

Building European Reference Networks in Health Care

28

Observatory
Studies Series

Exploring concepts and national practices in the European Union

Edited by
Willy Palm
Irene A. Glinos
Bernd Rechel
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**Willy Palm, Irene A. Glinos, Bernd Rechel, Pascal Garel,
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Foreword

Providing highly specialized and complex health care of quality is a challenge faced by all health systems. Medicine is constantly evolving and more innovation and technologies are now used in diagnostic techniques. A good response to this challenge therefore requires careful resource planning.

The common approach in European Union countries has been to allocate resources according to the level of complexity and the expected number of cases of any particular disease. This implies concentrating resources and cases, leading to the accumulation of experience and knowledge and the efficient use of costly technology and resources. Experience and knowledge are key in ensuring safe and high quality health care and, coupled with the efficient use of resources (economy of scale), essential for creating smart, responsive and sustainable health systems.

Establishment of referral networks or pathways, from the lowest to the highest level of complexity is inherent to the organization of all health care systems. However, there are currently neither agreed terminologies nor agreed standards when defining highly specialized centres (centres of excellence, expertise, reference, competence, etc.)

We will soon have a clearer framework at European Union level. The Directive on patient's rights in cross-border healthcare (2011/24/EU) provides, in Article 12, the mandate for the Commission, to define the criteria that the reference networks and health centres members of the networks should fulfil. This project is certainly ambitious and complex but I am convinced it will be a decisive step in the improvement of knowledge and the competitiveness of the European Union when dealing with highly complex pathologies.

The primary aim of European Reference Networks will be to benefit European citizens, allowing them to be referred, when needed, to qualified centres of expertise at European Union level. The European Reference Network will improve the capacity of local health-care providers to deal with highly complex diseases by making the knowledge and support of the centres working within a network accessible to them. Communication with members of reference networks and access to clinical and best practices tools in several domains

(clinical practice guidelines, protocols, telemedicine, etc.) will improve the capacity of local health providers to provide complex care to their patients as close as possible to their home, while guaranteeing high standards of care.

A necessary first step is to carefully and systematically analyse the current situation of reference networks and highly specialized centres in the different European Union countries. It is only by assessing existing models, and analysing experience and best practices, that the European Commission, in cooperation and coordination with Member States, can establish a logical, feasible and robust model of European Reference Networks for highly complex diseases in the European Union.

This study represents a valuable asset in the process of analysis and discussion of the future model of European Reference Networks to be defined in the European Union. It is based on a fruitful collaboration between the authors and the national health authorities to reflect the state of the art of this topic.

I would like to congratulate and thank all the people involved in the drafting of this study and I hope that readers will find this information relevant and useful.

Paola Testori

Director General

Directorate-General for Health and Consumers

European Commission

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List of abbreviations

AIM	International Association of Mutual Benefit Societies (Association Internationale de la Mutualité)
ARH	Regional Hospital Agencies (France)
BMBF	Federal Ministry of Research (Germany)
CCC	Comprehensive Cancer Centre (Czech Republic)
ChCC	Children's Cancer Centre (Czech Republic)
CHU	Centres Hospitaliers Universitaires (University Hospital Centres) (France)
CNMR	Centro Nazionale Malattie Rare (National Centre for Rare Diseases) (Italy)
CNT	Centro Nazionale Trapianti (National Transplant Centre) (Italy)
DG	Directorate General
EC	European Commission
EU	European Union
EUCERD	EU Committee of Experts on Rare Diseases
FJC	Federal Joint Committee (Germany)
GMP	good manufacturing practice
HLG	High Level Group
HNDP	Hospital Network Development Plan (Estonia)
HOPE	European Hospital and Healthcare Federation
HPSC	haemopoietic progenitors and stem cells
IHU	Institut Hospitalo-Universitaire (University/Hospital Institute) (France)
INCa	Institut National du Cancer (National Cancer Institute) (France)
ISS	Istituto Superiore di Sanità (National Health Institute) (Italy)
KST	Czech Transplantations Coordinating Centre
LHA	local health authority
NHS	National Health Service (England)
NNBC	National Network for Burn Care (England)
NRDC	National Rare Disease Centre (Hungary)
NSMC	National Specialized Medical Care (Sweden)
RCDU	reference centres, departments and units (Spain)
RDTF	Rare Diseases Task Force
RHS	Regional Health System(s) (Italy)
RNMR (Italy)	Rete Nazionale Malattie Rare (network for the treatment of rare pathologies)
SCG	Specialized Commissioning Group (England)
SHI	Social Health Insurance
SNS	Spanish National Health Service
SROS	Schéma Régional d'Organisation Sanitaire (Strategic regional health plan) (France)

SSNDS	Specialized Services National Definitions Set (England)
UMC	university medical centre
UMCL	University Medical Centre, Ljubljana (Slovenia)
WBMV	Wet Bijzondere Medische Verrichtingen (Special Medical Procedures Act) (Netherlands)

Introduction and objectives

In March 2011, after a political debate spanning more than ten years, Directive 2011/24/EU on the application of patients' rights in cross-border health care was adopted. This Directive aims to facilitate access to safe and high-quality cross-border health care within the European Union (EU) (Wismar et al., 2011), in accordance with the principles of free movement, while respecting the responsibilities of the Member States in organizing access to health care for their citizens. The Directive clarifies the rules of reimbursement for cross-border health care as well the conditions that need to be observed when providing these services. At the same time, it establishes a framework for future cooperation on health care between Member States.

One particular area of cooperation that was identified in the Directive is the development of European reference networks (ERNs) (Article 12). These networks are meant to improve access to and provision of high-quality health care to all patients who have conditions requiring a concentration of specialized resources or expertise and could also act as focal points for medical training and research, information dissemination and evaluation, especially for rare diseases (Article 54).

The European Commission (EC), which will support Member States in the implementation of this provision, is required to adopt a list of criteria and conditions for these ERNs as well as for providers wishing to join them. These criteria and conditions have to ensure that ERNs have the necessary knowledge and expertise, take a multidisciplinary and collaborative approach, and have links with research and training. They should also have the capacity to develop and disseminate good practice guidelines and expert information and implement outcome measures and quality control (Article 12.4). Before the Directive comes into force in October 2013, the EC is preparing a Delegated Act as well as implementation measures for evaluating the ERNs and facilitating the exchange of information and expertise. To support and advise the EC, a Cross-border Healthcare Expert Group was established with representatives from Member States.

In the light of these developments, in May 2011 the EC's Directorate General (DG) Health & Consumers asked the European Observatory on Health Systems and Policies to produce a preliminary scoping paper to explore national practices with regard to reference networks, looking at definitions used, criteria employed, and policies and legal frameworks developed. To develop this review a small working group was created that included staff from the Observatory and external experts. This group carried out a rapid assessment of existing information systems, documentation and published literature on the subject. In a second phase a range of key informants and country correspondents in various Member States were consulted, drawing on existing networks and including those within the Observatory and the European Hospital and Healthcare Federation (HOPE). Contributions of these experts were based on a set of questions to frame the type of information required and collect some basic evidence about how the concept of reference networks and centres is understood in Member States and how it is used as a tool for policy and the organization of health-care delivery, providing examples and illustrations. Following the presentation of the report to the Cross-border Healthcare Expert Group, its scope was extended to include more countries and additional input was provided.

This scoping paper, which was developed within a short time frame to inform the decision-making process begun by the Commission in early 2012, only provides a rough map of existing practices in Member States, highlighting the main information gaps and outlining key policy implications and challenges for developing the concept of reference networks at national and European levels. Ultimately we aim to provide a better understanding of the issues that may be encountered when implementing the Directive.

Historical background

The idea of establishing networks of excellence at the European level emerged very early in the aftermath of the first rulings of the European Court of Justice on the free provision of health services (cf. Kohll and Decker rulings). In a report looking at the implications of this jurisprudence, the idea of concentrating highly specialized clinical services in centres of excellence was promoted as an interesting avenue for developing a conscious, proactive policy towards cross-border care. Motivations were generally attributed to financial constraints of health-care systems and the need to realize economies of scale, as well as the objective of fostering safety and quality of care (Palm et al., 2000). The Standing Committee of HOPE is quoted in this report as saying:

... possible incentives will have to be devised for which the European Union, staying within its role under subsidiarity, could, for example, promote European

centres of excellence (the results of intra-European cooperation (not always evident) between hospitals concerning rare or very complicated diseases, or diseases which are too expensive to be treated within one particular country) ...

The concept of “centres of reference” (originally “centres of excellence”) was adopted as a way to describe one particular aspect of patient mobility. The paper on *Centres of reference/excellence* for the conference organized by the Spanish Presidency in Menorca on 31 May and 1 June 2002 stated: “the concept of European Centres of Reference is taken here to be synonymous with the concept of Centres of Excellence as discussed before in the context of the development of an internal European market in health”.

The 2003 high-level process of reflection on patient mobility and health-care developments in the EU identified the development of European centres of reference as an interesting mechanism for cross-border collaboration between health systems and the common sharing of resources (Rosenmoller, McKee & Baeten 2006). It invited the EC to carry out a mapping exercise and to explore how to foster networking and cooperation on these issues. It also suggested using the cohesion and structural funds to support the upgrading of infrastructure in potential centres of reference with existing high-level skills and capacities. At the same time, the high-level process warned that any system of European centres of reference should be flexible, objective and transparent and should leave choices as to its use open to the authorities responsible for the care concerned.

The actual work only started in 2005, via the High Level Group (HLG) on Health Services and Medical Care, which set up a specific working party on centres of reference. This working party regularly published its results in the reports of the HLG. The first and main objective was to define the scope and criteria for European centres of reference. Coordinating its activities with the Task Force on Rare Diseases, which in 2005 produced an overview of centres of reference for rare diseases, pilot projects were set up to test the feasibility of the approach. Different options were analysed for a procedure for identifying and developing European networks of centres of reference, including the call for proposals, the setting up of expert panels, the process of selection and the financial support to be provided. Some 11 pilot projects were supported under the Public Health Programme’s call for proposals in 2006 and 2007. Other projects were funded under the 5th, 6th and 7th Research Framework Programme. The experiences of these pilot projects, all located in the area of rare diseases, have been analysed in a recent report of the EU Committee of Experts on Rare Diseases (EUCERD) (EUCERD, 2011a).

All this work was then used in the EC’s consultation “Community Action on Health Services” of 26 September 2006. The idea of establishing a European

network of centres of reference was generally welcomed as a way to provide practical support to health systems in the provision of high-quality and cost-effective care. This was then the basis for the legislative process that started at this point.

In the context of the follow-up to the 2003 high-level process of reflection and the preparation of the cross-border care directive, the scope for promoting ERNs has always been kept broader than solely rare diseases. The working party within the HLG explicitly aimed to develop a general concept of a European system of centres of reference not limited to the area of rare diseases. Although ample reference is given in the new directive to the area of rare diseases, it is suggested that other conditions requiring specialized resources or expertise could also benefit from the idea of networking to provide high-quality and cost-effective care.

Despite the work that has been undertaken on the subject in various circles, including the high-level reflection process on patient mobility and health-care developments in the European Union, the EU HLG on Health Services and Medical Care and the Rare Diseases Task Force (RDTF), there is still a great deal of ambiguity as to the definition and scope of reference centres and networks. In addition, the terms “centres of excellence”, “centres of reference” and “centres of expertise” are often used inconsistently or interchangeably. The AIM report from 2000 (Palm et al., 2000) predicted the emergence of “large-scale centres of hospital excellence where intervention will be limited to specific fields and as a result there will be a catchment area for patients that will extend beyond the traditional geographical regions that the hospital formerly served”. The 2006 report by the RDTF acknowledged both the intuitive and ambiguous nature of the term “centre of reference” and defined it as “a place suitable for referring patients due to its expertise and scope of services” (RDTF, 2006). The two definitions respectively highlight the specialization and quality of services delivered in these centres. However, the focus has gradually shifted from identifying isolated European centres of reference, through establishing European networks of centres of reference, to creating ERNs connecting appropriate health-care providers and centres of expertise, thereby avoiding any hierarchy between the European and national levels. Simultaneously, the focus also seems to have shifted from “moving patients” to “moving knowledge and expertise”.

Definition, scope and dimensions

The lack of a common understanding of the exact meaning of the concept is also reflected in the way the concept is defined in Article 12 of Directive

2011/24/EU. Instead of providing a clear definition, the Article merely lists the objectives and characteristics for ERNs to qualify as such. They can pursue different objectives, ranging from the improvement of diagnosis and delivery, through the pooling and sharing of knowledge and expertise, to the concentration of resources or patients (Article 12.2). The functions and features of ERNs that are described (Article 12.4; emphasis added) are to:

1. have **knowledge and expertise to diagnose, follow up and manage patients with evidence of good outcomes**, as far as applicable;
2. follow a **multidisciplinary** approach;
3. offer a high level of expertise and have the capacity to produce good **practice guidelines** and to implement **outcome measures** and **quality control**;
4. make a contribution to **research**;
5. organize **teaching** and **training** activities; and
6. **collaborate** closely with other centres of expertise and networks at national and international level.

In view of the fact that no commonly accepted definition has been drawn up, a different approach was needed in this scoping exercise to try to capture what constitutes (European) reference networks. Based on the published literature and other written documentation that could be retrieved, five dimensions appeared to be particularly relevant to gaining a better understanding of reference networks, their functions and the different shapes they assume.

In essence, these dimensions are interlinked and relate to the following four questions (see Table 1).

- Who initiates the reference network and how is it structured? (governance)
- What is the purpose and motivation behind its creation? (objectives)
- What will it do? (function)
- What will it cover, both technically in terms of types of patients or interventions and geographically? (scope)

Although the evidence is still limited, these dimensions are useful to explore how existing variants of reference networks compare vis-à-vis the functions outlined in paragraph 4 of the Directive, whether they fulfil or exceed these functions, and what other elements characterize the networks. Annex I briefly describes examples of networks that we used to test and apply these five dimensions. In spite of the limited size of the sample, the cases provide a good illustration of the wide range and diversity of reference networks in Europe today.

Table 1 *Dimensions for reference centres and networks*

Governance	Objectives	Function	Material scope	Geographical scope
<ul style="list-style-type: none"> • Formal • Informal • Peer structure • Hub-and-spokes • Organic 	<ul style="list-style-type: none"> • Efficiency • Quality • Safety • (Equity) • Market position 	<ul style="list-style-type: none"> • Referral of patients • Transferring knowledge 	<ul style="list-style-type: none"> • Prevalence • Cost • Complexity • Rare • Critical • Chronic • Common 	<ul style="list-style-type: none"> • EU-wide • Transnational • National • Interregional • Regional



The rest of this section discusses each of the five dimensions in turn, giving the wider concepts emerging from the literature as well as specific examples, with the aim of broadening our understanding of what characterizes (European) reference networks.

Types of networks and governance

Network governance models (Lega, 2005) reflect the nature of the relationship between members of a network. These relationships can vary greatly, and are indeed what define different types of networks. According to Goodwin et al. (2004), “definitions [of networks] differ by whether links are loose or tight, weak or strong, bounded or unbounded, and formal or informal”. Based on the practical examples gathered for this exercise, we identified three broad types of networks that reflect the internal governance structure and the composition (membership) of networks:

- Networks can be composed of centres of reference/expertise with similar specializations (peer structure). These would fit under what Goodwin et al. (2004) identify as “enclave networks”, characterized by horizontal and egalitarian structures.
- Networks can have a hub-and-spoke structure, with one or more centres surrounded by other (non-specialized) providers. These reflect the “hierarchical networks” that Goodwin et al. (2004) characterize as having clearly defined rules and an organizational core that takes decisions.
- Networks can have an organic structure with a variety of members representing different kinds of health institutions.

These three types may be overlapping in practice. It is essential to understand the internal governance of a network and its membership – both are influenced by the actors that initiated the network and will in turn influence the purpose and

objectives that the network pursues. Some networks grow almost spontaneously through long-standing collaboration or based on a commonly recognized authority or reputation that a particular provider may have developed over time within a region, country or beyond. A network can also be deliberately initiated by a provider or a group of providers or by public authorities, based on either regulation or a business agreement.

Purpose and objectives

Health and financial objectives seem to encapsulate the basic rationales for the existence or creation of reference networks. As also demonstrated in the objectives listed in Article 12.2 of the Directive, the purpose of setting up a reference network is either to improve quality and safety of care by giving both health professionals and patients access to high-level, shared expertise in a given field, or to save costs by maximizing the cost-effective use of resources or realizing economies of scale. Equity can also be a motivation, since reference networks could allow Member States with insufficient numbers of patients or limited resources to invest in the necessary equipment and infrastructure to provide access to highly specialized services of the best quality for their population.

The compelling evidence that high volumes of care delivered (especially in terms of surgical interventions) improve health outcomes (in terms of mortality rates) (Begg et al., 1998; Birkmeyer et al., 2002, 2007; Dimick et al., 2002; Gouma et al., 2000; Kuo, Chang & Wright, 2001) is among the strongest arguments for concentrating certain medical procedures in a limited number of hospitals. Indeed, the debate on centres of reference and hospital networks is often closely linked to concepts and processes of specialization, concentration, centralization, regionalization and rationalization, as well as economies of scale, scope and know-how (Rechel et al., 2009a, 2009b; Saghatchian et al., 2008).

To improve treatments and outcomes, hospitals must reach a critical mass (of cases and patients) to ensure a sufficient level of activity and specialization (in certain clinical practices). Where hospitals become centres of reference for a wider catchment area, these processes that are taking place at the internal level of hospital organization set off wider, external processes whereby health services requiring particularly high levels of expertise and/or equipment are centralized or regionalized.¹ Both processes have clear managerial, territorial and economic implications for how health services and resources (public and private) are distributed over a territory, and may well lead to a rationalization of services. While the terminology is different, the logic of economies of scale, scope and

¹ The terms “centralization” and “regionalization” are rather confusingly often used synonymously in the literature on hospital networks and the impact of case volumes.

know-how (the latter being the result of “greater efficiency and efficacy in performing the work due to the experience of the worker” (Lega, 2005)) is similar, as unit costs are expected to fall with volume increasing.

