Involvement from the outset of European Patients Associations Groups (ePAGs) designated by EURORDIS in the Board of the Network and their active participation in the ERN actions has been cornerstone to contribute to patient empowerment and advocacy, keeping the ERN-EuroBloodNet patient-centered approach.

ERN-EuroBloodNet is a collaborative network that brings together Healthcare Providers (HCPs) nationally recognised centres of excellence and multidisciplinary teams with the main goal to promote excellence for best health care in RHDs at the EU level. Initially concentrating 66 members HCP from 15 EU Member States (MS), ERN-EuroBloodNet has been recently enlarged integrating 96 HCP from 18 EU MS. Country coverage is additionally promoted in MS where there is no official member designation with 7 Affiliated Partners from 6 EU MS.

ERN-EuroBloodNet involves more than 450 RHDs according to ORPHA classification encompassing oncological and non-oncological diseases, of inherited or acquired origin, and with significant differences on clinical manifestations (acute or chronic). Prevalences also range from 0,049% to 10⁻⁷%, meaning from 1 patient affected in 2.032 individuals to 1 patient affected in 101.600.000 individuals. Therefore, as for other RDs, knowledge and expertise available is even more fragmented and scarce on those ultra-rare diseases.

In this highly heterogeneous scenario, ERN-EuroBloodNet has succeeded during the five first years of implementation, on the establishment of the state-of-the art of RHDs and the identification of disease specific needs allowing the challenging implementation of multiple methodological strategies based on both transversal and disease-specific approaches, where actions focused on very rare RHD have been prioritized. The recent expansion of ERN-EuroBloodNet members coverage situates the network in an optimum position to consolidate and further expand the following key achievements obtained:

The European inventory of RHD experts and facilities available at the EU and Member State levels based on the implementation of [members, healthcare providers, departments and experts profiles](#) have been upgraded with the inclusion of 70 RHD Disease groups (RHD-DG) for becoming the center piece of a) the members' reporting of number of patients and new patients, b) make the expertise in ERN-EuroBloodNet searchable and c) classify the contents of the website, i.e. Guidelines, educational material. The inventory is in continuous expansion, currently 182 experts have completely fulfilled their profiles and are findable through the [disease search engine](#) offering the possibility of searching experts either by disease or by subnetwork with the possibility of including additional filters.

4 European mapping exercises were conducted among ERN-EuroBloodNet members and non-members to identify the European state of the art of highly specialized procedures key for the diagnosis or treatment of RHDs and presenting high inequalities for its access among MS: a) **Next generation sequencing (NGS) availability on non-oncological RHDs**, 50 answers from 12 countries led to the identification of gaps on the availability of NGS for rare anaemia disorders, b) **Bone marrow transplantation (BMT) on non-oncological disorders**, 18 answers from 14 countries led to the identification of gaps on the availability of BMT for Sickle cell disease, c) **Availability of diagnosis procedures for Primary vitreo-retinal lymphoma (PVRL)**, 86 answers from 18 countries led to identification of important disparities in clinical practice between physicians on diagnosis, treatment and assessment of treatment response and follow up, and therefore the high need for development of a Clinical Practice Guideline on the area that could be addressed by the ERN-EuroBloodNet Guidelines. The paper "[Primary vitreoretinal lymphoma: short review of the literature, results of a European survey and French guidelines of the LOC network for diagnosis, treatment and follow-up](#)" was published in Current opinion in oncology in September 2021 with the acknowledgement of ERN-EuroBloodNet, d) **Transcranial Doppler (TCD) availability for children with sickle cell disease (SCD)**, 81 answers from 16 countries demonstrates that less than 30% of children with SCD followed in European Centers receive annual TCD according to recognized guidelines. The abstract "[Limited Access to Transcranial Doppler Screening and Stroke Prevention for Children with Sickle Cell Disease in Europe: Results of a Multinational Eurobloodnet Survey](#)" presenting the results from the mapping was presented during the American Society of Hematology (ASH) 2021 edition.

24 RHD patients requesting Cross-Border health assistance have been supported by ERN-EuroBloodNet team, helping patients navigating the healthcare social systems in Europe by offering a mediation among National Contact Points for Cross Border Care and hospital administration. Moreover, an analysis on **patients experience on the cross border health accessibility to blood transfusions** across EU has also been performed by the participation of 6 patients in a survey conducted, allowing the evaluation of obstacles suffered by these patients.

