European Union Committee of Experts on Rare Diseases

EUCERD REPORT

HEALTH INDICATORS FOR RARE DISEASES

II – Conceptual framework for the use of health indicators for monitoring quality of care

September 2011

INTRODUCTION & METHODOLOGY

Introduction

This report was produced by a working group of the European Union Committee of Experts on Rare Diseases[1] (EUCERD, formerly the European Commission's Rare Disease Task Force), with the aim of defining suitable indicators to monitor quality of care in the field of rare diseases in different countries and year after year. This report is the result of a workshop organised by the EUCERD Scientific Secretariat on 25 November 2010 to follow up on the work carried out by the former European Commission Rare Disease Task Force working group on health indicators which has produced the following reports:

- Health indicators for rare diseases: State of the Art and Future Directions[2] (2008)
- Health indicators for rare diseases: Conceptual framework and development of indicators from existing sources[3] (2010)

The report "Health indicators for rare diseases: Conceptual framework and development of indicators from existing sources", identifies the main areas/dimensions in relation to the current need for indicators for rare diseases: indicators to monitor the development of health policies and initiatives for rare diseases at national and EU level; and indicators of health outcomes and health status. The RDTF/EUCERD working group on health indicators has, over the past 2 years, focused on two topics: registries for single rare diseases as sources of indicators, and quality of care indicators for RD. When there is progress in the knowledge of a rare disease and specific health care planning for rare diseases exists, there is potential to measure quality of care. As costs need to be justified and motivated, there is increasing emphasis on the use of quality of care indicators. Quality of care indicators can be used for areas such as health status/health outcomes, and healthcare/ healthcare services. One of the challenges in the field is to link these two areas.

Indicators should be validated for their validity, their reliability, their evidence base, the availability of internationally-comparable data across countries and the susceptibility of influence from health care systems. Validation of indicators can be carried out through a study of available literature and by adapting existing OECD criteria. The data should also be validated, i.e. the intrinsic quality of the database must be validated, the population base and its representativeness, the geographic coverage, and the collection over time.

Patient registries for specific rare diseases have been identified by the working group as one feasible source of data for building indicators for monitoring quality of care in the field of RD

[1] www.eucerd.eu
[2] http://www.eucerd.eu/upload/file/Publication/RDTFHI2008.pdf
[3] http://www.eucerd.eu/upload/file/RDTFReportIndicatorsApril2010.pdf

due to the professionalisation in the area and increased attention to quality of data. There is minimal codification bias in this field, some registries have been collected data for more than 20 years, and the use of outcomes has been validated by scientific societies. There are, however, drawbacks associated with patient registries, i.e. their representativeness, geographic coverage, quality of data and continuity of collection. However, the working group views a strategy based on existing registry data as a resource-saving strategy which could help avoid the duplication of efforts.

On 25 November 2010, the Scientific Secretariat of the EUCERD organised an expert workshop on health indicators for rare diseases in order to explore how indicators for rare diseases can be produced from existing registry data in order to monitor quality of health care. The present report is the result of this workshop.

The correct form when quoting this document is:
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http://nestor.orpha.net/EUCERD/upload/file/RDTFIndicators2011.pdf

Methodology

Following the RDTF Indicators workshop of November 2009[4], it was decided that a follow-up strategy would be implemented to concentrate further work on the demographic, health status and health outcome indicators which can be produced by existing registries, in particular registries for single rare diseases or clusters of rare diseases (usually but not exclusively run by academics) collecting data on rare diseases. The relationship of these indicators with quality of care and their suitability to be used for monitoring quality of care considering the way they have been generated and alternative ways of computation, has been explored and will be discussed.

Attention has been focused on ten registries, which were studied through the documents and publications they produce, past presentations of their data, and through direct interviews. The registries chosen have a European dimension and some form of data collection control. The diseases they cover are very heterogeneous and so are the registries are very heterogeneous as well.

The type of data collected by the registries was assessed, as was the methodology of their data collection which is relevant to the evaluation of their 'fitness' to produce indicators. This assessment was made on the basis of a questionnaire elaborated during, and finalised after, the 2009 RDTF workshop (available in annex of the 2010 Report "Health indicators for rare diseases: Conceptual framework and development of indicators from existing sources[5]").

A number of registry leaders who were interviewed for this questionnaire were selected to present their work at the workshop:

- ERCUSYN[6]: Cushing and related syndromes
- ENRAH[7]: alternating hemiplegia (an example of a very rare disease)
- EUROCARE CF[8]: Cystic fibrosis (an example of a relatively 'common' RD),
- MARFAN Cohort and Registry[9] (a disease where quality of care can make the difference to a prognosis)
- EUROFEVER[10]: rare autoinflammatory disorders (an example of a register covering a cluster of diseases).

[4] http://www.eucerd.eu/upload/file/RDTFReportIndicatorsApril2010.pdf
[5] http://www.eucerd.eu//upload/file/RDTFReportIndicatorsApril2010.pdf
[6] http://www.lohmann-birkner.de/ercusyn/
[7] http://www.enrah.net/
[8] http://www.eurocarecf.eu/
[9] http://www.orpha.net/consor/cgi-bin/ResearchTrials_RegistriesMaterials.php?lng=FR&data_id=67063&Nom%20du%20registre%20ou%20mat%E9riel=Cohorte-de-patients-presentant-un-syndrome-de-Marfan-ou-apparente&title=Cohorte-de-patients-presentant-un-syndrome-de-Marfan-ou-apparente&search=ResearchTrials_RegistriesMaterials_Simple
[10] http://www.printo.it/eurofever/

These registers collect information on health status (mortality/life expectancy), health outcomes, processes, and the onset of symptoms/date of diagnosis. The type of data less frequently collected is: the degree of severity of the disease, global health status, comorbidities, functional status/disabilities, quality of life, and working status/ social status/ social life/ activities.

These registry leaders prepared a presentation of indicators which could be derived from their registry data for discussion at the 2010 workshop. Particular attention was paid to the evaluation of the importance of these indicators and the relevance of the indicators in relation to what they are meant to measure. The relationship of the proposed indicators and their validity as measures of quality of care were discussed and evaluated.

Workshop participants were provided with detailed information on the proposed indicators, their relationship with quality of care, and their possible computations. Specific characteristics of the registries relevant to the generation of indicators, such as their opinion on the quality of the data, the number of years of data collection, the geographic representativeness, etc., were also provided to participants among others.

The present document gives an overview of the conceptual framework of the use of health indicators to monitor quality of care, as well as highlighting examples of indicators which can currently be derived from current registry data for this purpose. The present report has been elaborated using the preparatory workshop documentation and the outcomes of the discussions of the 2010 EUCERD workshop on Indicators.

CONCEPTUAL FRAMEWORK FOR THE USE OF HEALTH INDICATORS FOR MONITORING QUALITY OF CARE

The need for monitoring quality of care in the field of rare diseases

Rare diseases have been neglected for a long time in health care planning. In the past, there has often been no dedicated health care strategy in place for rare diseases, and so there was basically nothing to monitor. The increased awareness of rare diseases of the past years has brought the creation of specific health care initiatives, including the elaboration of national plans/strategies for rare diseases, centres of expertise, European networks, and increased attention to improvement of diagnosis and treatment of rare diseases. Even if health care for rare diseases is still far from ideal, and many diseases still do not receive any specific attention in health care systems, it is time to start monitoring health care interventions for rare diseases whenever possible.