According to one American study, three conditions must be present for centralization of care in centres of expertise to improve health: there must be safe transport links between the referring hospital and the receiving hospital; some hospital centres must show better results than others (e.g. regarding outcomes and quality); and patients must be referred to the better performing hospitals (Iwashyna et al., 2009). Yet the 2006 report by the RDTF (RDTF, 2006) mentioned that having to travel abroad to a treatment facility “can have several negative side effects” for patients as they would face an additional financial burden due to travel costs, as well as a psychological burden due to treatment being delivered in a foreign environment and language without family and community support. This suggests the importance of distance as a factor to be considered in the context of developing European reference networks and potentially finding ways of how best to manage patients having to travel within or even between countries. It also adds an argument in favour of moving knowledge, rather than patients.

However, it should not be forgotten that there may also be an underlying economic motive for establishing reference networks. Hospitals wishing to consolidate their position within a market or extend their catchment area, attracting more patients from a wider geographical area, may have an interest in self-declaring their expertise in a particular area. Looking at reference networks from a public health perspective differs from looking at them from a business perspective, where motivations for mergers and take-overs include market leverage, positioning and profits.

Functions and criteria

As mentioned before, the concept of reference networks can refer to moving patients as well as knowledge and expertise. In 2005 the HLG on Health Services and Medical Care expressed a preference for mobility of expertise (professionals, samples, information) but also stated that it should be possible for patients to travel to centres where this is necessary (Health & Consumer Protection DG, 2005). This seems especially to be the case in Member States with an insufficient number of patients with a particular medical condition or lacking technology or expertise to provide highly specialized services of high quality (Article 12.2.h of the Directive). The clearly identified aim is to organize at European level access to shared expertise in a given field for health professionals as well as for patients.

Even if the emphasis has gradually shifted from patient mobility to the mobility of knowledge and expertise between and within networks, these aspects cannot be entirely dissociated from each other. Clearly, centres of expertise involved in disseminating information, providing clinical support to providers, developing good practice guidelines on state-of-the-art treatment for specific conditions and contributing to research, epidemiological surveillance and training would also attract patients wanting to be referred to them, especially from Member States with an insufficient number of patients with that particular medical condition or lacking technology or expertise to provide highly specialized services of high quality.

Although the focus may vary to a certain extent, the expertise present within the network should be reflected through the multifaceted approach of dealing with the diagnosis and treatment of a particular condition. This is why the criteria for qualifying as reference networks generally refer to a whole set of different functions. Based on the report of the RDTF (RDTF, 2006), the HLG listed the following criteria to be fulfilled by European reference centres:

- appropriate capacities for diagnosing, following up and managing patients, with evidence of good outcomes, where applicable;
- sufficient activity and capacity to provide relevant services at a sustained level of quality;
- capacity to provide expert advice, diagnosis or confirmation of diagnosis, to produce and adhere to good practice guidelines and to implement outcome measures and quality control;
- demonstration of a multidisciplinary approach;
- high level of expertise and experience, as documented through publications, grants or honorific positions, teaching and training activities;
- strong contribution to research;
- involvement in epidemiological surveillance, such as registries;
- close links and collaboration with other expert national and international centres, and capacity to network;
- close links and collaboration with patient associations, where they exist.

These criteria demonstrate the specific features and approaches that would distinguish ERNs from other providers:

- a multidisciplinary approach in treating patients;
- coordination and continuity of care between different providers and stages;
- strong links between treatment, training and research;

- integrating evaluation and quality control;
- good communication skills;
- the involvement of patients and patient groups; and
- openness towards receiving new members in the network.

These elements are also to be found in the criteria described in Article 12.4 of the new directive. The HLG specified, however, that although an ERN should meet most of the above criteria, their comparative relevance would depend on the particular disease or group of diseases covered. New centres that meet all the conditions should be able to join a network at any time.

In addition to eligibility criteria, criteria will also need to be developed to designate the networks that demonstrate better value and quality in comparative terms. This may turn out to be even more challenging, especially as the assessment may have to focus on various functions at the same time. Quality, defined as “the degree to which health services increase the likelihood of desired health outcomes and are consistent with current professional knowledge” (IOM, 2001), is acknowledged to be multidimensional (see Table 2) and the choice of which dimensions to prioritize will very much determine the result. This is particularly so for the reference centres with very specific and highly specialized care in which quality can not only be measured on the basis of input and process indicators but also in terms of outcomes – adjusted by case–mix measures.

Technical scope (type of disease or intervention)

The scope of ERNs will also need to be defined in terms of the types of medical indications or interventions they will cover. Most reference networks focus on particular (groups of) diseases or conditions. Four categories (which are not mutually exclusive) have been identified in our review:

- rare conditions
- chronic conditions (e.g. diabetes)
- critical conditions (e.g. neonatal intensive care, burns, transplants, etc.),
- common conditions (e.g. cancer).

Different priority indicators can be used to determine the scope of reference networks.

- Most common is the frequency or prevalence of a certain medical condition in the population. This is the case with rare diseases (i.e. serious, chronic and often life-threatening medical conditions). As shown in Table 3, the number

Table 2 Dimensions of quality of care

Donabedian (1988)	Maxwell (1992)	United Kingdom Department of Health (1997)	Council of Europe (1998)	NLHI of the JCAHO (2006)	Institute of Medicine (2001)
Effectiveness	Effectiveness	Effectiveness	Effectiveness	Effectiveness	Effectiveness
Efficiency	Efficiency	Efficiency	Efficiency	Efficiency	Efficiency
Access	Access	Access	Access	Access	–
Safety	–	–	Safety	Safety	Safety
Appropriateness	Appropriateness	–	Appropriateness	Appropriateness	–
Equity	Equity	(Equity)	–	–	Equity
–	–	Timeliness	–	Timeliness	Timeliness
–	Acceptability	–	Acceptability	–	–
–	Respect	–	–	–	Respect/
–	Choice	–	–	–	Patient-centredness
–	Information	(Satisfaction)	Satisfaction	–	–
Health improvement	–	Health improvement	–	–	–
–	–	–	–	–	Continuity
–	Technical competence	–	Efficacy	Availability	–
–	Relevance	–	–	Prevention/early	–
–	–	–	–	detection	–

Sources: Donabedian, 1988; Maxwell, 1992; United Kingdom Department of Health, 1997; Council of Europe, 1998; IOM, 2001; JCAHO, 2006.

Note: NLHI: National Laboratory for HIV Immunology; JCAHO: Joint Commission on Accreditation of Health Care Organizations.

of patients with rare diseases varies widely between Member States due to the different sizes of population. Usually, the prevalence threshold is not more than five affected persons per 10 000. However, some countries apply much more stringent parameters (e.g. the United Kingdom: 2/100 000), which can decrease the nominal number of rare conditions considerably.

- Other parameters could be the cost per treatment or per patient or the investment cost for specific centres or units. This relates to interventions involving highly specialized and very expensive equipment and technologies.
- Another factor could be the complexity of a case requiring specific expertise or multidisciplinary skills as well as sufficient experience to ensure high quality and safe conditions for certain patients or procedures. This can translate into specifications as to the type of qualifications available, thresholds for minimum volumes of activity, or even limiting prescription of certain medicines to specialized centres.

Table 3 Selected rare diseases sorted by frequency per 100 000 population with estimated number of patients per country (selection)

Country	Erythropoietic protoporphyria 50/100 000	Systemic sclerosis 20/100 000	Cystic fibrosis 12/100 000	Gaucher's disease 1/100 000
Germany	41 250	16 500	9 900	825
Finland	2 600	1 040	624	52
Malta	200	80	48	4
Romania	10 850	4 340	2 604	217
Slovenia	1 000	400	240	120
United Kingdom	29 650	11 860	3 558	593

Source: Busse, van Ginneken & Wörz, 2011

Geographical scope

The geographical scope of networks can range from the regional to the European, in the latter case involving several countries. This geographical reach of networks is of particular relevance to patient referrals, as it has implications for the distance that patients have to travel. Five broad geographical levels of networks can be distinguished:

- EU wide: across all EU Member States
- transnational: between two or more countries
- national: within one country
- interregional: between two or more regions of one country
- regional: within one region of a country.

Mapping national practices and experiences

A key methodological challenge in conducting this review was to adopt a definition of what should be understood as reference networks. Given the lack of a clear consensus on how reference networks should be conceptualized or framed, we adopted a working definition in order to cover all relevant national practices and experiences. This working definition broadly relates to the functions and features that are generally attributed to reference networks, even if they would not necessarily be termed as such. A deliberate choice was made not to narrow the working definition too much, so that we could capture the variability of the concept in different countries and settings and explore a wider range of implications. In this sense, reference networks and centres are defined here as:

- EU-wide, transnational, national or regional provider networks and centres
- to which patients are referred from within a defined catchment area
- or that provide clinical support to other providers
- on the basis of a certified or generally recognized high level of expertise
- in a specific area of disease or for complex or highly technological interventions
- that require a particular concentration of resources and knowledge.

Typically, the networks would receive some formal or informal recognition on the basis of demonstrated skills of their members and follow a series of standardized processes in communicating, involving and empowering patients, linking practice to research, developing guidelines and protocols and evaluating outcomes.

Based on this working definition of reference networks, we developed a set of questions (see Box 1) and consulted a series of key informants and national correspondents in a sample of Member States, to collect evidence on national practices and experiences relating to reference networks.

Box 1 *List of questions*

- Definition and scope
 - To what extent are the concepts of reference centres and/or networks (or any similar concepts) known in a particular Member State?
 - Are they generally limited to specific pathologies, technologies and techniques?
 - What are the main areas commonly linked to the concept (e.g. rare diseases, transplants, burn treatment)?
 - What functions and features are generally used to define them?
- Policies and processes
 - Is the development of reference centres/networks a formal process steered by health system authorities or funding agencies, or is it rather a voluntary process initiated by the provider side?
 - To what extent is the diagnosis and treatment of specific diseases or highly specialized interventions limited to a restricted number of specific centres or providers?
 - Is there a formal system of authorizing/certifying/licensing/accrediting specific centres/providers as reference centres or networks?
 - Is the awarding of a special status related to general criteria (e.g. quality monitoring, treatment protocols, patients' rights, communication, continuity of care, etc.) or specific criteria (e.g. minimal treatment thresholds, use or availability of specific technology or equipment, etc.)?
 - What are the implications in terms of financing, quality assurance, information exchange, research and training, evaluation, etc?
 - To what extent are these reference centres/networks linked to the development of practice guidelines?
- Impacts and outcomes
 - What are the main drivers for developing reference centres/networks?
 - What have been the main impacts and challenges so far?
 - Can any policy implications and lessons be drawn at this point?
- References
 - To specific reports
 - To specific legislation

The information retrieved from our contacts was complemented by some illustrative examples of networks emerging from our literature review.² However, the limited time frame available for this exercise constrained the number and range of countries included, as well as the depth of the analysis carried out and the extent to which information could be standardized for comparative purposes. The assessments aim to provide a first approximation of the range of existing issues and practices in Member States.

Baltic states

In the Baltic states the concept of reference centres and networks has not yet been officially embraced. Highly specialized care is mainly centralized in the few main hospitals of each country.

As their respective populations are too small to sustain highly specialized services, the Baltic states are also considering how they may share resources and expertise. Within the Baltic Council of Ministers' Task Force for Health a subgroup was set up on the "Establishment of joint specialized medical centres for a more efficient use of professional skills in the Baltic states". Based on the analysis of existing patient flows between the Baltic States, its aim is to promote collaboration between clinics in these countries.

Estonia³

According to the Hospital Network Development Plan (HNDP) (approved by the Government in spring 2003) there are 19 acute care hospitals in Estonia, including 12 general and local hospitals, 4 central hospitals and 3 regional hospitals (see Table 4). There are three regional hospitals in Estonia, two of which (covering both secondary and tertiary care) each serve an area with about 500 000 people: North Estonian Regional Hospital and Tartu University Hospital. The third regional hospital, Tallinn Paediatric Hospital, provides tertiary medical services to children living in north and west Estonia. There are four central hospitals that provide some tertiary but mainly secondary care. Each serves an area with about 200 000 people.

Local and general hospitals provide secondary care for common conditions and have between 50 and 200 beds. There is at least one local or general hospital in each of the country's 15 counties. The exceptions are the counties of Tartu, Pärnu and Harju where, according to the HNDP, there will be no separate general hospital, as secondary services will be provided by the respective central

² More detailed information on national practices can be found in the various reports produced by the Rare Diseases Task Force and its successor, EUCERD.

³ References: National Audit Office of Estonia (2010); Koppel et al. (2008).

Table 4 Acute care hospital network in Estonia

Regional hospitals	Central hospitals	General hospitals	Local hospitals
North Estonia Medical Centre and Tallinn Children Hospital	East Tallinn Central Hospital	Järvamaa Hospital	Jõgeva Hospital
Tartu University Hospital	West Tallinn Central Hospital	Kuressaare Hospital	Põlva Hospital
	East-Viru Central Hospital	Läänemaa Hospital	Rapla Hospital
	Pärnu Hospital	Rakvere Hospital	
		South-Estonian Hospital	
		Narva Hospital	
		Viljandi Hospital	
		Valga Hospital	
		Hiiumaa Hospital	

Source: National Audit Office of Estonia, 2010

or regional hospital. A local hospital is deemed necessary in county centres or population centres that are more than 70 km away from a general, central or regional hospital (Koppel et al., 2008).

The level of care provided in each level of hospital is determined by the Ministry of Social Affairs' decree on "Requirements of hospital types". This decree established minimum standards for inputs and care provided in each type of hospital, although without specifying standards for specific conditions. According to the decree, the highest-level care is provided in regional hospitals.

There are no legislative acts specifying referral rules, but some clinical guidelines recommend patients with specific conditions be referred from lower- to higher-level hospitals (e.g. patients with acute myocardial infarctions are recommended to be referred to higher-level hospitals, where angioplastic procedures are available).

One of the latest developments on reference centres is related to the Strategy for Quality of Cancer Care⁴, which defines requirements for centres of excellence in cancer care. Centres of excellence are required to be able to provide multimodal cancer care, including chemotherapy, radiotherapy and surgery.

Lithuania

In Lithuania, the concept of reference centres and networks has not yet been officially embraced. Highly specialized care is mainly provided in two multiprofile

⁴ Available in Estonian at www.sm.ee (http://www.sm.ee/fileadmin/meedia/Dokumendid/Tervisevaldkond/Tervishoid/Eesti_v%C3%A4hiravi_kvaliteedi_tagamise_n%C3%B5uded.pdf).

university hospitals as well as a few specialized tertiary care institutions, such as the national oncology centre. These institutions, which are directly accountable to the Ministry of Health, fulfil all the basic requisites of reference centres: a multidisciplinary approach and high level of expertise, highly specialized services with a broad spectrum of diagnostic technologies, treatment, follow-up, teaching, training, research facilities, and international collaboration in the field of clinical practice and research. A mandatory licensing mechanism for all health facilities has been established by the State Accreditation Agency.

While in general patients are given free choice of providers and providers of tertiary care are competing for patients, rules for referral are only gradually being put in place. Under pressure from the global economic crisis, Lithuania has carried out a hospital reform aiming to centralize highly specialized services in university and national-level hospitals. Based on a threshold of surgical and obstetric activities, patients are redirected to hospitals of an appropriate level. However, ongoing efforts to establish stable referral systems are perceived by some observers as attempts by certain providers to establish a dominant market position.

Recently, a pilot centre of reference for cystic fibrosis has been established in a consulting room of one of the university clinics. The centre supervises about 50 cystic fibrosis patients per year. Before, cystic fibrosis patients could be treated by any pulmonologist.

As a way to address rare and extremely difficult medical cases, patients can be sent abroad for treatment. Each case is assessed by the University Hospital Council of Specialists, based on the capacity available in Lithuania to diagnose or treat the case. A special commission in the Ministry of Health advises the patient on the referral and confirms the compensation to the hosting hospital. The Compulsory Health Insurance Fund refunds the costs. About 50 to 60 patients per year are sent abroad for treatment, mostly for genetic or metabolic disorders, transplantation or surgical cases.

Latvia

The situation in Latvia is similar. Latvia has a special financial programme for specialized treatments or treatment of specific diseases, such as coronary angioplasty and multidrug-resistant tuberculosis, which are available in a restricted number of centres. Although their specific status is linked to postgraduate training and research activities, no specific criteria are applied for these hospitals.

Belgium

Structuring health-care delivery

Belgium has no formal referral system for health care that designates the provision of certain types of care to different types of health-care providers. There is a clear distinction between primary, secondary and tertiary care. Top-level clinical care, requiring a particular concentration of multidisciplinary expertise and equipment, has traditionally been developed in teaching hospitals and some larger hospitals. As part of the hospital planning and accreditation process, certain types of care (such as transplants, burns, neonatal intensive care, paediatric oncology) can only take place in a limited number of centres or units; and referral, as well as sharing of expertise, is specified in the context of collaboration agreements.

Despite the lack of a more comprehensive referral mechanism, policy has given more attention in recent years to a better integration between different levels of care and more multidisciplinary cooperation through the creation of care programmes, patient pathways and networks.

