State-of-Play Adoption/Implementation of the Orphanet RD nomenclature (ORPHAcodes) to Trace RD Diagnosis in Europe

June 2025

To be Revised and approved by the JARDIN MS representatives

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Co-funded by the European Union

Co-Funded by the European Union. Views and opinions expressed are however those of the author(s) only and do not necessarily reflect those of the European Union or HADEA. Neither the European Union nor the granting authority can be held responsible for them

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Background

The Orphanet nomenclature of RD (ORPHAcodes) is a multilingual, standardised, controlled medical terminology specific to rare diseases, it includes all clinical entities registered in the Orphanet knowledge base[i]. Each clinical entity (disorder, group of disorders, or subtype of a disorder) is associated with a unique numerical identifier named ORPHAcode, as well as a preferred term, synonyms, and a definition. The Orphanet nomenclature is organised in a classification system, structured around the major medical specialties, according to diagnostic and therapeutic relevance[ii],[iii]. This clinical coding system is mapped to the main generic clinical and genetic terminologies [iv], thus providing a common language across healthcare and research systems for effective monitoring and reporting on all rare diseases diagnosis (including undiagnosed[v]). Its production and maintenance started at the Inserm in 2007 and it is co-funded by Inserm & European Commission projects (see annex 3 for more info) since 2009 when "Improved codification for rare diseases " is cited as a priority in the COUNCIL RECOMMENDATION of 8 June 2009 on an action in the field of rare diseases 2009/C 151/02[vi]. Exploitation of ORPHAcodes' annotated health data increases the visibility of people living with a RD, compared to generic terminologies [vii], [viii], [ix],[x], [xi], [xii], [xiii], [xiv], [xv],[xvi],[xvii],[xviii], [xix], [xx], [xxi], [xxii]and thus contributes to better understanding the RD impact on the health of a community and facilitates ensuring that needs of all RD patients are met.

In 2014, the Commission Expert Group on Rare Diseases adopted a Recommendation on ways to improve codification for rare diseases[xxiii]. In this Recommendation, Member States are encouraged to consider and explore the feasibility of the use of ORPHAcodes at a national level and to include the codification of rare diseases as an area of their national plans/strategies for rare diseases.

In 2017 the EC Steering Group on Promotion and Prevention (SGPP) recognised the ORPHAcodes as best practice[xxiv].

Since 2019, ORPHAcodes are listed in the set of common data elements for Rare Diseases Registration released by the EU RD platform to ensure interoperability between registries [xxv].

The Orphanet nomenclature of RD is included in the 2011 Cross Border Health-care Directive as far as RD diagnosis is concerned. So, ORPHAcodes are the recommended code to trace RD diagnoses in the European Common Semantic Strategy 2019[xxvi] & in the Guidelines on Patient Summary, Release 3.2, Mar 2022, and Release 3.4, November 2024[xxvii] as such ORPHAcodes (disorder level - aggregation level- and subtypes) are included in the Code Systems used in the MVC - My Health @ EU - eHealth Digital Service Infrastructure (eHDSI)[xxviii].

The functional specifications for the EC's eHealth Network guidelines on the European Electronic Health Records format (EEHRxF) include the ORPHAcodes for inclusion in the Patient Summary [xxix],[xxx].

The WHA Resolution "Rare Diseases: a Global Health Priority for Equity and Inclusion", adopted on 24 May 2025, urges members to commit to considering the implementation of ICD-11, and where appropriate, interoperable codification systems for rare diseases such as the Orphanet nomenclature of rare diseases, at their earliest possibility, and in accordance with their available resources, in order to enable the recording, reporting and monitoring of rare diseases at the national and international levels[xxxi].

Guidelines and recommendations for ORPHAcoding implementation and exploitation in order to ensure internationally standardised data collection[xxxii] have been released in the frame of the EC co-funded RD-ACTION Joint Action and RD-CODE project (see Annex 3 for more info).

Since 2022 un Orphanet nomenclature national hubs network has been set up in order to support the implementation of ORPHAcodes at national level[xxxiii],[2].

State of Play

In order to assess the State of Play of ORPHAcodes implementation in European countries, complementary approaches have been used to cover both the legal frameworks available in the different countries and the real-life implementation cases.