The steadily increasing costs of health care (health spending across industrialised countries almost doubled in the last thirty years according to OECD data) imply the need to justify health care interventions and plans with accurate cost/benefit measures and by showing the impact of interventions on relevant outcomes. Rare diseases are in most cases chronic, heavily debilitating, and often life-threatening, and health care for such diseases can have quite high costs: for example rare diseases account for the largest number of conditions leading to solid organ transplantations, which are probably the most expensive health interventions. In addition diagnosis is often difficult and requiring costly highly specialised health care. It is therefore important that healthcare actions for rare diseases can be not only justified by principles of equity and solidarity but also legitimated by the demonstration that such interventions do indeed change outcomes of the diseases.

Interested parties in the monitoring of quality of care

Evaluation of the quality of care is usually carried out by specialised units belonging to the healthcare systems themselves, and through public health and surveillance institutions. In the field of rare diseases it has already been shown that in the majority of cases such institutions do not monitor quality of care for rare diseases, as this is not part of their traditional remit. Whenever they decide to start such monitoring, they face time and resources constraints, as data for rare diseases are usually not being collected in administrative data frameworks, or

collection is inappropriate due to inadequate coding. Some examples of collection of data from administrative sources and related difficulties have been shown during the 2009 RDTF Indicators Workshop[11] with the work performed by the *Institut de Veille Sanitaire* of France on mortality on four rare diseases (Hemophilia A and B, sickle cell disease, and cystic fibrosis). The example of health monitoring for specialised commissioned services in the UK was given during the 2010 EUCERD Indicators Workshop (see Annex 1).

Registries for single rare diseases or clusters of diseases are in the position of creating relevant indicators for monitoring quality of care, and in particular they are in a unique position in what concerns health outcome indicators. The rarity of the diseases also implies a rarity in expertise and the people involved in data collection, basically putting the whole process in the hands of a very small group of people, who:

i) Possess the necessary expertise to choose and validate health outcomes indicators (through publications, expert consensus);
ii) Belong to the health care structures where the patients are followed;
iii) Run/participate in registries where data on the specific disease object of the expertise are collected.

This puts registries for a single rare disease (or cluster of rare diseases) in the position of contributing to the generation of quality of care indicators in many cases, and even to be the only possible way of doing such monitoring in some cases.

This does not mean that there is no other way of monitoring quality of care for rare diseases apart from this type of registry. Some local (or regional, in some cases national) registries are collecting data on rare diseases and might have the advantage of a more valid population base than registries for single diseases/clusters of diseases: during the 2010 EUCERD Indicators Workshop the experience of the Veneto Region Registry was given (see Annex 1). On the other hand, they have the disadvantage of collecting only a limited number of fields of data, due to the large number of rare diseases that have to be monitored.

In addition, quality of care for rare diseases can be monitored using structure indicators, i.e. indicator of the characteristics of, or inputs to, health care. One classic example of a structure indicator is whether doctors are suitably qualified and whether hospitals are properly equipped. Such structure indicators are usually not supposed to be in the sphere of competence of registries such as the ones addressed in the two RDTF/EUCERD workshops. Structure indicators have been developed by Europlan[12], which measure whether structures exist for rare diseases. Due to the relative novelty of action planning for rare diseases and the fact that the Europlan indicators had to 'fit all sizes' (i.e. be usable from different countries with completely different health care systems), they are necessarily general, that it is to say they measure very general actions rather than specific ones. Specific actions will be decided by single countries and specific national structural indicators will need to be created. As an

[11] http://www.eucerd.eu/upload/file/RDTFReportIndicatorsApril2010.pdf
[12] http://www.europlanproject.eu/Home.aspx

example, the Europlan indicators measure whether centres of reference/expertise have been created in a country, and how many. However they could not be designed for measuring the performance of the centres of reference/expertise because such centres will be organised differently in each country, according to the different health care systems.

To conclude, it is interesting to give the example of the current strategy for the development of quality indicators (in general) of the UK national health system (NHS). Such a strategy involves clinical teams, universities, and specialist societies (together with Royal colleges, NHS information centre, and the commercial sector) more actively in different steps of the assessment of quality of care as compared to the past, not only as sources of evidence-based indicators for quality of health care, but also in benchmarking and measuring quality, with the aim of having indicators *'assured by clinicians for use by clinicians'*.

The quality pyramid represents a schema of such strategy and suggests the fact that stakeholders mainly involved in the clinical and scientific work of specific diseases can collaborate with the health care system for its quality control, at different stages.

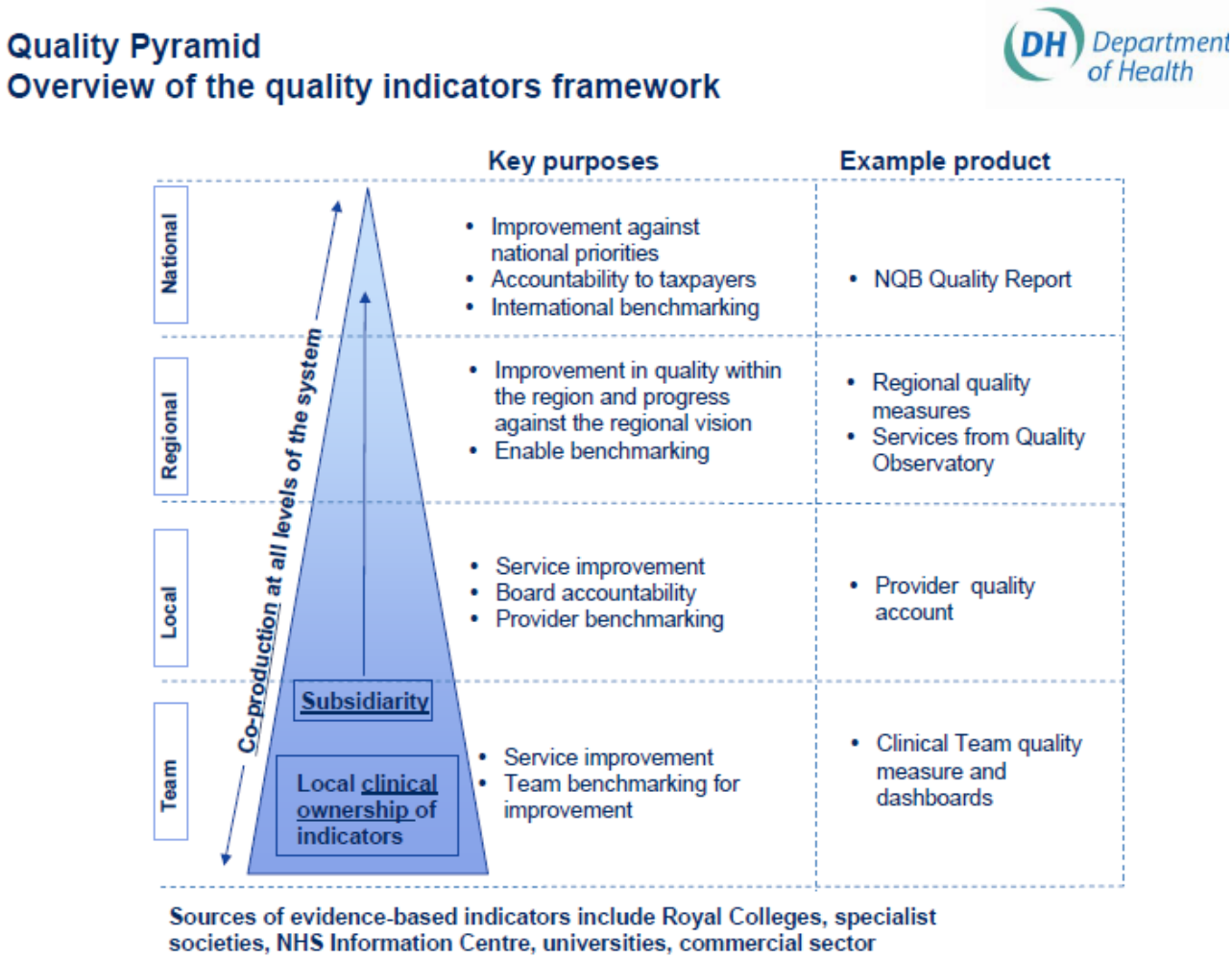

Figure 1: Source - UK Department of Healt

The dimensions of quality of care

In 1998 Donabedian[13] posed the basis of evaluation of quality of care:

