ERNs EVALUATION RESULTS REPORT

Independent Evaluations of European Reference Networks and of Healthcare Providers

Contract No HADEA-2022-P3-04

Report submitted by the Consortium:

IDOM, Consulting, Engineering, Architecture, S.A.U.

and Fundación Pública Andaluza Progreso y Salud

EUHealthSupport Consortium

October 2024

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Independent evaluation of European Reference Networks (ERNs) and of Healthcare Providers (HCPs)

Final Report
October 2024

Specific Contract No HADEA-2022-P3-04 in the context of the Implementing Framework Contract HADEA/2021/OP/0012

Written by the Consortium IDOM, Consulting, Engineering, Architecture, S.A.U. and Fundación Pública Andaluza Progreso y Salud

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Manuscript completed in October 2024

LEGAL NOTICE

EN PDF	ISBN 978-92-95239-24-1	DOI: 10.2925/6609809	HW-01-24-014-EN-N

Luxembourg: Publications Office of the European Union, 2024

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ACRONYMS

ACSA	Agencia de Calidad Sanitaria de Andalucía
BoMS	Board of Member States
CPMS	Clinical Patient Management System
CV	Curriculum Vitae
DG SANTE	Directorate-General for Health and Food Safety
ERN	European Reference Network
EC	European Commission
EHDS	European Health Data Space
ePAG	European Patient Advocacy Group
EU	European Union
FAD	Fundación Avedis Donabedian
FAQ	Frequently Asked Questions
FwC	Framework Contract
HaDEA	European Health and Digital Executive Agency
HCP	Healthcare Provider ERN member
IEB	Independent Evaluation Body
ME	Measurable Element
NC	Network Coordinator
NHS	National Health System
OEIT	Online Exchange Information Tool
WP	Work Packages

Project Identification Sheet

CONTRACT TITLE	Independent evaluation of European Reference Networks (ERNs) and of Healthcare Providers (HCPs)
SPECIFIC SERVICE CONTRACT	No HADEA-2022-P3-04
FRAMEWORK CONTRACT	No HADEA/2021/OP/0012
START DATE	9 November 2022
END DATE	8 December 2023
CONTRACTOR	IDOM, Consulting, Engineering, Architecture, S.A.U. (Spain). Leader Fundación Pública Andaluza Progreso y Salud (partner)
CONTRACTING AUTHORITY	Health and Digital Executive Agency, HaDEA
CONTRACT VALUE	€3,705,908

Abstract

The following report is a comprehensive evaluation of European Reference Networks (ERNs) and its members, the Healthcare Providers (HCPs), across Europe, focusing on their role in addressing complex and rare conditions. 24 ERNs and 836 HCPs from 24 EU Member States and Norway participated in the evaluation. The evaluation included self-evaluations, document reviews, ERN interviews, on-site HCP audits and stakeholder interviews.

The results showed a high level of commitment of ERNs to their objectives, with a significant proportion, 100% of ERNs and 89.7% of their members, achieving satisfactory results in the evaluation. Strengths were identified in the areas of Education and Training, Networks and Dissemination, Competence, Experience, and Patient-centred care, while Quality and Patient Safety, and Organization and Management are areas for improvement for both, ERNs, and HCPs respectively.

This report, drawing on a wide range of data, increases the understanding of the essential role of the ERN system in addressing rare diseases and conditions across Europe. It also presents relevant information on the structure, maturity, activity, and impact of the ERN system, and identifies opportunities for improvement based on the findings of the stakeholder interviews and the evaluation to further enhance the evaluation process and ensure the continued sustainability of the ERN system. The information and views set out in this report are those of the Independent Evaluation Body and do not necessarily reflect the official opinion of the Commission/Executive Agency.

Une évaluation complète des réseaux européens de référence (ERN) et de leurs membres, les unités de soins de santé (HCP) en Europe, axée sur leur rôle dans le traitement des maladies complexes ou rares, a couvert 24 ERN et 836 HCP dans 24 États membres de l'UE et en Norvège. Cette évaluation a inclus des auto-évaluations, des examens de documents, des entretiens, des audits sur site et des enquêtes auprès des parties prenantes.

Les résultats révèlent un fort engagement des ERN et des HCP envers leurs objectifs, avec un pourcentage notable – 100% des ERN et 89.7% des HCP – atteignant des résultats satisfaisants dans l'évaluation. Des points forts ont été identifiés dans l'éducation et de la formation, des réseaux et de la diffusion, de la compétence, de l'expérience et des soins centrés sur le patient, tandis que la qualité et la sécurité des patients, ainsi que l'organisation et la gestion, constituent des domaines à améliorer pour les ERN et les HCPs, respectivement.

Ce rapport, fondé sur de données diverses, améliore la compréhension du rôle vital du système ERN dans la lutte contre les maladies rares en Europe Il relève également des informations cruciales sur la structure, la maturité, l'activité et l'impact du système ERN, offrant des possibilités d'amélioration basées sur les entretiens avec les parties prenantes et de l'évaluation visent à affiner le processus d'évaluation et garantir la soutenabilité du système ERN.

Executive summary

INTRODUCTION

European Reference Networks (ERNs) are virtual networks that aim to improve the diagnosis, treatment, and care of patients with rare or complex diseases. They are networks of specialized clinical units of healthcare providers (HCPs) from across Europe, enabling the exchange of knowledge and highly specialized resources across borders. The networks cover a wide range of diseases, including cranioencephalic and metabolic disorders, childhood cancer and rare epilepsies, and serve a large number of patients at European level.

The network system is complex, involving 24 ERNs, around 1.600 HCP members, around 400 European Patient Advocacy Group (ePAG) advocates, numerous Affiliated Partners, and the designated representatives of the Member States and the European Commission. To ensure the system runs smoothly, it is essential for these actors to cooperate and maintain interoperability.

The Commission Implementing Decision 2014/287/EU[1] provides for the evaluation every five years of their performance and contribution to patient care. The objective of this evaluation is to assess compliance with the criteria and conditions set out in Delegated Decision 2014/286/EU[2], the degree of achievement of the objectives set out in Article 12(2) of Directive 2011/24/EU[3] and the results and performance of ERNs and the contribution of HCPs.

The IDOM-ACSA consortium was selected by the European Commission through a tender process as the Independent Evaluation Body (IEB) for the development of the first evaluation of 24 ERNs and 836 HCPs in 261 hospitals in 24 EU Member States and Norway.

This report - D.6.2.3 Results of the evaluation of the ERNs - presents a comprehensive overview of the findings and conclusions following the first evaluation exercise since the launch of the ERNs.

METHODOLOGY

The evaluation process and methodology has been carried out under the guidelines specified in the Evaluation Manual[4] and Evaluation Technical Toolbox[5], according to the Commission Implementing Decision 2014/287/EU. The evaluation process took 10 months in total, starting in December 2022.

The methodology is based on the verification of the operational criteria established for ERNs and HCPs, comprising a self-assessment by ERNs and HCPs, the review of the documentation provided by the

[1] 2014/287/EU: Commission Implementing Decision of 10 March 2014 setting out criteria for establishing and evaluating European Reference Networks and their Members and for facilitating the exchange of information and expertise on establishing and evaluating such Networks. Available at: https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=OJ:JOL_2014_147_R_0007

[2] 2014/286/EU: Commission Delegated Decision of 10 March 2014 setting out criteria and conditions that European Reference Networks and healthcare providers wishing to join a European Reference Network must fulfil Text with EEA relevance. Available at: https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=OJ:JOL_2014_147_R_0006

[3] Directive 2011/24/EU of the European Parliament and of the Council of 9 March 2011 on the application of patients' rights in cross-border healthcare. Available at: https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=celex:32011L0024

[4] Evaluation Manual for the ERNs evaluation. Available at: https://health.ec.europa.eu/document/download/4cff3905-7e55-46b3-8fb6-4e62a3d263f4_en?filename=erns_evaluation_manual_en.pdf

[5] Technical Toolbox for the ERNs evaluation. Available at: https://health.ec.europa.eu/document/download/d8fe72ce-94dd-4f98-8311-2ea7ab3b4e2d_en?filename=erns_evaluation_toolbox_en.pdf

evaluators, the execution of 24 interviews with the ERN coordination teams and a selection of ePAGs advocacies, the execution of 193 audits in a selection of HCPs and the resolution of comments on the preliminary results.

During the different stages, a team of 179 evaluators has verified the level of compliance with a series of aspects or Measurable Elements for the evaluation of the following areas:

Areas evaluated in the ERNs

1. *Governance and coordination:* The structural framework of the ERN is reviewed, to ensure effective coordination and monitoring. The governance set-up of the network is verified, including the regular assessment of the progress of the ERN, the involvement of patient organisations in strategic actions and the measures taken for long-term sustainability.
2. *Clinical care:* The ERN's approach to advising on clinical practice is evaluated, reviewing the adaptation and dissemination of clinical practice guidelines, care pathways and best practices. In addition, the implementation of a multidisciplinary approach to care and the integration of e-health tools into care is assessed.
3. *Quality and patient safety:* The ERN's strategy is evaluated to ensure quality of care and patient safety. The strategies defined to promote quality are reviewed, as well as the monitoring of indicators to track clinical performance and ensure positive outcomes of care within the network.
4. *Patient-centred care:* Emphasis is on patient empowerment and patient involvement in the ERN. The mechanisms in place to educate and involve patients are considered, as well as the strategies to engage patients in decision-making processes, and measures taken to measure and learn from patients' experience.
5. *Contribution to research:* The contribution of the ERN to medical science and research is evaluated. A review is carried out of the strategic actions to fill research gaps, promote innovation, establish collaborative research frameworks, and strengthen epidemiological surveillance through shared registries and databases at European level.
6. *Education and training:* The ERN's efforts to identify and address gaps in education, training, and professional development are reviewed to assess the extent to which the Network is improving educational activities and opportunities for health professionals within and outside the ERN.
7. *Networking and dissemination:* The ERN's networking capacity is assessed, looking for the existence of good systems for collaboration, knowledge sharing and resource pooling. In addition, the strategies for the dissemination of referral information between Member States and the efforts to share knowledge within and outside the ERN itself are examined.

Areas evaluated in HCPs

1. *Patient-centred care:* The evaluation addresses the prioritisation of patients' needs, while respecting their rights and preferences. This includes education programmes, clear information, the use of patient feedback, informed consent, transparency in the provision of information, pain management protocols, and collaboration with patient organisations.
2. *Organisation and management:* The efficient structuring and management of services is reviewed, especially for cross-border patients. The evaluation looks at the establishment of fee-for-service policies, coordination with other units, integration into national networks, use of the Clinical Patient Management System (CPMS), and implementation of effective communication strategies.
3. *Research, education, and training:* The participation of the HCP in education and training activities, both for patient care and research, is examined. In addition, the verification aims to ascertain the contribution of the HCP to the research activities of the ERN, the dissemination of the results of their research activities and clinical trials, and the inclusion of data in the registries or databases maintained by the ERN.

4. *Exchange of expertise, Information systems, and e-Health:* The capacity of the HCP to provide knowledge and support to other HCPs is evaluated. The degree of implementation of e-health tools and the alignment of the clinical information coding system with the national and international standards proposed by the ERN is also addressed.
5. *Quality and safety:* The monitoring and improvement of the quality of care and patient safety provided by the HCP is evaluated. Adherence to clinical practice guidelines disseminated by the ERN is also assessed.
6. *Competence, experience, and outcomes of care:* The evaluation examines whether the HCP is maintaining an established level of activity that demonstrates clinical competence in order to provide optimal care and outcomes within the network.
7. *Human resources:* The evaluation assesses whether the professionals who form part of the unit's team have the necessary competencies to provide comprehensive care through a multidisciplinary and specialised approach, guaranteeing a high quality of healthcare provision.

To test the preliminary results, the IEB conducted 24 additional interviews with selected stakeholders (ERNs, HCPs, evaluators, EURORDIS representatives and BoMS representatives). Additional information, suggestions and comments were also collected through online questionnaires sent to all HCPs, ERNs and ePAGs.

RESULTS

The main conclusions that can be drawn after an extensive exercise of aggregate analysis are the following:

- With 100% of ERNs and 97.61% of HCPs completing the self-assessment, both have demonstrated a high level of commitment to the assessment process.
- 100% of ERNs and 87.68% of HCPs achieved a satisfactory result, demonstrating a high commitment to the criteria set for ERNs and HCPs.
- Of the 84 HCPs with unsatisfactory results, 72 have submitted an improvement plan and have one year to implement the proposed actions, which represents 8.61% of the total 836 HCPs.
- 31 HCPs of the 836 under evaluation (corresponding to 3.71%) had their membership terminated as follows:
    - 16 HCPs have had their membership terminated by BoMS decision due to non-completion of the self-evaluation.9 HCPs out of the 84 that did not perform satisfactorily have had their membership terminated by the BoMS due to the non-submission of the improvement plan.6 HCPs have voluntarily withdrawn from the ERN to which they belonged during the evaluation process.

Importantly, all ERNs have successfully met the selected targets, which are set out in Article 12(2) of Directive 2011/24/EU, with most being rated as excellent and none below a poor or deficient standard.

Of the common thematic areas, which have been assessed for both ERNs and HCPs, *Education and training* was the area that received the highest average score for both.

Of the thematic areas that have been evaluated specifically for ERNs, *Networking and Dissemination* has received the best average score. However, there are other aspects that stand out in other areas. This is the case of the establishment of a governance structure that ensures the coordination and supervision of ERNs (*Governance and Coordination*), as well as the development of European-wide epidemiological registries and databases on rare diseases (*Contribution to Research*).

In the case of HCPs, the main thematic areas were competence, experience and outcomes of care and patient-centred care. Similarly, the integration into national networks in the area of organization and management stands out with excellent results.

In terms of areas for improvement, most ERNs scored low in the thematic area *Quality and patient safety*, specifically in the analysis of indicators for monitoring clinical performance and healthcare outcomes.

In the case of HCPs, the weakest thematic area was *Organisation and management*, where special attention should be given to the use of CPMS, which obtained an average score of 0.8 out of 2.

The main strengths of the ERNs identified include:

- The existence of a well-defined framework for the governance and implementation of the work packages. These structures foster collaboration among ERN members and facilitate their regular participation in the development of specific tasks that add value to the ERN and its mission. Furthermore, some ERNs were noted to include patient representatives on their governing bodies, thereby enhancing patient participation within the decision-making process.
- Due to the low prevalence of rare diseases, the development of common registries and databases as part of the ERNs roadmap is particularly noteworthy. Establishing them as European-wide patient registry tools facilitates data sharing and helps to advance research on rare or complex diseases.
- Identifying and addressing the training needs of professionals, both within and outside of ERNs, has been shown to be an important instrument for the dissemination of expertise and training in the care of rare or complex diseases.
- It's worth noting that all members of the ERN have a high level of expertise and experience in their fields of specialization. This facilitates the exchange of knowledge and strengthens the ERN's ability to promote cooperation among its members.

CONCLUSIONS

The main conclusions that can be drawn from the evaluation process are as follows:

Structure of the ERN system

According to the HCPs assessed in this first evaluation, the system has a broad geographical representation, although there are marked differences between Eastern and Western countries.

In terms of specialisation, the 24 networks collectively cover many rare or complex diseases, making it possible to reach a large number of patients and professionals.

In terms of its coordination structure, there are several formal and informal mechanisms that promote networking. However, there is a need to establish or strengthen communication channels with some key actors, such as national health authorities and hospital managers.

Maturity of the ERN system

The compliance of 92.39% of the objectives set in the ERNs was rated as "excellent" or "very good" overall. This indicates a satisfactory degree of achievement of the objectives set.

European funding has supported the existence of an ERN coordination team to ensure that the objectives of the ERN are met. However, the ERNs are currently viewed as project-based entities rather than permanent bodies. This view, together with the temporary nature of the grant funding, creates a certain discontinuity due to interruptions or delays in the arrival of funds. This has a real impact on the smooth and effective functioning of the ERNs.

Currently, hospital managers are in the lead of the ERN membership application process. However, hospital administration at many centres often do not recognize the time clinicians dedicate to ERN activities and do not allocate resources for these tasks. This lack of formal recognition and resource allocation prevents health professionals from integrating ERN responsibilities into their daily routines. Consequently, this threatens their sustained engagement with the network and hinders regular participation in its activities.

Although there has been clear progress in the governance structure, the integration, and recognition of the ERN centres in health systems at national level is one of the main challenges for the sustainability of the ERN systems. In this context, the Joint Action "JARDIN" funded under the EU4HEALTH programme is expected to be a catalyst for a better integration of the activities of ERNs into national health systems.

ERN system activity

During these first years of operation, with 84.5% of expected deliverables delivered on time, the ERNs have successfully developed the activities defined in the different work packages. However, some of them, such as the development and implementation of evidence-based clinical practice guidelines, have proved to be more complex than expected.

Similarly, there is a clear need to improve the added value and usability of the CPMS as a tool for virtual case discussion by participating units in the ERN system. However, despite the limited application of the CPMS, there is still a high level of cross-border cooperation and networking that should be highlighted.

Finally, given the impact of the COVID-19 pandemic and Brexit on health systems in general and the ERN structure in particular, it is worth noting the flexibility and resilience shown by the networks in carrying out their activities.

As regards the monitoring of the ERNs, the Integrated System for the Evaluation, Monitoring, Assessment and Quality Improvement of the Networks (AMEQUIS model) monitors a set of 18 indicators common to all ERNs, as well as indicators specific to each network. However, the evaluation highlighted the lack of baselines against which to analyse trends in these indicators.

Impact of the ERN system

This evaluation has shown that the ERN system has had a significant impact on the care of rare or complex diseases, mainly by helping to raise the visibility of the problems of patients with these types of minority diseases. According to the data reported, more than 2 million patients were diagnosed and treated by HCPs during the evaluation period.

The philosophy based on the doctor-patient binomial contributes to patient empowerment. The inclusion of networks of patient representatives in the governing bodies and the development of activities that incorporate their vision show clear progress in this area. However, it is necessary to promote tools for analysing the impact of this collaboration, as well as the experiences of patients treated in the member units of the networks.

For health professionals, ERNs have facilitated the exchange of expertise through the implementation of training actions and the development of registries at European level.

Similarly, the collaborative work developed over the years has been of great value in improving access to innovative treatments. This ultimately helps to reduce the burden on healthcare systems for these patients by improving specialised care and early treatment.

Several opportunities have been identified by the independent evaluation body based on the results of this evaluation and interviews with stakeholders.

Résumée exécutif

INTRODUCTION

Les Réseaux Européens de Référence (RER) sont des réseaux virtuels qui cherchent à améliorer le diagnostic, le traitement et la prise en charge des patients atteints de maladies rares ou complexes. Ces réseaux sont constitués d'unités cliniques spécialisées regroupant des professionnels de la santé (HCP) de toute l'Europe, permettant ainsi l'échange de connaissances et de ressources spécialisées au-delà des frontières. Ces réseaux abordent un large éventail de maladies, telles que les traumatismes cranio-encéphaliques et métaboliques, les cancers infantiles et les épilepsies rares, couvrant ainsi un grand nombre de patients au niveau européen.

Il s'agit d'un système de réseau complexe qui regroupe 24 RER, 1.629 membres HCP, environ 400 défenseurs des patients ePAG, un grand nombre de Partenaires Associés et les représentants des États membres et de la Commission européenne. La coopération et l'interopérabilité entre les acteurs sont indispensables pour assurer son bon fonctionnement.

La Décision 2014/287/EU[6] de la Commission prévoit de réaliser une évaluation de ses performances et contribution aux soins prodigués aux patients tous les cinq ans. L'objectif est d'analyser le respect des critères et des conditions énoncés dans la *Delegated Decision* 2014/286/EU[7], le degré d'atteinte des objectifs énoncés à l'article 12(2) de la Directive 2011/24/EU,[8] ainsi que les résultats et performances des RER et la contribution des HCP.

A l'issue d'un processus d'appel d'offres, le consortium IDOM-ACSA a été sélectionné par la Commission européenne en tant qu'organisme évaluateur indépendant (IEB - Independence Evaluation Body) pour le développement de la première évaluation des 24 RER et 836 HCP dans 261 hôpitaux de 24 États membres de l'UE et Norvège.

Ce rapport - D.6.2.3 Résultats de l'évaluation des RER - présente une vision intégrale des découvertes et conclusions issues du premier exercice d'évaluation depuis le lancement des RER.

MÉTHODOLOGIE

Le processus et la méthodologie d'évaluation ont été réalisés conformément aux lignes directrices stipulées dans le Manuel d'Evaluation[9] et les Outils Techniques[10] d'Evaluation, conformément à la décision 2014/287/EU de la Commission. Le processus d'évaluation a débuté en décembre 2022 pour une durée totale de 10 mois.

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[6] 2014/287/EU: Commission Implementing Decision of 10 March 2014 setting out criteria for establishing and evaluating European Reference Networks and their Members and for facilitating the exchange of information and expertise on establishing and evaluating such Networks. Disponible à : https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=OJ:JOL_2014_147_R_0007

[7] 2014/286/EU: Commission Delegated Decision of 10 March 2014 setting out criteria and conditions that European Reference Networks and healthcare providers wishing to join a European Reference Network must fulfil Text with EEA relevance. Disponible à : https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=OJ:JOL_2014_147_R_0006

[8] Directive 2011/24/EU of the European Parliament and of the Council of 9 March 2011 on the application of patients' rights in cross-border healthcare. Disponible à : https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=celex:32011L0024

[9] Manuel pour l'Evaluation des RER. Disponible à : https://health.ec.europa.eu/document/download/4cff3905-7e55-46b3-8fb6-4e62a3d263f4_en?filename=erns_evaluation_manual_en.pdf

[10] Outils techniques pour l'évaluation des RER. Disponible à : https://health.ec.europa.eu/document/download/d8fe72ce-94dd-4f98-8311-2ea7ab3b4e2d_en?filename=erns_evaluation_toolbox_en.pdf

La méthodologie comprend la vérification des critères opérationnels établis pour les RER et les HCP, via une auto-évaluation par les RER et les HCP, la révision des documents fournis par les évaluateurs, la réalisation de 24 entretiens avec les équipes de coordination des RER et une sélection de défenseurs ePAG, ainsi que 193 audits parmi une sélection de HCP et la résolution des commentaires aux résultats préliminaires.

Au cours des différentes étapes, une équipe de 179 évaluateurs a vérifié le niveau d'atteinte de plusieurs aspects ou Eléments Mesurables pour l'évaluation des domaines suivants :

Domaines évalués dans les RER

1. Gouvernance et coordination: Le cadre structurel du RER est révisé, pour garantir l'efficacité de la coordination et supervision. Pour cela, la configuration de la gouvernance du réseau, l'évaluation régulière des progrès du RER, l'implication des organisations de patients dans les actions stratégiques et les mesures prises pour la durabilité à long terme sont vérifiées.
2. Soins cliniques: L'approche du RER en matière de conseil sur la pratique clinique est analysée en examinant l'adaptation et la diffusion des directives de pratique clinique, des parcours de soins et des meilleures pratiques. La mise en œuvre d'une approche multidisciplinaire des soins et l'intégration des outils de e-santé dans les soins sont aussi évaluées.
3. Qualité et sécurité des patients: La stratégie du RER est évaluée pour assurer la qualité des soins et la sécurité des patients. Pour cela sont examinées les stratégies de promotion de la qualité, ainsi que le suivi des indicateurs pour superviser les performances cliniques et garantir des résultats positifs des soins au sein du réseau.
4. Soins axés sur le patient: L'accent est mis sur la formation du patient et son implication au sein du RER. Sont évalués les mécanismes mis en place pour éduquer et impliquer les patients, les stratégies d'intégration des patients dans les processus de prise de décision, et les initiatives développées pour mesurer et apprendre de l'expérience des patients.
5. Contribution à la recherche: La contribution du RER à la science et à la recherche médicales est évaluée. Sont examinées les actions stratégiques pour combler les lacunes dans la recherche, promouvoir l'innovation, établir des cadres de recherche collaborative et renforcer la surveillance épidémiologique grâce à des registres et des bases de données partagées au niveau européen.
6. Éducation et formation: Sont analysés les efforts des RER pour identifier et combler les lacunes en matière d'éducation, de formation et de développement professionnel afin d'évaluer dans quelle mesure le réseau améliore les activités éducatives et les opportunités de formation pour les professionnels de la santé à l'intérieur et à l'extérieur du domaine du RER.
7. Mise en réseau et diffusion: La capacité de mise en réseau du RER est évaluée pour identifier l'existence de systèmes solides de collaboration, de partage des connaissances et de mise en commun des ressources. Par ailleurs, sont examinées les stratégies de diffusion des informations de référence entre les États membres et les efforts de partage des connaissances au sein et en dehors du RER lui-même.

Domaines évalués dans les HCP

1. Soins axés sur le patient: L'évaluation porte sur la priorisation des besoins des patients, tout en respectant leurs droits et préférences. Cela comprend des programmes d'éducation, des informations claires, la considération des retours des patients, le consentement éclairé, la transparence dans la fourniture d'informations, les protocoles de gestion de la douleur et la collaboration avec les organisations de patients.
2. Organisation et gestion: La structuration et la gestion efficaces des services sont examinées, en particulier pour les patients transfrontaliers. Sont ainsi mesurées la mise en place de politiques sur les tarifs et les services, la coordination avec d'autres unités, l'intégration dans les réseaux nationaux, l'utilisation du Système de Gestion des Patients Cliniques (CPMS -

Clinical Patient Management System) et la mise en œuvre de stratégies de communication efficaces.

3. Recherche, éducation et formation: La participation du HCP aux activités d'éducation et de formation, tant pour les soins aux patients que pour la recherche, est examinée. De plus, est vérifiée la contribution du HCP aux activités de recherche dans le cadre du RER, la diffusion des résultats de ses activités de recherche et essais cliniques, et l'incorporation de données dans les registres ou bases de données tenues par le RER.
4. Échange d'expertise, systèmes d'information et e-santé: La capacité du HCP à fournir des connaissances et un soutien aux HCP est évaluée. Est aussi mesuré le degré de mise en œuvre des outils de e-santé et l'alignement du système de codification clinique sur les normes nationales et internationales proposées par le RER.
5. Qualité et sécurité: Le suivi et l'amélioration de la qualité des soins et de la sécurité des patients de la part du professionnel de la santé sont évalués. Le respect des directives de pratique clinique diffusées par le RER est également évalué.
6. Compétence, expérience et résultats des soins: L'évaluation examine si le HCP maintient les niveaux d'activité établis, démontrant sa compétence clinique afin de prodiguer des soins et de fournir des résultats optimaux au sein du réseau.
7. Ressources humaines: Evaluation des compétences des professionnels qui font partie de l'équipe de l'unité pour fournir des soins complets grâce à une approche multidisciplinaire et spécialisée, garantissant une prestation de soins de santé de grande qualité.
8. Pour comparer les résultats de manière préliminaire, le IEB a réalisé 24 entretiens supplémentaires avec une sélection d'agents impliqués dans le système (RER, HCP, évaluateurs, représentants d'EURORDIS et représentants du Conseil des États Membres). De plus, des informations supplémentaires, des suggestions et des commentaires ont été recueillis grâce à des questionnaires en ligne envoyés à tous les évaluateurs HCP, RER et ePAG.

RÉSULTATS

Après un vaste exercice d'analyse agrégée, les principaux résultats sont les suivants :

- 100 % des RER et 97,61 % des HCP qui ont complété l'auto-évaluation ont démontré un niveau élevé d'engagement envers le processus d'évaluation.
- 100 % des RER et 87,68 % des HCP (à l'exclusion de ceux qui n'ont pas réalisé l'auto-évaluation) ont obtenu un résultat satisfaisant, démontrant un engagement élevé envers les critères fixés pour les RER et les HCP.
- Parmi les 84 HCP qui ont obtenu des résultats insatisfaisants, 72 ont soumis un plan d'amélioration et disposent d'un délai d'un an pour mettre en œuvre les actions proposées, ce qui représente 8,61% du total des 836 HCP.
- 31 HCP parmi les 836 évalués (soit 3,71 %) ont vu leur adhésion résiliée comme indiquée ci-dessous:
    - L'adhésion de 16 HCP a été résiliée par décision du Conseil des Etats Membres en raison de la non-réalisation de l'auto-évaluation
    - L'adhésion de 9 HCP parmi les 84 qui n'ont pas obtenu de résultats satisfaisants a été résiliée par le Conseil de Etats Membres en raison de la non-soumission de plan d'amélioration.
    - 6 HCP se sont volontairement retirés du RER auquel ils appartenaient au cours du processus d'évaluation.

Il est important de noter que tous les RER ont atteint avec succès les objectifs marqués, établis dans l'article 12(2), de la Directive 2011/24/UE. La plupart ont été jugés excellents et aucun n'a reçu une note inférieure à un standard médiocre ou déficient.

Parmi les domaines d'évaluation communs aux RER et HCP, la catégorie de Education et formation est celle qui a reçu le score le plus élevé, aussi bien pour les RER que les HCP.

Parmi les domaines évalués spécifiquement pour les RER, la catégorie Mise en réseau et diffusion a reçu la meilleure note. Cependant, d'autres aspects se démarquent dans d'autres domaines, comme par exemple la mise en place d'une structure de gouvernance qui garantit la coordination et supervision des RER (Gouvernance et Coordination), ainsi que le développement de registres et bases de données épidémiologiques à l'échelle européenne sur les maladies rares (Contribution à la Recherche).

Dans le cas des HCP, les domaines les plus forts étaient Compétence, expérience et résultats des soins ainsi que Soins axés sur le patient. De même, l'intégration dans les réseaux nationaux pour le domaine Organisation et gestion se démarque avec d'excellents résultats.

En termes de domaines à améliorer, la majorité des RER ont obtenu un score faible dans le domaine Qualité et sécurité des patients, en particulier dans l'analyse des indicateurs de suivi des performances cliniques et des résultats en matière de soins de santé.

Pour ce qui est des HCP, le domaine le plus faible était Organisation et gestion, où une attention particulière devrait être accordée à l'utilisation des CPMS, ayant obtenu une note moyenne de 0,8 sur 2.

Les principaux points forts identifiés pour les RER comprennent :

- L'existence d'un cadre clairement défini pour la gouvernance et la mise en œuvre des lots de travaux. Ces structures favorisent la collaboration entre les membres du RER et facilitent leur participation régulière à l'élaboration de tâches spécifiques qui ajoutent de la valeur au RER et à sa mission. De plus, certains RER se sont démarqués pour avoir intégré des représentants des patients dans leurs organes directeurs, renforçant ainsi la participation des patients au processus décisionnel.
- En raison de la faible prévalence des maladies rares, le développement de registres et de bases de données communes dans le cadre de la feuille de route des RER est particulièrement remarquable. En faire des outils de registre des patients à l'échelle européenne facilite le partage des données et contribue à faire progresser la recherche sur les maladies rares ou complexes.
- L'identification et la réponse aux besoins de formation des professionnels, tant à l'intérieur qu'à l'extérieur des RER, se sont révélées être un instrument important pour la diffusion de la connaissance spécialisée et la formation dans la prise en charge de maladies rares ou complexes.
- Il convient de noter que tous les membres du RER présentent un haut niveau d'expertise et d'expérience dans leurs domaines de spécialisation, ce qui facilite l'échange de connaissances et renforce la capacité du RER à promouvoir la coopération entre ses membres.

CONCLUSIONS

Les principales conclusions qui peuvent être tirées du processus d'évaluation sont les suivantes :

Structure du système RER

Selon les HCP analysés dans cette première évaluation, le système est fortement représenté géographiquement, bien qu'il existe des différences entre les pays de l'Est et ceux de l'Ouest.

En termes de spécialisation, les 24 réseaux couvrent collectivement un grand nombre de maladies rares ou complexes, permettant d'atteindre un grand nombre de patients et de professionnels.

En termes de structure de coordination, il existe plusieurs mécanismes formels et informels qui favorisent la création de réseaux. Cependant, il est nécessaire d'établir ou de renforcer les canaux de communication avec certains acteurs clés, tels que les autorités sanitaires nationales et, en particulier, les directeurs d'hôpitaux.

Maturité du système RER

92,39 % des objectifs fixés pour les RER ont été jugés globalement « excellents » ou « très bons », ce qui indique un degré satisfaisant d'atteinte des objectifs fixés.

Le financement européen a soutenu l'existence d'une équipe de coordination du RER pour veiller à l'atteinte des objectifs du réseau. Cependant, les RER sont actuellement considérés comme des entités associées à des projets plutôt que des organes permanents. Cette vision ainsi que le caractère temporaire du financement dépendant de subventions créent une certaine discontinuité en raison d'interruptions ou de retards dans l'arrivée des fonds, ce qui a un impact réel sur le bon fonctionnement et l'efficacité des RER.

Actuellement, les directeurs d'hôpitaux gèrent le processus de demande d'adhésion au RER. Cependant, il est fréquent que les administrateurs de nombreux centres ne reconnaissent pas le temps que les cliniciens consacrent aux activités du RER. Ce manque de reconnaissance formelle et d'allocation de ressources empêche les professionnels de la santé d'intégrer les responsabilités des RER dans leurs activités quotidiennes. Par conséquent, cela menace la durabilité de leur engagement avec le réseau et limite leur participation aux activités du RERJ

Bien que des progrès évidents dans la structure de gouvernance aient été observés, l'intégration et la reconnaissance dans les systèmes de santé au niveau national constituent l'un des principaux défis pour la durabilité des systèmes RER. Dans ce contexte, l'action conjointe « JARDIN » dans le cadre du programme EU4HEALTH devrait être un catalyseur pour une meilleure intégration des activités des RER dans les systèmes de santé nationaux.

Activité du système RER

Au cours de ces premières années de fonctionnement, avec un taux de 84,5 % de réalisation des livrables dans les temps, les RER ont développé avec succès les activités définies dans les différents lots de travaux. Cependant, certaines de ces activités, telles que l'élaboration et la mise en œuvre de lignes directrices de pratique clinique basées sur des données probantes, se sont révélées plus complexes que prévu.