1) Feedback from the Orphanet National Nomenclature Hubs[3] or Orphanet National team (Luxembourg & Greece) was sought to collect information on the ORPHAcodes implementation status at national level and the political/legal framework of national ORPHAcodes implementation if relevant (table 1-2). Use-cases description has also been collected (tables 3a, 3b, 3c). In some cases, the information was also validated by National/Regional Registry Staff (as per indication).
2) Feedback from users was obtained from:
   - A survey to evaluate the 2024 situation of ORPHAcodes usage by health care providers (HCPs) linked to ERNs has been carried out by 15 Orphanet Nomenclature National Hubs *via* the OD4RD2 project.
   - A survey to better understand the first Capture of RD Patient data addressed to health care providers (HCPs) linked to ERNs in 26 MS plus Norway was performed in the frame of JARDIN Joint Action. It included a question regarding the use of ORPHAcodes in HCP Institutions.
3) Literature survey of available studies reporting benefits of ORPHAcoding or using ORPHAcoding to identify RD populations in their analysis.
4) Submission for revision and approval of the information in this document to the MS representatives of the JARDIN project.

[2] https://od4rd.eu/02-partners
[3] https://od4rd.eu/02-partners

1) Feedback from the Orphanet Nomenclature National Hubs

2025 ORPHAcodes Implementation* Assessment (Austria, Belgium, Bulgaria, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, Norway, The Netherlands, Poland, Portugal, Slovenia, Spain, Sweden & Switzerland)

As of January 2025, 24 countries were surveyed: Austria, Belgium, Bulgaria, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, Norway, The Netherlands, Poland, Portugal, Slovenia, Spain, Sweden & Switzerland. For: Hungary/Slovakia the information is presented in yellow as it has been obtained via the JARDIN T8.1 Survey, for Croatia/Cyprus/ the information is not yet available: this information will be collected during the T8.2 JARDIN Data Management Workshop in June.

In two participating countries ORPHAcodes are implemented in Electronic Health Records of the Health Information Systems of all hospitals via a reference list mapped to a partial subset of ORPHAcodes. In most countries ORPHAcodes are implemented in the Electronic Health records of the Health Information Systems of centers of expertise for RD, either nationally (7) or locally in some hospitals (13) (Fig.1a).
In most cases ORPHAcodes are used in registries, either RD national registries (14) and/or regional registries (2) and/or specific registries (11), (Fig.1b)
When exploring a selection of 5 Nation-wide implementation use-cases and 3 local implementation use-cases (table 3) we observe that primary ORPHAcoding is carried out only in 4 countries (fig 2), and that full ORPHAcodes integration (i.e. covering 100% of disorder level) is carried out only in 4 countries (fig.3).

MS	OC implementation in EHR	OC implementation in National RD Registry	OC implementation in other Registry	Is there a legal framework for ORPHAcodes use? (i.e. decision/law)	Links to official documents/websites
Austria	Officially designated RD centres of expertise (mandatory), Associated national centers in ERNs and other university clinics (process ongoing, to be finalized Jan 1, 2026)	No National RD Registry	Yes, in some local registries	Yes, beginning Jan 1, 2026, mandatory for officially designated CoEs.	
Belgium	Local	Yes	Yes, in some disease-specific registries: spinal muscular	No policy, but Recommendation in the 1st Belgian RD plan,	https://www.health.belgium.be/sites/default/files/uploads/fields/fpshealth

