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European Reference Network for rare or low prevalence complex diseases
Network Hematological Diseases (ERN EuroBloodNet)

European Reference Networks

4.1 ERN-EuroBloodNet Repository of Members

ERN-EuroBloodNet
European Reference Network on Rare Hematological Diseases

EUROPEAN REFERENCE NETWORKS
FOR RARE, LOW PREVALENCE AND COMPLEX DISEASES

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DOCUMENT INFORMATION

4.1 ERN-EuroBloodNet Repository of Members

Report document

ERN: **ERN-EuroBloodNet (European Reference Network on Rare Hematological Diseases)**

Call: **HP-ERN-SGA-2018**

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Short Description

Report on ERN-EuroBloodNet's members' profiles, including data on the HCPs, experts and multidisciplinary team, diseases covered, and core facilities for health provision. This will be also accessible through EuroBloodNet website

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1. INTRODUCTION

EUROPEAN COMMISSION STRATEGY FOR MONITORING RARE DISEASE PATIENTS POPULATION

The European Reference Networks (ERNs) legal framework sets out the objectives, principles and criteria of the ERNs and defines the general implementation process including the assessment, approval and evaluation of the ERNs. Once approved, ERNs are expected to be evaluated every five years. However, Member States (MS), ERNs and European Commission (EC) have identified the need to establish a solid continuous monitoring system of the ERNs to allow a closer follow up of the activities performed by the networks.

The process to set up such a monitoring and information system involves a huge challenge both at organisational and technical level including periodical self-assessment and reporting of the activities of the ERNs and Healthcare Providers (HCPs) to the EC and the Board of MS for ERNs.

In this context, ERN Continuous Monitoring Working Group of the Member States and the ERN Coordinators defined 18 Core indicators to be finally agreed by the ERN Board of MS and the ERN Coordinators Group in September 2018, several of them with specific focus the monitoring of two types of ERNs patient population:

- ERNs CPMS population: The patients that due to their complexity or need of expert advice are included in the CPMS
- ERNs total patient population: The aggregated number of patients looked after by each of the HCPs of a given ERN.

While the first one represents the individual patients and treating clinicians that would directly benefit from the expert advice of the ERNs from a cross border perspective, the second one will benefit as well in an indirect way from the improvements in the knowledge, tools and expertise of the HCP that is looking after them with a national perspective.

The aggregated total number of patients of an ERN will be the backbone of the ERNs capabilities as the pooling of the data and information provided by this population of patients will feed the whole system of ERNs and make possible the generation of knowledge and new evidence for the better diagnosis and treatment of those patients. Knowledge is also being transferred to the clinician treating the patient, as they usually participate in the panel review and so directly benefit from participating in the clinical discussions with the experts on these rare or complex cases.

CROSS-BORDER HEALTH IN THE FIELD OF RARE HEMATOLOGICAL DISEASES

As in other Rare Diseases (RDs), expertise in Rare Hematological Diseases (RHDs) is scarce and distributed heterogeneously across the EU and there is no accessible repository of human and technical resources available to challenge the difficulties of RHD at the EU or national levels.

As a result of the scarce and heterogeneous distributed expertise on RHDs, many patients suffer either a delay diagnose or remain undiagnosed over time, while it is also well known cases for specific diseases incorrectly diagnosed due to a trend on the awareness of close entities overlapping the clinical manifestations. Consequently, many patients are wrongly monitored resulting in an improper delivery of healthcare. In addition, highly specialized procedures for both cure or monitor long term complications including organ damage are not available or are not fully Implemented across Europe leading to big Inequalities on the access to healthcare.

The Directive 2011/24/EU on Cross-border health provides the keys for the establishment of a referral system for patients and samples in order to ensure the same level of access to healthcare across Europe. However, previous information on the expertise and services available at each MS is mandatory for the identification of needs and the establishment of evidence- based patients and cross-border pathways leading to a best healthcare care for each individual European patient, improvement of health services delivery for RHD across EU and better use of resources.

ERN-EUROBLOODNET MAPPING OF EXPERTS AND HIGHLY SPECIALIZED PROCEDURES

Mapping of experts

As starting point for the mapping of experts, an inventory of ERN-EuroBloodNet inventory of members and experts was created during previous period of the network implementation (2017-2018) for creating a public and accessible repository of the expertise available in the network.

ERN-EuroBloodNet inventory is based on Experts, Departments, and Members profiles. Profiles are editable through a set of applications forms allocated in the private area, and integrate the ORPHA classification for RHD in its back office, allowing the selection of health professionals' specific area of expertise as well as for the diseases covered by each of the departments directly from the classification and through a user-friendly disease- level format.

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In addition, a Disease Search tool has been implemented to exploit the data gathered through the inventory, making the expertise available in the network findable and searchable to the public. The engine searches experts based on the information gathered through the Experts' profile, offering the possibility of searching either by specific disease through the ORPHA classification, or by subnetwork. The tool also includes different filters to add to the search as patients' age coverage, area of expertise, country.

Highly Specialized Procedures in the context of Rare Hematological Diseases

As the basis for a cross-border health action, we define highly specialized procedures (HSP) as those procedures that for a number of reasons i.e. economical, lack of expertise or awareness, are not available in all EU-MS, thus preventing the delivery of the best care for EU citizens suffering from a rare haematological disease (RHD) independently of their country of origin.

These HSP are classified as "under the scope" of the Directive 2011/24/EU if they are defined as Standards of Care and/or included in the national basket of health services for patients or "out of the scope" in the cases that they are still performed on academic or experimental environment. In these cases, the European cooperation can be produced on the research field.

HSP involve both interventions for diagnosis and for treatment, and their complexity can rely on technological advances or expertise of multidisciplinary team, or both.

In this context, during previous period of ERN-EuroBloodNet implementation, the state of the art of Next generation sequencing (NGS) and Bone marrow transplantation (BMT) on non-oncological disorders was analysed as highly specialized procedures key for the diagnosis or treatment of many non-oncological RHD and presenting high inequalities for its access among EU-MS. Two questionnaires were conducted among ERN-EuroBloodNet members with the gathering of 50 and 39 and responses respectively. Answers allowed the identification of important gaps among the need and availability of a) NGS for rare anaemia disorders and b) BMT for Sickle cell disease.