The repository of 68 RHD Clinical Practice Guidelines (CPG) and Other Clinical Decision Making Tools (CDMTs) classified on Quality Domains for the red blood cell, bone marrow failures, haemochromatosis and other iron disorders and myeloid malignancies subnetworks are public available at ERN-EuroBloodNet website together with a [search engine](#) to allow the findability of documents by a) disease, b) topic, c) involvement of patients and d) quality of evidence and consensus approach. Classification of Bleeding and coagulation and lymphoid subnetworks documents on Quality Domains will be finalized in the upcoming period of implementation.

GAPS for **development of new guidelines and adaptation** of existing documents to clinical practice guidelines have been identified with a survey conducted among ERN-EuroBloodNet members gathering 29 answers that led to the identification of the Top 10 list for CPGs and other CDMTs priorities development to be addressed by two main actions a) DG SANTE supporting action to the development/adaptation of 2 new CPGs and 5 CDMTs per ERN: The **creation of a CPG on Adult Burkitt Lymphoma** is under development, while the second topic to be addressed is already identified for **CPG for long-term complications in hemoglobinopathies**. b) Collaboration with the European Hematology Association for the development of CPGs and other CDMTs: A first [Recommendations for diagnosis and treatment of methemoglobinemia](#) has been already published with the acknowledgement of EHA and ERN-EuroBloodNet. In addition, ERN-EuroBloodNet will develop patients' pathways & patients' summary on new generated CPG and CDMTs during the next period of implementation.

[ERN-EuroBloodNet Webinars programs for professionals](#) has been launched aiming to cope with the educational gaps identified in previous phases while focusing on a very innovative and specific disease, clinic or intervention area, including: 27 [Thursdays Webinars](#) (media of 27 participants) as single webinars addressing cutting edge knowledge on clinical management or treatment. Online educational program is reinforced with the [Topic on Focus Webinars program](#) launched in the frame of "Connecting EuroBloodnet II", including a set of webinars focusing on a very concrete area/disease for the provision of a comprehensive knowledge of the field, including: a) [Cutaneous Lymphoma](#), 9 webinars (media of 78 participants), accredited with 7 European Board for Accreditation in Hematology (EBAH) credits, b) [Thrombotic Microangiopathies](#), 15 webinars (media of 41 participants), accredited with 11 EBAH credits and, c) [Bone Marrow Failure Syndromes](#), 18 webinars (ongoing, media of 75 participants), accredited with 18 EBAH credits. Lastly, a collaboration has been established for the development of [EHA & ERN-EuroBloodNet Spotlight](#) as EBAH accredited programs in collaboration with EHA. To date, the area tackled has been tackled [Castleman Disease](#) with 4 webinars (ongoing, media of 63 participants) and 1 EBAH credit per webinar.

[ERN-EuroBloodNet Webinars programs for patients](#) are moderated by a duo of an expert physician and a patient representative, including 2 [Patients Webinars](#) (media of 43 participants) as webinars providing patients' community with highly specialized knowledge on a specific RHD or groups of disease. [Topic on Focus for patients](#) Webinars Program promote the awareness on a RHD or groups of disease targeting patients, to date the following diseases on Focus have been tackled: a) [Myelodysplastic syndromes](#), 8 webinars (media of 36 participants), b) [Sickle Cell Disease](#), 11 webinars (ongoing, media of 56 participants). Lastly, [Topic on Focus for Patients Organizations](#) Webinars Program promoting the awareness on a RHD or groups of disease targeting organizations and advocates, to date [Cutaneous lymphoma](#) included 6 webinars (media of 41 participants).

[Past webinars](#) are available at ERN-EuroBloodNet website dedicated sections and [EuroBloodNet EDU Youtube channel](#).

Preceptorships for health professionals on Sickle cell disease are being defined for its conduction in the coming period of the network. Hosting centers, coordinators and topics have already been identified.

[The eleven pan-European umbrella networks](#) of patients' organizations on RHDs, comprising more than 250 national and regional patient organisations, have been listed ERN-EuroBloodNet webpage in order to increase their visibility among RHD patients. In addition, [two new ePAGs](#) have been designated during the network implementation for Hereditary Hemochromatosis and Iron metabolism related disorders subnetwork and for Lymphoma subnetwork.

