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PEDROSO**

**Redes de Investigação Clínica na Europa**

**Clinical Research Networks in Europe**



**Universidade de Aveiro** Secção Autónoma das Ciências da  
2014 Saúde

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Dissertação apresentada à Universidade de Aveiro para cumprimento dos requisitos necessários à obtenção do grau de Mestre em Biomedicina Farmacêutica, realizado sob a orientação científica do Professor Doutor Bruno Gago, Professor Auxiliar Convidado da Secção Autónoma de Ciências da Saúde da Universidade de Aveiro.



Dedico este trabalho  
ao meu avô Arnaut Pedroso  
e ao meu tio Manuel Rodrigues de Matos



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**Palavras-chave** Investigação clínica, Redes de investigação clínica

**resumo** O tema da tese são as redes de investigação clínica Europeias e o seu impacto na investigação clínica e no desenvolvimento de novos medicamentos e terapias.

A tese apresenta o produto final de uma recolha exaustiva de informação sobre redes de investigação clínica existentes na Europa de forma a caracterizar o perfil atual destas redes na Europa. É também avaliado o seu impacto através da descrição das principais atividades dessas redes. Finalmente assinalam-se iniciativas que poderão potenciar a contribuição destas redes para uma investigação clínica mais efetiva na Europa.

A pesquisa foi realizada através da Internet entre dezembro de 2013 e maio de 2014, uma vez que um website é uma ferramenta essencial para o funcionamento de organizações desta natureza. Assim, partiu-se da premissa de que o número de websites de redes de investigação clínica existentes na Internet corresponde ao número de redes de investigação clínica efetivamente existente.

Não foi identificada nenhuma fonte que reunisse informação ou listagens referentes a redes de investigação clínica na Europa. Verificou-se ainda a existência de bastante informação na Internet, mas que esta se encontra dispersa de um modo aleatório na Internet e na maioria dos websites a informação não está muito trabalhada, o que incrementou o desafio desta recolha.

Uma vez que pesquisa se focou na região da Europa, o ponto de partida desta pesquisa foi o website da Agência Europeia do Medicamento, EMA.

Nesta tese apresentam-se os critérios definidos para a classificação de redes de investigação clínica, bem como os dados recolhidos sistematicamente de cada uma das redes. É feita ainda uma caracterização descritiva do conjunto das redes europeias de investigação clínica, a partir da qual se parte para uma discussão dos pontos fortes e pontos fracos. Finalmente, são apresentadas conclusões, perspetivas para o futuro e potenciais formas de otimizar/ maximizar a performance das redes europeias de investigação clínica.



**Keywords**

Clinical research, Clinical research networks

**Abstract**

The theme of the thesis is the European clinical research networks and their impact on clinical research and on the development of new drugs and therapies.

This report presents the final product of an exhaustive search about clinical research networks in Europe in order to characterize the profile of these networks in this region. It is also assessed its impact by describing the main relevant activities of these organisations. Finally, a few initiatives that may increase the contribution of these networks for a more effective clinical research are suggested.

The search was performed in the Internet between december 2013 and may 2014, as websites are an essential tool for organizations of this nature. Therefore, it was assumed that the number of websites of clinical research networks corresponds to the number of clinical research networks that exists effectively.

It was not identified any source that gathered information or that listed clinical research networks in Europe. It was also verified that there are much information in the Internet, but information is dispersed and in the majority of the websites the information is not very well processed, which increases the challenge of this search.

This search was focused in Europe, thus the starting point of the search was the website of the European Medicines Agency, EMA.

The thesis presents the criteria that were defined to classify the organizations as clinical research networks and the data collected from each identified clinical research network. It is also done a descriptive characterization of the clinical research networks to assess the strengths and weaknesses. Finally, conclusions, suggestions for the future and strategies to optimize/ maximize the performance of the clinical research networks are presented.



**Networking requires know-how and expertise, but also team spirit, team players, shared goals, natural trust and confidence.(1)**

**E. Napoleone**







## Abbreviation List

ACORRN	Academic Clinical Oncology and Radiobiology Research Network
AGMT	Study Group of Medical Tumor Therapy - Arbeitsgemeinschaft medikamentöse Tumorthherapie
AIDS	Acquired immunodeficiency syndrome
APS ACTION	AntiPhospholipid Syndrome Alliance for Clinical Trials and International Networking
ATCRIN	Austrian Clinical Research Infrastructure Network
BPDN	Belgian Pediatric Drug Network - Belgian Pediatric Clinical Trial Network
BIG	Breast International Group
CESAR	Central European Society for Anticancer Drug Research
CICPed	Paediatric Network of Clinical Investigators Centre
CIRM	Consorzio Italiano per la Ricerca in Medicina
CRP-Santé	Centre de Recherche Public de la Santé
CZECRIN	Czech Clinical Research Infrastructures Network
DCLLSG	Deutsche Chronic Lymphocytic Leukemia Study Group
DCRIN	Danish Clinical Research Infrastructures Network
EBIC	European Brain Injury Consortium
EBMT	European Group for Blood and Marrow Transplantation
EC	European Commission
ECFS-CTN	European Cystic Fibrosis Clinical Trial Network
ECRIN	European Clinical Research Infrastructures Network
EFPIA	European Federation of Pharmaceutical Industries and Associations
EMA	European Medicines Agency
Enpr-EMA	European Network of Paediatric Research at the European Medicines Agency.
ENSAT	European Network for the Study of Adrenal Tumours
EORTC	European Organisation for Research and Treatment of Cancer
EPOC	European Paediatric Oncology Off-patent Medicines Consortium
EpSSG	European Paediatric Soft Tissue Sarcoma Study Group
ESA CTN	European Society of Anaesthesiology Clinical Trial Network
ESN	European Stroke Network
ETOP	European Thoracic Oncology Platform
EU	European Union
EUNETHYDIS	European Network for Hyperkinetic Disorders
EuroHYP	European Stroke Research Network for Hypothermia
EuroNeoNet	European Neonatal Network
EURONICH	European Network for Intracerebral Haemorrhage

EVICR.net	European Vision Institute Clinical Research Network
EWOG-MDS	European Working Group on Myelodysplastic Syndromes
FCRIN	French Clinical Research Infrastructure Network
FIMP-MCRN	Family Paediatricians Medicines for Children Research Network
FINPEDMED	Finnish Investigators Network of Paediatric Medicines
Futurenest	Futurenest Paediatric Network
GA <sup>2</sup> LEN	Global Allergy and Asthma European Network
GCP	Good Clinical Practices
GECA	Groupe Européen de Chimiothérapie Anticancéreuse
GECP	Grupo Espanol de Cancer de Pulmón
GHSG	German Hodgkin Study Group
GNN	German Neonatal Network
HECRIN	Hungarian European Clinical Research Infrastructure Network
HOVON	Haemato Oncology Foundation for Adults in the Netherlands
HS	Histiocyte Society
IBCSG	International Breast Cancer Study Group
I-BFM-SG	International Berlin/ Frankfurt/ Munsten (BFM) Study Group
ICRIN	Irish Clinical Research Infrastructure Network
IDCT	Investigator Driven Clinical Trial
IELSG	International Extranodal Lymphoma Study Group
IMI	The Innovative Medicines Initiative
INRO / IGEH	International Neurotrauma Research Organization
	Internationale Gesellschaft zur Erforschung von Hirntraumata
IPCRN	Irish Paediatric Clinical Research Network
IRCI	International Rare Cancers Initiative
ItaCRIN	Italian Clinical Research Infrastructure Network
ITCC	Innovative Therapies for Children with Cancer
KKS-Network	Network of the Coordinating Centres for Clinical Trials
MCRN	Medicines for Children Research Network (NL)
MS	Member State
N-CCLG	Newcastle Children's Cancer & Leukaemia Group (CCLG) Pharmacology
NCI	National Cancer Institute
NFU	Dutch Federation of University Medical Centers
NICRN	Northern Ireland Clinical Research Network
NIHR-CRN	National Institute for Health Research Clinical Research Network
NISCHR CRC	National Institute for Social Care and Health Research Clinical Research Centre
NNI	Network Neonatale Italiano

NORCRIN	Norwegian Clinical Research Network
NRS	National Health Service Research Scotland
PEDDCReN	Paediatric European Digestive Diseases Clinical Research Network
PENTA-ID	Paediatric European Network for the treatment of AIDS and infectious diseases
PIGS	Pediatric Infectious Disease Group of Switzerland
POLCRIN	Polish Clinical Research Infrastructures Network
PREDIMED	Prevención con Dieta Mediterránea
PREPARE	Platform for European Preparedness Against (Re-)emerging Epidemics
PRINTO	Pediatric Rheumatology International Trials Organisation
PtCRIN	Portuguese Clinical Research Infrastructure Network
R&D	Research and Development
Red SAMID	Red de Investigación en Salud Materno-Infantil y del Desarrollo
REEM	Red Española de Esclerosis Múltiple
RIC	Red de Investigación Cardiovascular
RICET	Red de Investigación Cooperativa en Enfermedades Tropicales
RIPPS	Réseau d'Investigations Pédiatriques des Produits de Santé
ROCRIN	Romanian Clinical Research Infrastructure Network
RTICCC	Red Temática de Investigación Cooperativa de Centros de Cáncer
SAKK	Swiss Group for Clinical Cancer Research
SCTO	Swiss Clinical Trial Organisation
SIOPEL	Childhood Liver Tumours Strategy Group
SIOPEN-R-NET	International Society of Paediatric Oncology European Neuroblastoma Research Network
SIOP-RTSG	International Society of Paediatric Oncology Renal Tumour Study Group
SKIC	Network of Excellence for Research in Paediatric Critical Care
SPOG	Swiss Group for Clinical Cancer Research
SweCRIN	Swedish Clinical Research Infrastructure Network
SwissPedNet	Swiss Research Network of Clinical Paediatric
TARN	The Trauma Audit & Research Network
UK	United Kingdom
UKCRN	United Kingdom Clinical Research Network
UKPVG	United Kingdom Paediatric Vaccine Group
USA	United States of America
WHO	World Health Organisation

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# 1. Introduction

## 1.1. *General Introduction*

This report was written as part of the Master's degree in Pharmaceutical Medicine and it presents the information about the search of the existing European clinical research networks that was performed between december 2013 and may 2014.

The document is composed by 4 main sections: Introduction, Methodology, Results and Discussion and Conclusion.

The first section, Introduction, is divided into two main parts: 1) a brief status of clinical research in Europe and 2) networking in clinical research. In the first part it is described the aim of clinical research, the European clinical research landscape, the integration of the European clinical research in the world context, the economic impact of clinical research and finally the challenges of clinical research. In the second part it is described the definition and objectives of networking in clinical research, the history of the first clinical research network, the EORTC, and finally the rationale of this thesis.

Section 2, Methodology, describes how the search was conducted by presenting the main steps performed to do the search of the European clinical research networks and the criteria that were defined to classify an organisation as a clinical research network.

Afterwards, Section 3, Results and Discussion, presents the results of the search and the corresponding discussion.

Finally, Section 4, Conclusion, presents the main conclusions about the search and about the results obtained. It is also mentioned in this final section, actions to maximize the contribution of the European clinical research networks to the clinical research and to the development of new drugs and therapies.

## **1.2. Brief Status of clinical research in Europe – the maze**

### **1.2.1. The aim of clinical research**

Biomedical research is divided into basic, clinical and translational research. Basic research is a systematic study directed toward greater knowledge or understanding of the fundamental aspects of phenomena. Translational research was created to accelerate the transfer of knowledge from basic to clinical research (2). Clinical research plays an important role in understanding better the diseases, in the development of new health products (preventive, diagnostic and therapeutic) and in the optimisation of medical strategies as it produces evidence-based practice and healthcare cost containment. Thus, the main goal of clinical research is to obtain treatment, prevention and diagnosis of diseases. To succeed in clinical research it is necessary an easy access to patients and to overcome the fragmentation of the different national health and legislative systems and the difficulties of obtaining funding (especially for academic studies)(3). Appropriate funding and best practice for medical research are key factors to improve healthcare and also economy (2).

### **1.2.2. European clinical research landscape**

Clinical research has had a great impact on society. In the last 40 years, infant mortality has decreased significantly. In terms of adults, new medicines have revolutionised the treatment of many diseases such as, heart attacks, high blood pressure and acquired immunodeficiency syndrome (AIDS). Many fatal diseases are no longer life-threatening due to advances in medicine. In fact, death rates in Europe have fallen for all main causes of death (2).

Still, Europe is facing the grand challenges such as global warming; tightening supplies of energy, water and food; ageing societies; unequal public health; allergy and chronic diseases; cancer and cardiac diseases; pandemics and security that are changing the disease patterns and increasing the need of more medical

research (4). To address all these challenges, clinical research has to be prepared and well-organised. Therefore, a strong scientific environment and good quality research infrastructures are essential. Researchers' mobility, partnerships and motivation are key points in this environment (2).

The positive point is that medicine is advancing rapidly. For example, genome sequencing is almost a routine that can be useful in supporting individual treatment as many genetic variations have been related to an increased risk of disease (e.g. heart diseases, stroke, diabetes, dementia and cancer). Stem cell technology is also advancing and it is being used to replace damaged cells and tissues. Further, innovation in information technology is producing powerful new imaging, diagnostic techniques and almost infinitive data store. For example, storage of data was until recently measured in terabytes and now it is measured in tens of petabytes and it will definitely increase a further million-fold by 2020 (2). At the same time, medical research is turning into a demanding multidisciplinary area due to the improved computational power, the increased results in disciplines of the basic science such as human genomics (5).

It should also be highlighted that the study of the social, economic and environmental factors that influence health is as important as the genetic and biologic factors. For example, it is widely accepted that a poor diet, tobacco, alcohol and lack of physical exercise may have a negative impact in health. To improve lifestyles and habits it is needed the engagement and good coordination among all stakeholders of the society (2).