This first mapping approach requires now to be step-wise upgraded by a) including indicators linked to specific aspects of both HSP in the members profiles for their monitoring and analysis of facilities available / needs at the national level and b) the identification of other HSP candidates for a mapping exercise and monitoring through ERN-EuroBloodNet members.

2. OBJECTIVES

ERN-EuroBloodNet established five specific objectives as priorities to be accomplished in the frame of the 5 years of implementation, including the specific objective 1: Improve equal access to highly specialized healthcare delivery for RHD across Europe.

Through this activity ERN-EuroBloodNet aims to build a central repository of reliable sources of information on expertise and HSP on RHDs available at both national and European level allowing the:

a) Identification of needs for cross border health actions based on existing gaps in certain MS for clinical management of a specific condition
b) Monitoring of assessment of network and members' excellence
c) Contribution to the EC strategy on monitoring rare disease patients population
d) Establishment of new bridges for collaboration not only among experts but also with other European bodies

In this context, the specific objective of this action is to **upgrade ERN-EuroBloodNet inventory of members and experts** established during previous period of network implementation for:

- Monitoring members' activity based on the gathering of Key Performance Indicators (KPIs)
- Mapping availability of HSPs considered as essential for the delivery of best healthcare and thus, defined as priorities for the establishment of cross-border pathways.

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3. TASKS

TASK 1. RARE HEMATOLOGICAL DISEASES-DISEASE GROUPS DEFINITION FOR MONITORING OF MEMBERS ACTIVITY

ERN-EuroBloodNet disease coverage includes more than 450 different entities with differential clinical and etiological features i.e. oncological vs non-oncological, hereditary vs acquired, or significant difference frequency, among others. However, some of these entities, especially those of the deeper levels in the classification, can be grouped attending to the expertise and procedures required for the appropriate healthcare provision to patients and the need for its monitoring at national level.

In this context, efforts have been performed for the establishment of Rare Hematological Diseases-Disease Groups (RHD-DG) in order to become the center piece of the ERN-EuroBloodNet central repository for:

- Mapping of experts: disease coverage
- Mapping of patients and HSPs through members' reporting on KPIs: number of patients/new patients and number of procedures HSPs
- Classify the contents of the website, i.e. Guidelines, educational material.

With the definition of RHD-DG, two major specificity levels of RHD classification will be available in the ERN-EuroBloodNet inventory of experts and health services:

a) RHD ORPHA classification "entire": The whole tree classification of ORHPA for RHDs will be available for the Experts to select their specific expertise. Experts are searchable when a very concrete disease is searched in the search tool
b) RHD classification "Disease groups": The RHD-DG established based on ORPHA/ICD will become the center piece of the website for members' reporting and classification of website contents.

For the definition of the RHD-DG, the following tasks were performed:

1.1 ANALYSIS OF CODIFICATION SCHEMES: ORPHANET AND ICD

Nowadays, multiple codification schemes are available for the international classification and categorization of diseases and health conditions. Taking into consideration their characteristics two schemes have been focused on this analysis:

- ORPHA classification (promoted by Orphanet) represents the only structured nomenclature specifically created for Rare Diseases (RDs) and the one with wider coverage of RDs.
- ICD 10/11 classification (promoted by WHO) is the foundation for the identification of health trends and statistics globally, and the international standard for reporting diseases and health conditions. It represents the usual classification used in clinical practices.

Given the specificity addressing RDs, ORPHA classification was chosen as the one to be implemented in the back office of ERN-EuroBloodNet website with the inclusion of more than 450 entities under the scope of the network. In addition, ORPHA provides interoperability between international codifications, aligned with ICD10 and ICD11, and other nomenclatures including SNOMED-CT, MeSH, MedDRA and OMIM.

In order to define RHD-DG, ORPHA classification was used as the basis for the clustering. However, two major barriers were found:

a) Gaps for the codification of some RDs, specially affecting to the very rare diseases, as rare iron disorders.
b) Outdates for Lymphoid malignancies which are better classified under the latest version of ICD scheme.

In order to cope with both barriers, the following actions were performed:

Revision and update for ORPHA Classification on Hemochromatosis and other rare genetic disorders of iron metabolism and heme synthesis subnetwork

Diseases encompassed in the Hemochromatosis (HH) and other rare genetic disorders of iron metabolism and heme synthesis subnetwork are most of them very rare disorders that present an important gap in the classifications for rare diseases. In this context, while many of them are contemplated in the OMIM classification, there are still important gaps in their presence at the ORPHA classification.

ORPHA classification has been reviewed by the ERN-EuroBloodNet task force on HH and iron disorders aiming to analyse the existing gaps and propose a new classification to Orphanet.

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Correlation between ORPHA and ICD on Lymphoid malignancies

The most updated classification available for Lymphoid malignancies is the " The 2016 revision of the World Health Organization classification of lymphoid neoplasms" reflecting a consensus among hematopathologists, geneticists, and clinicians regarding both updates to current entities as well as the addition of a limited number of new provisional entities.

The revision clarifies the diagnosis and management of lesions at the very early stages of lymphomagenesis, refines the diagnostic criteria for some entities, details the expanding genetic/molecular landscape of numerous lymphoid neoplasms and their clinical correlates, and refers to investigations leading to more targeted therapeutic strategies.

A correlation exercise among the ORPHA and ICD classification for these diseases was performed (see section 4. Results)

1.2 Rare hematological diseases - disease groups definitions

Based on the results from the analysis of the ORPHA and ICD codification schemes, a first version of ERN-EuroBloodNet RHD-DG was prepared with the contribution of subnetwork coordinators and other experts in the field. This first version was discussed at the ERN-EuroBloodNet 3rd Board of Network meeting held on 13-14 November 2019 in Barcelona. During the parallel session dedicated to cross border health, the audience was divided into oncological and non-oncological working groups for practical discussion of:

a) RHD-DG proposal
b) Identification of those RHD-DG that, according to the experts, mapping of expertise is required given the specifity of the requirements for their diagnosis or management.
c) Definition of KPIs for those RHD-DG requiring monitoring, including:
    a. Minimum number of adult patients followed by the Healthcare provider
    b. Minimum number of new adult patients per year followed by the Healthcare provider
    c. Minimum number of pediatric patients followed by the Healthcare provider
    d. Minimum number of new pediatric patients per year followed by the Healthcare provider

Task 2. Upgrade of ERN-EuroBloodNet repository of members and experts for the monitoring of members activity