MS	OC implementation in EHR	OC implementation in National RD Registry	OC implementation in other Registry	Is there a legal framework for ORPHAcodes use? (i.e. decision/law)	Links to official documents/websites
			atrophy (SMA), neuromuscular diseases (NMD) and myasthenia gravis (MG).	action 2019-2021. The OC must be used in the data collection form for the Central Registry of Rare Diseases (CRRD) since September 2024.	_theme_file/plan_belge_maladies_rares.pdf
Bulgaria	National RD centres of expertise	Yes	No	Ministry of Health Ordinance N16, 30.07.2014	https://www.mh.government.bg/upload/4324/naredba16-ot-30-07-2014g-registrirane-redki-zaboliavania.pdf
Czechia	Local (ERN centres) ongoing to ALL ERN centres. Implementation in other hospitals/healthcare providers in progress.	National RD Registry in preparation, OC will be in the dataset.	OC implemented in the National Registry of Reimbursed Health Care and in the National Registry of Reproductive Health. Both registries are mandatory at the national level, completeness of OC coding not mandatory but on the rise.	Yes, official documentation of the National Registries, official guide for OC coding.	https://www.uzis.cz/index.php?pg=registry-sber-dat--klasifikace--orphanet#o-klasifikaci https://mzd.gov.cz/vestnik/vestnik-4-2024/
Denmark	Local	No RD Registry	Info not available	Info not available	
Estonia	Local	Yes	Yes	No	https://www.kliinikum.ee/harvikhaigused/
Finland	Local, Fully implemented in 2 out of 5 University Hospitals, partially in 3 out of 5	Yes	Yes, in all the 5 patient registries of The University Hospitals,	Consensus and a national plan/strategy to implement OC	National programme: https://urn.fi/URN:ISBN:978-952-408-251-8
France	National RD centres of expertise	Yes	Yes	Yes	[ix] [xlviii-xlvi]
Greece	Officially designated RD centres of expertise (mandatory), some are are part of the ERNs and other specialized centers	No, currently there are various registries under development	Not Known	Yes, official documentation of the National Registries, official guide for OC coding.	https://search.et.gr/el/fek/?fekId=620336 https://www.elinyae.gr/sites/default/files/2024-01/248%CE%B2_2024.pdf

MS	OC implementation in EHR	OC implementation in National RD Registry	OC implementation in other Registry	Is there a legal framework for ORPHAcodes use? (i.e. decision/law)	Links to official documents/websites
Germany	Mandatory by law in inpatient-sector , via a mapping to a reference list (Alpha-ID-SE file)	Yes	Yes	Yes	https://www.bundesgesundheitsministerium.de/themen/praevention/gesundheitsgefahren/seltene-erkrankungen/kodierung-von-seltenen-erkrankungen.html
Ireland	No	No National RD Registry	Yes, in two ERN Registries	No	
Italy	Local	Not yet but the National RD Plan envisages further OC use expansion (i.e. in the National RD Registry, starting with selected pilot groups of RDs).	Yes, RD Regional Registries	Yes	[xxi-xxii][li-liii]
Latvia	Local	Yes	Yes (Population based Cancer Registry)	Yes	https://likumi.lv/ta/id/336729-plans-reto-slimibu-joma-2023-2025-gadam
Lithuania	National RD centres of expertise	National RD Registry in development	Yes, ERN registries, RD local hospital registries	Yes (ORDER ON THE CODING OF RARE DISEASES WITH ORPHAcodes)	https://e-seimas.lrs.lt/portal/legalAct/lt/TAD/5cb702d1ee1e11ec8a3a9ec3b65fdf23
Luxembourg	Local in the National ERN Hub for the purpose of completing the specific ERN registries	No National RD Registry	Not known	No national policy	
Malta	National	Yes	Yes	No, voluntary submission to the registry via online form	https://dhir.gov.mt/en/registries/rare-diseases/ https://dhir.gov.mt/wp-content/uploads/2024/04/Annual_Report_Feb_2023.pdf https://dhir.gov.mt/wp-content/uploads/2024/04/Annual_Report_Feb_2024.pdf
The Netherlands	National , via a mapping to a reference list (the Diagnosis Thesaurus)	No National RD Registry	Yes, in ERN and several local registries	Consensus among relevant partners, no official legislation	Zeldzame aandoeningen in beeld - DHD
Norway	Local	Yes	Yes, Norwegian Rare Bone Disorders	No	arsrapport-sjeldenregisteret-2023.pdf

