Deliverable 5.1

Background Report exploring the "coding environment" of implementing countries

Co-funded by
the Health Programme
of the European Union

Disclaimer:

This report is part of the project RDCODE project which has received funding from the European Union's Health Programme (2014-2020).The content of the report represents the views of the author only and is his/her sole responsibility. It cannot be considered to reflect the views of the European Commission and/or the Consumers, Health, Agriculture and Food Executive Agency or any other body of the European Union.
The European Commission and the Agency do not accept any responsibility for use that may be made of the information it contains.

It constitutes the Deliverable 5.1: Background Report exploring the "coding environment" of implementing countries.
Issued on the 26.06.2019 by the WP5 members of the RD-CODE project (Veneto region, Italy- AP-HP, France, DIMDI, Germany).

The RD-CODE project was launched in January 2019 for a 36 months period.
More information on the activities of the RD-CODE project can be found at www.rd-code.eu

Table of content

Austria Report (RD-CODE observer country)

1. Austrian health-care system at a glance

In Austria responsibility for coordination and planning of health care provision and financing is shared between the federal Government, the social health insurance funds, the nine states, called Länder in German, and their municipalities. According to the Federal Constitution, almost all areas of the healthcare system are primarily the regulatory responsibility of the federal government. The most important exception is the hospital sector. In this area, the federal government is only responsible for enacting basic law; legislation on implementation and enforcement is the responsibility of the nine Länder.
Health care provision is based on a social insurance model based on compulsory insurance. All of the insured have a legal right to services, which are financed on the basis of solidarity. As of 2018, 21 social insurance institutions exist, of which 18 solely or also provide health insurance. Beginning 2019 the number of institutions has been reduced significantly via mergers. Austrian citizens normally are assigned to a social insurance mainly on the basis of their occupational group[1].

2. National Plan/Strategy and the coding issue

The Austrian National Plan for Rare Diseases (NAP.se) was developed and written by the National Coordination Center for Rare Diseases (CCRD), which was established by the Austrian Ministry of Health in April 2011. Two committees were established accompanying the activities of the CCRD, namely the Experts Committee on Rare Diseases, which includes representatives of a variety of stakeholders in the rare disease field in Austria, and the Strategic Platform, where delegates of the decision-makers in the Austrian health care and social system are represented. These two Expert Committees participated actively in the development of the NAP.se. Upon finishing the draft, the input of all relevant decision-makers was obtained, and the NAP.se was eventually approved by and published on behalf of the Austrian Ministry of Health as well as the Ministry of Labour, Social Affairs and Consumer Protection, and the Ministry of Science, Research and Economy. Taken together, a broad acceptance of the plan among stakeholders in health care, social services and research with respect to rare diseases can be assumed. However, there is no binding legal basis backing the NAP.se.
In the Austrian National Plan for Rare Diseases, the rare diseases coding issue is addressed in the field of Action #1. Specific identified measures to improve RD visibility in health information systems include the implementation of a suitable coding system for RD in Centres of expertise (CoEs), as well as (possibly) outside of designated CoEs. It has been common understanding lately that Orphacodes will be adopted as the coding system in question.
Specific funding was allocated to implement the National Plan for Rare Diseases. RD coding related activities were not specifically funded within this framework.

3. Morbidity coding framework

In Austria, a legal framework regulating the process of morbidity recording exists and is linked to reimbursement procedures. The International Classification of Diseases, Tenth Revision, (ICD-10) is used for the recording of in-patient morbidity data. ICD-10-BMSG 2017 (ICD-10-WHO 2016 translated into German except Chapter XX) is the Edition/modification in use[2].

The Austrian Diagnosis Related Groups (DRG) system was developed by local experts for the definition of inpatient hospital costs and has been in use since 1997. The Austrian DRG-model LKF provides a catalogue of diagnoses, an Austrian modification of the ICD-10, and a catalogue of selected procedures; namely the most frequent and expansive ones[3].
The morbidity recording process is compulsory only at inpatient-level. For outpatient care, it is performed only test wise in some regions or hospitals.
According to the Federal Act on Documentation in Health Care System all of the Austrian hospitals are legally obligated to collect administrative and medical data of their patients. Hospitals which are financed by the Regional Health Funds transmit their data to the respective funds. The Regional Health Funds checks completeness and plausibility of data and transfers them to the Austrian Ministry of Health (currently Federal Ministry of Labour, Social Affairs, Health and Consumer protection, (BMASGK). Hospitals which are not funded by a Regional Health Funds have to transmit data directly to the BMASGK. Finally, the BMASGK makes hospitals discharge data available for **Statistics Austria**.
Medical doctors have the final responsibility of the coding process, although they may be supported in this activity by "coding assistants", namely administrative personnel who received some training to perform this activity. The coding activities are performed both at the point of care and *a posteriori* and the process is software-based. Training activities for personnel involved in the coding process are performed at hospital, regional and national level.
The quality assurance of hospital discharges is not standardized and depends on specific conditions of the hospital owner and of the Regional Health Funds. Data collection within the Austrian DRG-model LKF is guided by detailed specifications defined by the BMASGK. Data quality controls take place at different levels. At hospital level data check are performed during data collection and then by hospital owners. Regional Health Funds can check for coding errors. Plausibility checks, the reporting of errors to the hospital owners or/and the Regional health fund are activities depending on the BMASGK. Statistics Austria cannot evaluate the external quality checks, but performs formal plausibility checks (i.e. by combination of codes, medical procedures, etc.)[4]. Coding of cancers, on the other hand, is performed directly by Statistics Austria with its own quality assurance process.

4. Mortality coding framework

ICD-10-BMSG 2017 (ICD-10-WHO 2016 translated into German except Chapter XX) is the Edition/modification is used for the coding of mortality data.
Cause of death has to be documented in the death certificate either by a pathologist, forensic pathologist, or coroner (in Austria an authorized physician). Based on these data, death statistics are regularly produced by Statistics Austria.

5. Patient identifier

Patients in Austria are identified through their social insurance number, which is used as an ID. Social insurances create this insurance number by demographic data. This number is not globally unique and can be reused after a person is deceased. Recently, an infrastructure has been developed, which allows the distribution of a unique number for each patient within the system. A central office distributes the numbers to the various healthcare providers and those then have a unique identifier. The link between the domain-specific identifiers and the central code cannot be

reconstructed, by the mean of a cryptographic process[5]. This **patient identifier is in use at hospital/inpatient level since 2015**.

6. Rare diseases registration

Currently, no RD registry having a national coverage exists in Austria. The only official national registry is the cancer registry, which monitors also rare cancers. At the moment, the main potential sources of information on RD epidemiology, affected by the well-known limitations of their underrepresentation in the coding systems used to record diagnoses, are the hospital discharge database and the death registry.
There are currently about 40 registries for individual rare diseases or groups of rare diseases in Austria. Apart from the cancer registry, all of them are individual initiatives and receive no national funding. They usually cover only patients that have been treated at the particular institution participating or running the registry.
Many Austrian research groups contribute to registries primarily located abroad, but do not have their own, local registries. Some European registries dealing with RD to which Austria contributes with data are: EUROCARE Cystic Fibrosis, RARECARE, the European registry and network for intoxication and metabolic diseases (EIMD), the European Multisystem Atrophy Study Group (EMSA-SG), EUROCAT, the Severe Chronic Neutropenia International Registry (SCNIR) and the European Network for research on alternating Hemiplegia (ENRAH)[6].