In line with the EC strategy for the monitoring of rare disease patients population, HCPs have to provide data on the number of patients followed every 6 months. So far, these monitoring exercises have been performed through Excel templates prepared by the coordination team indicating:

- Subnetworks covered by the HCP
- Number of patients and Number of new patients by Disease/diseases groups the HCP reported in the ERN application (2016)
- Number of patients and Number of new patients by Disease/diseases groups the HCP reported in the monitoring exercises already performed
- Cells dedicated to report the Number of patients and Number of new patients by Disease/diseases groups for the monitoring period

The upgrade of the ERN-EuroBloodNet inventory of members and experts will allow the direct reporting by the members through a dedicated application form available in their profiles avoiding the monitoring via excels files. To this aim, the following technical upgrades have been implemented:

2.1 Implementation of Rare hematological diseases - disease groups at the back office

In parallel to the definitions of the RHD-DG, the website developers implemented a tool at the back office of the inventory that allowed the coordination team to create the RHD-DG "boxes" for the inclusion of the different RHD ORPHA entities already implemented in the website.

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2.2 Creation of "HCPs Subnetwork coordinators" user role

The user role "HCP Subnetwork coordinator" was designed as those Experts profiles with authorization to report the HCP activity. In this way, if an HCP covers the Myeloid subnetwork and Red blood cell subnetwork, the HCP shall assign at least two "HCP Subnetworks coordinators" for the reporting of monitoring process.

In parallel to the technical implementation, the coordination team contacted ERN-EuroBloodNet members representatives and substitutes in order to create the list of HCPs Subnetworks coordinators.

2.3 Implementation of "Statistics" section for reporting KPIs

ERN-EuroBloodNet inventory of members and experts profiles have different sections for the edition of the information gathered:

- Professional information: Accessible by all the Experts to complete their personal profiles
- Healthcare providers: Information on the HCPs, only editable by members representatives and substitutes
- Departments: Information on the departments linked to the HCPs for the management of RHDs. Only editable by members representatives and substitutes
- Invite: Section for the possibility to have invitations to create the Expert profile to colleagues from their HCPs. Only accessible to members representatives and substitutes.

In order to allow the direct reporting of HCPs activity, a new section was designed to gather the following KPIs by RHD-DG and period of reporting:

- Number of New adultand Total adult patients
- Number of New pediatric and Total pediatric patients
- Number of New diagnostics and Total diagnostics procedures

This section will be only accessible to the HCPs subnetworks coordinators.

Task 3. Identification of Highly Specialized Procedures for European Mapping

A first approach for the identification of other HSP candidates for a mapping exercise and monitoring through ERN-EuroBloodNet members was performed taking advantage of the 3rd ERN-EuroBloodNet Board of Network meeting.

During the parallel session dedicated to cross border health, the audience was divided into oncological and non-oncological working groups for practical discussion of

a) Identification of HSP that experts consider essential to be mapped given inequalities on their availability across MS found.
b) Definition of KPIs for their monitoring, including number of minimum procedures performed to be consider an expert.

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4. RESULTS

LINKED TO TASK 1. RARE HEMATOLOGICAL DISEASES - DISEASE GROUPS DEFINITION FOR MONITORING OF MEMBERS ACTIVITY

1.1 ANALYSIS OF CODIFICATION SCHEMES: ORPHANET AND ICD

Revision and update for ORPHA Classification on Hemochromatosis and other rare genetic disorders of iron metabolism and heme synthesis subnetwork

7 new codes related to HH and other rare genetic disorders of iron metabolism and heme synthesis subnetwork were created for their inclusion at the back office at the ERN-EuroBloodNet website. Nevertheless, discussion among experts have continued during this period in order to reach an agreement on the final consensus to be submitted to Orphanet and subsequently to ERN-EuroBloodNet website.

Based on this discussion, an update on the first classification has been produced including the integration of porphyrias (defects of heme synthesis) and ferritinopathies (they are in the differential diagnosis of hypoferritinemias) and taking into consideration the following important aspects:

1) One of the points of concern was the use of the ORPHA classification of “symptomatic form” of HFE related hemochromatosis (Orpha code 465508). This term was created in order to respond to the issue of HH type 1 not being considered a rare disease because of the high prevalence of the genetic variant. The term, however, is unfortunate because there may be tissue damage “without” symptoms, and symptoms are not criteria to define the disease. The new proposal aims to simply remove the term “symptomatic form” and be sure that, in the info page a good reference be made about the low penetrance of the disease and the fact that the real prevalence is still unknown.

2) Agreement on separating hereditary hemochromatosis for the FTH related hereditary HH, or type 4B, and Ferroportin Disease to the type 4A, in two different primary level classifications. At the moment, covered by the same come either in OMIM or ORPHA classification.

3) Agreement among experts on no separating HH due to rare mutations in HFE as a different entity since the phenotype and pathophysiology are the same.

4) Agreement on substituting the term “non-HFE” by the respective mutated genes in order to avoid the mistaken indications included in the OMIM classification, which is indeed a major change in the nomenclature.

5) Concerns regarding the existence of HH type 5. There is a single family described in which a single mutation in H-ferritin was observed in the proband and two hyperferritinemic siblings, and in a 28 year daughter with normal ferritin. Clinical study in relatives was limited (no information on transferrin saturation, or evidence of iron overload) as well as genetic analysis that only tested mutations in HFE and TFR2 without excluding other genes. Nevertheless, animal studies suggest it may exist so at this stage it is included in the classification for further discussion.

6) Ferritinopathies due to ferritin deficiencies have been included as they constitute differential diagnosis for rare causes of low ferritin levels. These include L-ferritin deficiency (also in ERN-RND and in EpiCare) and Neurodegeneration with Brain Iron Accumulation 3 (NBIA3; 606159; also in ERN-RND).

7) Porphyrias have been also included as they belong to the group of pathologies of heme synthesis. Of course they are also considered in other ERNs such as RARE-LIVER, RARE-SKIN and ERN-RND.

Discussions among experts have continued during this period in order to reach an agreement on the final consensus to be submitted to Orphanet and subsequently to ERN-EuroBloodNet website.