De même, il est clairement nécessaire d'améliorer la valeur ajoutée et l'utilisation des CPMS en tant qu'outil de discussion virtuelle de cas par les unités intégrant le système RER. Cependant, malgré l'application limitée du CPMS, il existe toujours un niveau élevé de coopération et de mise en réseau transfrontalières.

Enfin, compte tenu de l'impact de la pandémie de la COVID-19 et du Brexit sur les systèmes de santé en général et la structure du RER en particulier, il convient de noter la flexibilité et la résilience dont les réseaux ont fait preuve dans la réalisation de leurs activités.

En ce qui concerne le suivi des RER, le Système intégré d'analyse, de suivi, d'évaluation et d'amélioration de la qualité des Réseaux (modèle AMEQUIS) suit un ensemble de 18 indicateurs communs à tous les RER, ainsi que des indicateurs spécifiques à chaque réseau. Cependant,

l'évaluation a mis en évidence l'absence de ligne de base permettant d'analyser les tendances de ces indicateurs.

Impact du système RER

Cette évaluation a montré que le système RER a eu un impact significatif sur la prise en charge des maladies rares ou complexes, principalement grâce à sa contribution dans l'augmentation de la visibilité des problèmes des patients atteints de ces types de maladies minoritaires. Selon les données rapportées, plus de 2 millions de patients ont été diagnostiqués et traités par des HCP au cours de la période d'évaluation.

La philosophie basée sur le binôme médecin-patient contribue à l'autonomisation des patients. L'inclusion de réseaux de représentants des patients dans les instances dirigeantes et le développement d'activités qui intègrent leur vision sont le reflet de progrès évidents dans ce domaine. Cependant, il est nécessaire de développer des outils permettant d'analyser l'impact de cette collaboration, ainsi que les expériences des patients traités dans les unités membres des réseaux.

Pour les professionnels de santé, les RER ont facilité l'échange d'expertise à travers la mise en place d'actions de formation et le développement de registres au niveau européen.

De même, en termes d'amélioration de l'accès à des traitements innovants, le travail collaboratif développé au fil des ans a été d'une grande valeur. Cela contribue à réduire la charge pesant sur les systèmes de santé de ces patients en améliorant les soins spécialisés et le traitement précoce.

Plusieurs opportunités ont été identifiées par l'organisme d'évaluation indépendant sur la base des résultats de cette évaluation et des entretiens avec les parties prenantes.

1. Introduction

The European Reference Networks (ERNs) are virtual networks involving Healthcare Providers (HCPs) across Europe, which aim to tackle complex or rare diseases and conditions that require highly specialised treatment and a concentration of knowledge and resources. These Networks cover major disease groups, from bone disorders, metabolic diseases, and paediatric cancer to immunodeficiency.

Following an international open tender (HADEA/2021/OP/0012), the Multiple Framework Contract in cascade for performing independent Assessments or Evaluations of European Reference Networks (ERNs) and of Healthcare Providers (HCPs), which this project is part of, was awarded to the Consortium led by IDOM, Consulting, Engineering, Architecture, S.A.U (IDOM) in partnership with Fundación Pública Andaluza de Progreso y Salud (FPS), hereafter, the Consortium.

The purpose of the first specific contract is to perform technical evaluations of the 24 existing ERNs and 836 HCPs, located in 24 EU Member States and Norway, under the framework of Article 12 of Directive 2011/24/EU on patients' rights in cross-border healthcare.

The evaluation process provides a standardised method for evaluating ERNs under the regulatory framework of the Commission Delegated and Implementing Decisions of 10th March 2014 and amendment of the Implementing Decision of 19th July 2019. As part of the evaluation process, the ERNs and their Members underwent a comprehensive evaluation that consisted of the following stages: self-evaluation of the ERNs and HCPs; evaluation through document review, 24 interviews with ERN coordination teams and patient representatives, and 193 onsite audits of some Members; and the review of the comments made by the HCPs. If the evaluation outcome was not satisfactory, an improvement plan was required to be submitted.

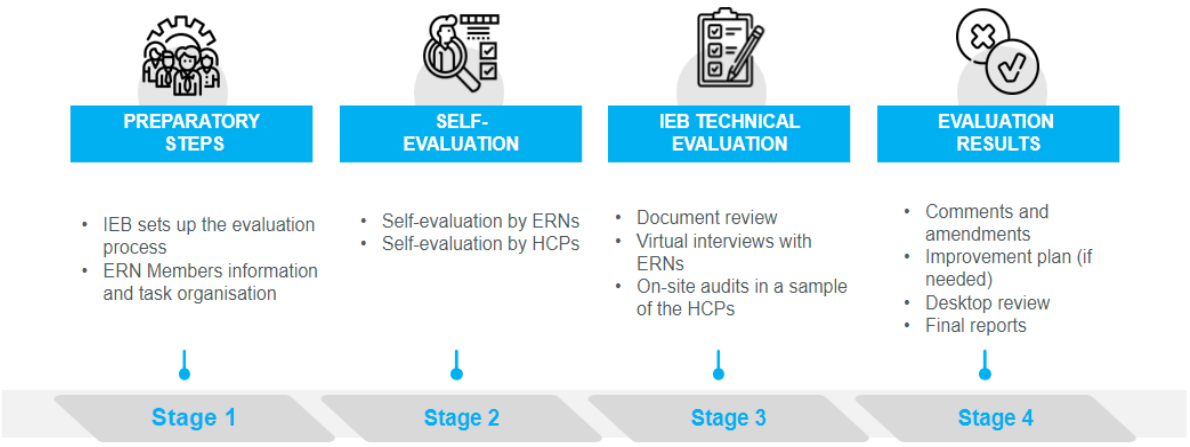


Figure 1. Scheme of the evaluation process

This report presents the final and overall results of the evaluation exercise, as well as a comprehensive analysis of the strengths, areas for improvement and other barriers in both the ERN system and the evaluation methodology.

A comprehensive approach involving multiple data sources and methodologies was used to reach the conclusions presented in this report. This rigorous process included:

- Evaluations: The evaluations provided by a diverse panel of 179 evaluators were analysed. These evaluations covered a range of operational criteria and the qualitative information included as strengths, suggestions for improvement, barriers, and outstanding practices.

- Surveys: To obtain an overall perception of the functionality of the network system and the evaluation methodology, a series of surveys were sent to the stakeholders of the system: 24 ERNs, 836 HCPs and 179 evaluators.

- Interviews: In-depth interviews were held between the Independent Evaluation Body (IEB) and representatives of all parties involved in the ERN system. The purpose of these 24 interviews with stakeholders was to confirm and validate the main hypothesis derived from the evaluation findings. A detailed list of the stakeholders interviewed can be found in **Annex** I.

An overview of the main stakeholders, the information collection methods and their purpose are detailed in Table 1.

Table 1. Overview of consultations held by the IEB with the different actors of the ERN system

Stakeholders	Entity	Tool	Objectives
ERN Coordinators	Forms submitted by ERN Coordinators	ERN survey	• ERN system conclusions • ERN interviews and methodology improvements/suggestions • HCPs inclusion in the ERN system
	Sample of ERN Coordinators (4)	Interview-Meeting	
HCPs with audit	Forms submitted by HCPs	General HCP survey	• HCPs onsite audit • HCPs inclusion in the ERN system • ERN system conclusions • HCPs evaluation methodology
	Sample of HCPs (5)	Interview-Meeting	
HCPs document review	Forms submitted by HCPs	General HCP survey	• HCPs evaluation methodology • HCPs inclusion in the ERN system • Consortium performance
Evaluators	Forms submitted by evaluators	Evaluators survey	• Insights from evaluators • ERN system conclusions • Evaluation methodology improvements/suggestions
	Evaluators Committee (8 evaluators chosen by involvement)	Interview-Meeting	• Insights from evaluators • ERN system conclusions • Evaluation methodology improvements/suggestions
Patient Organizations	European Patient Advocacy Groups (PAGs)	ePAG survey	• Insights from the Patient Organizations interviews • Involvement in the evaluation • ERN system
	EURORDIS	Interview-Meeting	• Insights from the Patient Organizations interviews • Involvement in the evaluation ERN system
Board of Member States (BoMS)	Sample of BoMS representatives (5)	Interview-Meeting	• ERN system conclusions • Integration of the ERN system in the National Health System (NHS)

This document is structured as follows to present the conclusions and main findings of the evaluation:

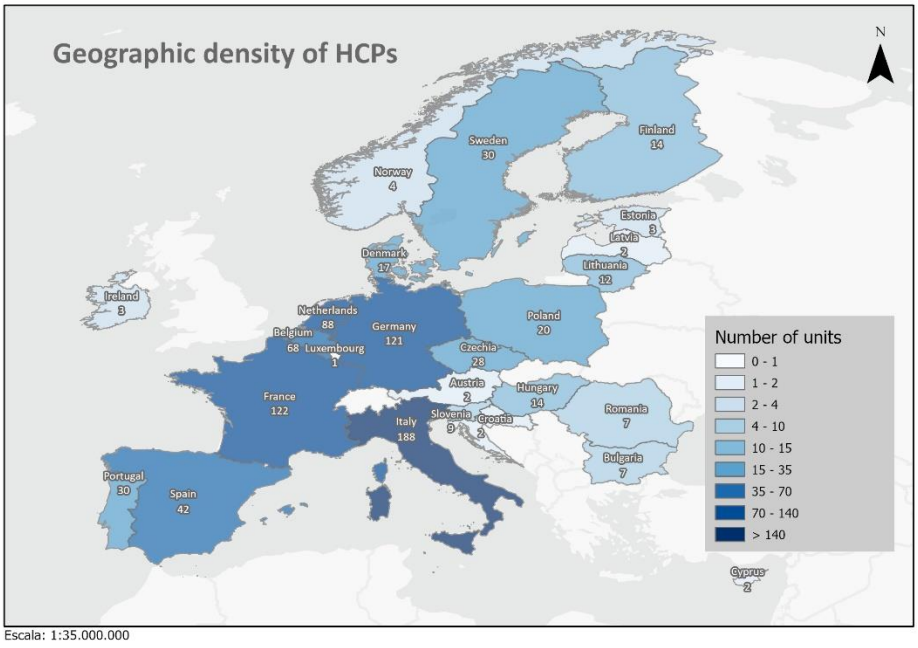
- Section 3 shows a comprehensive presentation of the evaluation results for ERNs and HCPs, including data and charts.
- Section 4 provides a summary of the analysis regarding the achievement of the Directive's objectives.
- Section 5 offers an analysis of the strengths and suggestions for improvement.
- Section 6 outlines the conclusions on the structure, maturity, activity, and impact of the network system, and
- Section 7 presents the opportunities for improvement identified by the IEB in both the evaluation system and the network system.

2. Map of geographical coverage of each Network

In the context of the expansion and evolution of ERNs in Europe, it is essential to understand the geographical distribution of HCPs. This geospatial analysis makes it possible to effectively visualise the presence of HCPs across Europe and to highlight the countries with the highest density of HCPs, allowing a more precise understanding of their territorial reach and the geographical coverage of the ERN system. However, this preliminary analysis is partial, as only the HCPs currently under evaluation (836 in total) are represented in the maps.

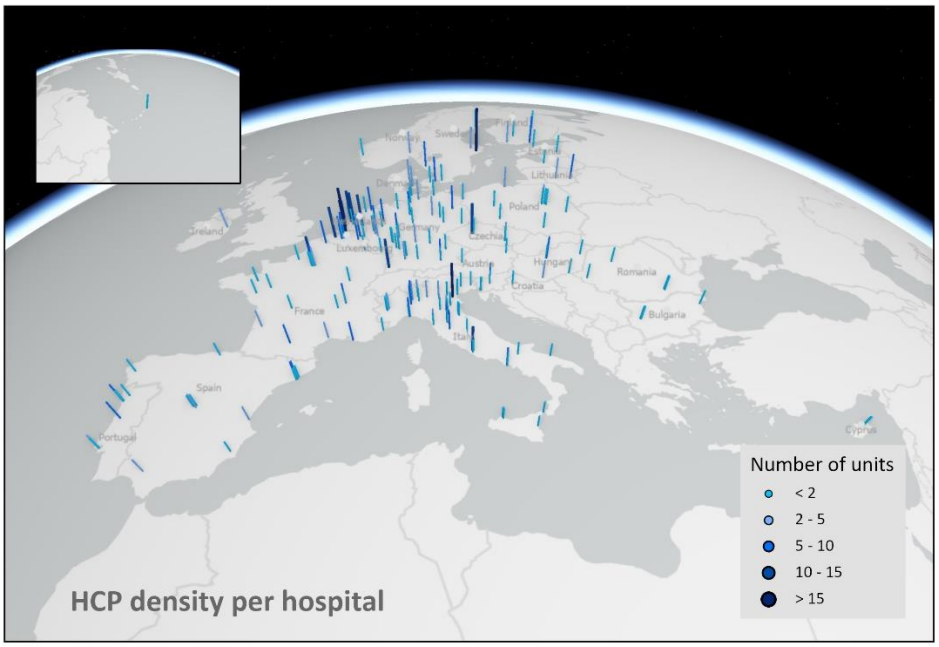
This map highlights the wide geographical coverage of the network system.

Figure 2 Geographic density of HCPs across Europe



As can be seen from the map, the ERN system is widely spread across Europe, with HCPs covered by the current evaluation being present in all EU countries with the exception of Slovakia, Greece, and Malta. However, it can also be seen that the coverage is not homogeneous, with some countries strongly represented and others less. For example, although Germany has a slightly larger population than Italy, Italy has 188 HCPs compared to 122 in Germany.

Figure 3 HCP density per hospital



Conversely, a map of HCP density per hospital is shown in Figure 3 there are certain countries and certain hospitals that show a higher level of participation in the ERN system. This may be because certain hospitals have policies that are more open to this type of inter-centre collaboration, or because these hospitals have taken more initiative to join these networks. It can also be seen that Belgium, Italy, Sweden, and the Netherlands have hospitals with higher participation in the ERN system. The hospitals with the highest participation in the ERN system (dark blue) are the University Hospital Leuven, the University Hospital Padova, the Karolinska University Hospital and the Erasmus MC: University Medical Rotterdam with 19, 18, 18 and 17 different ERN members respectively.

Maps showing the geographical coverage per ERN and country are included in **Annex II** and **Annex III**: Geographical coverage per each country.

3. Overall system results

All 24 networks successfully completed the evaluation process, resulting in a 100% completion rate. The evaluation completion rate for HCPs was an impressive 97.72%. This remarkable achievement can be attributed to the thorough understanding by both ERNs and HCPs of the importance of the evaluation and its direct impact on the future development of the ERNs and their members.

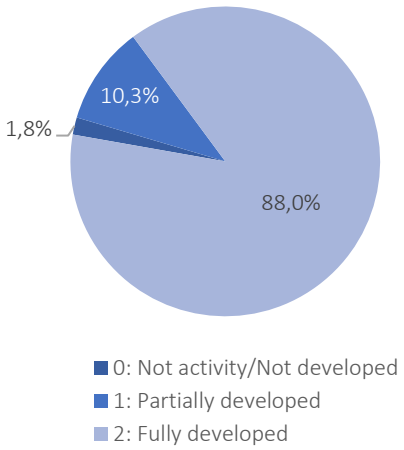
The results of the evaluation for both ERNs and HCPs are presented in this section. This includes general findings on compliance with the operational criteria set out in the methodology, as well as more specific findings highlighting the strongest and weakest areas and criteria.

3.1. ERNs

3.1.1. Overall results

The following figure shows the overall distribution of ratings for the 24 ERNs according to the evaluation of compliance with the Operational Criteria.

Figure 4. Overall compliance with operational criteria for ERNs



88% of all Measurable Elements (MEs) of the ERNs were rated as Fully Implemented, indicating that the ERNs are performing as expected and have provided the evidence to support this. However, there is room for improvement, particularly in the areas of development detailed in Section 3.1.2.

The final results of the evaluation of the ERNs are presented below. These results are based on the decision guidelines that determine whether the ERN has achieved a satisfactory result:

- A rating/score of 1 or 2 in 90% of core MEs
- An average score of at least 70% of the highest possible score in the group of core MEs

3.1.2. Overall results by thematic area

The Operational Criteria for the evaluation of ERNs are grouped into seven thematic areas, each of which consists of one or more criteria with different MEs.

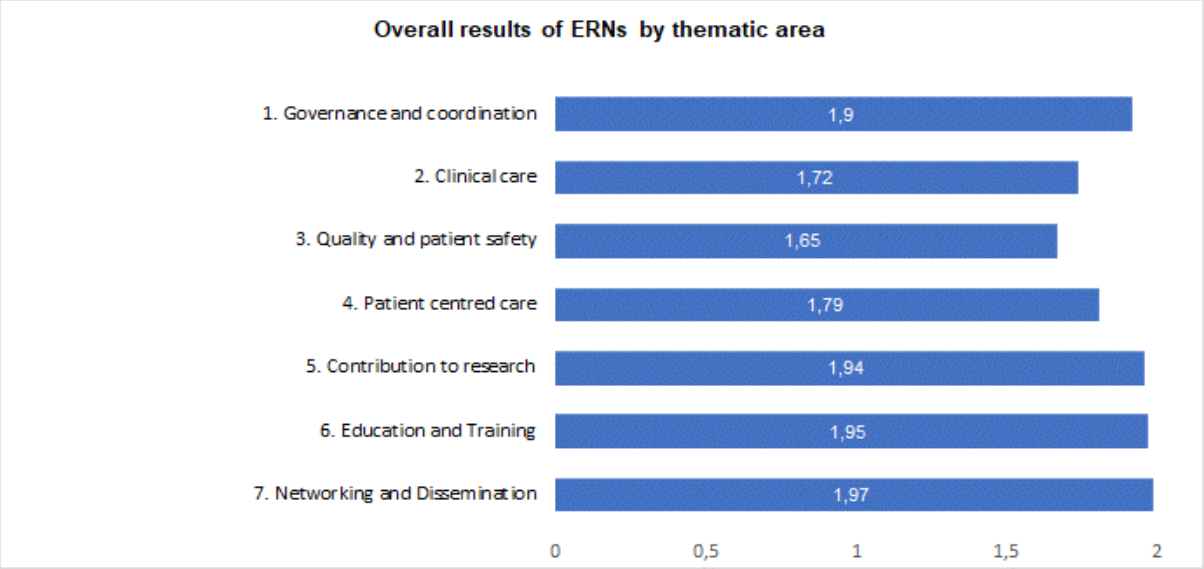
1. *Governance and coordination:* The structural framework of the ERN is reviewed, to ensure effective coordination and monitoring. The governance set-up of the network is verified,

including the regular assessment of the progress of the ERN, the integration of patient organisations in strategic actions and the measures taken for long-term sustainability.

2. *Clinical care:* The ERN's approach to advising on clinical practice is evaluated, reviewing the adaptation and dissemination of clinical practice guidelines, care pathways and best practices. In addition, the implementation of a multidisciplinary approach to care and the integration of e-health tools into care is assessed.
3. *Quality and patient safety:* The ERN's strategy is evaluated to ensure quality of care and patient safety. The strategies defined to promote quality are reviewed, as well as the monitoring of indicators to track clinical performance and ensure positive outcomes of care within the network.
4. *Patient-centred care:* Emphasis is on patient empowerment and patient involvement in the ERN. The mechanisms in place to educate and involve patients are considered, as well as the strategies to engage patients in decision-making processes, and measures taken to measure and learn from patients' experience.
5. *Contribution to research:* The contribution of the ERN to medical science and research is evaluated. A review is carried out of the strategic actions to fill research gaps, promote innovation, establish collaborative research frameworks, and strengthen epidemiological surveillance through shared registries and databases at European level.
6. *Education and training:* The ERN's efforts to identify and address gaps in education, training, and professional development are reviewed to assess the extent to which the Network is improving educational activities and opportunities for health professionals within and outside the ERN.
7. *Networking and dissemination:* The ERN's networking capacity is assessed, looking for the existence of good systems for collaboration, knowledge sharing and resource pooling. In addition, the strategies for the dissemination of referral information between Member States and the efforts to share knowledge within and outside the ERN itself are examined.

The following figure shows the average rating of the ERNs for each thematic area, calculated as the average score of all MEs within each area. The scores range from 0, the lowest, to 2, the highest.

Figure 5: Overall results of ERNs by thematic area



As shown in Figure 5, the strongest areas of ERNs are those focusing on *Networking and Dissemination*, and *Education and Training*. Conversely, the areas that need to be strengthened are *Quality and patient safety*, followed by *Clinical care* and *Patient-centred care*.

In terms of criteria, as shown in the figures in Annex IV: Overall results of each criterion (calculating exclusively its core MEs) of ERNs, the criteria with the best results (considering only the core ME) are evenly distributed between *Networking and Dissemination* and *Education and Training*. However, there are other aspects that stand out in other areas. This is the case for establishing a governance framework to ensure appropriate coordination and oversight of the ERNs (in the area of Governance and Coordination), and for developing European-level registries and epidemiological databases on rare diseases (in the area of Contributing to Research).

However, although the ERNs demonstrate a consolidated multidisciplinary approach to care, in the area of clinical care, there is still room for improvement in the development of evidence-based clinical guidelines and best practices to help standardise care among their members. The ERNs should focus on refining their oversight strategies to monitor the implementation of the guidelines, pathways, and protocols among their members. They should adjust the frequency of review of these decision support tools to ensure that they are based on the latest evidence. This adjustment would facilitate timely reassessment and allow for the incorporation of new advances or evolving best practice. Additionally, the ERNs should work on monitoring and feedback mechanisms to follow up and encourage their use across HCPs.

Finally, in the area of quality and patient safety, the low level of implementation of quality and patient safety indicators to monitor clinical processes should be highlighted.

3.2. HCPs

3.2.1. Overall results

From the 836 HCPs, 19 did not complete the self-evaluation (any ME), so the results presented below are from the remaining 817 HCPs (97.72%) who completed all stages of the evaluation process.

Based on the evaluation of compliance with the operational criteria, the following figure shows the overall distribution of ratings for the 817 HCPs.

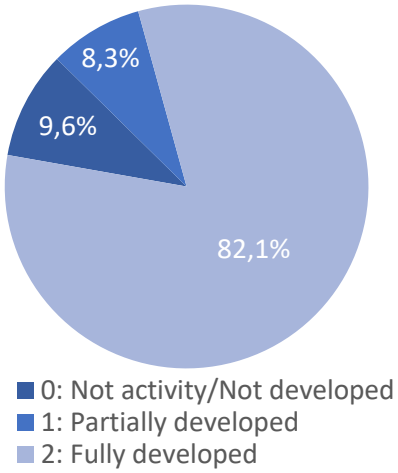


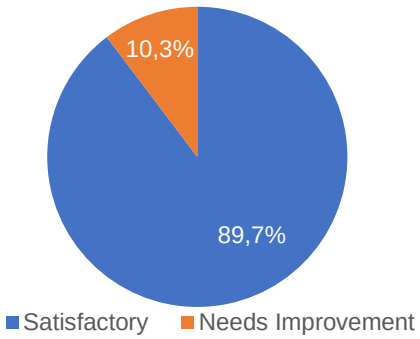
Figure 6. Overall compliance with operational criteria for HCPs

82.1% of all MEs within the HCP evaluations were rated as Fully Implemented, indicating that the HCPs are performing as expected and have provided the evidence to support this performance. However, there is still room for improvement, particularly in the development areas detailed in section 3.2.2.

The final results of the HCP evaluation are presented below. These results are based on the decision guidelines that determine whether an HCP team has achieved a satisfactory result:

- A rating/score of 1 or 2 in 90% of core MEs.
- An average score of at least 70% of the highest possible score in the group of core MEs.

Figure 7. Final results of the HCP evaluation process



Of the 817 HCPs who completed the self-evaluation, 733 (89.72%) received a *Satisfactory* rating, while a minority, 84 (10.28%), received a *Needs Improvement* rating.

3.2.2. Overall results by thematic area

The HCP operational criteria are grouped into seven thematic areas, each of which consists of one or more criteria with different MEs.

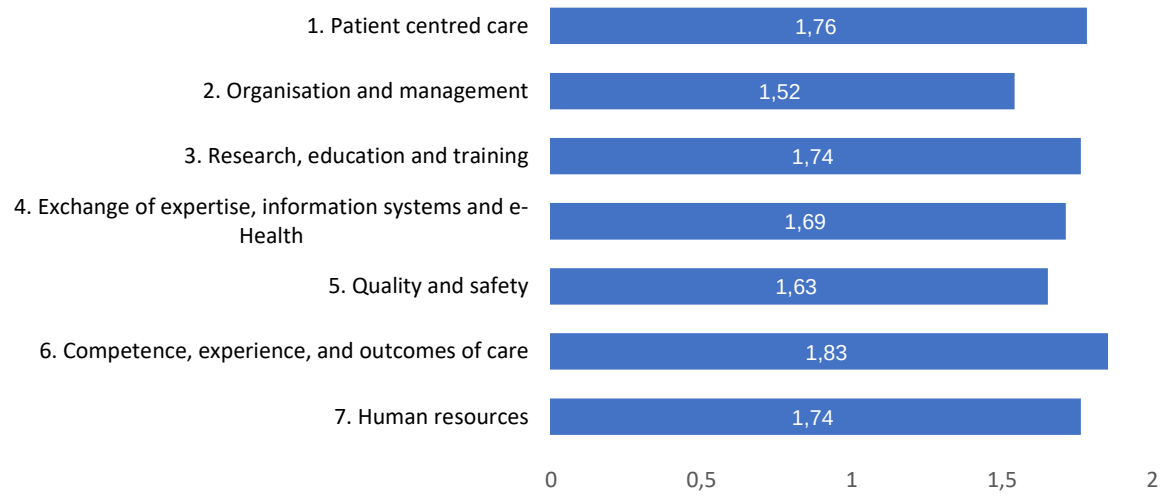
1. *Patient-centred care:* The evaluation addresses the prioritisation of patients' needs, while respecting their rights and preferences. This includes education programmes, clear

information, the use of patient feedback, informed consent, transparency in the provision of information, pain management protocols, and collaboration with patient organisations.

2. *Organisation and management:* The efficient structuring and management of services is reviewed, especially for cross-border patients. The evaluation looks at the establishment of fee-for-service policies, coordination with other units, integration into national networks, use of the Clinical Patient Management System (CPMS), and implementation of effective communication strategies.
3. *Research, education, and training:* The participation of the HCP in education and training activities, both for patient care and research, is examined. In addition, the verification aims to ascertain the contribution of the HCP to the research activities of the ERN, the dissemination of the results of their research activities and clinical trials, and the inclusion of data in the registries or databases maintained by the ERN.
4. *Exchange of expertise, Information systems, and e-Health:* The capacity of the HCP to provide knowledge and support to other HCPs is evaluated. The degree of implementation of e-health tools and the alignment of the clinical information coding system with the national and international standards proposed by the ERN is also addressed.
5. *Quality and safety:* The monitoring and improvement of the quality of care and patient safety provided by the HCP is evaluated. Adherence to clinical practice guidelines disseminated by the ERN is also assessed.
6. *Competence, experience, and outcomes of care:* The evaluation examines whether the HCP is maintaining an established level of activity that demonstrates clinical competence in order to provide optimal care and outcomes within the network.
7. *Human resources:* The evaluation assesses whether the professionals who form part of the unit's team have the necessary competencies to provide comprehensive care through a multidisciplinary and specialised approach, guaranteeing a high quality of healthcare provision.

The following figure shows the average HCP rating for each thematic area, calculated as the average score of all MEs within each area. The ratings range from 0, being the lowest, to 2, being the highest.

Figure 8. Overall results of HCPs by thematic area



As shown in Figure 8, the strongest areas for HCPs are *Competence, experience and outcomes of care*, and *Patient-centred care*. On the other hand, the areas that need to be strengthened are *Organisation and management*, followed by *Quality and safety*.

In terms of the analysis of criteria, as can be seen from the figures in Annex V: Overall results of each criterion (calculating exclusively its core MEs) of HCPs, the criteria with the best results in HCPs (considering exclusively core MEs) are the integration in national networks in the *Organisation and management* area, as well as the implementation of strategies for a patient-centred assistance in the *Patient-centred care* area.

In contrast, the criteria with the lowest ratings are the use of clinical guidelines in their specialty and the use of CPMS to review clinical cases with other healthcare professionals.

3.2.3. Overall results of the HCP teams' MEs reflecting their contribution to the ERNs

A total of 64 measurable elements have been defined in the evaluation methodology to measure the performance of HCPs as members of the ERN. Among these, 18 measurable elements have been identified to verify the contribution of each HCP to the network, as part of the logic of the methodology. Table 2 shows the distribution of these measurable elements across the thematic areas.

Table 2. Distribution of MEs that identify the HCP team contribution to the mission of the Network

AREA	Number of HCP contribution MEs	Total number of MEs	%
1.Patient care	2	19	10.5%
2.Organisation and Management	2	10	20.0%
3.Research, training, and education	7	11	63.6%
4.Exchange of expertise	2	7	28.6%
5.Quality and safety	3	9	33.3%
6.Competence, experience, and outcome of care	2	4	50.0%
7.Human Resources	0	4	0.0%
Total	**18**	**64**	**28.1%**

The results of the evaluation of the measurable elements that assess the contribution of the HCP team to the network's mission are shown in the figure below.

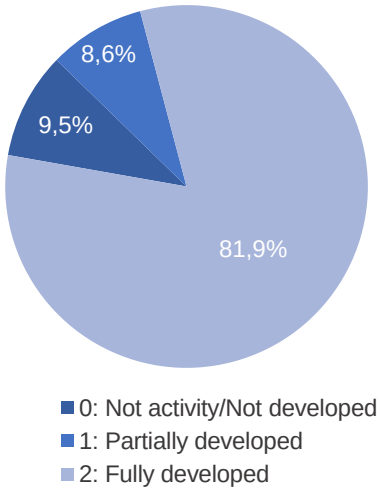


Figure 9. Overall results of HCPs reflecting their contribution to the ERN

As shown in Figure 9, 81.9% of the MEs measuring the contribution to the network have received the highest rating This result highlights the important contribution of HCPs to each ERN, although there are some MEs that have not yet been developed (8.6%).

In line with the previous section, the implementation of policies to ensure patient-centred care and respect for patients' rights and preferences, as well as the participation of HCPs in national networks for rare diseases, received the highest scores among the measurable elements defined to assess the contribution of HCPs to the mission of ERNs.

Similarly, the adoption of clinical guidelines in their area of expertise and the use of the CPMS received the lowest ratings. In the area of patient-centred care, the lack of standardised data collection on the experience or satisfaction of patients of HCPs in the areas of action of ERNs should be highlighted as one of the aspects to be strengthened.

4. Evaluation of the achievement of the objectives of the Directive

4.1. Analysis of the selection of objectives by the ERN

The following section assesses the achievement of the objectives set out in Article 12(2) of Directive 2011/24/EU (Table 3).

Table 3. Objectives set out in Article 12(2) of Directive 2011/24/EU

Objective Number	Objective description
1	To help realise the potential of European cooperation regarding highly specialised healthcare for patients and for healthcare systems by exploiting innovations in medical science and health technologies
2	To contribute to the pooling of knowledge regarding sickness prevention
3	To facilitate improvements in diagnosis and the delivery of high-quality, accessible, and cost-effective healthcare for all patients with a medical condition requiring a particular concentration of expertise in medical domains where expertise is rare
4	To maximise the cost-effective use of resources by concentrating them where appropriate
5	To reinforce research, epidemiological surveillance like registries and provide training for health professionals
6	To facilitate mobility of expertise, virtually or physically, and to develop, share and spread information, knowledge, and best practice and to foster developments of the diagnosis and treatment of rare diseases, within and outside the Networks
7	To encourage the development of quality and safety benchmarks and to help develop and spread best practice within and outside the Network

During the 2016 assessment, in their application form, each ERN was required to select some of the objectives set out in the Directive that they wished to pursue.

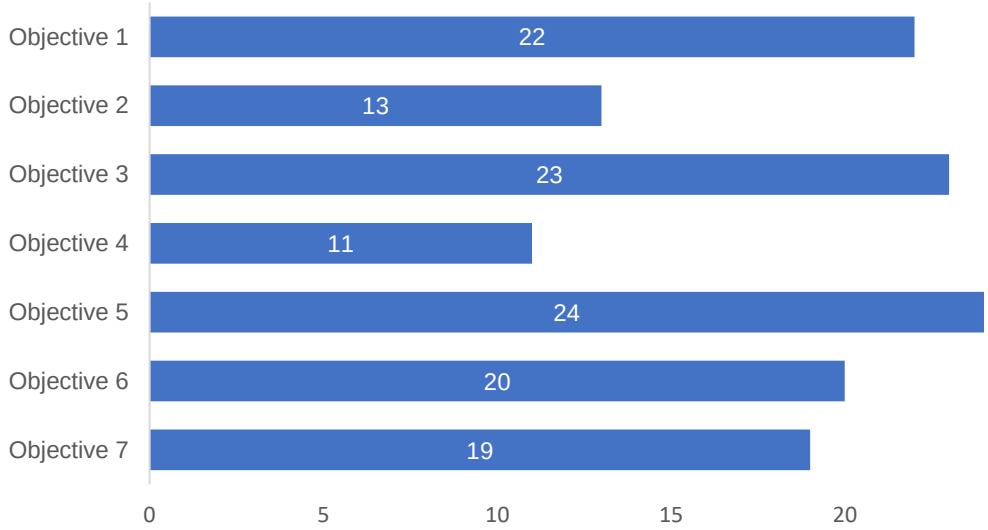


Figure 10. Selection of the objectives by the ERNs

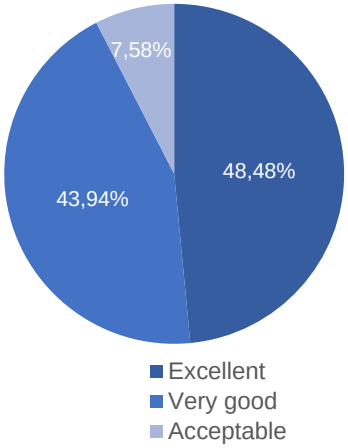
As can be seen from *Figure 10*, the most frequently chosen objective for ERNs was Objective 5. This was chosen by all ERNs, followed by Objectives 1 and 3.