- Since 1999, hospital accreditation has been gradually organized around care programmes (hospital activities organized around certain pathologies or patient groups). For each care programme, legal criteria have been set out relating to the target group, nature and content of care, minimum activity level, necessary infrastructure, required medical and nonmedical staff and their required expertise, standards for quality and quality monitoring, economic standards and geographical accessibility criteria. For each care programme, a college of expert physicians was created. These colleges are responsible for developing, assessing, implementing and disseminating good practice guidelines, and for developing quality indicators to assess clinical practice in the care programmes. However, they carry out no field visits by peers to validate implementation efforts and results, despite the fact that they are legally allowed to do so. It is therefore not clear which centres (teaching or non-teaching) provide higher standards of care. A distinction is made between basic programmes for common conditions and specialized programmes for rarer conditions, which will not be available in every hospital. At present, there are care programmes for reproductive medicine, cardiac pathology, oncology, and geriatric and paediatric activities. A specialized care programme for breast cancer has a minimum annual number of 150 diagnoses.
- Since 2000, more than 450 clinical pathways for hospital care (i.e. a collection of methods and tools to guide the members of a multidisciplinary and interdisciplinary team towards patient-focused collaboration for a specific

patient population) have been under development. In 2003 two Belgian universities (Katholieke Universiteit Leuven and Université Catholique de Louvain) and the Dutch Institute for Health Care Improvement established the Network of Clinical Pathways, linking over 100 care institutions. This network provides education on clinical pathways and related concepts (such as patient safety, quality control, multidisciplinary teamwork, operations management and evidence-based medicine); supports multidisciplinary teamwork, in-hospital projects on pathways and multicentre research projects and benchmarking; and promotes research and international collaboration in this field. Since 2009, the federal government has also promoted care pathways in ambulatory care for the treatment and follow-up of certain chronic diseases to enhance the collaboration in care between the patient, the GP, the specialist and other caregivers. So far, pathways for chronic renal failure and type 2 diabetes have been started.

- The concept of pathways is often complemented by the concept of networks, as a way to enhance collaboration between caregivers, care organizations and services, and coordinate care for a specific target group. These multidisciplinary networks are especially found at local, outpatient level. Specific networks have been set up in the field of palliative care and mental health services.

Developing the concept of reference networks

More formally, the concept of reference networks is mentioned in Article 14 of the Federal Hospital Act. It provides for the specification of characteristics for designating reference centres. Even though the Minister in 2005 indicated the intention to implement this article, it has not been done so far. The lack of a clearly defined role for university hospitals, the risk of the criteria being contested, and the possible negative effects for cooperation between hospitals were considered significant obstacles by the National Hospital Council. At the same time, in the absence of any systematic quality monitoring system for care processes, there are no tools for distinguishing between centres with recognized expertise and self-declared ones, which often build their excellence around the acquisition of specific highly specialized equipment or innovative technologies. Several hospitals decided to validate the quality of their services by external institutions accredited by the International Society for Quality in Health Care (such as the Netherlands Institute for Accreditation in Healthcare and Joint Commission International).

Currently, the concept of reference centres in Belgium is generally linked to the treatment of rare diseases and chronic conditions. The National Health Insurance Institute concludes specific agreements with these reference centres and provides

for a fixed daily, monthly or yearly rate. These agreements define the therapeutic project, including the target group, the composition of a multidisciplinary team of providers, and the package of care. Reference centres are selected through spontaneous applications or calls, on the basis of criteria established by specialists and adopted by the National Health Insurance Institute's college of medical directors. These criteria take into account the multidisciplinary approach, the expertise of the centre's team members, the number of patients treated and monitored, as well as the geographical distribution and networking with local providers. There are no clear criteria for selecting the type of pathologies. In addition to eight centres for human genetics, there are some 25 multidisciplinary reference centres specializing in neuromuscular disorders (6), refractor epilepsy (4), cystic fibrosis (7), and rare monogenetic hereditary metabolic illnesses (8). Other centres specialize in the treatment of chronic diseases, such as AIDS, chronic breathing disorders, chronic fatigue syndrome, chronic pain, autism, brain paralysis or cerebral palsy and spina bifida. As many of these agreements are developed ad hoc, often at the centre's request and without any systematic quality assessment and control, consideration is being given to organizing funding of these reference centres as specific care programmes for rare diseases, which would allow stricter standards and criteria, quality control, better containment of the number of centres and integrating them into a national network.

This also fits with the National Plan for Rare Diseases that has been in the process of preparation by the federal government since 2008, based on EC recommendations. The task was entrusted to the Fund for Rare Diseases and Orphan Drugs, which submitted a full plan in 2011. One of the main concerns is the fragmentation of specialized services and the lack of coordination and formal recognition, leading to late diagnosis and sub-optimal treatment. Therefore, one of the first measures proposed under this action plan is the creation of centres of expertise for a specific rare disease or group of rare diseases. The centres of expertise would be required to develop, implement and promote best practice guidelines for diagnosis and treatment, enrolling patients onto a national register, creating networks with both local providers and European centres, developing training and research, and interacting with patients' organizations and the media. Patients suffering from rare conditions that cannot yet be diagnosed, or for whom no expertise is available in Belgium, would be referred to liaison centres for multidisciplinary consultation and eventually to a centre of expertise elsewhere in Europe. The Plan also proposes a set of accreditation criteria for these centres, which would replace the reference centres accredited under the health insurance system. In the context of the Directive on the application of patients' rights in cross-border health care, a framework for reference networks is being developed by the federal administrations of health insurance and public health.

Similarly, the National Cancer Plan, which was introduced in 2008, also aims to increase multidisciplinary working and improve coordination between health-care providers. One of the actions it envisages is the establishment of a Belgian Cancer Centre. Its tasks will consist of centralizing all the available expertise and data to improve the fight against cancer; coordinating, supporting and evaluating all initiatives in this field; promoting the exchange of information; assessing and disseminating good practice guidelines; and evaluating the National Cancer Plan and cancer policy. The centre is designed to facilitate and improve communication between health-care providers.

Czech Republic

Developing a network of centres for rare diseases

Currently, there is no specialized reference network in the Czech Republic, although specialized centres for Gaucher's disease, cystic fibrosis, Fabry's disease, pulmonary hypertension, hereditary ataxia, rare tumours and skin disorders do exist. The activities of these centres, such as the Institute for Inherited Metabolic Disorders in Prague, and the Centre for Epidermolysis Bullosa (a Czech branch of Debra International) at the University Hospital Brno, are coordinated under the National Coordination Centre for Rare Diseases.

The recently adopted Act 372/11 on Healthcare Services sets out the general conditions for the establishment of centres for highly specialized health care, which also assumes their possible connection to European reference networks. The functioning of these centres will be subject to further expert assessment according to national strategies on specific diagnoses (such as the National Rare Diseases Action Plan).

In June 2010 the Czech government adopted a ten-year strategy (2010–2020) for rare diseases. The strategy is to be set out in more detail in a three-year national action plan. To develop this plan a dedicated task force was created: the Interministerial and Interdisciplinary Commission for Rare Diseases. It consists of leading rare diseases experts, biotech industry representatives, lawyers, representatives from the State Institute for Drug Control, patients' representatives, medical statisticians, health insurance representatives and representatives from the Ministry of Social Affairs.

The care of patients with rare diseases is to be concentrated in 10–20 centres under the umbrella of the National Coordination Centre in Prague and Brno. This centre was expected to assure its funding through the Norway Grants scheme by June 2012. A major objective is to identify additional *de facto*

centres of expertise and propose their transformation into *de jure* centres by the Ministry of Health.

The Czech Cancer Centre Network

The Czech Republic also has an extensive network of cancer centres. Since January 2006, the Ministry of Health and the Czech Society for Oncology have accredited a network of 18 medical centres to which the most complex and expensive care in the field of diagnostics and treatment of tumours is transferred. The network consists of dedicated medical facilities bearing the status of Comprehensive Cancer Centre (CCC) and Children's Cancer Centre (ChCC), where patients are guaranteed complex care in the area of diagnosis and treatment of tumours. The core of a cancer centre consists of a cancer care facility that is comprehensively equipped to provide radiotherapy and systemic treatment (including drugs that can only be administered in the CCCs and ChCCs), both to hospitalized patients and to outpatients treated in short-stay wards.

In 2008, audits were carried out at these CCCs by the Ministry of Health to assess the quality of care provided and compare quality levels between the CCCs. Not all centres were able to fulfil the criteria and so the audit resulted in the reduction of the number of centres from 18 to 13 (of which two are also paediatric-oncological centres and six haemato-oncological). The innovative, targeted anti-cancer treatment is assured and reimbursed in all 13 CCCs.

To be accredited, a centre must fulfil a series of meticulously defined criteria (published in the Ministry of Health Official Journal No. 7 of 28 November 2008) on staffing (e.g. number of medical specialists, nurses, radiological technicians and biomedical engineers), technical equipment and medical requirements and responsibilities (e.g. on interdisciplinary cooperation; education, research and training; diagnostic methods; surgical and radiation treatment; palliative care; follow-up; clinical trials; participation in the regional network of cancer care facilities, etc). For the centres specializing in haemato-oncology, minimum annual numbers of patient cases are also established.

The Czech Transplantations Coordinating Centre

The Czech Transplantations Coordinating Centre (KST) is an organizational unit of the state, established by the Ministry of Health under the Transplantation Act (No. 285/2002 Coll., as amended). KST works under direct governance of the Ministry of Health in the field of arrangement and intermediation of transplants, being assigned several basic tasks.⁵

⁵ The main responsibilities of KST are set out at <http://www.kst.cz/web/tasks-en.php>.

Denmark⁶

Specialized hospital functions

The Health Care Act of 2007 profoundly changed the Danish health-care landscape by dividing Denmark into five hospital regions. Each hospital region owns and operates public hospitals and is in charge of hospital planning. Following the creation of the five hospital regions, efforts were stepped up to decide where various types of hospital care would be provided and a national master plan of specialized hospital services was implemented in 2010–2011. The plan is being monitored; revision will take place every three years with smaller adjustments being possible when appropriate.

The Health Care Act gives the National Board of Health mandate to define the requirements and approval criteria applicable to the so-called specialized functions. Specialized functions represent some 10% of all hospital services, the remaining 90% being considered basic functions. Specialized functions can involve prevention, diagnosis, treatment, rehabilitation and/or control of diseases or conditions where services are of considerable complexity and presuppose the presence of several multidisciplinary functions/partners, where the diseases or the health system's services are rare and therefore create a need for concentration of experience and/or which are particularly resource intensive. (Sundhedsstyrelsen, 2012). The main guiding criteria are thus complexity, rarity and resource allocation.

A specialized function can only be delivered at a department of a public or private hospital that has been recognized for that purpose, effectively making the facility a regional or a national centre of reference.

Out of 36 recognized specialties, some 1100 specialized functions have been established. These fall into two groups depending on the complexity, rarity and resources required.

- **Regional functions**, taking place at one to three hospitals per region, showing some level of complexity, are relatively infrequent and/or require considerable resources, such as collaboration with several other specialties.
- **Highly specialized functions**, taking place at one to three hospitals countrywide with a high level of complexity, are infrequent and/or require considerable resources, such as collaboration with several other specialties.

Criteria taken into account to evaluate whether a hospital department can be approved for performing a specialized function are divided into core professional criteria (capacity and stability; volume, experience and expertise; competence; collaboration and facilities; quality and documentation; collaborative care and

⁶ Reference: Sundhedsstyrelsen, 2012.

continuity of care) and secondary criteria covering research, development and education, assessment of new technologies and treatments, and collaboration. Other factors such as geographical distribution, regional characteristics and national capacity are also considered as part of the wider national context. Public and private hospitals are assessed on the same criteria. Hospitals may only perform the functions that they have been recognized to do by the National Board.

By late 2010, 2500 hospital departments had been recognized to perform highly specialized functions. Some 75 functions such as decompression sickness, intrauterine blood sampling, extremely dangerous psychiatric patients, and Wilson's disease, are only present at one treatment centre in the country. For a small number of specialized functions, such as small intestine transplant, particle radiotherapy, fetal surgery, and extracranial to intercranial bypass, patients have been referred to hospitals outside Denmark.

The main challenges, according to the health authorities, are the approval of good clinics (as opposed to those good at writing applications), finding the right national balance in terms of geographical coverage and capacity, and monitoring and evaluating the system.

Finland⁷

From voluntary networks to a more formal framework

Finland is a sparsely populated country with a relatively large territory, so despite the decentralized system it has been both natural and necessary to gather medical know-how in a few centres to provide quality treatment. Each of the country's five university hospitals provides a more or less full-scale spectrum of highly specialized services. University hospitals are nationally responsible for providing the most demanding and expensive care and treating rare illnesses. This network of university hospitals, independent as they may be, has in reality served as the Finnish model of reference networks so far.

Public health-care providers are not formally accredited in Finland but they are inspected and monitored by the national regulatory authority (Valvira). For the limited number of private sector providers a formal licensing procedure performed by Valvira is required. Hospitals until recently did not have to comply with general or specific criteria in order to be awarded a certain status. However, an entirely new decree is now being considered that will indicate (at least indirectly) the volume and quality criteria for hospitals providing acute and emergency care.

⁷ References: National Institute for Health and Welfare, 2012; Meretoja. 2011; Ministry of Social Affairs and Health, 2010; Tapper, 2011; National Institute for Health and Welfare, 2010.

A number of highly specialized, costly and/or rare treatments, methods or disease groups have been centralized in one to three centres, usually connected to a university hospital, by a governmental decree. A governmental intervention also became necessary after the bankruptcy of the Rheumatism Foundation Hospital in Heinola in March 2010, which had traditionally been the centre of excellence for paediatric rheumatology. Despite these limitations, some criteria are considered “guidelines” and not followed precisely.

There are also voluntary mutual agreements of centralization between hospitals belonging to a certain university hospital district, or even nationwide between university hospitals. Some centralized services have been provided by nongovernmental organizations (NGOs), such as rehabilitation services for neurological diseases, and were then commissioned by municipalities and hospital districts.

The main areas linked to reference centres include rare (paediatric) diseases, transplants, very severe burns, some complicated surgical treatments (e.g. cleft palate), and traumatic spinal injury. The focus appears to be more often on the pathologies and the expertise needed to treat these patients by multi-professional teams rather than the specific technologies or physical facilities required. However, the process of defining what care should be provided by reference centres has so far not been systematic.

Until recently, voluntary reference network agreements or decisions to centralize health care at national level were mainly based on discussions between the university hospitals and specialist associations, without much government involvement. However, the situation is now changing as there are government-supported actions to build more formal reference networks for cancer, rare diseases and perhaps other areas too. The forthcoming health and social care reform will provide the legal basis by enforcing the legal status of the five university hospital districts and by strengthening state governance and/or financing of the reference networks (to be determined in more detail by the end of 2012).

Being designated as reference centre does not have any financial implications: each centre is financed through treatment (patient) fees (based on diagnosis-related groups whenever applicable). Nor are reference centres involved with the development of practice guidelines, as current national guidelines are created and updated by independent medical associations (which is unlikely to change).

Know-how, research and finance are the main drivers for developing reference centres and networks. In the future, the very uneven geographical distribution of the ageing population, available skilled personnel and other resources may

be a driver for Finland to reshape its health-care system. The tendency is from decentralization to a more structured provision of specialized services. This opens a window of opportunity to consider new kinds of reference networks. However, the municipalities (now more than 300, but soon maybe only 100–150) continue to have the main responsibility for organizing and financing all health care even in the future.

The main challenges are very long distances (from the patient's perspective) and personal opinions of some professionals (lobbying against centralization). From the perspective of some municipalities, reference networks may be seen as a significant and unwanted government intervention. Thus, a stronger legal and financial basis and national consensus is clearly needed. As criticism is to be expected, it has to be demonstrated that reference networks would not contradict the core values of universality and equity, as well as the need to reduce socioeconomic health gaps. The networks should also not be seen as a means to set health priorities.

France

Hospital organization and planning

As in many other European countries, the French public hospitals are hierarchically organized. The most specialized ones are those to which patients are referred from within a defined catchment area and which provide clinical support to other providers on the basis of a certified or recognized high level of expertise in a specific group of diseases or for complex or highly technological interventions and that require a particular concentration of resources and expertise.

The 1958 law that created teaching and research hospital centres (*Centres Hospitaliers Universitaires* (CHU)) arose from this idea of allocating different tasks to hospitals with different skill levels, devoting to the highest level (the CHU) the highest level of complexity. The 1970 hospital law crystallized this concept by defining three levels of public hospitals (regional, general and local), detailing what could be found in terms of medical specialties and equipment at each level, implicitly creating a referral mechanism.

- The 32 Regional Hospital Centres provide a series of highly specialized diagnostics and treatments thanks to specialized staff and high performing equipment. The Regional Hospital Centre serves as a resource for other institutions in the region. In practice, the Regional Hospital Centre also provides day-to-day care for the local population. Indeed, they account for more than one-third of the activities of the French public hospital sector.

As part of an agreement with one or several training and research units, 30 Regional Hospital Centres have Regional Teaching Hospital status (*Centre Hospitalier Régional Universitaire* (CHRU)). They therefore perform a triple role: patient care, teaching and research.

- General Hospital Centres account for over half of hospital beds and the majority of public sector daily admissions. They perform diagnoses and provide a series of treatments linked to acute conditions in the medical, obstetrics and surgery fields. They also provide follow-up, rehabilitation and long-term treatment.
- The formerly called local hospitals account for a third of public hospitals. Usually located in rural municipalities, they provide short-term basic medical treatment. They comprise the first level of hospital care and are also specialists in medium- and long-term stays for follow-up and rehabilitation treatment, or care for dependent elderly people and in-home care. Referral works both ways from lower to upper and from upper to lower levels. The hospitals themselves are favourable to the concepts of hospital hierarchy, networking and expertise, which are present in various policy documents (Romatet, 2002). For instance a CHU cannot significantly cover all healthcare, research and innovation domains.