7. Centres of expertise and European Reference Networks (ERNs)

In Austria, an official policy for identifying Centres of expertise for RD is in place at national level. In 2016, the first official Centre was designated through this process. The National Plan for Rare diseases (NAP.se) lists criteria to be fulfilled by Centres of expertise. These criteria are closely related to the Eucerd ones and to those established for healthcare providers (HCPs) participating in an ERN (a combination of general and specific ones, according to the area of expertise).
Currently **6 Centres of expertise** have been designated. Three others will be identified by the end of 2019 and 8 more are in an advanced application phase.
The plan is to implement Orphacodes use in all CoE.
A formal process is in place for the endorsement of health care providers (HCP) to participate as full-members of an ERN. Currently, one HCP, St. Anna Kinderspital & St. Anna Kinderkrebsforschung, is the coordinator of **ERN PaedCan**, and one, EB-Haus Austria, participates in **ERN skin** [7].

8. Undiagnosed RD patients

The issue of undiagnosed patients has been addressed in the Austrian National Plan (field of action #3), and general rare disease centers with undiagnosed diseases programs are mentioned there. An official definition of who is a rare disease patient is not mentioned and has not been adopted though.

Initiatives to address this issue take place mainly at local level. Several university medical centers have started initiatives with rare disease boards and local networks dealing with unsolved cases,

with Innsbruck and Salzburg having pilot roles. There is currently no specific funding for these actions.

Future plans include the establishment of a clear designation process for centers for undiagnosed rare diseases. The criteria for these centers have to be elaborated, but they should include having a tracking system for undiagnosed patients in place. This would include official registration of these patients and hopefully an official "undiagnosed" status for them.

This report is based on information, which is accurate to the best of the Authors' knowledge. However, contents of this report should be considered indicative and not exhaustive of the addressed topics.

Czech Republic Report (RD-CODE participant country)

1. Czech Republic health-care system at a glance

The Czech Republic has a system of statutory health insurance (SHI) based on compulsory membership in a health insurance fund. The funds are quasi-public self-governing bodies that act as payers and purchasers of care. The Ministry of Health responsibilities include setting the health care policy agenda, supervising the health system and preparing health legislation.
The regional authorities and the health insurance funds play an important role in ensuring the accessibility of health care, the former by registering health care providers, the latter by contracting them. Eligible residents can freely choose their health insurance fund and health care providers. The health insurance fund must accept all applicants who have a legal basis for entitlements regardless of age or health status[8].

2. National Plan/Strategy and the coding issue

In 2010 the Government of the Czech Republic (CZ), via Government Resolution No. 466, adopted the "National Strategy for Rare Diseases for 2010-2020" (NAS). The Strategy established the frame for action and identified the main measures for improving the care of RD patients in the country.
The subsequent first "National Action Plan for Rare Diseases for 2012-2014" (NAP1) further specified priority tasks and activities within this biennium.
Further developments were the National Action Plan for Rare Diseases 2012-2014 and the National Action Plan for Rare Diseases 2015-2017.
Currently, the third National Action Plan for Rare Diseases 2018-2020 is in force.
The actions included in the Plans have been funded through specific projects supporting their concrete implementation. Other actions have been carried out through research funding schemes.

Within the National Strategy 2010-2020, the improved representation of RD in health information systems, as well as the development of European cooperation in this area, were identified as primary goals.

The topic of rare diseases coding was further specifically addressed in the first National Plan 2012-2014, under action 8 “Harmonisation and development of data collection and biological sampling”. The achievement of an appropriate identification of RD patients both at national and regional level, through the **support of data collections on RD in the pre-natal, peri-natal and post-natal periods** was recognized as a specific goal. The responsibility for this activity was assigned to the Institute of Health Information and Statistics of the Czech Republic (IHIS; UZIS) and to the National Registry of Reproductive Health.
Furthermore, a broader action aimed at improving awareness about RDs among both professionals and citizens, realized through the participation in the Orphanet activities, was recognized as pivotal. The expansion of a dedicated Czech portal (www.orphanet.cz) implying the **translation of the Orphanet database** contents in Czech language is part of this strategy. This activity has been identified as the basis for the further implementation of the Orphanet nomenclature, including the use of Orphacodes, into Czech health information systems.

Following the adoption of the first and the second RD National Action Plan, a report evaluating the fulfillment of the tasks and activities listed in the Plans was issued.

The underrepresentation of RD in codification systems used for morbidity and mortality recording and the absence of a minimal data set for the collection of RD-related data were the main identified areas for action. IHIS was in charge of introducing OMIM, Orphacodes and the SSIEM (Society for the Study of Inborn Errors of Metabolism) classification system into the National Registry of Reproduction Health and into the Ministry of Health "Data Standard". The IHIS established a **minimum data set for the collection of RD data** to be used in any new **RD registries** and incorporated in existing ones.
In the National Action Plan 2018-2020 the topic of rare diseases coding is further addressed under action 8 "Unification and development of data collection and biological samples". The Orphanet nomenclature is recognized as the leading system for RD coding.
Starting from the translation into Czech of the entire Orphanet terminology, completed in 2017, the document explores ways to enable further accurate **identification of RD patients through Orphacodes in other data collections**. A considered action consists in the integration of at least some RD terms into the ICD-10 alphabetical list modelled on the German Alpha-id system of enhanced terminology.

3. Morbidity coding framework

In the Czech Republic the International Classification of Diseases Tenth Revision (ICD-10) has been used since 1994 for mortality and morbidity coding.
WHO commissioned the IHIS with updating of the Czech version of the classification.
The IHIS has a dedicate webpage through which ICD-10 can be accessed in different formats, including a web-browser. The tabular part is available in ClaML since 2016. Revisions of the Tabular part, the Alphabetical list and the Instruction manual are periodically issued.

In the Czech Republic a legal framework regulating the process of morbidity recording exists and is linked to reimbursement procedures. Reimbursement for in-patient care on the basis of in-patient cases payments (mainly referred to as Diagnosis Related Groups – DRGs) started to be considered in the 90s, in the context of the transformation of the Czech healthcare system, and started its concrete implementation in 1995. The Ministry of Health chose the "International Refined Diagnosis Related Groups" (IR-DRG) as the preferred system in 2002. In 2012, the DRG system started to be used more extensively in the country[9].

The Government of the Czech Republic accepted by its Resolution No. 1046/2002 the Long Term Program for Improvement of Health Care Status of the Czech Population (The Health for All in the 21st century). This Resolution calls for establishing the DRG system for controlling high quality of health care provided and for more effective allocation of financial resources.
For the recording of morbidity data, ICD-10 is enforced with specific classifications/coding systems for particular use: e.g. ICD-O for cancers and, partially, Orphacodes for rare diseases. This activity is in charge to the IHIS.
National guidelines for morbidity and mortality recording with ICD-10 are available in Czech language and accessible through the IHIS website. The guidelines are included in the instruction manual. This resource includes also practical instructions for mortality and morbidity coders and guidelines for presentation and interpretation of data[10].

The Czech Ministry of Health launched in 2015 a project aimed at promoting and implementing a more transparent and effective in-patient care reimbursement system, redesigning the national

Diagnosis Related Groups (DRG) system. Within this project, a specific methodology for improving morbidity coding for acute in-patient care was developed and is available for users[11].

The morbidity recording process takes place both at hospital level and in the primary care setting; it involves medical doctors, nurses and administrative personnel, and differs in its modalities according to the type of healthcare facility in which it takes place.