Correlation between ORPHA and ICD on Lymphoid malignancies

As result of the ORPHA and ICD correlation on Lymphoid malignancies, a total of 106 terms were analyzed with the following results:

- 3 disparities were found:
  - Erdheim-chester disease: not classified as a rare hematological disorder according to ORPHA classification
  - AL amyloidosis / Castleman disease: not classified as a hematological disorder according to ICD classifcation
- 6 GAPs were found in ICD-10, all of them for non-malignant haematological disorders
- 23 GAPs were found in ORPHA classification

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Results show important gaps and disparities and the need for harmonization among both schemes. A proposal will be sent to ORPHANET / WHO teams as a comprehensive ERN-EuroBloodNet document on codification schemes for identification of RHD.

1.2 Rare hematological diseases - disease groups definitions

As a result of the revision and discussion of the RHD-DGs during the Board of the Network meeting, a total of 70 RHD-DG has been identified, as follows:

- Red blood cell defects: 10 disease groups encompassing 59 disorders
- Bone marrow failure and hematopoietic disorders: 12 disease groups encompassing 42 disorders
- HH and other rare genetic disorders of iron metabolism and heme synthesis: 11 disease groups encompassing 29 disorders
- Rare bleeding-coagulation disorders and related diseases: 9 disease groups encompassing 70 disorders
- Lymphoid malignancies: 19 disease groups encompassing 98 disorders
- Myeloid malignancies: 9 disease groups

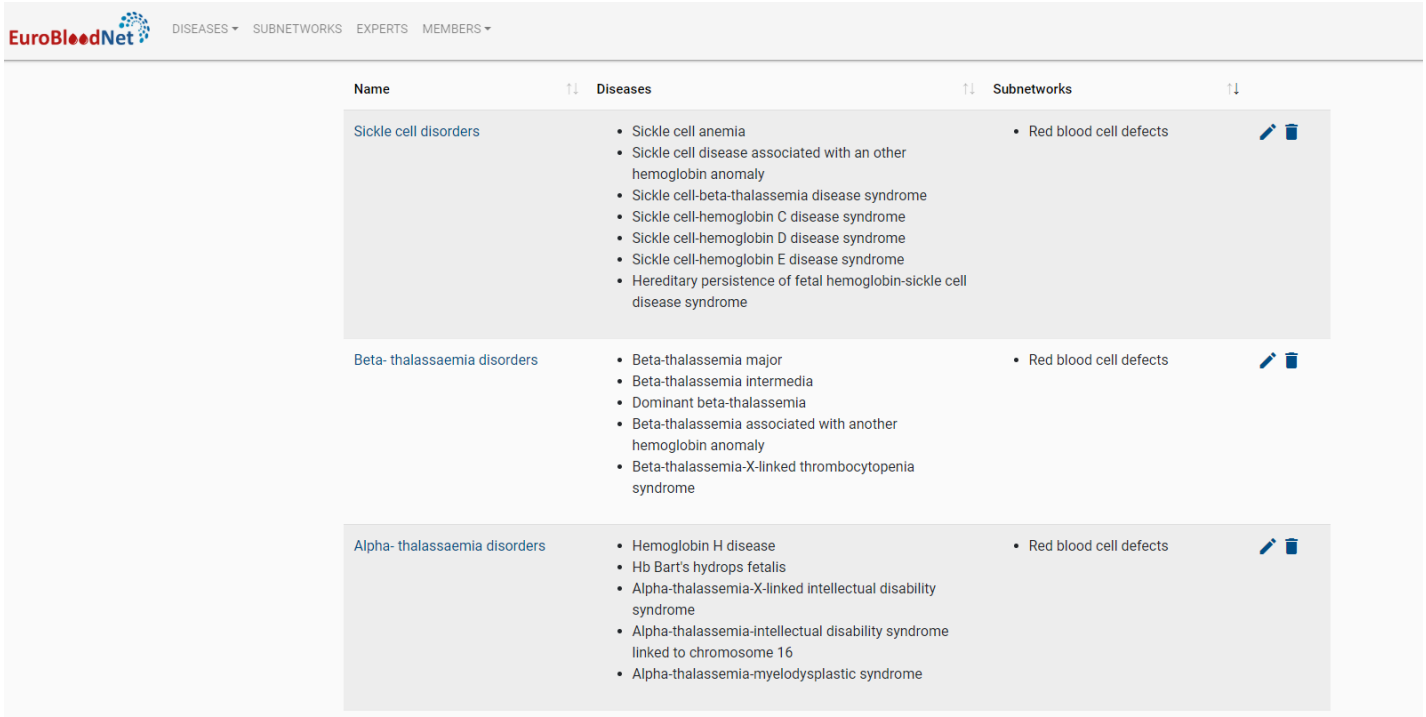
RHD-DGs and disorders included under each group are available at Cross Border health section in ERN-EuroBloodNet website.

Discussions for the identification of RHD-DG needing to be monitored through the gathering of KPIs is still ongoing.

Linked to task 2. Upgrade of ERN-EuroBloodNet repository of members and experts for the monitoring of members activity

2.1 Implementation of Rare hematological diseases - disease groups at the back office

The back office tool implemented by the Web developers for the creation of the disease groups allowed their linkage to a) the specific subnetworks and b) the diseases encompassed. The 70 disease groups identified were implemented by the coordination team as follows:



Name	Diseases	Subnetworks
Sickle cell disorders	• Sickle cell anemia • Sickle cell disease associated with an other hemoglobin anomaly • Sickle cell-beta-thalassemia disease syndrome • Sickle cell-hemoglobin C disease syndrome • Sickle cell-hemoglobin D disease syndrome • Sickle cell-hemoglobin E disease syndrome • Hereditary persistence of fetal hemoglobin-sickle cell disease syndrome	• Red blood cell defects
Beta- thalassaemia disorders	• Beta-thalassemia major • Beta-thalassemia intermedia • Dominant beta-thalassemia • Beta-thalassemia associated with another hemoglobin anomaly • Beta-thalassemia-X-linked thrombocytopenia syndrome	• Red blood cell defects
Alpha- thalassaemia disorders	• Hemoglobin H disease • Hb Bart's hydrops fetalis • Alpha-thalassemia-X-linked intellectual disability syndrome • Alpha-thalassemia-intellectual disability syndrome linked to chromosome 16 • Alpha-thalassemia-myelodysplastic syndrome	• Red blood cell defects