Hospital planning can be perceived as a way to establish a division of labour and optimize the referral of patients. The Regional Public Health Organization Programme (SROS) is a planning tool that sets patient care priorities at the regional level over a period of five years, with the aim of rationalizing hospital treatment provision in the region and improving the quality of treatment. The programme oversees the gradual organization of specialist platforms. Regional Hospital Agencies (ARH) were responsible for allocating the hospital budget in their region, delivering, authorizing, and promoting cooperation between public and private care institutions. As part of the latest hospital reform, ARHs were replaced by Regional Health Agencies (ARS) in 2010; those agencies now manage regional health-care policy within a broader scope, including the social sector.

Hospital collaboration and networking

The 1996 social security reform opened up the possibility of developing forms of provider networks “*réseaux*” at regional level. These experiments were meant to try out new forms of coordination between professionals providing ambulatory care or between ambulatory care and hospital care. They could either target whole populations or focus on a specific chronic disease (for example diabetes or asthma), a specific population (for example elderly people), and a specific type of health care (for example palliative care). The 2002 Patients’ Rights and Quality

of Care Act brought together diverse provider network initiatives under the simple concept of “health networks”, which were defined as a form of managed care that aims to strengthen the coordination, continuity or inter-disciplinarity of health care provision, with particular focus on selected population groups, diseases or activities. Funding for these provider network experiments has been unified under the Social Security Finance Act of 2007 into a single Intervention Fund for Quality and Care Coordination (*Fonds d'Intervention pour la Qualité et la Coordination des Soins* - FIQCS), which is controlled by the Ministry of Health and the Social Health Insurance Fund. There are now several hundred local networks. Currently, there is a tendency to redefine these local networks as tools for coordinating providers for all care, rather than focusing on specific groups or diseases.

At the hospital level cooperation is promoted through the creation of Local Hospital Communities (*Communauté Hospitalière de Territoire*). The 2009 hospital reform allowed provision of care according to a group model. Public institutions within a single area are called upon to cooperate under the supervision of a benchmark hospital that has a significant amount of technical resources and is responsible for a common strategy. The implementation of a consistent medical plan at local level involves the delegation of specific activities to the benchmark hospital and the pooling of resources. Along similar lines, cooperation between public and private institutions is made easier by the creation of Public Health Cooperation Groups (*Groupements de Coopération Sanitaire*).

In specific areas, national networks of hospitals are developed around a central agency. The University/Hospital Institute (*Institut Hospitalo-Universitaire* (IHU)) is primarily a centre of excellence and a collaboration mechanism between tertiary care hospitals and universities. It is built on four pillars: one or more health-care services; recognized teams of world-famous biomedical researchers; a high-quality university education; and partnerships for translational research. It should improve the provision of care both within the IHU and elsewhere in France. The IHUs also aim to promote the emergence of partnerships with industry. Following a completely open selection process, five IHUs were selected in early 2011. The criteria were the excellence, relevance and innovative nature of four aspects: nursing, teaching, research and technology transfer. However, the emphasis was mainly on the sharing of local resources, since IHUs, should primarily rely on existing structures. The five IHUs benefit from government subsidies.

One example is the Biomedicine Agency (*Agence de la biomédecine*) that was created under the 2004 Bioethics Act (No. 2004-800 of 6 August 2004). This public agency, under the supervision of the Ministry of Health, plays a key

role in the organization of the network of hospitals performing organ, tissue and cell transplantations. It also operates in other areas of human biology and medicine: assisted reproductive technologies, prenatal and genetic diagnosis, embryo and stem cell research

Another example is the National Institute for Cancer (*Institut National du Cancer* (INCa)). This national health and scientific agency in oncology was set up by the first national cancer plan implemented for the period 2003–2006 and created by the 2004 Public Health Act. INCa is entrusted with the task of overseeing and assessing cancer policy in France, as well as developing guidelines for the management of cancer patients and contributing to continuing medical education in the field of cancer. It also plays a key role in providing information and expert opinion on any cancer-related topic. INCa also helps design the procedure for inspection visits to hospitals providing cancer care performed under the authority of the ARH. In order to obtain authorization to provide specific types of cancer care (surgery, chemo- or radiotherapy, etc.), hospitals have to fulfil certain criteria, including staff and quality assurance. Among other things, the hospital has to prove that it is a member of the regional cancer network.

Since 2009, the INCa has authorized the creation of 17 clinical centres for rare cancers of adult patients at the national level, on the model of the reference centres for rare diseases. Each national centre coordinates regional or inter-regional centres. Four reference networks in pathological anatomy complete this organization for rare cancers.

In the field of rare diseases, France launched its first National Plan in November 2004, covering the period 2005–2008. The plan includes specific provision for care management of rare diseases, to overcome the somewhat unstructured care situation that existed previously. The selected national reference centres provide expertise on a rare disease or a group of rare diseases based on their multidisciplinary competences, which are organized around highly specialized medical teams and specific equipment. They provide diagnostics, define therapeutic strategies, conceive and disseminate care protocols, and coordinate research activities. Information and patient education, information and training of professionals, patients and their families are also among their activities. Finally, they organize health and social care networks and have a referral mission nationally, or even internationally. Today some 131 national reference centres for rare diseases have been designated. They are linked to a network of 500 regional centres (*centres de compétences maladies rares*), which contribute to the local provision of specialized health care and advice to patients, under the supervision of the reference centre.

The second French National Plan for Rare Disease 2011–2014 planned the creation of clinical networks of reference centers (*filières maladies rares*). These clinical networks are to coordinate and structure the activities between the national and regional centres, the technical platforms for genetic diagnosis, medical imaging and functional exploration, or any other structure involved in care for patients affected by a rare disease. They should facilitate identifying rare disease patients and their medical practitioners, and orienting them within the health care system.

Developing a framework for reference centres and corresponding networks

Based upon the experience acquired with rare diseases, the French health administration is developing a new doctrine to clarify the situation and roles of reference centres and to define their position vis-à-vis other centres delivering highly specialized care. This should help to contain the creation of new centres frequently advocated by both patients and professionals. Next to specifying their mission, this doctrine aims to develop a framework for selecting, monitoring and evaluating the centres as well as listing the financial tools available. At the same time, it should also pave the way for French participation in European reference networks.

Taking into account the experience with already existing reference centres (e.g. centres for pain treatment, osteo-articular infections, cerebrovascular accidents in children, severe obesity), the concept of national and inter-regional reference centres should be limited to already existing facilities that have the expertise to deal in a multidisciplinary way with complex and less frequent cases. It is expected that no more than 10 reference centres would be recognized on French territory for a given pathology.

The mission of a reference centre should include all of the five following items: coordination between care providers and linking with patients; expertise including epidemiological studies, protocol writing, referral; highly specialized care provision for severe situations; contribution to international level research and teaching. Other hospitals that only partially comply with these criteria, or play a more sub-regional role of concentration and collaboration, would be termed specialized (referral) centres. They would be more numerous (e.g. 200 specialized centres).

To establish reference centres and their corresponding networks a detailed procedure is proposed. It starts with specifying their scope and purpose and defining their functions, based on the characteristics of the medical condition and the treatment pathways. Under national terms of reference, a call for

applications would be launched at regional level, leading to the selection of reference centres and their affiliated facilities. The designation would apply for a period of three to five years, subject to periodic evaluation. The funding should, in principle, only cover extra expenses associated with research, training, coordination and evaluation that are not already financed otherwise.

Germany

Concentrating health care in a decentralized health system

The German health system, owing to its characteristics of federalism and delegated decision-making, poses difficulties when it comes to identifying, developing, designating and financing reference centres or networks. Furthermore, it is mainly through the combination of fixed pricing and free provider choice for patients that hospitals are induced to pursue the goals of achieving efficiency and quality of care.

German federal law regulates the basics of providing and financing health care but leaves details to delegated decision-making bodies (mainly the Federal Joint Committee (FJC)) in which the providers (ambulatory care physicians and hospitals) and the funders (sickness funds) are represented. This is further complicated by the fact that the 16 states have the authority (and the duty) to plan hospital structures and capacities (and to provide capital funding accordingly). Therefore, each state plans hospital capacities from basic to the most advanced levels – each with different ideas and terminology (even the number of levels differs). However, types and numbers of actual services are negotiated for each hospital between the respective hospital and the sickness funds. Federal law and the delegated decision-makers can only indirectly intervene through financing mechanisms (which may make the provision of certain services more or less attractive) or in order to guarantee better quality. A few instruments deserve particular attention.

- Minimum service volumes were legally prescribed for selected hospital services in 2002. Contract partners – the former federal associations of sickness funds, the German Hospital Federation and the Federal Chamber of Physicians – were required by law to develop a list of elective services in which there is a clear positive relationship between the volume of services and the quality of health outcomes. For those services, delivery of a predefined minimum volume during the previous year is the condition to become (or stay) eligible for reimbursement. Examples include liver and renal transplants or oesophagus cancer operations. However, the use of these activity thresholds is still politically very sensitive, with measures linking quality to service volumes being contested before federal courts.

- Furthermore, ambulatory care for patients with certain rare diseases and special forms of disease progression as well as highly specialized services have been declared areas of hospital activity by the Social Health Insurance (SHI) Modernization Act. In such cases, sickness funds may conclude special contracts with hospitals (§ 116b SGB V). The SHI Competition Enhancement Act has expanded this provision since 2007, allowing hospitals to deliver outpatient care services pursuant to § 116b SGB V without prior authorization from the sickness funds, insofar as the prerequisites for delivering these services are present and an application has been approved by the accrediting agency. Of the diseases listed in the act, the FJC has selected the following to date: oncological diseases, mucoviscidosis, pulmonary hypertension, haemophilia, tuberculosis, multiple sclerosis, severe heart failure, HIV/AIDS, rheumatism, primary sclerotic cholangitis, Wilson's disease and Marfan's syndrome. In addition, the FJC has listed criteria according to which new diseases are to be selected for hospital-based outpatient care. The list of disease conditions is anticipated to be reviewed every two years.

Additionally, other instruments are used to steer the demand of highly specialized services by setting quality standards and certifying services.

- The FJC has the legal task of assuring quality in accredited hospitals. It defines minimum requirements for specific diagnostic or therapeutic inpatient services, including the quality of structures, processes and outcomes. They cover the configuration of human resources, equipment, special procedures and forms of cooperation in the hospital as well as the occupational training of medical staff.
- The FJC is also involved in so-called external quality assurance. This is a homogenous federal procedure according to which hospitals have to collect and provide care data to assess and compare the quality of services against specific indicators. The data submitted are collected, validated, assessed and analysed at state and federal level. If striking differences are observed between a particular hospital and similar facilities in the same region, a structured dialogue is initiated. External experts and the hospital concerned will then look for the reasons and try to remedy them.
- Additionally, the FJC defines the content, scope and format of data of the structured quality report in which hospitals have to account for the quality of their services. The public nature of these data allows patients and doctors to compare quality between hospitals and is an important motivation for continuous improvement of the quality of inpatient services.

- Beside the (binding) quality standards of the FJC, hospitals can also apply for certification, for example by scientific organizations such as the Federal Cancer Society or by KTQ® (or KTQ-GmbH – Cooperation for Transparency and Quality in Health Care), a practice-related certification procedure on quality management in hospitals.

Competence networks and research centres

Another complication is that responsibility for providing health care lies in different hands to those for medical training, continuing medical education, research or public health.

To overcome the divided landscape in clinical and applied research among the 36 medical faculties – in order to become more competitive internationally as well as to improve population health – the Federal Ministry of Research (BMBF) initiated the Competence Networks in Medicine at the end of the 1990s. The goal of these competence networks is to establish and promote competence on specific diseases for the benefit of doctors and other health service providers as well as patients and their relatives.

The competence networks are oriented around specific functions. The most important, best and most innovative research institutions for a specific disease area are united within an individual competence network. This horizontal networking of scientific competence supports the development of new medical solutions more quickly and more efficiently and avoids redundancies in research. The vertical networking between scientists and doctors is intended to accelerate the communication and exchange of information in order to accelerate research transfer. Methods of standardization and quality assurance are also developed for clinical research and medical care. Seventeen competence networks in medicine are currently being funded. In the area of neurological and psychiatric diseases, networks exist for depression and suicidal feelings, schizophrenia, Parkinson's disease, stroke and dementia; in cancer for acute and chronic leukaemia, malignant lymphomas, paediatric oncology and haematology; in infectious and inflammatory diseases for chronic inflammatory intestinal diseases, rheumatism, community-acquired pneumonia, hepatitis, HIV/AIDS and sepsis; and in cardiovascular diseases for congenital heart defects, cardiac insufficiency and atrial fibrillation.

Similarly, the BMBF supported 10 networks for rare diseases in the 2000s to integrate national capacities in research and care in order to establish the prerequisites for a specific diagnosis, systematic research, optimal information transfer and competent patient care. The funding of the individual networks was provided for an initial period of three years from 2003. After a successful

interim evaluation, nine of the networks for rare diseases were funded for another two years until 2008.

Greece

Specialized centres

The Greek legislation governing the National Health Service (NHS) provides that a department of a peripheral or specialized hospital can be designated a Specialized Centre if it is involved in the provision of specialized care in a specific area of medicine and nursing; the coordination of the provided services; the training and specialization of medical, nursing and other personnel; as well as the development of research.

The NHS legislation outlines the procedure through which such centres are recognized and governed, whereas the details of their function and objectives are expected to be specified in the official decision nominating the centre. The same applies to clinical units and laboratories belonging to universities or other bodies of the public sector that can be recognized as reference centres for specific topics of public health and which can be commissioned to carry out research programmes, studies and/or the provision of specialized services.

The terms and conditions governing the operation of such centres are established on a case-by-case basis, through an agreement between the Ministry of Health and the organization/institution to which these centres belong.

In the context of the above-mentioned legislative provisions, a number of specialized centres were formally recognized through this process:

- The Specialized Centre for the follow-up and care of patients suffering from Tuberculosis (General Hospital “Sotiria”, Athens);
- The Specialized Centre on Primary Immunodeficiencies (“Aghia Sophia” Children’s Hospital, Athens);
- The Specialized Centre on Developmental and Adolescent Medicine (“Aghia Sophia” Children’s Hospital, Athens);
- The Specialized Centre for Craniofacial Anomalies in Children (“Aghia Sophia” Children’s Hospital, Athens);
- The Specialized Centre on Haemorrhagic Disorders of Children and Adolescents (General Hospital “Ippokrateion”, Thessaloniki).

Finally, there is special reference to specialized centres or centres of reference for occupational diseases.

Reference centres for rare diseases

In addition to these centres there are a number of laboratories or clinics that offer specialized services, in particular in the field of rare disorders, that act, in effect, as reference centres for their respective activities.

The Institute of Child Health in Athens is effectively the reference centre for:

- the National Neonatal Screening Programme for Greece, covering all neonates born in the country and four diseases (congenital hypothyroidism, phenylketonuria, galactosaemia, glucose-6-phosphate dehydrogenase deficiency) (the programme is organized according to WHO guidelines);
- congenital metabolic disorders (e.g. peroxisomal disorders or lysosomal storage diseases) (the services provided cover the whole country);
- genetic disorders and syndromes (e.g. congenital deafness, glaucoma, Cohen syndrome);
- diseases of bone and mineral metabolism in children.

The Institute of Child Health participates in international quality control programmes. In addition, it is the focal point for Orphanet.

With regard to cystic fibrosis, the clinical management of patients is carried out in two centres in Athens (“Aghia Sophia” Children’s Hospital and Sismanoglio Hospital, for children and adults respectively) and three university clinics organized in one centre in Thessaloniki. The molecular diagnosis is carried out at the Department of Genetics of the Medical School of the University of Athens. Furthermore, there are centres offering specialized services for other diseases, such as muscular dystrophies⁸.

The need to define criteria, standardize operating procedures and set up an overall framework governing reference centres in Greece has been recognized. The Advisory Committee on Rare Disorders, supervised by KEELPNO (Hellenic Centre for Disease Control and Prevention) and collaborating with EUCERD, is currently mapping all ongoing activities relating to rare disorders and defining the criteria that should be implemented in the procedure of recognizing reference centres.

Hungary

Reference centres in Hungary are mainly connected to university hospitals, which provide the highest level of care in the country. Reference centres are mostly linked to specific and rare diseases (such as the Hungarian Reference

⁸ Additional information can be retrieved from the latest EUCERD report (EUCERD, 2012).

Centre for Human Prion Disease, the Neuropathology and Prion Disease Reference Centre, the Malignant Lymphoma Reference Centre, and the Children's Allergy Educational and Methodological Reference Centre), acquiring expertise in a specific field, and providing patients with access to diagnostics, necessary equipment and care. Their activity usually covers research, as well as training and education.

With regard to rare diseases, Hungary joined the EU EuroPlan programme, the main aim of which is to prepare a national plan and strategy for rare diseases until 2013, based on EC recommendations. A decree of the Ministry of Health established the National Rare Disease Centre (NRDC) in Hungary in 2008 as part of the National Centre for Health Care Audit and Inspection. The aim of the NRDC is to improve the quality of life of patients with rare diseases by coordinating multidisciplinary activities and establishing coherent health policies handling rare diseases. According to its remit, the NRDC has the following functions:

- defining indicators for rare diseases;
- elaborating its own data-collecting technology;
- cooperating with other agencies in order to collect data on rare diseases;
- initiating the elaboration of guidelines on the treatment of rare diseases;
- carrying out audits;
- maintaining the national database of health-care providers specializing in rare diseases;
- contributing to the assignment of national centres of expertise and their participation in European networks;
- facilitating the establishment and operation of quality management programmes for rare disease laboratories;
- facilitating e-health applications in health care related to rare diseases;
- initiating teaching programmes on rare diseases in universities;
- participating in the work of national agencies responsible for orphan drug and orphan medical device legislation; and
- assessing the availability of special social services for patients with rare diseases (EUROPLAN, 2010).