"Before assessment can begin we must decide how quality is to be defined and that depends on whether one assesses only the performance of practitioners or also the contribution of patients and of the health care system; on how broadly health and the responsibility for health are defined; on whether the maximally effective or optimally effective care is sought,; and on whether individual or social preferences define the optimum. We also need detailed information about the causal linkages among the structural attributes of the settings in which care occurs, the processes of care, and the outcomes of care. Specifying the components of outcomes of care to be sampled, formulating the appropriate criteria and standards, and obtaining the necessary information are the steps that follow".

Several dimensions of quality of care can be measured, where dimensions are defined as those definable, preferably measurable and actionable, attributes of the system that are related to its functioning to maintain, restore and improve health (JCHO, 1971). Such dimensions have been extensively studied and used in different types of projects concerning indicators. We present as example the dimensions as graphically illustrated in the OECD Health Care Quality Indicators Project Conceptual Framework published in 2006[14].

[13] A. Donabedian "The quality of care: how can it be assessed?", *JAMA*. 1988;260:1743-1748
[14] http://www.oecd.org/dataoecd/1/36/36262363.pdf

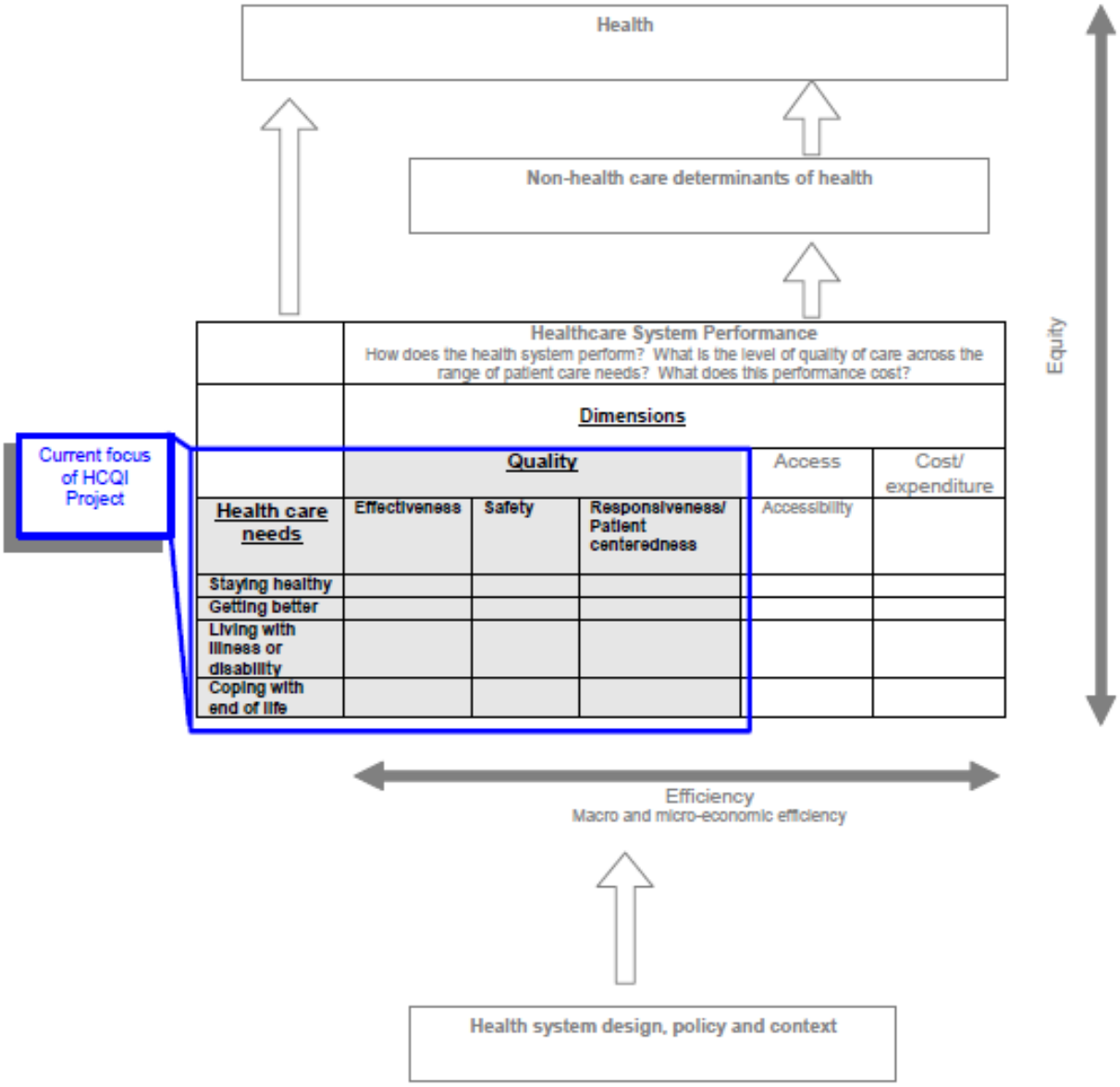

Figure 2: Proposed conceptual framework for OECD health care quality indicators project[15]

The OECD schema shows all main measurable dimensions of health and it puts in evidence (highlighted by the blue box/darker area) the dimensions related to quality of care: effectiveness, safety and responsiveness/patient centeredness. Such dimensions are the core attributes of quality of care, i.e. the attributes which increase the likelihood of desired outcomes.

The indicators explored by the RDTF/EUCERD with the registries involved in the present workshop almost exclusively address the dimension of effectiveness, as other dimensions are

[15] http://www.oecd.org/dataoecd/1/36/36262363.pdf

out of the current scope of the data collection from registries for single diseases such as safety. Responsiveness/patient centeredness is from a theoretical point of view a dimension of interest in the field of rare diseases, as it is the degree to which a system functions by placing the patient/user at its centre and it is usually addressed in terms of patients' experience and perception of the health care. However such a dimension is at present difficult to assess in the field of rare diseases, for the paucity of validated instruments. The main components of quality of care which are of interest in rare diseases and can be addressed using registries for single diseases/clusters of diseases are:

- Recognition of patients at risk for the disease;
- Start the appropriate evaluation;
- Make the appropriate diagnosis;
- Start the appropriate treatment;
- Schedule the appropriate follow-up;
- Stimulate the appropriate compliance/adherence to treatment.