The coding process is mostly software-based. As already mentioned, several tools are accessible online to support the coders. Specific training modules are regularly performed for personnel involved in coding activities. They are based on the translated ICD-10 training tool and on other material developed for improving the correctness of the DRG system use. All these activities are carried out by the IHIS and involve users from universities, hospitals, other healthcare institutions as well as from health insurance funds.

4. Mortality coding framework

The International Classification of Diseases Tenth Revision (ICD-10) is in use since 1994 for mortality and morbidity coding.
In the Czech Republic a national legal framework regulating the process of mortality recording exists. It is based on Decree no. 297/2012 about Medical Death Certification.

5. Patient identifier

At birth, all **citizens are assigned a personal identification number**. This unique national patient identifier is used both in morbidity and in mortality data collections. Currently, some technical problems with its use exist in the new registry of healthcare reimbursement data, which is the main source of information for out-patient cases.
The legal framework for the generation and use of this ID is based on the following official Acts:
Act n. 133/2000 and Act n. 296/2004.

6. Rare diseases registration

The Czech Republic accepts the European definition of rare disease included in the European Regulation on Orphan Medicinal Products (prevalence of no more than 5 in 10,000 individuals).
A national legal framework establishing a list of RD whose affected patients can access specific benefits has not been defined.

In the Czech Republic, specific experiences on RD codification within health information systems exist and are carried out both at local level (i.e. within selected hospitals) and at national level.

Currently, no global data on the number of citizens living with a RD in Czech Republic are available. Nevertheless, some sources of information from which epidemiological data on RD can be derived, are available at local, regional and national level. They mainly consist in treatments' registries and in the congenital malformation registry.

Although a national RD registry is not in place, since 2016 RD cases can be recorded in the national **registry of congenital malformations**, in addition to the cases usually monitored through this source.
The Czech registry participates in the Eurocat network.
RD diagnoses can be entered into the congenital malformations Registry using Orphacodes.
Data quality control is mainly based on some automated processes taking place at the level of data entry (i.e. completion of required fields, defined range values for specific fields, etc.)
A communication pathway between coders and the registry staff regarding coding issues exists, but areas for improvement have been identified.

Of note, a registry of rare examinations (www.registr-raritnich-vysetreni.cz) was also developed in collaboration with NCCRD and the Czech Society of Clinical Biochemistry.

Various research groups have developed their own data collections, in some cases in collaboration with scientific societies.
In the Czech Republic, 5 registries collecting data on specific rare diseases or group of rare diseases are currently ongoing[12].

CZ - CZECH REPUBLIC (5 registries)		
ENGLISH LABEL OF THE ACTIVITY	COVERAGE	AFFILIATION
Autoimmune neuromuscular disease	National	Not defined
Czech cystic fibrosis patient registry - contributes to the EUROCARE CF registry	National	Public
Czech severe chronic neutropenia registry - contributes to the SCN international registry (SCNIR)	National	Public
Duchenne and Becker muscular dystrophy patient registry in the Czech Republic and Slovakia - contributes to the TREAT-NMD network	National	Private for-profit
Spinal muscular atrophy patient registry in the Czech Republic - part of the TREAT- NMD network	National	Private for-profit

7. Centres of Expertise and European Reference Networks (ERNs)

In the Czech Republic an official process for **designating Centers of expertise for groups of RD has not been defined yet**. A pilot project for the designation of 4 Centres of expertise has been initiated this year and potentially could include in the near future other Centres of expertise already participating in ERNs.

In the Czech Republic at the Ministry of Health level a formal process is in place for the endorsement of health care providers (HCP) to participate as full-members of an ERN. Currently, a total of **9 HCPs participate as full members of 17 ERNs**.
In fact, a single HCP can be member of various ERNs. As an example, the Motol University Hospital in Prague is full member of 12 ERNs.
For a complete list of HCP of the Czech Republic participating in ERNs, please consult the EC dedicated page: *https://ec.europa.eu/health/ern_en*

Czech Republic

Representative in the ERN Board of Member States:
MACEK Milan, *Charles University Prague*

Members:

Charles University	ERN-RND
General University Hospital in Prague	ERN EYE ERN LUNG MetabERN ERN RITA ERN RND
Hospital Na Bulovce	ERN Skin
Masaryk Memorial Cancer Institute	EURACAN
Motol University Hospital	ERN BOND Endo-ERN ERN CRANIO ERN LUNG ERN EURACAN ERN EpiCARE ERN EURO-NMD ERN GUARD-HEART ERN ITHACA ERN PaedCan ERN-RND ErkNET
Saint Anna University Hospital in Brno	EPICARE ERN Skin
Thomayer Hospital, Prague	ERN LUNG
University Hospital Královské Vinohrady	Endo-ERN ERN Skin
University Hospital Brno	EURO NMD Paedcan EuroBloodNet ERN SKIN

A national policy according to which CoE should use Orphacodes to record RD patients in health information systems is not currently in place. Nevertheless, clinicians involved in various ERNs can use Orphacodes in the context of registries developed as part of the ERNs activities. Currently 5 ERNs received specific funding for the development of registries: ERKNet, Endo-ERN, MetabERN, ERN-LUNG and ERN PaedCan. HCPs of the Czech Republic participate in all these ERNs.

8. Undiagnosed RD patients

The timely identification and diagnosis of RD is recognized as a priority in the National Strategy and in the National Action plans issued so far. Nevertheless, the issue of undiagnosed patients has not been specifically identified as a clear area for action in these documents.
The topic of the representation of undiagnosed RD patients in health information systems has not been discussed yet.
A proposal to improve undiagnosed RD patients' traceability could be to use a specific label (i.e. U) to trace the health care pathways of these patients within health information systems.

Malta Report (RD-CODE participant country)

1. Maltese health-care system at a glance

The Maltese healthcare system, publicly funded, is the key provider of health services. The private sector complements provision, especially in the area of primary care and ambulatory specialist care. The responsibility for the healthcare system is of the Government. The Ministry for Health is responsible for the provision of health services and health regulation and standards. The Maltese health system provides a comprehensive basket of health benefits. Few services, such as elective dental care, optical services and some medicines, are not included in the basket. Primary and ambulatory care is available both through the public and the private sector. Secondary and tertiary care is currently provided mainly through public hospitals[13].

2. National Plan/Strategy and the coding issue

A draft of the National Plan on Rare Diseases was completed in 2012, followed by an internal consultation exercise. Nevertheless, it has not been officially approved, yet. As a consequence, **currently no national plan/strategy** for rare diseases is yet in place in Malta.
However, rare diseases are mentioned in a broader action plan, issued by the Ministry of Health. Among the identified priorities, there are the establishment of a RD registry and the creation of the **Treatment Abroad Service**, addressing the needs of some RD patients to be treated for specialised care abroad.

3. Morbidity coding framework

In Malta, a legal framework regulating the process of morbidity recording exists. The Hospitals Information System collects hospital activity data from state and private hospitals and store them into the National Hospital Information System (NHIS) database. The collected data are used for health planning purposes.
ICD-10 Version 2016 (WHO) is the Edition used for the coding of diagnoses and external causes of injuries/accidents for hospitalized patients[14]. Operations and procedures are coded in ICD-9 CM.
Morbidity coding is not linked to reimbursement procedures. In the future, it is envisaged that diagnosis-related groups (DRGs) could be introduced, but they are not used at the moment[13].
The morbidity recording process take place both at hospital and at the primary care setting level.
Medical doctors are in charge of the coding process. The coding activities are performed *a posteriori*, based on clinical documentation available. The process is both paper and software-based. A data quality control process has not been defined, yet.