The health policy programme of the government elected in 2010 was summarized in a discussion paper entitled *Revived health care, recovering Hungary – Semmelweis Plan to save health care*, which presented the planned structural

changes for health-care provision in Hungary. According to this document, national professional centres and sub-centres represent the highest level of health-care provision in the country. These centres are envisaged to provide expensive and specialized care. Their centralization at national level is seen as necessary to ensure efficiency and patient safety. In addition to diagnostics and provision of care, these centres are envisaged to be involved in education and training activities, as well as in international cooperation (National Institute for Strategic Health Research, 2011).

Italy

Decentralized organization of health care

The Italian National Health System (*Servizio Sanitario Nazionale*) relies on a well-established principle of decentralized health-care provision based on 21 Regional Health Systems (RHS). The regional level is presently the most relevant policy-maker in the health domain. Each RHS is responsible and accountable for the health of its resident population.

Treatment and care are delivered through three different actors: local health authorities (LHAs), free-standing public hospital trusts and private providers accredited by the regions. LHAs are vertically integrated organizations that aim to build the most complete and cost-effective continuum of care for their catchment area. LHAs regroup facilities that provide care at different levels, including primary, secondary and tertiary care (academic medical centre and specialty hospital). There are roughly 145 LHAs across the whole Italian territory, plus 80 hospital trusts.

Given this structure, reference networks have developed along three main levels of geographical aggregation:

- the LHA level, since the majority of the LHAs manage more than one hospital (on average three) and are expected to create a network between them;
- the regional level; and
- the national level.

Since Italian regions vary greatly in population size (LHAs cover populations ranging from 700 000 inhabitants in Lombardia to 200 000 in Friuli Venezia Giulia region), some regions have started to reorganize their LHAs and hospital trusts across sub-regional zones (including the private providers through commissioning) in order to achieve higher scale economies. Zones (*area vasta*, or wide area) are intermediate levels between the region and the LHAs.

Multihospital networks increasingly consolidate at zone level, marking a fourth geographical level at which reference networks are developing in Italy.

The creation of networks at different levels

Centres of expertise and reference networks started to emerge in the mid-1990s, similar to other European countries, in an effort by policy-makers and practitioners to improve the safety and quality of treatments.

Networks initially developed at LHA level with a view to integrating clinical processes and rationalizing or integrating resources. At national level the concept was used to identify reference centres for rare diseases, complex procedures (transplants), and research-oriented activities (centres where trials, innovative practices and latest technology should be introduced).

Later, networks also developed at zone and regional levels. These mainly took the form of managed clinical networks – hierarchically linked groups of health professionals and organizations from primary, secondary and tertiary care working together in a coordinated manner, unconstrained by existing professional (and organizational) boundaries, to ensure equitable provision of high-quality and effective services. They include networks for oncology, cardiovascular disease and neuroscience and have both a formal and informal nature: they are formally recognized at the regional level, where the regions identify the reference centres for each specialty area, but they also represent informal communities that link professionals belonging to the same area of expertise.

The different networks have different characteristics. Whereas reference networks at local and zone level have more structural features (they are based on organizational structures that facilitate the integration and coordination of resources and clinical pathways in hospitals), regional and national networks have a mostly functional nature, as they focus on sharing knowledge and coordinate referral paths to reference centres.

LHA and zone-level networks

Many large LHAs managing several hospitals have pursued their network strategies with the introduction of clinical directorates across different hospitals. For instance, the LHA of Bologna (Emilia Romagna region), which manages nine hospitals, has designed eight clinical directorates (for medical services, surgery, diagnostics, oncology, etc.) that regroup units and professionals located in the different hospitals. The same reconfiguration was pursued by the hospital trust of Melegnano (Lombardy region), with clinical directorates cutting across five hospitals. Furthermore, Melegnano introduced a “pendulum movement” of physicians in ophthalmology and cardiovascular disease, where highly

specialized medical teams move between network providers to harmonize supply, ensure equitable access for all patients in the territory and homogenize the clinical behaviour of physicians.

Regional-level networks

More than 100 regional reference networks are formally active throughout Italy. However, about 40% are not functional, whilst the remainder, although formally recognized by the respective regional authority, are mainly operating as enclave or individualistic networks. Only a minority, around 10%, are acting as managed clinical networks. Examples include the oncology networks developed in different regions (Piedmont, Lombardy, Veneto, Emilia Romagna, etc.). Other diffuse regional networks exist in the areas of cardiovascular disease (Olivari, 2005), orthopaedics, nephrology, burn care, neuroscience and rehabilitation. They are usually limited to LHAs and public hospital trusts, although some have included private providers. The majority were started as a voluntary, bottom-up process initiated by a single person or a group of peers, and then recognized and regulated by the regional health department. Few originated as formal initiatives orchestrated by the regional level. Their focus has so far been on sharing knowledge and designing care and clinical pathways that identify referral paths of simple versus complex cases and expected activities by professionals. Pathways aim to increase equity of treatment and facilitate the integration between acute, sub-acute and primary care.

National-level networks

These networks address the treatment of the most complex and rare conditions. The high technological and scientific specialization required calls for the concentration of a critical mass of human and physical resources in a very limited number of geographical sites across the national area. Two examples are elaborated below.

National networks for rare diseases and transplants

The first example is the network for the treatment of rare pathologies (RNMR – *Rete Nazionale Malattie Rare*), established by Government Decree DM 279/2001, with the aim of developing prevention initiatives, enhancing surveillance, improving diagnostic and therapeutic interventions and promoting information and education relating to the treatment of rare pathologies. The network comprises certified care providers who have been given a mandate by regional authorities for diagnosis and treatment of rare pathologies according to predetermined clinical protocols. The certified centres also coordinate the relationship with local primary health care and related services.

The National Centre for Rare Diseases (CNMR – *Centro Nazionale Malattie Rare*) of the National Health Institute (ISS – *Istituto Superiore di Sanità*) is responsible for the surveillance of the national network for rare diseases, with the aim of mapping the distribution of rare pathologies and improving knowledge of associated causes and risk factors. Interregional centres have a prominent role in the network, as they ensure:

- the exchange of information and documents about rare pathologies;
- the coordination of network centres to ensure timely diagnosis and adequate treatment, if existing, also through shared protocols of interventions; and
- the dissemination of information relating to rare conditions and related drug availability to citizens, patient associations and family members.

The RNMR is thus centrally coordinated and monitored, while certified health care providers constitute the reference points at the regional level. However, because of the absence of national-level bodies specializing in the research, diagnosis and treatment of specific rare disorders, and the still very limited specialization of competences across different units, the network appears to remain at functional/organizational level rather than implying the coordination of care provision between different providers.

The case is different for the national network for transplants of organs, cells, tissue and bone marrow. Resource scarcity, the need for equitable access to transplant opportunities at the national level, and the urgency as regards treatment have shaped a provider network characterized by strict coordination and central monitoring. Most importantly, the supply of organs, tissues and cells is centrally planned.

The National Transplant Centre (CNT – *Centro Nazionale Trapianti*), established as a branch of the ISS in 1999, constitutes the central body that controls and coordinates transplants in Italy. Unlike the CNMR, however, the CNT decides on the supply of services within Italy by rationing the scarce resources in accordance with local demands. In particular, the CNT:

- manages at central level the national lists of patients waiting for transplants;
- establishes the procedures and protocols for collecting patient data;
- identifies criteria for the assignment of available organs, tissues and cells on the basis of the urgency of the intervention and of the compatibility between donors and recipients;
- defines guidelines for extraction and transplant within national boundaries;
- defines guidelines and criteria for quality and safety control;

- identifies national needs for transplants;
- regulates the minimum threshold of activity for accredited bodies and the criteria for an equitable distribution of services;
- coordinates the relationship with European and international bodies for donations and transplant of organs, tissues and cells;
- acts as a regional or interregional centre for those types of transplant considered of national competence; and
- verifies and controls all of the above.

Directly dependent on the CNT are three interregional centres and 114 regional centres for transplants, responsible for enabling timely transmission of local data to the national database, managing the relationship between CNT and the local health-care institutions, and ensuring the reliability, quality and safety of all local activities related to the extraction and transplant of organs, tissues and cells.

It is worth underlining that both examples of national-level networks are the outcome of a formal process steered by health authorities and orchestrated through regulatory change.

Malta

Given its small population and correspondingly small structures and availability of specialized expertise, expertise in Malta is concentrated around single, or a small group of, professionals. Secondary and tertiary care are mainly provided by specialized public hospitals of varying size and function. The main acute general services are provided by one main teaching hospital incorporating all specialized, ambulatory, inpatient care and intensive care services. Patients are sent overseas only for highly specialized care. In addition, Malta is currently working on the drafting of a National Strategy on Rare Diseases. The criteria for the designation of centres of expertise and participation in European reference networks will be tackled in this strategy.

The National Highly Specialized Referrals Programme

Malta has a National Highly Specialized Referrals Programme. This health-care services programme is mainly operated between Malta and the United Kingdom and has been functioning for more than 60 years. These bilateral operations were strengthened in 1975 when the Malta–United Kingdom Health Care Agreement was signed. This agreement has since been renewed three times. Through this agreement, Maltese patients are offered highly specialized medical

treatment in NHS hospitals in the United Kingdom. In 2011, 314 patients (474 episodes) were sent to the United Kingdom for treatment under this programme.

The services offered through this programme are considered an extension to the services offered in Malta. Cases referred to the United Kingdom require specialized equipment and interventions that can be offered in very few highly specialized centres in the United Kingdom. Referrals under this programme are not limited by specific pathology, technologies or techniques. Conditions include cases of rare diseases (including cancers for specialized oncological treatments), polytrauma, cerebral palsy and congenital anomalies such as profound hearing loss and complex congenital heart defects. The local consultants are in close contact with United Kingdom consultants in order to ensure continuity of care once the patients return to Malta.

Furthermore, consultants from the United Kingdom visit Malta and conduct specialized operations/ procedures and hold shared care clinics at Mater Dei Hospital⁹. During 2011, 64 such visits were organized with visiting consultants in spinal surgery, paediatric interventional cardiology, hand surgery, orthopaedic surgery, urology surgery, paediatric surgery, pain management, ophthalmic surgery, interventional radiology, interventional oncology, orthognathic surgery and neurosurgery performing operations or procedures at Mater Dei Hospital. Furthermore, visiting consultants in paediatric respiratory diseases, paediatric cardiology, paediatric nephrology, paediatric oncology, paediatric endocrinology, paediatric gastroenterology, paediatric neuromuscular diseases, paediatric neurology, paediatric neurosurgery, haemato-oncology, respiratory diseases, and retinoblastoma ophthalmology held shared care clinics at Mater Dei Hospital during 2011.

The National Highly Specialized Referrals Programme is coordinated by the Treatment Abroad Coordination Office. This office answers directly to the Chief Medical Officer and monitors the expenditure of an annual public budget that is dedicated to the programme. The Treatment Abroad Coordination Office is mandated to give administrative and secretarial support to the Treatment Abroad Committee, which is made up of a chairperson, eight members and a secretary. The committee members are appointed by the Minister for Health and their responsibility is to evaluate all referral forms for patients who are being recommended for further treatment abroad. Seven of the committee members are consultants who work in different areas at Mater Dei Hospital and one member is a lay person representing the public. The committee is also responsible for providing clinical recommendations to the Ministry of Health

⁹ Mater Dei Hospital: this is the major acute public general teaching hospital in Malta. It offers a full range of hospital services, including an extensive range of specialist services.

for the introduction of new services in the health-care system via treatment abroad or overseas visiting consultants. The Treatment Abroad Coordination Office is also responsible for the coordination and logistical arrangements in relation to clinics and theatre lists carried out by overseas visiting consultants at Mater Dei Hospital. Furthermore, a Treatment Abroad Section takes care of all arrangements relating to hospital appointments, accommodation, travel, transport and subsistence for patients and escorts, together with the associated verification, payment and reimbursement processes.

The bilateral agreement with the United Kingdom has provided Malta with a robust and practical means to operate a long-standing method for referrals of patients requiring highly specialized management to centres of expertise outside the country. Malta is seeking to develop working relationships to operate similar networks in other countries. In 2011, Malta signed an agreement with a specialized centre in respiratory medicine in Sicily (*Istituto Mediterraneo per i Trapianti e Terapie ad Alta Specializzazione – ISMETT*). Through this agreement, Maltese patients can benefit from lung transplant services in Palermo. Furthermore, Malta has for several years been providing organs for transplantation to other countries (for which transplantation operations are not performed in Malta, e.g., for liver transplants). These organs are harvested from Maltese patients by a team that comes to Malta from Italy and the transplant operations are then performed in Italy.

Over the years, Malta has gained a lot of experience with regard to issues and practical methods needed to support the referral of patients abroad and the movement of foreign expertise to give specialized health-care services in Malta. These include the importance of having a system that ensures adequate follow-up and after-care upon the return of patients to Malta and the importance of building good clinical and administrative working relationships.

Netherlands¹⁰

Concentration of specialized health care

In the Netherlands, the legislation that regulates the provision and distribution of specialized care is the 1997 Special Medical Procedures Act (*Wet Bijzondere Medische Verrichtingen, WBMV*). On the basis of the WBMV, the Ministry of Health, Welfare and Sports grants permits to the university medical centres (UMCs) and other health-care establishments to provide specialized procedures. The ministry has used this tool primarily to concentrate care from the viewpoint of safety but not to formally set up reference networks, which was left to the UMCs. The UMCs provide the majority of the care regulated

¹⁰ References: NFU, 2007a, 2007b, 2009; Rooijen, de Jong & Rijken, 2011.

under the WBMV. However, for certain WBMV procedures, such as open heart surgery and placing stents, general hospitals perform the majority of cases (NFU, 2007a).

Another tool used to concentrate care are activity thresholds for interventions that are rarely performed in Dutch hospitals. As an example, the Dutch Healthcare Inspectorate (*Inspectie voor de Gezondheidszorg*, IGZ) has set a minimum of 20 oesophagus cardia resections per year per hospital. Hospitals which fall below this threshold are not allowed to perform these resections at all.

Specialized clinical care (*topklinische zorg*) in the Netherlands is concentrated at the level of eight UMCs. These UMCs treat so-called tertiary referral patients (*topreferentie patienten*), who are patients with rare and complex diseases who need highly specialized multidisciplinary treatment. They account for approximately 40% of all UMC patients (NFU, 2009). For every UMC about 100 tertiary referral functions are identified. Some can treat 10–20 patients per year, others 100 or more (NFU, 2007b). For these patients the UMC is their last resort, as there is no option for further referral. The Dutch Federation of University Medical Centres (NFU) is developing a special web site¹¹ to help patients and providers identify the appropriate reference centre for their disease. This type of care is financially supported by the government.

Building reference networks

The establishment of reference networks and centres is high on the agenda of the Ministry of Health, Welfare and Sports. The government adopted the view that these centres enable better access to specialized medical procedures, nurture research and help to build up experience and knowledge with regard to treatment and diagnosis. An implicit assumption is that these centres would also cooperate with each other and form a network.

As of September 2010, the Dutch government has stated its intentions to take a more active role in the development of reference networks. Some very preliminary plans foresee the involvement of the UMCs and, in some cases, the larger general hospitals. The centres involved should be able to conduct basic and applied research into specific diseases, but also organize or participate in clinical studies. Furthermore, there should be a willingness to share knowledge with other specialized centres, but also with smaller hospitals and primary care centres, both nationally and internationally.

One particular example of a reference network involving other health-care providers is ParkinsonNet.¹² This network was initiated by one of the UMCs

¹¹ <http://www.nfu.nl/trf/>.

¹² <http://www.parkinsonnet.nl>.

in collaboration with other professionals. The network represents regional communities of closely cooperating health-care professionals who specialize in treating patients with Parkinson's disease.

Another example of a network that was initiated by patients is the Alliance for Heredity Issues (VSOP).¹³ This alliance of several organizations of patients with a genetic, congenital or rare disorder develops guidelines for rare diseases for reference centres, supports the reference centres with ideas concerning IT infrastructures, and develops quality criteria for concentrated multidisciplinary care.

Norway

Specialist Health Services

The Norwegian health-care system has three tiers. Whereas overall responsibility for the health-care sector rests at the national level with the Ministry of Health and Care Services, specialized health-care services are provided by four regional health authorities. The hospitals are organized as hospital trusts, owned by the regional health authorities. Each regional health authority has a statutory duty to provide equal access to specialized health-care services for those who live in its catchment area. Each hospital is a distinct legal entity, with a managerial board responsible for all its activities. The health authorities may contract out some services to private hospitals or agencies. Each region has a different degree of tertiary level services, but most are provided in university hospitals situated in urban areas.

National services are identified within the Specialist Health Services and consist of national treatment services and national competence services. In 2006 the Ministry of Health and Care Services decided to evaluate all national services and to strengthen their national steering. The high level of quality of these services is to be ensured by establishing new criteria for the development of national services and by introducing a more dynamic steering system. In 2011 a new regulation was introduced for the approval of hospitals and the use of the terms “university hospital” and “national services” within the Specialist Health Services. The aim was to increase the quality of treatment and enhance management by objectives and results.

Furthermore, a strong emphasis is put on research, participation in national and international research networks, education of health-care personnel and performance management. Annual reporting and equal access to the national services is a requirement. Equal access to and use of the national services is to

¹³ <http://www.vsop.nl> (in Dutch only).

be ensured by establishing professional reference groups with representatives from the four regional health authorities, as well as representation from patient associations when appropriate. The Norwegian Directorate of Health is tasked with evaluating all national services every five years and advising the ministry regarding the establishment or decentralization of the national services.