Europe has a variety of world-leading researchers, higher education institutions, public research organisations, public universities and public university hospitals with excellent and recognised health professionals. European countries have also well organised and well equipped healthcare systems widely accessed by the population and a great number of university hospitals with high level of healthcare. Finally, history has proved that Europe is able to face complex challenges (2). Nevertheless, the variety of national clinical research strategies may be a

weakness. Moreover, 84% of the public funding in Europe is concentrated in a few countries. Therefore, European clinical research is considered heterogeneous and disparate. Europe has a number of major clusters that are strong, competitive, visible and attractive. Thus, Europe should align all its potential(2).

Another negative aspect is the fact that the mobility of researchers and ideas are limited by the different national regulatory frameworks, by the lack of harmonisation policies that leads to different ways of implementing the European Union (EU) Directives and by the gaps in the legislation (2). An exception is the case of Sweden, Norway and Denmark that are independent countries that have similar legislation that facilitates collaboration among them. Clinical research network can improve the efficiency of the clinical research by creating communication between the different institutions and planning strategies for clinical research development (4).

To fight against the limiting factors in Europe, large research infrastructures are another way of increasing European competitiveness in clinical research as they create scientific communities across Europe. These communities facilitate the researchers' mobility and training (2).

In fact, the Member States (MS) of the European Union share the same European Directives to elaborate their national laws. Nevertheless, due to the different interpretations, a complete harmonization among the MS is never achieved, turning the conduct of multinational clinical trials into a complex mission for the pharmaceutical industry and academy (6).

The *"Eurocan plus report"*, a feasibility study for coordination of national cancer research activities in Europe, can be extrapolated for European clinical research in general. This report concluded that fragmentation and lack of sustainability are the two main challenges that clinical research faces in Europe. This fragmentation leads to duplication of clinical research work that consequently leads to avoidable waste of time and money that could be used in other projects. There is also lack of



communication between the stakeholders, namely, funders and researchers. Other relevant disadvantages identified in Europe are:

- 1) the shortage of leadership;
- 2) the fact that each institution has its own agenda lacking a global vision;
- 3) lack of functional contact between academy and industry;
- 4) inadequate training and non-existent career paths;
- 5) low personnel mobility in research;
- 6) lack of functional translational research continuum process;
- 7) lack of epidemiological research integrated with clinical research;
- 8) lack of functional information flow;
- 9) lack of efficient funding (e.g. difficulty in obtaining long-term financing, grants are usually slow to be obtained)
- 10) lack of efficient networking (7).

It should also be noticed that society is not involved as much as advisable in the clinical research issues. Many people consider that patients are not considered in the centre of clinical research. Moreover, it is not only the interpretation of the European Directives that differs from Member State to Member State. In fact, Europe is not a homogenous area; the different countries have different cultures, habits and legislations. Further, there is not a common plan in clinical research neither harmonisation in what concerns approvals, evaluation, assessment, education and training. Europe also lacks clinical research career tracks, mobility for investigators and a common educational programme. It should be highlighted that medical research has never been considered as important as it is nowadays, playing a key role in health of society. Further, the unmet medical needs are creating new complex challenges and new paradigms such as personalized medicine. The economic models of the pharmaceutical industry are also shifting and the first large scale initiatives of partnerships between academia and industry are showing relevant results. Finally, Europe has to learn how to take advantage of its diversity (2).

It is a fact that Europe has excellent basic, clinical and innovative etiological research that should be better explored. While, Phase III clinical trials are migrating to Asia, clinical trials of Phase I and Phase II remain in Europe due to the unique expertise. This region also detains important and unique biobanking resources (7).

The European Science Foundation in a report on the European Biomedical Research, White Paper II, gives 5 main recommendations regarding the future of the European biomedical research, as follows:

- 1 - "Citizens and patients should be closely engaged with biomedical research."
- 2 - "The results of biomedical research should be rapidly and efficiently brought to the patient."
- 3 - "Biomedical research should be conducted with high quality in an open, honest and transparent way."
- 4 - "European biomedical research should be conducted within a global context."
- 5 - "Investment should be increased to create the right world-class biomedical research. (2)"

### **1.2.3. Clinical research: Europe versus the rest of the World**

As previously mentioned, Europe is widely known of being an "*excellence in science*". The European investigators and the health universities are worldwide recognised (2). Biomedical research generates about half of the European scientific publications. At the moment the United States of America (USA) have higher funding than Europe does (funding in Europe is about half of the USA funding (2), being consequently the clinical research output lower in Europe than in the USA. Since the 1990, USA has replaced Europe in the top of the developers of medicines (2). Nevertheless, the number of publications in Europe is greater than in the USA (2). Thus, it can be concluded that Europe presents a very efficient biomedical research with a strong and large health industry in spite of a lower funding than in the USA (2).

In terms of publishing, USA and EU together produce almost 2 thirds of the world publishing. This world share tends to decrease due the emerging countries such as Brazil, China and India (2).

In fact, geopolitical is changing as new powerful economies are growing (e.g., China, India and Brazil). Many of the scientists of these countries are studying in the USA what contributes to the creation of stronger links with the USA rather than with Europe (2).

To summarize, the major threats to European clinical research are the USA that has greater funding than Europe and the emerging countries such as India, China, Brazil. This can cause a loss of attractiveness and leadership of Europe in the industry perspective. Consequently, there is the threat of potential increase of the European healthcare costs. Therefore, Europe has to create a single science policy involving all stakeholders, society, academia and industry (small and large enterprises) to be able to influence the global healthcare to improve the quality of life of the European and world citizens (2).

Although globalisation increases competition, as it was previously described, at the same time it opens great opportunities for international partnerships. Global collaboration is becoming fundamental to overcome the great challenges (2).

#### ***1.2.4. The economic impact of clinical research***

Clinical research presents a positive economic return due to the health gains and commercial gains. To assess the economic impact of medical research it is necessary a complex calculation with limitations due to the assumptions that are needed. Therefore, the studies are scarce. A study in the USA concluded that investment on medical research returns many times over in social benefits. Nevertheless, Europe has a different reality and results cannot be extrapolated. The existing European studies do not have an adequate approach of the issue of economic research. The results of the investment on medical research should be considered essential to choose the best strategies for the future of medical

research (5). Therefore, the economic impact of clinical research in Europe should be assessed. Clinical research networks may help in this area, as they can gather data from the different member institutions.

### **1.2.5. Clinical research global challenges**

Despite the increase of investment in Research & Development (R&D), the productivity of the big pharmaceutical companies is decreasing and a significant number of patents is expiring. At the same time, the biotech companies that are creating new drugs have difficulties in obtaining partners for funding due to the high cost and high risk of R&D.

One of the challenges of clinical research is the translation of the biomedical discoveries into new drugs and therapies. Moreover, regulatory authorities are changing the approaches to assess benefit-risk profiles and patients are willing to be part of the stakeholders in the healthcare sector.

Further, the present crisis imposes the cut of investments, increasing the challenge of obtaining new drugs.

All the described challenges that clinical research is facing influence directly the pharmaceutical industry. The major challenges of the industry are:

- Complexity and quantity of data are increasing;
- There is a move towards the 4P medicine: personalised, predictive, preventative and participatory;
- The number of market approvals are decreasing and R&D costs continue to increase;
- The emergence of the generic medicines;
- The need to enhance anticipation and minimisation of risk within the industry;

These challenges pushed the industry to establish relationships with academy, biotechs, small and medium enterprises and even with multinational companies. Pharmacy industry understands that in-house research is not enough for the success (2).

In fact, collaborations between industry, academia, regulatory authorities and patients' organisations are seen more and more the key factor for the success of obtaining new drugs. One significant example in Europe is The Innovative Medicines Initiative (IMI) that is a European public-private partnership between the European Commission (EC) and the European Federation of Pharmaceutical Industries and Associations (EFPIA) that started in 2008 to improve the competitiveness of the pharmaceutical industry in Europe. It has 46 projects on-going with a budget of €2 billion between 2008 and 2013 and a budget of €3.3 billion between 2014 and 2024 (8, 9). Although this type of initiatives is more than welcome, it is also essential that these initiatives are not limited in time to avoid the fragmentation by projects. Well established networks are a fruitful option as know-how and data is accumulated from project to project.

Another weakness in Europe is the low number of academic studies and multinational academic studies. In fact, less than 10% of the Investigator Driven Clinical Trials (IDCT) are multinational, whereas in the case of the commercial clinical trials, about 50% are multinational. IDCT are clinical trials whose sponsors are academic researchers and, like in the industry-driven clinical trials, the aim is to obtain scientific knowledge and evidence about a drug, therapy or about the disease. Usually these studies have not commercial interest. Some examples are: proof of concept studies, studies on orphan diseases, comparison of diagnostics or therapeutic interventions, surgical therapies or novel indications for registered drugs. IDCT have an important role in terms of patient-oriented clinical research, being the basis for continually improving patient care. In a conference organized by the European Science Foundation in 2008 while discussing the reasons for the reduced number of IDCT in Europe, a vast number of recommendations were produced, such as:

1. Scientists who participate in IDCTs should have access to better education, training, career structure and opportunities;
2. Funding for IDCT should be increased;
3. Regulation of IDCT should have a specific "risk-based" approach;

4. The procedures for obtaining authorization for IDCT should be streamlined;
5. It should be ensured that IDCT have the adequate number of subjects to obtain statistically reliable results;
6. IDCT are an advantage for the society that will have access to improved patient care and also for the industry with the transfer of scientific innovation from the laboratory to the bedside.

Efficient IDCT demand specialised competences and advanced infrastructure. They are performed in academic medical centres and university hospitals. Nevertheless, data management, quality assurance, monitoring, regulatory affairs are lacking in Europe for this type of trials (10). This is one of the challenges that clinical research networks are able to respond.

In fact, to invert this trend of the low number of multinational IDCT, national networks were developed in most of the MS to increase the number of multicentre clinical trials and create common procedures for submission and conduction of the clinical trials, focusing in IDCT. The European Clinical Research Infrastructures Network (ECRIN) was created in 2004, it was funded by the FP6 Health and it is a net of national networks. This network aims to overcome the fragmentation of health and legislative system in Europe by providing information, consulting, coordination, management and other services to investigators and sponsors in the preparation and conduct of multinational clinical trials with focus in IDCT. The final goal is to create a common pan-European culture among clinical research professionals by implementing common training and communication and also by creating common procedures and standards for investigation in the different areas (11).

### ***Key message***

Although clinical research has had a great impact on drug development and consequently on the health of the European society, clinical research has never faced such a tremendous number of challenges. The most relevant are:

- 1) high number of unmet medical needs;
- 2) massive volume of information being produced everyday;
- 3) demanding of multidisciplinary in clinical research;

- 4) heterogeneous environment of clinical research due to different regulatory frameworks and different cultures from country to country;
- 5) high costs of clinical research;
- 6) reduced productivity of the pharmaceutical industry.

If efforts of the different stakeholders in clinical research are aligned, the probability of success increases exponentially. Clinical research networks can be a useful tool to align the different stakeholders and create a common strategy to optimize the productivity of the each element.

### **1.3. Networking in clinical research**

#### **1.3.1 Definition and objectives**

The definition of *networking* is: a supportive system of sharing information and services among individuals and groups that have a common interest. (12).

Clinical research networks fit exactly in this definition as they are formed by independent groups with independent management that share a common interest in clinical research and that are aware that gathering expertise, know-how and efforts of the different members will certainly bring better and faster outcomes. It is now fully accepted that collaboration among individual research groups is no longer the solution and that solid and permanent partnerships are proving to be the key factor to achieve success.

With the exponential growth of the scientific and technical discoveries, clinical research is getting more complex and is demanding expertise from many different fields. For instance, the discoveries in the field of genetics, epigenetics and genomics changed the approaches to cancer risk identification and management, cancer diagnosis, prognostic evaluation and therapies (13). In most of the cases it is not possible to gather in one single institution the know-how of all the involved fields of a research project, hence, networking can make the difference between failure and success.

Medical Societies were the first networks of the biomedical history. These academies or learned scientific societies are member organisations for physicians and researchers and are specialised in certain fields or disciplines. In most of the cases there are national societies and European-wide scientific societies. The latter usually have an English language peer review journal.

We have been assisting to a shift in science from an individual-based model to a teamwork model. This is explained by the huge amount of data that is now possible to produce and to store due to the innovation in technology and it is also explained by the need of having multidisciplinary teams to face the high demanding of science. Moreover, sharing knowledge, techniques, equipment and ideas, pooling data and research resources are some of the advantages of networking that can lead to successful results more rapidly and with more quality. Nevertheless, among networks there might be miscommunication, difficulties with the coordination of meetings, travel expenses and disagreements in the main goals of research. The increase of costs should also be taken into account (14).