4.2. Qualitative assessment of the degree of achievement of each objective

In the current evaluation, performance against all selected objectives has been assessed using different performance categories as defined in the evaluation manual ('Excellent', 'Very Good', 'Acceptable', 'Poor', 'Unsatisfactory'). The evaluators relied on the information provided by the ERNs during the documentary review of the grant reports, the self-evaluation form (in which the ERNs described their main achievements and assessed the level of achievement of the objectives after five years) and the information gathered during the interviews.

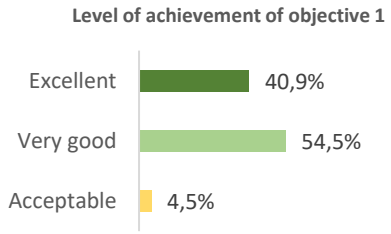
Figure 11 shows that most ERNs were rated Excellent (48.48%) and Very Good (43.94%) in terms of their performance in achieving their objectives, while only 7.58% were rated Acceptable. It is also important to note that in no case was the level of achievement of the networks' objectives rated as Poor or Failing.

Figure 11. Qualitative assessment of the level of achievement of the ERNs' objectives



The degree of achievement for each objective is summarised below:

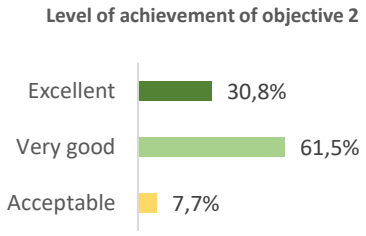
1 To help realise the potential of European cooperation regarding highly specialised healthcare for patients and for healthcare systems by exploiting innovations in medical science and health technologies



The broad geographical representation of the ERN system allows healthcare systems to access experts and share knowledge, facilitating the diagnosis and treatment of patients with rare or complex diseases in Europe. In this sense, some networks have worked on the development of databases of experts according to their expertise and on mapping activities to understand the actual access to specialised treatments and procedures among their members.

The organisation of sub-networks and thematic working groups, as well as collaboration with scientific societies and other networks, helps to foster collaborative efforts and knowledge sharing. Other activities of the networks in European collaboration include the promotion of multicentre projects and joint clinical and research initiatives to increase knowledge of innovative techniques, promote the use of technologies and also develop innovative tools.

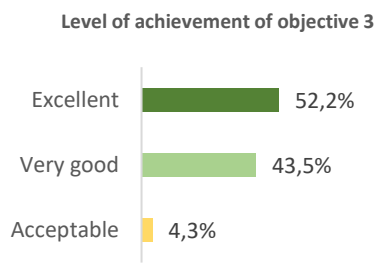
2 To contribute to the pooling of knowledge regarding sickness prevention



While recognising that many rare diseases are not preventable in themselves, ERNs have focused their efforts on disseminating knowledge through education, developing patient pathways, and establishing clinical practice guidelines to inform how certain abnormalities can be detected at an early stage. Some ERNs have complemented these prevention and early detection strategies with initiatives such as newborn screening.

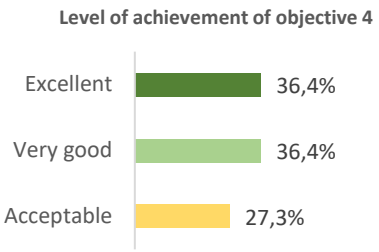
In addition, some ERNs have actively engaged in ERN-related research, established ERN-specific registries and expanded the use of CPMS to facilitate the dissemination of information on rare diseases and complex individual cases..

3 **To facilitate improvements in diagnosis and the delivery of high-quality, accessible, and cost-effective healthcare for all patients with a medical condition requiring a particular concentration of expertise in medical domains where expertise is rare**



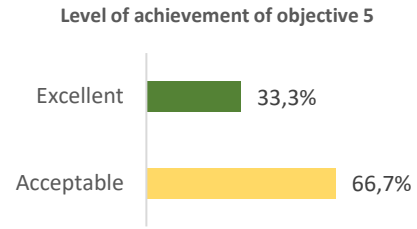
It is clear that each ERN has done its utmost to contribute to this objective. Developing clinical practice guidelines, promoting knowledge exchange through the CPMS, organising various workshops and other training activities, publishing scientific papers and defining indicators to measure clinical outcomes. Each of these activities focuses on disseminating information and finding a clear way to improve cost-effective and high-quality diagnosis of rare diseases..

4 **To maximise the cost-effective use of resources by concentrating them where appropriate**



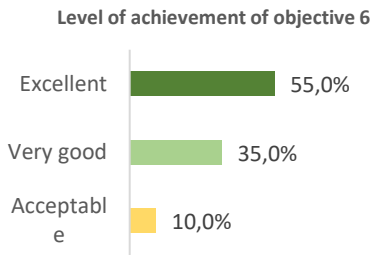
The vast majority of ERNs have a second department or subcontractor, most often the hospital's own general management department, to help them prepare a cost-effective budget. In order to determine where and when to invest resources, some of the ERNs have carried out a resource assessment. In general, all ERNs prioritise patient needs as part of the cost-effective use of resources..

5 **To reinforce research, epidemiological surveillance like registries and provide training for health professionals**



Many ERNs have established registries to collect data on patients with rare diseases. These registries are very valuable as they serve research and epidemiological purposes, as well as providing a better understanding and management of rare diseases. In addition, ERNs have been active in promoting research to advance treatments for rare diseases and have also been involved in clinical trials. In terms of education, ERNs have provided various trainings, educational materials and platforms to increase the knowledge of healthcare professionals and improve patient outcomes.

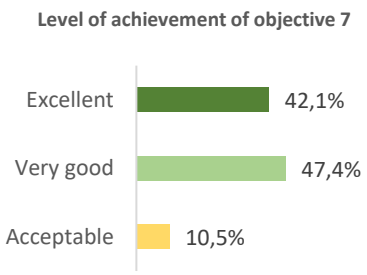
6 **To facilitate mobility of expertise, virtually or physically, and to develop, share and spread information, knowledge, and best practice and to foster developments of the diagnosis and treatment of rare diseases, within and outside the Networks**



To facilitate the dissemination of information and the training of health professionals, some ERNs have implemented mobility programmes. In addition, some ERNs have used the ERN Academy platform to host educational webinars to facilitate knowledge transfer. Clinical practice guidelines for implementation by HCPs have been developed and disseminated. Publications have also been produced to

promote the treatment and care of rare disease patients by disseminating the information gathered.

7 **To encourage the development of quality and safety benchmarks and to help develop and spread best practice within and outside the Network**



Different ERNs have achieved varying degrees of success in this objective. Some ERNs have excelled in developing quality and safety frameworks, guidelines and registries to monitor and improve patient care. Other ERNs have also made excellent progress in developing organisational reference pathways, organising multi-stakeholder workshops, and fostering collaboration for research and knowledge dissemination. On the other hand, some ERNs have made very good progress in their efforts to develop best practice and approaches to patient safety. Many ERNs are making commendable progress in developing disease-specific quality indicators and monitoring clinical outcomes. However, a few ERNs are still in the early stages of their quality and safety initiatives, with plans for future development. Overall, the qualitative assessment shows a commitment to improving patient care and safety within the ERNs, with varying levels of achievement reflecting the diversity of rare diseases and conditions they address.

5. Analysis of strengths and suggestions for improvement by thematic area

The evaluation of the ERN has identified a number of strengths and weaknesses in different thematic areas, by examining the ratings given to the operational criteria and the activities carried out by its members that have a direct impact on the achievement of its objectives.

This chapter reviews the specific strengths and suggestions for improvement identified by the evaluation. The thematic areas that received the highest and lowest ratings in their ME in the evaluation of 24 ERNs are presented.

5.1. Strengths

Governance and coordination

The establishment of a clear governance framework plays an important role in the ERN system, facilitating the performance of essential coordination and supervisory tasks. This governance structure, which has been thoroughly defined in all ERNs, has played a crucial role in defining the objectives, activities and dynamic relationships between HCPs and ERNs.

Most of the ERNs have elaborated work programmes that enable their members to work together. They also have the necessary structure to carry out their activities. Similarly, ERNs have co-ordinating structures that support the governing bodies and regularly involve their members in the development of specific tasks.

These working structures also include representatives of patient organisations with an interest in the ERN's field of activity. In several ERNs, patient organisations are part of the ERN governing body. ERNs are therefore moving forward and including the patient voice in the development of their strategy and activities.

Contribution to research

Progress in research depends on the availability of reliable, unbiased, and representative data on the specific populations being studied. The low prevalence of rare diseases poses a challenge in accessing such data.

The ERNs have been instrumental in sharing data between all members of the networks and in establishing registries and databases at EU level. The creation of collaborative registries by ERNs can make a significant contribution to the epidemiology of rare diseases and guide future research priorities.

ERNs received financial support from the 3rd EU Health Programme (Annual Work Plan 2016 and Annual Work Programme 2019 to develop a comprehensive approach for rare disease registries covering their entire ERN, following JRC standards and tools.

Education and training

Training initiatives should involve a wider range of professionals, not only ERN members, but also affiliates and centres of expertise across Europe.

The ERNs as a whole have undertaken an important process of identifying education, training, and professional development needs in the rare disease care ecosystem. As a result of this work, the networks have initiated various education and training activities for professionals involved in rare disease care across Europe, facilitating the participation of those professionals, whether they are part of the network or not.

Networking and dissemination

In order to effectively disseminate information on its activities, good practices and expertise, the ERN system is required to develop a clear communication strategy. This approach is essential to increase the visibility of the ERNs and to raise awareness of their contributions within the EU.

Key findings indicate that ERNs are effective in developing a precise message, identifying audiences that need information and tailoring content to those audiences.

In addition, the evaluation has shown that HCPs have extensive and in-depth knowledge of rare or complex diseases or conditions. This knowledge serves as a basis for providing accurate information to other healthcare professionals, including clinicians in local hospitals, local referring physicians, general practitioners, and other specialised centres. The active involvement of HCPs in expertise-sharing advisory services enhances the ability of ERNs to provide effective support and foster collaboration between different groups of practitioners.

5.2. Suggestions for improvement

Clinical care

It is essential to ensure that all members and relevant stakeholders have access to Clinical Practice Guidelines through consistent updates, as this has the potential to establish standardised best practice and reduce differences in healthcare across EU countries.

Adopting and implementing these clinical guidelines and recommendations by the HCPs plays a crucial role in standardising care processes, reducing risks, ensuring timely clinical interventions, optimising resource use, and providing consistently high-quality care based on evidence-based practices.

ERNs should continue to develop and update evidence-based guidelines and identify best practices to disseminate to their members. Other key aspects for the development of a sound clinical care management strategy are:

- Developing processes to facilitate the transition from childhood to adulthood or in special circumstances such as pregnancy.
- Progress in developing proposals for the design of cross-border care pathways that provide equitable access to care in their specialty.
- Translating these clinical guidelines or best practices into different languages could significantly improve their dissemination to a wider range of professionals and patients.
- Evaluation of adherence to clinical guidelines through monitoring indicators developed by HCPs, which provide aggregated information on the implementation of clinical guidelines by their members.

The use of the Clinical Patient Management System (CPMS) to share clinical data, images and related information is also important.

The number of cases discussed using this online tool was low, mainly due to the time-consuming process of uploading virtual panels. Another reason that may have had an impact is that sometimes a

cross-border discussion of the case is not necessary if the case has already been resolved through the national networks to which the HCPs belong.

Patient-centred care

Patient experience, including the systematic collection and regular analysis of this feedback by HCPs, is an important component of patient-centred care. This practice gives patients a clear voice and provides valuable insights for making improvements from the patient's point of view. It also addresses issues that the team may not be aware of.

While the concept of patient-centred care offers enormous potential, the development of common tools in the ERN measuring patient and family experience or satisfaction remains underdeveloped. ERNs should encourage HCPs to regularly use a standardised tool and analyse the results to identify opportunities to improve the patient experience of their members.

Quality and patient safety

In order for ERNs to identify areas for improvement in the effectiveness of clinical processes, a comprehensive set of measures or indicators should be developed to monitor clinical processes, performance, and outcomes of care. ERNs are encouraged to continue to work on the analysis of the results of these clinical indicators collected from their members on a regular basis, as the evaluation of these results will stimulate collective reflection for learning and improvement.

Reliable data on the activities of HCPs with a particular type of patient or procedure, the clinical trials in which they are involved, and the reported clinical outcomes can contribute to a meaningful analysis of the collected data, such as surveillance or clinical indicators.

5.3. Best practices

During its first 5 years of operation, the ERN system has made a significant contribution to healthcare by addressing the challenges of rare and complex diseases. The ERNs have demonstrated good practice in all areas of their operational criteria. They have promoted collaboration, knowledge sharing and patient involvement. The evaluators highlighted several outstanding contributions across the 24 ERNs. For each of the thematic areas, several notable examples have been highlighted. These examples are drawn from the specific evaluations conducted for individual ERNs and HCPs. It is important to note that these are not generalised examples of good practice, but rather specific cases extracted from the evaluations.

Governance and coordination

- The activities, results and initiatives of the ERN and each HCP can be monitored by using a robust and efficient dashboard. A specific evaluation system, as is used by one of the networks, to assess the contribution of its members, has shown itself to be a best practice which adds value. (ReCONNET)
- A SWOT analysis to identify their strengths, weaknesses, opportunities, and threats in the competitive environment is a valuable instrument for strategic planning. By analysing the internal and external environment, ERNs gain a better understanding of their organisation's current position and potential for growth. (CRANIO)

Clinical care

- Establishing a Clinical Practice Guideline Expert Panel that includes both internal and external experts and involving scientific societies and other key stakeholders in creating organisational reference models for patient pathways. This initiative demonstrates the network's commitment to evidence-based and collaborative healthcare. It also promotes transparency, reliability, and integration of the latest research, ultimately improving the overall quality of care and patient outcomes within the network. (ReCONNET)
  On the contrary, some ERNs have not yet implemented clinical practice guidelines to assist with the transition from childhood to adulthood. However, a plan to develop such guidelines is underway. A review of the literature and a survey of HCPs have already been carried out and this has identified some transition protocols that are already being used by some of their members. (ERN-RND)

Patient-centred care

- One element to be emphasized is the involvement of patient representatives in all areas of the network. Their role as experts on the disease and their participation on an equal footing with professionals in most of the ERNs is a crucial element in the decision-making process and leads to a clear patient-centred strategy, objectives, and actions. (Endo-ERN)
- Some ERNs translate clinical guidelines, consensus statements and patient journeys into several languages. This goes beyond basic dissemination and reflects a real concern for patients' needs and preferences, recognising that language barriers should not hinder access to important medical information. (ERNICA)

Contribution to Research

- The development of a European registry platform will allow healthcare providers and researchers to analyse trends and identify areas for improvement by collecting comprehensive data on pre-, peri- and post-natal care for specific conditions. (ERNICA)

Education and Training

- The implementation of the ERN Exchange Programme, which focuses on long-term sustainability and excellence in patient care. The programme will provide training and mentoring opportunities for young researchers, with an emphasis on the development of future leaders in healthcare. The ERN ensures a continuous pool of skilled professionals dedicated to advancing medical research and improving patient outcomes by investing in the growth and education of young talent. This collaborative approach enriches the Network's expertise and helps to improve patient care and medical practice. (ITHACA)

Networking and Dissemination

- Activities such as organising regular meetings, collecting feedback via email, launching calls for interest, or using communication platforms, among other strategies, contribute to the collaborative approach of the network. All of these contribute to sustaining and improving cooperation between ERN members, affiliated partners and ePAG advocates. (ReCONNET)

The following good practices are examples that highlight the different strategies, effective methods and noteworthy initiatives that have emerged in all areas of the HCP operational criteria:

Patient-centred care

- Providing in-house services for diagnosis, treatment and care within the hospital has significant benefits from a patient perspective, despite increasing management demands and the complexity of care pathways. Patient experience and outcomes are improved by providing all necessary services within the hospital, eliminating the need for referral to external units. (Karolinska University Hospital – ERKNet)
- The development of a Rare Disease Card by the HCP personalised for each patient and provided free of charge. The card contains the patient's diagnosis and specific information that other clinicians may need in an emergency. The card also contains the contact details of the clinicians who are responsible for the HCP in question. This patient-centred approach prioritizes safety, empowerment, and effective collaboration, showcasing the HCP's commitment to individualized care and improved patient outcomes. (Centro Hospitalar de Lisboa Norte, EPE – MetabERN)
- The provision of 'welcome bags' for young patients on arrival, containing toys, games, and useful information. This demonstrates a compassionate and patient-centred approach to healthcare for young patients, adding a personal touch to hospitalisation and helping children feel more at ease during their stay. A specially designed waiting room with access to games, sports and musical instruments creates a child-friendly environment, reducing the anxiety and fear associated with hospital visits. The presence of a toy MRI scanner for children to familiarise themselves with the scanning process is particularly noteworthy, helping to reduce the stress of undergoing a real MRI scan. (University Children Hospital in Lublin, UCHL – PaedCAN)

Organisation and management

- Coordinating appointments that involve multiple specialists at the same time, putting the patient at the centre of care. This comprehensive strategy, exemplified by the presence of several specialists during a single visit, ensures a holistic approach to the management of medical conditions. (Hôpitaux Universitaires de Strasbourg – RITA)
- The availability of the multidisciplinary team, even outside normal working hours, demonstrates a genuine concern for patients' wellbeing and provides reassurance that urgent health matters will be dealt with promptly. The level of personal attention and care provided by the professional staff sets the HCP team apart from others and makes patients feel valued and supported throughout their healthcare journey. (AO San Camillo Forlanini – Rome – ReCONNET)

Research, education, and training

- Creating educational packages on specific diseases demonstrates a commitment to training and patient safety. The provision of these training packages, which are available to staff both nationally and internationally, reflects a commitment to disseminating knowledge and making a positive contribution to the wider medical community. (Oslo University Hospital – MetabERN)
- Some HCP representatives regularly participate in simulation laboratories to improve their medical care. This commitment to continuous learning and knowledge sharing fosters a culture of improvement, resulting in higher quality patient care and ensuring that healthcare professionals are up to date with the latest advances in their field. (AOU Careggi, Florence – VASCERN)

Exchange of expertise, Information Systems, and e-Health

- A website developed by the HCP that enables patients and families to contact various patient organisations for additional support and information. By providing a centralised platform for patients to access valuable resources and connect with relevant support networks, the HCP ensures that patients receive comprehensive support in managing their condition. (Amsterdam University Medical Centers Location AMC – VASCERN)

Quality and safety

- A flagging system to identify patients diagnosed with rare diseases in electronic health records alerts HCPs to the potential complexities and unique needs of these patients. This procedure goes beyond standard requirements and ensures that rare disease patients receive specialised attention and customised treatments. (University Hospitals Saint-Luc – ReCONNET)

Competence, Experience, and outcomes of care

- Whole genome sequencing for all patients is an excellent practice. The use of this advanced genomic technology has achieved remarkable results in healthcare, such as a significant reduction in the percentage of undiagnosed cases, ensuring that patients receive accurate and timely diagnoses of their conditions. (Karolinska University Hospital – ITHACA)
- Interdisciplinary collaboration within the same hospital is an important practice as it enables the medical team to provide more comprehensive and personalised care, which can lead to improved outcomes and overall quality of life for patients with rare diseases. (Karolinska University Hospital – CRANIO)

Human resources

- The appointment of a dedicated 'support nurse', responsible for both the patient and their family, is another example of the focus on the patient. This nurse provides ongoing information and acts as the first point of contact from the patient's first visit.

6. Conclusions

6.1. Structure of the ERN system

The coverage of geographical areas, diseases and conditions, and patient populations by the ERNs has shown varying degrees of success.

The ERNs have made efforts to cover a wide range of geographical areas, diseases and conditions, and patient populations. This chapter describes the evolution of the structure of the ERN system over the last five years and the way in which the ERNs are currently provide care in these areas.

Geographical representativeness

ERNs are present in 24 EU countries and Norway. They have played a crucial role in improving healthcare across Europe through their network of specialised healthcare facilities. 7 of these countries host the network's coordinating nodes. This enhances their effectiveness in promoting collaboration and sharing expertise.

The ERNs have efficiently facilitated the delivery of specialised care and treatment to patients across several countries, achieving widespread coverage and interconnecting healthcare facilities. As previously mentioned, the overview is still not full as the current evaluation has considered approximately 60% of the current HCPs in the ERN system. However, it has become clear that there is a notable lack of uniformity in the distribution of HCPs across Europe. The Western European region has a higher concentration of HCPs, Italy (22.49%), Germany (14.47%), France (14.59%), the Netherlands (10.53%), Belgium (8.13) and Spain (5.02%). In contrast, Eastern Europe has significantly fewer HCPs: Croatia (0.24%), Hungary (1.67%), Romania (0.84%), Bulgaria (0.84%), Estonia (0.36%) and Latvia (0.24%). At the lower end of the scale in Western Europe are Austria (0.24%) and Luxembourg (0.12%).

There is not only disparity between Member States, but also within countries, with a higher concentration of HCPs in certain regions. Some hospitals show a clear strategic commitment to high specialization in the field of rare diseases by being part of a large number of ERNs.

In terms of ERN membership, besides the full membership, healthcare providers can be classified as 'associated' if their focus is on the provision of healthcare, or 'collaborative' if their focus is on the production of knowledge and tools to improve the quality of care. Together they are referred to as affiliated partners. The Affiliated Partner status may be more suited to some centres in the ERN system to address concerns related to the geographical reach of the ERNs.

ERN now has around 200 affiliated partners that can participate in ERN activities. Their involvement is significant because of their recognised expertise and collaborative approach.

The conclusion of the Brexit transition period marked the end of the participation of UK centres in the ERNs. Specifically, six ERNs (EpiCARE, RARE-LIVER, EURO-NMD, ITHACA, RITA and eUrogen) suffered structural changes, and a total of 118 HCPs from the UK departed the network. Brexit has therefore led to the loss of important knowledge in the ERN system. As a result, there has been a growing interest in expanding collaborations beyond the EU to build partnerships that cross geographical boundaries.

Diseases and conditions

The ERN system is made up of 24 different ERNs, each specialising in a particular area of medical expertise. While the exact number of diseases covered by the ERN system may vary, together these ERNs cover a wide range of rare diseases and complex medical conditions.

Collectively, ERN coverage reaches a significant patient population, ensuring widespread access to tailored and up-to-date care. The ERNs are committed to improving their disease coverage and providing comprehensive care to a wide range of patients, but they face several challenges along the way. Limited funding is the main obstacle, preventing the expansion of thematic groups and the implementation of certain initiatives to increase coverage. Despite these challenges, concerted efforts have been made to overcome them, such as the establishment of new working groups and the development of policies to facilitate the organisation of ERNs.

The ERICA (European Research Infrastructure Consortium) project, presented as a cross-cutting initiative between different ERNs, is an example of a systemic initiative. This initiative advocates the advancement of research and development (R&D) and highlights the importance of collaboration to comprehensively address complex and multisystemic diseases.

Through ERICA and other initiatives, ERNs can influence the research pathway and promote the importance of not only their individual efforts, but also collaboration to advance the knowledge and management of multisystemic diseases.

Coordination structure

Several successful structural elements have emerged from the coordination structure within the ERNs. The matrix-based governance structure used by some ERNs, such as EuroBloodNet and MetabERN, has enabled comprehensive disease and country coverage.

A regular coordination group meeting is held with the participation of all ERN coordinators. In addition to regular meetings, informal interactions between project leaders from different ERNs are organized to address specific issues.

Collaboration and communication between ERNs and HCPs vary considerably within each network. While some ERNs work closely and effectively with their members, this is not uniform across the ERN system. Small ERNs tend to be better in this respect, while larger ERNs with a large number of members find it more difficult to closely monitor all their activities.

Patient representation plays an important role in the ERNs, helping to ensure patient-centred care and reduce geographical inequalities. However, the level of involvement in the different activities and working groups varies among Networks. Nevertheless, these patient representatives advocate for greater recognition and involvement in decision-making, and their patient-centred perspective adds value to many ERN activities.

Board of Member States (BoMS) representatives are in regular contact with ERN coordinators in most ERNs, participating in specific ERN working groups to provide insights from different national stakeholders. ERN Coordinators and BoMS representatives also hold periodic meetings with the European Commission.

In terms of coordination with hospital managers, the evaluation identified a lack of communication with hospital managers. They are often unaware of the activities of the ERN and are not actively involved in the ERN system.

The lack of coordination structures in the hospitals participating in the different ERNs was also highlighted, resulting in healthcare professionals having to manage administrative tasks without standardised processes for common aspects shared across ERNs.

6.2. Maturity of the ERN system

An evaluation of the state of development of the system in terms of purpose, sustainability and integration into national health systems was carried out after the first five years since the ERNs were approved.

Purpose of the ERN system

All ERNs have made great efforts to achieve their objectives and contribute to the advancement of medical knowledge and patient care for rare diseases during these five years. Based on the evaluation, it was found that most ERNs performed exceptionally well in achieving their objectives, with 48.48% rated as Excellent and 43.94% rated as Very Good. This data, together with the information gathered from the interviews with the different stakeholders, shows that the objectives of the ERN system are correctly pursued, keeping in mind that the system has been in place for five years and is still evolving.

One of the main purposes of the ERN system is to bring together healthcare professionals from different European countries. While the ERNs now have a robust structure, there is an urgent need to support and motivate HCPs to ensure their continued involvement in the ERNs and national health systems.

Sustainability

Although both the European Commission and the Member States have areas of shared competence in the field of public health in the European Union, they have different but complementary approaches, particularly with regard to the financing of health initiatives and policies.

The European Commission plays a key role in formulating common public health strategies and policies to ensure coherence and collaboration between Member States. In contrast, Member States retain responsibility for organizing, managing, and financing their national healthcare systems, as well as implementing health policies tailored to their specific needs. They have autonomy in allocating financial and human resources to healthcare and health management within their borders, including the education and training of healthcare professionals.

Despite the shared competences and common objectives between the EU and Member States, a significant challenge remains, which is likely to have a negative impact on initiatives such as the ERNs.

To ensure coordination and activities between ERNs, a common funding mechanism has been established for all ERNs, consisting of direct and specific grants from the EU under the EU4Health programme. At present, as their main sources of funding are EU grants under the EU health programmes, the sustainability of the ERN system is largely dependent on EU funding.

The EU4Health grants were originally based on a single beneficiary approach, with a single HCP designated as the Network Coordinator (NC). This HCP receives all of the ERN's funding. It is extremely challenging or impossible to distribute the funding to other HCPs who play a more active role in the ERN's activities. New initiatives to innovate funding schemes are being explored in response to this challenge. The aim is to broaden the range of HCPs who receive funding for their direct contributions to the network's activities and objectives. By identifying and designating more beneficiaries among HCPs, the ERNs will motivate increased engagement and meaningful participation.

The current funding system considers ERNs as project-based entities rather than permanent bodies. This view, together with the temporary nature of grant funding, creates a discontinuity of funding in the ERN system. If the NC cannot provide the necessary resources, administrative factors such as interruptions or delays in the arrival of funds have a real impact on the smooth and efficient operation of the ERNs.

However, European fundings are intended to support the ERN coordination structures. The new multi-beneficiary approach for EU4Health grants aims to optimize resource allocation for HCPs serving as work package leaders. Nevertheless, many HCPs currently operate on a voluntary basis within the ERN system based on the legislative framework. Despite hospital managers endorsing membership agreements, ERN activities are not formally recognized as part of healthcare professionals' daily workload.

The ERN model is still in an early stage of deployment, but it is a unique and innovative initiative to pool efforts in the care of patients with rare or complex diseases in Europe, providing a supranational collaborative framework. This structure has made it possible to establish connections and offer healthcare professionals the opportunity to have their expertise "recognised" at the European level, to stimulate national centralisation of care and cross-border collaboration.

However, the functioning of ERNs and their success in improving care for patients with rare or complex diseases across Europe depends to a large extent on the support of the Member States. The integration of ERN activities into National Health Systems and the support of national health authorities to HCPs for participation in ERN activities and implementation of clinical guidelines revised or adopted by ERNs is critical for the sustainability of ERNs. The lack of financial support and recognition of the ERN system at national level by Member States poses a major risk to ERNs, as it demotivates HCPs professionals, threatening their level of commitment and engagement.

There is also a need to strengthen the role of patient representation in ERNs. In 80.00% of the networks, there is good patient collaboration, but there are still barriers for patients and clinicians to work together. Some of the barriers are related to cultural differences between Member States in terms of working with patient representatives and their contribution to clinical practice. In addition, the scarce methodological approach to identifying patient needs within the ERNs and the lack of recognition of the voluntary contribution of patient representatives and their value in the ERN system could prevent the full potential of this collaboration from being realised.

Level of integration into NHS

ERNs have an important role to play in providing care for rare and complex diseases across Europe. However, ERNs need to be linked to Member States' healthcare systems in a clear and stable way. Therefore, in order to ensure the long-term sustainability of the ERN system, the ERN inclusion should address challenges such as:

- The efforts of healthcare professionals to demonstrate their expertise and performance are duplicated by the lack of integration of the activities of clinical units, both at ERN and national level.
- The adaptation of clinical guidelines and care pathways to the national healthcare context is necessary for a robust clinical care management strategy of the ERNs. However, the evaluation reveals that national authorities have not provided sufficient support to facilitate the implementation of clinical practice guidelines by HCPs and the development of care pathways by ERNs, hindering the creation of clear and well-defined pathways.
- Issues of data sharing have been identified as a barrier to the inclusion of patients in the CPMS and in the ERN registries.

- The CPMS is the foundation within the ERN to ensure that knowledge "flows" across Europe. However, HCPs struggle with the extra workload caused by the lack of integration of this electronic tool at national level. This is due to the lack of data transfer from the hospital EHR to the CPMS and the fact that these virtual consultations, which provide specialist advice, take place outside the national system.

It is in this context that the JA JARDIN project is currently being developed. This is a European initiative that aims to improve the integration of the ERNs into the NHS of the Member States. The Project, in the grant agreement preparation phase, is expected to be launched in February 2024 and finalised in February 2027.

JA JARDIN brings together 60 partner organisations, of which 28 are competent authorities, 31 are affiliated organisations and 1 is an associated partner from 29 different Member States. The total budget of this Joint Action is €18.75 million.

In order to improve the link between ERNs, healthcare providers, specialists and patients, JA JARDIN is addressing different aspects. Key areas include information campaigns, data management, governance, and sustainability through the following work packages:

- WP4: Sustainability
- WP5: National governance and quality assurance models
- WP6: National care pathways and ERN referral systems
- WP7: National reference networks and undiagnosed disease programs or equivalent
- WP8: Data management
- WP9: National support options for ERN-HCP

6.3. Activity of the ERN System

These activities, as described in their Specific Grant Agreements, include the development of clinical practice guidelines, the conduct of research studies, the establishment of patient registries, the promotion of education and knowledge sharing, and cross-border collaboration. Following an analysis of the extent to which the networks have completed the activities planned to meet the objectives set out in the Specific Grant Agreements, this section presents the highlights.

Network activity status

Most ERNs showed a strong commitment to developing the planned tasks and deliverables for the different work packages, as 84.5% of the deliverables reviewed were fit for purpose and produced on time.

The ERNs have evolved in different ways, with some ERNs building on pre-existing national networks, providing an informal foundation for their creation. As a result, the more mature ERNs have been able to maintain and develop the activities that were the basis of their creation. Some of them have started from scratch and worked hard over the last five years to get their basic structures in place. These ERNs have focused on setting their standards to acquire expertise, and while progress has been made, certain activities are still undergoing development.

In this regard, the development of evidence-based clinical guidelines has proven to be a more complex process than expected, given the difficulties in obtaining recommendations based on scientific evidence in the field of rare diseases. In many cases, intermediate steps that will allow the development of these clinical practice guidelines in the future, such as expert panels and sharing of scientific references, have been taken.

Furthermore, the difficult health scenario caused by the COVID-19 pandemic, which lasted for two years and had a significant impact on all HCPs, Affiliated Partners and ePAG Advocates, needs to be highlighted when developing activities. Although many HCPs had to close during the first waves of the pandemic in order to care for COVID patients, the ERNs responded from the beginning by adapting their practices to provide immediate support and advice to rare disease patients.

Cross-border collaboration

ERNs have also fostered cross-border cooperation and networking, recognising the importance of multidisciplinary approaches and shared expertise in the management of rare diseases. Through their extensive networks, ERNs have facilitated the pooling of resources, knowledge, and experience. This has led to improved patient outcomes and a better understanding of rare diseases.

Despite notable achievements, challenges have emerged within the CPMS, the cornerstone for obtaining expert advice from HCPs. CPMS activities have been limited by technical difficulties and lack of integration of national networks. There have also been barriers to the development and implementation of CPMSs for clinical data exchange. The ERNs have worked hard to encourage their members to adopt CPMS; however, it has been noted that difficulties arise from the legal framework for sharing clinical data and from insufficient integration with national systems.

ERN Continuous Monitoring and Quality Improvement System

To facilitate regular evaluation and monitoring, it is essential that ERNs identify and disseminate evaluation criteria. In terms of monitoring ERNs, an ERN Continuous Monitoring and Quality Improvement System (ERN CMQS) has been introduced, as part of the integrated Assessment, Monitoring, Evaluation, and Quality Improvement System (AMEQUIS). This system consists of a set of 18 indicators common to all ERNs, as well as network-specific indicators. Although, these 18 generic indicators are applicable across the different ERNs, because they differ dramatically in size and disease scope, the data collected should be used to benchmark each ERN itself. Interpretation must therefore take into account the unique characteristics of each network.

This evaluation has highlighted the lack of reference baselines for the ERN-specific indicators. The implementation of these would be beneficial for trend analysis and compliance assessment. This is an opportunity for continuous improvement in the work of the ERN.

6.4. Impact of the ERN System

This section assesses the impact of the ERN system on patients' experience and journey through the healthcare system. By improving access to expert care, promoting multidisciplinary approaches, facilitating cross-border healthcare, sharing best practice, and involving patients in decision-making, ERNs aim to add value for patients. Across several ERNs, there is evidence of a significant impact of the ERN system on patients' healthcare experiences and pathways.