4. Mortality coding framework

Malta has a National Mortality Registry, which collects information from the medical death certificates of all persons who die in the country. ICD-10 Version 2016 (WHO) is the Edition used for the coding of mortality data.
The Directorate for Health Information and Research (DHIR) is the institution responsible for the collection, analysis and delivery of health-related information in Malta. The DHIR manages the

national health data sets on mortality, cancer, congenital anomalies, organ transplants, obstetrics, hospital information system, as well as a number of other databases on health service activity. For the purpose above, the **DHIR has been designated a National Statistical Institute by EUROSTAT**.

5. Patient identifier

Since the 90's, in Malta a **unique citizen identifier** (ID number) has been in use in the Patient Administration System (PAS), which is a centralized system accessible from all public hospitals and health Centres. Since 2005, Malta has an electronic registry, which stores health insurance/healthcare patient information and processes all claims and payments related to social security benefits. For healthcare purposes, the registry stores information on the national ID[15].

6. Rare diseases registration

Malta accepts the European Regulation on Orphan Medicinal Products definition of a prevalence of no more than 5 in 10,000 individuals.
The RD Registry initiative was launched in 2016, collecting data from 2008 onwards. It can be defined as a secondary registry and it is based at the Department of Health Information. Existing data collections used to identify within them RD cases are the national cancer registry for rare cancers, the congenital anomalies registry, specific diseases registries and the DB of patients sent to other countries, mainly the UK, for tertiary care not available in Malta. In all these sources of data, coding of these cases is currently done manually. An attempt to estimate RD cases from these sources has been recently carried out, but published data are not available yet.
Two Maltese registries having a national coverage contribute to European registries and networks: EUROCAT and RARECARE[16].

7. Centres of expertise and European Reference Networks (ERNs)

In Malta, there are five public hospitals. Two of these are acute general hospitals (one in Malta and a smaller one in Gozo) and three are specialized hospitals (for oncology, mental health and rehabilitation services, respectively). Mater Dei Hospital (MDH), a newly built modern hospital, is the major acute general and teaching hospital in Malta, offering a full range of hospital services and employing almost half of all the public healthcare employees.
An official policy for identifying Centres of expertise for RD is in not place, but the adoption of a formal designation process is under discussion. Part of this strategy includes also the possible adoption of Orphacodes for the recording of RD patients' data by the Centres of expertise that will be officially labelled.
Specific agreements and pathways for authorization exist for the referral to the UK or to some Italian regions of patients with complex conditions requiring care not available in Malta. Currently, **no Maltese HCP has been designated for participation in ERNs**. At national level, it is under discussion the establishment of an endorsement procedure for application to ERNs of Maltese HCP.

8. Undiagnosed RD patients

The issue of undiagnosed patients has not been addressed yet in Malta.

Spain Report (RD-CODE participant country)

1. Spain health-care system at a glance

The main features of the Spanish health care system are public financing and universal access to public health care services free of charge at the point of use. The Spanish National Health System (SNHS) is a **decentralized** one. The regional governments of the 17 Autonomous Communities have full responsibility for policy making, planning, and financing at a regional level. The NHS is financed by general taxes. Furthermore, each AC can collect additional resources through marginal add-on taxes on income. Health care coverage can be defined as universal. Provision is free of charge at the point of delivery, with the exception of outpatient pharmaceutical prescriptions and specific orthesis and prosthesis[17].

2. National Plan/Strategy and the coding issue

The Rare Diseases Strategy of the Spanish National Health System was approved by the *Consejo Interterritorial del Sistema Nacional de Salud* on 3 June 2009[18]. The elements defined in the Strategy reflect the recommendations established by the European Council Recommendation on an Action in the field of Rare Diseases. The content of the Strategy was evaluated three years after its approval. During 2013, an update of the objectives and recommendations of the strategy was carried out and the updated Rare Diseases Strategy was officially approved on 11 June 2014[19].
As all health strategies of the Spanish NHS, the Rare Diseases one is evaluated and updated every 4-5 years. Some Autonomous Community (AC) approved regional plans or strategies based on the National RD Strategy. In addition, some AC set up Advisory Commissions on rare diseases, with the aim of implementation the specific health policies outlined in the Plans.
At national level, the 2009 Rare Diseases Strategy identifies 7 lines of action. For each action, objectives and recommendations are clearly defined. The issue of RD codification is addressed within the strategy line “Information on RD”. The document outlines extensively the issue of RD codification and classification.
General and specific objectives are listed. Among them, the participation of Spanish experts in European and international coding and classification activities and the establishment of coordination mechanisms with these groups. Furthermore, the need to create a working group, within the framework of the Strategy, to tackle the RD classification issue and evaluate proposals was outlined.
The updated Rare Diseases Strategy of the Spanish National Health System, approved in 2014, further addresses the issue of coding and classification under the “Registries” chapter.

As Spain has a decentralized healthcare system, the funding of the RD Strategy is transferred from the national level to the regional one in the framework of a more general funding process. It is up to each region to establish which percentage of those funds is specifically dedicated to rare diseases-related activities. RD coding related activities were not specifically funded within the National Strategy, but regions could decide to allocate part of the funds received to coding activities.

3. Morbidity coding framework

In Spain, a legal framework regulating the process of morbidity recording exists and is linked to reimbursement procedures. The operating DRG systems for the reimbursement for in-patient care is the All Patient (AP-)DRG system[20]. The International Classification of Diseases, Ninth Revision, clinical modification (ICD9-CM) for the coding of diagnostics and clinical procedures has been compulsory used in Spain since 1987.
The Ministry of Health, Social Services and Equality is responsible for ICD translation and update. In 2011, a process for the translation and validation of the original materials of the ICD-10 for diagnoses and procedures started and lead to the issue of the ICD-10-ES (Spanish version of the ICD-10-CM)[21]. The translation and validation works were carried out by a Technical Unit, a group of designated experts, responsible for generating and maintaining the coding materials related to the ICD-10 for Spain and from which criteria are established for the normalization, training and use of the classification. The group is composed by representatives of the Ministry and of all the Autonomous Communities. It works in collaboration with Medical Societies and experts in clinical documentation.
Its main tasks are:
-the revision and validation of the translation of the classification currently in use (ICD-10-ES, 2nd edition, 2018).
-the periodic update of the versions of the ICD-10-ES, incorporating the addenda corresponding to the original classification of the United States.
-the revision and validation of the materials associated with this classification (i.e. reference tables, validation tables, correspondences, etc.)
- the elaboration of the official coding rules and guidelines with ICD-10-ES as a classification of reference for clinical coding in Spain
Since January 1st, 2016, the ICD-10-ES has been implemented in Spain as the reference classification for clinical coding and for the collection of morbidity in-patient data, in accordance with the Royal Decree 69/2015. A gradual implementation, according to the type of hospital and the care setting, of a new data model of the minimum basic data set was established.
Currently, morbidity data at hospital level are still collected using the ICD9-CM. In addition to ICD9-CM, ICD-10 and ICD-10-ES are used in some regions[22]. One region responding to the survey, reported to use for morbidity coding in addition to ICD, the International Classification of Primary Care (ICPC), a coding and classification system used in the domain of family medicine.
The Ministry of Health website has a dedicated webpage through which helping coding tools are accessible by users. In particular, a **tool allows the cross-referencing between ICD9-CM and ICD-10-ES codes**[23]. The Institute of health information (*Instituto de Información Sanitaria*) regularly releases publications with clarifications on specific coding issues.
In most of the regions consulted, the morbidity recording process takes place at both hospital and in the primary care setting, whilst in others is performed only at hospital level. The coding activities are performed both at the point of care and *a posteriori* and, in most cases, the process is both paper and software-based.