The European Network of Sickle Cell Disease Patients Organisations is being established in collaboration with EURORIDS as a bottom-up umbrella network of national and local organizations of SCD patients' advocates, whose objective is to give a strong representation of the disease and make its needs visible at European level. From the national representatives elected, one will be trained to become ERN-EuroBloodNet Epag. More than 50 SCD patients association have been reached in Europe and three national meetings have been held, as an opportunity to raise national needs that could be translated into a European concrete action. 4 national representatives have been elected so far (France, Italy, Portugal and Spain). [A video with 9 patients' testimonies on their experience on National meetings](#) was published in ERN-EuroBloodNet EDU Youtube Channel during World Sickle Cell Disease Awareness Day 2020.

The Sickle Cell Disease Research Prioritisation Workshop at the Annual Scientific Conference on Sickle Cell and Thalassaemia (ASCAT) was a joint project of the ERN-EuroBloodNet together with ASCAT members aiming to train patients to Public Patient Involvement in Research and health professionals on a patient research center approach. Workshop was held the October 2019 with 28 participants coming from 7 EU countries, 5 non-EU countries. Participants were able to define the Top 10 priority research topics to be most urgently tackled, allowing the identification of direct and indirect educational actions. [A video with 5 patients' testimonies on their experience on the Research prioritisation workshop at ASCAT](#) was published in ERN-EuroBloodNet EDU Youtube Channel during World Sickle Cell Disease Awareness Day 2020. Collaboration with ASCAT has continued for the organization of Patients Educational Session at a) ASCAT 2020 (held October 2020 online) addressing three major topics: Living with SCD and coping with COVID19 Pandemic Outbreak, the participations of SCD patients to Research and Peer Reviewing and three panels (one "meet the experts" and two "meet the patients' session"). With a total of 68 participants the Educational Online Session is available at Youtube channel into 2 different playlists: [Patient's Testimony](#) and [SCD Patients' Educational Session at ASCAT 2020](#). b) ASCAT 2021 (held January 2022 online) where a total of 54 participants had the opportunity to participate in interactive panels on Racism, Mental Health, Pregnancy and Bone Marrow Transplant (a dedicated video is under edition). Collaboration with ASCAT is ongoing for 2022 edition.

Other educational action for SCD patients has been the creation of the [SCD patient Priority Blog](#), as a virtual space for people living with SCD, when they can express themselves about what they consider relevant topics. Moreover, **a pilot project of SCD patients' conversation group with a psychotherapist** has been launched by the Spanish National SCD Patient Association: Asociación Española de Enfermedad Falciforme (ASAFE) promoted by ERN-EuroBloodNet.

Analysis of the existing available educational material for Cutaneous lymphoma patients has been performed in collaboration with Lymphoma patients associations (Europe Lymphoma Coalition, France Lymphoma Espoir, Cutaneous Lymphoma Foundation) and EURORDIS. A first list of the educational material has been collected from Lymphoma patients associations. The CL task force will review the materials compiled for its publication in ERN-EuroBloodNet and identification of needs for development of new materials.

The use and awareness of CPMS has been promoted among members. As a result 43 panels have been created for RHDs since the launch of the CPMS, from which 21 are closed with outcome report produced. Moreover, 100 users are currently registered at the platform.

In addition, [the CPMS Virtual Board model has been developed based on a pilot for Cutaneous Lymphoma \(CL\)](#) as an ultra-rare cancer with very concrete expert needs with the aim to a) train experts in the use of the CPMS, b) establish regular CPMS video meetings, and c) develop logistics for open consultation to non-member requests and timely outcome delivered to patient. This model has been created in the frame of Connecting EuroBloodNet II and will be expanded to other ultra-rare diseases through pilot schemes including financial compensation for panels.

An estimation of the ERN-EuroBloodNet members activity by number of patients have been performed based on the monitoring exercises conducted so far, gathering the number of patients and number of new patients referred to the center per group of disease covered and period of reporting. A total 65.000 RHD patients is estimated to be covered by ERN-EuroBloodNet, with the inclusion of around 5.000 new RHD patients per year.

184 RHD registries have been identified through the exploratory exercise conducted for the creation of an Inventory of EU-RHD registries. The high number of national registries identified (64%) highlights the need of the joining efforts towards as a European pooling of data through initiatives as the [European Rare Blood Disease Platform \(ENROL\)](#). ENROL, starting from 1st June 2020, has been conceived in the core of ERN-EuroBloodNet and endorsed by the EHA, as the umbrella for both new and already existing registries on RHDs. ENROL aims at avoiding fragmentation of data by promoting the standards for patient registries' interoperability released by the EU RD platform. The exploratory exercise of existing registries provide a solid source of potential data providers in the short term.