MS	OC implementation in EHR	OC implementation in National RD Registry	OC implementation in other Registry	Is there a legal framework for ORPHAcodes use? (i.e. decision/law)	Links to official documents/websites
Poland	Local , ERN centres. Gradually introduced to NRN	Yes	No	Yes	[45]
Portugal	National RD Centres of expertise	No National RD Registry	No	Yes	https://diariodarepublica.pt/dr/detalhe/resolucao-assembleia-republica/34-2009-608018
Romania	Local	No National RD Registry	No	No	
Slovenia	Local	Yes, but NRDR not fully operational	Not known	Yes, part of national RD plan	https://www.gov.si/teme/redke-bolezni/
Spain	Local/Regional/Gradually introduced at National RD Centres of Expertise	Yes (33 RD)	RD Regional Registries	Yes	https://www.boe.es/eli/es/rd/2015/12/04/1091 [xii] [lx]
Sweden	No	Yes	No	No	
Switzerland	National RD centres of expertise	Yes	Not known	A legal framework is under development by the Federal Office of Public Health and should be implemented by 2028.	
Hungary	Jardin Survey - Voluntary integration; no legal obligation to adopt ORPHAcodes	*Info not available*	*Info not available*	*Info not available*	*Info not available*
Slovakia	Jardin Survey: Mandated within the National RD Registry; no obligation for general EHR use.	*Info not available*	*Info not available*	*Info not available*	*Info not available*
Croatia/ Cyprus/	*Info not available*	*Info not available*	*Info not available*	*Info not available*	*Info not available*

Table 1 Summary of ORPHAcodes (OC) implementation status by country as per Orphanet National Nomenclature Hub or Orphanet Network Feedback (2025) in HIS (a) & in registries (b)

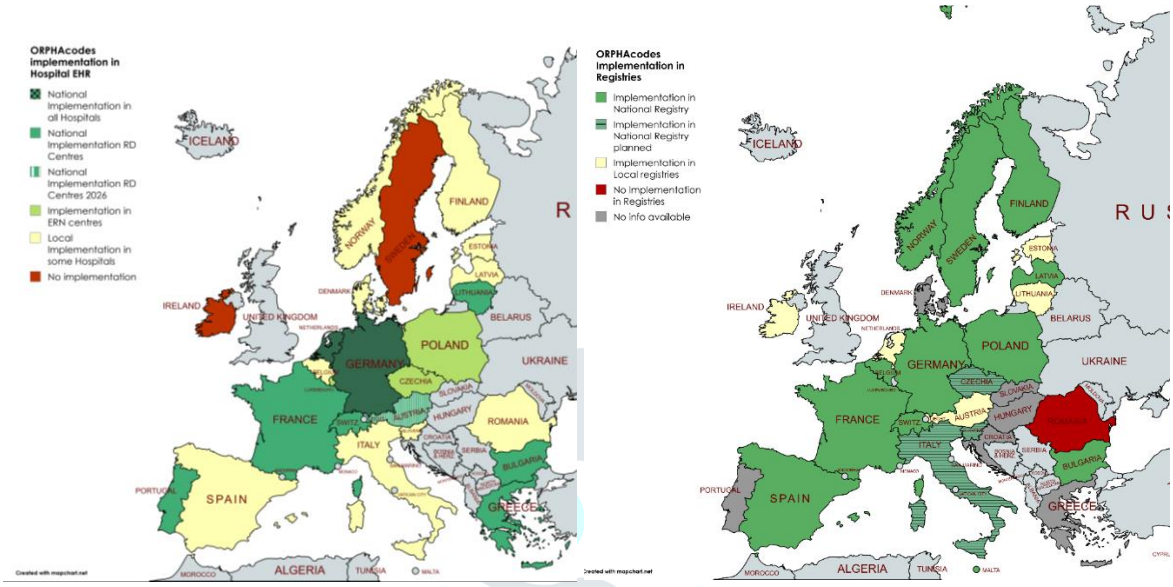

Fig.1 ORPHAcodes Implementation in HER of Hospitals or RD centres (a) and in Registries (b) as of beginning 2025

The same kind of survey was carried out in 2023 [xxxiv]and 2022 [xxxv], allowing to observe the evolution of ORPHAcodes implementation over the years. Although the number of countries surveyed increased over the years, we still observe a decrease in the number of countries where ORPHAcodes were not implemented at all (from 5 in 2022 to 0 in 2025) with also a considerable increase of local implementations (13 in 2025) (Table2).