National and multiregional treatment services

National treatment services involve highly specialized tertiary care, localized in one or two hospitals (regional health authorities) in Norway. They have the responsibility to treat all patients nationally with the need for the relevant highly specialized treatment, with emphasis on competence and resources to provide treatment of the highest quality. The national treatment services are also responsible for communicating treatment outcomes, participating in research and establishment of research networks, and contributing to relevant teaching. Furthermore, the national treatment services have an obligation to ensure the provision of guidance and the dissemination of knowledge and competence to the health services, other service providers and clients. The national treatment services should also contribute to the implementation of national guidelines and evidence-based practice.

At present 39 national treatment services and seven multiregional treatment services (shared between two regional health authorities) have been approved by the Ministry of Health and Care Services. Areas covered include organ transplants, treatment of severe burns, cochlear implants (for infants), epilepsy surgery, advanced invasive fetal medicine and paediatric heart surgery.

National competence services

The main goal for national competence services is to build and disseminate knowledge and competence to all health services nationally. The national competence services are required to monitor and communicate treatment outcomes, participate in research and the establishment of research networks, contribute to relevant teaching of health personnel and ensure the provision of guidance and dissemination of knowledge and competence to other service providers and clients. Furthermore, the national competence services will support the implementation of measures to ensure equal access and contribute to the implementation of national guidelines and evidence-based practice.

At present 42 national competence services have been approved by the Ministry of Health and Care Services. Examples of national competence services include long-term effects of cancer treatment, women's health, sarcoma, multiple sclerosis, pregnancy and rheumatic disease, and advanced laparoscopic surgery.

Poland

Former structuring of hospital care

The first approach to reference centres or networks for Poland's health-care system was linked to the idea of creating a network of hospitals. Plans were formalized in 1997 in a draft national plan for a revised structure and location of health-care facilities (national network of hospitals), aiming to rationalize the use of resources and adapt supply to demand. This project was prepared by the Centre for Health Organization and Economics to implement the provisions of the 1991 Act on Healthcare Units.

The hospital network was understood as a coordinated plan, under which hospitals of appropriate profile and with qualified staff were located in the right place, taking into account the demand for health-care services. The network was envisaged to be constantly monitored, modified and adapted to changing population health needs. The draft plan was part of wider government activities with the aim of hospital restructuring, rationalization of health expenditures and a more efficient use of existing hospitals and their respective affiliates. The model was based on regional division, with highly specialized services assigned to university hospitals. Indicators typically used in the planning process (staff and structural indicators, i.e. the total number of hospital beds and specialties in relation to the population) were assigned only secondary value.

The draft national network of hospitals in 1997 became the basis for the regulation of the national network of hospitals and their reference levels by the Ministry of Health and Social Welfare, which came into force on 1 January 1999. This regulation introduced three reference levels.

- Level 1 included hospitals providing health-care services in internal medicine, general surgery, obstetrics and gynaecology, paediatrics, anaesthesiology and intensive care.
- Level 2 included regional hospitals, providing health-care services in the disciplines specified for the first level plus at least four of the following specialties: cardiology, neurology, dermatology, pathology of pregnancy and neonatal care, ophthalmology, laryngology, orthopaedic surgery, urology, neurosurgery, paediatric surgery and surgical oncology.
- Level 3 included state hospitals, medical institutes and state medical universities teaching and conducting research in the field of medical science.

Furthermore, it was assumed that university hospitals are authorized to provide health services in the third reference level in an area bigger than one region, while the activity of state hospitals (medical institutes) covered the whole country. After a change in the structure of the public funders, through the

amalgamation of 17 autonomous sickness funds into one single National Health Fund, this system lost legitimacy and has not been valid since 1 April 2003. However, it is still in informal use owing to the routine activities of medical professionals.

Centres of excellence

When it comes to providers with a recognized high level of expertise, there are a number of hospitals that deal with the most complicated cases in a particular area. Their role is emphasized by ownership status, as they are supervised directly by the Ministry of Health. The list includes the Institute of Psychiatry and Neurology, the Institute of Physiology and Pathology of Hearing, the Institute of Mother and Child Health, the Institute of Rheumatology, the Silesian Centre for Heart Diseases, two institutes for occupational and environmental health, the Institute of Cardiology, the Oncology Centre, the Institute of Rural Health, the Institute of Tuberculosis and Pulmonary Diseases, the Polish Mother's Memorial Hospital Research Institute, and the Children's Memorial Health Institute of Haematology and Transfusion Medicine. These hospitals, however, do not operate within a formal referral system. One network has been recognized: the Ministry of Health has established 13 trauma centres, which are responsible for providing specialist medical care to polytrauma patients.

The status of a reference centre, regardless of whether it is formal or informal, does not translate directly into increased reimbursement by the National Health Fund. However, the Ministry of Health, by specifying the conditions for providing health services, attempts to direct the most complicated cases to hospitals with the highest institutional volume, the best medical equipment and the most qualified staff. In the case of neonatology, gynaecology and obstetrics, and anaesthesiology and intensive care, competences have been divided into two or three levels, depending on the standard (which applies to the full scope of services in these disciplines). Furthermore, if they meet additional requirements above the minimum standards set out in the regulation, hospitals are granted the opportunity to provide selected highly specialized services, such as endovascular surgery, teleradiotherapy, brachytherapy, haemodialysis or hyperbaric oxygenation. Patients with severe burns are also referred to selected centres. Another group of highly specialized services that can be provided by hospitals that have concluded a contract with the Ministry of Health includes organ transplants or selected cardiac surgeries. Fulfilment of the higher standard authorizes hospitals to receive increased reimbursement for the provision of more complex services.

It seems essential to continue with the identification of areas that require better specified conditions for care delivery and improvements of referral systems.

Romania¹⁴

Structuring of hospital care

The concept of a reference system in Romania relates to the capacity of the health system to deal with complex cases based on adequate high-technology medical equipment, techniques and very experienced medical personnel. It relies on the historical development of the health system. According to Title VII of the Health Reform Law 95/2006, hospitals are organized on the basis of geographical criteria into regional, district and local hospitals. Each of the 41 districts, as well as Bucharest municipality, has a district emergency hospital where patients from the respective district are referred if the local health unit cannot resolve the case. The next level of reference is the tertiary level, represented by university hospitals. There are eight university centres and each of them has its own catchment area represented by the surrounding districts. However, the centres in Bucharest, Cluj and Iasi cover the majority of severe cases due to their long history and professional recognition.

According to Ministry of Health Order 1408/2010, hospitals in Romania are classified into five categories: I – very high level of competence; II – high level of competence; III – medium level of competence; IV – basic level of competence; and V – limited level of competence. The main legal criteria for classifying a hospital in one of the five categories relate to the level of professional expertise, the quality of existing medical equipment, the availability of human resources, and the range and complexity of health services provided. The hospitals in the first category also act as teaching units as well as recognized research centres. These first-class hospitals usually serve as reference units for patients in the catchment area, or even for the whole country.

Reference centres

The Romanian health sector has several reference centres, usually part of university hospitals in the larger cities. They are mainly public health facilities or departments/wards of hospital facilities, and cover specific pathologies: certain chronic diseases (e.g. diabetes, cancers, rare diseases), critical care (transplantation, burns), communicable diseases (HIV/AIDS, epidemics of certain communicable diseases), specific parts of the body (e.g. breast pathology), or specific techniques (laser therapy and minimally invasive treatment of urological conditions). Most reference centres have a national scope but some operate at the regional level (e.g. for imaging or reproductive health).

¹⁴ References: Vladescu, Scintee & Olsavski, 2008; Government of Romania, 2006; Ministry of Health, 2002.

Here are some examples of areas where the concept of reference centres is applied in Romania:

Transplants

Ministry of Health Order 534/2005 establishes a list of accredited health units authorized to perform organ transplantation. All patients in need of an organ transplant and registered on the waiting list are referred to one of these units. The National Transplant Agency, established in 2004, coordinates the activity of the entire transplantation network in Romania.

Burns

The Emergency Clinical Hospital for Plastic Surgery and Burns of Bucharest is the only specialized hospital in Romania to provide these services. All severe cases from across Romania are referred to this hospital.

Diabetes

The National Institute for Diabetes, Nutrition and Metabolic Diseases was established in 1993 as a centre of excellence for treatment, teaching and research. The institute coordinates the whole network for diabetes treatment in Romania. Severe cases are referred to the National Institute from all over the country.

HIV/AIDS

Patients with HIV/AIDS are referred to eight regional reference centres. Coordination at national level is carried out by the Institute of Communicable Diseases, Bucharest, which is also a reference centre for communicable diseases in specific circumstances, as during the avian influenza pandemic.

The process of becoming a reference centre is voluntary and initiated by the provider, usually through the following key stages: firstly, a specific medical ward, clinic or hospital with a very good medical team tries to obtain the best medical equipment and be up to date with the latest medical techniques and procedures, including training of staff. At the next stage, the complexity and severity of cases treated in the facility are high and the physicians have a good reputation, which might include running clinical studies and providing medical training. Once the expertise of physicians and the centre of reference is commonly recognized, official recognition by the Ministry of Health is obtained through a long, bureaucratic process. There are very detailed standards for accrediting reference centres (Ministry of Health Order 431/2002 and amendments). Reference centres are approved after evidencing compliance with specified criteria for infrastructure, equipment, medical personnel and availability (working 24 hours per day throughout the year). Hospitals may have referral arrangements with these centres or doctors refer their patients directly to such facilities when needed. The health reform law 95/2006 describes

all networks with their reference centres. These centres are centrally financed through national health programmes. So far there has been no recognition for reference centres within the system of reimbursement. However, new legislation for hospital classification and accreditation has been implemented that allows for reimbursing hospitals with reference centres for medical equipment and personnel, but not for other structural costs.

Slovenia

The organization of tertiary health care

Currently, the provision of health-care services is organized in three levels, defined by the Health Services Act. The tertiary level covers clinics, clinical institutes or clinical departments. They are basically high-standard hospitals, hospital departments or university institute departments providing the highest professional, technological and educational services in Slovenia. Although the catchment area of hospitals is often not clearly defined, the geographical scope for these tertiary centres is generally the whole country.

Following an objective, detailed and transparent process the title of “tertiary centre” is granted by the Ministry of Health based on the fulfilment of educational, scientific, professional, personnel and other requirements that are specified in detail in the Health Services Act. It lists criteria such as a sufficient number of adequately educated and trained medical and other staff, material capacities required for performing the work, international cooperation and conditions for performing professional, educational and scientific research work. General criteria, such as quality monitoring or patients’ rights, are not yet included in the criteria.

As stated in Article 17 of the Health Services Act, these clinics, clinical institutes or clinical departments, which in a way represent national reference centres for specific areas of expertise, are entrusted with performing the most demanding specialist ambulatory or hospital treatments that cannot be carried out at lower levels due to professional, staff, technological and organizational requirements. They are expected to introduce new treatment and diagnostic interventions, in some cases develop guidelines for prevention, diagnosis, treatment and rehabilitation, as well as to disseminate information to other hospitals, medical practitioners and health-care workers. Where different clinical guidelines have been formulated for the same medical condition at the national level, the Health Council (which confirms clinical guidelines) leads the process of their harmonization. Clinics are also involved in scientific research and educational work for the medical faculty, as well as other faculties and colleges. They are expected to perform basic, applied and developmental research for health-

care needs and provide for the development of top researchers and research staff. In addition, they cooperate with competent bodies for designing and implementing undergraduate and postgraduate education of medical doctors, dentists and other health-care workers in higher education.

Although formally patients are free to choose the provider to whom they will entrust their own health care, they will be referred to the above-mentioned tertiary centres if they are in need of highly specialized care. In some fields, expertise is concentrated in one particular centre.

- The Institute of Oncology in Ljubljana is a national institution that is entirely dedicated to the area of cancer. While it does not diagnose and treat all oncology patients, it is the only institution in charge of the care of patients with some rare cancers.
- A document issued by the highest professional advisory body (the General Expert Collegium) in the area of paediatrics outlines the competences for hospital treatment of paediatric patients in Slovenia. For instance, it recognizes the University Children's Hospital at the University Medical Centre, Ljubljana (UMCL) as being responsible for the treatment of metabolic diseases.
- There is one tertiary genetic centre, the Clinical Institute of Medical Genetics at UMCL, providing genetic testing (pre-implantation/prenatal/postnatal) and counselling for any kind of genetic disorder.
- Organ transplantations are carried out at the moment only at the University Clinical Centre of Ljubljana. However, a new law about donation and transplantation of human body parts is being prepared.
- In the field of rare diseases it is expected that one of the above-mentioned tertiary institutions (University Children's Hospital, Clinical Institute of Medical Genetics or UMCL) will take the role of national centre for rare diseases, with the establishment of national reference centres to follow later on.
- There is also a centre for Fabry's disease within one of the regional hospitals, to which patients from the whole country are referred.

Reference centres

The concept of reference centre in the context of provision of health-care services is not defined in any law or other legislation. Reference centres are generally considered as those centres that are the target of referral for complex medical cases, provide support to other institutions and through research and publications have gained international recognition.

The Ministry of Health has recognized the need to concentrate the treatment of certain conditions in one or a small number of centres. It also recognized the need to award special status and hence give support to centres showing exceptional achievements in their area of expertise, as stated in the work plan in the area of rare diseases, issued in February 2012. The process for developing a legal framework for the recognition of reference centres began in 2008 with the creation of a working group at the Ministry of Health. Its mission was to draft criteria for the recognition of reference centres, translating the expectations into specific requirements and assessment procedures. This work is ongoing.

The need for reference centres has been recognized particularly in the areas of rare diseases, human genetics and paediatric metabolic diseases. However, the draft criteria do not prevent reference centres being established in other areas, such as in vitro fertilization or rheumatic diseases. Furthermore, the draft criteria also allow for the recognition of reference centres that actually do not treat patients, such as genetic services. The proposal to delegate the responsibility for the drafting and/or approval of practice guidelines to reference centres is being discussed. At present, this responsibility is entrusted to the tertiary level by clinics, clinical institutes or clinical departments.

Once the framework is established, the provider will probably be the one to initiate the recognition process. To be awarded the title of reference centre, the provider will have to prove excellence in its area of expertise through the fulfilment of specific criteria. As the advantages of obtaining reference centre status are currently unclear and a mechanism to financially recognize and award outstanding achievements in medical treatment is lacking, interest in the initiative has been lower than expected.

Spain

Designating reference services

The legal base for designating reference centres, departments and units (RCDUs) in Spain is the Spanish National Health Service (SNS) Cohesion and Quality Act (16/2003). It sets out the legal framework for coordination and cooperation between public health authorities in the exercise of their respective functions and defines reference services that require the centralization of cases in a small number of centres for their best management and to guarantee equitable access to high-quality, safe and efficient health care for patients affected by conditions that require highly specialized care.

Royal Decree 1302/2006 establishes the procedure and principles for designating and accrediting centres, departments or units within the SNS that would provide these reference services. The task of designating

reference services, defining their number and strategic location within the national health system, based on a joint planning approach, fundamentally belongs to the SNS's Interterritorial Council. This is the permanent body for coordination, cooperation, communication and information between health services and the state administration. However, most of the work is delegated to a special designation committee that was set up in 2006 and is composed of representatives of the different Autonomous Regions, the Ministry of Health, Social Policy and Equity and the Healthcare Technologies Evaluation Agency. Its first mission is to identify the diseases and procedures that justify the designation of RCDU, following priority criteria it has established. For each area of specialization the actual assessment is done by a group of experts appointed by the Autonomous Regions, the scientific societies and the Ministry of Health. The need for concentration could be motivated by the use of very advanced technologies (e.g. total skin electron radiation), the involvement of a high level of specialization or the low prevalence of cases (rare diseases, transplants). For rare diseases, reference services would include support for confirming diagnoses, and defining treatments and follow-up strategies. Reference centres would also act as consulting bodies for clinical units that regularly care for these patients.

Reference services can only be established for treatments that are already included in the public basket of health services. New techniques, technologies or procedures, prior to deciding on the advisability or need to include them in the portfolio of SNS services, are introduced at centres that have been explicitly authorized for that purpose, and in accordance with specific protocols for guaranteeing safety, respect for bioethics and achieving good patient outcomes. This supervised use aims to establish the degree of safety, efficacy, effectiveness and efficiency and will be conducted in accordance with a research format, for limited periods of time.

The expert groups also propose designation criteria for each area of specialization. They refer to professional experience, staff and technical resources as well as performance and clinical outcome indicators.

Selection and designation procedure

Once the diseases and procedures have been identified and the criteria for designation have been specified, the actual selection and designation of RCDUs can start. Based on a formal decision of the Interterritorial Council, the Autonomous Regions can propose eligible centres to the Designation Committee. Proposals accepted by the Designation Committee are subsequently sent to the Quality Agency of the SNS to start the qualification process. During this process, the centre is audited against the designation criteria. If a positive report is issued and the centre fulfils all the requirements, the Designation

Committee proposes its designation as an RCDU. After agreement of the Interterritorial Council, an official resolution from the Ministry of Health, Social Policy and Equity confirms the designation for a maximum period of five years. Before this period ends, a renewal of the designation is required following a reassessment by the Quality Agency.

So far, the Interterritorial Council has identified 46 diseases or procedures requiring the designation of an RCDU. The designation criteria for 13 areas of specialization have been defined, with nearly 250 professionals participating in this process. For 35 diseases or procedures, 132 reference centres, departments or units have been designated (68 started operating in 2009, 22 in 2010 and 42 in 2011).

Reference services are monitored annually. An information system is in place to report on how the activities performed comply with the designation criteria and meet the procedure and result indicators that were included in the designation criteria. The information system has begun gathering data for 90 RCDUs that started operation in 2009 and 2010, covering 26 diseases and procedures. The definition of these procedures and result indicators by the corresponding expert groups (agreed by the Interterritorial Council) is very complex, due to the diversity of diseases and procedures, considering that every disease and procedure has its own information system.