In fact, there are a significant number of good reasons to have a networking approach in clinical research:

- To contribute to the translational research from the lab to the bed of the patient and vice versa. (15, 16)
- To decrease the gap between basic and clinical research and the gap between clinical research and implementation in real life.
- To facilitate clinical research between academy and industry. (15, 17, 18)
- To increase the collaboration between the elements of the network. (19, 20)
- To develop multidisciplinary research partnership. (19)
- To promote the collaboration between centres to guarantee infrastructure support, critical mass of expertise and resources such as patients and data.
- To stimulate the creation of new networks. (19)
- To promote high quality research, focusing on multicentre activities and randomized clinical trials. (15-17, 21)



- To study rare diseases, as recruitment can be facilitated. (16)
- To ensure the training in clinical research, trial methodology, Good Clinical Practices and Good Laboratory Practices of the health professionals such as, medicines, pharmacists and nurses. (15, 18, 19, 22)
- To promote education and training in specific areas of medicine, such as vaccinology. (20, 22)
- To support the patients, their families and patient organisations by informing them about clinical research during their participation in clinical research. (15)
- To be a source of information and expertise for health professionals and researchers. (18, 19, 22)
- To create a forum of scientific discussion. (19)
- To create scientific and operational quality standards and to create guidelines and templates to harmonise operational models. (18, 19, 22)
- To avoid duplication of clinical trials or other studies. (19)
- To raise awareness on the need for clinical trials that the industry is not interested, such as off-patent medicines and observational studies on natural history of diseases. (19)
- To contribute to the compliance of GCP and advocate for ethical research. (19)
- To facilitate clinical trials among different countries and to facilitate recruitment. (19)
- To promote communication and information exchange between institutions. (20)
- To activate cooperative projects for biological research. (16)
- To support the study conduct in the sites that are part of the network. (22)
- To increase scientific competitiveness. (23)
- Optimize scientific potential and expertise. (23)
- To increase recruitment and speed up recruitment that impact in the statistical power, duration of the trials, publications and also in the innovation for the patients. (23)
- To attract industry. (23)

- To increase solid partnerships with the rest of the world. (23)

As previously mentioned, networks can give an effective contribute to Europe to(11):

- Play a leader role in major research and innovation challenges.
- Develop new healthcare models (personalized and stratified medicine).
- Address health challenges (rare diseases, ageing, health technology)
- Translate clinical research into clinical practice.
- Achieve health cost containment.
- Promote evidence-based medical practice and enhance health
- Reduce health inequalities in Europe and ensure equal access to healthcare.

### **1.3.2. EORTC – the first clinical research network**

The European Organisation for Research and Treatment of Cancer (EORTC) is the oldest and the best example of success of networking in clinical research. It is a unique association that conducts multinational clinical trials of all types of cancer. It is not possible to write about clinical research networking without referring to EORTC.

The goal of EORTC is to develop, conduct and motivate translational and clinical research in Europe to improve the health care of patients with cancer by improving the standard of cancer treatment. Extensive and comprehensive research is usually not possible by individual hospitals and can be best accomplished through the multidisciplinary multinational contributions of basic scientists and clinicians.

EORTC was created in 1968 from the Groupe Européen de Chimiothérapie Anticancéreuse (GECA) that had been founded by Prof. Henri Tagnon in 1962. By that time that group of experts were already aware of the relevance of a multidisciplinary approach and international collaboration in clinical research in Europe.

The EORTC Network associates more than 300 hospitals in more than 30 countries that includes about 2500 elements from the different disciplines needed for cancer research. The EORTC headquarters are located in Brussels, Belgium. Between 2000 and 2011, 71905 patients participated in clinical trials of EORTC, being about 90% of them from the European Union.

The EORTC has multiple sources of funding such as the European national cancer leagues and the US National Cancer Institute (NCI).

The greatest achievements of EORTC are that the clinical trials performed within the EORTC framework have led to increased survival rates for childhood cancers, Hodgkin's disease and leukaemia, melanoma, breast, uterine, prostate, testicular and bladder cancers, lung and larynx cancers and other rare tumours (brain and sarcoma). (24)

### **1.3.3. Rationale**

Considering that:

- Clinical research is facing a significant number of challenges and networking can be a key strategy to increase productivity in clinical research.
- Networking has multiple advantages such as flexibility, convenient ways to share resources, lower costs, less administrative burden and easiness in gathering multidisciplinary teams.
- Clinical research network can provide centralised resource and adequate access to patient populations for the execution of clinical trials. This is important to obtain adequately powered clinical trials, to facilitate the development drugs for orphan diseases and to enhance the medical science of the sites.
- Well identified clinical research networks can lead to new projects among the stakeholders: industry, academy, regulatory authorities and society.
- It seems that the number of clinical research networks has been increasing significantly in the last 2 decades.
- There is not any systematic investigation about the existing clinical research networks in Europe, neither a list of the networks.

This project aims:

- 1) to gather a full list of the existing clinical research networks working in Europe;
- 2) to characterise the profile of the existing European clinical research networks;
- 3) to sort out possible actions to maximize the benefits that clinical research can take from the clinical research networks.

## **2. Methodology**

### ***2.1. Search of clinical research networks***

In a preliminary stage, it was conducted a search to assess whether there was already any project, thesis, document or website with systematic information about European clinical research networks. It was not identified any source with information regarding clinical research networks in Europe. Further, from this preliminary search, it was verified that the information about clinical research networks is almost found exclusively in the websites of the clinical research networks.

The search of information about the existing European clinical research networks was performed between december 2013 and may 2014. Search was done using the Internet, as websites were considered an essential tool to such a type of organisation as a network. Therefore, search was done with the assumption that the number of websites of clinical research networks corresponds to the effective number of the existing clinical research networks.

The steps of the search in the Internet were done as follows:

- 1) As search was focused in the European region, the starting point of this search was the website of the European Medicines Agency (EMA). The website was carefully reviewed to identify all the names of clinical research networks. All the networks that were identified in the website of EMA were verified in the search engine of Google to obtain their websites' links.
- 2) Each website of a potential clinical research network was carefully reviewed and relevant information was collected.
- 3) Further, in each website of a potential clinical research network that was reviewed to collect data, it was kept in mind to check if there was any reference or link to another clinical research network. This step was very fruitful, as it led to the identification of a significant number of other clinical research networks and step 2 was repeated to these new networks.

- 4) In order to identify as many clinical research networks as possible, the websites of European medical societies were reviewed to check if clinical research networks were mentioned in their websites and also to check if the medical societies had any production of clinical research. To make sure that as many medical societies websites as possible were reviewed, it was used the search engine of Google writing “society” and the various disciplines of medicine. In each website of the medical society, sections such as: “Clinical Research”, “Publications” and “Links” were carefully verified.
- 5) Other searches were done in the search engine of Google, using key words such as: “clinical research”, “network”, “networking“, “investigator driven clinical trials”, etc. This search was not successful.
- 6) Finally the website of the World Health Organization was carefully verified to identify any clinical research networks. No positive results were obtained.

As the type, quantity and complexity of information released by each website differ widely from network to network due to the different policies, it was defined a set of parameters to organise the collection of data in each website:

- Name of the clinical research network;
- Acronym of the clinical research network;
- Brief description of the clinical research network with the main goals;
- National/international clinical research networks;
- Number of members;
- Relevant activities;
- Website address;
- Country;
- Year of establishment;
- Nature: private/public;
- Target disease.

## **2.2. Criteria for the classification of clinical research network**

One of the great challenges of this search was how to decide whether an organisation could be considered a clinical research network or not. Therefore, it was essential to establish since the beginning of the search a set of criteria to assess whether each organisation could be considered as a clinical research network.

The criteria used are as follows:

- Headquarters in Europe or networks with headquarters outside Europe but with European members (search was limited to the European region);
- Organisation with associated members (to validate the network definition);
- Organisation with projects with undetermined time (to ensure that consortiums and single projects were not included in the search);
- Evidence of production of clinical research by presenting the number of clinical trials and/or publications (to ensure that it is a network of clinical research).





### 3. Results and discussion

#### 3.1. Results

Eighty-eight clinical research networks were identified in the Internet between december 2013 and may 2014. The identified clinical research networks are listed in Table 2. Table 2 presents the name, acronym, brief description, country and year of establishment of the networks.

Almost all European countries have clinical research networks: Austria, Belgium, Czech Republic, Denmark, Finland, France, Germany, Hungary, Ireland, Italy, Luxembourg, the Netherlands, Northern Ireland, Poland, Portugal, Romania, Scotland, Spain, Switzerland, the United Kingdom and Wales. The UK is the country with the highest number of clinical research networks, 11 networks, followed by Germany with 10 networks. Spain and Switzerland have 8 networks, Belgium and Italy have 7 networks and Austria, France, and the Netherlands have 5 networks. Hungary, Ireland, Poland, Portugal, Scotland and the USA have 2 networks. Finally, Czech Republic, Denmark, Finland, Ireland, Luxemburg, Northern Ireland, Norway, Romania, Sweden and Wales have 1 network.

Clinical research networks were established between 1962 and 2014. The oldest one is the EORTC and the newest one is under construction at the moment, and it is the International Society of Paediatric Oncology European Neuroblastoma Research Network (SIOPEN-R-NET). The number of new clinical research networks established per decade is presented in Table 1.

**Table 1** – Number of new clinical research networks per decade.

<b>Decade</b>	<b>Number of networks</b>
Before the 1980s	4
1980s	5
1990s	10
2000s	42
Between 2010 and 2014	15
Date of establishment not available	12

**Table 2** – List of the European Clinical Networks: name, acronym, brief description, country and year of establishment.

Line	Name	Acronym	Brief description	Country	Year
1	Academic Clinical Oncology and Radiobiology Research Network (25, 26)	ACORRN	The network aims to bring together all disciplines needed for radiotherapy and to support radiotherapy research, dissemination and implementation.	UK	2005
2	AntiPhospholipid Syndrome Alliance for Clinical Trials and International Networking (27)	APS ACTION	The aim of the network is to design and conduct well-designed, large-scale, multicentre clinical trials in persistently antiphospholipid antibody (aPL)-positive patients.	USA	2010
3	Austrian Clinical Research Infrastructure Network (28)	ATCRIN	The network aims to provide support to biomedical research by facilitating non-commercial multinational trials with clinical sites in Austria. The network also provides training.	Austria	2007
4	Belgian Pediatric Drug Network - Belgian Pediatric Clinical Trial Network (29)	BPDN	The aim of the network is to place child health, rights and interest as the primary consideration by: enforcing good clinical practice, establishing a network of active units in clinical research and collaborating with other European networks.	Belgium	2005
5	Breast International Group (30)	BIG	The network aims to accelerate breast cancer research by promoting collaboration between its members and other academic networks. This network works independently of the pharmaceutical industry. Collaborative groups based in Europe, Canada, Latin America, Asia and Australia.	Belgium	1999
6	Central European Society for Anticancer Drug Research (31)	CESAR	The network aims to increase the cooperation between academic study groups, individual institutions in Oncology and pharmaceutical industries, fostering translation of basic research into clinical application via integral drug development. CESAR as European Economic Interest Grouping is the umbrella organisation of the registered societies CESAR Germany and CESAR Austria.	Austria	2001
7	Centre de Recherche Public de la Santé (32)	CRP-Santé	The aim of the network is to perform clinical research studies, clinically-oriented biomedical research and public health. These activities will lead to new knowledge in disease mechanisms, epidemiology, diagnostics and treatment of diseases.	Luxembourg	1988

**Table 2** – List of the European Clinical Networks: name, acronym, brief description, country and year of establishment (cont.1).

<b>Line</b>	<b>Name</b>	<b>Acronym</b>	<b>Brief description</b>	<b>Country</b>	<b>Year</b>
8	Childhood Liver Tumours Strategy Group (33)	SIOPEL	The aim of the network is to promote cooperative clinical and basic research in the field of primary childhood liver tumours. The ultimate goal of the study group is to ameliorate the prognosis and the quality of life of children affected by this rare neoplasm.	Poland	1987
9	Czech Clinical Research Infrastructures Network (23)	CZECRIN	The aim of the network is to develop an infrastructure and capacity to facilitate clinical research primarily academic driven.	Czech Republic	2011
10	Consorzio Italiano per la Ricerca in Medicina (34)	CIRM	The aim of the network is to establish partnerships to develop national and European research projects, namely, biologic, medical, non-medical healthcare, socio-economic and biostatistical areas.	Italy	1997
11	Danish Clinical Research Infrastructures Network (28)	DCRIN	The aim of the network is to improve the quality of clinical research at a national and international level by promoting harmonised research procedures, reducing the time with administrative procedures, sharing expertise.	Denmark	2003
12	Deutsche Chronic Lymphocytic Leukemia Study Group (35)	DCLLSG	The aim of the network is to optimize the diagnosis and treatment of chronic lymphocytic leukemia by performing controlled prospective clinical trials.	Germany	1996
13	Dutch Federation of University Medical Centers (36)	NFU	The aim of the network is to ensure that the bodies that decide on health care, education and science in the Netherlands take into account the vision of this network. The network also aims to strengthen the research infrastructure. It is focused on biobanks, translational research and patient-related research.	Netherlands	2004
14	European Brain Injury Consortium (37)	EBIC	The aim of the network is to establish close co-operation between European Neurotrauma Centers and Investigators in the management of Traumatic Brain Injury (TBI) and other types of acute brain damage and to act as an advisory organ in both practical and theoretical issues concerning brain injury studies.	Netherlands	1994

**Table 2** – List of the European Clinical Networks: name, acronym, brief description, country and year of establishment (cont.2).

<b>Line</b>	<b>Name</b>	<b>Acronym</b>	<b>Brief description</b>	<b>Country</b>	<b>Year</b>
15	European Clinical Research Infrastructures Network (23, 38)	ECRIN	Network of national clinical research networks that aims to provide consulting, coordination, management and all the needed services to investigators and sponsors in the conduction of multinational clinical trials. The main target are the academic sponsored clinical trials.	France	2004
16	European Cystic Fibrosis Clinical Trial Network (22)	ECFS-CTN	The aim of the network is to increase the quality and quantity of clinical research in the area of cystic fibrosis and to bring new medicines to the patients as quickly as possible.	Belgium	2009
17	European Group for Blood and Marrow Transplantation (39)	EBMT	The aim of the network is to allow scientists and physicians involved in clinical bone marrow transplantation to share their experience and develop cooperative studies.	UK	1974
18	European Neonatal Network (40)	EuroNeoNet	The network aims to give European neonatologists a tool to perform their own quality assurance and a framework to facilitate the development of high-quality outcome epidemiological research and randomised clinical trials.	Spain	Not available
19	European Network for Hyperkinetic Disorders (41)	EUNETHYDIS	Network of scientists, clinicians, clinical researchers, cardiologists, pharmacologists and neuroscientists dedicated to the study and treatment of children with Attention Deficit Hyperactivity Disorder (ADHD) or Hyperkinesis.	Scotland	1994
20	European Network of Paediatric Research at the European Medicines Agency (19)	Enpr-EMA	The objectives of the network are: to increase collaboration between the existing networks, to build competences to be shared among the networks, to avoid unnecessary studies, to stimulate high quality research, to strengthen the European Research Area to facilitate recruitment and clinical trials' implementation.	UK	2008
21	European Organisation for Research and Treatment of Cancer (24)	EORTC	The aims of the network are to develop, conduct, coordinate translational and clinical research in Europe to improve the treatments of cancer.	Belgium	1962

**Table 2** – List of the European Clinical Networks: name, acronym, brief description, country and year of establishment (cont.3).