	Countries surveyed	ORPHAcodes used to produce data or statistics for RD in all hospitals	ORPHAcodes used in National Registry	ORPHAcodes used in centres of expertise at national level	ORPHAcodes used at local level in Hospitals	ORPHAcodes used in local registries/regional registries	No use
2022	17	1	8	5	4	3	5
2023	20	2	10	5	3	3	3
2025	25	2	14	7	13	14	0

Table 2. Evolution of ORPHAcodes evolution 2022-2023-2025

Czechia

ORPHAcodes are utilised in collaboration with Czech Society of Medical Genetics and Genomics [xxxvi] and the General Health Insurance Company [xxxvii] for the pilot reimbursement of extra funding for members of the Czech members of the European Reference Networks for Rare Diseases (legally codified as per art. 133a of act 372/2011 Coll as official national centres of "highly specialised care") and for reimbursement of next generation sequencing in rare diseases/rare cancers. The methodology for coding rare diseases through ORPHAcodes was also developed, which can be found on the website of the Ministry of Health of the Czech Republic, on the website of the Institute of Health Information and Statistics [xxxviii], as it was also published in the Bulletin of the Ministry of Health 4/2024 [xxxix], [xl].

France

In 2012, an instruction was issued that the French hospital system database would use ORPHAcodes alongside the French modification of ICD-10 (PMSI) to code all diagnosis of inpatients seen in as soon as a patient with a rare disease is taken into care, whatever the conditions and the cause of the treatment (Instruction DGOS/PF2 no 2012-389 du 16 novembre 2012 relative aux modalités de codage PMSI concernant les patients atteints de maladies rares) [xli], however this instruction was unsufficient. It was followed by an instruction given to RD Centres of reference for rare diseases and centres of competence for rare diseases in 2016 (Instruction DGOS/PF4 no 2016-11 du 11 janvier 2016 relative aux missions et périmètres des centres de référence, centres de compétences et des filières de santé dans le domaine des maladies rares)[xlii], which made mandatory for them to feed the national database for RD (BNDMR) using ORPHAcodes, importantly, financial incentives accompanied this measure. Information is daily transmitted to the National RD Registry (Banque Nationale Données Maladies Rares- BNDMR). The aim was to better identify patients in the healthcare system so as to improve knowledge of their healthcare pathways.

The introduction of ORPHAcodes allows the National RD Registry-BNDMR to be used in studies regarding, amongst others, the diagnostic delay[xliii], the mortality as well as health-economic studies that would not have been possible without this codification [xliv], [xlv], such as the annual report on Number of cases per rare disease registered in the French National Rare Disease Registry (BNDMR)[xlvi]. As far as RD are concerned, BNDMR data also automatically feeds the National Platform for National agencies & administrations: PIRAMIG. This platform collects, analyses and compares activity reports of officially designated RD expert centres and RD competence centres with the aim to assess the relevance of allocated resources to establishments and, where necessary and if necessary, to resize funding more equitably [xlvii]. Data from BNDMR is also used to feed specific repositories (for diagnosis and for treatment surveillance); for e-prescription for genomic testing and to conduct epidemiological studies and to monitor policy indicators.

Within the French third National Plan for Rare Diseases and also because of the development of electronic health records in France, the French Ministry of Health set up in 2015 an advisory

committee for the codification of RD, which concludes to the use of ORPHAcodes in the BNDMR.

Germany

With the entry into force of the Digital Supply and Care-Modernisation Act (DVPMG) in 2023, the legal basis was created in Germany to be make ORPHAcoding mandatory in inpatient clinics in all hospitals [xlviii]. Outpatient clinics can use ORPHAcodes at their discretion.

The implementation of the ORPHAcodes was initiated early in Germany as part of the Federal Ministry of Health (BMG)-funded national project "Coding of Rare Diseases" (2013-2019) [xlix]. It was an initiative under the National Action Plan for People with Rare Diseases of the National Action Alliance for People with Rare Diseases (NAMSE). It started in July 2013, was initially planned for 3 years and was extended until October 2019 under the project name "Coding of Rare Diseases II".

In 2015, the German Institute for Medical Documentation and Information (DIMDI) released an extended variant of the Alpha ID file (File containing all Diagnostic Terms from the Alphabetical Index of ICD-10-GM, aligned with ICD-10-GM codes and machine-readable specific Alpha-ID-Codes) for the first time. This Alpha-ID-SE file, also aligns ORPHAcodes in case of diagnostic terms of RD. The annually updated version comes into force at the beginning of the year and is valid until the end of the respective year. By using the Alpha-ID-SE file, coders will be provided with ICD-10-GM and ORPHAcodes by selecting the disease's diagnostic term. This makes it possible to carry out a standardised and simplified coding of Rare Diseases and thus enable their mapping in the health system without additional coding effort [l].