Since 2010 the care provided to patients transferred from an Autonomous Region to an RCDU has been funded from the Cohesion Fund for Care Services. The Cohesion Fund covers 80% of the cost of the health care provided to patients transferred from regions outside that which hosts the reference centre, department or unit. A Ministerial Order is published annually, listing the diseases and procedures that require RCDUs and the amounts that have to be provided as compensation in each case. The amounts and rates will be regularly updated.

Sweden¹⁵

The organization of specialized care

In Sweden, most secondary and tertiary care is provided by public hospitals owned and administered by county councils. For highly specialized care, and for research and medical training of doctors, the county councils cooperate in six medical care regions. The population of these regions varied in 2011 from 0.9 to 2.1 million and in each medical care region there is at least one university hospital.

¹⁵ References: National Board of Health and Welfare, 2011; RDTE, 2005; Glenngård et al., 2005, EUCERD, 2011b.

Sweden has approximately 60 hospitals that provide specialist care, including emergency services. Seven of these are university hospitals where highly specialized care is offered. They are affiliated with a medical school and also function as research and teaching hospitals (Glenngård et al., 2005). Patients with complex or rare diseases and injuries who need highly specialized care are referred to one of these university hospitals. If they come from another county, their costs will be covered by the county council of the county where they usually reside.

National centres of expertise on rare diseases are mostly located at university hospitals. In 2010, the Swedish Government decided to establish a national focal point for coordination of efforts in the field of rare diseases. Since 1999, the Swedish Information Centre for Rare Diseases, located at the University of Gothenburg, has run the Rare Disease Database commissioned by the National Board of Health and Welfare. The database currently includes detailed and expert-validated information about almost 300 rare diseases (about 500 according to Orphanet categorizations), including information on national medical specialists and national (and sometimes international) medical centres (EUCERD, 2011b).

National Specialized Medical Care

The concept of reference centres was established in Sweden in 1990 and has become widely known in the country (RDTE, 2005). The main areas linked to the concept are treatments designated as National Specialized Medical Care (NSMC). After initial attempts to improve coordination of highly specialized services, the national coordination of NSMC was established by law in 2007. According to the Health and Medical Services Act, NSMC “refers to medical care provided by a certain county council and coordinated with the entire country as its service area” (National Board of Health and Welfare, 2011). NSMC is thus provided by county councils for the population of the entire country. It differs from other levels of care: Regional Specialized Medical Care (RSMC), county care and primary care.

The type of health care that would qualify for NSMC is treatment of a “national character”, for which patients would normally be referred between regional hospitals. This includes rare diseases and areas of highly specialized treatment requiring special technology and medical competence. The criteria used for designating treatments as NSMC are: the disease is rare (defined as affecting less than 1 in 10 000 individuals); the diagnosis/treatment is complicated, requiring special competence; and/or diagnosis/treatment requires a high level of resources (advanced or expensive equipment). The following areas have been designated so far as NSMC (National Board of Health and Welfare, 2011):

cochlear implantation in infants, craniofacial surgery, heart transplantation, liver transplantation, lung transplantation, ocular oncology, paediatric heart surgery, treatment of severe burns, glaucoma in children and intrauterine treatments. Treatments that are currently under consideration include brachial plexus injuries and treatments as well as advanced paediatric surgery (National Board of Health and Welfare, 2011).

All decisions about what types of treatment will be designated as NSMC and which health-care units will provide this care are taken by the National Board of Health and Welfare, but delegated to a special Committee for National Specialized Medical Care that includes representatives of the county councils, the Swedish Research Council, the Swedish Council of Technology Assessment in Health Care, and the Stockholm Administrative Court of Appeal. The chairman of this committee is the Director General of the National Board of Health and Welfare.

After having decided what medical areas are eligible, a working group with representatives from all university hospitals draws up a comprehensive description of the highly specialized service, mapping the critical medical competence, medical equipment and other important components, referral patterns, care pathways and patient volumes. Next, an impact analysis of the particular NSMC is undertaken, exploring the consequences for patient safety, research, education and also taking into account the patient perspective and future scenarios.

Applications for designation as NSMC have to be endorsed by a county council. A maximum of two county councils will be awarded a licence to perform a particular NSMC. A formal system of accrediting reference centres is in place. In order to provide NSMC, providers will need to be licensed by the National Board of Health and Welfare. In the appraisal the Board will investigate the applicants' competence (medical, organizational, international), their ability to provide good care (quality management system for quality and patient safety), and their ability to ensure medical care provision in case of unexpected resource failure, as well as the need to expand their activities (to ensure treatment for all referred Swedish patients).¹⁶ One of the main challenges in the designation of reference centres for NSMC has been that some of the decisions of the Committee and the National Board of Health and Welfare have been questioned by some providers or by the county councils. However, acceptance has increased over time as a result of the transparent and cooperative approach throughout the process. Consensus is growing that a systematic and orderly distinction between national and regional services enhances efficiency

¹⁶ Since 2005, patients referred by a general practitioner should get an appointment with a specialist within 90 days and not have to wait more than a further 90 days after being diagnosed to receive treatment. The guarantee applies to the whole country and includes all elective care.

and concentration of services, increases the number of patients per surgeon, and generates better access for all patients to the best service available. Legislative support has also been a key factor in establishing NSMC successfully.

Sweden also investigates cross-border cooperation with its neighbouring countries in the field of reference networks. One example between Sweden and Denmark is the Joint Unit for Breast and Endocrine Surgery project between the University Hospital in Lund and Copenhagen University Hospital. This three-year project, which started in 2001, aimed to achieve optimal surgical treatment for patients with breast cancer, melanoma, goitre and diseases of the pancreas and other glands. Since the sub-specialized departments for breast and endocrine surgery were too small to meet the accreditation criteria of the European Union of Medical Specialists (UEMS), cross-border cooperation was seen as an alternative way to strengthen the profiles of both hospitals by increasing the critical patient population, broadening the basis for research and enhancing cooperation in research and development. The ultimate goal was to become a centre of excellence for breast and endocrine surgery in northern Europe. One of the achievements of the project was to develop a web-based quality system for endocrine surgery. The cross-border system was based on the data that the two hospitals fed into it. Although networks for research were created, the creation of the centre of excellence did not materialize.

United Kingdom (England)

Reference centres for specialized services

In England's NHS, a separate system exists for the commissioning (planning and contracting) of specialized services. Specialized services are typically provided in relatively few specialist centres that cover a planning population (catchment area) of more than a million people. This means that a specialized service would not be provided by every hospital in England; generally, it would be provided by less than 50 hospitals.

In England, 10 Specialised Commissioning Groups (SCGs) commission specialized services for their regional populations, which range in size from 2.8 million people to 7.5 million people. Examples of such services include haemophilia and blood and marrow transplantation, rare cancers, specialized burn care, medical genetics, renal services and specialist cardiac services. The National Specialised Commissioning Group (NSCG) facilitates working across the SCGs at regional and pan-regional level.

The Specialised Services National Definitions Set (SSNDS) lists and describes these services in detail. Specialized services are constantly developing and

changing; new specialized services will be provided by the NHS while other services will become more commonplace and cease to be specialized. The SSNDS has to be seen as an ongoing process with new editions being produced from time to time.¹⁷

Specialized services are complex and/or expensive services provided in a small number of specialist centres that serve a large geographical area, larger than the area normally served by local hospitals or community services. The process of designation of such a service involves checking that providers deliver an agreed quality and level of care to their patients within clear financial and clinical standards. In particular, the designation strategy aims to make best use of and ensure the sustainability of specialized service providers' skills, experience and facilities; encourage provider innovation and development where appropriate; and help to inform patients and carers about the services commissioned.

Many aspects of the designation strategy are already part of the NHS commissioning process; however, there will be an expectation of:

- more detailed service specifications, including explicit quality standards and measurable outcomes;
- a formal process of quality reviews of providers, involving service users and clinicians;
- formal designation decisions taken by the SCGs;
- more information for the public about designation and quality of services.

Reference centres for highly specialized services

Alongside specialized services, which are commissioned by regional SCGs, there are about 60 services that have been designated as highly specialized and are commissioned nationally.¹⁸ Generally speaking, these are services that affect fewer than 500 people across England or involve services where fewer than 500 highly specialized procedures are undertaken each year. Examples of such services include the diagnosis and treatment of rare conditions¹⁹, heart transplantation (about 270 transplants each year) and secure forensic mental health services for young people (about 80 new patients each year).

Nationally commissioned services that are rare or highly specialized – and those eligible to provide them – are specifically designated by the Secretary of State for Health. The system is a reactive one: there is no specific call but rather

¹⁷ Detailed information on the SSNDS is available at <http://www.specialisedservices.nhs.uk/info/specialised-services-national-definitions>.

¹⁸ The list of highly specialized services and the name of specialized centres authorised to provide them is available at <http://www.specialisedservices.nhs.uk/services>.

¹⁹ The UK definition of rare diseases is much narrower than the EU definition: 2 per 100 000 or lower.

providers wishing to be designated reference centres for specialized services have to submit an application. Applicants have to provide evidence that the proposed product, service or technology can deliver better clinical outcomes than any current NHS alternatives. Applicants also have to outline what support the application has from relevant professional and patient groups. If there is a relevant patient group for the target condition(s), the expectation is that applicants should seek, and present in their application, evidence of its support for the proposed provision. If there is no organized patient group, patient feedback could be presented.

The NHS pays for these services collectively and they are commissioned through the National Specialised Commissioning Group, which ensures that they are provided to the highest standards of quality and meet patient needs. Services and providers are initially designated when the service is first deemed appropriate to be commissioned on a national basis. Designation is renewed when the Secretary of State accepts a recommendation from the Advisory Group for National Specialised Services (AGNSS) to continue to designate the service and specific service providers.

Through the process of renewal of the designation, the National Specialised Commissioning Group will assess providers to determine how they are meeting the contractually agreed quality and performance criteria and, where appropriate, improvement plans may be identified.²⁰

The evolution of specialist networks in England

Clinical networks have developed at national or regional level in relation to several specialized services. These networks have strong links with commissioners of specialized services, working in partnership with them to ensure that services are developed and coordinated appropriately.

By their nature networks are driven from the bottom up and therefore differ in definition and scope. Below are a selection of networks that exist on a regional and national basis in England and whose development was driven by both health-care providers and professionals, working together to improve access to and the provision of health care to patients.

- The National Network for Burn Care (NNBC)²¹ aims to improve the quality of NHS burn care services in England and Wales. Specialist burn care providers (including burn care centres, units and facilities) are required to work collaboratively in the United Kingdom to deliver coordinated services

²⁰ The list of NHS trusts designated as reference centres for very specialized care is available at http://www.specialisedservices.nhs.uk/library/24/Location_of_NCG_Services_and_Designated_Centres_by_NHS_Trust.pdf.

²¹ <http://www.specialisedservices.nhs.uk/burncare>.

to patients, and membership of the NNBC reflects the interests of all those involved in burn care, including the four regional burn care networks, NHS specialized commissioners and patient representatives.

- The NHS Cancer Programme for England web portal²² was designed to assist in finding cancer-related information quickly and easily from one central resource. This web site provides links to some of the major areas of work and services for patients, the general public, NHS staff and other health-care professionals involved in cancer care. In particular, it links the NHS cancer networks, which bring together all commissions, providers, local authorities and charities at all stages of the cancer journey at a regional level. The cancer networks were established in 2000 as key players in the delivery of improvements to cancer services. A series of coordinated committees (clinical outcomes groups) made up of specialists has been created to oversee the development of guidelines and specialist standards for different cancers. These have been used as the basis for decision-making by local networks about which hospitals are permitted to administer highly specialist procedures or treatments.²³
- The North Central London CardioVascular & Stroke Network²⁴ is an example of a regional network that increased in prominence and broadened its clinical coverage following successive government reports. The network brings together users, clinicians and managers in primary, secondary and tertiary care to ensure that cardiac and stroke services develop to meet the standards in the National Service Framework and national strategy respectively, and to establish support for a sector-wide approach to planning, commissioning and assessing the performance of heart disease and stroke services and to develop robust mechanisms for involving local people, commissioners and trusts in this approach.
- Although not networks as such, national service frameworks and strategies set quality requirements for specific types of care and are designed with input from patients and professionals.²⁵

²² <http://www.cancer.nhs.uk/index.htm>.

²³ http://www.ncin.org.uk/cancer_type_and_topic_specific_work/cog.aspx.

²⁴ <http://www.nclcn.org.uk/>.

²⁵ <http://www.nhs.uk/nhsengland/NSF/pages/Nationalserviceframeworks.aspx>.

Discussion and preliminary conclusions

This scoping study throws light on a series of issues and challenges encountered when defining the scope of ERNs. These relate mainly to questions on how the concept of reference centres and networks should best be defined; how the political aspects (and especially the selection process) can be managed effectively; and around the implications for funding and coverage.

The questions in all three areas are strongly shaped by the fact that much of the experience with reference networks has focused on rare diseases. Certainly, most of the European literature and reporting is found in this area, not least because the work in the context of the HLG on Health Services and Medical Care, and particularly EUCERD, has led to a range of pilot projects and incentives in this field.

It is the success of these initiatives, as recognized by the 2008 Communication on Rare Diseases (European Commission, 2008), that has prompted discussion about establishing ERNs as a promising way to tackle coordination of clinical research, support and treatment options and to add value, strengthening national health systems. However, the focus to date on reference centres and networks to meet a particular set of needs skews the debate and offers a relatively narrow range of evidence on how the concept could be implemented and supported beyond the field of rare diseases.

Provision of care or knowledge-orientation

The review of national practices conducted here demonstrates the diversity and different rates of progress in developing the concept of reference centres and networks. In some countries the creation of reference networks is mainly motivated by the need to concentrate or centralize the provision of highly specialized services in a limited number of medical institutions. In others it was inspired more by the desire to improve clinical expertise and research on the treatment of specific (mainly rare) diseases. Some countries have developed well-established systems and procedures for defining scope and designating

centres and networks as well as for monitoring their activities and outcomes, whereas others have *de facto* systems, where certain hospitals or departments because of their traditional position or professional recognition have become the natural leading centre to which patients are referred, without any clear criteria or quality control mechanisms.

The technical focus also varies, with some Member States essentially targeting rare diseases and others extending the scope towards more common and chronic conditions (e.g. cancer, diabetes). Networks are often built around a central coordination centre, especially in the field of critical care (transplants, burns). All this variety makes it difficult to conceptualize reference networks at the European level.

Two main dimensions have emerged, and although both are intrinsically linked to the concept of reference networks, they are, to a certain extent, in competition with each other. The tension that exists is between:

- the concentration of expertise and care on the one hand (as encapsulated in the notion of reference centres); and
- the transfer of this expertise between and within networks, on the other (as encapsulated in the notion of reference networks).

This translates into a single key question for the future – should the network concept relate mainly to the idea of referring patients (provision of health care) or referring providers (knowledge transfer)? In existing examples the emphasis on one dimension or the other stems largely from the motivation which underpinned the establishment of the network in the first place. This can also be seen to have shaped the scope and focus of the network, and also the way the network is governed, with major implications for future developments.

Even if, in many respects, it may seem more appropriate and easier to promote the knowledge-oriented, expert/provider referral model, these two aspects cannot be fully or easily disentangled. Not only is much of the national experience built around the idea of centralizing specialized health care for reasons of economies of scale, but also out of considerations for quality and safety, which implies that patients are to be referred to the higher-level facilities. Besides that, we should also remind ourselves that ERNs are being developed as part of the patients' rights directive, which is closely connected to the idea of choice, opening up options for patients and facilitating cross-border care. To exclude the question of patients' access to reference centres for specialized treatment under this article would seem illogical. It is likely, then, that the formal recognition – or even listing – of reference networks and centres at EU level will be interpreted as signalling quality and will attract patients seeking care. This may in turn prompt providers to promote themselves as self-declared

reference centres as a marketing ploy, or encourage Member States to seek ERN status to enable them to use spare health-care services capacity as an export product.

Reference networks and the scale of the issues addressed

The lack of “critical mass” in terms of rare diseases in many Member States prompted the development of multinational responses. This is entirely understandable given the low numbers of patients affected per country, the limited knowledge and expertise available locally, and the high cost associated with diagnosis, treatment and monitoring, so that rare diseases can indeed be addressed more effectively in a broader European context.

However, as argued above, prevalence is just one, and not the only or necessarily most relevant, indicator that points to the setting up of ERNs. The question of whether there is sufficient critical mass within a country or a region to address rare diseases does depend on the size of the country (after all, the European definition of rare diseases still results in about 30 000 cases in the United Kingdom alone), but the available expertise and treatment capacity are also highly relevant. Nor does prevalence tell policy-makers much about the type of disease, how well established the treatment options are, what is required in terms of interventions and support, or whether it involves a short period of treatment or ongoing care. The incentives for Member States to participate in reference networks are therefore very diverse. Not just smaller countries but countries with less financial capacity may prefer not to invest in their own responses but to look to access (reference) centres abroad, as for example with the Maltese national referrals programme for complex care. Other countries will want to share expertise around very complicated diseases or cost-intensive interventions.

Moreover, the concept of reference networks can be useful in other areas beyond rare diseases. Creating ERNs has considerable appeal in the field of chronic diseases, although many of these are far from rare. Here, the growing burden of disease has brought home to policy-makers the need to optimize health system responses. Working across borders to improve treatment protocols and coordinate training and research through reference networks is therefore happening with common conditions such as diabetes, Parkinson’s or cancer (as in the country examples above). This is in line with reform trends in Member States, building on increased national expectations that health systems should integrate and coordinate care to achieve better quality, to ensure efficiency and to make best use of scarce resources. The idea of establishing provider networks fits with these concerns and is supported by convincing evidence that better

quality and better outcomes are achieved if complex interventions for diagnosis and treatment are concentrated in specialized centres with a critical mass of expertise, equipment and experience.