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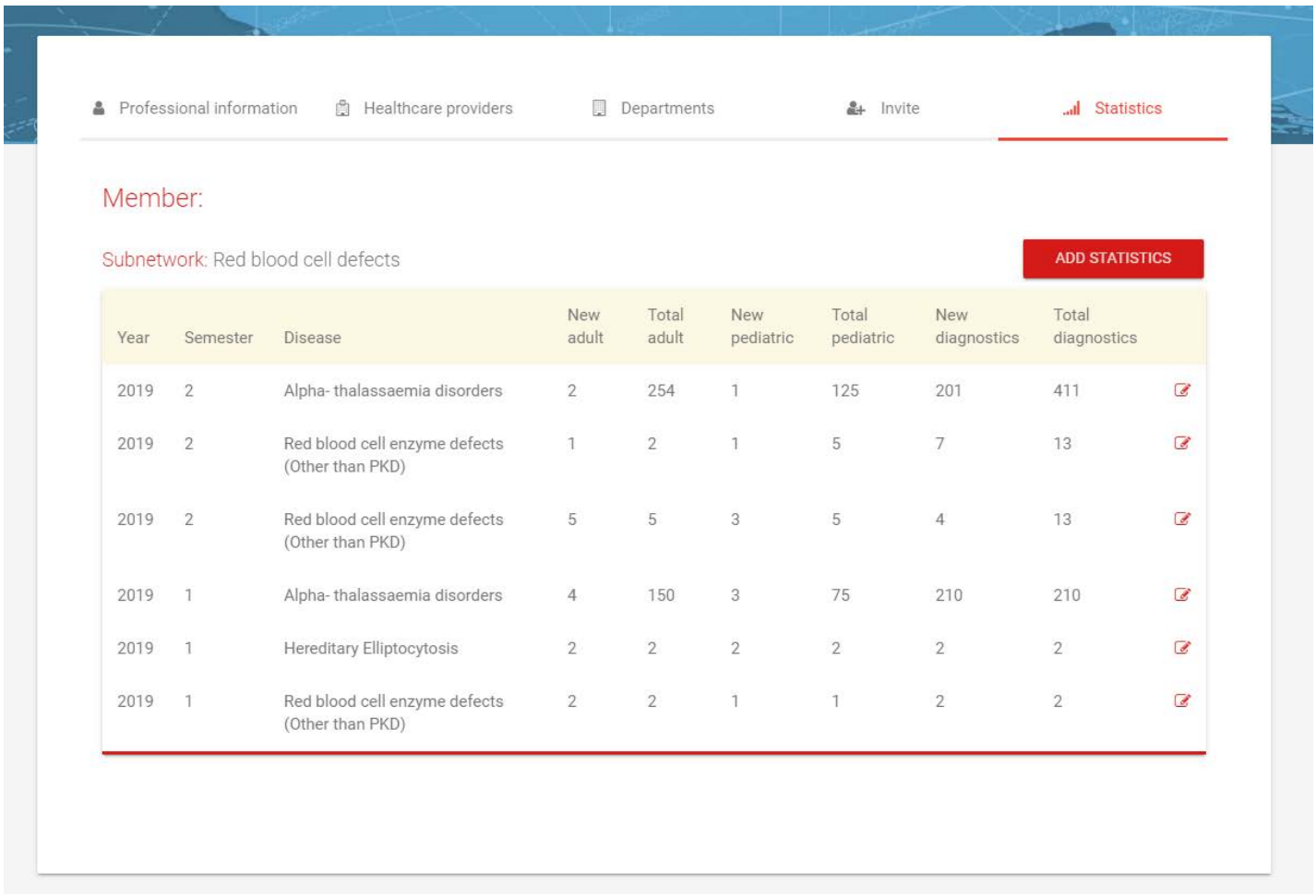
2.2 Creation of "HCPs Subnetwork coordinators" user role

The role of "HCP Subnetwork coordinator" was implemented at the back office of the inventory, allowing the coordination team to assign the role to the specific subnetwork identified by the HCPs representatives and substitutes:

The list of HCPs Subnetworks coordinators was compiled by the coordination team with the feedback from members representatives and substitutes.

2.3 Implementation of "Statistics" section for reporting KPIs

The section "Statistics" has been implemented in the Experts profiles with the role of "HCPs subnetwork coordinator" application form to report the period of monitoring, disease group, number of patients and diagnostic procedures as follows:



Year	Semester	Disease	New adult	Total adult	New pediatric	Total pediatric	New diagnostics	Total diagnostics
2019	2	Alpha- thalassaemia disorders	2	254	1	125	201	411
2019	2	Red blood cell enzyme defects (Other than PKD)	1	2	1	5	7	13
2019	2	Red blood cell enzyme defects (Other than PKD)	5	5	3	5	4	13
2019	1	Alpha- thalassaemia disorders	4	150	3	75	210	210
2019	1	Hereditary Elliptocytosis	2	2	2	2	2	2
2019	1	Red blood cell enzyme defects (Other than PKD)	2	2	1	1	2	2