Incentives: In order to receive the status of an “expert centre for RD” by the German Federal Joint Committee it is amongst other prerequisites necessary to code with ORPHAcodes. This status comes with extra funding.

The Netherlands

For the implementation of ORPHAcodes in the Dutch hospital information systems a working group of DHD (Dutch Hospital Data), Nictiz, NFU (Dutch Federation of University Medical Centers) and Orphanet Netherlands included in the “Diagnosethesaurus” terms mapped with ORPHAcodes derived from the SNOMED/ORPHAcodes mapping files. All Dutch hospitals supply data to the DHD on the patients they treat (LBZ) since 2022. DHD uses this data to give information back to the hospitals (benchmarks/dashboards), to governmental institutions, and others [li].

DHD developed a viewer on this database to give insight in number of patients with rare diseases: ORPHA-viewer. ORPHA-viewer will be used in future by hospitals to supply data to the Ministry of Health, but also it will support hospitals in providing patient numbers for the assessment procedure for the recognition of expertise centres or ERN’s centres.

Italy

The 2021 national plan regarding the policies on rare diseases (LEGGE 10 novembre 2021, n. 175 Disposizioni per la cura delle malattie rare e per il sostegno della ricerca e della produzione dei farmaci orfani) has been released in November 2021 [lii]. The article 4 states that the updated list of rare diseases/groups of rare diseases to be covered by the Essential Levels of Care (LEA), must refer to the ORPHAcodes and to the Orphanet classification system. The 2016 Italy report issued by RD-Action [liii] indicates that 11 Regional registries out of 19 in Italy use ORPHAcodes to code rare diseases. These Regional registries issue reports to regional authorities and contribute to studies [vii], [xxi], [xxii], [liv].

Portugal

The Directorate-General of Health (DGS), through the Department of Quality in Health, developed an instrument for the special protection of people living with a rare disease, titled the 'Rare Disease Person's Card' (RDPC) – in Portuguese, “Cartão da Pessoa com Doença Rara (CPDR).

The Orphanet nomenclature of RD (ORPHAcodes) is the mandatory classification to be used by all rare disease reference centres for the Rare Disease Card (CPRD) registration. The RDPC is requested by a clinician through a dedicated tab of the electronic patient record on the Portuguese Health Data Sharing Platform (Plataforma do Registo de Saúde Eletrónico), which provides a list of rare diseases with their correspondent ORPHAcodes and clinical guidelines in emergent or urgent situations. The clinician can edit the clinical guidelines and, if necessary, personalize and adjust the information according to each individual patient’s case, enabling the customization of urgent/emergency care. In order to simplify the process and clarify the RDPC issuance procedure, the DGS guideline (DGS Norma No. 01/2018) defines its emission and review conditions [lv]. A Technical Report on Rare Disease person’s card production is issued regularly [lvi]. The Legal base to use ORPHAcodes is the following diploma "Resolution of the Assembly of the Republic n.º 34/2009, may 7th 2009, published in Republic Diary No. 88/2009, Series 1 of 2009-05-07, available at https://diariodarepublica.pt/dr/detalhe/resolucao-assembleia-republica/34-2009-608018

Poland

Since 1st July 2024 a new policy of reimbursement of medical consultations for RD patients, financed by the National Health Fund is in place. The condition for obtaining better financing of medical consultations is entering the ORPHAcode when diagnosing a rare disease. ALL Patients with RD diagnosis will be automatically included into the Registry, with mandatory assignment of the ORPHAcode, by the Expert Centres of Rare Disease (currently 44 HCPs – members of ERNs, with the perspective of granting “expert centres” status for other highly specialized centres (non-ERN members)). National Health Funds currently obtains reports from manually collected data at the HCP level. The National RD Registry will be operational in 2025 and will provide these reports to the National Health Funds [lvii].

Switzerland

In 2014, the Federal Council adopted the National Concept for Rare Diseases and its implementation plan, which included the creation of a national registry. This initiative established the political framework for implementing the Swiss Rare Disease Registry (SRDR).

The SRDR is governed by the Federal Act on Research Involving Human Beings and the Federal Data Protection Act. The project was reviewed by the Cantonal Ethics Committee of Bern and received approval on December 11, 2018, granting authorization to collect data on rare diseases in Switzerland.