According to the considered region, different professionals are in charge of the coding process. Among them, nurses, medical doctors, administrative personnel and other coding experts (i.e. technicians in health documentation, clinical coders, etc.).
National guidelines for morbidity recording with ICD-9-CM are available and accessible through the Ministry of Health website. These guidelines are included in the coding manual[24].

A Codification Manual with the ICD-10-ES, prepared by the Technical Unit of the ICD-10-ES, is forthcoming. For Catalonia, a manual in Catalan for the coding with ICD-10-CM is available for users[25].
Specific training activities are performed for personnel involved in the coding process at local, regional and national level. During the last years, the training of the coders has been an activity for which Autonomous Communities are responsible. The Ministry of Health, Consumer Affairs and Social Welfare has a coordination role, produces materials that can be used for training activities and organizes specific update workshops. Furthermore, it manages a web-based training platform on ICD-10-ES. Other institutions directly involved in coding training activities are the Catalan Health Service and the Escola Valenciana d'Estudis de la Salut (EVES).

A data quality control process has been officially defined at local, regional and national level. At national level external audits are periodically performed.
In addition, Autonomous Communities Health Authorities and hospitals are responsible for data quality controls concrete implementation. At hospital level the sampling of cases to be reviewed by administrative staff to verify the correctness of reported data occurs.
The quality control process includes the use of software with flags for certain codes; automated quality control procedures (validity of input values, assessment of internal consistency and consistency with established norms); variation analyses carried out after data consolidation.

4. Mortality coding framework

The International Classification of Diseases Tenth Revision, Spanish version (ICD-10-ES) is used for the coding of mortality data. In Spain, a national legal framework regulating the process of mortality recording exists. Three are the sources of data from which mortality statistics are produced: medical death certificates (MDC), the Statistical Birth Bulletin (BB) and the Judicial Statistical Death Bulletin (JDB). A project named “Certifica” is in place for the self-training of medical doctors in charge of filling death certificates, in order to improve the quality and comparability of mortality statistics.

5. Patient identifier

The Royal Decree 183/2004 regulated the issue of the individual health card. Article 4 of the Royal Decree is the legal basis for the generation and use of the personal identification code of the National Health System. However, it is not used in health information systems recording morbidity /mortality data.
In addition to the personal identification code for the National Health System, there is a specific ID assigned by each Autonomous Community. As soon as a citizen is included in the population database, he/she is assigned to an identification number. This is a key link among the possible various autonomic personal identification codes that a person can have throughout his life. Both, the autonomous communities and the Ministry of Health provide databases that contain protected records of citizens[26].

6. Rare diseases registration

Spain accepts the European definition of rare disease (prevalence of no more than 5 in 10,000 individuals). An official list of RD whose affected patients can access specific benefits either at national or regional level has not been defined.

Currently, in Spain several experiences on RD registration within databases and health information systems exist. The level of implementation is local (i.e. within selected hospitals), regional and national.
The Strategy for Rare Diseases of the NHS, approved by the Interterritorial Council of the NHS in 2009, and updated in 2014, addresses extensively the issue of RD registration. An overview of existing experiences is included in the section "Health registries".
The first initiative, developed since 2002 as an epidemiological research programme for rare diseases, is REpIER[27]. REpIER, composed of research centres/groups from 11 of the Autonomous Communities and from the Carlos III Health Institute (ISCIII), explored the possibility, starting from by the existing databases established at different level, to set up a more comprehensive epidemiological information system on RD.
The National Strategy for Rare Diseases, approved in 2009, outlined clearly the need to estimate the incidence and prevalence of rare diseases to improve knowledge on their natural history, to adapt health care actions and be able to monitor better these diseases. One of the objectives identified by the Strategy is to obtain the necessary epidemiological information allowing for the development of effective social, health and research policies.

Interestingly, in 2006 a descriptive study was carried out to assess the existence of health registries in the field of rare diseases. Existing registries were classified in the following categories: 'specifically on RD', 'not specific, but with information on RD' and 'no information on RD'. The report concluded that in 2005 in Spain there were a total of 19 health information sources, mechanisms and registries collecting data 'specifically on rare diseases' and 58 'non-RD specific, but with information on RD'[28].

In 2011, the Carlos III Institute of Health (ISCIII) joined the International Rare Disease Research Consortium (IRDiRC) and financed the consolidation of the Spanish Registry Network for Research for Rare Disorders (SpainRDR).
All Autonomous Communities have participated in SpainRDR, coordinated by the Research Institute for Rare Diseases (IIER) of the Carlos III Institute of Health. During the period 2012-2015, the network contributed to the standardization of procedures and the development of regulatory frameworks in most regional governments to set up regional registries or information systems for rare diseases.
The main objective of **SpainRDR Network** was to create a **nationwide population-based rare diseases registry**, gathering data from the population-based registries of each Spanish Region and from specific patients' registries. This work started from the identification of ICD9-CM and ICD-10 codes to be used to trace RD cases in already existing different social and health data sources.
In 2015, the Royal Decree n.1091 was approved. The Decree established and regulated the State Registry of Rare Diseases, allowing for appropriate collaboration and coordination between the Regions, the Ministry of Health and the IIER. The Ministry of Health is the responsible of the National Registry of Rare Diseases[29].
Within this rich scenario, the issue of RD patients' codification has been tackled at all the levels of implementations of data collection on RD (local, regional and national).
As rare diseases can be recorded in different systems or in the same system using different classification and terminologies, a specific working group within the National Registry of Rare

Diseases was set up to **produce and maintain a standardized mapping of codifications** between ICDs, Orphacodes, SNOMED, OMIM and ERA-EDTA.
In one region, clinical units officially designated as of expertise for RD, report cases to a RD registry using Orphacodes during the recording process.

Starting from the REpIER experience, several studies on the prevalence of rare diseases per Autonomous Community were carried out. They represented a first attempt to describe the RD epidemiology at population level. Nevertheless, they were affected by some limitations depending on the nature of the sources of information used.
During the years, the consolidation of data collections on rare diseases made it possible to have more epidemiologic data available at the local/regional level. Autonomous Communities have issued official acts defining the functioning and the governance of regional registries[30,31,32,33,34,35,36 37,38,39, 40, 41 ,42 ,43].
At the national level, the Ministry of Health has data available, coming from regional registries, but they have not been fully processed yet.
Other sources of information from which epidemiological data on rare diseases can be derived, are available at local, regional and national level. They include population-based registries as cancer registries for rare cancers, congenital malformations registries, treatments registries, death registries and hospital discharge registries. Additional data sources considered at regional level in some AC are the specialized Health Services databases and the Spanish database of Persons with Disabilities (DBPD).

Where regional RD are ongoing, in most cases a communication mechanism between who performs the cases codification, namely at hospital level, and the RD registries' staff is not in place. In some regions, a communication is in place, with the possibility to submit queries on issues arising during the codification of specific cases. In addition, follow-up and review of inconsistent cases takes place in at least one of the consulted regions.

Several RD patient registries are ongoing in Spain and have been developed as part of the activities carried out by various research groups, in many cases in collaboration with scientific societies and/or in the context of European projects.
As reported in the Orphanet Report Series "RD registries in Europe", updated in May 2018[44], in Spain 58 registries, collecting data on specific rare diseases or group of rare diseases, are currently ongoing. Of them, 11 have a regional coverage, 43 a national coverage, 2 are European registries and one can be considered having a global coverage.