Monitoring quality of care with health outcome indicators

As first stated by Lalonde[16] in 1974, health is determined by a number of factors, one of which is health care. When evaluating health care by means of health outcomes indicators, it is therefore important to focus on those indicators which are more related to this aspect than to other determinants of health such as e.g. lifestyle, environment or the biologic characteristics of a disease. As an example in the field of rare diseases, subjects with alpha1-antitrypsin deficiency are at risk of developing severe emphysema at young age; therefore an early diagnosis is recommended and can represent an indicator of quality of care. However once the deficiency is diagnosed, the development of the disease is linked to smoking in most cases, therefore indicators aiming at evaluating quality of care after the moment of diagnosis will have to take this lifestyle factor into account and correct for it.

The same considerations hold true when the diagnosis of a disease is particularly difficult or many intermediate phenotypes exist, or some very generic symptoms are followed by a long latency period before the development of more specific symptoms that can lead to a diagnosis. In these cases diagnosis delay might not be the most appropriate indicator to measure quality of care, as the signal of the effects of the health care system in achieving a timely diagnosis of the disease will be confounded by the characteristics of the disease itself: "*We can only be sure to improve what we can actually measure"* (Lord Darzi, High Quality Care for All, June 2008[17]).

[16] http://www.hc-sc.gc.ca/hcs-sss/pubs/system-regime/1974-lalonde/index-eng.php
[17] http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_085825

Outcome indicators seek to represent measures of health improvement (or deterioration) attributable to medical care (OECD 2006), based on health/clinical outcomes (a classical example is the rate of 1 year survival following acute myocardial infarction). Many of the indicators proposed by the registries are health/clinical outcomes (e.g. cortisol measurements in Cushing disease, aortic dissection in Marfan disease). As already mentioned, the main concern of outcome indicators is that they may be influenced by other factors than quality of care, therefore there has to be sufficient evidence that quality of care makes an independent contribution to the outcome and adjustment for the confounding factors should be performed.

However process indicators can also be derived by the data of the registries participating in the preparation of the 2010 EUCERD workshop, and were presented to workshop participants. **Process indicators** represent measure of the delivery of appropriate (or inappropriate) healthy care to the relevant population at risk[18]. Examples of process indicators from participating registries include: the number of tonsillectomies performed in the population of interest (undetermined fever), or number of echocardiography assessments in a specific time-frame per patient with Marfan disease. It is important to remember that the degree to which the proposed measurements are related to clinically desirable outcomes should be considered when using process indicators.

Quality of care indicators from registries for single rare diseases/clusters of rare diseases

The type of data collected by registries for single rare diseases/clusters of diseases is usually decided at the creation of the registry by a steering group/expert group. Relevant data fields are based on scientific rationale, existing literature evidences, and experience of the experts on the specific rare disease or cluster of rare diseases. Usually the type of data which are collected depends on the aims of the register. The interviews carried out with different registries prior to the 2010 EUCERD Indicators workshop confirmed that none of them had the aim of producing indicators other than epidemiological ones, such as prevalence and mortality of the disease.

Nevertheless, as can be seen from the possible indicators proposed by the five registries interviewed prior to the 2010 EUCERD Indicators workshop, some of the data collected are usually suitable to be thought of in terms of indicators. Whether they can be used or not depends also on all the methodological considerations addressed by this report. Besides the characteristics of the indicators, the characteristics of data collection are also extremely important for evaluating the possibility (feasibility/fitness for purpose) of producing indicators from the available data.

[18] OECD 2006

The development of quality indicators for rare diseases from the registries requires the following approach:

1. *Selection of the indicator(s)*
2. *Provision of appropriate computations*
3. *Verification of characteristics of data collection for the specific indicator (i.e. Who should carry out this verification?).*

Steps 1 and 3 are the most crucial. The criteria for choosing indicators of quality of care are extensively discussed in the main literature on indicators and several series of criteria have been proposed. The OECD criteria for quality indicators are as follows[19].

1. *Importance* of what is being measured

Impact of disease or risk on health and on health expenditure. What is the impact on health and on health expenditure associated with each disease, risk or client group? To help understand these impacts, the OECD has prepared a list of conditions with the highest costs, morbidity, and mortality. Preferably, the measure will address areas in which there is a clear gap between the actual and potential levels of health that can be influenced by improvements in the quality of care.

Policy importance. Are policy makers and consumers concerned about this disease or risk group area?

Susceptibility to being influenced by the health care system. Can the health care system meaningfully address this disease area or problem? The measure should reflect an aspect of health that can be influenced by the health care system as it exists or as it is envisioned. That is, policy makers can take specific actions (generally at the structural or process level) to improve health care in that area and, ultimately, health status. Injuries caused by automobile accidents, for example, are the leading cause of death among young adults, but most remedies (for example, changing car design or reducing the speed limit) lie outside the influence of the health care sector.

2. *Scientific soundness* of the measure

Validity. Does the measure actually measure what it is intended to measure? The measure should make sense logically and clinically (face validity); it should correlate well with other measures of the same aspects of the quality of care (construct validity) and should capture meaningful aspects of the quality of care (content validity) (Carmines and Zeller, 1991; Nunnally, 1978). In general, measures should be linked to significant processes or outcomes of care as demonstrated by scientific studies. For

[19] This list, reproduced in the previously cited OECD report http://www.oecd.org/dataoecd/1/36/36262363.pdf has been modified directly from the report "Envisioning the National Health Care Quality Report" by the US Institute of Medicine (Hurtado MP, Swift EK, and Corrigan JM, eds., (Washington: National Academy Press, 2001)).*References* Nunnally, J.C. 1978. *Psychometric Theory*. 2nd ed. New York: McGraw-Hill. Carmines EG and Zeller RA. 1991. *Reliability and Validity Assessment*. Newbury Park, Calif.: Sage Publications.

example, the provision of selected screening tests in a timely manner is a process measure of quality that has construct validity when the screening is linked to earlier detection of disease and a better prognosis or outcome. Outcome measures should be examined for validity in a similar manner.

Reliability. Does the measure provide stable results across various populations and circumstances? The measure should produce consistent results when repeated in the same populations and settings, even when assessed by different people or at different times. Measure variability should result from changes in the subject of measurement rather than from artefacts of measurement (for example, a change in the definition of the measure or, for rare events, restricted sample size or small numbers of cases). This aspect is particularly important for periodic data collection. Most measures will have to be repeated every year, and any changes in the measure should reflect a true change in quality.
Explicitness of the evidence base. Is there scientific evidence available to support the measure? There should be a clearly documented scientific foundation for the measure in the literature. An explicit evidence base could also mean that there is some other specific, formal process by which the measure has been accepted as a valid marker for quality, such as review by an expert panel.

3. *Feasibility* of obtaining internationally comparable data for the measure

***Existence of prototypes*.** Is the measure in use? A further question is if the measure is in use at the national level, or for sub-national population groups.

Availability of internationally-comparable data across countries. Can internationally-comparable information needed for the measure be collected for sufficient countries in the time frame required? At one extreme, a few indicators of the technical quality of health care can already be found for most countries in *OECD Health Data*. At the other extreme, there will be many potential indicators for which few if any countries could provide any data in the foreseeable future. In between these extremes, there are likely to be some indicators for which data would be readily available at national level for a significant group of countries, but with variations in the precise definitions of numerators and denominators. There are likely to be other indicators for which national data has not yet been assembled (say, from local or clinical databases) and which could be put together according to a common definition only with considerable effort.

Cost or burden of measurement. How much will it cost to collect the data needed for the measure?