Empowered Patient-Centric Approach

The impact of the ERNs on the patient experience has been notable, facilitated by the strong involvement of patients, driven by patient organisations and EURORDIS (the European Organisation for Rare Diseases). Patient involvement has become a fundamental aspect of many ERNs. Patients and their families are proactively involved in critical decision-making and policy formulation. However, the evaluation shows that they need to improve in collecting information on patient experience and satisfaction with care in the ERN's area of expertise. Most ERNs have not developed a standardised common tool for members to report patient experience data. In addition, it was found that when services are provided via telemedicine, satisfaction with telemedicine and other e-health tools is not assessed.

Similarly, few ERNs collect data to monitor and evaluate the participation of patient representatives in ERN activities. There is also no standardised methodology to facilitate common rules for this evaluation across ERNs.

Beyond advocacy, patient organisations have played a crucial role in raising awareness, supporting each other, and working in harmony within the ERN. From developing clinical guidelines and sharing first-hand patient experiences to contributing to clinical trials, their active involvement covers a wide range of aspects. The strong commitment to improving patient wellbeing and overall outcomes is underlined by the collaboration between patients, patient groups, and ERNs.

Enhanced knowledge dissemination

ERNs have also been a catalyst for the exchange of best practices, education, and training, which has led to an increase in the visibility and awareness of rare diseases. In terms of knowledge exchange between healthcare professionals and patients, ERNs have a clear and positive impact.

The ERN system facilitates a wide range of activities that contribute significantly to the improvement of the expertise of healthcare professionals by providing them with valuable learning experiences and an enhanced exchange of knowledge for the direct benefit of patients.

ERNs provide a platform not only for healthcare professionals but also for patients. They give visibility to rare diseases that often go unnoticed. This is particularly important as clinical decisions within ERNs are multidisciplinary, ensuring comprehensive and informed assessments. As part of this commitment, ERNs produce patient-focused materials, such as fact sheets on different diseases. These are designed to increase patient understanding and involvement. In addition, and particularly in the complex landscape of rare diseases and specific pathologies, the organisation of workshops and training courses by ERNs amplifies their impact by providing a continuous flow of expertise and insight.

Furthermore, ERNs are a solid foundation for the exchange of the latest advances, practical guidelines, and treatment standardisation, thus promoting a more equitable approach to healthcare in different countries. The ERN system enables professionals dedicated to providing the best possible care to stay updated and well-informed about how to treat and care for their patients.

Transforming Specialized Care and Access to Treatment

The ERNs have led to transformative improvements in the provision of specialised care and improved access to diagnosis and treatments for patients. According to the data reported, more than 2 million patients were diagnosed and treated by HCPs during the evaluation period.

The network-based structure has the potential to facilitate large-scale studies. This will lead to a deeper understanding of rare diseases and more comprehensive research results.

The ERN framework also helps to alleviate congestion within healthcare systems. By establishing multiple centres of reference, patients will be more evenly distributed. This will reduce the burden on individual healthcare institutions and streamline patient management.

Many ERNs have facilitated access to multidisciplinary expertise. This has improved the quality and efficiency of care for rare diseases. All ERNs have worked on the development of ERN registries. The aim of these registries is to bring together all the information from their members in order to facilitate the monitoring of specific diseases and to provide an overview of the situation of rare diseases in Europe. In addition, ERNs provide direct access to experts and promote collaboration and knowledge sharing among healthcare professionals through the use of tools such as the CPMS.

It is clear that ERNs have had a transformative impact. However, certain challenges should be taken into account. Specifically, language barriers and resource allocation to support HCP activities for the ERN have been identified as areas for improvement.

7. Opportunities for improvement detected by the IEB

ERNs are a major breakthrough in the management of rare diseases and healthcare collaboration throughout Europe. These networks have proven to be valuable forums for healthcare professionals, patient organisations, and stakeholders to work together to address the challenges of rare diseases. The ERN system operates in a complex landscape but has proven to be flexible and resilient to the impact of the COVID-19 pandemic and the Brexit. This section examines key components of the ERN system, highlighting barriers and opportunities to improve its effectiveness in different areas.

Several conclusions and suggestions are drawn from the findings identified by the IEB during the first evaluation. These suggestions were based on the experience of the IEB, the consortium and the evaluators, and cover various aspects of the ERN system. In addition to the lessons learned, these suggestions were then cross-checked with information gathered through satisfaction surveys of HCPs, ERNs, and evaluators, as well as through interviews with a selection of stakeholders.

OPPORTUNITY 1

COORDINATION WITHIN THE ERN SYSTEM

While regular meetings between BoMS and ERN coordinators take place, there is a recognised need for a more formalised and structured approach to promote multidisciplinary collaboration within ERNs. Therefore, prescriptive rules could be established to standardise collaboration expectations between BoMS representatives, ERNs, and HCPs. These collaboration rules may form a basis for national governance models for ERN-HCP, thereby facilitating ERN integration into NHS.

At hospital level, the involvement of hospital managers is highly recommended, as they are often unaware of ERN activities. In addition, internal collaboration between different HCPs within different ERNs in the same hospital is not systematic. Therefore, coordination mechanisms between HCPs at hospital level are recommended to facilitate internal communication.

Priority should be given to revitalising national plans and strategies for rare diseases to improve coordination with ERN activities. This will allow for the integration of existing national pathways where possible, and their linkage to ERNs where such integration has not been previously considered.

Establishing stronger collaborative mechanisms is essential for addressing cross-cutting issues and enhancing care for patients with rare diseases. Key areas of focus include ensuring continuity of care from childhood to adulthood, effectively managing pregnancy, and addressing mental health needs. Continuity of care is crucial involving the development of standardized protocols that facilitate seamless transitions from paediatric to adult services, ensuring that patients receive consistent and appropriate care throughout their lives.

In the "Recommendations to Achieve a Mature ERN System by 2030" EURORDIS emphasizes the need to address cross-cutting issues within the ERNs to improve care for patients with rare diseases. Existing working groups are focusing on areas of common interest to develop guidelines and best practices for comprehensive and coordinated care. For example, the Pregnancy and Family Planning working group aims to manage pregnancies in women with rare diseases more effectively, ensuring safe and evidence-based care.

Building on these initiatives, the creation of new ERNs has been explored to address gaps and further enhance care in these cross-cutting areas. Specifically, a proposed standalone Gynaeco-Obstetrics ERN would address complex gynaecological and obstetrical conditions, enhancing collaboration among existing ERNs and strengthening national healthcare capacities. This network would also partner with

the European Medicines Agency (EMA) to systematically collect data on pregnancy outcomes and adverse effects in clinical trials and post-approval contexts. These steps aim to ensure a comprehensive, coordinated, and multidisciplinary approach to addressing the needs of rare disease patients across Europe.

Furthermore, given the multisystemic nature of many diseases, it is vital to establish formal ways of collaboration between different ERNs. Adopting a proactive approach and working collaboratively to take advantage of multiple areas of expertise and knowledge is highly recommended to effectively address the complexity of these conditions from a holistic perspective.

OPPORTUNITY 2

VISIBILITY AND RECOGNITION FOR ERNS AND THEIR MEMBERS

The structure and operational framework of ERNs pose significant challenges to their recognition and visibility. ERNs operate as project-based systems without a legal entity, which limits their ability to attract specific funding and recognition. While this project-based approach is proving useful for scientific endeavours, it is not fully compatible with the broad scope and enduring objectives of ERNs. This mismatch may hamper the ability of ERNs to secure long-term funding and resources, to gain legal recognition, and to gain prominence within the European and national health landscape. It is therefore advisable to seek a legal entity for ERNs to enable their participation in funding programmes, collaborations and partnerships that require specific organisational structures**.**

The lack of sufficient support from national health authorities exacerbates the challenge for HCP representatives. This lack of support is further exacerbated by a lack of awareness and understanding of ERNs at both national and European level. It is therefore essential to establish national recognition for HCPs involved in ERNs, as this would encourage their engagement and contribution. In this context, a more structured approach to national support for healthcare professionals (HCPs) is necessary.

To ensure the long-lasting sustainability of ERNs and commitment of its volunteers, it is crucial to improve the recognition and visibility of the ERNs. This requires strategic dissemination of information about the existence, purpose, and accomplishments of ERNs to a broader audience. By raising awareness among healthcare professionals, health institutions, policymakers, and the public, ERNs can receive more recognition for their significant role in the management and care of rare diseases.

OPPORTUNITY 3

LEGAL ISSUES

Healthcare in each country is overseen by its national health ministry, resulting in differences in regulations that impede the standardization of care in the ERN system. This regulatory disparity creates an obstacle to providing consistent care for patients with rare diseases. A prime instance is the variance in national data protection rules, which obstructs the exchange of medical information.

The ERN system fosters a fresh mindset, aided by the digitisation of all services, that relies on collaborative research involving sharing clinical data among various professionals. To ensure patient data privacy and security, this joint data sharing process must abide by strict policies. However, patient registration in the ERNs is not necessarily integrated with national registries. This leads to duplication

of work. There is currently no information system that allows clinical data to be exchanged between different levels and across national and European borders.

The European Health Data Space (EHDS) addresses these regulatory challenges by establishing a unified framework for cross-border data exchange, ensuring rigorous data privacy and security standards are upheld. By introducing standardized data protocols and secure access mechanisms, the EHDS has the potential to harmonize the regulatory disparities among national health systems, thereby facilitating the seamless access and sharing of clinical data within the ERN system. This integration would reduce duplication of efforts, streamline patient registration processes, and support the ERNs' collaborative research initiatives by enabling healthcare professionals to access a comprehensive, interoperable data repository.

OPPORTUNITY 4

LACK OF RESOURCES

The issue of inadequate recognition, support, and funding within the ERN, highlighted by many HCPs, highlights a notable challenge that requires attention. A particular concern is the payment mechanism for uploading data to the CPMS. The lack of a standardized payment mechanism may lead to variations in data submission rates and data quality. At the same time, HCPs encounter challenges as their healthcare-related activities on this platform are uncompensated, whereas they increase their workload. Consequently, proposals for nationwide and hospital-level backing of ERN-HCP and a compensation strategy for CPMS activities ought to be formulated to ease the assimilation of ERNs into the national healthcare systems.

The current distribution of funding within the ERNs has sparked concerns regarding its structure. Presently, the funding structure directs most of its resources towards the organizational system of the ERNs and the HCPs functioning as NCs. While these functions are crucial, a more uniform allocation of funds may stimulate wider HCP participation. Ergo, it has become crucial to undertake a comprehensive review of the funding system to ensure its adaptability and cohesion.

Ensuring the ERNs long-term sustainability requires support from the Member States at the highest political level. EU funding mechanisms have been put in place to support the coordination of the networks, but for a real integration of the ERN system activities into NHS financial support from Member States will be required to provide the infrastructure and resources needed to address the gap between the national health system and each ERN.

Therefore, the operational effectiveness and long-term sustainability of the ERN system require that all Member States to take ownership the ERN model, providing the resources to facilitate the participation of HCPs. To address the funding challenge impacting the sustainability of ERNs, several opportunities for improvement can be considered:

First, it is essential to promote closer cooperation between the EU and individual Member States through the existing Board of Member States. This could include establishing more structured dialogues within this forum, where both entities actively participate in discussions related to the ERN, aiming to harmonise strategies for allocating resources and standards of care.

Secondly, the resources available for these networks could be increased by incentivising Member States to increase their financial commitment to HCPs involved in ERNs through funding schemes or grants. Exploring innovative funding mechanisms, such as public-private partnerships or leveraging EU funding to attract additional private investment, could significantly increase financial support for ERNs.

Lastly, advocating for clearer guidelines or directives that encourage Member states to allocate a specific portion of their healthcare budgets to support ERNs could help ensure consistent and adequate funding across participating HCPs.

OPPORTUNITY 5

PATIENT EMPOWERMENT

Patient associations play a crucial role in ERNs, with roughly 80% demonstrating a firm dedication to involving the patient perspective in rare disease management and decision making. This partnership between clinicians and patients has the potential to enhance patient care, treatment outcomes, and overall healthcare experiences. To ensure the optimal impact of this partnership, it is vital to create concise organizational tools and guidelines that facilitate and streamline the collaboration. These guidelines must specify when and how patients should be involved in various ERN activities, such as research initiatives and the development of clinical guidelines. This approach will ensure that patient involvement is meaningful and significant, leading to solutions that benefit patients.

Patient representatives also need more recognition for their voluntary work as ERN members in the legislation. They are not mere spectators, but active participants in discussions, providing input and contributing to decision-making. Their involvement covers a wide range of areas, including the design of clinical trials, the creation of patient-centred educational resources and the evaluation of health services from a patient perspective. Henceforth, mechanisms for patient engagement, delineation of patient representatives' roles within the European Reference Networks (ERNs), and allocation of resources to bolster their efforts therein necessitate clear definition to establish a foundational framework across all ERNs.

In addition, efforts to improve the culture of patient-centred care within ERNs and HCPs should focus on two fronts.

The first is to identify opportunities for improvement from the experiences of patients with rare or complex diseases. It is recommended that a validated methodology be developed to collect and analyse the experiences of patients receiving care in specialised units. Ideally, this methodology should be consistent across networks.

On the other hand, despite numerous attempts by different networks to assess the involvement of patient representatives in their activities, it is imperative to establish process and outcome metrics to track their real impact. These metrics need to be consistent across networks, so that levels of engagement and collaboration can be routinely assessed. By analysing this data, ERNs should be able to understand the requirements of their collaboration, identify real needs and make changes where necessary.

OPPORTUNITY 6

REVISION OF THE CPMS

The CPMS is the main IT platform for clinical consultations between ERN members. Therefore, both the uploading of cases and the participation of experts in these cases are equally important. As a result, the CPMS tool can be very useful for the exchange of knowledge and expertise across borders allowing health care professionals to work with a multidisciplinary approach. Low uptake of this tool by practitioners, due to technical difficulties and lack of time, requires revision and improvement to make this tool more user-friendly and intuitive.

In addition, this revision of the CPMS tool should result a complete picture of the patient's condition. The CPMS should provide a collection of information and data on the patient's physical, psychological, and social needs, as well as their medical history, for a comprehensive assessment of the patient. This information is essential for appropriate decision making, facilitating diagnosis and treatment by virtual panels of professionals.

OPPORTUNITY 7

GEOGRAPHICAL DISTRIBUTION

Geographical disparities in the ERN system have become apparent. Several countries have emerged with larger numbers. They have made significant progress in their activities and have a high level of experience and expertise within the ERN system. In contrast, certain countries, primarily located in Eastern Europe, find themselves in a beneficiary role within the ERN system. Extensive support in terms of both case and knowledge exchange enables them to access the collective expertise of the ERN system. Nonetheless, this highlights the educational and training gap present especially in Eastern European nations. Although the system is beneficial, discrepancies in proficiency and experience could impede consistent and homogeneous quality standards of care throughout the ERN system.

The ERNs have a particular opportunity to promote a shared learning experience in order to address inequalities and gaps in expertise. ERNs must actively seek to bridge the education/training gap that hinders the creation of consistent quality standards by promoting collaboration, knowledge sharing and educational initiatives.

In countries with limited representation, geographical coverage can be improved by prioritising the inclusion of centres with relevant experience to ensure that their activities benefit from skilled professionals.

It is essential to maintain a balanced and inclusive participation of HCPs from different countries in the activities of ERNs. This is particularly important for countries with a limited number of specialised centres. It is therefore recommended to encourage the active involvement of countries such as Croatia, Bulgaria, Romania, Greece, and Poland to increase their representation in all ERNs.

OPPORTUNITY 8

REVISION OF THE MONITORING INDICATORS

Given their inherent heterogeneity and lack of comparability in terms of disease, scope, and coverage, designing universal monitoring indicators for 24 different ERNs is a complex challenge. In addition, the inclusion of intermediate milestones in the indicator framework is essential due to the different stages of maturity of the ERNs.

For example, the development of clinical guidelines involves several initial steps, including surveys, focus groups and document review. It is important to recognise and acknowledge these steps as they are essential and should be included in any future evaluation process. Adopting this all-encompassing perspective, which looks at progress along the whole journey rather than focusing solely on the end results, provides a better perspective.

Rather, it is essential to establish the criteria for measuring the ePAG's contribution to the ERN and the patient's satisfaction or experience under the care of the HCP.

It is important to underline that the actions taken by the HCPs are evaluated collectively when analysing the results of the ERN. It is therefore essential to define and implement a validation system for the information reported by HCPs to ensure that it is monitored in a consistent manner.

In addition, an integrated quality management system must be established to help ERNs identify trends, targets and opportunities for improvement using a standardised methodology. This system should effectively link the analysis of indicators to the objectives of the network, taking into account the objectives and KPIs set out in the technical reports of the grant.

All these aspects should be taken into account in the revision of the monitoring system with the aim of streamlining the ERN assessment process in the future and enabling sustainable improvement of the ERN.

Annex I: Stakeholders interviewed by the IEB

ERN Coordinators

- EpiCARE
- TransplantChild
- ReCONNET
- MetabERN

HCPs with onsite audit

- Assistance Publique-Hôpitaux de Paris, Hôpital Necker-Enfants Malades – TransplantChild
- Erasmus MC: University Medical Center Rotterdam – ERNICA
- Hospital Clínic i Provincial de Barcelona – ERN-LUNG
- Hospital Universitari Vall d'Hebron – EuroBlood
- Hospital Universitario y Politécnico La Fe – PaedCAN
- Karolinska University Hospital
- University Hospital 'Alexandrovska' Sofia – MetabERN

Evaluators

- President of the Board. Instituto de Excelencia Europea SL.
- Rare Disease Program Manager. Servei Català de la Salut.
- Scientific Director. myOmics SL.
- President of the Board. ANDO Portugal.
- Higher Education Lecturer. University of Granada.
- Coordinator of the Hereditary Metabolic Diseases Unit and Associate Professor of Pediatrics. Hospital Universitario Cruces and University of the Basque Country.
- Postdoctoral Research Fellow. Institute of Biomedicine of Seville.
- Head of Cancer Genetics Clinic. Institute of Oncology Ljubljana.
- MD PhD. Quality and Hospitalization Manager. Cardiology Department. Virgen del Rocío University Hospital.
- Childhood Cancer and Blood Disorders. Vall d´Hebron Research Institute.

Patient Organizations

- EURORDIS

Board of Member States (BoMS)

- Denmark. Danish Health Authority.
- Lithuania. Vilnius University Hospital.
- Belgium. Federal Public Service of Health.
- Spain. Ministry of Health, Social Services and Equality.
- Czech Republic. Charles University in Prague.
- Austria. University of Vienna.

HaDEA

- Project Advisor at HaDEA

Annex II: Geographical coverage of each Network

BOND

Table 4. Information of BOND

Network node	Italy
Network Coordinator	Rizzoli Orthopaedic Institute of Bologna
Countries covered	9
HCPs	24

Figure 12. Geographical coverage of BOND

Table 5. Healthcare Providers in BOND

Country	HCP	Onsite Audit
Belgium	University Hospital Antwerp	No
	University Hospital Ghent	Yes
Czech Republic	Motol University Hospital	No
Estonia	Tartu University Hospital	Yes
France	Assistance Publique-Hôpitaux de Paris, Hôpital Cochin	No
	Assistance Publique-Hôpitaux de Paris, Hôpital Bicêtre	Yes

Country	HCP	Onsite Audit
	Assistance Publique-Hôpitaux de Paris, Hôpital Necker-Enfants Malades	No
	CHU de Toulouse	No
	Hospices Civils de Lyon	Yes
Germany	Klinikum der Universität München	No
	Universitätsklinikum Essen	No
	Universitätsklinikum Freiburg	No
	Universitätsklinikum Köln	No
	Universitätsklinikum Magdeburg	No
Italy	AOU Careggi, Florence	No
	AOUI Verona	No
	Foundation IRCCS CA'Granda Ospedale Maggiore polyclinic - Milan	No
	IRCCS Burlo Garofolo - Trieste	No
	IRCCS Institute Giannina Gaslini - Genoa	Yes
	Rizzoli Orthopaedic Institute of Bologna	No
	University Hospital of Padova	No
Netherlands	Erasmus MC: University Medical Center Rotterdam	No
	Leiden University Medical Center	No
Portugal	Centro Hospitalar e Universitário de Coimbra, EPE	Yes
Sweden	Karolinska University Hospital	No

CRANIO

Table 6. Information of CRANIO

Network node	Netherlands
ERN Coordinator	Erasmus MC: University Medical Center Rotterdam
Countries	10
HCPs	21

Figure 13. Geographical coverage of CRANIO

Table 7. Healthcare Providers in CRANIO

Country	HCP	Onsite Audit
Czech Republic	Motol University Hospital	No
Finland	Helsinki University Hospital (HUS)	No
France	Assistance Publique-Hôpitaux de Paris, Hôpital Necker-Enfants Malades	No
	Hôpitaux Universitaires de Strasbourg	No
Germany	Charité Universitätsmedizin Berlin	No
Hungary	University of Pécs	No
Italy	Fondazione IRCCS Ospedale San Gerardo dei Tintori di Monza	No

Country	HCP	Onsite Audit
	Fondazione Policlinico Gemelli, IRCCs, Rome	No
	Foundation IRCCS neurological institute Carlo Besta - Milan	No
	Hospital San Paolo - Milan	Yes
	San Bortolo Hospital - Vicenza	No
	University Hospital of Padova	No
Netherlands	Erasmus MC: University Medical Center Rotterdam	No
	Radboud University Medical Centre Nijmegen	Yes
	University Medical Center Utrecht	No
Portugal	Centro Hospitalar de Lisboa Norte, EPE	Yes
Spain	Hospital Universitari Vall d'Hebron	No
	Hospital Universitario 12 de Octubre	Yes
Sweden	Karolinska University Hospital	No
	Sahlgrenska University Hospital	No
	Uppsala University Hospital	Yes

ENDO-ERN

Table 8. Information of ENDO-ERN

Network node	The Netherlands
ERN Coordinator	Amsterdam University Medical Centers Location AMC
Countries	18
HCPs	62

Figure 14. Geographical coverage of ENDO-ERN

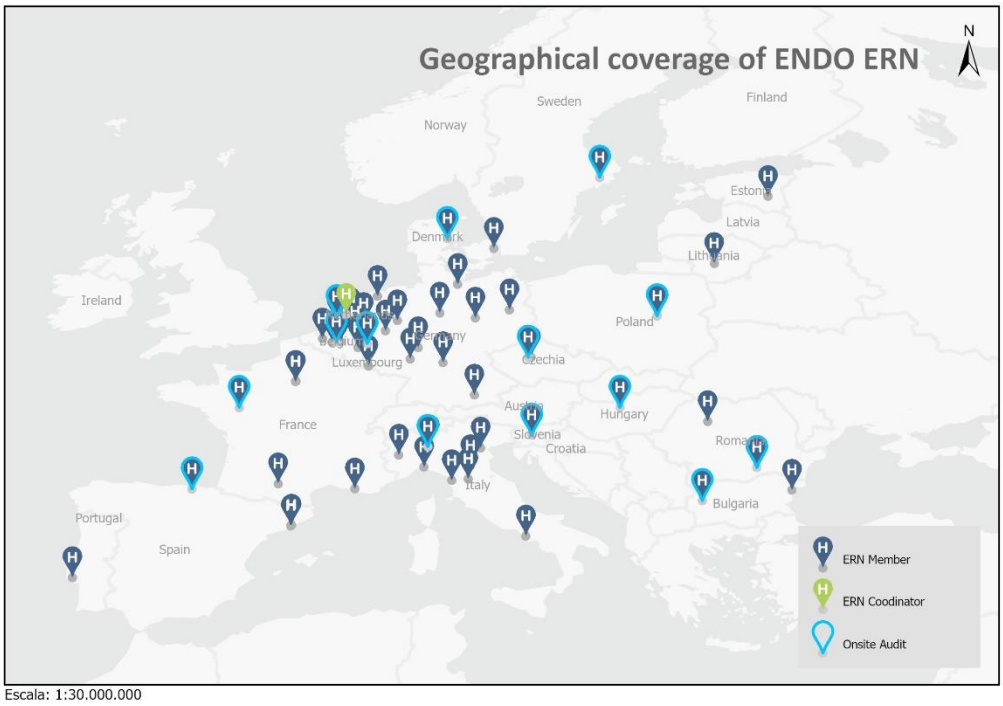


Table 9. Healthcare Providers in ENDO-ERN

Country	HCP	Onsite Audit
Belgium	Erasme Hospital	No
	University Hospital Brussels	No
	University Hospital Ghent	No
	University Hospital Leuven	No
	University Hospital Liège	No
	University Hospitals Saint-Luc	Yes
Bulgaria	MHAT 'Sveta Marina'	No
	USHATE 'Acad Ivan Penchev'	Yes
Czech Republic	Motol University Hospital	Yes

Country	HCP	Onsite Audit
	University Hospital Královské Vinohrady	No
Denmark	Aarhus University Hospital	Yes
	Copenhagen University Hospital, Rigshospitalet	No
Estonia	Tartu University Hospital	No
France	Assistance Publique-Hôpitaux de Marseille	No
	Assistance Publique-Hôpitaux de Paris, Hôpital Cochin	No
	Assistance Publique-Hôpitaux de Paris, Hôpital Bicêtre	No
	Assistance Publique-Hôpitaux de Paris, Hôpital Necker-Enfants Malades	No
	Assistance Publique-Hôpitaux de Paris, Hôpital Pitié-Salpétrière	No
	CHU d'Angers	Yes
	CHU de Toulouse	No
Germany	Charité Universitätsmedizin Berlin	No
	Hannoversche Kinderheilanstalt	No
	Klinikum der Universität München	No
	Uniklinik RWTH Aachen	Yes
	Universitätsklinikum Essen	No
	Universitätsklinikum Gießen und Marburg	No
	Universitätsklinikum Magdeburg	No
	Universitätsklinikum Münster	No
	Universitätsklinikum Schleswig-Holstein	No
	Universitätsklinikum Würzburg	No
	Universitätsmedizin Mainz	No
Hungary	Semmelweis University	Yes
Italy	AO City of Health and Science - Turin	No
	AOU - Bologna	No
	AOU Careggi, Florence	No
	AOU Federico II - Naples	No
	AOU Meyer - Florence	No
	AOU Pisan	No
	IRCCS Auxologico Italian Institute - Milan	Yes
	IRCCS Ospedale Policlinico San Martino – Genova	No
	San Raffaele hospital - Milan	No
	University Hospital of Padova	No
Lithuania	Hospital of Lithuanian University of Health Sciences Kauno Klinikos	No
Luxembourg	Centre Hospitalier de Luxembourg	No
Netherlands	Amsterdam University Medical Centers Location AMC	No

Country	HCP	Onsite Audit
	Erasmus MC: University Medical Center Rotterdam	No
	Leiden University Medical Center	Yes
	Maastricht University Medical Center+	No
	Máxima Medisch Centrum Veldhoven	No
	Radboud University Medical Centre Nijmegen	No
	University Medical Center Utrecht	No
	University Medical Centre Groningen	No
Poland	Maria Sklodowska-Curie National Research Institute of Oncology (MSCNRIO)	No
	Public Pediatric Teaching Hospital	Yes
Portugal	APDP - Associação de Diabéticos de Portugal	No
Romania	Institute of Oncology 'Prof dr. Lon Chiricuta' Cluj-Napoca	No
Slovenia	University Medical Centre Ljubljana	Yes
Spain	Hospital Universitari Vall d'Hebron	No
	Hospital Universitario de Cruces	Yes
	Sant Joan de Déu Hospital	No
Sweden	Karolinska University Hospital	Yes

EPICARE

Table 10. Information of EPICARE

Network node	France
ERN Coordinator	Hospices Civils de Lyon
Countries	12
HCPs	24

Figure 15. Geographical coverage of EPICARE

Table 11. Healthcare Providers in EPICARE

Country	HCP	Onsite Audit
Belgium	University Hospital Leuven	No
Czech Republic	Motol University Hospital	Yes
	Saint Anna University Hospital in Brno	No
Finland	Kuopio University Hospital, Finland	No
France	Assistance Publique-Hôpitaux de Paris, Hôpital Necker-Enfants Malades	Yes
	CHU de Lille	No
	Hospices Civils de Lyon	No
Germany	Universitätsklinikum Bonn	No
	Universitätsklinikum Freiburg	No
Italy	AOU Meyer - Florence	No
	AUSL of Bologna – IRCCS Institute of Neurological Sciences	No
	Foundation IRCCS neurological institute Carlo Besta - Milan	No
	National Neurological Institute Foundation C. Mondino - Pavia	No
	Pediatric hospital Bambino Gesù, Rome	No
Netherlands	University Medical Center Utrecht	Yes
Poland	The Children's Memorial Health Institute	No
Portugal	Centro Hospitalar de Lisboa Norte, EPE	Yes
	Centro Hospitalar do Porto, EPE	No

Country	HCP	Onsite Audit
	Centro Hospitalar e Universitário de Coimbra, EPE	No
Romania	Clinical Psychiatric Hospital 'Alexandru Obregia'	No
Spain	Hospital del Mar	No
	Hospital Universitario y Politécnico La Fe	No
	Sant Joan de Déu Hospital	No
Sweden	Sahlgrenska University Hospital	Yes

ERKNET

Table 12. Information of ERKNet

Network node	Germany
ERN Coordinator	Universitätsklinikum Heidelberg
Countries	11
HCPs	33

Figure 16. Geographical coverage of ERKNet

Table 13. Healthcare Providers in ERKNet

Country	HCP	Onsite Audit
Belgium	University Hospital Leuven	No
	University Hospitals Saint-Luc	Yes
Czech Republic	Motol University Hospital	No
Finland	Helsinki University Hospital (HUS)	Yes
France	Assistance Publique-Hôpitaux de Paris, Hôpital Henri-Mondor	No
	Assistance Publique-Hôpitaux de Paris, Hôpital Necker-Enfants Malades	No
	Assistance Publique-Hôpitaux de Paris, Hôpital Tenon	No
	CHU de Toulouse	No

Country	HCP	Onsite Audit
	Hospices Civils de Lyon	Yes
Germany	Medizinische Hochschule Hannover	Yes
	Universitätsklinikum Essen	No
	Universitätsklinikum Hamburg-Eppendorf	No
	Universitätsklinikum Heidelberg	No
	Universitätsklinikum Köln	No
	Universitätsklinikum Münster	No
Italy	A.S.L. Turin 2 - Hub O. Giovanni Bosco	No
	AO Santobono-Pausilipon - Naples	No
	AOU Meyer - Florence	No
	AOU Siena	No
	AOU University of Campania 'Luigi Vanvitelli', Naples	Yes
	Fondazione Policlinico Gemelli, IRCCs, Rome	No
	Foundation IRCCS CA'Granda Ospedale Maggiore polyclinic - Milan	No
	Hospital Pope John XXIII - Bergamo	No
	IRCCS Institute Giannina Gaslini - Genoa	No
	Pediatric hospital Bambino Gesù, Rome	No
	University Hospital of Padova	No
Lithuania	Vilnius University Hospital Santaros Klinikos	Yes
Netherlands	Amsterdam University Medical Centers Location AMC	Yes
	Radboud University Medical Centre Nijmegen	No
	University Medical Center Utrecht	No
Poland	University Clinical Hospital of Medical University Gdansk	No
Spain	Hospital Universitari Vall d'Hebron	No
Sweden	Karolinska University Hospital	Yes

ERN RND

Table 14. Information of ERN RND

Network node	Germany
ERN Coordinator	University Hospital and Faculty of Medicine Tübingen
Countries	12
HCPs	31

Figure 17. Geographical coverage of ERN RND

Table 15. Healthcare Providers in ERN RND

Country	HCP	Onsite Audit
Belgium	Erasme Hospital	No
	University Hospital Leuven	No
Bulgaria	University Neurological Hospital 'ST. Naum' Sofia	Yes
Czech Republic	General University Hospital in Prague	No
	Motol University Hospital	No
France	Assistance Publique-Hôpitaux de Paris, Hôpital Henri-Mondor	No
	Assistance Publique-Hôpitaux de Paris, Hôpital Pitié-Salpétrière	No

Country	HCP	Onsite Audit
	Assistance Publique-Hôpitaux de Paris, Hôpital Pitié-Salpétrière	No
	Assistance Publique-Hôpitaux de Paris, Hôpital Robert-Debré	No
	CHU de Bordeaux	No
	CHU de Toulouse	Yes
Germany	Klinikum der Universität München	No
	Universitätsklinikum Bonn	No
	Universitätsklinikum Schleswig-Holstein	Yes
	Universitätsklinikum Ulm	No
	University Hospital and Faculty of Medicine Tübingen	No
Hungary	Semmelweis University	No
	University of Pécs	Yes
Italy	AOU Siena	Yes
	Foundation IRCCS neurological institute Carlo Besta - Milan	No
	IRCCS Clinical Institute Humanitas - Rozzano	No
	Pediatric hospital Bambino Gesù, Rome	No
Lithuania	Vilnius University Hospital Santaros Klinikos	Yes
Netherlands	Amsterdam University Medical Centers location: VUMC	Yes
	Erasmus MC: University Medical Center Rotterdam	No
	Radboud University Medical Centre Nijmegen	No
	University Medical Centre Groningen	No
Poland	University Hospital in Krakow	No
Slovenia	University Medical Centre Ljubljana	No
Spain	Hospital Universitari Vall d'Hebron	No
	Sant Joan de Déu Hospital	No

ERN-EYE

Table 16. Information of ERN-EYE

Network node	France
ERN Coordinator	Hôpitaux Universitaires de Strasbourg
Countries	12
HCPs	24

Figure 18. Geographical coverage of ERN-EYE

Table 17. Healthcare Providers in ERN-EYE

Country	HCP	Onsite Audit
Belgium	University Hospital Ghent	No
Czech Republic	General University Hospital in Prague	No
Denmark	Copenhagen University Hospital, Rigshospitalet	Yes
Estonia	East Tallinn Central Hospital	No
France	Assistance Publique-Hôpitaux de Paris, Hôpital Necker-Enfants Malades	No
	Centre Hospitalier National d'Ophtalmologie des Quinze-Vingts	Yes
	CHU de Montpellier	No
	CHU de Toulouse	No