7. Centres of expertise and European Reference Networks (ERNs)

In Spain, an official policy for identifying Centres of expertise for RD is in place, both at regional and at national level. However, considering the national level, the designation procedure is not RD-specific.
The legal framework supports the identification of Centers of Expertise (CSUR), when the referral of cases in a limited number of Centres for their best management is necessary to guarantee equitable access to high-quality, safe and efficient health care. The Royal Decree 1302/2006[45] establishes the procedures and principles for the designation and accreditation of these Centres and the characteristics to be met by diseases in order to have a designated CSUR. CSUR are designated for

diseases needing procedures that require high technology use for their prevention, diagnosis or treatment or a high level of expertise for their diagnosis and management and for rare diseases.
Some regions have established their own official procedures for the designation of Centers of expertise for RD or RD groups.
Currently, there are **281 designated Centers of Expertise** (CSUR), located in 50 hospitals of the National Health System (NHS), for 44 diseases or procedures, including some related to rare diseases. Although **not all of them are specific for rare diseases**, some are highly specialized in procedures that are provided mainly to rare diseases patients.
In Spain, a formal process is in place for the endorsement of health care providers (HCP) to participate as full-members of an ERN. Currently, a total of **16 HCPs participate as full members of 16 ERNs.**
For a complete list of HCP of Spain participating in ERNs, please access the EC dedicated page:
[*https://ec.europa.eu/health/ern_en*]

Members:	
Complejo Hospitalario Regional Virgen del Rocío	ERN EURACAN
	ERN EURO-NMD
	ERN PaedCan
Complexo Hospitalario Universitario de Santiago	MetabERN
Hospital Clínic i Provincial de Barcelona	ERN LUNG
	ERN RARE-LIVER
Hospital Clínic i Provincial de Barcelona y Hospital de Sant Joan de Déu	ERN EpiCARE
	ERN Skin
	ERN-RND
Hospital de la Santa Creu i Sant Pau	ERN EURACAN
	ERN EURO-NMD
Hospital de Sant Joan de Déu	Endo-ERN
	ERN EURO-NMD
	ERN GENTURIS
	ERN GUARD-HEART
	MetabERN
	ERN PaedCan
Hospital del Mar	ERN EpiCARE
Hospital Universitari Germans Trias i Pujol y ICO Badalona	ERN GENTURIS
Hospital Universitari Vall d'Hebron	Endo-ERN
	ERKNet
	ERN CRANIO
	ERN LUNG
	ERN EuroBloodNet
	ERN EURO-NMD
	MetabERN
	ERN PaedCan
	ERN RITA
	ERN-RND
Hospital Universitario 12 de Octubre	ERN CRANIO
	ERN LUNG
	MetabERN
Hospital Universitario de Cruces	Endo-ERN
	MetabERN
Hospital Universitario La Paz	RARE-LIVER
Hospital Universitario Puerta de Hierro Majadahonda	ERN GUARD-HEART
Hospital Universitario Virgen de la Arrixaca	ERN GUARD-HEART
Hospital Universitario y Politécnico La Fe	ERN EpiCARE
	ERN EURO-NMD
	ERN PaedCan
ICO L´Hospitalet y Hospital Universitari de Bellvitge	ERN EURACAN

8. Undiagnosed RD patients

The importance of a timely diagnosis of RD has been recognized as a priority in the National RD Strategy under the strategy line “Early detection” and in its updated version, issued in 2014.
Nevertheless, the issues of undiagnosed patients and of their potential representation in data collections and in health information systems have not been specifically mentioned in these documents.
Despite this, different Spanish institutions, research groups and experts are involved in initiatives related to undiagnosed RD patients. These initiatives take place at local level (in selected

hospitals/Centres of expertise), at regional and at national level, including the participation in international/European projects and programs. A list with a brief description of these initiatives is reported.

Solve-RD

"Solve-RD - solving the unsolved rare diseases" is a research project funded by the European Commission for five years (2018-2022). It addresses one of the goals of the International Rare Diseases Research Consortium (IRDiRC) that consists in the delivery of diagnostic tests for most rare diseases by 2020. The Solve-RD consortium consists of 21 European academic institutions and one academic partner from the United States. The Centro Nacional de Análisis Genómico (CNAG-CRG) in Barcelona is a full partner in this European project and the Spanish Undiagnosed Rare Diseases Program (SpainUDP) is a collaborator.

The Spanish Undiagnosed Rare Diseases Program (SpainUDP)

The Spanish Undiagnosed Rare Diseases Program (SpainUDP) is implemented by the Institute of Rare Diseases Research (IIER)[46,47] of the Instituto de Salud Carlos III (ISCIII). The program is based on a multidisciplinary evaluation of undiagnosed patients based on a standardized protocol that establishes the criteria for patient selection, data collection, laboratory investigation and diagnosis. Patients with undiagnosed diseases or their family members can apply to SpainUDP individually, through patients' organizations or hospitals.

Genetic analyses are performed and phenotypic data (mapped to the Human Phenotype Ontology, HPO) are collected for each patient. SpainUDP is part of international/European initiatives: RD-Connect, Solve-RD, the Undiagnosed Diseases Network International (UDNI), and the MatchMaker Exchange (MME) platform.

URDCat

This program implemented in Catalonia aims to develop a model of health care directed to patients affected by non-Diagnosed Neurological Rare Diseases (nDRD)[48]. The Project is developed around 4 tasks: Selection and characterization of patients affected by neurological nDRD; genomic characterization and data analysis; development of a platform that allows data analysis and interpretation (RDCat); legal, ethical and social integration of the Genomic Medicine in RD.

EnoD

The Program for Undiagnosed Rare diseases (EnoD)[49] is an initiative of the Center for Biomedical Research on Rare Diseases (CIBERER) with the aim of discovering new genes and variants involved in the etiology of rare diseases to contribute ultimately to the accurate molecular diagnosis of unsolved clinical cases.

FEDER

Of notice, the Spanish Federation of Patients Associations (FEDER)[50] has constituted a Scientific Committee where unsolved cases are discussed.

Learning from these initiatives, some discussions have started on how to code undiagnosed RD patients within registries and /or health information systems.

ABOUT

This report is based on information which is accurate to the best of the Authors' knowledge. However, contents of this report should be considered illustrative and not exhaustive.

This document has been elaborated by the RD-CODE WP5 members, lead by the Veneto Region team, with the input of:

For Austria

Dr. Ursula Unterberger
Orphanet Austria/Medical University of Vienna

For Czech Republic

Dr. Miroslav Zvolský
Department of Clinical Classifications, DRG
Institute of Health Information and Statistics of the Czech Republic

For Malta

Dr. Francis Agius
Directorate Health Information and Research, Department of Health, Ministry for Health, the Elderly and Community Care, Malta

For Spain

Centro de Investigación Biomédica en Red de Enfermedades Raras (CIBERER)
Fundación para el Fomento de la Investigacion Sanitaria y Biomedica de la Comunitat Valenciana (FISABIO)
Ministerio de Sanidad, Consumo y Bienestar Social (MSCBS)
Consejería de Salud. Región de Murcia.
Servei Català de la Salut (CatSalut)
Departamento de Salud del Gobierno de Navarra
Dirección General de Salud Pública de la Junta de Castilla y León
Departamento de Salud Donostia-San Sebastian, Gobierno Vasco
Dirección General de Salud Pública. Generalitat Valenciana

BIBLIOGRAPHY AND SOURCES

All websites and documents were last accessed in June 2019.