There is clearly scope therefore for ERNs to expand from the area of rare diseases and this is reinforced by Article 12 of the cross-border patients' rights directive. An important first step in fulfilling this potential and in implementing the directive will be to frame the concept of ERNs better, specifying whether their core role is in health-care provision or the transfer of expertise and knowledge, and doing more to tease out when and for what purposes ERNs might be established. This is necessary because the second paragraph of Article 12 defines no less than eight objectives for reference networks and calls for at least three to be pursued, allowing for a wide range of network types. The focus of networks is crucial for determining how best they are selected, managed and funded.

Managing ERNs: the selection process and beyond

The most efficient way to manage the scope of ERNs flows from the decisions taken on the network concept and the focus that ERNs will take. Notwithstanding these decisions, it is already clear that there are important challenges in ensuring that the various (potentially competing) regional, national and international concerns are reconciled, not least when it comes to selecting the potential reference networks.

This scoping exercise suggests several ways forward. First of all, ERNs need to be more comprehensively identified and mapped. National (and/or regional) authorities are well placed to review and assess the expert/reference centres located on their territory (and in the long term to oversee them and maintain regular contact), and so need to play an active role in this process. However, national authorities cannot be entirely disinterested, so self-declared or nationally determined status will not be sufficient to identify (or rule out) all eligible candidates or to choose between them.

Here the European dimension is important. As highlighted by the RDTF expert group, there is a need for explicit comparison of the quality of the services provided and a centre of expertise should only be recognized as such where it can demonstrate that it is indisputably better than other hospital centres in the same specialty, either because its technical platform is unique or because its clinicians are of international stature (being particularly well qualified and covering a range of disciplines). This is less straightforward than it seems since it depends entirely on agreement of an accepted set of outcome measures to define and capture (superior) quality. Given that Member States are at different stages in defining and monitoring reference centres nationally, it is fortunate that the

directive has focused on networks rather than centres, since this helps to avoid the different national centres taking part in networks having to compete against each other. Yet certain actors can function as benchmarks for others within the same network. Agreeing which quality indicators should be used is already challenging in itself; it will be just as complex to reach agreement on how to gather, validate and compare data from across Member States. Furthermore, monitoring mechanisms will be needed to ensure compliance with the eligibility conditions, as well as to reassess quality criteria on an ongoing basis.

In many respects, the field of rare diseases has significant competitive advantages here. Although the definitions of rare diseases, and indeed centres of reference, vary widely between countries (including on issues of density, focus and level of specialization), the ERN concept for rare diseases is already well known by Member States. Networks have already been mapped for a range of rare diseases and criteria have (sometimes) been developed. Similarly, specialized clinics have been identified (through the Orphanet database), while several EU Member States have recognized centres of reference. Where there are existing networks in place or under development, these help to demonstrate the feasibility and value of the approach and allow experience to be built up with criteria, selection and designation. Rare diseases also have the advantage of having smaller numbers of eligible centres and a more limited group of experts, which tends to make it easier (or less controversial) to define eligibility, choose between centres and actually designate ERNs. It is also easier to monitor relatively small networks, reducing the burden of assessing compliance with criteria over time. All these elements, combined with the clear added value of work on rare diseases, can be expected to minimize any opposition from Member States to the concept of ERNs.

The implications for funding and coverage

The issues of focus, criteria and selection require considerable further thought. However, even at this early stage it is worth also raising some questions on funding and coverage. Although Article 12 of the Directive does not specifically provide for EU funding, it is likely to create pressure for ERNs to benefit from core support or from seed monies. This will, inevitably, raise questions as to which specific aspect(s) of ERNs the EU should be paying for, how priorities will be defined, and how any financial support should be made sustainable over the longer term. It is too soon to formulate answers to these questions, but it is interesting to observe that national health systems do typically not include financial incentives for centres of expertise to allow them to provide clinical support to other network members, particularly where these are international.

The cross-border referral of patients is another important consideration. Even where this is not an explicit or prime intention of ERNs, the simple act of designation is likely to generate flows of patients. In these cases, questions will be posed as to the impact on Member State budgets and their ability to refuse prior authorization for treatment (under Regulation (EC) No 883/2004); or to refuse reimbursement for services or treatment methods not covered in the competent state. Recent cases brought to the European Free Trade Association Court, such as *Rindal and Slinning* (E-11/07 and E-1/08), and the European Court of Justice, such as *Elchinov* (C-173/09), have reopened the debate as to whether national systems can refuse to reimburse so-called experimental (or better, not nationally recognized) treatments or innovative treatment methods that prove to be more effective than the options available at home. Even though the Directive specifies that the creation of ERNs shall not be seen to harmonize any national laws or regulations and confirms Member States' responsibilities for the organization and delivery of health care, creating these ERNs may well create demand to open them to all EU citizens alike, thus increasing financial pressure on the respective statutory health systems. Certainly, in the area of rare diseases (and given the high costs involved), ERNs are likely to prompt discussions around differences in resources allocated to health care and solidarity across Europe. However, even in areas where cost may be a lesser consideration, the additional transparency and the highlighting of models of excellence may well be challenging for some Member States.

Despite the many questions and challenges still to address, the idea of creating ERNs seems to have sound roots and be relatively well supported as a way of fostering cross-border cooperation in health care at the European level. The concept itself has value not just in promoting excellence, but also in that it embodies a comprehensive range of key concerns, such as quality and safety, accessibility, cost-effectiveness, coordination and continuity of care, and patient orientation. In that sense, the move towards ERNs may generate a broader and highly pertinent debate on how best to support Member States in developing their health systems.

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Annex I

Some examples of (European) reference networks

Organisation of European Cancer Institutes (OECI)

Web site <http://www.oeci-eeig.org/>

Level European (27 countries)

Composition The network is composed of 67 centres specializing in oncology. To become a member, a cancer institute must work in the area of cancer, including research, prevention and care.

Objectives To bring together cancer research and cancer institutes of the EU to create a critical mass of expertise and competence with the view of building and maintaining a consensus on the best models of oncology, developing concrete, affordable and realistic solutions to effectively combat cancer, and fostering the widest deployment of oncology models and solutions to improve the quality of life for the patients in the EU.

Governance European Economic Interest Grouping

Scope Common (cancer)

Better control in Pediatric and Adolescent diabetes: working to create Centres of Reference (SWEET project)

Web site <http://www.sweet-project.eu/>

Level European

Composition The project comprises a group of established European and national diabetes organizations that have joined together to improve diabetes management in children and adolescents.

Objectives To enhance the health and quality of life of children and young people affected by type 1 and type 2 diabetes in Europe by improving: secondary prevention, early diagnosis and control, effective management. SWEET will address these, e.g. by stimulating the exchange of information and good practice, developing recommendations for standards of care and education. With this support, SWEET wishes to achieve something in the framework of the European Union that may have importance beyond the European boards: the establishment of Centers of Reference for Pediatric Diabetes (CORs).

Governance Centres of Reference for Pediatric Diabetes are accredited through the governing bodies of SWEET and the International Society for Pediatric and Adolescent Diabetes (ISPAD). In 2011, the accreditation procedure for the first 13 centres of reference had started (Danne, 2011).

Scope Paediatric and adolescent diabetes

Belgian–Dutch Clinical Pathway Network (NKP)

Web site	http://www.nkp.be/default.html
Level	Transnational
Composition	The network has over 100 members covering different types of health-care organizations such as acute hospital trusts, rehabilitation centres and home care providers.
Objectives	The aim of the network is not to refer patients between member hospitals but to improve patient pathways through education in clinical pathways, multidisciplinary research and cooperation in pathways (within and between hospitals), cross-border training, international collaboration (with other universities), benchmarking, clinical peer reviewing, etc. The network has developed and/or implemented more than 1200 pathways.
Governance	Joint venture since 2003 between the Dutch Institute for Healthcare Improvement (CBO) and the Université Catholique de Louvain (UCL) in Belgium.
Scope	Various

Planning of highly specialized functions in Denmark

Web site	http://www.sst.dk/Planlaegning%20og%20kvalitet/Specialeplanlaegning/Specialeplan_2010.aspx
Level	National
Composition	The network comprises departments or units of public and private hospitals in Denmark that may be recognized as regional or national referral centres.
Objectives	By late 2010, 2500 highly specialized functions had been recognized in Denmark. Such functions can involve prevention, diagnosis, treatment, rehabilitation and/or control of diseases or conditions where services are of considerable complexity and presuppose the presence of several multidisciplinary functions/partners, where the diseases or the health system's services are rare and therefore create a need for concentration of experience and/or which are particularly resource intensive. To obtain accreditation, hospital departments must fulfil criteria on experience, case volumes, multidisciplinary work, capacity for research and training, as well as robustness and sustainability (e.g. to avoid the specialized functions being centred around a particular individual).
Governance	Based on the Health Law of 2007 giving the National Board of Health mandate to define the criteria for accrediting national/regional reference centres with highly specialized functions.
Scope	Various, including about 100 diagnoses or diagnosis groups on rare diseases

Italian National Network on Rare Diseases

Web site	http://www.iss.it/cnrmr/ccmr/chis/index.php?lang=1&tipo=10&anno=2011
Level	National
Composition	The network is composed of accredited centres, of which certain are nominated interregional centres of reference. Centres must have documented experience in diagnostic or therapeutic activities specifically for the disease in question, suitable support structures and complementary services, and where necessary, emergency services and biochemical and genetic-molecular diagnostics.
Objectives	The national network on the prevention, surveillance, diagnosis and therapy of rare diseases is set up to assist and protect patients with such disease. These patients are exempt from contributing to the costs of their treatments.
Governance	Based on ministerial decree of 2001.
Scope	Rare diseases

Interregional network of Piedmont and Vale d'Aosta for rare disease

Web site	http://www.malattierarepiemonte.it/
Level	Interregional (two neighbouring Italian regions)
Composition	University hospital(s) and local health-care providers
Objectives	The interregional network is based on the pre-existing regional network of Piedmont built upon a model of care for rare diseases that encourages access to centres of excellence in the diagnostic phases and the decentralization of treatment and rehabilitation to local health units, especially for repeated interventions. The model includes multihospital working groups setting up treatment protocols and patient pathways. The interregional structure gives residents of both regions access to the same treatment options, particularly relevant since there are no academic hospitals in the smaller region of Valle d'Aosta.
Governance	Convention signed in 2008 between Piedmont Region and Valle d'Aosta Autonomous Region on the creation of an interregional coordination centre for rare diseases and an interregional registry of rare diseases.
Scope	Rare diseases (based on ministerial decree of 2001)

Networking of European cord-blood-bank-based GMP (good manufacturing practice) laboratories suitable to prepare clinical grade cell therapy products for European Clinical Reference Centres

In the late 1980s, the discovery of the presence of large numbers of haemopoietic progenitors and stem cells (HPSC) in cord blood paved the way for the development of cord blood banking programmes in Europe and the United States of America. The creation of 36 internationally accessible cord blood banks with an inventory of more than 180 000 donations has permitted transplantation for about 6000 patients (two thirds of them children) in need of bone marrow replacement. These achievements can now be considered a consolidated development of a form of therapy traditionally called bone marrow transplantation. Based on the availability of a particularly well-developed EUROCORD/NETCORD²⁶ public cord blood banking network of the highest international accreditation and a joint inventory of over 60 000 units, a large expertise has been accumulated about the GMP requirements for the procurement and testing of human tissues and cells under European regulation.

In parallel, and as a result of the increasing success of cord blood, a new type of financially expensive infrastructure, technologically and operationally not dissimilar from a small- to medium-size GMP pharmaceutical industry and called “Cell Factory”, has been developed by most European cord blood banks active in this nascent field with academic institutions mainly involved in the treatment of cancer, hereditary diseases and degenerative conditions.

²⁶ <http://eurocord.org/index.php?setLang=EN>; <http://www.netcord.org>.

Annex II

Overview table

Country	Main technical focus	Geographical scope	Procedure
Belgium	Rare diseases Chronic conditions	National	Article 14 of the Federal Hospital Act refers to the concept of reference networks, but has not been implemented so far. The National Institute for Health and Disability Insurance concludes specific agreements with reference centres.
Czech Republic	Rare diseases Highly specialized care Cancer Transplants	National	National Coordination Centre for Rare Diseases Act 372/2011 on Health Care Services Comprehensive Cancer Centres Transplantations Coordinating Centre (KST)
Denmark	Specialized hospital functions	National and regional	National Board of Health: mandate to define requirements and criteria for specialized functions
Estonia	Tertiary care provided in regional and central hospitals Excellence centres in cancer care	National and regional	Types of hospitals are specified in the Hospital Network Development Plan. The level of care provided in each level of hospital is determined by the Ministry of Social Affairs. The Strategy for Quality of Cancer Care defines requirements for excellence centres in cancer care.
Finland	Rare diseases Highly specialized interventions	National and regional	Voluntary mutual agreements to establish networks Governmental decrees centralizing specific highly specialized care in 1–3 centres
France	Highly specialized care Cancer Rare diseases	National and interregional	Structuring of hospital care at three levels (local, general, regional) National certification of centres of excellence among university hospital centres and institutes Creation of national networks around a central agency: e.g. the French Biomedicine Agency (transplants), the National Institute for Cancer 34 centres of reference designated for rare diseases

Germany	Rare diseases Specific areas of medical practice (also common and chronic diseases)	National and regional	National funding arrangements and activity thresholds to stimulate concentration and integration of specialized care 17 competence networks in medicine to establish and promote clinical competence in a specific disease, bringing together the most important and innovative research institutions Four innovative research and treatment centres: disease-related clinical research centres to overcome structural deficits in academic medicine German centre for diabetes research: combining expertise of federal institutes and universities
Greece	Rare and chronic diseases	National	National certification as specialized centre De facto reference centres
Hungary	Specific and rare diseases	National	Assignment of national centres of expertise through the National Rare Disease Centre
Italy	Rare diseases Complex procedures, including transplants	National, regional and interregional	Structuring of health care at three levels (local, regional, national) + intermediate sub-national certification of networks (e.g. rare diseases and transplants)
Lithuania	Highly specialized care	National	Activity threshold to centralize highly specialized care in two university clinics and some specialized tertiary care institutions (e.g., national oncology centre) Cross-border referral of patients for rare and complex cases
Malta	Highly specialized care	National	National Highly Specialized Referrals Programme to send patients overseas for treatment of complex cases
Netherlands	Special medical procedures Patients with rare and complex diseases Chronic and genetic, congenital or rare diseases	National	National certification of university medical centres and other hospitals under the 1997 Special Medical Procedures Act Concentration of highly specialized multidisciplinary treatment for tertiary referral patients in university medical centres Networks for Parkinson's disease and genetic, congenital or rare diseases
Norway	Highly specialized care Advanced treatments Chronic conditions	National and regional	39 national treatment services and 7 multiregional treatment services to concentrate highly specialized tertiary care 42 national competence services to build and disseminate expertise

Country	Main technical focus	Geographical scope	Procedure
Poland	Highly specialized services Most complicated cases	National and regional	National institutes and centres for most complicated cases, directly supervised, contracted or accredited by the Ministry of Health Certified network of trauma centres Highly specialized services reserved for hospitals meeting additional requirements (with increased reimbursement)
Romania	Tertiary care and care for complex cases Critical care (e.g., burns, transplants) Chronic diseases	National and regional	Classification of hospitals into five categories (highest level also acting as teaching units, research centres and reference units) Reference centres established by order of the Minister of Health according to certain criteria
Slovenia	Tertiary care	National	National certification of clinics, clinical institutes and clinical departments by the Ministry of Health
Spain	Selected reference services that require concentration of diagnostic and therapeutic resources (advanced technologies, rare expertise, low prevalence of cases)	National and regional	National designation of centres, departments or units within the Spanish National Health Service to provide reference services by the Interterritorial Council and the Ministry of Health, Social Policy and Equity
Sweden	Rare diseases Areas of highly specialized treatment requiring special technology and medical competence	National and regional	Designation of National Specialized Medical Care by the National Board of Health and Welfare and the Committee for National Specialized Medical Care.
United Kingdom (England)	Highly specialized services that are complex, rare and/or expensive Rare diseases	National, regional and pan-regional	(Inter)Regional concentration of specialized services through 10 Specialised Commissioning Groups that commission specialized services for their regional populations (e.g. haemophilia and blood and marrow transplantation, rare cancers, specialized burn care, medical genetics, renal services and specialist cardiac services) National concentration of 60 highly specialized services through the National Specialised Commissioning Group (e.g. rare conditions, heart transplantation) Clinical specialist networks at national or regional level in relation to several specialized services (e.g. burn care, cancer, cardiac and stroke)

Under the European Directive on the application of patients' rights in cross-border health care that was adopted in March 2011, the development of European reference networks was promoted as one of the prime areas for cross-border cooperation among Member States. These networks are meant to improve access to and provision of high-quality health care to all patients who have conditions requiring a concentration of specialized resources or expertise. At the same time they could act as focal points for medical training and research, information dissemination and evaluation, especially for rare diseases.

The idea of pooling resources in order to better address medical conditions that are rare or require very specialized expertise or equipment corresponds with moves towards concentration of specialized health care services, often motivated by common health systems challenges such as tightening financial constraints, workforce shortages and growing attention to quality and safety.

This book examines the different ways in which the concept of reference networks has been implemented in European countries, and what kind of medical conditions or interventions it covers in various countries. It also looks at the motivations behind the establishment of such networks, the regulatory and administrative processes for identifying and designating them, as well as the financial arrangements needed for their proper functioning. This study outlines the key policy implications and challenges for developing the concept of reference networks at national and European levels. Ultimately it aims to provide a better understanding of the issues that may be encountered when implementing the Directive.

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