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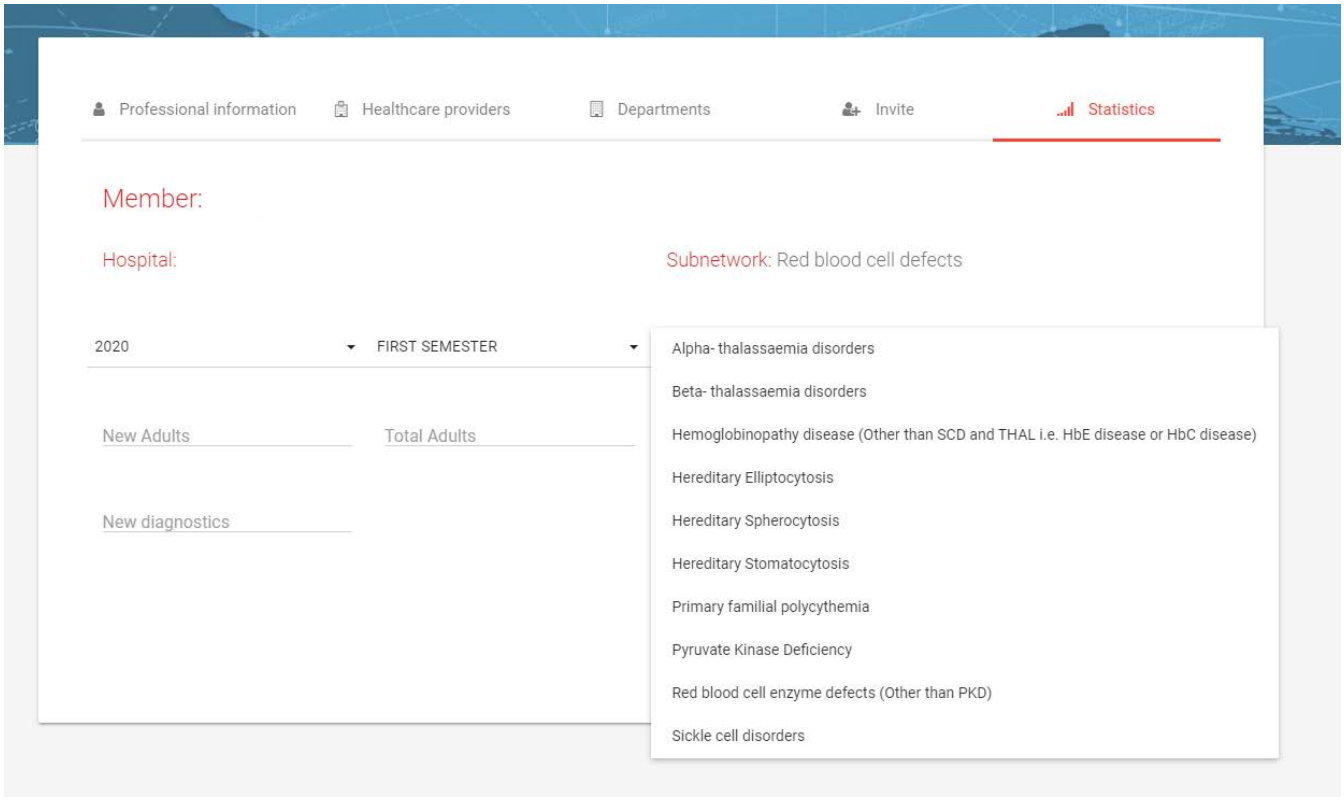
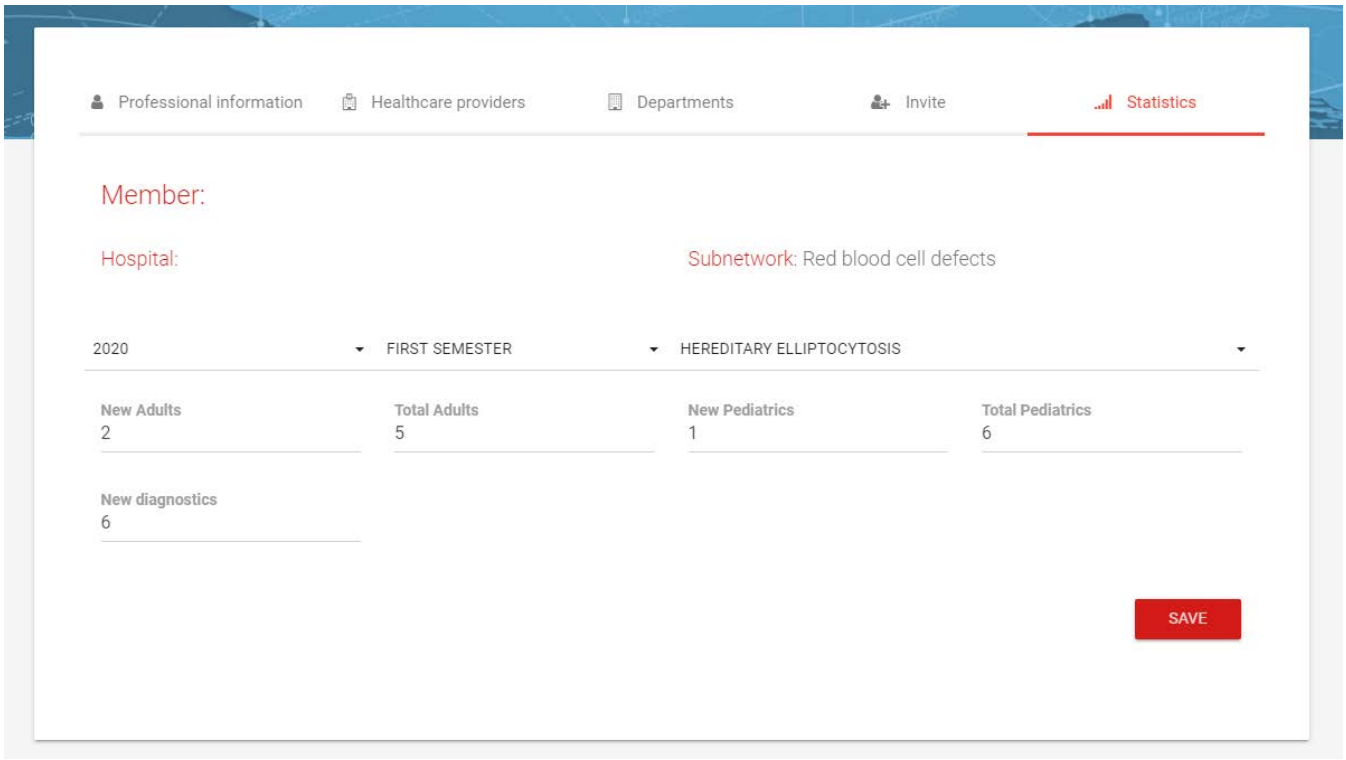
In order to facilitate the reporting, it is only possible to include the numbers for the subnetwork to which the expert is linked. In addition, the selection of the RHD-DGs to be reported is selectable from a list filtered by the given subnetwork.