1. Selection of the indicator(s)

Even though it is not necessary that the indicators for monitoring quality of care in rare disease fulfil all these criteria, some of them are particularly important and they should be taken into account. We suggest the following as the most important for the work of developing health indicators for quality of care in rare diseases:

i) susceptibility to being influenced by the health care system;
ii) validity;
iii) reliability;
iv) explicitness of the evidence base;

v) **availability (or feasibility when not available) of internationally-comparable data across countries**.

Other criteria, even though very important, are at present difficult to fulfil in the case of rare diseases.

2. Provision of appropriate computations

Computations of indicators have been extensively studied and published, therefore once the indicator has been chosen it should not be a problem to find the most appropriate computation for it. Again, slightly different computations might be chosen for the same indicator depending on the type of data and the message that we want to put in evidence with the indicator (e.g. data on death can be used to show that more people die of a disease in a country than in another; the same data, if we use the age of death, can be used to demonstrate that people die at earlier age in one country than in another). In this context 'appropriate' refers to 'appropriateness for the purpose'.

3. Verification characteristics of data collection for the specific indicator

The feasibility of an indicator depends largely on data collection and its quality. In the fields where indicators are now being produced for many years, substantial work has been done on the analysis of the quality of data and their fitness for international comparisons. The methodology of the project RareCare[20] (see Annex 1), created for studying indicators (epidemiologic to start with) for rare cancers, is an important example of such quality analysis. In the case of rare cancers, data from all European countries were analysed. The analysis concerned cancer data such as topographies and morphologies, including combinations of data fields such as; consistency between date of birth, diagnosis and follow-up; consistency of site-morphology combinations; consistency of age-site, age-morphology, sex-site and sex-morphology combinations; consistency of morphology-behaviour combinations. This analysis is specific for cancer data; the methodology of RareCare is explained in Annex 1. Analysis of the data is a very important step in order to check the correctness and consistency of diagnosis, and to assess the extent of missing data and correct this deficiency. In general, for the production of indicators in rare diseases registries should consider: i) quality, ii) geographical coverage and iii) population base, as the most important characteristics of data collection to be kept in mind for the development of quality of care indicators.

Data quality

Data are collected from the expert clinical/scientific centres belonging to the registry, and in some cases from additional centres 'accredited' by the registries, and pooled in a single

[20] http://www.rarecare.eu/

database. In general national databases are also maintained. Significant differences in the quantity and quality of data collection between countries can be observed, with some registries collecting data of 'gold' quality and other countries performing very poorly.

The level of data quality that we need for the purpose of generating indicators for rare disease still has to be discussed. Main issues are how to treat the data which are not 'gold' standard, which is the level of quality needed, and for which indicators. In general the needed level of quality of the data (and related issues such as population base and geographic representativeness) must be discussed case by case and possibly some minimum common requirements must be considered.

What can registries for single rare diseases/ groups of diseases measure?

When we think of measuring quality of care in rare disease we can think of different ways to do it. For registries wanting to embark in this task, we can start with some examples of how this has been done (or partially done) by the interviewed registries and comment on this. Data collected from registries dedicated to single rare diseases many are in some cases still quite immature for the purpose of generating indicators, i.e. some registries had never thought about a way to compute their data in the form of indicators, and not many are currently carrying out longitudinal data collection. This is obviously a consequence of the fact that the vast majority of registries for single rare diseases/clusters of diseases have not been created to serve as data sources for indicators other than demographic and some epidemiologic ones (prevalence and incidence).

Impact of specific actions and impact of general health care

The age distribution study carried out by EuroCare CF (see Annex 1)[21] correlates the age at distribution of subjects affected by the disease with the general health care provision of a country, assuming that the higher the GDP the higher the healthcare expenditure, therefore basically correlating the epidemiologic indicator with countries' GDP: in this case the EU countries had higher GDP than the non-EU countries. Assuming this holds, it was demonstrated that a better-financed health care system (EU countries) had a positive effect on the life expectancy of people with the disease. The results of the EuroCare CF study give an important 'sentinel' signal regarding the impact of an assumed richer/better health care system on the life expectancy of rare diseases.

One other possible approach to a similar correlation/evaluation of the global impact of different health care systems would be that of a direct correlation with health care expenditure, as such data exist. To this purpose, it is also been shown that the countries with the highest expenditure are not always the ones with the best results (OECD, 2004 b;

[21] *Comparative demographics of the European cystic fibrosis population: a cross-sectional database analysis*, *Jonathan McCormick MD, Gita Mehta MPhil, Hanne V Olesen MD, Laura Viviani MSc, Prof Milan Macek MD, Anil Mehta FRCP*, The Lancet, March 2010, Vol. 375 No. 9719 pp 1007-1013

Anderson et al 2003: Leatherman and Sutherland, 2004), therefore it is not taken for granted that the same type of results will be replicable by all single rare diseases.

Indicators such as the ones proposed by, for example, the Marfan cohort and registry, on the other hand, are aimed at evaluating quality of the health care actions for the specific disease, by measuring clinical outcome indicators such as number of surgeries and aortic dissections, the number of which can be decrease in the presence of appropriate health care. Monitoring use of beta-blockers can also be used as indicator of quality of care, as such treatment has been demonstrated to have an impact on mortality and morbidity of the disease (including reducing the number of surgeries and of aortic dissections). These types of indicators are conceptually in line with e.g. those developed for more common cardiovascular diseases in the framework of health monitoring programs of morbidity and mortality financed by the EU (e.g. Eurociss). Considerations on the computations of the use of beta-blockers and on the limitation of such indicator are discussed in the tables of indicators.

Which indicators can be feasibly used today?

Indicators related to morbidity at baseline or changes in morbidity over time (e.g. if patients with cystic fibrosis live longer, how 'good' is the quality of the additional years of life gained and if they live longer when do they develop the most severe clinical features of the disease?) seem at present difficult to be derived from the data colleted by registries, with the exception of some possible examples. The Ercusyn register collects data on residual morbidity after treatment, once Cushing disease has been treated and is supposed to be cured. From this type of information figures of a sort of 'disability free life expectancy' could be calculated if data are collected longitudinally for a sufficient number of years in a sufficient population.

Apart from this example, the majority of the registries interviewed prior to the 2010 EUCERD Workshop do not collect data on functional status of the patients/disability, nor on global health status, apart from Ercusyn where data on quality of life are also collected, using a specific validated questionnaire and a more generic European one, the latter allowing international comparisons and comparisons with other diseases.

If we place the proposed indicators from registries who participated in the preparation of the 2010 EUCERD Workshop in the perspective of such criteria we can provide several observations:

- In the field of rare diseases the **choice of indicators is linked to research and level of knowledge of the disease** as not many information are available on standards of care, and guidelines do often not exist. To develop quality of care indicators information on diseases (e.g. for more common diseases it is necessary to know that a pap smear is a good method of diagnosing cervical cancer and to have an idea/estimate of which is the optimal frequency of assessment of the test that can result in reduction of the incidence, therefore the number of pap smears in a country in a certain time is an

indicator if quality of care). This is important for validity, where validity can be understood as the measurement under consideration corresponding to the true condition of the event being measured. Because a quality indicator reflects a minimally acceptable standard of care, validity also relates to the degree of relevance of the proposed recommendations (e.g. clinical practice guidelines, standards of care or in the case of rare diseases often only experts consensus).

- Mortality is considered a very important indicator from all registries and it is one of the very few data which are collected by all registries. Other indicator data collected by all registries points to diagnosis delay (time from symptoms to diagnosis/treatment).