<b>Line</b>	<b>Name</b>	<b>Acronym</b>	<b>Brief description</b>	<b>Country</b>	<b>Year</b>
22	European Paediatric Oncology Off-patent Medicines Consortium (42)	EPOC	Network that performs paediatric oncology pharmacology clinical trials.	UK	2009
23	European Paediatric Soft Tissue Sarcoma Study Group (43)	EpSSG	The aim of the network is to promote and manage clinical trials, encourage and facilitate clinical and basic science research, foster optimal standards of care, organise educational meetings for its members and other professionals, and advocate for patients with Soft Tissue Sarcoma.	Italy	Not available
24	European Society of Anaesthesiology Clinical Trial Network (44)	ESA CTN	The aim of the network is to provide an infrastructure for clinical research in the fields of Anaesthesia Pain, Intensive Care and Emergency Medicine by transnational European collaborative studies.	Belgium	2010
25	European Stroke Network (45)	ESN	The aims of the network is to bring together researchers, government, industry and patients group associations to decrease physical, social and economic consequences of strokes on society by developing basic and clinical research. The network has the ESN Clinical Trial Platform that is composed of stroke centres and that also supports the design of Phase I and II studies and deals with the ethical and regulatory issues.	Germany	2008
26	European Stroke Research Network for Hypothermia (46)	EuroHYP	The network aims to develop, support and promote medical research and dissemination activities related to stroke and brain diseases in general, especially considering the experimental and clinical research related to hypothermia and its therapeutic aiming to protect the human health.	Belgium	2008
27	European Thoracic Oncology Platform (47)	ETOP	The aim of the network is to promote and to improve collaboration in clinical and translational research in lung cancer and mesothelioma in Europe.	Switzerland	2009
28	European Network for Intracerebral Haemorrhage (48)	EURONICH	The aim of the network is to set research priorities and conduct clinical trials dedicated to intracerebral haemorrhage.	Germany	Not available

**Table 2 – List of the European Clinical Networks: name, acronym, brief description, country and year of establishment (cont.4).**

Line	Name	Acronym	Brief description	Country	Year
29	European Network for the Study of Adrenal Tumours (49)	ENSAT	The network aims to improve the understanding of the genetics, tumourigenesis and hypersecretion in patients with adrenal tumours and associated familial syndromes.	Not available	2002
30	European Vision Institute Clinical Research (50)	EVICR.net	The aim of the network is to guarantee a high level of quality and excellence in ophthalmology clinical research collaborative work performed by the members.	Portugal	2010
31	European Working Group on Myelodysplastic Syndromes (51)	EWOG-MDS	The network aims to bring together clinicians and researchers with an interest in childhood myelodysplastic syndromes (MDS) and juvenile myelomonocytic leukemia (JMML), initiate collaborative studies, disseminate information about childhood MDS and serve as a resource for those being interested in childhood MDS.	Germany	1993
32	Family Paediatricians Medicines for Children Research Network (1, 52)	FIMP-MCRN	The network aims to develop competence, infrastructure, networking and training for paediatric clinical trials. This network is composed by 20 Local Research Networks and 6 Sub- speciality Networks (vaccines, nutrition, phytotherapy, allergology, dermatology and gastroenterology).	Italy	2003
33	Finnish Investigators Network of Paediatric Medicines (18)	FINPEDMED	The network aims to improve both academic and commercial paediatric clinical trials for the benefit of children's health. The network facilitates reliable expert services related to designing and conducting paediatric clinical trials.	Finland	2007
34	French Clinical Research Infrastructure Network (53)	FCRIN	The network aims to support investigators and sponsors to increase attractiveness and efficiency by gathering clinical trial units. The network provides information on existing structures and regulatory framework; consultancy on protocol, study design and services needed for the the conduct of clinical trials such as methodology, training, monitoring, pharmacovigilance, quality assurance, etc.	France	2010

**Table 2** – List of the European Clinical Networks: name, acronym, brief description, country and year of establishment (cont.5).

Line	Name	Acronym	Brief description	Country	Year
35	Futurenest Paediatric Network (54)	Futurenest	The network aims to ensure that clinical trials with children are conducted in an efficient way to increase the access of the population to innovative medicines. This network facilitates the recruitment of experts and investigators to the clinical trials.	Hungary	2008
36	German Hodgkin Study Group (55)	GHSG	The aim of the network is to optimize and standardize diagnostics, therapy and follow-up care in Hodgkin lymphoma patients.	Germany	1978
37	German Neonatal Network (56)	GNN	The network is focussed on the long-term effects of genetic, clinical and social risks factors, the influence of center specific treatment strategies and in the support of randomized clinical trials in Very Low Birth Weight infants.	Germany	2008
38	Global Allergy and Asthma European Network (57, 58)	GA <sup>2</sup> LEN	The network aims to bring together research and clinical units to overcome the fragmentation in Europe in terms of allergy and asthma research where the diseases' prevalence continues to grow. The services available are a web platform for data transfer and storage, knowledge in biobanking, platform for clinical trials, administrative support and collaboration among partners.	Germany	2005
39	Grupo Espanol de Cancer de Pulmón (59)	GECP	The aim of the network is to develop the treatment of lung cancer by clinic research and prevention.	Spain	1991
40	Hungarian European Clinical Research Infrastructure Network (60)	HECRIN	The network aims to develop clinical research by providing infrastructures.	Hungary	2006
41	Haemato Oncology Foundation for Adults in the Netherlands (61)	HOVON	The aim of the network is to improve and promote treatment methods for adult patients with malignant haematological disorders, such as leukaemia and lymphoma.	Netherlands	1985
42	Histiocyte Society (62)	HS	The aim of the network is to advance knowledge about and improve outcomes for patients with histiocytic disorders through clinical and basic research and education.	USA	1985

**Table 2 – List of the European Clinical Networks: name, acronym, brief description, country and year of establishment (cont.6).**

Line	Name	Acronym	Brief description	Country	Year
43	Innovative Therapies for Children with Cancer (63)	ITCC	The aim of the network is to develop novel therapies for the treatment of paediatric and adolescent cancers in cooperation with regulatory bodies, pharmaceutical companies, parents and patients. The expertise of the network is in conducting early phase trials.	France	2003
44	International Breast Cancer Study Group (64)	IBCSG	The aim of the network is to develop innovative clinical cancer research to improve the outcome of women with breast cancer.	Switzerland	1977
45	International Berlin/ Frankfurt/ Munster (BFM) Study Group (16)	I-BFM-SG	The aim of the network is to promote both research and clinical care for children and adolescents with leukemia and lymphoma, making use of the large population of patients.	Germany	1987
46	International Extranodal Lymphoma Study Group (65)	IELSG	The aim of the network is to bring together scientists from different institutions to study specific extranodal sites of involvement by a lymphoma.	Switzerland	1998
47	International Neurotrauma Research Organization Internationale Gesellschaft zur Erforschung von Hirntraumata (66)	INRO / IGEH	The aim of the network is to improve the recovery of patients who suffer a brain or spinal cord injury through helping hospitals to implement evidence-based medical care by collaborating on clinical research to continuously improve the scientific foundations.	Austria	Not available
48	International Rare Cancers Initiative (67)	IRCI	The aim of the network is to facilitate the development of international clinical trials for patients with rare cancers in order to boost the progress of new treatments for these patients. This is an initiative between UK National Cancer Research Network (UK CRN), Cancer Research UK (CR-UK), US National Cancer Institute (US NCI) and the EORTC.	UK	2011
49	International Society of Paediatric Oncology European Neuroblastoma Research Network (68)	SIOPEN-R-NET	The network aims to co-ordinate prospective multinational risk adapted trials and to be the basis to exchange the experience acquired, to disseminate results and to inform users.	Austria	2014
50	International Society of Paediatric Oncology Renal Tumour Study Group (69)	SIOP-RTSG	The network aims to plan and implement new studies in children and adolescents affected by kidney tumours.	Germany	2007



**Table 2 – List of the European Clinical Networks: name, acronym, brief description, country and year of establishment (cont.7).**

Line	Name	Acronym	Brief description	Country	Year
51	Irish Clinical Research Infrastructure Network (70)	ICRIN	The network supports clinical research and investigators in assuring that the standards of efficiency, ethical principals and national regulatory requirements are complied in order to improve the quality of research. The network provides templates, forms, SOPs to be used in clinical trials.	Ireland	2006
52	Irish Paediatric Clinical Research Network (71)	IPCRN	It is a network of key opinion leaders in paediatric care created to promote high-quality basic and clinical research in children to further the understanding of paediatric illness and to develop safe and effective treatment options.	Ireland	2009
53	Italian Clinical Research Infrastructure Network (72)	ItaCRIN	A network of Italian institutions of excellence in the field of clinical research. It is coordinated by the Istituto Superiore di Sanità. The aim of the network is to support clinical trials of European projects involving different ECRIN partners and Italy by giving support of technical and scientific nature.	Italy	2012
54	Medicines for Children Research Network (NL) (21)	MCRN	The aim of the network is to stimulate high quality research on drugs in children in the Netherlands, to ultimately improve drug therapy by providing expertise and to coordinate logistical support to academic investigators and pharmaceutical companies.	Netherlands	2008
55	National Health Service Research Scotland (73)	NRS	The network aims to provide the best environment to high quality clinical research and to give support to the patients that participate in clinical research. The network is organised in 5 regional nodes: North, East, South-East and West. The network includes 6 topic research networks (Cancer (SCRN that is divide in 4 hubs: West, North, South East and East), Medicines for Children (ScotCRN), Dementia (SDCRN), Diabetes (SDRN, 2006), Mental Health (SMHRN, 2009), Primary Care (SPCRN, 2002) and Stroke (SSRN, 2006)).	Scotland	2010

**Table 2 – List of the European Clinical Networks: name, acronym, brief description, country and year of establishment (cont.8).**

Line	Name	Acronym	Brief description	Country	Year
56	National Institute for Health Research Clinical Research Network (74)	NIHR-CRN	The network aims to provide the infrastructure that allows high quality research and to give support to the patients that participate in clinical research. This network is organized in 6 topic research networks (Cancer, Dementia and Neurodegenerative Diseases, Diabetes, Medicine for Children, Mental Health and Stroke), a Primary Care Research Network and a Comprehensive Clinical Research Network that cover all other disease areas and 15 Local Research Networks.	UK	2006
57	National Institute for Social Care and Health Research Clinical Research Centre (75)	NISCHR CRC	The network aims to support the development and delivery of high-quality clinical research. The network also provides training for people involved in clinical research, namely Good Clinical Practice, Informed Consent Form, Communication Skills and Core Research Skills and an annual meeting. This network is organized in 9 topic research networks (Children and Young People's (CYPRN, 2006), Dementias and Neurodegenerative Diseases (NEURODEM Cymru), Diabetes (DRN Wales), Thematic RN for Emergency and Unscheduled Treat (TRUST), Wales Epilepsy (WERN, 2004), Learning Disabilities, Autism and Neurodevelopmental Disorders (LDAN), Mental Health (MHRN-C, 2006), Public Health Improvement (PHIRN, 2006) and Older People & Ageing & Development (OPAN Cymru) and also the Wales Cancer Research Network (WCRN, 1998), all networks with websites . The main organization of the network is the regional networks: North Wales, South East and South West Research Networks and Primary Care.	Wales	2010
58	Network of the Coordinating Centres for Clinical Trials (76)	KKS-Network	The network is a scientific service provider with the aim of implementing clinical trials among the network to ensure the successful implementation of clinical trials. The network also provides training and it has a relevant role in improving the regulatory framework.	Germany	Not available
59	Network of Excellence for Research in Paediatric Critical Care (77)	SKIC	The network aims to create guidelines in the Intensive Care Units for children with scientific basis.	Netherlands	2009

**Table 2 – List of the European Clinical Networks: name, acronym, brief description, country and year of establishment (cont.9).**

Line	Name	Acronym	Brief description	Country	Year
60	Network Neonatale Italiano (78)	NNI	The aim of the network is to improve the quality and care of newborns and their families by research programs, education and quality improvement. This network is associated to the Vermont-Oxford Network (VON).	Italy	1999
61	Newcastle Children's Cancer & Leukaemia Group (CCLG) Pharmacology (79)	N-CCLG	The network aims to promote the conduction of clinical pharmacology trials for children and adolescents. The coordinating Centre is the Northern Institute for Cancer Research at Newcastle University.	UK	2000
62	Northern Ireland Clinical Research Network (80)	NICRN	The aim of the network is to enable a well-resourced network of skilled staff which facilitates investigators and patients and delivers high quality clinical research studies among the Health and Social Care in the Northern Ireland. The network is organized in the following Groups: Cardiovascular, Children, Critical Care, Dementia, Diabetes, Mental Health, Primary Care, Renal, Respiratory Health, Stroke and Vision.	Northern Ireland	2008
63	Norwegian Clinical Research Network (81)	NORCRIN	The aim of the network is to strengthen and facilitate collaboration on clinical research in Norway and to integrate clinical research in Europe by providing research support to clinical trials.	Norway	Not available
64	Paediatric European Digestive Diseases Clinical Research Network (82)	PEDDCReN	The aim of the network is to study effective medicines for paediatric patients in the speciality of gastroenterology, hepatology and nutrition. The network also aims to play a role in influencing the development of study plans and protocols.	UK	2013
65	Paediatric European Network for the treatment of AIDS and infectious diseases (83)	PENTA-ID	Collaboration between paediatric HIV centres to address questions about treatment for children with HIV that are not answered, performing clinical trials, cohort studies and training. Close collaboration with adult trial networks.	Italy	2004
66	Paediatric Network of Clinical Investigators Centre (15)	CICPed	The aim of the network is to create interactions between the researchers, the paediatricians and the pharmaceutical industry to conduct paediatric clinical research projects in France.	France	2000

**Table 2** – List of the European Clinical Networks: name, acronym, brief description, country and year of establishment (cont.10).