[1] Federal Ministry of Labour, Social Affairs, Health and Consumer Protection (BMASGK). The Austrian Health Care System Key Facts. Updated edition 2019. ISBN 978-3-902611-38-3

[2] European Commission. Current status of the use of ICD by eHDSI deploying countries (2018). [https://ec.europa.eu/cefdigital/wiki/pages/viewpage.action?pageId=62884034]

[3] Busse R, Geissler A, Quentin W, Wiley M, eds. Diagnosis related groups in Europe: moving towards transparency, efficiency and quality in hospitals. Open University Press, 2011. [http://eurodrg.projects.tu-berlin.de/wiki/doku.php?id=publications:drgbook]

[4] Statistics Austria. Standard-documentation Meta information (Definitions, comments, methods, quality) on Hospital Discharge Statistics. [http://www.statistik.at/web_en/statistics/index.html]

[5] European Commission, DG Information Society and Media. Country Brief: Austria. [http://ehealth-strategies.eu/database/documents/Austria_CountryBrief_eHStrategies.pdf]

[6] Orphanet Report Series - Disease Registries in Europe. May 2018. [http://www.orpha.net/orphacom/cahiers/docs/GB/Registries.pdf].

[7] European Commission. [https://ec.europa.eu/health/ern_en]

[8] Bryndova L, Pavlokova K, Roubal T, et al. 2009. Czech Republic: health system review. Health Systems in Transition. European Observatory on Health Systems and Policies. 11: 1–121.

[9] European Social Policy Network (ESPN) - Flash report 2015/30 DRG Restart: Moving towards a more transparent in-patient care reimbursement system in the Czech Republic

[10] https://www.uzis.cz/en/catalogue/classifitions/international-statistical-classification-diseases-and-related-health-problems-instruction-manual

[11] https://drg.uzis.cz/res/file/metodiky/metodika-kodovani-diagnoz-v-drg-v016.pdf

[12] Orphanet Report Series - Disease Registries in Europe. May 2018. [http://www.orpha.net/orphacom/cahiers/docs/GB/Registries.pdf].

[13] Azzopardi-Muscat N, Buttigieg S, Calleja N, Merkur S (2017). Malta: Health system review. Health Systems in Transition, 2017; 19(1):1–137.

[14] European Commission. Current status of the use of ICD by eHDSI deploying countries (2018). [https://ec.europa.eu/cefdigital/wiki/pages/viewpage.action?pageId=62884034]

[15] European Commission, DG Information Society and Media. Country Brief: Malta. [http://ehealth-strategies.eu/database/documents/Austria_CountryBrief_eHStrategies.pdf]

[16] Orphanet Report Series - Disease Registries in Europe. May 2018. [http://www.orpha.net/orphacom/cahiers/docs/GB/Registries.pdf].

[17] Bernal-Delgado E, García-Armesto S, Oliva J, Sánchez Martínez FI, Repullo JR, PeñaLongobardo LM, Ridao-López M, Hernández-Quevedo C. Spain: Health system review. Health Systems in Transition, 2018;20(2):1–179.

[18] MINISTRY OF HEALTH AND SOCIAL POLICY. Rare Diseases Strategy of the Spanish National Health System. [http://www.mscbs.gob.es/organizacion/sns/planCalidadSNS/docs/RareDiseases.pdf]

[19] MINISTRY OF HEALTH AND SOCIAL POLICY. Estrategia en Enfermedades Raras del Sistema Nacional de Salud. [https://enfermedades-raras.org/images/feder/Documentos_ultimas_noticias/2014_Estrategia_nacional_ER.pdf]

[20] Busse R, Geissler A, Quentin W, Wiley M, eds. Diagnosis related groups in Europe: moving towards transparency, efficiency and quality in hospitals. Open University Press, 2011. [http://eurodrg.projects.tu-berlin.de/wiki/doku.php?id=publications:drgbook]

[21] http://www.cie10formacion.es/

[22] European Commission. Current status of the use of ICD by eHDSI deploying countries (2018). [https://ec.europa.eu/cefdigital/wiki/pages/viewpage.action?pageId=62884034]

[23] http://www.mscbs.gob.es/estadEstudios/estadisticas/normalizacion/home.htm

[24] http://www.mscbs.gob.es/en/estadEstudios/estadisticas/docs/Manual_de_codificacion.pdf

[25]https://catsalut.gencat.cat/web/.content/minisite/catsalut/proveidors_professionals/registres_catalegs/catalegs/cim-10-mc-scp/documents/manual-codificacio-CIM-10-MC-diagnostics.pdf

[26] European Commission, DG Information Society and Media. Country Brief: Spain. http://ehealth-strategies.eu/database/documents/Spain_CountryBrief_eHStrategies.pdf

[27] REpIER – Spanish Network of Rare Diseases Research on Epidemiology. Information System on Rare Diseases in Spain [https://registroraras.isciii.es/Comun/Inicio.aspx]

[28] Zurriaga Lloréns O, Martínez García C, Arizo Luque V, Sánchez Pérez MJ, Ramos Aceitero JM, García Blasco MJ, Ferrari Arroyo MJ, Perestelo Peréz L, Ramalle Gómara E, Martínez Frías ML, Posada de la Paz M; Red REpIER. [Disease registries in the epidemiological researching of rare diseases in Spain]. Rev Esp Salud Publica. 2006;80(3):249-57.

[29] Ministerio de Sanidad, Servicios Sociales e Igualdad. Real Decreto 1091/2015, de 4 de diciembre, por el que se crea y regula el Registro Estatal de Enfermedades Raras. [https://www.boe.es/diario_boe/txt.php?id=BOE-A-2015-14083]

[30] Boletín Oficial de la Junta de Andalucía [http://www.juntadeandalucia.es/boja/2013/126/BOJA13-126-00001-10823-01_00029685.pdf]

[31] Boletín Ofi cial de Aragón. [http://benasque.aragob.es:443/cgi-bin/EBOA/BRSCGI?CMD=VEROBJ&MLKOB=723989725252]

[32] BOLETÍN OFICIAL DEL PRINCIPADO DE ASTURIAS. [https://sedemovil.asturias.es/bopa/2013/04/29/2013-07667.pdf]

[33] BOLETÍN OFICIAL DEL ISLAS BALEARIAS. [http://www.caib.es/eboibfront/es/2013/8140/516721/orden-del-consejero-de-salud-de-6-de-mayo-de-2013-]

[34] BOLETÍN OFICIAL DE CANARIAS [http://www.gobiernodecanarias.org/boc/2011/162/002.html]

[35] BOLETÍN OFICIAL DE CANTABRIA [http://www.saludcantabria.es/uploads/SAS/Orden%20SAN-25-2012.pdf]

[36] Diario Oficial del Castiilla La Mancha [http://sescam.castillalamancha.es/sites/sescam.castillalamancha.es/files/documentos/legislacion/20131019/orden_22_09_2010_0.pdf]

[37] Boletín Oficial de Castilla y León. [http://www.saludcastillayleon.es/institucion/es/resumen-bocyl-legislacion-sanitaria/orden-san-113-2014-18-febrero-crea-registro-poblacional-enf]

[38] http://www.madrid.org/wleg/servlet/Servidor?opcion=VerHtml&idnorma=10146&word=S&wordperfect=N&pdf=S

[39] Boletín Oficial de la Región de Murcia. [http://sid.usal.es/bleyes/discapacidad/19880/3-2-2/decreto-n-223-2015-de-16-de-septiembre-por-el-que-seestablecen-los-criterios-de-gestion-y-funcionamiento-del-sistemade-informacion-sobre-enfermedade.aspx]

[40] Boletín Oficial de la Región de Navarra. [http://www.lexnavarra.navarra.es/detalle.asp?r=32271]

[41] Boletín Oficial del Pais Vasco. [http://www.lehendakaritza.ejgv.euskadi.eus/r48-bopv2/es/p43aBOPVWebWar/VerParalelo.do?cd2014000196]

[42] Boletín Oficial de la Comunitat valenciana [https://www.dogv.gva.es/va/eli/es-vc/o/2012/04/04/4/]

[43] Boletín Oficial de la Región de Galixia [http://www.docv.gva.es/portal/ficha_disposicion.jsp?L=1&sig=003421/2012

[44] Orphanet Report Series - Disease Registries in Europe. May 2018. [http://www.orpha.net/orphacom/cahiers/docs/GB/Registries.pdf].