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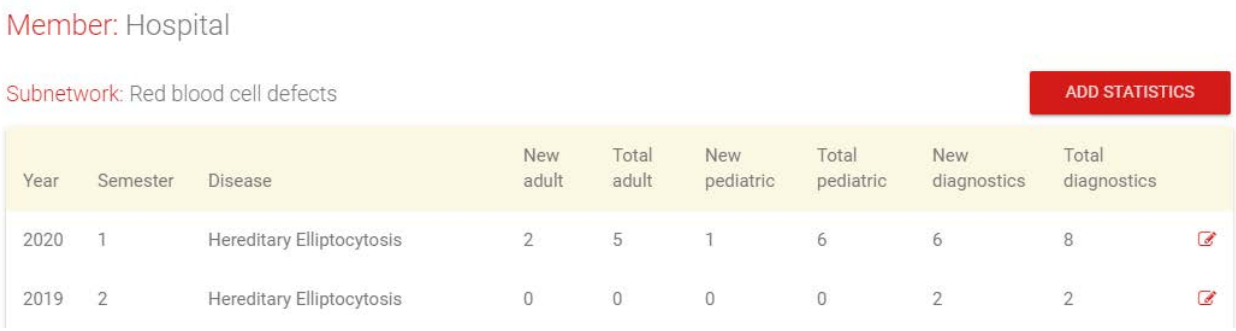
The number of total diagnostics is automatically calculated with the summatory of the previous numbers introduced and the new numbers reported



Year	Semester	Disease	New adult	Total adult	New pediatric	Total pediatric	New diagnostics	Total diagnostics	
2020	1	Hereditary Elliptocytosis	2	5	1	6	6	8	
2019	2	Hereditary Elliptocytosis	0	0	0	0	2	2	

The "Statistics" section is already programmed and is currently being tested by the coordination team for potential improvements on its visualization.

LINKED TO TASK 3. IDENTIFICATION OF HIGHLY SPECIALIZED PROCEDURES FOR EUROPEAN MAPPING OF AVAILABILITY

During the 3rd Board of Network meeting HSP that are only available in members and not always available at the national level were discussed among the audience as potential targets of Cross border health were discussed.

Besides de on-going projects on European mapping of availability for BMT and NGS for non-oncological disorders, new HSP for mapping were proposed:

- Non-oncological: European mapping on availability of
  - Transcranial Doppler for SCD
  - T2*MRI for assessment of iron overload for beta- thalassaemia
  - Gene therapy for beta – thalassaemia.
- Oncological: European mapping on availability of:
  - CAR-T cell therapy
  - Diagnostic procedures, treatment and follow-up of primary intra-ocular lymphomas

KPIs linked to specific aspects of HSP identified will be defined and implemented in the members profiles for their monitoring and analysis of facilities available / needs at the national level.

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5. CURRENT STATE OF THE ERN-EUROBLOODNET INVENTORY OF MEMBERS AND EXPERTS

A total of 254 experts have already created their profiles in the ERN-EuroBloodNet directory, including both members representatives and substitutes and experts invited by them. 173 of them have fulfilled completely their profiles while the rest is in progress.

With the aim to integrate the relevant data introduced so far in the ERN-EuroBloodNet directory of members, the results reported in this deliverable are focused on the profiles completely fulfilled.

Comparing to previous year, a total of 7 new profiles have been created. However it is normal considering the remarkable expansion achieved in the previous period of network implementation (70 new profiles).

Results of the number of experts by Member State dealing with oncological or non-oncological subnetworks are shown in table 1. In addition, the specific subnetworks by Member State are detailed in Figure 1.

MS	Experts	Non-Onc	Onc
BE	**10**	8	3
BG	**1**	1	
CY	**15**	15	
CZ	**1**		1
DE	**2**		2
ES	**5**	5	
FR	**30**	23	7
GB	**14**	9	5
IE	**1**	1	
IT	**63**	45	21
LT	**2**	1	1
NL	**16**	15	1
PL	**4**		4
PT	**5**	4	1
SE	**4**	4	
Total	**173**	**131**	**46**

Table 1. Number of experts dealing with non-oncological and oncological subnetworks by Country

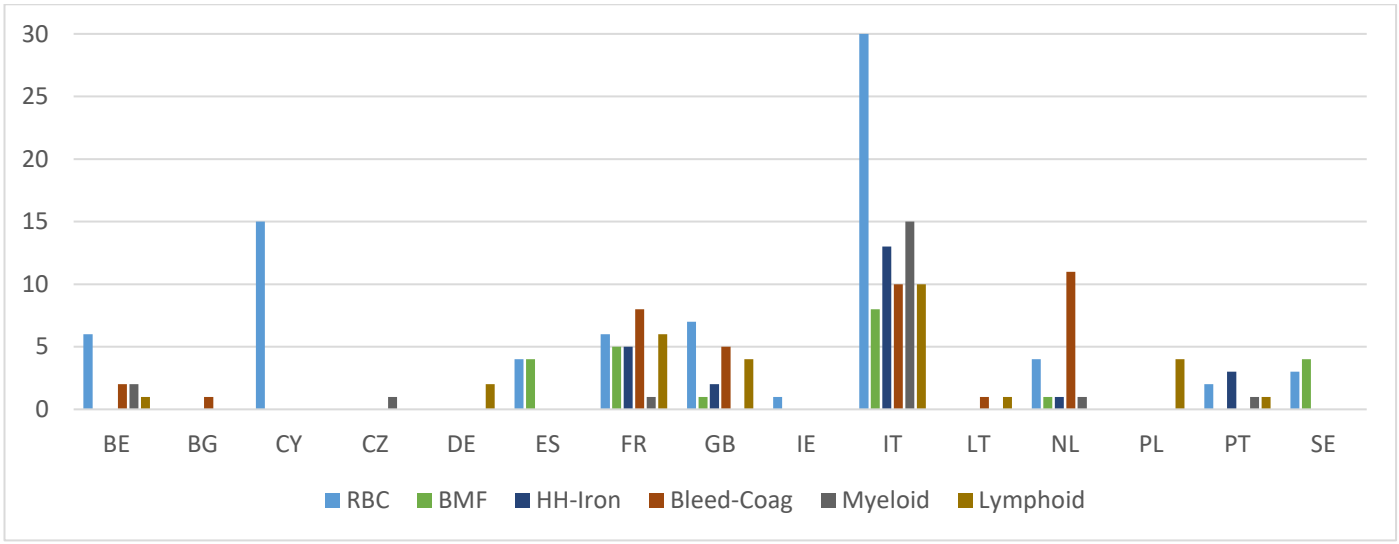

Fig 1. Number of experts by subnetwork and country. Subnetworks: Red blood cell disorders (RBC), bone marrow failures (BMF), Haemochromatosis and iron defects (HH-Iron), bleeding and coagulation (Bleed-Coag), Myeloid malignancies and lymphoid malignancies

In line with the results from the previous year, Italy is the country with the highest number of experts in the ERN-EuroBloodNet inventory, which is normal taking into consideration that the number of Italian members is the highest in ERN-EuroBloodNet (21 from 66 members). Also their involvement in the Red Blood Cell disorders subnetwork, together with the high number of experts in Cyprus for this subnetwork, is logic since Thalassaemia is endemic in the Mediterranean area and the prevalence of this disorder belonging to the red blood cell subnetwork is very high comparing to non-endemic areas.