The ENROL strategy for data gathering combines the exhaustiveness of data collection at EU level for health planning and epidemiological purposes, with a higher level of RHD data granularity for promoting research and identification of patients' cohorts. The platform has been designed to integrate data from available sources (healthcare providers hospital records, EU/national/local existing registries) with different levels of granularity to pursue ENROL aims: a) counts/aggregated level to facilitate the increase of exhaustiveness of data gathered at the EU level required for the epidemiological surveillance, b) pseudonymised individual data to promote research and facilitate the identification of trial groups. As final result, ENROL will not only provide epidemiological surveillance for RHD, but also facilitate the re-use of data by exploratory study population queries aiming to identify adequate target populations to include in clinical trials and research projects. This will promote the development of clinical trials, especially in those countries with limited access to drugs, and –OMICS based research on drug-able targets.

Another epidemiological initiative promoted by ERN-EuroBloodNet during this period has been the launch of the [Collaborative Platform on Red Blood Cell and COVID-19 patients](#), a unique platform resulting from a European effort aiming to pool evidence for supporting daily medical practice on the clinical management of patients affected by red blood cell disorders and COVID-19. To date the platform counts with 373 patients. The abstract "[ERN-EuroBloodNet European Registry of Patients Affected by Red Blood Cell Disorders and COVID-19](#)" was presented during the American Society of Hematology (ASH) 2021 edition.

ERN-EuroBloodNet is sponsoring the use of innovative drugs in clinical trials. Those trials can be activated simultaneously in several member states through a EU directive on clinical trials allowing one country to be "main sponsor" and a few other countries to be "delegate sponsors". MDS-RS will be the first trial promoted through the association, and two new candidates have been identified.

ERN-EuroBloodNet is promoting the establishment of collaborative research projects among ERN-EuroBloodNet members through their endorsement and contribution. Some examples of joint proposals submitted under the current period of implementation are H2020 Call for RHD as [Genomics and Personalized Medicine for all through Artificial Intelligence in Haematological Diseases \(GenoMed4All\)](#) and the [Erythrocytes properties and viability in dependence of flow and extra-cellular environment \(EVIDENCE\)](#) projects, as well as the [International Hemoglobinopathy Research Network \(INHERENT\)](#) as the European network to integrate existing knowledge for rare anaemias (epidemiology, genetic variation, genotype-phenotype relationships).

Dissemination and communication channels have been consolidated in order to increase the outreach of network actions, including: a) [ERN-EuroBloodNet EDU Youtube channel](#), with 262 subscribers and 79 educational videos created/endorsed by the network for the benefit of the EuroBloodNet Community (patients and experts), providing a direct and open access to the knowledge in the field of rare blood diseases, b) [@ERN-EuroBloodNet Twitter](#) account registers more than 2170 Tweets and 1154 followers, c) [ERN-EuroBloodNet Facebook](#) with 197 followers, as one of the major social networks mainly addressing general audience, d) [ERN-EuroBloodNet LinkedIn](#) with 260 followers as one of the major social networks connecting professionals, e) [ERN-EuroBloodNet newsletter](#) with 440 subscribers to transmit stakeholders the most relevant RHD news while keeping them updated with the main achievements of ERN-EuroBloodNet, maximizing the impact of ERN-EuroBloodNet activities.

In conclusion, during its first 5 years of implementation ERN-EuroBloodNet has contributed to 3rd EU Health Programme by supporting innovative, efficient and sustainable health systems and facilitate access to better and safer healthcare for EU citizens while decreasing the cross-border health barriers currently existing for information, samples and patient mobility in RHDs.

ERN-EuroBloodNet has succeeded in positioning as a key player for strengthening the use and re-use of RHD health data for the provision of best healthcare and research while enhancing access to quality and patient-centred healthcare by supporting integrated work among MS and health systems, in particular strengthening and scaling up networking with other ERNs and other transnational networks.

The implementation of well defined tailored strategies to transversal and RHD specific needs has undoubtedly led to the development of a solid matrix of cross border health, best practices, education, telemedicine and epidemiological surveillance actions that set the bases to scale up towards strengthening health systems in the field of RHDs under the frame of the new EU4Health Programme.



https://ec.europa.eu/health/ern_en



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