- The reason for entering the register is a very important issue when considering the use of registry data of diseases with different phenotypes and degrees of severity of the disease in order to avoid ascertainment bias in the results. The source population should be in this respect carefully specified by the registries and the conclusions generalised to the specific population represented by the registry.

  As an example, AIR the Alpha1 International Registry, collects data from patients with lung disease related to alpha1-antitrypsin deficiency: 68% of the patients entered the registry because they were diagnosed with lung disease and the remaining 32% were detected with family screenings. Mortality data cannot be produced for the whole registry; the two populations should be divided and examined separately. As an example, the Dutch AIR registry collects almost all lung patients in the country (around 68% of 330 subjects registered) but most likely only a small percentage of all subjects affected by alpha1-antitrypsin deficiency who are not symptomatic or only mildly symptomatic. In addition it does not collect data from patients with liver disease (which are mostly children). This means that if mortality data is generated from the registry this will be mortality data for the population with lung disease from alpha1-antitrypsin deficiency and not for all individuals affected by alpha-1 antitrypsin deficiency (due to the fact that main referral reason for entering the registry is lung disease).

Diagnosis delay/time from symptoms to diagnosis

Diagnosis delay is one of the most relevant indicators in the field of rare diseases. As mentioned for other indicators, the relationship of this indicator with quality of care is different by disease, due to the enormous heterogeneity of rare diseases. Most of the interviewed registries considered information on diagnosis as one of the most relevant at the moment the registry was built. As such, onset of symptoms and date of diagnosis are fields included the majority of registries for single rare diseases/clusters of rare diseases.

The definition of the time of diagnosis is not always obvious, and the same applies to the definition of ‘onset of symptoms’ or ‘first symptoms’. Diagnosis can be recorded as a

clinical/instrumental/genetic diagnosis or in some cases it is registered as the time when the patients first receive (appropriate) treatment for the specific condition. Diagnosis delay is usually calculated as the period from when an individual first experiences symptoms to the time when they are diagnosed. It can be calculated as the time between first symptoms and treatment e.g. in the case when diagnosing a condition implies that the patient is immediately put under treatment, or when the moment of starting the treatment is considered a more important information (e.g. when there is a well-established relationship between early treatment and favourable outcome).

When planning to compute diagnosis delay from such data, it has to be considered that several biases can affect the data recorded as 'first symptoms'. An obvious one is referral bias; when patients know that they have the diseases they might recall first symptoms that they now know to be connected to the disease. Depending on the type of disease, adding a specific field to register the first time the symptoms were communicated to a doctor might be more appropriate for computing diagnosis delay for quality of care evaluation purposes.

The characteristics of first symptoms, such as e.g. their specificity for the disease, can also influence the time which passes between such first symptoms and the actual diagnosis. In one British study on ovarian cancer, the interval between the first reported symptoms and a definite diagnosis varied according to symptoms (Tate AR et al, BMC medical research methodology 2009). The most common reported symptoms were abdominal pain (41%), urogenital problems (25%), abdominal distension (24%), constipation/change in bowel habits (23%). The median time between first reporting each of these and a definite diagnosis was 13, 21, 9.5 and 8.5 weeks respectively.

Cancer registries have adopted specific methodology and invest time in clarifying the definition of diagnosis and of 'first symptoms'. The definition of a disease and the establishment of diagnostic criteria and appropriate treatment for such disease is therefore crucial information in order to interpret the meaningfulness of the data 'time between first symptoms and diagnosis. This has to be kept in mind by those registries that want to explore diagnosis delay, as they might consider computing it as 'time between first symptoms to diagnosis/treatment instead of as 'diagnosis delay' depending on the real meaning of the indicator. One other indicator of interest if diagnosis coverage: percentage of those who experience symptoms who are actually diagnosed.

For the specific situation of rare diseases even more than for more common diseases each indicator that can point to diagnosis delay or lack of proper diagnosis in the population is a priority. In a framework in which registries periodically do critical reviews of their databases and data collection it can be worthwhile to stimulate collection of data related to diagnosis, such as onset of symptoms and date of diagnosis, methods of diagnosis, and other information relevant to diagnosis which are relevant to the specific disease. Data that could allow the pooling of information with other rare diseases (e.g. diagnosis delay) would be welcome.

Mortality and its relation with quality of care

Mortality is a very important indicator and linked to quality of care in that it shows the life-threatening burden of a disease therefore claiming the need of improved quality of care. The feasibility/costs of obtaining such indicator in usually favourable since data are already being collected. However if we aim at using mortality data for evaluating quality of care some basic assumptions on the importance and soundness should be fulfilled, i.e. the fact that mortality from a disease is dependent on quality of care (e.g. if no treatment for a disease exist which can prevent death, or an early diagnosis has no influence of the age of death of the disease, it is usually not possible to relate mortality to quality of care). Mortality can also be related to quality of care when the natural history of a life-threatening disease can, for example, be modified by treatment. One example among the interviewed registries is Marfan disease. When the disease is promptly diagnosed and treatment with beta-blockers is started early, some of the most life-threatening complications of the disease can be avoided, such as aortic dissection.

Population-based indicators

A population-based practice is a practice (an action, a collection of data such as a registry, etcetera) which focuses on the entire population. A population-based indicator has been defined as "an indicator which pertains to the entire population in a particular area. It does not include indicators based on a subset of the population involved in a select program"[22]. The use of population-based registries has become more and more fostered in the field of cancer as they offer several advantages as compared to, for example, hospital cancer registries. The advantages result from the fact that population-based registries serve a wider range of purposes and in this way they are suitable for cancer control programs, patient care programs, administrative programs, and cancer research programs. In more practical terms, a population-based cancer register monitors the frequency of new cancer cases (also called incident cases) every year in a well defined population and over time by collecting case reports from different sources (e.g. treatment facilities, hospital files/registries, death certificates).

As expected, data collection from registries for single diseases is almost never population-based as conceived, with the exception of rare cancers.

However in several cases the registries reported that the registry actually covers the vast majority of the cases in a country (with approximate figures up to 90-100%), as one or more centres of reference are active in the country since several years and they can estimate, by considering the expected prevalence of the disease in the country and cross-checking with patients' associations, that almost all patients of the country have been registered. This is

[22] www.idph.state.ia.us

bound to happen more often in the case of small countries and, for example, for diseases which are very rare.

For example, the Netherlands the activity of the Alpha1 international registry started in 1997. Out of a country of around 16'000'000 persons there are currently 330 patients in the registry. If we consider that not all subjects registered are patients (32% are family screenings) we can end up with around 224 patients affected by lung disease related to alpha1-antitrypsin deficiency in the country. In line with the expected prevalence data of the disease in European countries we can conclude that the Dutch alpha1-antitrypsin registry includes most of the expected patients in the country and can therefore be approximated to a population-based registry.

In order to establish whether the registry population represents the real population affected by the disease in the country, and to approximate the coverage of the registry to the entire population of a country, it would be ideal to cross-check the data on the registry with other data sources, such as administrative data whenever possible, data from the centres of reference/hospitals, patients' associations. Such a check against administrative data in one country could show that one patient is registered several times in the administrative data, resulting in a higher number of cases than in the registry, thus establishing that the registry data reported the real number of cases in the country, while the administrative data may over estimate the number of cases.

Appropriate coding of rare diseases in population-based registries is also an issue: the visibility of rare diseases will be improved in the next version of the WHO International Classification of Diseases (ICD11) which should help the collection of data for indicators.