Line	Name	Acronym	Brief description	Country	Year
67	Pediatric Infectious Disease Group of Switzerland (84)	PIGS	The aims of the network are to set standards of care for pediatric patients with infectious diseases and to develop protocols for studies in the area of pediatric infectious disease.	Switzerland	2001
68	Pediatric Rheumatology International Trials Organisation (17)	PRINTO	The aim of the network is to perform clinical trials for paediatric with and without the support of pharmaceutical industry.	Italy	1996
69	Platform for European Preparedness Against (Re-)emerging Epidemics (85)	PREPARE	The network aims to conduct observational studies and randomised clinical trials in children and in adults. The network will develop pre-emptive solutions to ethical, administrative, regulatory and logistical bottlenecks that prevent a rapid response in the face of new threats.	Belgium	2014
70	Prevención con Dieta Mediterránea (86)	PREDIMED	The network was created to perform a clinical trial to assess the influence that the Mediterranean Diet may have in people with high cardiovascular risk. The network also aims to develop an epidemiologic nutritional study and other sub-studies (interventional and observational).	Spain	2002
71	Polish Clinical Research Infrastructures Network (23)	POLCRIN	The network aims to integrate and strengthen medical science in Poland.	Poland	2007
72	Portuguese Clinical Research Infrastructure Network (87)	PtCRIN	The network aims to facilitate and improve quality in clinical research and to increase research collaboration for the benefit of the patients by developing clinical research infrastructures.	Portugal	2012
73	Red Española de Esclerosis Múltiple (88)	REEM	The aim of the network is to study the causes and treatment of multiple sclerosis by the collaboration between national investigational groups.	Spain	2007
74	Red de Investigación Cardiovascular (89)	RIC	The aim of the network is to reduce the impact of the cardiovascular diseases on the survival and quality of life by promoting translational research. This network resulted from the union of 3 former networks: RECAVA, REDINSCOR and HERACLES.	Spain	2012

**Table 2** – List of the European Clinical Networks: name, acronym, brief description, country and year of establishment (cont.11).

Line	Name	Acronym	Brief description	Country	Year
75	Red de Investigación Cooperativa en Enfermedades Tropicales (90)	RICET	The aim of the network is to study the tropical diseases that are becoming to be present in Europe due to the international mobility.	Spain	2002
76	Red de Investigación en Salud Materno-Infantil y del Desarrollo (91)	Red SAMID	The aim of the network is to generate high quality scientific knowledge in the area of neonatology to improve the quality of health care. The main lines of work is to assess the potential impact of certain perinatal processes on children's growth and development. One of the RETIC Network (Redes Temáticas de Investigación Cooperativa en Salud) of Spain that promotes the collaboration between institutions of the National Health System.	Spain	2008
77	Red Temática de Investigación Cooperativa de Centros de Cáncer (92)	RTICCC	The aim of the network is to stimulate the research in cancer diseases and to consolidate the infrastructures of collaboration between institutions of the National Health System.	Spain	2003
78	Réseau d'Investigations Pédiatriques des Produits de Santé (93)	RIPPS	The aim of the network is to facilitate the conduct of clinical trials with children in France and to ensure the quality of the medicinal products. This network is organized by sub-networks: RIPPS DéfiScience (multidisciplinary), PERENE Epilepsy, RMNMI (pediatric neuromusculaires diseases) and Pediatric Emergency Network).	France	2005 (PERENE, 2011), (RMNMI, 2010)
79	Romanian Clinical Research Infrastructure Network (23)	ROCRIN	The aim of the network is to develop clinical research.	Romania	Not available
80	Study Group of Medical Tumor Therapy - Arbeitsgemeinschaft medikamentöse Tumorthherapie (94)	AGMT	The aim of the network is to carry out clinical trials to improve the results of patients suffering from malignant tumours and to perform translational research.	Austria	2007
81	Swedish Clinical Research Infrastructure Network (95)	SweCRIN	The aim of the network is to improve the quality and the efficacy of clinical research in Sweden by facilitating the collaboration between clinical trial units and also with international clinical research. The network intends to stimulate the dialogue with the regulatory authorities, associations and networks.	Sweden	2003

**Table 2** – List of the European Clinical Networks: name, acronym, brief description, country and year of establishment (cont.12).

Line	Name	Acronym	Brief description	Country	Year
82	Swiss Clinical Trial Organisation (96)	SCTO	The network aims to position swiss clinical research in the international competition with respect to innovation and quality. The network provides quality assurance, data management, education and training, coordination of clinical trials, information for the public, funding opportunites and meetings.	Switzerland	Not available
83	Swiss Group for Clinical Cancer Research (97)	SAKK	The aim of the network is to investigate new cancer therapies and to improve the existing tumor treatments in order to cure the disease, prolong survival and improve life quality of patients. The network is organised by project groups: breast cancer, lung cancer, leukemia, lymphoma, gastrointestinal cancer, new anticancer drugs and urogenital tumors. The network has 2 sections of pathology and radio-oncology; 2 networks: for cancer predisposition testing and counseling (CPTC) and for outcomes research; and 4 working groups (central nervous system tumors, head and neck cancer, melanoma and control and palliative cancer care.	Switzerland	Not available
84	Swiss Group for Clinical Cancer Research (98)	SPOG	The aim of the network is to promote patient-oriented cancer research in the field of paediatric oncology through cooperative, predominantely international studies. This network has the Swiss Childhood Cancer Registry and the SPOG's Tumor Bank.	Switzerland	Not available
85	Swiss Research Network of Clinical Paediatric (99)	SwissPedNet	The aim of the network is to promote, facilitate, coordinate and conduct clinical trials devoted to children ranging from newborns to adoloscents in all paediatric diseases. The ultimate goal is to enhance clinical research in pediatrics both by supporting pediatric clinician scientists to foster their commitment to high-quality clinical research and by encouraging an overall increased acceptance in the community of trials in children.	Switzerland	2012
86	The Trauma Audit & Research Network (100)	TARN	The aim of the network is to perform research with highly skilled teams to provide relevant information to help health professionals and managers to improve their services.	UK	Not available

**Table 2** – List of the European Clinical Networks: name, acronym, brief description, country and year of establishment (cont.13).

Line	Name	Acronym	Brief description	Country	Year
87	United Kingdom Clinical Research Network (101)	UKCRN	The aim of the network is to ensure that the clinical research networks across the UK work together in an integrated manner to share experiences, develop joint initiatives and promote partnership between networks. The network is formed by the national networks of UK: National Institute for Health Research (NIHR CRN), Northern Ireland Clinical Research Network (NICRN), National Health Service Research Scotland (NRS) and National Institute for Social Care and Health Research Clinical Research Centre (NISCHR CRC).	UK	Not available
88	United Kingdom Paediatric Vaccine Group (20)	UKPVG	The aim of the network is to improve education, training and high quality research through collaboration among the participating centres.	UK	2001

Table 3 (See Appendix 1) lists other parameters that help to characterise the networks: national/international networks, number of members, public/private networks, target disease, relevant activities (e.g., studies, publications) and website address.

According to the collected data, 51 of the networks are national, i.e., 58% of the networks perform their activities among members inside of the country of the network. The other 42% of the networks are international.

The number of members varies from network to network. 14 of the networks have 10 or less members; 27 networks have between 11 and 50 members and 13 networks have between 51 and 100 members. 11 networks have more than 100 members and the number of members varies from 100 to 6200. Finally, 6 networks have as members all the hospitals of the corresponding country and in this case it was not possible to quantify. There are other 17 networks that it was not possible to quantify neither qualify the number of members.

Considering the identified networks, 61% (54 networks) of them are private organisations, whereas 38% (33 networks) are public organisations and 1% (1 network) is a public/private organisation.

Further, 64% (56 networks) of the networks are thematic, whereas 36% (32 networks) are general. Among the 32 general networks, 30% (10 networks) are focused in paediatric diseases. Among the 55 thematic networks, 31% (17 networks) are focused in paediatric diseases.

The thematic networks are related to diseases such as: radiotherapy, AntiPhospholipid Syndrome, disease and long-term development of preterm infants, allergology and asthma, ophthalmology, intracerebral haemorrhage, anaesthesiology, stroke, traumatic brain injury, cystic fibrosis, blood and marrow, neonatal diseases, attention deficit hyperactivity disorder (ADHD) and hyperkinesis, histiocytic disorders, intensive care, gastroenterology, hepatology, nutrition, HIV and other infectious diseases, infectious diseases, rheumatic



diseases, infectious diseases outbreak, multiple sclerosis, heart diseases, tropical diseases, trauma, vaccines, oncology and specific areas of oncology like breast cancer, liver tumor, chronic lymphocytic leukemia, soft tissue sarcoma, lung cancer and mesothelioma, adrenal tumors, myelodysplastic syndromes (MDS) in childhood and juvenile myelomonocytic leukemia (JMML), Hodgkin lymphoma and malignant haematological disorders.

Among the thematic networks (55 networks), 45% of the networks are cancer related.

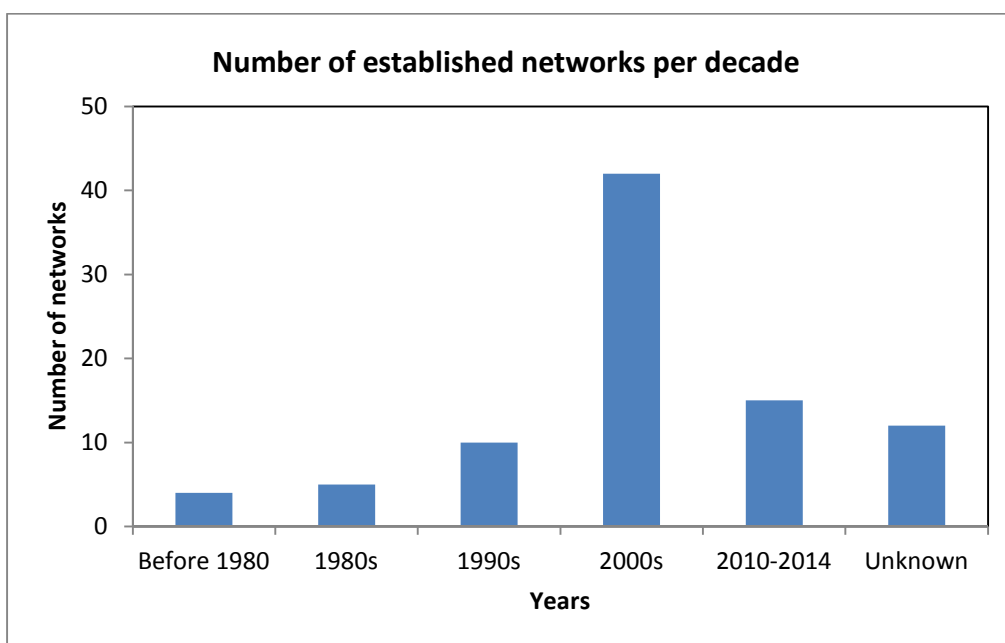
Relevant activities of the networks were also collected from the corresponding websites. Therefore, networks may have other activities that as are not referred in the website are not mentioned here. Relevant activities were defined as all activities that contribute to clinical research such as: clinical trials, observational studies, projects, meetings, trainings and publications.

### **3.2. Discussion**

Almost all European countries have networks. The UK is the country with the highest number of CRN, 11 networks, followed by Germany with 10 networks, Spain and Switzerland with 8 networks, Belgium and Italy with 7 networks and Austria, France, and the Netherlands with 5 networks. Hungary, Ireland, Poland, Portugal, Scotland and the USA have 2 networks. Finally, Czech Republic, Denmark, Finland, Ireland, Luxemburg, Northern Ireland, Norway, Romania, Sweden and Wales have 1 network. Therefore, it can be concluded that the richest countries have a higher number of networks. This fact was already expected as wealthy countries have a stronger clinical research tradition, better clinical research policies and greater budget to dedicate to this type of organisations and research.

The identified networks were established between 1962 and 2014. Figure 1 presents the number of established networks per decade in Europe. The 2000s was the decade of the “*baby boom*” of networks in Europe with 42 new networks.

Apparently, the odds are that the current decade will also have a great number of new networks. This tendency comes in line with the new paradigm in Drug Development where stakeholders have been progressively concluding that the success of innovative drugs and therapies will not happen in an isolated lab of the academy, or in the lab of a pharmaceutical company or in the bed of a University Hospital. Collaboration and partnership are essential in Drug Development and Clinical Research.