Country	HCP	Onsite Audit
	Hôpitaux Universitaires de Strasbourg	No
Germany	Universitätsklinikum Freiburg	No
	Universitätsklinikum Gießen und Marburg	No
	University Hospital and Faculty of Medicine Tübingen	Yes
Italy	AOU Careggi, Florence	No
	AOU University of Campania 'Luigi Vanvitelli', Naples	No
	AULLS 12 – Mestre hospital – rare eye diseases	No
	Pediatric hospital Bambino Gesù, Rome	No
	ULSS 15 - Hospital - Camposampiero	No
	University Hospital of Padova	No
Latvia	Children's Clinical University Hospital, Riga	Yes
Lithuania	Hospital of Lithuanian University of Health Sciences Kauno Klinikos	No
Netherlands	Leiden University Medical Center	Yes
	Radboud University Medical Centre Nijmegen	No
	Rotterdam Eye Clinic	No
Poland	The Independent Public Clinical Hospital No1 in Lublin	No
Portugal	Centro Hospitalar e Universitário de Coimbra, EPE	Yes

ERN-LUNG

Table 18. Information of ERN-LUNG

Network node	Germany
ERN Coordinator	Universitätsklinikum Frankfurt
Countries	11
HCPs	50

Figure 19. Geographical coverage of ERN-LUNG

Table 19. Healthcare Providers in ERN-LUNG

Country	HCP	Onsite Audit
Belgium	Erasme Hospital	Yes
	University Hospital Antwerp	No
	University Hospital Leuven	No
Czech Republic	General University Hospital in Prague	Yes
	Motol University Hospital	No

Country	HCP	Onsite Audit
	Thomayer Hospital, Prague	No
Denmark	Aarhus University Hospital	No
	Copenhagen University Hospital, Rigshospitalet	Yes
France	Assistance Publique-Hôpitaux de Paris, Hôpital Cochin	No
	Assistance Publique-Hôpitaux de Paris, Hôpital Bicêtre	No
	Assistance Publique-Hôpitaux de Paris, Hôpital Necker-Enfants Malades	Yes
	Assistance Publique-Hôpitaux de Paris, Hôpital Trousseau	No
	Hospices Civils de Lyon	No
Germany	Charité Universitätsmedizin Berlin	No
	Medizinische Hochschule Hannover	No
	Ruhrlandklinik - Westdeutsches Lungenzentrum	No
	Thoraxklinik University Hospital Heidelberg	No
	Universitätsklinikum Frankfurt	No
	Universitätsklinikum Freiburg	No
	Universitätsklinikum Gießen und Marburg	No
	Universitätsklinikum Köln	No
	Universitätsklinikum Münster	Yes
	Universitätsklinikum Würzburg	No
Italy	AOU - Bologna	Yes
	AOU - Modena	No
	AOU Federico II - Naples	No
	AOU Meyer - Florence	No
	AOU Pisan	No
	AOU S. Luigi - Turin	No
	AOU Siena	No
	AOUI Verona	No
	Foundation IRCCS Polyclinic San Matteo, Pavia	No
	Pediatric hospital Bambino Gesù, Rome	No
	Riuniti' Hospitals - Trieste	No
	St. Joseph Hospital - Milan	Yes
	University Hospital of Padova	No
	University Hospital Policlinico G.Rodolico-San Marco	No
	USL Romagna company (Hospital G.B.Morgagni-L.Pierantoni)	No
Netherlands	Amsterdam University Medical Centers location: VUMC	No
	Erasmus MC: University Medical Center Rotterdam	No
	Leiden University Medical Center	Yes

Country	HCP	Onsite Audit
	St Antonius Hospital Utrecht	No
	University Medical Center Utrecht	No
Poland	European Health Center Otwock	Yes
	National Tuberculosis and Lung Diseases Research Institute	No
Portugal	Centro Hospitalar do Porto, EPE	Yes
Spain	Hospital Clínic i Provincial de Barcelona	Yes
	Hospital Universitari Vall d'Hebron	No
	Hospital Universitario 12 de Octubre	No
Sweden	Karolinska University Hospital	Yes

ERN-SKIN

Table 20. Information of ERN-SKIN

Network node	France
ERN Coordinator	Assistance Publique-Hôpitaux de Paris; Hôpital Necker-Enfants Malades
Countries	16
HCPs	46

Figure 20. Geographical coverage of ERN-SKIN

Table 21. Healthcare Providers in ERN-SKIN

Country	HCP	Onsite Audit
Austria	EB-Haus	No
Belgium	Erasme Hospital	Yes
	University Hospital Ghent	No
	University Hospital Leuven	No
Croatia	University Hospital Center Zagreb	Yes
Czech Republic	Hospital Na Bulovce	No
	Saint Anna University Hospital in Brno	No
	University Hospital Brno	No

Country	HCP	Onsite Audit
	University Hospital Královské Vinohrady	Yes
Denmark	Odense University Hospital	No
	Zealand University Hospital	No
Finland	Helsinki University Hospital (HUS)	No
France	Assistance Publique-Hôpitaux de Paris, Hôpital Henri-Mondor	No
	Assistance Publique-Hôpitaux de Paris, Hôpital Necker-Enfants Malades	No
	CHU de Bordeaux	Yes
	CHU de Nice	No
	CHU de Rouen	No
	CHU de Toulouse	No
Germany	Klinikum der Universität München	No
	Städtisches Klinikum Dessau	No
	Universitätsklinikum Erlangen	No
	Universitätsklinikum Freiburg	No
	Universitätsklinikum Freiburg	No
	Universitätsklinikum Münster	Yes
	Universitätsklinikum Regensburg	No
	Universitätsklinikum Schleswig-Holstein	No
	Universitätsklinikum Würzburg	No
	Universitätsmedizin Rostock	No
Hungary	Semmelweis University	No
	Szent-Györgyi Albert Medical Center, University of Szeged	Yes
	University of Debrecen	No
Ireland	Children's Health Ireland	No
Italy	AOU - Bologna	No
	ASL Tuscan Centre	No
	Foundation IRCCS CA'Granda Ospedale Maggiore polyclinic - Milan	Yes
	IRCCS IDI foundation Luigi Maria Monti - Rome	No
	Pediatric hospital Bambino Gesù, Rome	No
	University Hospital of Padova	No
Lithuania	Hospital of Lithuanian University of Health Sciences Kauno Klinikos	Yes
Netherlands	Amsterdam University Medical Centers Location AMC	No
	Erasmus MC: University Medical Center Rotterdam	No
	Maastricht University Medical Center+	No
	University Medical Centre Groningen	Yes
Poland	University Swiecicki Hospital in Poznan	No

Country	HCP	Onsite Audit
Romania	Colentina Clinical Hospital	No
Spain	Sant Joan de Déu Hospital	No
Sweden	Uppsala University Hospital	Yes

ERNICA

Table 22. Information of ERNICA

Network node	Netherlands
ERN Coordinator	Erasmus MC: University Medical Center Rotterdam
Countries	9
HCPs	19

Figure 21. Geographical coverage of ERNICA

Table 23. Healthcare Providers in ERNICA

Country	HCP	Onsite Audit
Belgium	University Hospital Leuven	No
Denmark	Copenhagen University Hospital, Rigshospitalet	Yes
	Odense University Hospital	No
Finland	Helsinki University Hospital (HUS)	No
France	Assistance Publique-Hôpitaux de Marseille	No
	Assistance Publique-Hôpitaux de Paris, Hôpital Antoine-Béclère.	Yes
	Assistance Publique-Hôpitaux de Paris, Hôpital Beaujon	No
	Assistance Publique-Hôpitaux de Paris, Hôpital Necker-Enfants Malades	No

Country	HCP	Onsite Audit
	Assistance Publique-Hôpitaux de Paris, Hôpital Robert-Debré	No
	CHU de Lille	No
Germany	Medizinische Hochschule Hannover	No
	Universitätsklinikum Mannheim	No
Italy	University Hospital of Padova	Yes
Netherlands	Amsterdam University Medical Centers Location AMC	No
	Erasmus MC: University Medical Center Rotterdam	No
	Radboud University Medical Centre Nijmegen	No
	University Medical Center Utrecht	No
Norway	Oslo University Hospital	Yes
Sweden	Karolinska University Hospital	No

EURACAN

Table 24. Information of EURACAN

Network node	France
ERN Coordinator	Centre Léon Bérard
Countries	16
HCPs	57

Figure 22. Geographical coverage of EURACAN

Table 25. Healthcare Providers in EURACAN

Country	HCP	Onsite Audit
Belgium	Jules Bordet Institut	No
	University Hospital Antwerp	Yes
	University Hospital Leuven	No
	University Hospital Liège	No
Czech Republic	Masaryk Memorial Cancer Institute	Yes
	Motol University Hospital	No
Denmark	Aarhus University Hospital	Yes
Finland	Turku University Hospital, Finland	Yes
France	Assistance Publique-Hôpitaux de Paris, Hôpital Cochin	Yes

Country	HCP	Onsite Audit
	Assistance Publique-Hôpitaux de Paris, Hôpital Pitié-Salpétrière	No
	Assistance Publique-Hôpitaux de Paris, Hôpital Tenon	No
	Centre Léon Bérard	No
	Hospices Civils de Lyon	No
	Institut Curie	No
	Institut Gustave Roussy	No
Germany	Charité Universitätsmedizin Berlin	No
	Universitätsklinikum Essen	No
	Universitätsklinikum Gießen und Marburg	No
	Universitätsklinikum Hamburg-Eppendorf	No
	Universitätsklinikum Mannheim	Yes
	Universitätsklinikum Würzburg	No
Hungary	National Insttitue of Oncology	Yes
Italy	AO City of Health and Science - Turin	No
	AOU - Bologna	No
	AOU Careggi, Florence	No
	AOU Federico II - Naples	No
	AOU Siena	No
	AULSS 2 Marca trevigiana	No
	AUSL of Bologna – IRCCS Institute of Neurological Sciences	No
	Candiolo Institute - IRCCS	No
	Fondazione IRCCS Istituto Nazionale dei Tumori, Milano	No
	Foundation IRCCS neurological institute Carlo Besta - Milan	No
	IRCCS Clinical Institute Humanitas - Rozzano	No
	IRCCS IFO Regina Elena - San Gallicano	No
	IRCCS Ospedale Policlinico San Martino – Genova	No
	IRST - Meldola	No
	Oncological Referral Center - Aviano	No
	Rizzoli Orthopaedic Institute of Bologna	Yes
	San Raffaele hospital - Milan	No
Lithuania	Hospital of Lithuanian University of Health Sciences Kauno Klinikos	No
Netherlands	Amsterdam University Medical Centers Location AMC	No
	Amsterdam University Medical Centers location: VUMC	No
	Erasmus MC: University Medical Center Rotterdam	No
	Leiden University Medical Center	No
	Maastricht University Medical Center+	Yes

Country	HCP	Onsite Audit
	Netherlands Cancer Institute - Antoni van Leeuwenhoek	No
	Radboud University Medical Centre Nijmegen	No
	University Medical Centre Groningen	No
Norway	Oslo University Hospital	No
Poland	Maria Sklodowska-Curie National Research Institute of Oncology (MSCNRIO)	Yes
Portugal	Cancer Institute Lisbon	Yes
	Centro Hospitalar do Porto, EPE	No
	Centro Hospitalar e Universitário de Coimbra, EPE	No
Slovenia	Institute of Oncology, Ljubjlana	Yes
Spain	Complejo Hospitalario Regional Virgen del Rocio	No
	Hospital de la Santa Creu i Sant Pau	Yes
	Hospital Universitari de Bellvitge	No
Sweden	Karolinska University Hospital	Yes
	Uppsala University Hospital	No

EURO NMD

Table 26. Information of EURO NMD

Network node	France
ERN Coordinator	Assistance Publique-Hôpitaux de Paris; Hôpital Pitié-Salpétrière
Countries	13
HCPs	57

Figure 23. Geographical coverage of EURO NMD

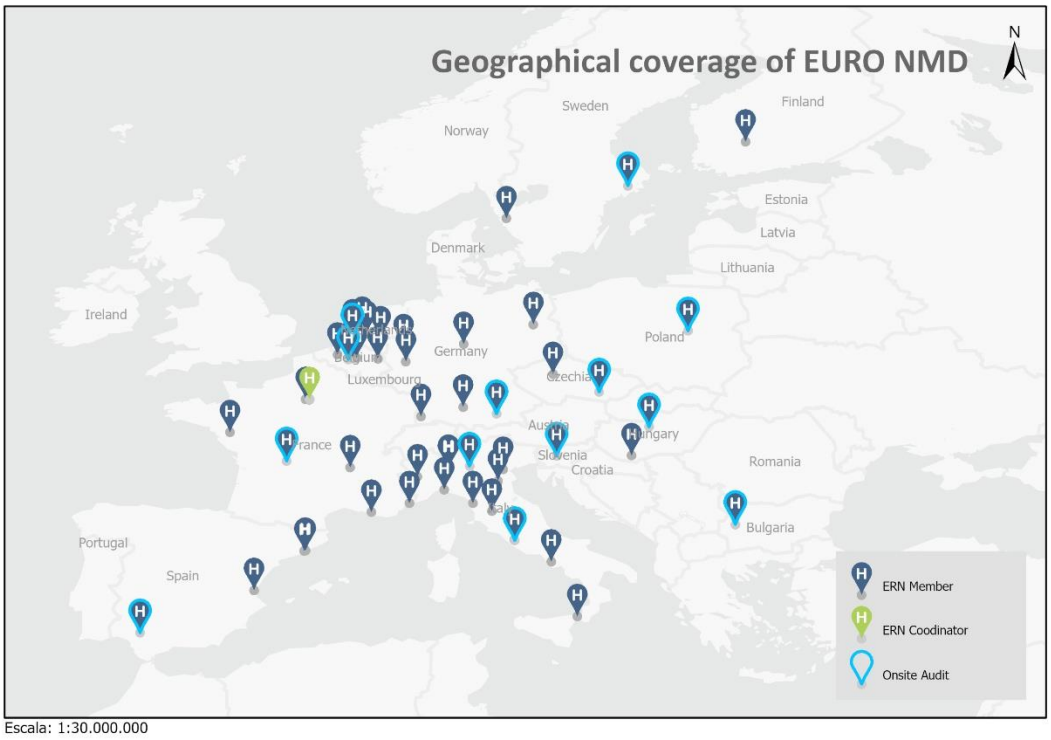


Table 27. Healthcare Providers in EURO NMD

Country	HCP	Onsite Audit
Belgium	Erasme Hospital	Yes
	University Hospital Antwerp	No
	University Hospital Ghent	No
	University Hospital Leuven	No
	University Hospitals Saint-Luc	No
Bulgaria	Expert Centre for Hereditary Neurologic and Metabolic Disorders	Yes
Czech Republic	Motol University Hospital	No
	University Hospital Brno	Yes
Finland	Tampere University Hospital, Finland	No

Country	HCP	Onsite Audit
France	Assistance Publique-Hôpitaux de Marseille	No
	Assistance Publique-Hôpitaux de Paris, Hôpital Bicêtre	No
	Assistance Publique-Hôpitaux de Paris, Hôpital Pitié-Salpétrière	No
	Assistance Publique-Hôpitaux de Paris, Hôpital Raymond Poincaré	No
	CHU de Limoges	Yes
	CHU de Nantes	No
	CHU de Nice	No
	CHU de Saint-Etienne	No
Germany	Charité Universitätsmedizin Berlin	No
	Friedrich-Baur Institut, Klinikum der Universität München	No
	Klinikum der Universität München	Yes
	Universitätsklinikum Bonn	No
	Universitätsklinikum Essen	No
	Universitätsklinikum Freiburg	No
	Universitätsklinikum Ulm	No
	Universitätsmedizin Göttingen	No
Hungary	Semmelweis University	Yes
	University of Pécs	No
Italy	AO City of Health and Science - Turin	No
	AOU - Ferrara	No
	AOU Pisan	No
	AOU polyclinic 'G.Martino' of Messina	No
	AOU Siena	No
	AOU University of Campania 'Luigi Vanvitelli', Naples	No
	Civil Hospital - Brescia	Yes
	Fondazione Policlinico Gemelli, IRCCs, Rome	No
	Foundation IRCCS CA'Granda Ospedale Maggiore polyclinic - Milan	No
	Foundation IRCCS neurological institute Carlo Besta - Milan	No
	IRCCS Auxologico Italian Institute - Milan	No
	IRCCS Institute Giannina Gaslini - Genoa	No
	Niguarda hospital - Milan	No
	Pediatric hospital Bambino Gesù, Rome	Yes
	University Hospital of Padova	No
Netherlands	Amsterdam University Medical Centers Location AMC	No
	Erasmus MC: University Medical Center Rotterdam	Yes
	Leiden University Medical Center	No

Country	HCP	Onsite Audit
	Maastricht University Medical Center+	No
	Radboud University Medical Centre Nijmegen	No
	University Medical Center Utrecht	No
Poland	University Hospital, Banacha, Warsaw	Yes
Slovenia	University Medical Centre Ljubljana	Yes
Spain	Complejo Hospitalario Regional Virgen del Rocio	Yes
	Hospital de la Santa Creu i Sant Pau	No
	Hospital Universitari Vall d'Hebron	No
	Hospital Universitario y Politécnico La Fe	No
	Sant Joan de Déu Hospital	No
Sweden	Karolinska University Hospital	Yes
	Sahlgrenska University Hospital	No

EUROBLOODNET

Table 28. Information of EuroBloodNet

Network node	France
ERN Coordinator	Assistance Publique-Hôpitaux de Paris; Hôpital Saint-Louis
Countries	14
HCPs	54

Figure 24. Geographical coverage of EuroBloodNet

Table 29. Healthcare Providers in EuroBloodNet

Country	HCP	Onsite Audit
Belgium	Erasme Hospital	No
	Jules Bordet Institut	Yes
	University Hospital Leuven	No
	University Hospital Liège	No
	University Hospitals Saint-Luc	No
Bulgaria	Expert Center on coagolopathias and Congenital Anemias	Yes
	Varna Expert Center of coagulopathies and rare anemias	No
Cyprus	Archbishop Makarios III Hospital	Yes

Country	HCP	Onsite Audit
Czech Republic	University Hospital Brno	Yes
France	Assistance Publique-Hôpitaux de Marseille	No
	Assistance Publique-Hôpitaux de Paris, Hôpital Henri-Mondor	No
	Assistance Publique-Hôpitaux de Paris, Hôpital Necker-Enfants Malades	No
	Assistance Publique-Hôpitaux de Paris, Hôpital Saint-Antoine	Yes
	Assistance Publique-Hôpitaux de Paris, Hôpital Saint-Louis	No
	Assistance Publique-Hôpitaux de Paris, Hôpital Trousseau	No
	CHU de Lille	No
	CHU de la Guadeloupe	No
	CHU de Limoges	No
	CHU de Montpellier	No
	CHU de Rennes	No
	Institut Curie	No
Germany	Charité Universitätsmedizin Berlin	No
	Universitätsklinikum Carl Gustav Carus	Yes
	Universitätsklinikum Heidelberg	No
	Universitätsklinikum Köln	No
Ireland	Children's Health Ireland	Yes
Italy	AOU - Modena	No
	AOU Careggi, Florence	No
	AOU Consorziale polyclinic - Bari	No
	AOU Federico II - Naples	No
	AOU Policlinico Umberto I - Rome	No
	AOU S.Luigi Gonzaga	No
	AOU Siena	No
	AOU University of Campania 'Luigi Vanvitelli', Naples	No
	AOUI Verona	No
	E.O. Ospedali Galliera, Genoa	No
	Fondazione IRCCS Ospedale San Gerardo dei Tintori di Monza	Yes
	Fondazione Policlinico Gemelli, IRCCs, Rome	No
	Foundation CNR Tuscany Region G. Monasterio	No
	Foundation IRCCS CA'Granda Ospedale Maggiore polyclinic - Milan	No
	Foundation IRCCS Polyclinic San Matteo, Pavia	No
	Hospital Pope John XXIII - Bergamo	No
	IRCCS Clinical Institute Humanitas - Rozzano	No
	IRCCS Institute Giannina Gaslini - Genoa	No

Country	HCP	Onsite Audit
	Riuniti' hospitals Villa Sofia-Cervello - Palermo	No
	San Bortolo Hospital - Vicenza	No
	University Hospital of Padova	No
Lithuania	Vilnius University Hospital Santaros Klinikos	Yes
Netherlands	Amsterdam University Medical Centers Location AMC	No
	Erasmus MC: University Medical Center Rotterdam	No
	Leiden University Medical Center	No
	Radboud University Medical Centre Nijmegen	No
	University Medical Center Utrecht	Yes
	University Medical Centre Groningen	No
Poland	Maria Sklodowska-Curie National Research Institute of Oncology (MSCNRIO)	Yes
Portugal	Centro Hospitalar do Porto, EPE	No
	Centro Hospitalar e Universitário de Coimbra, EPE	Yes
	Instituto Português de Oncologia do Porto	No
Spain	Hospital Universitari Vall d'Hebron	Yes
Sweden	Karolinska University Hospital	Yes

EUROGEN

Table 30. Information of EUROGEN

Network node	Netherlands
ERN Coordinator	Radboud University Medical Centre Nijmegen
Countries	10
HCPs	22

Figure 25. Geographical coverage of EUROGEN

Table 31. Healthcare Providers in EUROGEN

Country	HCP	Onsite Audit
Belgium	University Hospital Ghent	No
	University Hospital Leuven	No
	University Hospital Liège	No
Denmark	Aarhus University Hospital	No
	Copenhagen University Hospital, Rigshospitalet	Yes
France	Assistance Publique-Hôpitaux de Paris, Hôpital Necker-Enfants Malades	No
Germany	Charité Universitätsmedizin Berlin	Yes
	Klinikum Bremen-Mitte	No
	Klinikum der Universität München	No
	Universitätsklinikum Leipzig	No
	Universitätsklinikum Hamburg-Eppendorf	No
	Universitätsklinikum Regensburg	No
Italy	Fondazione Policlinico Gemelli, IRCCs, Rome	Yes
	Foundation IRCCS CA'Granda Ospedale Maggiore polyclinic - Milan	No
	Pediatric hospital Bambino Gesù, Rome	No
	University Hospital of Padova	No
Lithuania	Vilnius University Hospital Santaros Klinikos	No
Netherlands	Erasmus MC: University Medical Center Rotterdam	Yes

Country	HCP	Onsite Audit
	Radboud University Medical Centre Nijmegen	No
Poland	University Clinical Hospital of Medical University Gdansk	No
Portugal	Instituto Português de Oncologia do Porto	No
Sweden	Karolinska University Hospital	No
	Sahlgrenska University Hospital	Yes

GENTURIS

Table 32. Information of GENTURIS

Network node	Netherlands
ERN Coordinator	Radboud University Medical Centre Nijmegen
Countries	11
HCPs	20

Figure 26. Geographical coverage of GENTURIS

Table 33. Healthcare Providers in GENTURIS

Country	HCP	Onsite Audit
Belgium	University Hospital Ghent	No
	University Hospital Leuven	No
	University Hospital Liège	No
Finland	Turku University Hospital, Finland	No
France	Assistance Publique-Hôpitaux de Paris, Hôpital Henri-Mondor	No
	CHU de Rouen	Yes
	Institut Curie	No

Country	HCP	Onsite Audit
Germany	MGZ - Medizinisch Genetisches Zentrum	No
	Universitätsklinikum Bonn	No
	Universitätsklinikum Carl Gustav Carus	No
Hungary	University of Pécs	No
Netherlands	Erasmus MC: University Medical Center Rotterdam	No
	Radboud University Medical Centre Nijmegen	No
	University Medical Centre Groningen	Yes
Poland	University Clinical Hospital No 1, Pomeranian Medical University in Szczecin	No
Portugal	Porto. Centro Compreensivo de Cancro	No
Slovenia	Institute of Oncology, Ljubjlana	No
Spain	Hospital Universitari Germans Trias i Pujol y ICO Badalona	No
	Sant Joan de Déu Hospital	Yes
Sweden	Karolinska University Hospital	Yes

GUARD HEART

Table 34. Information of GUARD HEART

Network node	Netherlands
ERN Coordinator	Amsterdam University Medical Centers Location AMC
Countries	11
HCPs	21

Figure 27. Geographical coverage of GUARD HEART

Table 35. Healthcare Providers in GUARD HEART

Country	HCP	Onsite Audit
Belgium	University Hospital Brussels	Yes
	University Hospital Leuven	No
Czech Republic	Motol University Hospital	No
Denmark	Copenhagen University Hospital, Rigshospitalet	No
Finland	Helsinki University Hospital (HUS)	Yes
France	Assistance Publique-Hôpitaux de Paris, Hôpital Pitié-Salpétrière	No
	CHU de Nantes	No

Country	HCP	Onsite Audit
	Hospices Civils de Lyon	No
Germany	Universitätsklinikum Münster	No
Italy	AORN Colli	No
	Foundation IRCCS Polyclinic San Matteo, Pavia	Yes
	IRCCS Auxologico Italian Institute - Milan	No
	IRCCS Foundation Salvatore Maugeri	No
	Pediatric hospital Bambino Gesù, Rome	No
	University Hospital of Padova	No
Netherlands	Amsterdam University Medical Centers Location AMC	No
Romania	Emergency Institute for cardiovascular disease : Prof dr. C. C. Iliescu	No
Spain	Hospital Universitario Puerta de Hierro Majadahonda	Yes
	Hospital Universitario Virgen de la Arrixaca	No
	Sant Joan de Déu Hospital	No
Sweden	Umea University Hospital	Yes

ITHACA

Table 36. Information of ITHACA

Network node	France
ERN Coordinator	Assistance Publique-Hôpitaux de Paris; Hôpital Robert-Debré
Countries	12
HCPs	34

Figure 28. Geographical coverage of ITHACA

Table 37. Healthcare Providers in ITHACA

Country	HCP	Onsite Audit
Belgium	Erasme Hospital	No
	University Hospital Antwerp	No
	University Hospital Leuven	No
Cyprus	Cyprus Institute of Neurology and Genetics	Yes
Czech Republic	Motol University Hospital	Yes
Finland	Helsinki University Hospital (HUS)	Yes
France	Assistance Publique-Hôpitaux de Marseille	No
	Assistance Publique-Hôpitaux de Paris, Hôpital Robert-Debré	No
	CHU de Lille	No

Country	HCP	Onsite Audit
	CHU de Bordeaux	No
	CHU de Dijon	Yes
	CHU de Montpellier	No
	CHU de Rennes	No
	Hospices Civils de Lyon	No
Germany	Universitätsklinikum Düsseldorf	No
	Universitätsklinikum Schleswig-Holstein	No
	University Hospital and Faculty of Medicine Tübingen	Yes
Italy	AOU - Bologna	No
	AOU Federico II - Naples	No
	AOU Meyer - Florence	No
	AOU Siena	Yes
	Fondazione Policlinico Gemelli, IRCCs, Rome	No
	Foundation IRCCS CA'Granda Ospedale Maggiore polyclinic - Milan	No
	Pediatric hospital Bambino Gesù, Rome	No
	University Hospital of Padova	No
Lithuania	Vilnius University Hospital Santaros Klinikos	No
Netherlands	Amsterdam University Medical Centers Location AMC	Yes
	Erasmus MC: University Medical Center Rotterdam	No
	Maastricht University Medical Center+	No
	Radboud University Medical Centre Nijmegen	No
	University Medical Centre Groningen	No
Portugal	Centro Hospitalar e Universitário de Coimbra, EPE	No
Romania	RoNetwork Multiple Congenital Abnormalities with ID	No
Sweden	Karolinska University Hospital	Yes

METABERN

Table 38. Information of MetabERN

Network node	Italy
Ern Coordinator	Azienda sanitaria universitaria friuli centrale
Countries	17
HCPs	60

Figure 29. Geographical coverage of MetabERN

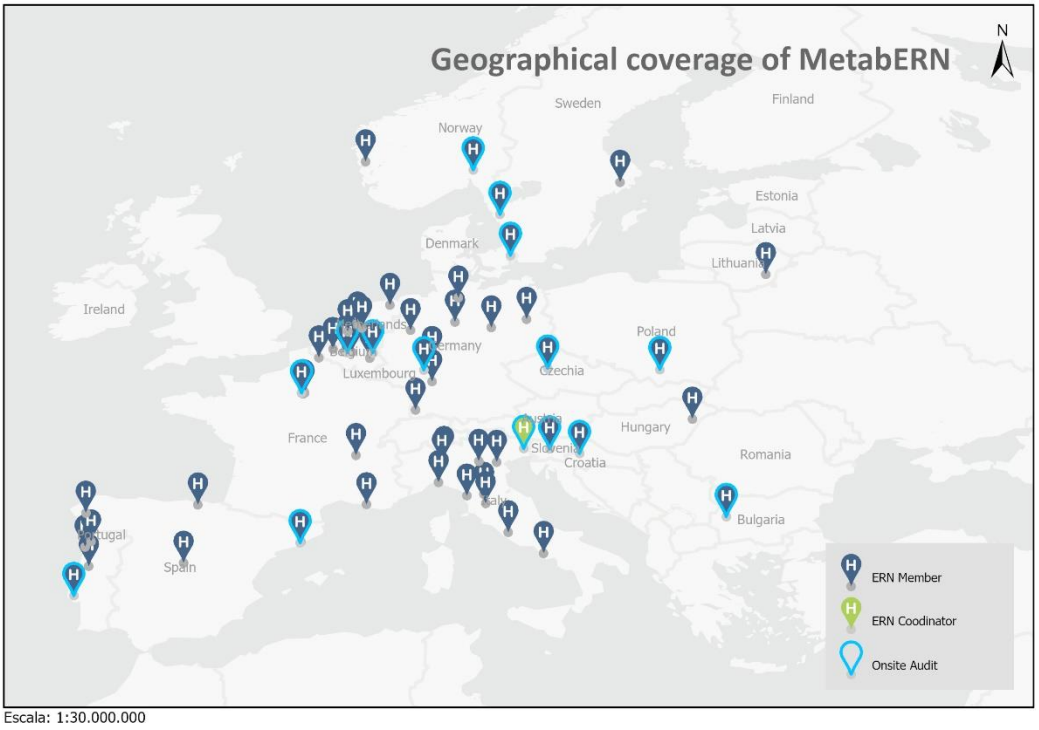


Table 39. Healthcare Providers in MetabERN

Country	HCP	Onsite Audit
Belgium	University Hospital Antwerp	No
	University Hospital Brussels	No
	University Hospital Ghent	No
	University Hospital Leuven	No
	University Hospital Liège	No
	University Hospitals Saint-Luc	Yes

Country	HCP	Onsite Audit
Bulgaria	University Hospital 'Alexandrovska' Sofia	Yes
Croatia	University Hospital Center Zagreb	Yes
Czech Republic	General University Hospital in Prague	Yes
Denmark	Copenhagen University Hospital, Rigshospitalet	Yes
France	Assistance Publique-Hôpitaux de Marseille	No
	Assistance Publique-Hôpitaux de Paris, Hôpital Antoine-Béclère.	No
	Assistance Publique-Hôpitaux de Paris, Hôpital Beaujon	No
	Assistance Publique-Hôpitaux de Paris, Hôpital Louis-Mourier	No
	Assistance Publique-Hôpitaux de Paris, Hôpital Necker-Enfants Malades	No
	Assistance Publique-Hôpitaux de Paris, Hôpital Raymond Poincaré	Yes
	Assistance Publique-Hôpitaux de Paris, Hôpital Robert-Debré	No
	CHU de Lille	No
	Hospices Civils de Lyon	No
Germany	Charité Universitätsmedizin Berlin	No
	Helios Dr. Horst Schmidt Kliniken	No
	Medizinische Hochschule Hannover	No
	Universitätsklinikum Freiburg	No
	Universitätsklinikum Gießen und Marburg	No
	Universitätsklinikum Hamburg-Eppendorf	No
	Universitätsklinikum Heidelberg	No
	Universitätsklinikum Magdeburg	No
	Universitätsklinikum Münster	No
	Universitätsmedizin Mainz	Yes
Hungary	University of Debrecen	No
Italy	AOU Federico II - Naples	No
	AOU Meyer - Florence	No
	AOU Pisan	No
	AOU Siena	No
	AOUI Verona	No
	AZIENDA SANITARIA UNIVERSITARIA FRIULI CENTRALE	Yes
	Fondazione IRCCS Ospedale San Gerardo dei Tintori di Monza	No
	Hospital San Paolo - Milan	No
	IRCCS Institute Giannina Gaslini - Genoa	No
	Pediatric hospital Bambino Gesù, Rome	No
	University Hospital of Padova	No
Lithuania	Vilnius University Hospital Santaros Klinikos	No

Country	HCP	Onsite Audit
Netherlands	Amsterdam University Medical Centers Location AMC	No
	Erasmus MC: University Medical Center Rotterdam	No
	Maastricht University Medical Center+	Yes
	University Medical Center Utrecht	No
	University Medical Centre Groningen	No
Norway	Bergen Hospital Trust	No
	Oslo University Hospital	Yes
Poland	University Hospital in Krakow	Yes
Portugal	Centro Hospitalar de Lisboa Norte, EPE	Yes
	Centro Hospitalar do Porto, EPE	No
	Centro Hospitalar e Universitário de Coimbra, EPE	No
	Centro Hospitalar Universitário de São João (CHUSJ)	No
	Hospital Senhora da Oliveira, Guimarães, EPE	No
Slovenia	University Medical Centre Ljubljana	Yes
Spain	Complexo Hospitalario Universitario de Santiago	No
	Hospital Universitari Vall d'Hebron	No
	Hospital Universitario 12 de Octubre	No
	Hospital Universitario de Cruces	No
	Sant Joan de Déu Hospital	Yes
Sweden	Karolinska University Hospital	No
	Sahlgrenska University Hospital	Yes

PAEDCAN

Table 40. Information of PaedCAN

Network node	Austria
ERN Coordinator	St, Anna Kinderspital & St, Anna Kinderkrebsforschung
Countries	17
HCPs	50