Conclusion

The aim is not to monitor RD in general, but to be pragmatic and define some diseases which can be monitored in different countries and followed up year after year. It is for this reason that disease registries have been selected as the best source of data. As RD are heterogeneous, different indicators and variables will apply from disease to disease.

Cited registries/projects

A number of disease registry leaders/related project leaders were interviewed prior to the 2010 EUCERD Indicators workshop to identify potential indicators to be computed from their data, and who were selected to present their work at the workshop. Case examples presented during the 2010 EUCERD Indicators workshop are available in Annex 1.

- Veneto Region Registry of Rare Diseases, Italy: Population registry
- ERCUSYN[23]: Cushing and related syndromes
- ENRAH[24]: alternating hemiplegia (an example of a very rare disease)
- EUROCARE CF[25]: Cystic fibrosis (an example of a relatively 'common' RD),
- MARFAN Cohort and Registry[26] (a disease where quality of care can make the difference to a prognosis)
- EUROFEVER[27]: Rare autoinflammatory disorders (an example of a register covering a cluster of diseases)
- RARECARE project[28]: Surveillance of rare cancers in Europe

[23] http://www.lohmann-birkner.de/ercusyn/ and www.ercusyn.eu
[24] http://www.enrah.net/
[25] http://www.eurocarecf.eu/
[26] http://www.orpha.net/consor/cgi-bin/ResearchTrials_RegistriesMaterials.php?lng=FR&data_id=67063&Nom%20du%20registre%20ou%20mat%E9riel=Cohorte-de-patients-presentant-un-syndrome-de-Marfan-ou-apparente&title=Cohorte-de-patients-presentant-un-syndrome-de-Marfan-ou-apparente&search=ResearchTrials_RegistriesMaterials_Simple
[27] http://www.printo.it/eurofever/
[28] http://www.rarecare.eu/

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Annex 1: Case studies presented at the EUCERD Workshop on Quality of Care Indicators for Rare Diseases - 25 November 2010

1. Monitoring quality of care: the experience of England *(Edmund Jessop)*

Clinical outcomes for specialised services (interventions, treatments, care and/or diagnostic services for a population of less than 0.1 persons per 10,000) are measured in England by acquiring data on all patients treated in all National Commissioning Group services: these services are also required to solicit patients' opinions every 3 years. Administrative data systems cannot be used to obtain this data: clinical teams have to set up a manual or IT system to do this. It was highlighted that currently there is a problem with the representation of RD in ICD10. It is possible to track mortality of survival, and short term outcomes through annual assessment and adapted evaluation criteria. It is very difficult to collect information/data on quality of life, however. It was highlighted that these clinics are also visited twice a year by the Commissioning services for monitoring purposes.

The difficulties of interpreting data were exposed: firstly there are small numbers of patients and therefore less data, secondly confounding is a problem due to the case mix, thirdly it takes time to become familiar with the metrics of the context and finally inexperience in interpreting data in this field can pose a real problem.

It is also possible to monitor adverse events, patient opinion, and equity (i.e. geographical access). Equity can be monitored both in terms of equity of access and equity of outcome. An example of monitoring of equity of access for pancreatic transplants was provided.

The possible indicators and monitoring systems that could be put into place by national health authorities were highlighted.

2. Population registries as a source of indicators: the experience of the Veneto Region Population Registry *(Paola Facchin)*

The Veneto region population registry registers 50'000 new births per year for a region of 4.9 million inhabitants. In Italy there is a defined list of RD for reimbursement purposes (covering 2295 specific diseases under 581 names/groups), and RD patients must be registered in order to receive reimbursement for their treatment. Regional authorities are obliged to define centres of expertise for specified groups of rare

diseases through a formal procedure: the organistion of these centres was explained. A unique IT platform connects the centres of expertise, hospitals, local health units and pharamaceutical services, therefore unifying the processes related to diagnosis and certification, identification of patients, exemption from costs, entitlement to benefits/benefits allocation, clinical health records, clinical management, prescriptions, diet therapies etc. Patients can enroll either at the centres of expertise or in local health districts/units: bias is evaluated by current health statistics. In the Veneto region around 19,500 RD patients are registered, with most patients inhabiting the region and receiving diagnosis/treatment in the region.

Data from the registry was then presented for rates of prevalence and incidence of RD in different age groups: this has allowed the Region to evaluate the prevalence of RD in the Region at 3.53 – 5 inhabitants per 1'000. Data was also presented for age and mortality rates, and figures for lost life years were also presented for rare diseases and other examples including diabetes, myocardial infarction, infectious diseases and road injuries. The prevalence, incidence, mortality and fatality rates by nosological group were presented. The data for hospitalisation rates were also presented which shows that hospitalisation rates are higher for RD patients than for all inhabitants. Age distribution at first admission was presented for Italian patients and patients from abroad. Interventions on RD patients were presented by nosological group.

Finally, it was highlighted that population registries have a relevant plus value in the quality and comprehensiveness of data. However, monitoring based on the currently collected data has some limitations. A network of registries of sample areas may be a good next in addition to obtaining more exhaustive current statistics.

3. Indicators for rare cancers: the experience of the RARECARE project *(Gemma Gatta)*

Indictors have been developed as a result of the DG Sanco funded RARECARE project on rare cancers in Europe. The project aimed to estimate the burden of rare cancers in Europe. To do this a definition of "rare cancers" and a list of cancers was given. Further objectives were: to improve the quality of data in cancer registration and to develop strategies for the diffusion of information among all key players. Cases from 1995-2002 were examined as part of this project. Data was taken from 89 European population-based cancer registries from 21 EU MS, covering a total population of 162 million people. This included 4 million malignant cases.

Indicators of burden related to frequency (incidence/prevalence/mortality) and outcome (relative survival/% cured) by sex, age, European region and economic macro-indicators were estimated and the methodological approaches for the analyses explained in the reports (www.rarecare.eu).

This surveillance shows that rare cancers represent a burden in terms of incidence, prevalence and survival rates, and that incidence is the best indicator to define rare cancers.

4. Examples of indicators for patient registries: ENRAH *(Tsveta Schyns)*

The ENRAH Registry for Research on Alternating Hemiplegia is funded through the FP6 ENRAH for SMEs project. It covers 9 EU MS, including clinical centres, patient organisations and research institutes, and includes all cases with a probable AHC diagnosis (whether typical or atypical). Collection of data is retrospective and was carried out between October 2006 and May 2007 through a natural history cohort study.

Data on incidence and age at diagnosis were presented in detail, and a selection of indicators which could be derived from registry data and used to monitor quality of care were presented:

- Incidence
- Age of first diagnosis
- Age of AHC diagnosis
- Age of death

These indicators could be compared across the participating EU countries.

5. Examples of indicators for patient registries: Marfan registry and cohort *(Guillaume Jondeau)*

In Marfan syndrome aortic dissection is one of the main causes of mortality, and the data collected by the registry on the reasons for aortic surgery (i.e. dilation versus dissection) was presented as a possible indicator to monitor over time. The aortic surgical techniques used (valve sparing, supracoronary and Bentall) to treat the condition can also be monitored over time in relation to the aforementioned data collected on dilation and dissection. By comparing this data it can be seen that overtime the reasons for aortic surgery are more often dilation rather than dissection, which reflects a preemptory approach to dealing with this disease.