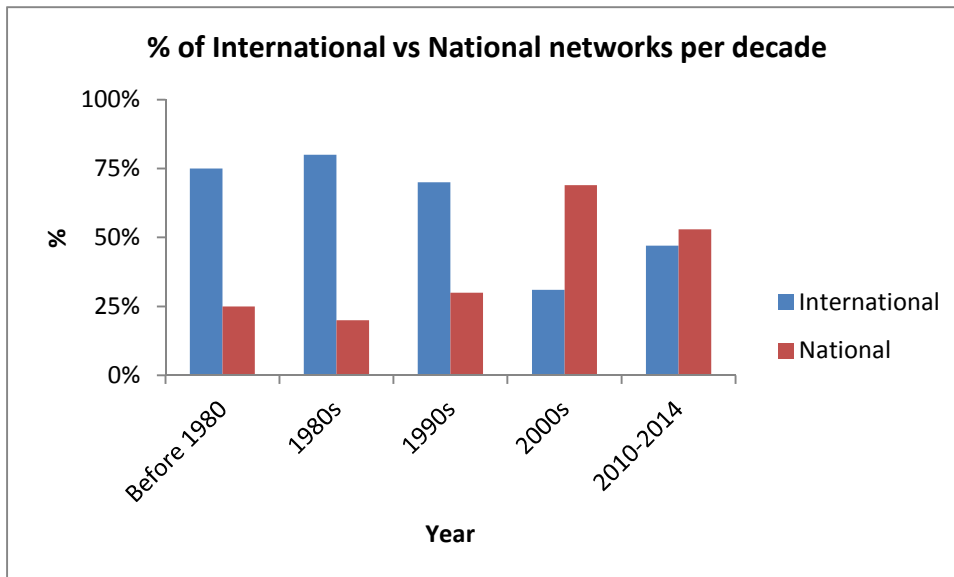


**Figure 1** - Number of established networks per decade

Table 3 (See Appendix 1) lists other parameters that help to characterise the networks: national/international networks, number of members, public/private networks, target disease, relevant activities (e.g., studies, publications) and website address.

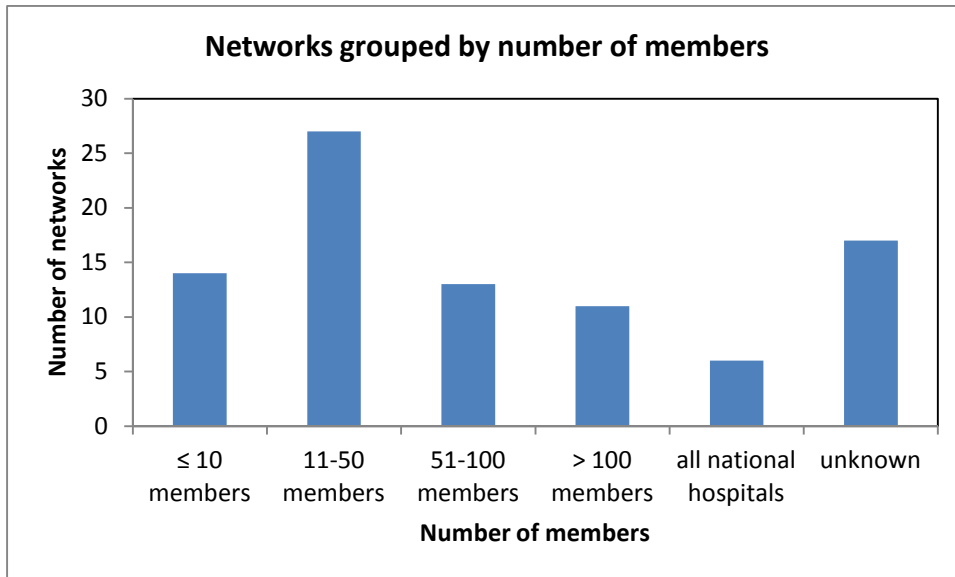
According to the collected data, 51 of the networks are national, i.e., 58% of the networks perform their activities among members inside of the country of the network. The other 42% of the networks are international. Therefore, there is a balance between the number of international and national networks. Nevertheless, if analysed along time, the conclusion is not the same (See Figure 2). Until the 2000s, there is a predominance of the international networks, whereas in the

2000s there is a predominance of the national networks and in the 2010s it seems that there is a balance between the number of international and national networks. The predominance of the national networks in the 2000s is related to the creation of the national clinical research infrastructure networks.



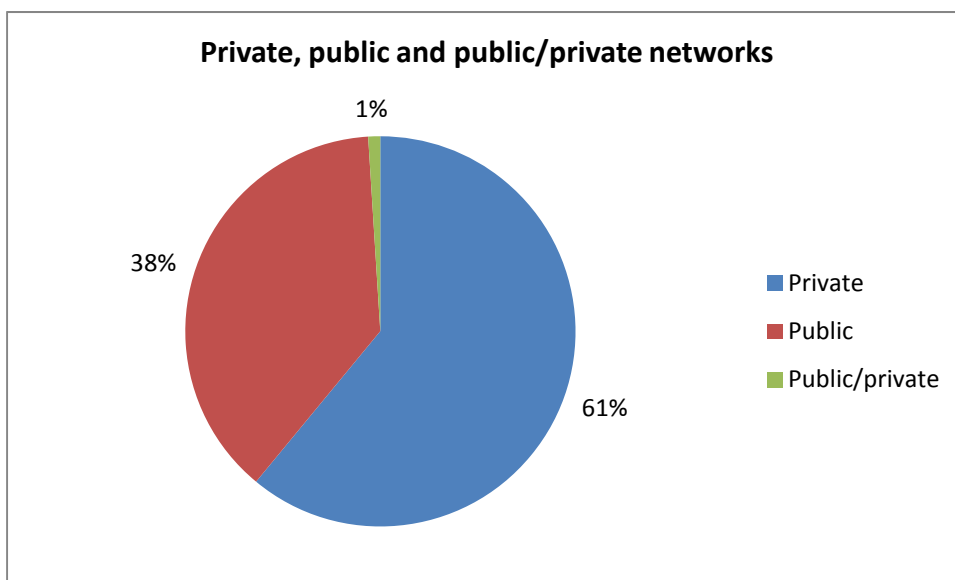
**Figure 2 - % of International versus National networks per decade**

The number of members varies from network to network. As represented in the graph of Figure 3, 14 networks have 10 or less members; 27 networks have between 11 and 50 members and 13 networks have between 51 and 100 members. 11 networks have more than 100 members where the number of members varies from 100 to 6200. Finally, 6 networks have as members all the hospitals of the corresponding country and in this case it was not possible to quantify. There are other 17 networks that it was not possible to quantify neither qualify the number of members. The most common number of members is between 11 and 50 members. Therefore, the number of member between 11 and 55 seems to be the optimal number to the well work of a network.



**Figure 3 – Networks grouped by number of members.**

61% (54 networks) of the networks are private organisations, whereas 38% (33 networks) are public organisations and 1% (1 network) is a public/private organisation (Figure 4). Although the majority of the networks are private, significant part of the budget of these networks are paid by public funding from the country national budget and from the European Commission.

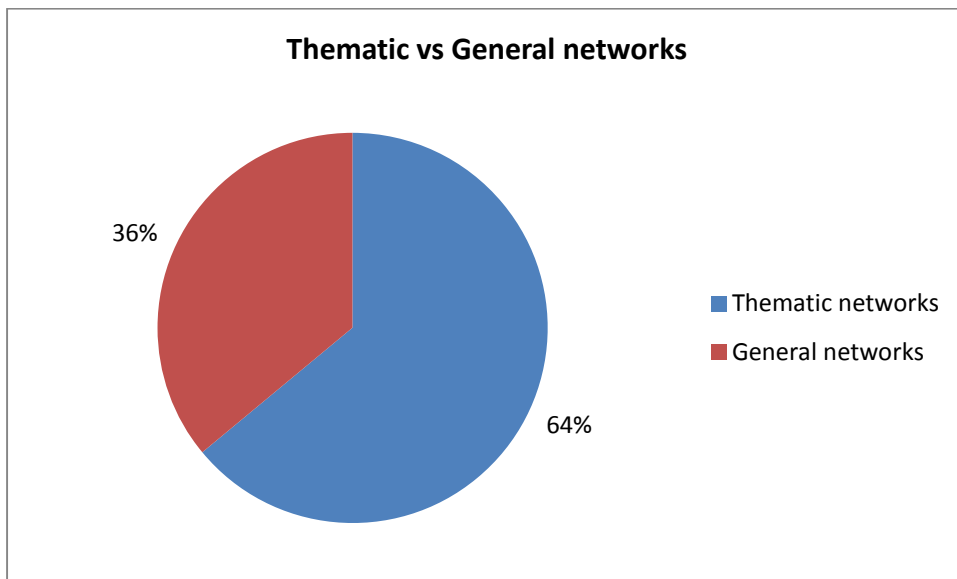


**Figure 4 – Private, public and public/private networks.**

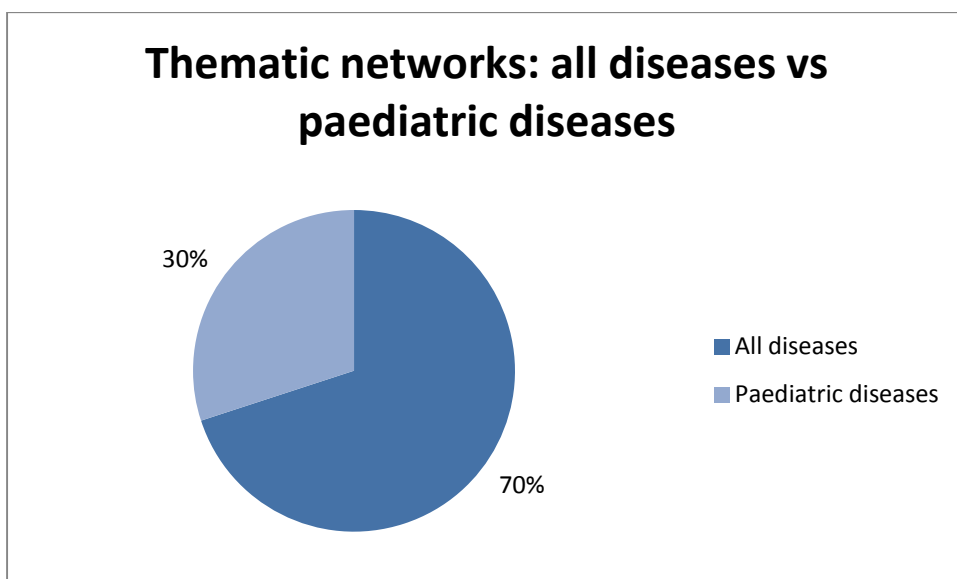
64% (56 networks) of the networks are thematic, whereas 36% (32 networks) are general. The significant higher number of thematic networks was expected as the

philosophy of the networks is the share of a common interest, in this case a disease or an area of medicine.

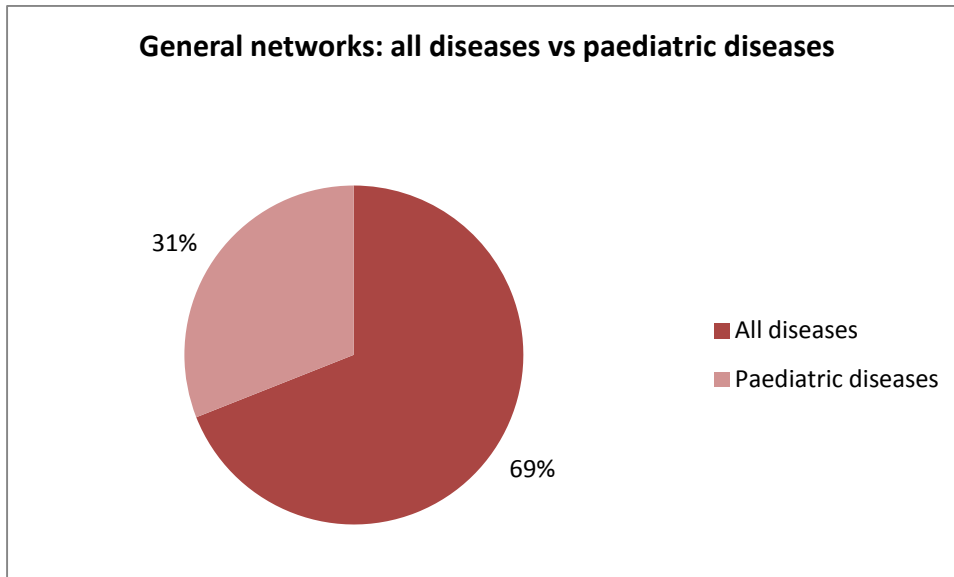
Among the 32 general networks, 30% (10 networks) are focused in paediatric diseases. Among the 55 thematic networks, 31% (17 networks) are focused in paediatric diseases (Figures 5.1, 5.2 and 5.3). It can be concluded that the interest by paediatric disease is the same among the thematic and the general networks.



**Figure 5.1** - Thematic networks *versus* general networks.



**Figure 5.2** - Thematic networks: all diseases *versus* paediatric diseases.



**Figure 5.3** - General networks: all diseases *versus* paediatric diseases.

The thematic networks are related to diseases such as: radiotherapy, AntiPhospholipid Syndrome, disease and long-term development of preterm infants, allergology and asthma, ophthalmology, intracerebral haemorrhage, anaesthesiology, stroke, traumatic brain injury, cystic fibrosis, blood and marrow, neonatal diseases, attention deficit hyperactivity disorder (ADHD) and hyperkinesis, histiocytic disorders, intensive care, gastroenterology, hepatology, nutrition, HIV and other infectious diseases, infectious diseases, rheumatic diseases, infectious diseases outbreak, multiple sclerosis, heart diseases, tropical diseases, trauma, vaccines, oncology and specific areas of oncology like breast cancer, liver tumor, chronic lymphocytic leukemia, soft tissue sarcoma, lung cancer and mesothelioma, adrenal tumors, myelodysplastic syndromes (MDS) in childhood and juvenile myelomonocytic leukemia (JMML), Hodgkin lymphoma and malignant haematological disorders.

Among the thematic networks (55 networks), 45% are cancer related networks.

It can be concluded that among the clinical research environment, there is a special focus in the cancer diseases and in paediatric diseases. This is probably due to the high number of unmet medical needs in oncology and in paediatric populations.

Relevant activities of the networks were also collected from the corresponding websites. Therefore, networks may have other activities that as are not referred in the website are not mentioned here. Relevant activities were defined as all activities that contribute to clinical research such as: clinical trials, observational studies, projects, meetings, trainings and publications. Analysing the relevant activities of the clinical research networks, there are significant evidences that clinical research networks have a positive impact in clinical research and are considered a valid stakeholder in clinical research environment. It is also a fact that this impact could be optimized.