Figure 30. Geographical coverage of PaedCAN

Table 41. Healthcare Providers in PaedCAN

Country	HCP	Onsite Audit
Austria	St. Anna Kinderspital & St. Anna Kinderkrebsforschung	Yes
Belgium	Queen Fabiola Children's University Hospital	No
	University Hospital Ghent	Yes
	University Hospital Leuven	No
Czech Republic	Motol University Hospital	No
	University Hospital Brno	Yes
Denmark	Copenhagen University Hospital, Rigshospitalet	No
Finland	Kuopio University Hospital, Finland	Yes

Country	HCP	Onsite Audit
	Tampere University Hospital, Finland	No
	Turku University Hospital, Finland	No
France	Assistance Publique-Hôpitaux de Paris, Hôpital Bicêtre	No
	Assistance Publique-Hôpitaux de Paris, Hôpital Necker-Enfants Malades	No
	Assistance Publique-Hôpitaux de Paris, Hôpital Trousseau	No
	Centre Léon Bérard	Yes
	Hôpital Fondation Adolphe de Rothschild	No
	Institut Curie	No
	Institut Gustave Roussy	No
Germany	Charité Universitätsmedizin Berlin	No
	Christian-Albrechts-Universitat zu Kiel (CAU)	No
	Klinikum der Universität München	No
	Klinikum Dortmund gGmbH	No
	Klinikum Stuttgart	No
	Medizinische Hochschule Hannover	No
	Universitätsklinikum Bonn	No
	Universitätsklinikum Freiburg	No
	Universitätsklinikum Gießen und Marburg	Yes
	University Children's Hospital Tübingen	Yes
Hungary	Semmelweis University	No
Italy	AO City of Health and Science - Turin	Yes
	AOU - Perugia	No
	AOU Meyer - Florence	No
	AOU Siena	No
	Foundation IRCCS Polyclinic San Matteo, Pavia	No
	IRCCS Institute Giannina Gaslini - Genoa	No
	MBBM Foundation – pediatrics – S.Gerardo hospital, Monza	No
	Pediatric hospital Bambino Gesù, Rome	No
	University Hospital of Padova	No
Latvia	Children's Clinical University Hospital, Riga	Yes
Lithuania	Vilnius University Hospital Santaros Klinikos	No
Netherlands	Amsterdam University Medical Centers location:VUMC	No
Poland	T. Marciniak Lower Silesian Specialist Hospital - Emergency Hospital	No
	University Children Hospital in Lublin (UCHL)	Yes
	University Clinical Hospital of Medical University Gdansk	No
Portugal	Cancer Institute Lisbon	No

Country	HCP	Onsite Audit
	Centro Hospitalar e Universitário de Coimbra, EPE	No
Slovenia	University Medical Centre Ljubljana	No
Spain	Complejo Hospitalario Regional Virgen del Rocio	No
	Hospital Universitari Vall d'Hebron	No
	Hospital Universitario y Politécnico La Fe	Yes
	Sant Joan de Déu Hospital	No
Sweden	Karolinska University Hospital	Yes
	Skåne University Hospital	No

RARE-LIVER

Table 42. Information of RARE-LIVER

Network node	Germany
ERN Coordinator	Universitätsklinikum Hamburg-Eppendorf
Countries	10
HCPs	23

Figure 31. Geographical coverage of RARE-LIVER

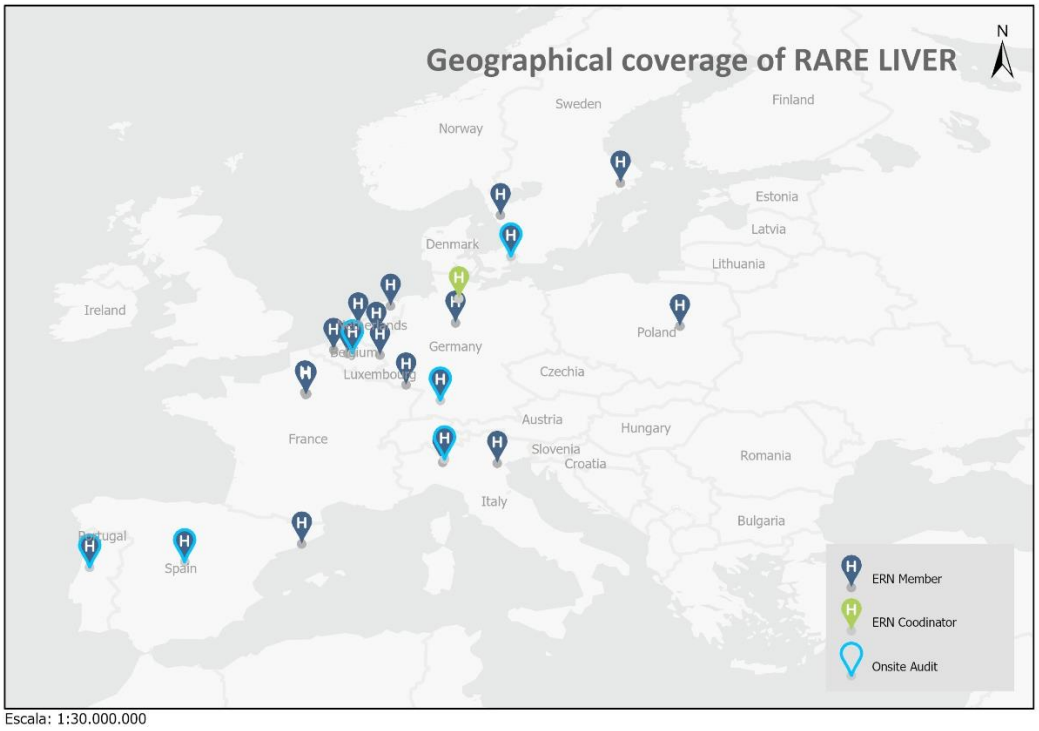


Table 43. Healthcare Providers in RARE-LIVER

Country	HCP	Onsite Audit
Belgium	University Hospital Ghent	No
	University Hospital Leuven	Yes
	University Hospitals Saint-Luc	No
Denmark	Copenhagen University Hospital, Rigshospitalet	Yes
France	Assistance Publique-Hôpitaux de Paris, Hôpital Beaujon	No
	Assistance Publique-Hôpitaux de Paris, Hôpital Bicêtre	No
	Assistance Publique-Hôpitaux de Paris, Hôpital Saint-Antoine	No
Germany	Medizinische Hochschule Hannover	No

Country	HCP	Onsite Audit
	Uniklinik RWTH Aachen	No
	Universitätsklinikum des Saarlandes	No
	Universitätsklinikum Hamburg-Eppendorf	No
	University Hospital and Faculty of Medicine Tübingen	Yes
Italy	Fondazione IRCCS Ospedale San Gerardo dei Tintori di Monza	Yes
	Hospital San Paolo - Milan	No
	University Hospital of Padova	No
Netherlands	Amsterdam University Medical Centers Location AMC	No
	Radboud University Medical Centre Nijmegen	No
	University Medical Centre Groningen	No
Poland	University Hospital, Banacha, Warsaw	No
Portugal	Centro Hospitalar e Universitário de Coimbra, EPE	Yes
Spain	Hospital Clínic i Provincial de Barcelona	No
	Hospital Universitario La Paz	Yes
Sweden	Karolinska University Hospital	No
	Sahlgrenska University Hospital	No

RECONNET

Table 44. Information of RECONNET

Network node	Italy
ERN Coordinator	AOU Pisan
Countries	8
HCPs	26

Figure 32. Geographical coverage of RECONNET

Table 45. Healthcare Providers in RECONNET

Country	HCP	Onsite Audit
Belgium	University Hospital Ghent	No
	University Hospital Ghent	No
	University Hospitals Saint-Luc	Yes
France	Assistance Publique-Hôpitaux de Paris, Hôpital Cochin	Yes
	Assistance Publique-Hôpitaux de Paris, Hôpital Pitié-Salpétrière	No
	CHU de Lille	No
	Hôpitaux Universitaires de Strasbourg	No
Germany	Charité Universitätsmedizin Berlin	No

Country	HCP	Onsite Audit
	Kerckhoff Klinik	No
	Universitätsklinikum Düsseldorf	Yes
	Universitätsklinikum Köln	No
Italy	AO San Camillo Forlanini - Rome	Yes
	AOU Careggi, Florence	No
	AOU Pisan	No
	Civil Hospital - Brescia	No
	Foundation IRCCS CA'Granda Ospedale Maggiore polyclinic - Milan	No
	Foundation IRCCS Polyclinic San Matteo, Pavia	No
	IRCCS Ospedale Policlinico San Martino – Genova	No
	University Hospital of Padova	No
Netherlands	Erasmus MC: University Medical Center Rotterdam	No
	Leiden University Medical Center	Yes
	University Medical Center Utrecht	No
Portugal	Centro Hospitalar de Lisboa Central, EPE	No
	Centro Hospitalar de Lisboa Norte, EPE	No
Romania	County Emergency Clinical Hospital	No
Slovenia	University Medical Centre Ljubljana	Yes

RITA

Table 46. Information of RITA

Network node	Netherlands
Ern Coordinator	University Medical Center Utrecht
Countries	9
HCPs	19

Figure 33. Geographical coverage of RITA

Table 47. Healthcare Providers in RITA

Country	HCP	Onsite Audit
Belgium	University Hospital Leuven	No
Czech Republic	General University Hospital in Prague	Yes
France	Assistance Publique-Hôpitaux de Paris, Hôpital Cochin	No
	Assistance Publique-Hôpitaux de Paris, Hôpital Bicêtre	No
	Assistance Publique-Hôpitaux de Paris, Hôpital Necker-Enfants Malades	No
	Hôpitaux Universitaires de Strasbourg	No
Germany	Klinikum der Universität München	Yes
	Universitätsklinikum Freiburg	No
	Universitätsklinikum Münster	No
Italy	Civil Hospital - Brescia	No

Country	HCP	Onsite Audit
	Foundation IRCCS Polyclinic San Matteo, Pavia	No
	IRCCS Institute Giannina Gaslini - Genoa	No
	Pediatric hospital Bambino Gesù, Rome	Yes
	San Raffaele hospital - Milan	No
Netherlands	Erasmus MC: University Medical Center Rotterdam	No
	University Medical Center Utrecht	No
	University Medical Centre Groningen	No
Slovenia	University Medical Centre Ljubljana	No
Spain	Hospital Universitari Vall d'Hebron	No
Sweden	Karolinska University Hospital	Yes

TRANSPLANTCHILD

Table 48. Information of TRANSPLANTCHILD

Network node	Spain
ERN Coordinator	Hospital Universitario La Paz
Countries	10
HCPs	17

Figure 34. Geographical coverage of TRANSPLANTCHILD

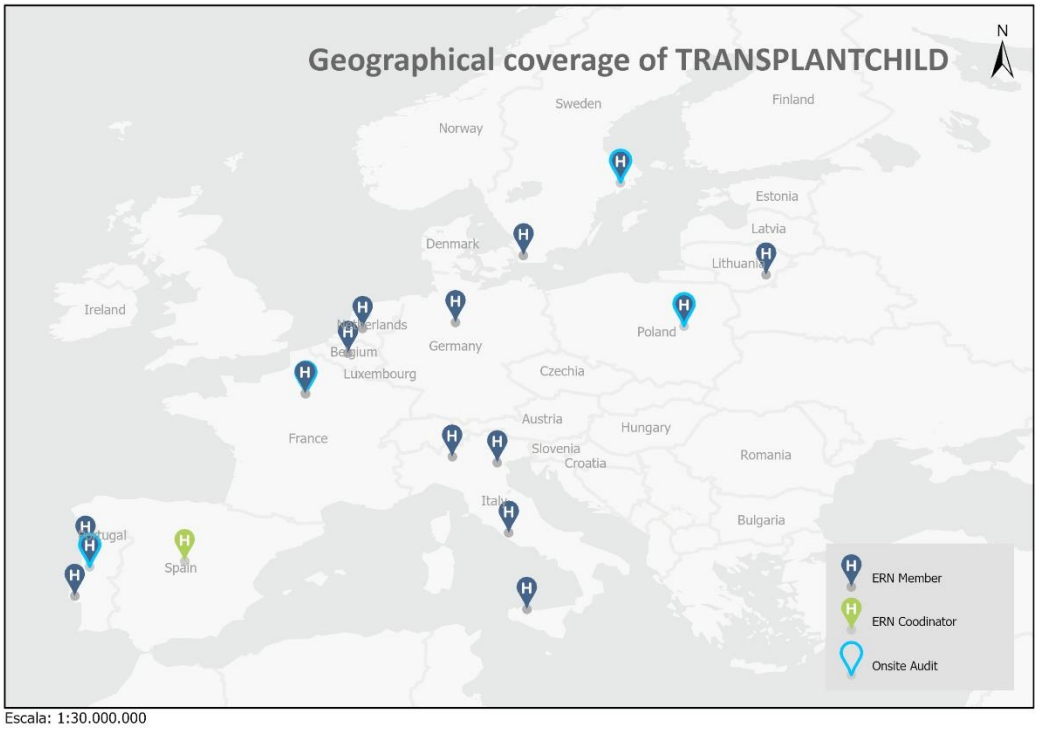


Table 49. Healthcare Providers in TRANSPLANTCHILD

Country	HCP	Onsite Audit
Belgium	University Hospitals Saint-Luc	No
France	Assistance Publique-Hôpitaux de Paris, Hôpital Bicêtre	Yes
	Assistance Publique-Hôpitaux de Paris, Hôpital Necker-Enfants Malades	No
Germany	Medizinische Hochschule Hannover	No
Italy	Hospital Pope John XXIII - Bergamo	No
	IRCCS ISMETT - Palermo	No
	Pediatric hospital Bambino Gesù, Rome	No
	University Hospital of Padova	No
Lithuania	Vilnius University Hospital Santaros Klinikos	No
Netherlands	University Medical Center Utrecht	No

Country	HCP	Onsite Audit
Poland	The Children's Memorial Health Institute	Yes
Portugal	Centro Hospitalar de Lisboa Norte, EPE	No
	Centro Hospitalar do Porto, EPE	No
	Centro Hospitalar e Universitário de Coimbra, EPE	Yes
Spain	Hospital Universitario La Paz	No
Sweden	Karolinska University Hospital	Yes
	Skåne University Hospital	No

VASCERN

Table 50. Information of VASCERN

Network node	France
ERN Coordinator	Assistance Publique-Hôpitaux de Paris; Hôpital Bichat
Countries	10
HCPs	26

Figure 35. Geographical coverage of VASCERN

Table 51. Healthcare Providers in VASCERN

Country	HCP	Onsite Audit
Belgium	AZ Sint-Marteen	No
	University Hospital Antwerp	No
	University Hospital Ghent	Yes
	University Hospital Leuven	No
	University Hospitals Saint-Luc	No
Denmark	Odense University Hospital	Yes
Finland	Helsinki University Hospital (HUS)	No

Country	HCP	Onsite Audit
France	Assistance Publique-Hôpitaux de Paris, Hôpital Bichat	Yes
	Assistance Publique-Hôpitaux de Paris, Hôpital Européen Georges-Pompidou	No
	Hospices Civils de Lyon	No
Germany	Universitäres Herzzentrum Hamburg	No
	Universitätsklinikum Essen	Yes
	Universitätsklinikum Freiburg	No
Hungary	Semmelweis University	No
Ireland	Children's Health Ireland	Yes
Italy	AOU Careggi, Florence	Yes
	AOU Consorziale polyclinic - Bari	No
	ASST-Fatebenefratelli-Sacco - Milan	No
	Foundation IRCCS Polyclinic San Matteo, Pavia	No
	Maggiore' hospital - Crema	No
	Pediatric hospital Bambino Gesù, Rome	No
Netherlands	Amsterdam University Medical Centers Location AMC	No
	Erasmus MC: University Medical Center Rotterdam	No
	Radboud University Medical Centre Nijmegen	No
	St Antonius Hospital Utrecht	No
	University Medical Center Groningen together with Nij Smellinghe Drachten	No
Sweden	Karolinska University Hospital	No

Annex III: Geographical coverage per each country

AUSTRIA

Table 52. Information of Austria

ERN	1
HCPs	2

Figure 36. Geographical coverage of Austria

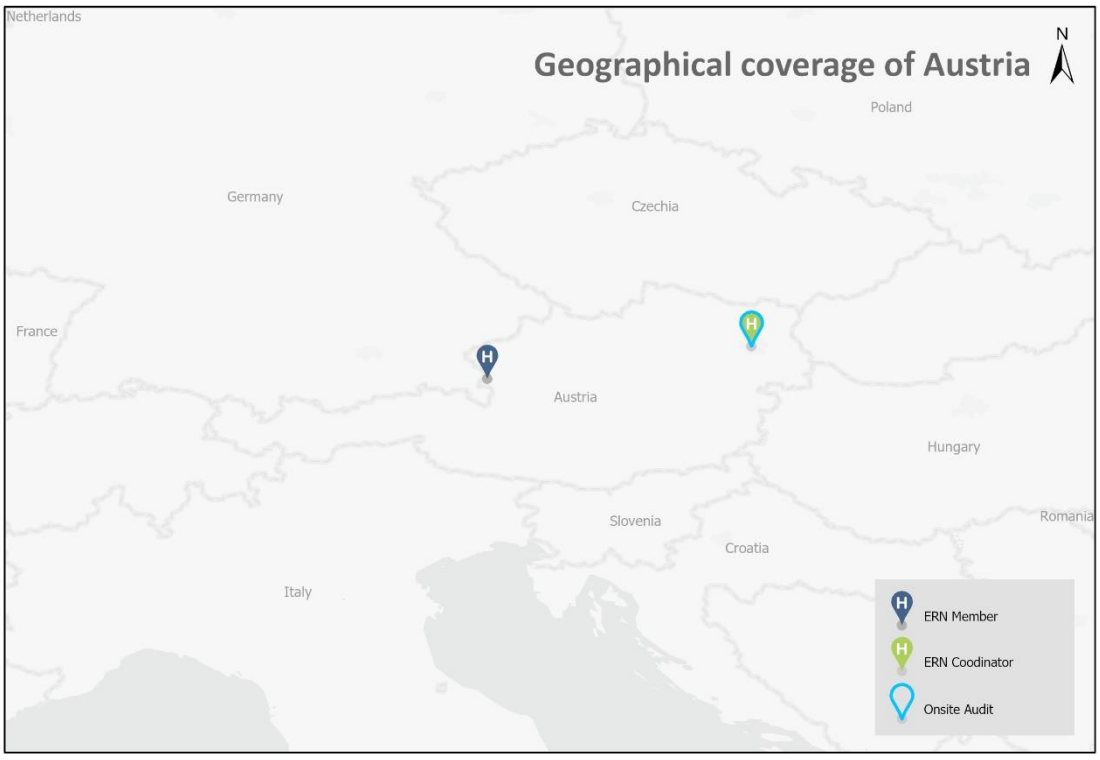


Table 53. Healthcare Providers in Austria

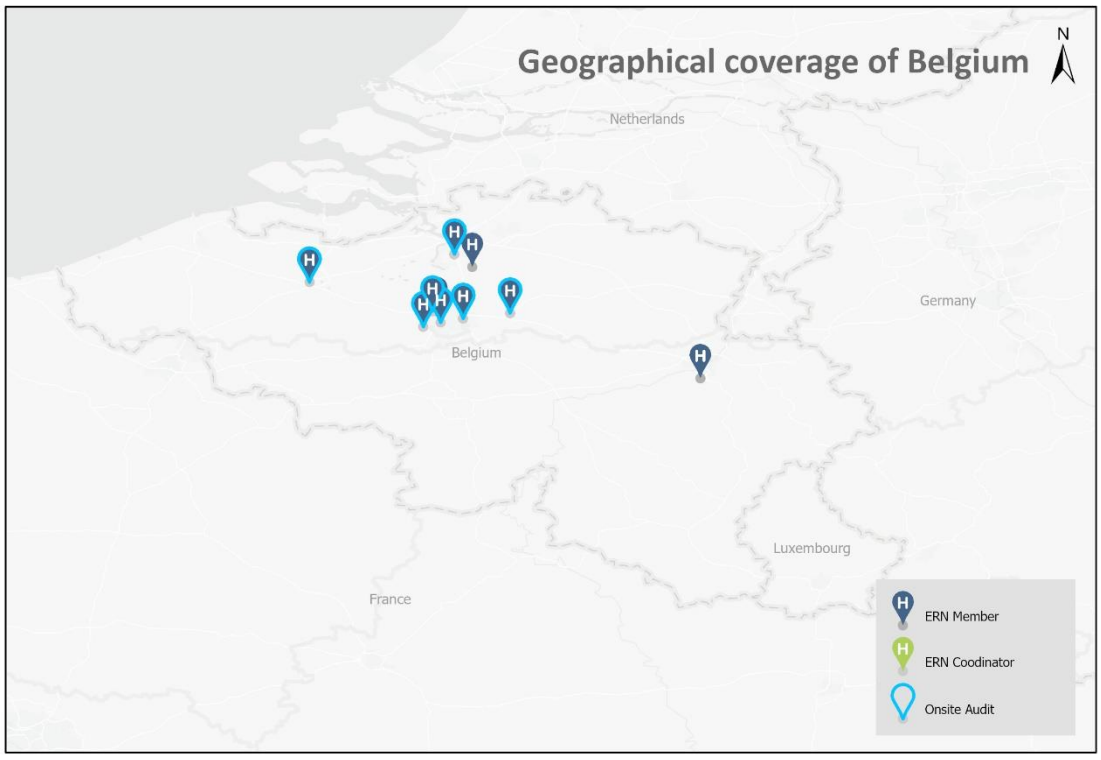
Hospital	Number of HCPs	Network
EB-Haus	1	ERN-Skin
St. Anna Kinderspital & St. Anna Kinderkrebsforschung	1	PaedCan

BELGIUM

Table 54. Information of Belgium

HCPs	68

Figure 37. Geographical coverage of Belgium



Escala: 1:3.000.000

Table 55. Healthcare Providers in Belgium

Hospital	Number of HCPs	Network
AZ Sint-Maarten	1	VASCern
CHU de Liège	6	Endo-ERN EuroBloodNet EURACAN GENTURIS MetabERN eUrogen
Cliniques universitaires Saint-Luc	9	EURO-NMD ReCONNET Endo-ERN ERKNet EuroBloodNet MetabERN RARE-LIVER TransplantChild VASCern

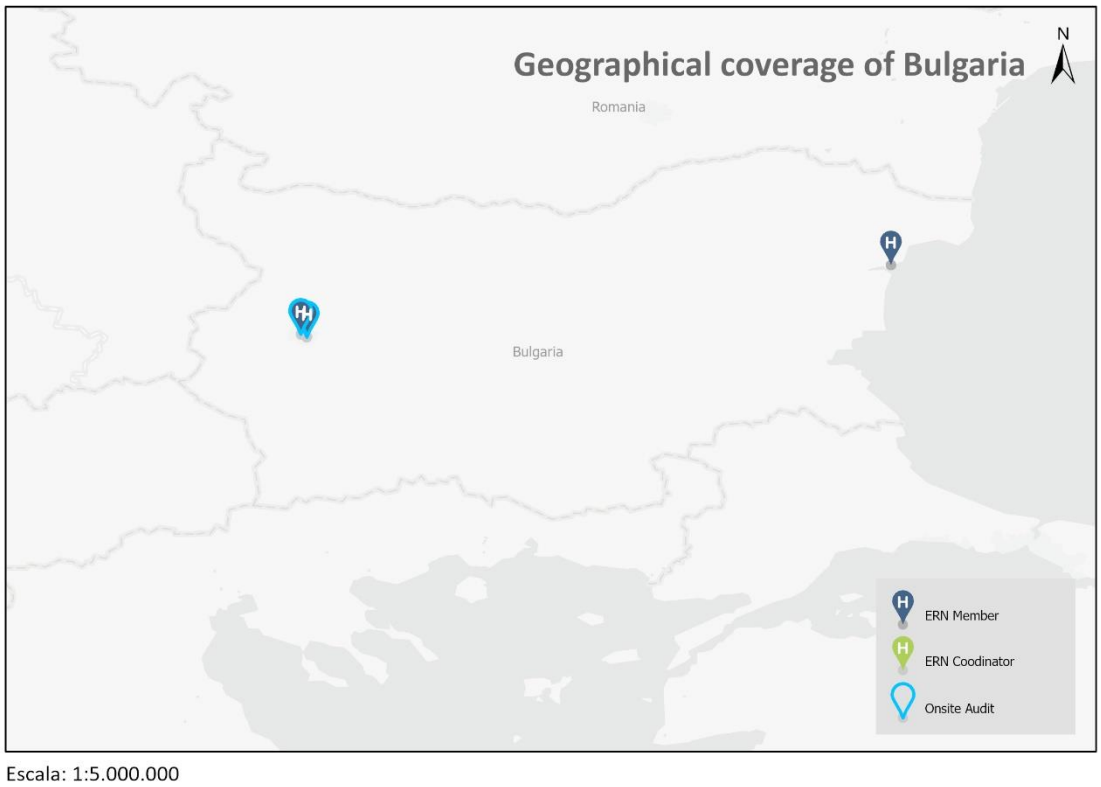
Hospital	Number of HCPs	Network
CUB-Hôpital Erasme	7	ERN-RND ERN-LUNG Endo-ERN ERN-Skin EuroBloodNet ITHACA EURO-NMD
Hôpital Universitaire des Enfants Reine Fabiola	1	PaedCan
Institut Jules Bordet	2	EURACAN EuroBloodNet
Universitair Ziekenhuis Antwerpen	7	EURACAN BOND ERN-LUNG EURO-NMD ITHACA VASCern MetabERN
UZ Brussel	3	Endo-ERN GUARD-HEART MetabERN
UZ Gent	13	EURO-NMD GENTURIS BOND Endo-ERN ERN-Skin MetabERN ERN-EYE eUrogen PaedCan RARE-LIVER ReCONNET ReCONNET VASCern
UZ Leuven	19	ERKNet ERN-Skin EURACAN EpiCARE ERN-RND GUARD-HEART MetabERN Endo-ERN ERNICA ERN-LUNG EuroBloodNet eUrogen EURO-NMD ITHACA RITA GENTURIS PaedCan RARE-LIVER VASCern

BULGARIA

Table 56. Information of Bulgaria

HCPs	7

Figure 38. Geographical coverage of Bulgaria



Escala: 1:5.000.000

Table 57. Healthcare Providers in Bulgaria

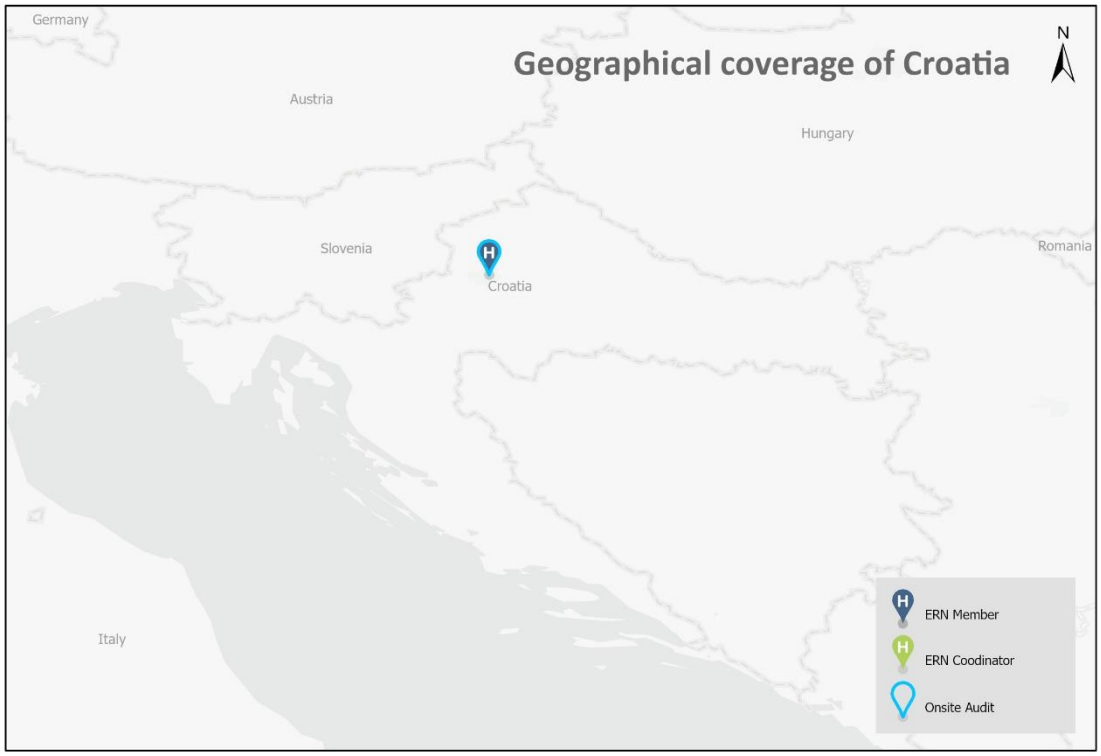
Hospital	Number of HCPs	Network
Expert Center on coagolopathias and Congenital Anemias	1	EuroBloodNet
Expert Centre for Hereditary Neurologic and Metabolic Disorders	1	EURO-NMD
MHAT 'Sveta Marina'	1	Endo-ERN
University Hospital 'Alexandrovska' Sofia	1	MetabERN
University Neurological Hospital 'ST. Naum' Sofia	1	ERN-RND
USHATE 'Acad Ivan Penchev'	1	Endo-ERN
Varna Expert Center of coagulopathies and rare anemias	1	EuroBloodNet

CROATIA

Table 58. Information of Croatia

HCPs	2

Figure 39. Geographical coverage of Croatia



Escala: 1:5.000.000

Table 59. Healthcare Providers in Croatia

Hospital	Number of HCPs	Network
Klinicki bolnicki centar Zagreb	2	MetabERN ERN-Skin

CYPRUS

Table 60. Information of Cyprus

HCPs	2

Figure 40. Geographical coverage of Cyprus

Escala: 1:1.500.000

Table 61. Healthcare Providers in Cyprus

Hospital	Number of HCPs	Network
Archbishop Makarios III Hospital	1	EuroBloodNet
Cyprus Institute of Neurology and Genetics	1	ITHACA

CZECH REPUBLIC

Table 62. Information of Czech Republic

HCPs	28

Figure 41. Geographical coverage of Czech Republic

Escala: 1:5.000.000

Table 63. Healthcare Providers in Czech Republic

Hospital	Number of HCPs	Network
Fakultní nemocnice Brno	4	PaedCan EuroBloodNet ERN-Skin EURO-NMD
Fakultní nemocnice Královské Vinohrady	2	ERN-Skin Endo-ERN

Hospital	Number of HCPs	Network
Fakultní nemocnice U Sv. Anny v Brne	2	EpiCARE ERN-Skin
Fakultní nemocnice v Motole	12	ERN-RND ERKNet Endo-ERN EpiCARE ITHACA PaedCan BOND CRANIO ERN-LUNG EURACAN EURO-NMD GUARD-HEART
Masarykuv onkologický ústav	1	EURACAN
Nemocnice Na Bulovce	1	ERN-Skin
Thomayerova nemocnice v Praze	1	ERN-LUNG
Všeobecná fakultní nemocnice v Praze	5	ERN-EYE ERN-LUNG ERN-RND RITA MetabERN

DENMARK

Table 64. Information of Denmark

HCPs	17

Figure 42. Geographical coverage of Denmark

Escala: 1:5.000.000

Table 65. Healthcare Providers in Denmark

Hospital	Number of HCPs	Network
Aarhus Universitets Hospital	4	Endo-ERN ERN-LUNG EURACAN eUrogen
Odense Universitetshospital	3	ERNICA ERN-Skin VASCern

Hospital	Number of HCPs	Network
Rigshospitalet	9	GUARD-HEART Endo-ERN MetabERN PaedCan RARE-LIVER eUrogen ERN-EYE ERNICA ERN-LUNG
Sjællands Universitetshospital	1	ERN-Skin

