Table S1. Rare disease activities in ERN ReCONNET countries

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| **Activities / Countries** | **Belgium** | **France** | **Germany** | **Italy** | **Portugal** | **Romania** | **Slovenia** | **The Netherlands** |
| **Centers of expertise for rare diseases** | National Plan for Rare Diseases receives an annual national funding (15 million euro per year).  Centres of expertise (university hospitals) have both federal and central designation. Some of them work under a convention and are recognised by the National Institute for Health and Disability (NIHDI). Among the others, covered diseases are: cystic fibrosis, metabolic diseases, neuromuscular diseases, and haemophilia. Three levels of networks for rare diseases: university hospitals; university hospitals and other surrounding hospitals; European level. Flemish Region authorities supported the Flemish University Hospitals in the recognition of rare disease networks. In October 2017 the first five networks were launched each of theme covering metabolic diseases, neuromuscular diseases, multi-systemic and cardio-vascular diseases, musculoskeletal and connective tissue diseases, and bone diseases. | Since 2004 France has a national plan for rare diseases (approved third plan 2018-2022 on July 2018). The plan provided the funding for about 131 expertise centres (reference centres for rare diseases) forming the first release of the national network for rare diseases. In 2008, the network was completed by the introduction of regional centres of expertise in close collaboration with the reference centres, but without dedicated resources. The regional centres cover the diagnosis, treatment and follow-up of the patients closer to where they live. | Centres of expertise for rare diseases were implemented by the federal structure of the healthcare system, with reference to a limited list of complex and rare diseases. Since 2012, high specialized outpatient care has been reinforced by the law provision of the gradual establishment of a new specialist care sector aimed to achieve seamless care provision between outpatient and inpatient settings.  Social-pediatric centres and university clinics for outpatient care are involved in the treatment of patients with rare diseases. | The Italian National Plan for Rare Diseases 2013-2016 was approved by a formal agreement by the State and the Italian Regions in October 2014. The Plan does not have dedicated funding source for rare diseases as the objective and actions planned are included within the basic health benefits, a minimum package of healthcare services available for all Italian citizens (Livelli Essenziali di Assistenza – LEA).  Since 2001 a national and regional designation process is in place for the identification of centres of expertise for rare diseases (hospitals). The officially-recognized centres designed by the Regions represent the national rare disease network for prevention, surveillance, diagnosis, access to treatments and the promotion of information and education activities about rare diseases. Criteria adopted by Italy for the designation of centres of expertise in rare diseases are EUCERD-EC expert group on rare diseases criteria. In addition, in 2008 the Italian Minister of Health identified various national centres of expertise for ultra-rare diseases. | Centres of expertise for rare diseases are recognized by an official act of the Minister of Health under a National strategy for rare diseases. | National Plan for Rare Diseases has been adopted at the end of 2013. The Plan was included in the National Healthcare Programs for the years 2015, 2016 and 2017 and funded through national legislation (not dedicated budget). A national network of medical genetics was established in 2014.  During 2016 nine healthcare providers have been accredited as centres of expertise for rare diseases. | The Plan for Rare Diseases has been adopted covering the period 2012-2020.  No official policies have been adopted for the designation of centres of expertise for rare diseases, and university medical hospitals have been considered the centres of expertise without a formal assessment. | The National Plan for Rare Diseases has been adopted in 2003, with a structured budget allocated.  Centres of expertise for rare diseases are designated following national criteria fully based on the EUCERD-criteria. |
| **Sharing information, patient support** | National level information on rare diseases is managed by the umbrella association for rare diseases organizations named RaDiOrg; the organization based on network of voluntaries managed both online and via post queries. | Information on rare diseases and orphan medicines has been developed by Orphanet, and a national helpline for patients was setup. | Information on rare diseases and orphan medicines has been developed by Orphanet, and a national helpline for patients was setup. | Orphanet operates with a national team producing information material and using the national website Orphanet Italy and Social Media Networks.  Moreover, a national helpline with a toll-free number managed by the National Centre for RDs and regional helplines are in place. | Information on rare diseases and orphan medicines has been developed by Orphanet.  An helpline is in place with private funding and only for the use of patients. | At national level a RDs dedicated helpline available for healthcare professionals and patients; this service is funded by the Romanian Prader Willi Association and it is part of EURORDIS’s Network of Helplines. | Public funded national rare diseases information helplines are in place for both patients and healthcare professionals (website, e-mail, telephone). | Orphanet operates with a national team producing information material.  National helpline is in place dedicated to the general public and healthcare professionals. |