In order to maximise the contribution of clinical research networks to the development of new drugs and therapies, it is essential to increase and improve the communication among stakeholders.

It would be useful to create an on-line database of clinical research networks, allowing the use of tools such as search engines that could be located in a dynamic website. The website could be fed with updated news about the clinical research networks, such as an updated list of the clinical research networks and contacts, active clinical trials, meetings, trainings and main achievements and could also have a forum for scientific discussion for all stakeholders (industry, academy, researchers, investigators, patients and authorities).

It could also be helpful to the clinical research networks to have access to a set of basic rules/tips to help in the management and communication of the networks.

For example, regular newsletters help to keep the members informed and motivated to participate in the network activities.

Other good tip is to keep a public updated portfolio of the projects. Portfolios are very useful as they characterise the network activities, avoid the duplication of projects already done and also work as a brainstorm for new projects.





## 4. Conclusion

This report was written as part of the Master's degree in Pharmaceutical Medicine and it presents the information about the search of the existing European clinical research networks that performed between December 2013 and May 2014.

The data collected from each clinical research network was: name, acronym, brief description, country, year of establishment, national/international networks, number of members, public/private networks, target disease, relevant activities (e.g., studies, publications) and website address.

Eighty-eight clinical research networks were identified in the Internet between december 2013 and may 2014. It was a great challenge to identify the networks, as information about networks can only be obtained in the websites of each network. Further, most of the websites do not provide much information and part of the websites were not updated.

Networks should give special attention to the design and contents of the websites, as websites are the interface/ image of the organisation. In order to better characterise this landscape of research networks and complete the information in this thesis, more information should be obtained to achieve better quality. By the use of a well developed questionnaire administered to the networks will allow to gather complete and accurate information, especially regarding the relevant activities.

Clinical research networks were identified in almost all European countries and the wealthiest countries have the higher number of networks.

The year of establishment of the networks vary between 1962 and 2014. The 2000s was the decade of the "*baby boom*" of networks in Europe with 42 new networks. It is expected that the current decade will also have a great number of new networks. This confirms that stakeholders believe that the success of

innovative drugs and therapies depends of the collaboration between academy and pharmaceutical companies.

It was verified that the majority of the networks are thematic and that there is a special focus in cancer diseases and in paediatric diseases. It seems that clinical research networks are being created due to the number of unmet medical needs in oncology and in paediatric diseases.

Analysing the relevant activities of the clinical research networks, there is evidence that clinical research networks have a positive impact in clinical research and are considered a valid stakeholder in the clinical research environment. It is also a fact that this impact could be optimized. It would be useful to create a search engine with an on-line database of the clinical research networks. Further, this search engine could be located in a dynamic website. The website could be fed with updated news about the clinical research networks, such as active clinical trials, scientific meetings and main achievements. Finally, it could also have a forum for scientific discussion for all stakeholders (industry, academy, researchers, investigators, patients and authorities).

Following this first step of collection of the European clinical research networks, conclusions should be analysed and released in a publication. The next step is to analyse the American clinical research networks.

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100. [19/05/2014]. Available from: <https://www.tarn.ac.uk>.
101. [07/04/2014]. Available from: <http://public.ukcrn.org.uk>.



## **6. Appendix**

### ***Appendix 1***

**Table 3** – List of the European Clinical Networks: acronym, national versus international, number of members, public versus private, target disease, relevant activities and website address.

	Acronym	Nat/ Inter	Members	Nature	Target	Relevant activities	Website address
1	ACORRN	Nat	Not available	private	radiotherapy	In the first 4 years this network achieved: 7 grant applications, 8 peer reviewed publications, 1 Lancet Oncology editorial, 1 audit of the Royal College of Radiologists guidelines, 2 working party reports, research radiographer starter pack, £41 million strategy document and business plan and Image Guided Radiotherapy Road Map.	<a href="http://www.actionradiotherapy.org/">http://www.actionradiotherapy.org/</a>
2	APS ACTION	Inter	31	public/ private	AntiPhospholipid Syndrome	Not available.	<a href="http://www.apsaction.org">http://www.apsaction.org</a>
3	ATCRIN	Nat	Not available	public	all diseases	Not available.	<a href="http://atcrin.at">http://atcrin.at</a>
4	BPDN	Nat	7	private	paediatric diseases	One survey ongoing.	<a href="http://www.pediatrie.be/pediatricdrug.htm">http://www.pediatrie.be/pediatricdrug.htm</a>
5	BIG	Inter	49	private	breast cancer	24 ongoing clinical trials and 8 closed clinical trials. 3 ongoing projects (INTEGRATE, EURECA and BIOMATERIAL INVENTORY).	<a href="http://www.bigagainstbreastcancer.org">http://www.bigagainstbreastcancer.org</a>
6	CESAR	Inter	Not available	private	oncology	This network provides education, training and several meetings per year and the CESAR award. 23 publications between 2002 and 2012, 20 abstracts and 7 ongoing clinical trials and 29 closed clinical trials.	<a href="http://www.cesar.or.at">http://www.cesar.or.at</a>
7	CRP-Santé	Nat	48	public	all diseases	154 research projects and publication of 107 peer-reviewed papers until 2012, 14 ongoing projects.	<a href="https://www.crp-sante.lu">https://www.crp-sante.lu</a>
8	SIOPEL	Inter	100	private	childhood liver tumor	7 ongoing projects, 7 closed clinical trials, 64 publications between 1993 and 2014.	<a href="http://www.siopel.org/">http://www.siopel.org/</a>
9	CZECRIN	Nat	Not available	public	all diseases	Not available.	This network does not have website.
10	CIRM	Nat	10	private	all diseases	2 ongoing multicenter clinical trials funded by 7th Framework Programme and 7 Italian projects.	<a href="http://www.cirm.net">http://www.cirm.net</a>



**Table 3** – List of the European Clinical Networks: acronym, national versus international, number of members, public versus private, target disease, relevant activities and website address (cont. 1).

	Acronym	Nat/ Inter	Members	Nature	Target	Relevant activities	Website address
11	DCRIN	Nat	Not available	public	all diseases	8 ongoing clinical trials.	<a href="http://ctu.dk">http://ctu.dk</a>
12	DCLLSG	Nat	Not available	private	chronic lymphocytic leukemia	2 ongoing clinical trials, 33 closed clinical trials and 75 publications between 1996 and 2014.	<a href="http://www.dcllsg.de">http://www.dcllsg.de</a>
13	NFU	Nat	8	public	all diseases	Clinical researchers from the network are obliged to attend the Basic Regulation and Organisation for Clinical Research (CHUNK course). The network has also a PhD program, where researchers are trained to become independent.	<a href="http://www.nfu.nl">http://www.nfu.nl</a>
14	EBIC	Inter	Not available	private	traumatic brain injury	The network provides different meetings per year. 5 closed studies and 5 ongoing studies, 59 publications between 1997 and 2011.	<a href="http://www.ebic.nl">http://www.ebic.nl</a>
15	ECRIN	Inter	22 national hubs + 12 institutions	private	all diseases	The network provides information, consultancy and services for non-profit academic clinical trials.	<a href="http://www.ecriin.org">www.ecriin.org</a>
16	ECFS-CTN	Inter	30	private	cystic fibrosis	23 ongoing studies and 7 new studies have been reviewed to be started in 2014, 7 publications and Annual training day on Clinical Research and annual conference.	<a href="https://www.ecfs.eu/ctn">https://www.ecfs.eu/ctn</a>
17	EBMT	Inter	Not available	private	blood and marrow	15 non-interventional prospective studies, 30 retrospective studies, 7 prospective clinical trials, more than 560 publications in peer-reviewed scientific journals.	<a href="https://www.ebmt.org/Contents/Pages/Default.aspx">https://www.ebmt.org/Contents/Pages/Default.aspx</a>
18	EuroNeoNet	Inter	Not available	private	neonatal diseases	The network has an up-to-date technological neonatal platform based on the Internet. A follow-up minimal dataset for long-term outcomes evaluated at 48 months is being developed.	<a href="http://www.euroneonet.eu">http://www.euroneonet.eu</a>

**Table 3** – List of the European Clinical Networks: acronym, national versus international, number of members, public versus private, target disease, relevant activities and website address (cont. 2).

	Acronym	Nat/ Inter	Members	Nature	Target	Relevant activities	Website address
19	EUNETHYDIS	Inter	160	private	attention deficit hyperactivity disorder (ADHD) or hyperkinesia	The networks has held an annual for the last 20 years, and it has a "Guideline Group" that has published 5 papers.	<a href="http://adhd-adduce.org/page/view/35/EUNETHYDIS">http://adhd-adduce.org/page/view/35/EUNETHYDIS</a>
20	Enpr-EMA	Inter	18	public	paediatric diseases	Annual workshop since 2008, creation EnprEMA Network Database, avaluation of the members of the network.	<a href="http://www.ema.europa.eu/ema/index.jsp?curl=pages/partners_and_networks/general/general_content_00_0303.jsp&amp;mid=WC0b01ac05801df74a">http://www.ema.europa.eu/ema/index.jsp?curl=pages/partners_and_networks/general/general_content_00_0303.jsp&amp;mid=WC0b01ac05801df74a</a>
21	EORTC	Inter	300 hospitals	private	oncology	Every year about 6000 new patients are enrolled in the EORTC clinical trials; 30 protocols are in the recruitment period and over 50000 patients are in the follow-up. EORTC has more than 180000 patients. EORTC has an official journal and every they organise courses and meetings.	<a href="http://www.eortc.org/">http://www.eortc.org/</a>
22	EPOC	Inter	Not available	private	paediatric oncology	Not available.	<a href="http://research.ncl.ac.uk/epoc/">http://research.ncl.ac.uk/epoc/</a>
23	EpSSG	Inter	163	private	paediatric soft tissue sarcoma	3 clinical trials in the recruitment period.	<a href="http://www.epssgassociation.it/">http://www.epssgassociation.it/</a>
24	ESA CTN	Inter	6200	private	Anaesthesiology	3 ongoing clinical trials and 6 closed clinical trials.	<a href="http://www.esahq.org/research/clinical-trial-network">http://www.esahq.org/research/clinical-trial-network</a>
25	ESN	Inter	29	private	Stroke	96 publications between 2009 and 2012.	<a href="http://www.europeanstrokenetwork.eu">http://www.europeanstrokenetwork.eu</a>
26	EuroHYP	Inter	25	private	Stroke	Annual Meeting, 8 ongoing clinical trials, 7 publications.	<a href="http://www.eurohyp.org">http://www.eurohyp.org</a>
27	ETOP	Inter	51	private	lung cancer mesothelioma	5 projects that include ongoing clinical trials.	<a href="http://www.etop-eu.org">http://www.etop-eu.org</a>
28	EURONICH	Inter	14 countries	private	intracerebral haemorrhage	3 ongoing clinical trials.	<a href="http://www.euronich.de">http://www.euronich.de</a> (Not working)

**Table 3** – List of the European Clinical Networks: acronym, national versus international, number of members, public versus private, target disease, relevant activities and website address (cont. 3).

	Acronym	Nat/ Inter	Members	Nature	Target	Relevant activities	Website address
29	ENSAT	Inter	Not available	private	adrenal tumors	4 ongoing clinical trials and 9 publications.	<a href="http://www.ensat.org">http://www.ensat.org</a>
30	EVICR.net	Inter	86	private	Ophthalmology	The network provides annual meeting, certification of the clinical sites. 11 ongoing clinical trials.	<a href="http://www.evicr.net">http://www.evicr.net</a>
31	EWOG-MDS	Inter	11	private	myelodysplastic syndromes (MDS) in childhood and juvenile myelomonocytic leukemia (JMML)	5 ongoing studies and 32 publications between 1997 and 2012.	<a href="http://www.ewog-mds.org/">http://www.ewog-mds.org/</a>
32	FIMP-MCRN	Nat	6000 paediatricians	private	paediatric diseases	Training programme with training courses for the researchers, 3 epidemiological post-marketing studies.	This network does not have website.
33	FINPEDMED	Nat	95	private	paediatric diseases	Not available.	<a href="http://www.finpedmed.com/index.php?page=141&amp;lang=2">http://www.finpedmed.com/index.php?page=141&amp;lang=2</a>
34	FCRIN	Nat	Not available	public	all diseases	Not available.	<a href="http://www.fcrin.org/en">http://www.fcrin.org/en</a>
35	Futurenest	Nat	5	private	paediatric diseases	Not available.	<a href="http://www.futurenest.hu/">http://www.futurenest.hu/</a>
36	GHSQ	Nat	400	governmental	Hodgkin lymphoma	The network provides an international symposium every 3 years, 4 ongoing clinical trials and 18 closed clinical trials.	<a href="http://en.ghsq.org">http://en.ghsq.org</a>

**Table 3** – List of the European Clinical Networks: acronym, national versus international, number of members, public versus private, target disease, relevant activities and website address (cont. 4).