ESTONIA

Table 66. Information of Estonia

HCPs	3

Figure 43. Geographical coverage of Estonia

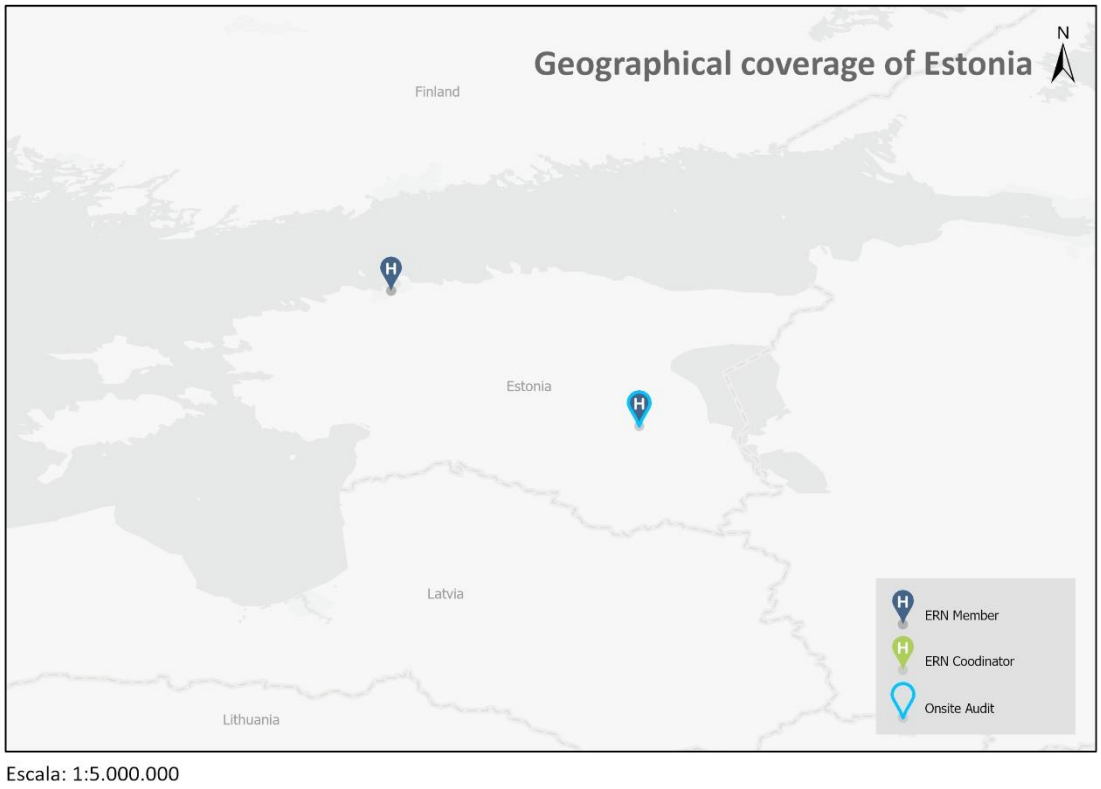


Table 67. Healthcare Providers in Estonia

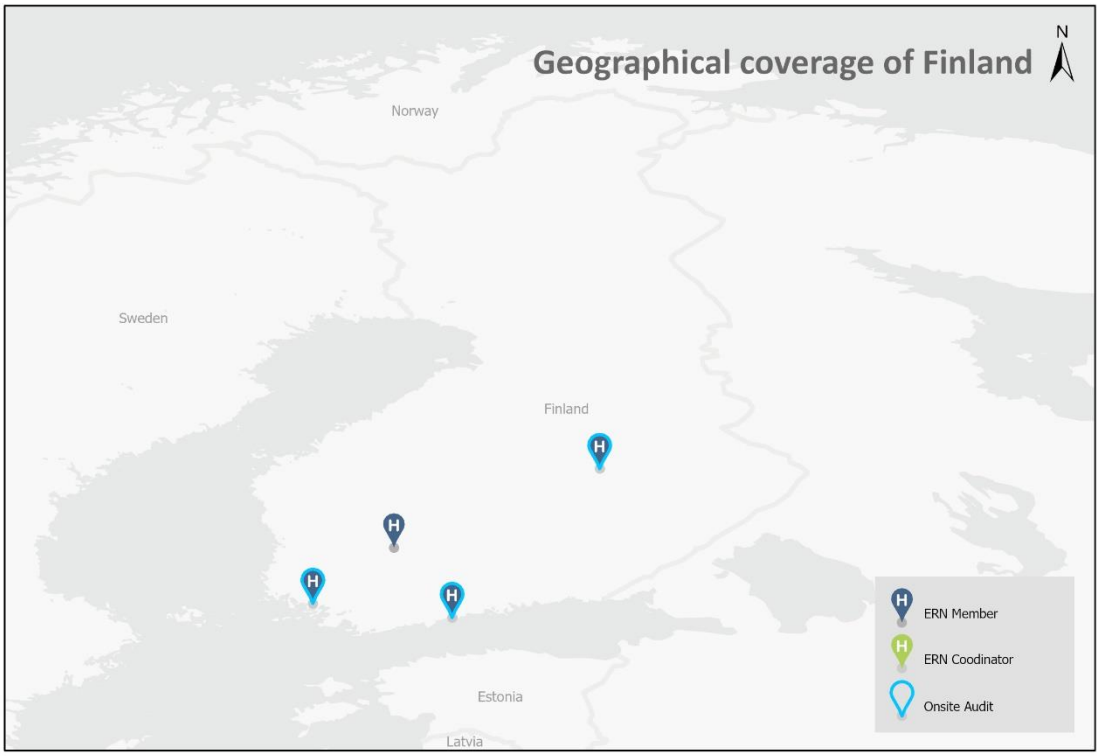
Hospital	Number of HCPs	Network
Ida-Tallinna Keskhaigla	1	ERN-EYE
Tartu Ülikooli Kliinikum	2	Endo-ERN BOND

FINLAND

Table 68. Information of Finland

HCPs	14

Figure 44. Geographical coverage of Finland



Escala: 1:12.000.000

Table 69. Healthcare Providers in Finland

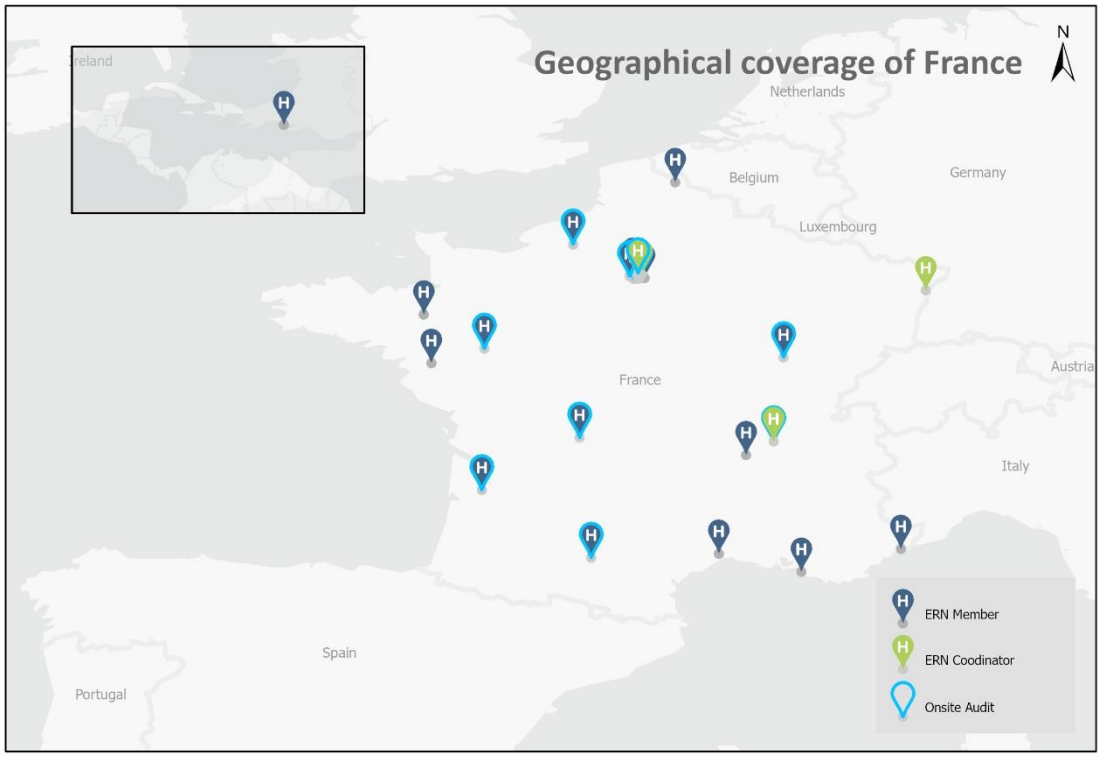
Hospital	Number of HCPs	Network
Helsinki University Hospital (HUS)	7	CRANIO ERKNet ERNICA ERN-Skin GUARD-HEART ITHACA VASCern
Kuopio University Hospital, Finland	2	EpiCARE PaedCan
Tampere University Hospital, Finland	2	PaedCan EURO-NMD
Turku University Hospital, Finland	3	EURACAN GENTURIS PaedCan

FRANCE

Table 70. Information of France

ERNs	8
HCPs	122

Figure 45. Geographical coverage of France



Escala: 1:12.000.000

Table 71. Healthcare Providers in France

Hospital	Number of HCPs	Network
Assistance Publique-Hôpitaux de Marseille	6	MetabERN Endo-ERN ERNICA EuroBloodNet EURO-NMD ITHACA
Assistance Publique-Hôpitaux de Paris, Hôpital Cochin	6	Endo-ERN ERN-LUNG EURACAN ReCONNET BOND RITA

Hospital	Number of HCPs	Network
Assistance Publique-Hôpitaux de Paris, Hôpital Antoine-Béclère.	2	MetabERN ERNICA
Assistance Publique-Hôpitaux de Paris, Hôpital Beaujon	3	MetabERN RARE-LIVER ERNICA
Assistance Publique-Hôpitaux de Paris, Hôpital Bicêtre	8	RARE-LIVER ERN-LUNG BOND Endo-ERN PaedCan RITA TransplantChild EURO-NMD
Assistance Publique-Hôpitaux de Paris, Hôpital Bichat	1	VASCern
Assistance Publique-Hôpitaux de Paris, Hôpital Européen Georges-Pompidou	1	VASCern
Assistance Publique-Hôpitaux de Paris, Hôpital Henri-Mondor	5	ERN-Skin ERKNet ERN-RND EuroBloodNet GENTURIS
Assistance Publique-Hôpitaux de Paris, Hôpital Louis-Mourier	1	MetabERN
Assistance Publique-Hôpitaux de Paris, Hôpital Necker-Enfants Malades	14	ERN-Skin ERKNet BOND CRANIO ERN-LUNG TransplantChild EpiCARE ERN-EYE eUrogen MetabERN PaedCan RITA EuroBloodNet ERNICA
Assistance Publique-Hôpitaux de Paris, Hôpital Pitié-Salpétrière	7	EURO-NMD GUARD-HEART Endo-ERN ERN-RND ERN-RND ReCONNET EURACAN
Assistance Publique-Hôpitaux de Paris, Hôpital Raymond Poincaré	2	EURO-NMD MetabERN
Assistance Publique-Hôpitaux de Paris, Hôpital Robert-Debré	3	ERNICA ERN-RND ITHACA
Assistance Publique-Hôpitaux de Paris, Hôpital Saint-Antoine	2	EuroBloodNet RARE-LIVER
Assistance Publique-Hôpitaux de Paris, Hôpital Saint-Louis	1	EuroBloodNet
Assistance Publique-Hôpitaux de Paris, Hôpital Tenon	2	EURACAN ERKNet
Assistance Publique-Hôpitaux de Paris, Hôpital Trousseau	3	ERN-LUNG PaedCan EuroBloodNet
Centre Hospitalier National d'Ophtalmologie des Quinze-Vingts	1	ERN-EYE
Centre Léon Bérard	2	EURACAN PaedCan
CHU d'Angers	1	Endo-ERN

Hospital	Number of HCPs	Network
CHU de Bordeaux	3	ERN-RND ERN-Skin ITHACA
CHU de Dijon	1	ITHACA
CHU de la Guadeloupe	1	EuroBloodNet
CHU de Lille	6	ITHACA EpiCARE ERNICA EuroBloodNet MetabERN ReCONNET
CHU de Limoges	2	EuroBloodNet EURO-NMD
CHU de Montpellier	3	ERN-EYE EuroBloodNet ITHACA
CHU de Nantes	2	GUARD-HEART EURO-NMD
CHU de Nice	2	EURO-NMD ERN-Skin
CHU de Rennes	2	ITHACA EuroBloodNeT
CHU de Rouen	2	ERN-Skin GENTURIS
CHU de Saint-Etienne	1	EURO-NMD
CHU de Toulouse	6	ERN-EYE BOND Endo-ERN ERN-RND ERN-Skin ERKNet
Hôpital Fondation Adolphe de Rothschild	1	PaedCan
Hôpitaux Universitaires de Strasbourg	4	CRANIO ERN-EYE ReCONNET RITA
Hospices Civils de Lyon	9	EpiCARE ERKNet ERN-LUNG EURACAN GUARD-HEART ITHACA VASCern BOND MetabERN
Institut Curie	4	EuroBloodNet GENTURIS PaedCan EURACAN
Institut Gustave Roussy	2	PaedCan EURACAN

GERMANY

Table 72. Information of Germany

ERNs	4
HCPs	121

Figure 46. Geographical coverage of Germany

Escala: 1:7.500.000

Table 73. Healthcare Providers in Germany

Hospital	Number of HCPs	Network
Charité Universitätsmedizin Berlin	10	ERN-LUNG EuroBloodNet CRANIO Endo-ERN EURO-NMD ReCONNET EURACAN MetabERN PaedCan eUrogen
Christian-Albrechts-Universität zu Kiel (CAU)	1	PaedCan
Friedrich-Baur Institut, Klinikum der Universität München	1	EURO-NMD
Hannoversche Kinderheilanstalt	1	Endo-ERN
Kerckhoff Klinik	1	ReCONNET
Klinikum Bremen-Mitte	1	eUrogen
Klinikum der Universität München	8	ERN-RND Endo-ERN EURO-NMD RITA ERN-Skin eUrogen BOND PaedCan
Klinikum Dortmund gGmbH	1	PaedCan
Klinikum Stuttgart	1	PaedCan
Medizinische Hochschule Hannover	7	TransplantChild ERNICA ERKNet ERN-LUNG MetabERN PaedCan RARE-LIVER
MGZ - Medizinisch Genetisches Zentrum	1	GENTURIS
Ruhrlandklinik - Westdeutsches Lungenzentrum	1	ERN-LUNG
Städtisches Klinikum Dessau	1	ERN-Skin
Thoraxklinik Universitätsklinikum Heidelberg	1	ERN-LUNG
Uniklinik RWTH Aachen	2	RARE-LIVER Endo-ERN
Universitäres Herzzentrum Hamburg	1	VASCern
Universitätsklinikum Leipzig	1	eUrogen
Universitätsklinikum Bonn	5	EpiCARE GENTURIS PaedCan ERN-RND EURO-NMD
Universitätsklinikum Carl Gustav Carus	2	GENTURIS EuroBloodNet
Universitätsklinikum des Saarlandes	1	RARE-LIVER
Universitätsklinikum Düsseldorf	2	ITHACA ReCONNET
Universitätsklinikum Erlangen	1	ERN-Skin

Hospital	Number of HCPs	Network
Universitätsklinikum Essen	6	Endo-ERN ERKNet VASCern EURO-NMD BOND EURACAN
Universitätsklinikum Frankfurt	1	ERN-LUNG
Universitätsklinikum Freiburg	11	EpiCARE MetabERN BOND ERN-EYE ERN-Skin EURO-NMD ERN-Skin PaedCan RITA VASCern ERN-LUNG
Universitätsklinikum Gießen und Marburg	6	ERN-EYE ERN-LUNG EURACAN MetabERN PaedCan Endo-ERN
Universitätsklinikum Hamburg-Eppendorf	5	eUrogen ERKNet EURACAN MetabERN RARE-LIVER
Universitätsklinikum Heidelberg	3	ERKNet EuroBloodNet MetabERN
Universitätsklinikum Köln	4	ERKNet ERN-LUNG BOND ReCONNET EuroBloodNet
Universitätsklinikum Magdeburg	3	BOND Endo-ERN MetabERN
Universitätsklinikum Mannheim	2	EURACAN ERNICA
Universitätsklinikum Münster	7	GUARD-HEART ERKNet ERN-LUNG ERN-Skin MetabERN RITA Endo-ERN
Universitätsklinikum Regensburg	2	ERN-Skin eUrogen
Universitätsklinikum Schleswig-Holstein	4	Endo-ERN ERN-RND ITHACA ERN-Skin
Universitätsklinikum Tübingen	4	ITHACA ERN-EYE ERN-RND RARE-LIVER

Hospital	Number of HCPs	Network
Universitätsklinikum Ulm	2	ERN-RND EURO-NMD
Universitätsklinikum Würzburg	4	Endo-ERN ERN-LUNG ERN-Skin EURACAN
Universitätsmedizin Göttingen	1	EURO-NMD
Universitätsmedizin Mainz	2	Endo-ERN MetabERN
Universitätsmedizin Rostock	1	ERN-Skin
University Children's Hospital Tübingen	1	PaedCan

HUNGARY

Table 74. Information of Hungary

HCPs	14

Figure 47. Geographical coverage of Hungary

Escala: 1:5.000.000

Table 75. Healthcare Providers in Hungary

Hospital	Number of HCPs	Network
Országos Onkológiai Intézet	1	EURACAN
Semmelweis University	6	ERN-RND VASCern Endo-ERN ERN-Skin EURO-NMD PaedCan
Szent-Györgyi Albert Medical Center, University of Szeged	1	ERN-Skin
University of Debrecen	2	MetabERN ERN-Skin
University of Pécs	4	ERN-RND CRANIO EURO-NMD GENTURIS

IRELAND

Table 76. Information of Ireland

HCPs	3

Figure 48. Geographical coverage of Ireland

Escala: 1:5.000.000

Table 77. Healthcare Providers in Ireland

Hospital	Number of HCPs	Network
Children's Health Ireland	3	ERN-Skin EuroBloodNet VASCern

ITALY

Table 78. Information of Italy

ERNs	3
HCPs	188

Figure 49. Geographical coverage of Italy

Escala: 1:10.000.000

Table 79. Healthcare Providers in Italy

Hospital	Number of HCPs	Network
A. ASL Toscana Centro	1	ERN-Skin
A. ULSS 15 - Ospedale di Camposampiero	1	ERN-EYE
A. ULSS6 - Ospedale San Bortolo di Vicenza	2	CRANIO EuroBloodNet
A. USL della Romagna (Ospedale G.B.Morgagni-L.Pierantoni)	1	ERN-LUNG
A.S.L. Torino 2 - Hub O. Giovanni Bosco	1	ERKNet

Hospital	Number of HCPs	Network
AO Città della Salute e della Scienza di Torino	4	EURO-NMD Endo-ERN EURACAN PaedCan
AO Ospedali Riuniti Villa Sofia-Cervello Palermo	1	EuroBloodNet
AO San Camillo Forlanini - Roma	1	ReCONNET
AO Santobono-Pausilipon - Napoli	1	ERKNet
AORN Colli	1	GUARD-HEART
AOU Careggi, Firenze	7	EURACAN BOND Endo-ERN ERN-EYE EuroBloodNet ReCONNET VASCern
AOU Consorziale policlinico di Bari	2	VASCern EuroBloodNet
AOU di Bologna	5	ERN-Skin Endo-ERN ERN-LUNG EURACAN ITHACA
AOU di Ferrara	1	EURO-NMD
AOU di Modena	2	EuroBloodNet ERN-LUNG
AOU di Perugia	1	PaedCan
AOU Federico II di Napoli	6	Endo-ERN EuroBloodNet EURACAN ITHACA MetabERN ERN-LUNG
AOU Meyer di Firenze	7	ITHACA Endo-ERN EpiCARE ERKNet ERN-LUNG MetabERN PaedCan
AOU Ospedali riuniti di Trieste	1	ERN-LUNG
AOU Pisana	5	Endo-ERN MetabERN ERN-LUNG EURO-NMD ReCONNET
AOU policlinico 'G.Martino' Messina	1	EURO-NMD
AOU Policlinico Umberto I di Roma	1	EuroBloodNet
AOU S. Luigi di Torino	1	ERN-LUNG
AOU S.Luigi Gonzaga	1	EuroBloodNet
AOU Senese	9	ERN-LUNG ERKNet EURACAN EuroBloodNet ITHACA PaedCan ERN-RND MetabERN EURO-NMD

Hospital	Number of HCPs	Network
AOU Università degli Studi della Campania 'Luigi Vanvitelli', Napoli	4	EURO-NMD ERN-EYE ERKNet EuroBloodNet
AOUI di Verona	4	BOND EuroBloodNet ERN-LUNG MetabERN
AULSS 2 Marca trevigiana	1	EURACAN
Azienda Ospedale - Università Padova	18	BOND CRANIO ERKNet eUrogen GUARD-HEART RARE-LIVER Endo-ERN ERN-EYE ERNICA ERN-LUNG ERN-Skin PaedCan ReCONNET TransplantChild EuroBloodNet EURO-NMD ITHACA MetabERN
Azienda Ospedaliero-Universitaria G. Rodolico-San Marco	1	ERN-LUNG
AZIENDA SANITARIA UNIVERSITARIA FRIULI CENTRALE	1	MetabERN
Azienda USL di Bologna - IRCCS Istituto delle Scienze Neurologiche	2	EpiCARE EURACAN
Fondazione CNR Regione Toscana G. Monasterio	1	EuroBloodNet
Fondazione IRCCS CA'Granda Ospedale Maggiore Policlinico , Milano	8	EURO-NMD eUrogen BOND ERKNet EuroBloodNet ReCONNET ERN-Skin ITHACA
Fondazione IRCCS Istituto Neurologico Carlo Besta di Milano	5	EURO-NMD CRANIO EpiCARE ERN-RND EURACAN
Fondazione IRCCS Ospedale San Gerardo dei Tintori di Monza	4	RARE-LIVER EuroBloodNet CRANIO MetabERN
Fondazione IRCCS Policlinico San Matteo, Pavia	7	ERN-LUNG RITA EuroBloodNet GUARD-HEART PaedCan VASCern ReCONNET
Fondazione Istituto Neurologico Nazionale C. Mondino di Pavia	1	EpiCARE
Fondazione MBBM – Pediatria – Ospedale S.Gerardo, Monza	1	PaedCan

Hospital	Number of HCPs	Network
Fondazione Policlinico Gemelli, IRCCs, Rome	6	ITHACA CRANIO ERKNet EuroBloodNet eUrogen EURO-NMD
IRCCS Burlo Garofolo di Trieste	1	BOND
IRCCS Fondazione Salvatore Maugeri	1	GUARD-HEART
IRCCS IDI Fondazione Luigi Maria Monti - Roma	1	ERN-Skin
IRCCS IFO Regina Elena - San Gallicano	1	EURACAN
IRCCS ISMETT - Palermo	1	TransplantChild
IRCCS Istituto Auxologico Italiano di Milano	3	Endo-ERN EURO-NMD GUARD-HEART
IRCCS Istituto Clinico Humanitas di Rozzano	3	EURACAN EuroBloodNet ERN-RND
IRCCS Istituto Giannina Gaslini, Genova	7	ERKNet EURO-NMD BOND MetabERN PaedCan EuroBloodNet RITA
IRCCS Ospedale Pediatrico Bambino Gesù, Roma	15	ERN-RND EURO-NMD EpiCARE MetabERN TransplantChild VASCern ERKNet ERN-EYE ERN-LUNG ERN-Skin eUrogen GUARD-HEART ITHACA PaedCan RITA
IRCCS Ospedale Policlinico San Martino – Genova	3	EURACAN Endo-ERN ReCONNET
IRCCS Ospedale San Raffaele di Milano	3	RITA Endo-ERN EURACAN
IRST di Meldola	1	EURACAN
Istituto di Candiolo - IRCCS	1	EURACAN
Istituto Nazionale tumori di Milano	1	EURACAN
Istituto Ortopedico Rizzoli di Bologna	2	BOND EURACAN
Ospedale Maggiore di Crema	1	VASCern
Ospedale Niguarda di Milano	1	EURO-NMD
Ospedale Papa Giovanni XXIII di Bergamo	3	ERKNet EuroBloodNet TransplantChild
Ospedale S. Paolo di Milano	3	CRANIO MetabERN RARE-LIVER

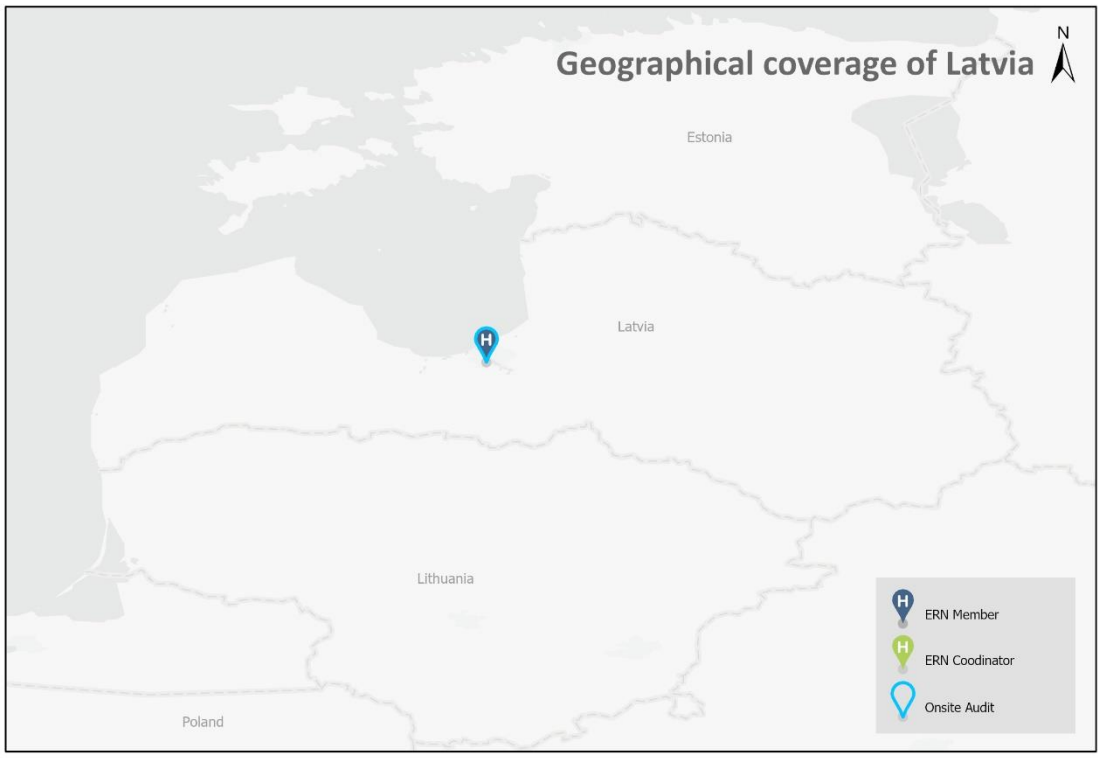
Hospital	Number of HCPs	Network
Ospedale San Giuseppe di Milano	1	ERN-LUNG
Spedali Civili di Brescia	3	RITA EURO-NMD ReCONNET
ASST-Fatebenefratelli-Sacco - Milan	1	VASCern
Oncological Referral Center - Aviano	1	EURACAN
AULLS 12 – Mestre hospital – rare eye diseases	1	ERN-EYE
E.O. Ospedali Galliera, Genoa	1	EuroBloodNet

LATVIA

Table 80. Information of Latvia

HCPs	2

Figure 50. Geographical coverage of Latvia



Escala: 1:5.000.000

Table 81. Healthcare Providers in Latvia

Hospital	Number of HCPs	Network
Bernu kliniska universitates slimnica	2	ERN-EYE PaedCan

LITHUANIA

Table 82. Information of Lithuania

HCPs	12

Figure 51. Geographical coverage of Lithuania

Escala: 1:5.000.000

Table 83. Healthcare Providers in Lithuania

Hospital	Number of HCPs	Network
Lietuvos Sveikatos Mokslu Universiteto Ligonine Kauno Klinikos	4	Endo-ERN ERN-EYE ERN-Skin EURACAN
Vilniaus Universiteto Ligonines Santariškiu Klinikos	8	ERKNet ERN-RND EuroBloodNet eUrogen ITHACA MetabERN PaedCan TransplantChild

LUXEMBOURG

Table 84. Table 85. Information of Luxembourg

HCPs	1

Figure 52. Geographical coverage of Luxembourg

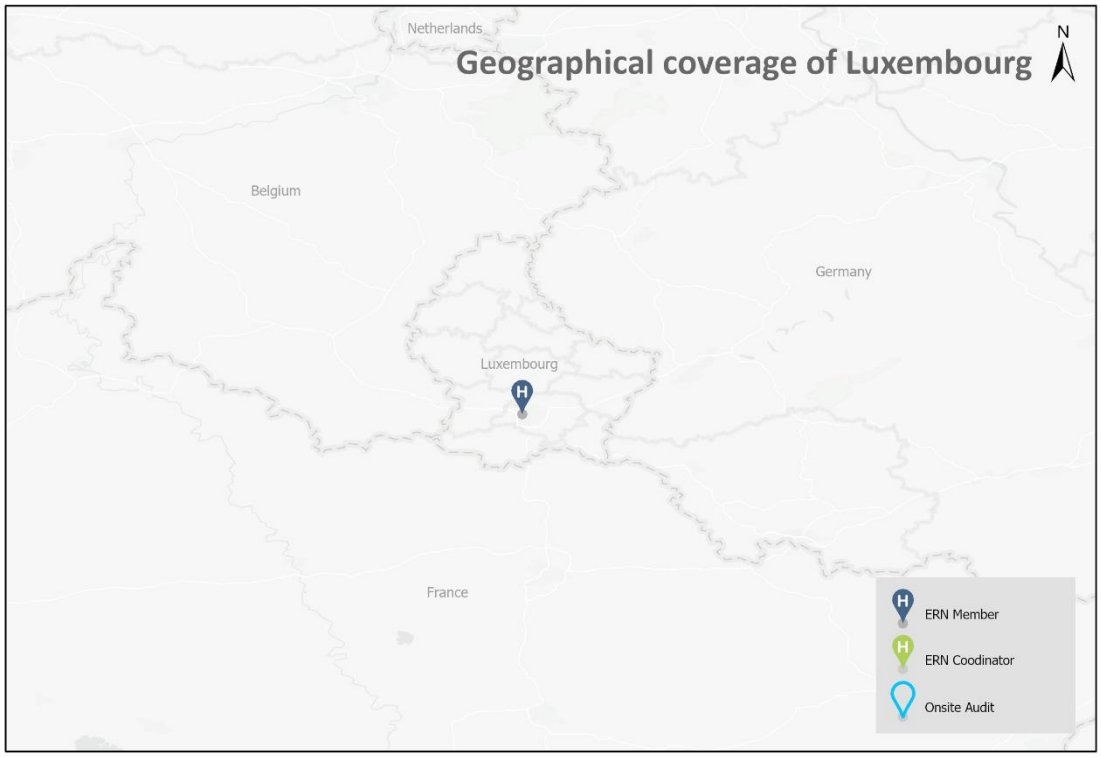


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Table 86. Table 87. Healthcare Providers in Luxembourg

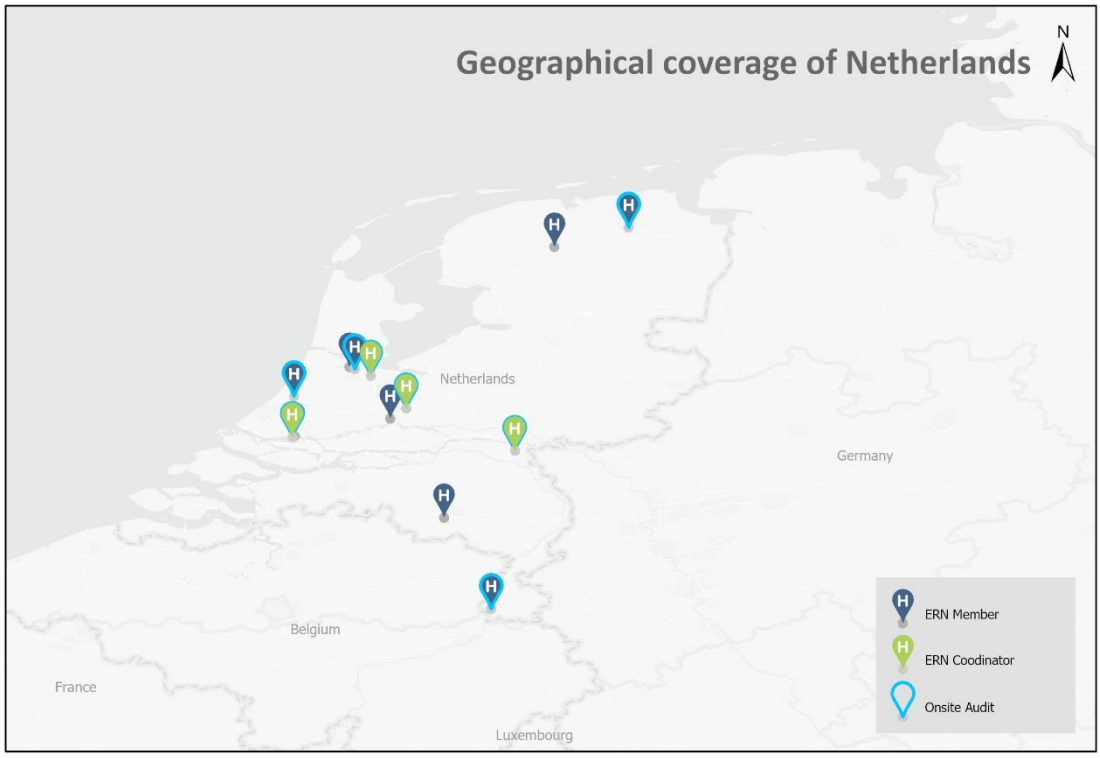
Hospital	Number of HCPs	Network
Centre Hospitalier de Luxembourg	1	Endo-ERN

NETHERLANDS

Table 88. Information of Netherlands

ERNs	7
HCPs	88

Figure 53. Geographical coverage of Netherlands



Escala: 1:4.000.000

Table 89. Healthcare providers in Netherlands

Hospital	Number of HCPs	Network
Amsterdam University Medical Centers Location AMC	12	Endo-ERN ERNICA ERKNet ERN-Skin EURACAN ITHACA EuroBloodNet EURO-NMD GUARD-HEART MetabERN VASCern RARE-LIVER
Amsterdam University Medical Centers location: VUMC	3	PaedCan ERN-LUNG ERN-RND
Erasmus MC: University Medical Center Rotterdam	17	EURACAN CRANIO BOND Endo-ERN ERNICA ERN-LUNG ERN-RND ERN-Skin EuroBloodNet eUrogen EURO-NMD GENTURIS ITHACA VASCern MetabERN ReCONNET RITA
Leiden University Medical Center	8	Endo-ERN BOND ERN-EYE ERN-LUNG EURACAN EuroBloodNet EURO-NMD ReCONNET
Maastricht University Medical Center+	6	ITHACA Endo-ERN ERN-Skin EURACAN EURO-NMD MetabERN
Máxima Medisch Centrum Veldhoven	1	Endo-ERN
Netherlands Cancer Institute - Antoni van Leeuwenhoek	1	EURACAN

Hospital	Number of HCPs	Network
Radboud University Medical Centre Nijmegen	14	GENTURIS Endo-ERN ERN-RND EuroBloodNet eUrogen RARE-LIVER CRANIO ERKNet EURACAN EURO-NMD ITHACA VASCern ERN-EYE ERNICA
Rotterdam Eye Clinic	1	ERN-EYE
St Antonius Hospital Utrecht	2	ERN-LUNG VASCern
University Medical Center Groningen together with Nij Smellinghe Drachten	1	VASCern
University Medical Center Utrecht	12	ERN-LUNG RITA ERKNet EuroBloodNet EURO-NMD ReCONNET CRANIO Endo-ERN EpiCARE ERNICA MetabERN TransplantChild
University Medical Centre Groningen	10	ERN-RND EURACAN Endo-ERN GENTURIS ITHACA MetabERN ERN-Skin RARE-LIVER RITA EuroBloodNet