In 2023, there was a decision for an organisation restructure and the registry is currently suspended while preparing to apply for an Advisory Opinion.

A specific legal framework for rare diseases is under development by the Federal Office of Public Health and should be implemented by 2028.

While registration of rare disease (RD) patients—both inpatient and outpatient—in the SRDR is not currently mandatory, it is strongly recommended through officially recognized RD centers and reference centers designated by the National Coordination for Rare Diseases (kosek). The SRDR utilizes ORPHAcodes [lviii] and publishes annual reports and scientific publications [lix].

Spain

The Spanish Network of Rare Disease Registries for Research, Spain-RDR, was a project of the Carlos III Health Institute IRDiRC Call (2012-2015). The main objective of Spain-RDR Network was to create a nationwide population-based RD registry in Spain, gathering the population-based registries of each Spanish Region as well as the specific registries of patients. To achieve this, each of the 17 Spanish Regions had to develop a regional population-based RDR that could work in coordination with the rest of registries to establish a nationwide registries network. Once the project Spain-RDR ended (June 2015), the Ministry of Health, Social Services and Equality (MSSSI) decided to continue this work with the creation of the Spanish Registry of Rare Diseases (ReeR), currently in force [lx].The ReeR, established by Royal Decree 1091/2015, aims at understanding and addressing the complexities of rare diseases in Spain. By consolidating regional registers, this system represents a milestone in the management of information on these pathologies. The latest ReeR report published (2023) provides epidemiological information about rare diseases in Spain in the period 2010-2020, to guide health planning and management in the field of rare diseases [lxi]. The Registry incorporates cases for 33 entities codified using different terminologies, including ORPHAcodes. In addition to the ReeR, many of the Regional RD Registries gather epidemiological data for a higher number of rare diseases.

In 2023, the Reference Terminology Server of the National Health System became operational. This platform, created by the Ministry of Health, offers users the possibility of consulting

terminological resources commonly used within the national clinical field, with special attention to SNOMED-CT. Additionally, it will provide the necessary tools for integration via REST or FHIR. In this first phase, its use will be aimed at autonomous communities, with the objective of consolidating its operation to subsequently open it to other agents in the health sector. Among the semantic resources available we can highlight: SNOMED CT (International Edition and national extensions); ICD-10-ES, ICD-10-PCS, ICD-O-3.1, CIAP-2 and ICD-9-CM and ORPHA.

Use cases of ORPHAcodes Implementation at National Level (France, Portugal, Germany, the Netherlands, Switzerland, Italy, Norway & Poland)

- table 3a RD diagnosis coding
- table 3b Additional info/specific Use cases
- table 3c Data Exploitation

Table 3a RD diagnosis coding

Country	Where	Inpatient/Outpatient	Registration of diagnosis	Who codes	Coding diagnosis: file used in the System	Number of OC available	Visibility of the OC or RD diagnosis in the EHR (further encounter)
	Mandatory in ALL Official RD centres in Hospitals	Both	Tab RD available in the EHR and daily transmission to intermediate system (BaMaRa) (after pseudonymization) which feeds specific registries and the National RD registry (BNDMR) and other data repository and ePrescription.	Clinicians/Coders from expert centres (with specific funding to increase coding capacity)	Flat list of diagnosis linked to OC, from the Nomenclature Pack file. Tool: search by disease name and retrieval of OC and ICD-10 code	As per Nomenclature Pack	Only accessible in the Hospital where the OC has been diagnosed
	In official RD centres	Both	Tab RD is available in the EHR for the request of an RD card: OC are mandatory for the request of the RD Card. This OC inserted for the request will be then available in the EHR. Whenever a RD Card is not requested the ICD10 code is used	Clinicians	Flat list of diagnosis linked to OC from Nomenclature Pack (but manual update) in RD Card Tab	As per Nomenclature Pack but no yearly update => manual lookup for more recent codes	Yes for the patients having an RD Card
	Mandatory for ALL Hospitals	Inpatient mandatory (outpatient optional)	Clinicians provide a diagnosis	Clinicians register the diagnosis and then Coders or Clinicians assign a code	Alpha-ID-SE file linked to OC aligned to ICD10-GM by the Orphanet DE/BfArM experts	7,022 If no ICD10 term => no OC	Yes (if EHR exists, not mandatory yet)
	RD Centres of reference and ERN RD Centres located in hospitals in some regions.	Both	Clinician assigns a diagnosis => this issues a certificate & the local public health authority of the patient's place of residence issues an exemption document for benefits to which they are legally entitled, including specific drugs or medical devices indicated in the treatment plan drawn up at the RD Centre of reference). These regions use a common	Clinicians register the diagnosis at the point of care from the official national list (expanded and with OC	List of diagnoses linked to OC from Nomenclature Pack/ classification included. Official National list of RD (entitles benefits).	The conditions mandatorily monitored by the RD registry are the ones included in the national official list of RD. (~65% of RD included in the	Yes