	Acronym	Nat/ Inter	Members	Nature	Target	Relevant activities	Website address
37	GNN	Nat	38	public	disease and long-term development of preterm infants	1 multicenter study completed and 1 ongoing study.	<a href="http://www.vlbw.info/index-e.html">http://www.vlbw.info/index-e.html</a>
38	GA <sup>2</sup> LEN	Inter	87	private	allergology and asthma	4 ongoing projects.	<a href="http://www.ga2len.net/">http://www.ga2len.net/</a>
39	GECP	Nat	132	private	lung cancer	7 ongoing clinical trials and 60 closed clinical trials.	<a href="http://www.gecp.org">http://www.gecp.org</a>
40	HECRIN	Nat	143	public	all diseases	Not available.	<a href="http://www.ett.hu/hecrin/hecrin.htm">http://www.ett.hu/hecrin/hecrin.htm</a>
41	HOVON	Inter	80% of the hospitals of Belgium and Netherlands	private	malignant haematological disorders	6 planned clinical trials, 21 ongoing clinical trials and 56 closed clinical trials.	<a href="http://www.hovon.nl">http://www.hovon.nl</a>
42	HS	Inter	220	private	histiocytic disorders	1 ongoing clinical trial, 3 closed studies, 33 publications.	<a href="http://www.histiocytesociety.org/">http://www.histiocytesociety.org/</a>
43	ITCC	Inter	52	private	paediatric cancer diseases	13 ongoing clinical trials, training and education of the healthcare professionals in clinical research; clarification of parents about clinical research.	<a href="http://www.itcc-consortium.org/itcc-clinical-trial-committee.php">http://www.itcc-consortium.org/itcc-clinical-trial-committee.php</a>
44	IBCSG	Inter	88	private	breast cancer	3 ongoing clinical trials and 38 closed clinical trials. 301 publications between 1982 and 2014. The network also has the IBCSG Tissue Bank and the Central Pathology Office.	<a href="http://www.ibcsg.org">http://www.ibcsg.org</a>
45	I-BFM-SG	Inter	32	private	paediatric leukemia and lymphoma	15 closed multicenter studies and ongoing 20 studies.	<a href="http://www.bfm-international.org/index.php">http://www.bfm-international.org/index.php</a>

**Table 3** – List of the European Clinical Networks: acronym, national versus international, number of members, public versus private, target disease, relevant activities and website address (cont. 5).

	Acronym	Nat/ Inter	Members	Nature	Target	Relevant activities	Website address
46	IELSG	Inter	54	private	extranodal lymphoma	9 ongoing clinical trials, 49 publications between 1999 and 2014, 33 oral presentations between 1999 and 2013 and 42 posters between 1998 and 2013.	<a href="http://www.ielsg.org">http://www.ielsg.org</a>
47	INRO / IGEH	Inter	Not available	private	brain injury	2 ongoing projects, 8 closed projects, 28 publications between 2000 and 2014.	<a href="http://www.igeh.org">http://www.igeh.org</a>
48	IRCI	Inter	4	private	rare cancers	11 ongoing clinical trials, 2 meetings per year.	<a href="http://www.irci.info">http://www.irci.info</a>
49	SIOPEN-R-NET	Inter	21	private	neuroblastoma	Network under construction.	<a href="https://www.siopen-r-net.org/">https://www.siopen-r-net.org/</a>
50	SIOP-RTSG	Inter	10	private	paediatric kidney tumors	1 ongoing clinical trial, 6 closed clinical trials, 154 publications between 2003 and 2014.	<a href="http://web.visu.uni-saarland.de/rtsg/">http://web.visu.uni-saarland.de/rtsg/</a>
51	ICRIN	Nat	7	public	all diseases	The network provides courses and workshops.	<a href="http://www.molecularmedicineireland.ie/icrin">http://www.molecularmedicineireland.ie/icrin</a>
52	IPCRN	Nat	64 members from more than 23 hospitals	public	paediatric diseases	10 ongoing clinical trials, 39 funded research projects.	<a href="http://www.nationalchildrensresearchcentre.ie/research/ipcrn">http://www.nationalchildrensresearchcentre.ie/research/ipcrn</a>
53	ItaCRIN	Nat	Not available	public	all diseases	Not available.	<a href="http://www.itacrin.it/ecrin/mod/resource/view.php?id=48">http://www.itacrin.it/ecrin/mod/resource/view.php?id=48</a>
54	MCRN	Nat	8 Regional Research Clusters	public	paediatric diseases	Not available.	<a href="http://www.mcrn.nl">http://www.mcrn.nl</a>

**Table 3** – List of the European Clinical Networks: acronym, national versus international, number of members, public versus private, target disease, relevant activities and website address (cont. 6).

	Acronym	Nat/ Inter	Members	Nature	Target	Relevant activities	Website address
55	NRS	Nat	all public hospitals in Scotland	public	all diseases	Studies of the Scottish network are registered on the UK Clinical Research Network Portfolio Database. The UK Clinical Research Network Portfolio Database has 14251 studies (closed and ongoing) since 2006.	<a href="http://www.nhsresearchscotland.org.uk/">http://www.nhsresearchscotland.org.uk/</a> <a href="http://www.scrn.org.uk">http://www.scrn.org.uk</a> <a href="http://www.scotcrn.org/">http://www.scotcrn.org/</a> <a href="http://www.sdcrn.org.uk">http://www.sdcrn.org.uk</a> <a href="http://www.sdrn.org.uk">http://www.sdrn.org.uk</a> <a href="http://www.smhrn.org.uk">http://www.smhrn.org.uk</a> <a href="http://www.sspc.ac.uk/">http://www.sspc.ac.uk/</a> <a href="http://www.ssrn.org.uk">http://www.ssrn.org.uk</a>
56	NIHR-CRN	Nat	all public hospitals in England	public	all diseases	Studies of the English network are registered on the UK Clinical Research Network Portfolio Database. The UK Clinical Research Network Portfolio Database has 14251 studies (closed and ongoing) since 2006.	<a href="http://www.crnc.nihr.ac.uk">http://www.crnc.nihr.ac.uk</a>
57	NISCHR CRC	Nat	24 hospitals sites	public	all diseases	The studies on the NISCHR Clinical Research Portfolio has 953 studies (in set-up, open and closed) since 2008. Studies of the Welsh network are also registered on the UK Clinical Research Network Portfolio Database. The UK Clinical Research Network Portfolio Database has 14251 studies (closed and ongoing) since 2006. 117 articles between 2008 and 2013.	<a href="http://www.wales.nhs.uk/sites3/home.cfm?orgid=580">http://www.wales.nhs.uk/sites3/home.cfm?orgid=580</a> <a href="http://www.wales.nhs.uk/sites3/home.cfm?orgid=970">http://www.wales.nhs.uk/sites3/home.cfm?orgid=970</a> <a href="http://www.neurodemcymru.org/">http://www.neurodemcymru.org/</a> <a href="http://diabeteswales.org.uk">http://diabeteswales.org.uk</a> <a href="http://www.trustresearch.org.uk/en">http://www.trustresearch.org.uk/en</a> <a href="http://www.wern.swan.ac.uk">http://www.wern.swan.ac.uk</a> <a href="http://www.ldancymru.org.uk/">http://www.ldancymru.org.uk/</a> <a href="http://www.mhrnc.org">http://www.mhrnc.org</a> <a href="http://phirn.org.uk">http://phirn.org.uk</a> <a href="http://www.opanwales.org.uk">http://www.opanwales.org.uk</a> <a href="http://wcrn.wales.nhs.uk">http://wcrn.wales.nhs.uk</a>
58	KKS-Network	Nat	19	public	all diseases	74 publications between 2009 and 2014.	<a href="http://www.kks-netzwerk.de/en/network.html">http://www.kks-netzwerk.de/en/network.html</a>
59	SKIC	Nat	8	private	intensive care	4 ongoing studies.	<a href="http://www.stichtingkinderik.nl">http://www.stichtingkinderik.nl</a>
60	NNI	Nat	94	private	neonatal diseases	Collection of data from the centers of Neonatal Intensive Care Unit in Italy. 7 publications between 2011 and 2014.	<a href="http://www.neonatalnet.org/doku.php">http://www.neonatalnet.org/doku.php</a>

**Table 3** – List of the European Clinical Networks: acronym, national versus international, number of members, public versus private, target disease, relevant activities and website address (cont. 7).

	Acronym	Nat/ Inter	Members	Nature	Target	Relevant activities	Website address
61	N-CCLG	Nat	25	private	paediatric cancer diseases	5 closed studies, 7 ongoing studies, newsletter and publications (not quantified).	<a href="https://cclg.arithmostech.com/">https://cclg.arithmostech.com/</a>
62	NICRN	Nat	all hospitals of Northern Ireland	public	all diseases	Studies of the Northern Ireland network are registered on the UK Clinical Research Network Portfolio Database. The UK Clinical Research Network Portfolio Database has 14251 studies (closed and ongoing) since 2006.	<a href="http://www.nicrn.hscni.net/">http://www.nicrn.hscni.net/</a>
63	NORCRIN	Nat	6	public	all diseases	2 observational prospective studies, guidance for medical research, web CRF, national procedures for clinical trials, advanced course in Good Clinical Practices, partner meetings and conferences.	<a href="http://www.norcrin.no">http://www.norcrin.no</a>
64	PEDDCReN	Inter	Not available	private	gastroenterology, hepatology, nutrition	It is being done an on-line survey across Europe (at the moment in the UK) to establish the interest, expertise and resources in conducting clinical trials in this area.	<a href="https://www.ueg.eu/fileadmin/user_upload/document/s/Awards/LINK.Award.2012.PEDDCReN_November%202013.pdf">https://www.ueg.eu/fileadmin/user_upload/document/s/Awards/LINK.Award.2012.PEDDCReN_November%202013.pdf</a>
65	PENTA-ID	Inter	Not available	private	paediatric HIV and other infectious diseases	3 ongoing clinical trials, 11 closed clinical trials.	<a href="http://www.pentatrials.org">http://www.pentatrials.org</a>
66	CICPed	Nat	15	private	paediatric diseases	The number of clinical trials was 109 in 2010 and 121 in 2011.	<a href="http://cic-pediatriques.com/index.php/objectifs/objectifs">http://cic-pediatriques.com/index.php/objectifs/objectifs</a>
67	PIGS	Nat	40	private	paediatric infectious diseases	16 publications, recommendations and guidelines since 2004.	<a href="http://www.pigs.ch/">http://www.pigs.ch/</a>
68	PRINTO	Inter	350	private	paediatric rheumatic diseases	6 ongoing projects, 10 closed projects, more than 100 papers between 1997 and 2013. The network elaborates proceedings and a newsletter.	<a href="http://www.printo.it/index.asp">http://www.printo.it/index.asp</a>

**Table 3** – List of the European Clinical Networks: acronym, national versus international, number of members, public versus private, target disease, relevant activities and website address (cont. 8).

	Acronym	Nat/ Inter	Members	Nature	Target	Relevant activities	Website address
69	PREPARE	Inter	22	private	infectious diseases outbreak	Clinical trials and training are planned to start in 2014. Kickoff of this network was on 5-7 February 2014, an FP7 project.	<a href="https://www.combacte.com/?q=node/115">https://www.combacte.com/?q=node/115</a>
70	PREDIMED	Nat	19	public	nutrition	1 ongoing clinical trial. 674 publications between 2007 and 2011.	<a href="http://www.unav.edu/departamento/preventiva/predimed">http://www.unav.edu/departamento/preventiva/predimed</a>
71	POLCRIN	Nat	12	public	all diseases	Not available.	No website available.
72	PtCRIN	Nat	15	public	all diseases	Not available.	<a href="http://web.fcm.unl.pt/ptcrin">http://web.fcm.unl.pt/ptcrin</a>
73	REEM	Nat	15	public	multiple sclerosis	Not available.	<a href="http://www.reem.es">http://www.reem.es</a>
74	RIC	Nat	64	public	heart diseases	936 publications, 34 patents, 509 projects and 117 courses.	<a href="http://www.redcardiovascular.com">http://www.redcardiovascular.com</a>
75	RICET	Nat	20	public	tropical diseases	110 publications between 2007 and 2012.	<a href="http://www.ricet.es">http://www.ricet.es</a>
76	Red SAMID	Nat	13	public	neonatal diseases	8 ongoing clinical trials.	<a href="http://www.redsamid.net">http://www.redsamid.net</a>
77	RTICCC	Nat	73	public	oncology	11 clinical trials, 243 projects, 12 courses, 158 publications and 4 guides between 2003 and 2012.	<a href="http://www.rticc.org">http://www.rticc.org</a>
78	RIPPS	Nat	(PERENE, 19) (RMNMI, 29)	public	paediatric diseases	3 studies (PERENE).	<a href="http://www.ripps.eu/site/default/">http://www.ripps.eu/site/default/</a>
79	ROCRIN	Nat	6	public	all diseases	Not available.	<a href="http://www.rocrin.umfcv.ro">http://www.rocrin.umfcv.ro</a>
80	AGMT	Nat	130	private	oncology	22 ongoing clinical trials and 2 closed clinical trials.	<a href="http://www.agmt.at">http://www.agmt.at</a>



**Table 3** – List of the European Clinical Networks: acronym, national versus international, number of members, public versus private, target disease, relevant activities and website address (cont. 9).

	Acronym	Nat/ Inter	Members	Nature	Target	Relevant activities	Website address
81	SweCRIN	Nat	40	public	all diseases	Not available.	<a href="http://www.swecrin.se">http://www.swecrin.se</a>
82	SCTO	Nat	6	private	all diseases	4 articles between 2011 and 2014.	<a href="http://www.scto.ch/">http://www.scto.ch/</a>
83	SAKK	Nat	22	private	oncology	198 articles between 2008 and 2013.	<a href="http://sakk.ch">http://sakk.ch</a>
84	SPOG	Nat	9	private	paediatric cancer diseases	57 ongoing clinical trials in 2012. 306 articles between 2006 and 2013.	<a href="http://www.spog.ch">http://www.spog.ch</a>
85	SwissPedNet	Nat	8	private	paediatric diseases	Not available.	<a href="http://www.swisspednet.ch">http://www.swisspednet.ch</a>
86	TARN	Nat	Not available	public	Trauma	The network provides annual meeting and trainings. 86 publications between 1992 and 2014.	<a href="http://www.tarn.ac.uk">http://www.tarn.ac.uk</a>
87	UKCRN	Nat	all hospitals and primary care services in the UK	public	all diseases	UK Clinical Research Network Portfolio Database has 14251 studies (closed and ongoing) since 2006.	<a href="http://public.ukcrn.org.uk">http://public.ukcrn.org.uk</a>
88	UKPVG	Nat	10	private	paediatric vaccines	Not available.	<a href="http://www.ukpvg.org/ukpvg/internet/en/index.html">http://www.ukpvg.org/ukpvg/internet/en/index.html</a>