NORWAY

Table 90. Information of Norway

HCPs	4

Figure 54. Geographical coverage of Norway

Escala: 1:14.000.000

Table 91. Healthcare providers in Norway

Hospital	Number of HCPs	Network
Helse Bergen HF	1	MetabERN
Oslo Universitetssykehus	3	ERNICA EURACAN MetabERN

POLAND

Table 92. Information of Poland

HCPs	20

Figure 55. Geographical coverage of Poland

Escala: 1:8.000.000

Table 93. Healthcare providers in Poland

Hospital	Number of HCPs	Network
Europejskie Centrum Zdrowia - Otwock	1	ERN-LUNG
Instytut 'Pomnik-Centrum Zdrowia Dziecka'	2	TransplantChild EpiCARE
Instytut Gruzlicy i Chorób Pluc	1	ERN-LUNG
Narodowy Instytut Onkologii im. Marii Sklodowskiej-Curie – Panstwowy Instytut Badawczy (NIO-PIB)	3	EURACAN EuroBloodNet Endo-ERN
Samodzielny Publiczny Dzieciecy Szpital Kliniczny w Warszawie	1	Endo-ERN

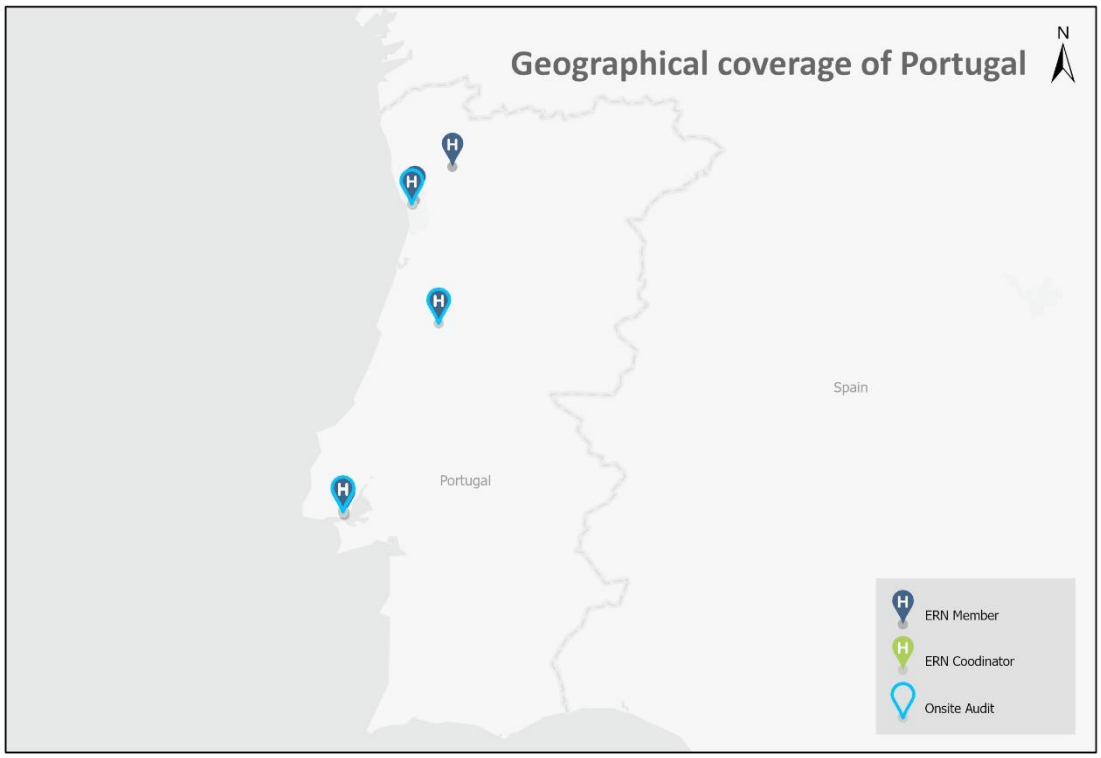
Hospital	Number of HCPs	Network
Samodzielny Publiczny Szpital Kliniczny nr 1 w Lublinie	1	ERN-EYE
Samodzielny Publiczny Szpital Kliniczny nr 1, PUM w Szczecinie. Poland	1	GENTURIS
SPCSK, Banacha, Warszawa	2	EURO-NMD RARE-LIVER
Szpital im. Marciniaka - Centrum Medycyny Ratunkowej	1	PaedCan
Szpital Uniwesytecki w Krakowie	2	ERN-RND MetabERN
Uniwersytecki Szpital Dzieciecy w Lublinie	1	PaedCan
Uniwersyteckie Centrum Kliniczne przy Gdanskim Uniwersytecie Medycznym	3	PaedCan Eurogen ERKNet
University Swiecicki Hospital in Poznan	1	ERN-SKIN

PORTUGAL

Table 94. Information of Portugal

HCPs	30

Figure 56. Geographical coverage of Portugal



Escala: 1:5.000.000

Table 95. Healthcare providers in Portugal

Hospital	Number of HCPs	Network
APDP - Associação de Diabéticos de Portugal	1	Endo-ERN
Centro Hospitalar de Lisboa Central, EPE	1	ReCONNET
Centro Hospitalar de Lisboa Norte, EPE	5	MetabERN CRANIO EpiCARE ReCONNET TransplantChild

Hospital	Number of HCPs	Network
Centro Hospitalar do Porto, EPE	6	ERN-LUNG TransplantChild EpiCARE EuroBloodNet MetabERN EURACAN
Centro Hospitalar e Universitário de Coimbra, EPE	10	TransplantChild ERN-EYE EpiCARE ITHACA MetabERN RARE-LIVER EURACAN BOND EuroBloodNet PaedCan
Centro Hospitalar Universitário de São João (CHUSJ)	1	MetabERN
Hospital Senhora da Oliveira, Guimarães, EPE	1	MetabERN
Instituto Português de Oncologia de Lisboa Francisco Gentil, EPE	2	EURACAN PaedCan
Instituto Português de Oncologia do Porto	2	eUrogen EuroBloodNet
Porto. Centro Compreensivo de Cancro	1	GENTURIS

ROMANIA

Table 96. Information of Romania

HCPs	7

Figure 57. Geographical coverage of Romania

Escala: 1:6.000.000

Table 97. Healthcare providers in Romania

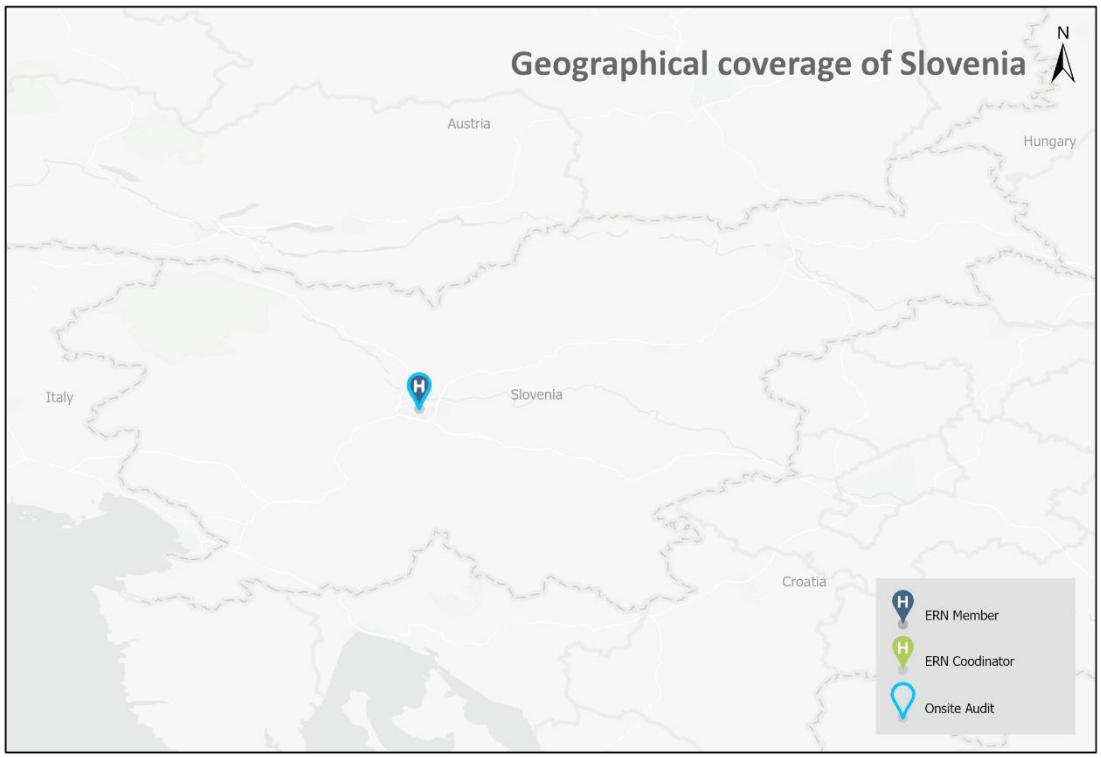
Hospital	Number of HCPs	Network
Institutul de Urgenta pentru Boli Cardiovasculare 'CC Iliescu'	1	GUARD-HEART
Institutul Oncologic 'Prof. dr. Lon Chiricuta' Cluj-Napoca	1	Endo-ERN
Rețea pentru Malformațiile Congenitale Asociate cu Dizabilitați Intelectuale	1	ITHACA
Spitalul Clinic Judetean de Urgenta Cluj	1	ReCONNET
Spitalul Clinic Colentina	1	ERN-Skin
Spitalul Clinic de Psihiatrie 'Alexandru Obregia'	2	Endo-ERN EpiCARE

SLOVENIA

Table 98. Information of Slovenia

HCPs	9

Figure 58. Geographical coverage of Slovenia



Escala: 1:2.000.000

Table 99. Healthcare providers in Slovenia

Hospital	Number of HCPs	Satisfactory
Onkološki inštitut Ljubljana	2	GENTURIS EURACAN

Hospital	Number of HCPs	Satisfactory
Univerzitetni klinicni center Ljubljana	7	MetabERN ERN-RND Endo-ERN EURO-NMD ReCONNET RITA PaedCan

SPAIN

Table 100. Information of Spain

ERNs	1
HCPs	42

Figure 59. Geographical coverage of Spain

Escala: 1:8.000.000

Table 101. Healthcare providers in Spain

Hospital	Number of HCPs	Network
Complejo Hospitalario Regional Virgen del Rocío	3	EURACAN EURO-NMD PaedCan
Complexo Hospitalario Universitario de Santiago	1	MetabERN
Hospital Clínic i Provincial de Barcelona	2	ERN-LUNG RARE-LIVER
Hospital de la Santa Creu i Sant Pau	2	EURACAN EURO-NMD

Hospital	Number of HCPs	Network
Hospital de Sant Joan de Déu	9	ERN-Skin Endo-ERN EURO-NMD GENTURIS GUARD-HEART MetabERN EpiCARE ERN-RND PaedCan
Hospital del Mar	1	EpiCARE
Hospital Universitari de Bellvitge	1	EURACAN
Hospital Universitari Germans Trias i Pujol y ICO Badalona	1	GENTURIS
Hospital Universitari Vall d'Hebron	10	CRANIO Endo-ERN ERKNet ERN-LUNG ERN-RND EuroBloodNet MetabERN PaedCan RITA EURO-NMD
Hospital Universitario 12 de Octubre	3	MetabERN CRANIO ERN-LUNG
Hospital Universitario de Cruces	2	Endo-ERN MetabERN
Hospital Universitario La Paz	2	RARE-LIVER TransplantChild
Hospital Universitario Puerta de Hierro Majadahonda	1	GUARD-HEART
Hospital Universitario Virgen de la Arrixaca	1	GUARD-HEART
Hospital Universitario y Politécnico La Fe	3	EpiCARE PaedCan EURO-NMD

SWEDEN

Table 102. Information of Sweden

HCPs	30

Figure 60. Geographical coverage of Sweden

Escala: 1:12.500.000

Table 103. Healthcare Providers in Sweden

Hospital	Number of HCPs	Network
Akademiska Sjukhuset	3	CRANIO ERN-Skin EURACAN

Hospital	Number of HCPs	Network
Karolinska Universitetssjukhuset	18	BOND MetabERN CRANIO ERNICA eUrogen ITHACA Endo-ERN ERKNet ERN-LUNG EURACAN EuroBloodNet EURO-NMD RITA TransplantChild GENTURIS PaedCan RARE-LIVER VASCern
Norrlands universitetssjukhus	1	GUARD-HEART
Sahlgrenska Universitetssjukhuset	6	CRANIO EpiCARE eUrogen EURO-NMD MetabERN RARE-LIVER
Skånes universitetssjukhus	2	PaedCan TransplantChild

Annex IV: Overall results of each criterion (calculating exclusively its core MEs) of ERNs

The following figures show the average rating of all the ERNs within each criterion in each thematic area.

Figure 61. Overall results of the ERNs in Area 1 criteria

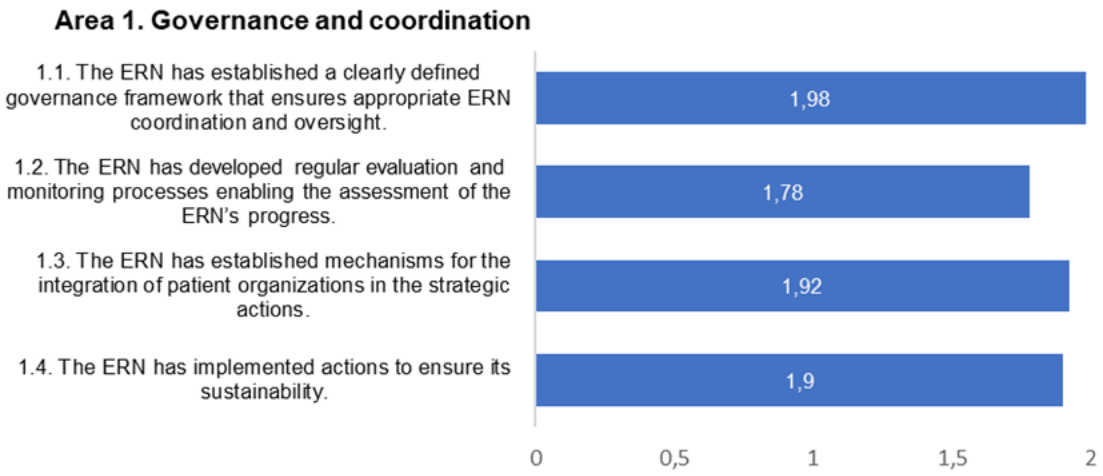


Figure 62. Overall results of the ERNs in Area 2 criteria

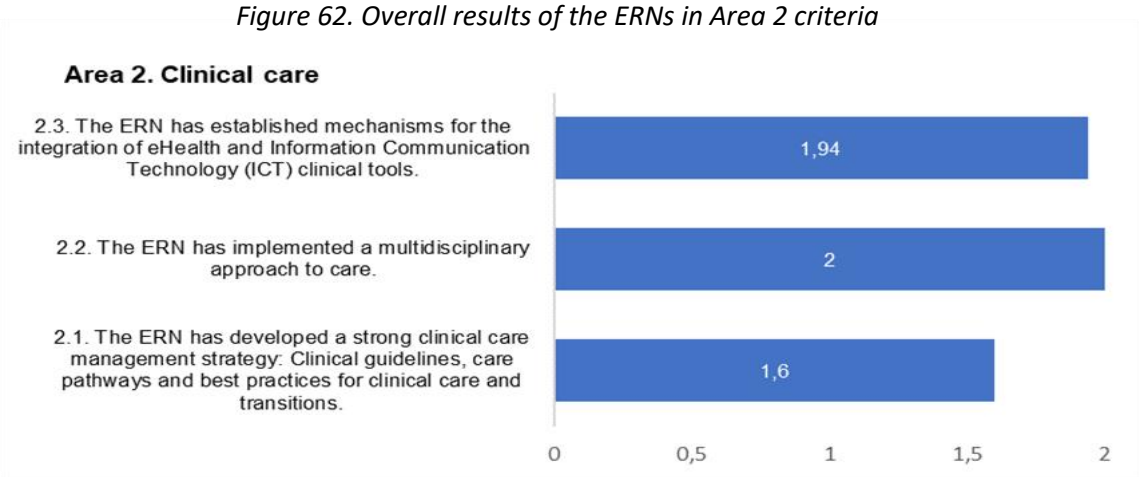


Figure 63. Overall results of the ERNs in Area 3 criteria

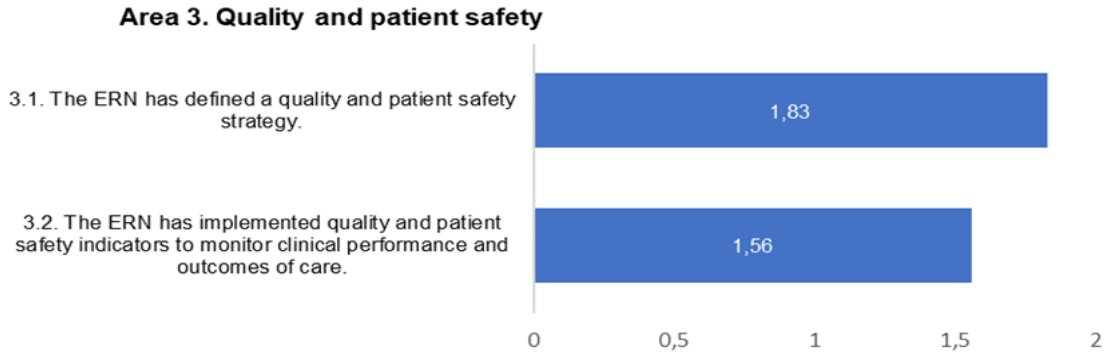


Figure 64: Overall results of the ERNs in Area 4 criteria

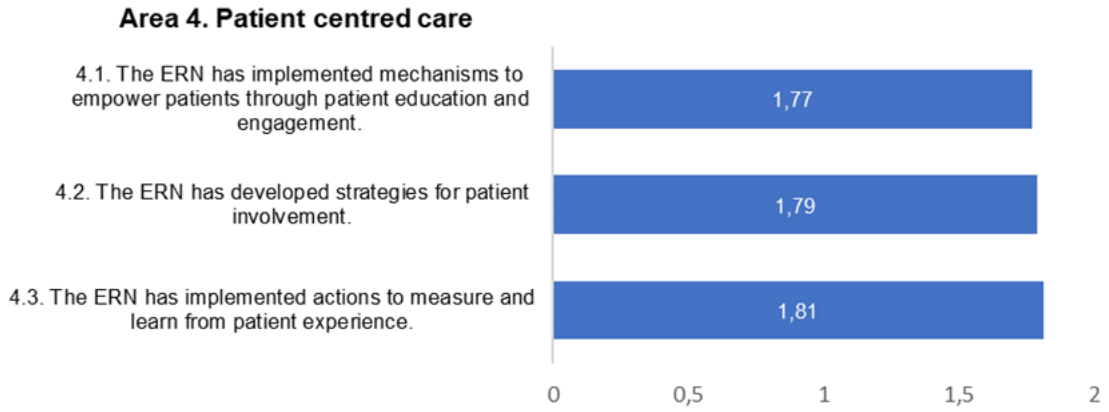


Figure 65. Overall results of the ERNs in Area 5 criteria

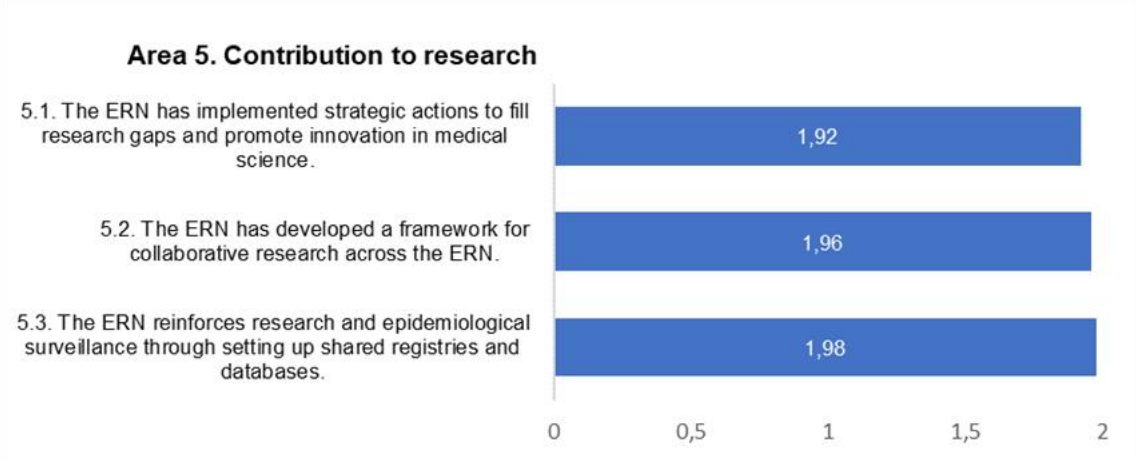


Figure 66. Overall results of the ERNs in Area 6 criteria

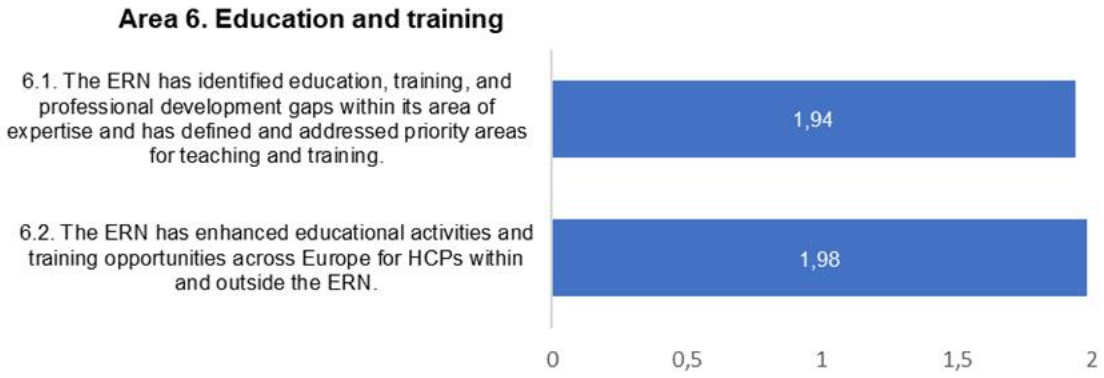
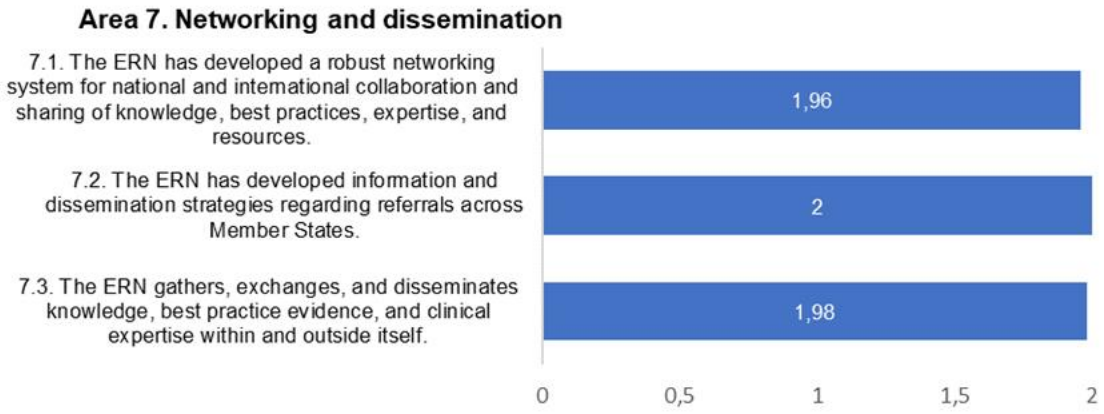


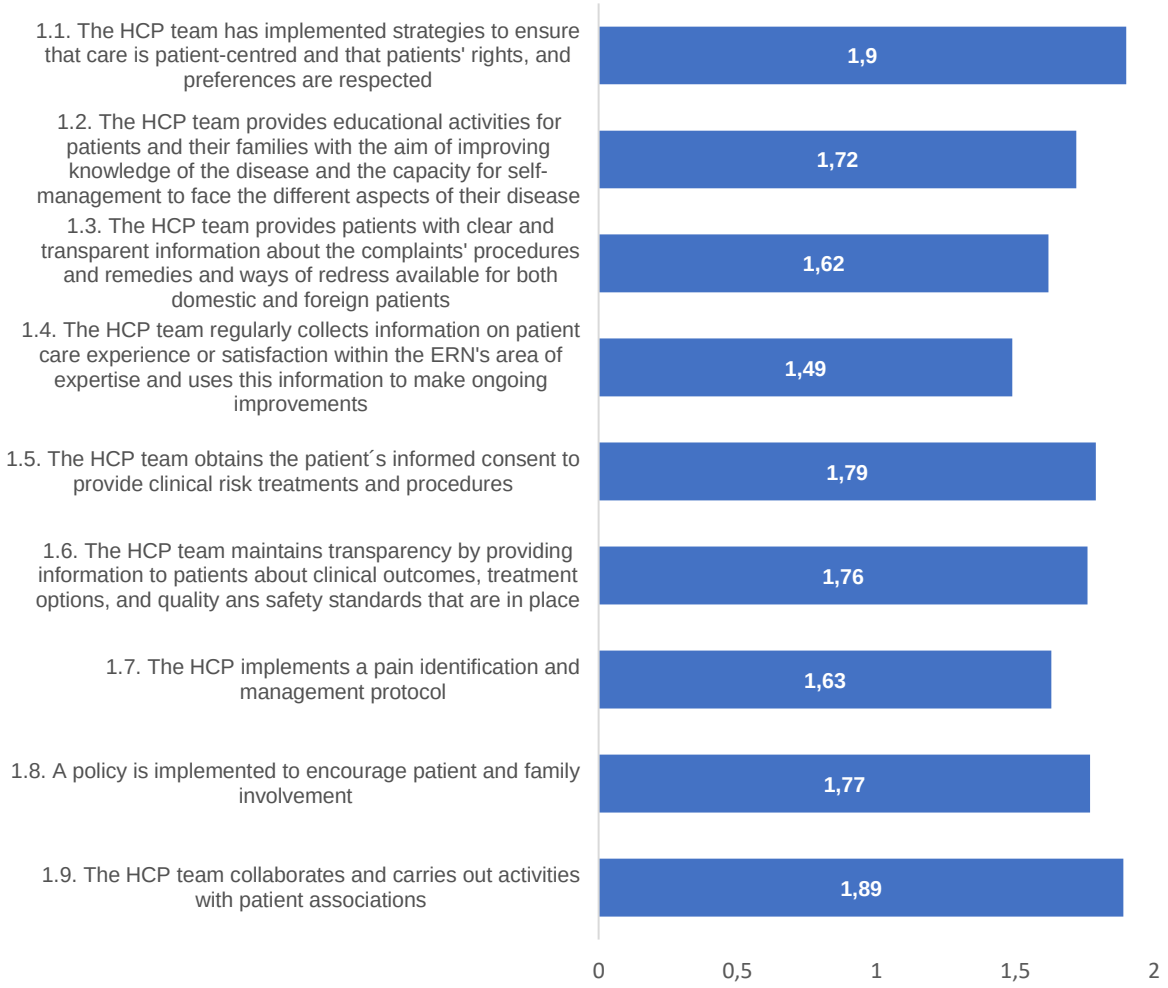
Figure 67. Overall results of the ERNs in Area 7 criteria



Annex V: Overall results of each criterion (calculating exclusively its core MEs) of HCPs

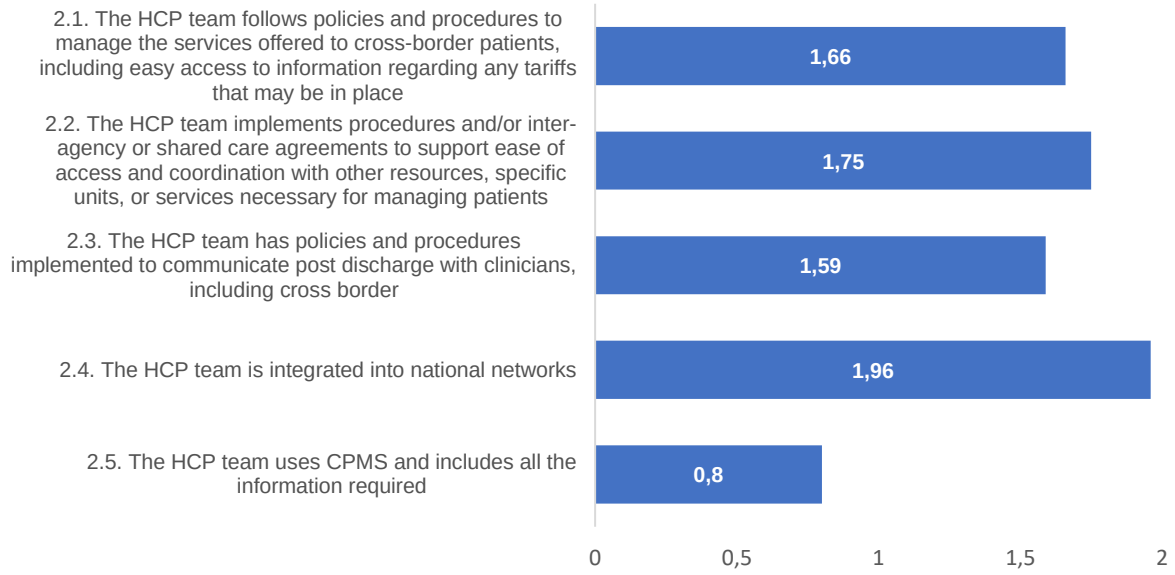
The following figures show the average rating of all the ERNs within each criterion in each thematic area.

Figure 68. Overall results of the HCPs in Area 1 criteria



Area 1. Patient centred care

Figure 69. Overall results of the HCPs in Area 2 criteria



Area 2. Organisation and Management

Figure 70. Overall results of the HCPs in Area 3 criteria

Area 3. Research, Education and Training.

Area 4. Exchange of expertise, Information systems and e-Health

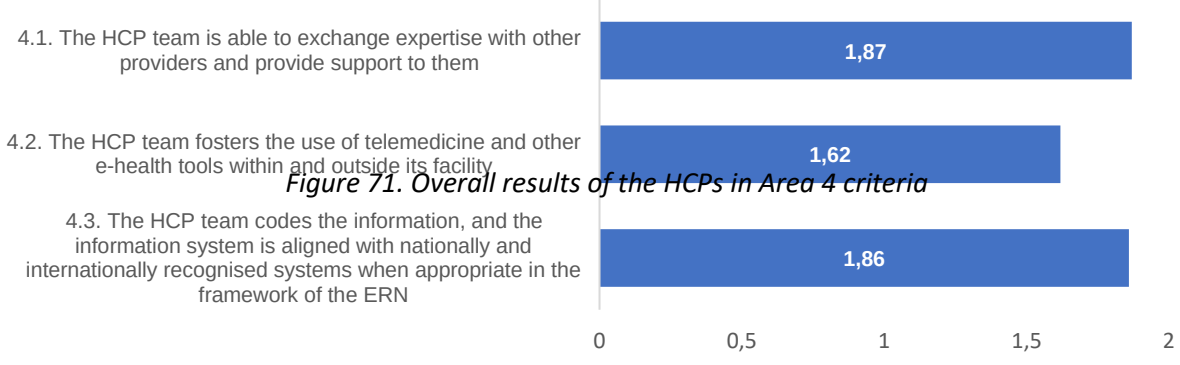
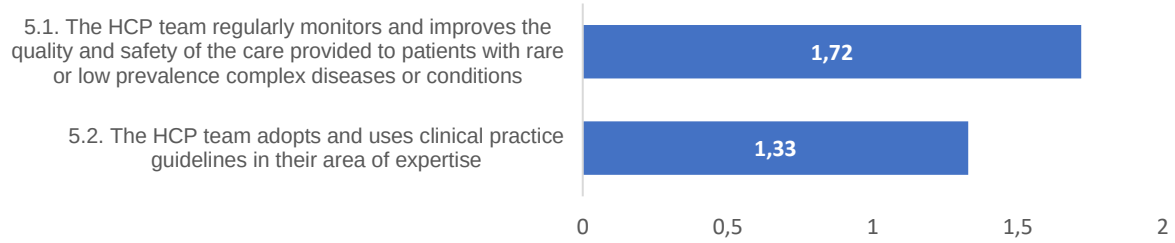


Figure 71. Overall results of the HCPs in Area 4 criteria

Figure 72. Overall results of the HCPs in Area 5 criteria



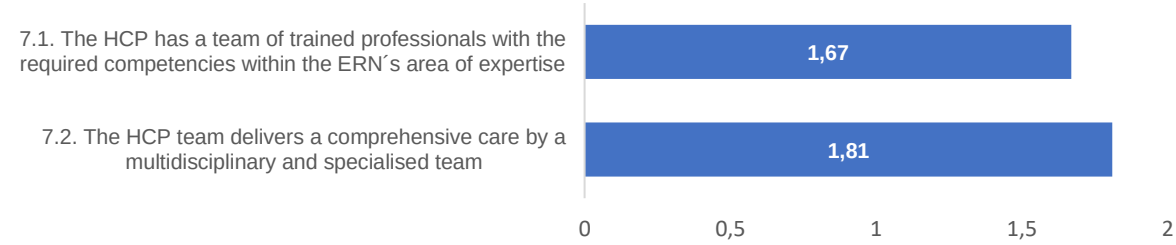
Area 5. Quality and Safety

Figure 73. Overall results of the HCPs in Area 6 criteria

Area 6. Competence, Experience and Outcomes of care

Figure 74. Overall results of the HCPs in Area 7 criteria

Area 7: Human resources



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ISBN 978-92-95239-24-1