[45] ROYAL DECREE 1302/2006 of 10th November 2006, that establishes the foundations of the procedure to designate and accredit benchmark centres, departments and units of the National Health Service [https://www.mscbs.gob.es/profesionales/CentrosDeReferencia/docs/RD_CSUR_EV.pdf]

[46] Spanish Undiagnosed Rare Diseases Program [http://spainudp.isciii.es/home/]

[47] López-Martín E., Martínez-Delgado B., Bermejo-Sánchez E., Alonso J.; SpainUDP Network, Posada M. SpainUDP: The Spanish Undiagnosed Rare Diseases Program. Int J Environ Res Public Health. 2018;15(8).

[48] [https://www.urdcat.cat/home]

[49] [https://www.ciberer.es/programas-transversales/proyectos/otros-proyectos/programa-de-enfermedades-raras-no-diagnosticadas]

[50] Federacion Espanola de Enfermedades Raras.[https://enfermedades-raras.org/]

List of relevant publications and websites providing RD data in Spain

https://www.boe.es/buscar/doc.php?id=BOE-A-2015-14083

http://www.euskadi.eus/contenidos/informacion/registro_enfermedades_raras/es_def/adjuntos/informe-rer-2018.pdf

http://www.euskadi.eus/contenidos/informacion/registro_enfermedades_raras/es_def/adjuntos/informe-rer-2017.pdf

Yepes García P, Mira Escolano MP, Cano Candela F, Maceda Roldán LA, Sánchez Escámez A, Seiquer de la Peña C, et al. Esclerosis tuberosa. Informe sobre Enfermedades Raras, IER 1902. Murcia: Consejería de Salud; 2019. Available in: http://www.murciasalud.es//publicaciones.php?op=mostrar_publicacion&id=2688&idsec=88

Mira Escolano MP, Cano Candela F, Maceda Roldán LA, Sánchez Escámez A, Seiquer de la Peña C, Serrano Pinto A, et al. Fibrosis quística. Informe sobre Enfermedades Raras, IER 1901. Murcia: Consejería de Salud; 2019. Available in: http://www.murciasalud.es//publicaciones.php?op=mostrar_publicacion&id=2679&idsec=88

Mira Escolano MP, Cano Candela F, Maceda Roldán LA, Sánchez Escámez A, Seiquer de la Peña C, Serrano Pinto A, et al. Prevalencia de enfermedades raras en la Región de Murcia 2015. Murcia: Consejería de Salud; 2018. Available in: http://www.murciasalud.es//publicaciones.php?op=mostrar_publicacion&id=2638&idsec=88

Titos Gil S, Segura Aroca M, Moreno López AB, Sánchez Escámez A, Sánchez Pardo M, Abellán Pérez MV, et al. Prevalencia de enfermedades raras en la Región de Murcia 2013. Murcia: Consejería de Sanidad; 2015. Available in: http://www.murciasalud.es// publicaciones.php?op=mostrar_publicacion&id=2379&idsec=88

Titos Gil S, Arizo Luque V, Palomar Rodríguez JA. Aproximación a las enfermedades raras en la Región de Murcia 2002-2009. Murcia: Consejería de Sanidad y Política Social; 2011. Available in: http://www.murciasalud.es//publicaciones.php?op=mostrar_ publicacion&id=1884&idsec=88

Titos Gil S, Hernando Arizaleta L, Palomar Rodríguez JA. Ingresos hospitalarios de personas con enfermedades raras. Región de Murcia, 2002-2007. Serie Informes sobre el Sistema Regional de Salud, nº 0901. Murcia: Consejería Sanidad y Consumo; 2009. Available in: http://www.murciasalud.es//publicaciones.php?op=mostrar_publicacion&id=1275&idsec=88 23

Titos Gil S, Palomar Rodríguez JA. Morbilidad hospitalaria por enfermedades raras en la Región de Murcia, 2002-2007. Serie Informes sobre el Sistema Regional de Salud, nº 0905. Murcia: Consejería Sanidad y Consumo; 2009. Available in: http://www. murciasalud.es//publicaciones.php?op=mostrar_publicacion&id=1542&idsec=88 24

León León J, Palomar Rodríguez JA. Coste de las altas hospitalarias con diagnóstico principal de enfermedad rara. Región de Murcia, 2002-2007. Serie Informes sobre el Sistema Regional de Salud, nº 1002. Murcia: Consejería Sanidad y Consumo; 2010.

Pastor-García M, Gimeno-Martos S, Zurriaga O, Sorlí JV, Cavero-Carbonell C. Anomalías congénitas cardíacas en la Comunitat Valenciana 2007-2014, el registro poblacional de anomalías congénitas. An Pediatr (Barc). 2019.

Gimeno-Martos S, Pérez-Riera C, Guardiola-Vilarroig S, Cavero-Carbonell C. Epidemiología de la Osteogénesis Imperfecta: una Enfermedad Rara en la Comunitat Valenciana. Rev Esp Salud Pública. 2017; 91: e1-e10.

Cavero-Carbonell C., Gimeno-Martos S., Zurriaga O., Rabanaque-Hernandez MJ., Martos-Jimenez C. La validez del Conjunto Mínimo Básico de Datos como fuente de identificación de las Anomalías Congénitas en la Comunitat Valenciana. Gac Sanit. 2017; 31: 220-226.
Gimeno-Martos S., Cavero-Carbonell C., López-Maside A., Bosch-Sánchez S., Martos-Jiménez C., Zurriaga O. Chromosomal anomalies: The experience of the Congenital Anomalies Registry of the Valencia Region. An Pediatr (Barc). 2016; 84: 203-10.

Verónica Alonso, Ignacio Abaitua, Óscar Zurriaga, Jenaro Astray, Manuel Errezola, Josefa M Aldana-Espinal, Mario J Margolles, Josep Jiménez, Joaquín A Palomar, Milagrosa Santana, Enrique Ramalle-Gomarra, Julián M Ramos, Federico E Arribas, Rufino Álamo, Gonzalo Gutiérrez-Ávila, Antònia Galmés, Miguel García-Ribes, Carmen Navarro, Eva Ardanaz, Manuel Posada de la Paz; Spain-RDR Group. National rare diseases registry in Spain: pilot study of the Spanish Rare Diseases Registries Research Network (SpainRDR). Orphanet J Rare Dis. 2014; 9: P5.

Cavero Carbonell C, Zurriaga O, Pérez Panadés J, Barona Vilar C, Martos Jiménez C. Variación temporal y distribución geográfica de las cardiopatías congénitas en la Comunitat Valenciana. An Pediatr (Barc). 2013; 79:149-56.