| **Clinical Practice guidelines and best practice;**  **Registries** | Not produced at national levels.  The Central Registry for Rare Diseases is in place (all rare diseases).  Specific registries: Cystic Fibrosis; Neuromuscular Diseases. Registries are funded by the National Institute of Health and Disability Insurance. | Reference centres provided the specific clinical practice guidelines (*protocole national de diagnostic et de soins* – PNDS), that are clinical protocols defining the national standard of care for rare diseases in France.  Data from centers of expertise are organized at national level by the *Banque Nationale de Données Maladies Rares* | Practice clinical guidelines exist for some diseases i.e. cystic fibrosis, diagnostic of myopathy, congenital adrenal hyperplasia. | Clinical Practices Guidelines are produced and implemented at national level.  Rare registries:  NHS funds the National Rare Registry. Regional registries projects receive funding from NHS but not from the Regions.  Additional disease specific registries are funded by NHS through specific projects, or by the Regions, or by non-profit organizations or patients’ organizations. | Clinical Practices Guidelines are produced and implemented at national level.  No National or regional registries are in place. Disease specific registries are available. | No CPGs for rare diseases (at the date of 2016).  National or regional registries are missing. Disease specific registries are in place and managed by academia, clinicians or patients organizations. | At the present, Clinical Practice Guidelines have been adopted at national level for Fabry Disease, Haemophilia and Cystic Fibrosis.  Regional-level registries are in place and governed by dedicated legislation. | National Clinical Practice Guidelines for rare diseases are produced; a national policy for the development of CPGs, the adoption of CPGs and the implementation of CPGs is in place in The Netherlands. |
| **Access to healthcare services and orphan drugs** | At the end of 2016 about n. 78 ODs available.  Reimbursement decisions are taken by the Ministry of Health and the committee of clinicians. | Each PNDS contains indication on the services and products considered essential for the patients’ healthcare and may be reimbursed, included off-label products.  ODs reimbursement from 65% to 100%; often complementary insurance covers the difference.  ODs prescribed only in competence centers. Not specific funding for ODs. | Once authorized, all orphan medicinal products are fully reimbursed by statutory health insurance.  Not specific funding for ODs. | ODs are provided by the National Healthcare System following the same coverage for all other medicinal products.  At the end of 2016 about n. 89 ODs available.  Patients with rare diseases are able to obtain the exemption for healthcare services (they do not pay tickets for services and treatments). The exemption refers to the rare disease instead of to the services (due to complexity and variety of rare diseases). The exemption provision for rare diseases does not define the detail of the services and treatments that are free of charge but it provides the right of exemption for all the services within LEA, prescribed by expert physician necessary to confirm the diagnosis, appropriate for the disease monitoring and for the prevention of aggravation.  In general, drugs, integrated care, and prostheses are not included within rare disease exemption as they follow different specific regulations.  Moreover, the Regions include additional benefits for rare disease patients using their own financial resources; the benefits include services and treatments and some pharmaceutical products that for rare disease patients are provided free of charge under specific prescription protocols and pathways. | Since 2013, patients with rare diseases can request for a card. The main services linked are: ensuring access to relevant information to doctors and nurses on clinical data and recommendations regarding emergencies and urgencies acts; improving the integrated management of the disease to avoid delay, error and harmful procedures; a correct referral to Reference Centres, and the improvement of the continuity of care, between all the levels of care.  The National Health System covers all citizens covered for positive drugs decision on a national reimbursement list basis.  At the end of 2016 about n. 90 ODs available. | Health insurance does not cover the costs of all genetic tests. Some genetic tests are free of charge (for children and adults enrolled in the national health program for congenital malformations).  A national list of Orphan Drugs includes more than n. 60 products both commercialized and free of charge. | Specific programs and facilities are in place to support people with rare diseases as individual care plans including access to social and support services.  At the end of 2016 about n. 39 ODs available. | Orphan drugs are reimbursed or directly provided by the health system (100% reimbursed). Hospitals are financially supported for prescribing ODs. |
| **Organization of care** | Neonatal screening regulated by regional law.  Flanders region: n. 11 diseases covered;  French region: n. 13 congenital anomalies. | Neonatal screening available for 5 RDs; inequality access to tests. | Neonatal screening: available for 14 pathologies; screening and genetic testing mandatory but not specific RDs policies. | Neonatal screening: available for a number of inherited metabolic disorders for all newborn from 2016.  Rare disease patient pathway: it starts with a suspected diagnosis of rare disease formulated by a hospital physician or by a local healthcare service professional. The general practitioner (GP) or the territorial pediatrician sends the patient to one of the centre of expertise of the national network in order to finalize the correct diagnosis of rare disease. The patient with a rare disease can present a formal request to its local healthcare unit (ASL) in order to obtain the certificate of exemption and benefit for free of the services included within the LEA list. | Neonatal screening: available for about 26 diseases. | Not found. | Neonatal screening mandatory for Phenylketonuria and Congenital Hypothyroidism. | Neonatal screening: available for about 31diseases. |