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On the other hand, attending to the area of expertise of the experts fulfilling the profiles, some differences can be observed among the oncological and non oncological hub. Figure 2 shows the percentage of experts based on their expertise and hub.

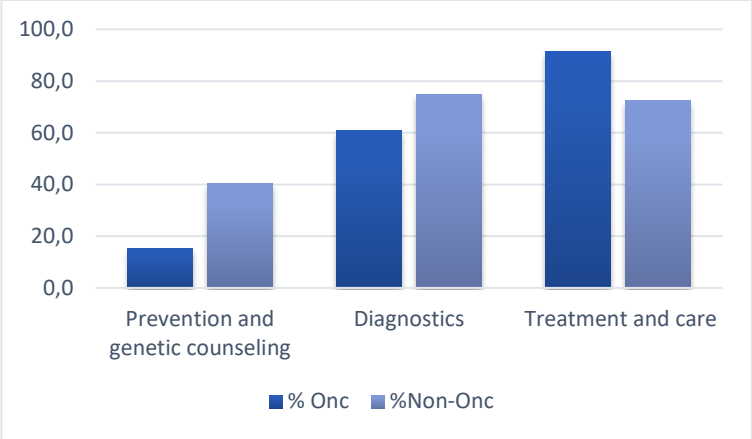

Fig 2 Percentage of experts by their area of expertise and dedicated hub

When focusing on the oncological diseases the trends has been maintained with regards to data from previous year in the area of treatment and care, being almost 100% of the health professionals involved. On the other hand, the percentage of diagnostics field has decreased from to 63% to 60,9% of the experts devoted to this area and in the prevention and genetic area from 16% to 15,2%.

When analyzing the non-oncological hub, it is remarkable that the new experts included in the inventory have caused that the percentage of professionals dealing with diagnostics decreased from 76% to 74,8%, while the treatment and care has decreased from 76% to 72,5%, making almost equal the number of experts in both fields. The number of experts in the prevention and genetic counselling has been maintained with regards to the previous year, which could be explained due to the more preventive character of these disorders in comparison with the oncological diseases.

Experts filling their profiles are also able to select their patients' age coverage. Figure 3 shows the percentage of experts dealing with children, adults or aged people by hub.

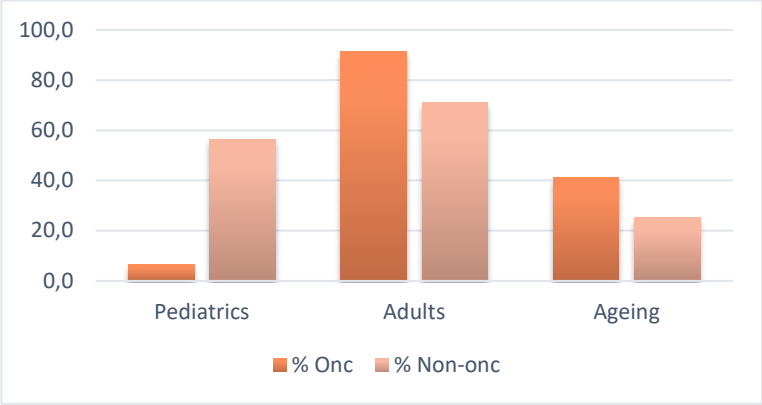

Fig 3 Percentage of experts by the patients' age dealing with and dedicated hub

The trends of this figure has been maintained with compared to previous year. Also, it is important to clarify that the low number of experts from the oncological hub dealing with pediatrics is given since the oncological diseases in children are out of the scope of our ERN, however these experts declared to deal with pediatrics, adults and ageing.

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6. EXPECTED OUTCOMES & NEXT STEPS

ERN-EuroBloodNet mapping of healthcare services in Rare Hematological Diseases (RHDs) and its monitoring based on key performance indicators (KPIs) is cornerstone for setting the basis for a European model of networking. They rely on a validated identification of experts and Highly specialized procedures (HSP) at both the national and European levels. It also arises the need for cross border health based on existing gaps in certain Member State for clinical management of a specific condition while allows health planning and better allocation of resources.

Making this expertise public through ERN-EuroBloodNet members' profile allows the establishment of **new bridges for collaboration** not only among experts but also with other European bodies such as EMA while enabling health professionals and patients seeking for best healthcare services across Europe. The **EuroBloodNet mapping of healthcare services** in RHD will also provide valuable information for identifying needs on best practices, continuing medical education and clinical and translational research. In addition, the **incorporation of KPIs** on patients' activity and HSPs will also contribute to the EC assessment of network and members' excellence.

Through this activity ERN-EuroBloodNet aims to build **a central repository of reliable sources** of information on expertise available at both national and European level in RHDs. To this aim, RHDs have been grouped into disease or disease groups (RHD-DGs) based on the analysis of codification schemes (ORPHA and ICD) for definition of rare diseases. **Disparities and gaps identified** will be reported to corresponding bodies.

RHD-DGs will be used for 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.

Based on the results from this period of implementation, the following next steps are foreseen:

1. Following the disparities and gaps identified in the correlation between ORPHA and ICD on Lymphoid malignancies, a proposal will be sent to ORPHANET / WHO teams as a comprehensive ERN-EuroBloodNet document on codification schemes for identification of RHD.
2. Final improvements of the "Statistics" section for the direct reporting of ERN-EuroBloodNet members activity are foreseen before its release to the members. Once the "Statistics" section will be ready the HCPs subnetworks coordinators identified will be invited to create their profiles (if they do not have it created yet) and assigned with the role at back office for the reporting of activity.
3. The activity reported in the ERNs application in 2016 and on the last monitoring exercises will be transferred to the back office for having the whole analysis of members activity in recent years.
4. The ERN-EuroBloodNet inventory will be upgraded for the inclusion in the members profiles of KPIs linked to specific aspects of HSP identified for the mapping for identify both the needs and the opportunities for a better allocation of resources, establishment of cross border agreements and promotion of networking for better delivery of care and engagement of clinical research.
5. Creation of experts profiles for the recent incorporation of Affiliated partners is envisaged for the next period of implementation.

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European Reference Networks

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

European Reference Network
for rare or low prevalence complex diseases
Network Hematological Diseases (ERN EuroBloodNet)

www.eurobloodnet.eu

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