The quality of care indicators which could be monitored with the collected data are

- % patients with annual echocardiography, ophthalmological examination, rheumatologic examination
- % patients receiving beta blockers
- % familial screening realised
    - Age of diagnosis

Furthermore the following indicators of the results of quality of care were proposed

- Age of death
- % aortic surgery for dissection

Discussion after the presentation included concerns that indicators of results of quality of care should be examined to be sure that external factors (other than the quality of care) are not at play. It was highlighted that age of death, mortality and survival rates are different indicators (survival is the period between diagnosis and death and mortality is the number of people to die in a given period), but which can often be monitored with the same registry data.

6. Examples of indicators for patient registries: ERCUSYN *(Susan Webb)*

The ERCUSYN registry's (European Registry on Cushing's Syndrome Registry) goals are to collect epidemiological data at EU level, to collect data on mortality, outcome of therapies, co-morbidities, to assess diagnostic and therapeutic strategies, to validate a disease-generated questionnaire on quality of life developed by partners of this study and to increase awareness in primary care to shorten delay to diagnosis, aimed at improving long-term prognosis ("residual" morbidity).

The database was opened in September 2008 and over 500 patients were registered by the end of October 2010 (74% with complete data). Patients included in the registry come from 24 countries and 36 centres. Data was presented on the age at diagnosis, the cause of Cushing's syndrome in these patients, the delay between onset of symptoms and diagnosis, other specialists consulted prior to correct diagnosis, morbidities at diagnosis, prevalence of CV risk factors in patients with Cushing's syndrome, fractures and bone mineral density, and also results of the quality of life questionnaire addressed to registered patients.

It was highlighted that there is a long delay before correct diagnosis for this disease (3 years) and high morbidity at diagnosis and that there is residual morbidity in "cured" patients. This data could be monitored as indicators of quality of care. Data also shows that quality of life is impaired, and only one third of patients work actively.

7. Examples of indicators for patient registries: EUROCARE CF/ECFS Registry *(Jonathan McCormick)*

The Eurocare CF project ran from 2006-2010 and is now run as the European Cystic Fibrosis Society Patient Registry. Data is collected in 35 EU and non EU countries. An article has been published in The Lancet using this data ("A matter of life and death" McCormick et al. *The Lancet* 2010: 375: 1007-13).

The data shows differences between EU and non EU-countries. Data on the distribution of age of the patients in EU and non-EU countries was presented as was data reflecting the percentage change in the size of the CF population from a previous 10-year age group in EU and non-EU countries. Data was then presented on CF genotype proportion changes over time in non-EU patients and EU patients, along with a population pyramid of mean age of patients with cystic fibrosis and homozygous Phe508del in EU and non-EU countries (showing a pyramid shape for non-EU countries, and an onion shape for EU countries).
It was then shown that death rates can be used as an indicator of quality of care. The topic of how to improve outcomes (i.e. newborn screening) was discussed, as was costing.

The quality of care indicators being collected for the ECFS Registry were presented:

- Demographics (age, age at diagnosis, death etc.)
- Therapy (severity indicators with costings)
- Longitudinal clinical parameters (best lung function in past year)
- Complications, transplant (may or may not indicate quality of care)
- Microbiology (can indicate severity and indirectly indicate quality of care).

The presentation concluded with three take home messages: international registries can be used persuasively for lobbying for increased resources; in CF registry work has shown how outcomes can be measured and costed; and simplicity is the key when collecting data for registries.

Discussion following the presentation focused on the interest of concentrating on collecting data on severe cases of CF, as in non-EU countries these forms are more easily diagnosed, and if there is a homogeneity in the genetics of patients for whom data is collected in EU and non-EU countries, then differences are more likely to be due to quality of care.

It was also suggested that quality of care may be based on the GDP of a country. It was highlighted that quality of life is difficult to measure as this is subjective and depends on a person's perception of what is important to them.

8. Examples of indicators for patient registries: Eurofevers *(Marco Gattorno)*

The EuroFever project registry was financed by the 2007 Public Health Programme, in collaboration with the Paediatric Rhuematology European Society Autoinflammatory Diseases' Working Party. The objective of the project is to create a web-based registry for all known autoinflammatory diseases in collaboration with the EUROTRAPS project. The aim of the registry is to collect information on the clinical presentation, outcome and response to treatment of patients affected by major autoinflammatory diseases.

Secondary aims were to provide evidence-based classification criteria for the autoinflammatory diseases lacking a precise genetic characterisation, to develop guidelines to justify genetic testing for each disease, to create a permanent network of centres dealing with patients affected by these diseases (for future clinical, pathogenic, genetic and therapeutic studies), to identify informative families or clusters of genetically negative patients for possible future genetic studies, and to establish a baseline cohort for future outcome studies. Enrolment started in November 2009 in 54 centres from 37 countries, and to date over 1100 patients are registered (baseline information and clinical manifestations). Base line information has been validated for nearly all of the enrolled patients.

Some possible indicators of quality of care were proposed:

- Diagnosis delay
- Actual prevalence in Eastern European countries
- Delay in receiving treatment
- Availability of expensive drugs
- Incidence of complications (by disease)

9. The experience of the OECD with quality of care indicators *(Niek Klazinga)*

In 2000 the Organisation for Economic Cooperation and Development (OECD) started a project on health care quality indicators: an expert and subgroups were founded and currently 37 countries from across the world are involved. A conceptual framework was established and quality indicators were systematically selected and pilot tested. The methodology was refined, and publications have since appeared in Health at a Glance (2007, 2009).

Currently the OECD has populated a matrix with 40 indicators. There is a real dependency on hospital administration databases, which are sometimes too heterogenous for building indicators.

The areas of interest in the project are:

- health promotion, prevention and primary care (monitored through hospital admissions data)
- acute care (monitoring 30 day case-fatality rates AMI and stroke)
- mental health care (monitoring re-admission rates in schizophrenia and bipolar disorders)
- cancer care (monitoring screening and survival rates for breast, cervical and colorectal cancer)

- patient safety (monitoring indicators such as: foreign body left in during procedure, catheter related bloodstream infections, postoperative sepsis etc)
- patient experiences (monitoring a common set of questions for population based statistics under development on access, autonomy and communication/ basic set of principles for setting up national systems for measuring patient experience).

These indicators have been chosen as they can be monitored using existing data.
There are of course limitations to national information infrastructures and data has to be gathered from different, heterogenous sources: mortality databases, registries, administrative databases, electronic health records, household and patient surveys. It can be seen that there are therefore methodological problems even for common diseases.
Ministerial recommendations were made by the OECD in October 2010, highlighting the need for:

- Legislation balancing privacy and data with quality-led governance
- Unique patient identifiers, secondary diagnosis, coding, present-on-admission flags
- Electronic health records for population statistics
- National patient experiences measurement
- Linking with Q policies on health system input, design, monitoring and improvement
- Good performance and mutual learning

The following indicators suitable for monitoring quality of care in the field of rare diseases were proposed:

- Link with mortality statistics (length of life)
- Link with cancer registries (coding, staging)
- Specific registries owned by health care providers and/or patient organisations
- Link with administrative data-bases (coding rare diseases/ volume parameters)
- Link with patient experience measurement
- Link with quality improvement policies

It was highlighted that it is essential to link databases and registries if we want to increased possibilities for monitoring. For RD the major issue is coding. Another concern is the ownership of the registry and barriers to linking databases for privacy reasons. The possibilities of linking types of data and databases should be explored. Indicators of improvement are a vital tool for policy makers: life expectancy is one of the sorts of information they need and are used in health care planning.