Country	Where	Inpatient/Outpatient	Registration of diagnosis	Who codes	Coding diagnosis: file used in the System	Number of OC available	Visibility of the OC or RD diagnosis in the EHR (further encounter)
			information system (RD Registry) connecting RD Centres, other hospitals, local health units, including primary care services and pharmaceutical services. The system is interoperable with the Administrative Health Database AHD (in the Veneto region).	available at the Registry level).		Orphanet Nomenclature Pack [excluding rare cancers which are recorded in the regional cancer registry & infectious diseases]. The Remaining ~35% OC can be recorded as well, but do not lead to the provision of benefits for diagnosed patients.	
	ALL Hospitals using the Diagnosis Thesaurus (DT)	Both	Diagnosis Thesaurus (DT) is used to register diagnosis in EHR. The EHR feeds the DHD ORPHA-viewer.	Clinicians register the diagnosis and the linked ORPHAcode is automatically retrieved.	Diagnosis Thesaurus. SNOMED CT-ORPHAcode mapping file used to map Diagnosis Thesaurus terms with ORPHAcodes (via SNOMED CT)	Diagnosis Thesaurus (DT) currently contains 5,500 diagnoses with a linked ORPHAcode ,the objective is to cover 100% of the disorder level	Specific field for the RD thesaurus name Local implementation of specific ORPHAcode field ongoing
	All hospitals in one of 4 health regions (Oslo University Hospital: simplified version	Both	OC registered by the clinicians in a dedicated tab of the EHR and feed the National registry (manually).	Clinicians in specialized health care service	List of diagnosis linked to OC retrieved by the ORPHAcodes API and Orphadata API for	As per Nomenclature Pack	Yes, an icon appears next to the patient name whenever an OC has been attributed

Country	Where	Inpatient/Outpatient	Registration of diagnosis	Who codes	Coding diagnosis: file used in the System	Number of OC available	Visibility of the OC or RD diagnosis in the EHR (further encounter)
	implemented since 2021)				classifications & associated genes.		
	Official RD expert centres for RD in 44 HCPs which belong to ERNs, will be expanded to NRN. This allows benefits for the patient and incentives for the centre + the code is then available in RD card	Outpatients (will be followed by inpatients)	Paperwork & then registration in EHR (with direct link to Nom & classification). National Health fund collects OC for the purpose of reimbursement manually, while for the national RD Registry it will be an automatic upload from officially designated RD. In the EHR/paperwork only one OC per patient can be registered. While in the RD registry: up to 3 different OC can be registered per patient in case of multiple RDs	Clinicians in non genetic expert centres , in genetic expert centres after genetic confirmation, on paper documentation, and then if the EHR is available in the Hospital by a secretary.	List of diagnosis linked to OC from Nomenclature Pack	All the Nomenclature pack but when requested by the HCP (currently 7 ERNs) delivery of subsets by medical field derived from the Nomenclature Pack.	Not yet as there is no connection between HCPs records yet, but genetic cards goes with the patient (OC +OMIM & ICD10).
	All five university hospitals and some cantonal ones.	Both	In most hospitals diagnosis is registered in Electronic Health Record and then transferred to national registry (automatically or manually, depends on the hospital)	Coders or clinicians (depends on the hospital)	List of diagnosis linked to OC from Nomenclature Pack	ALL	Depends on the hospital- not yet implemented in most

Table 3b Additional Info/ use cases

Country	Diagnosis status options available in the EHR	Transcoding to Generic Terminology if relevant	Additional descriptors in the EHR to further annotate the RD diagnosis	Inactivated codes	Undiagnosed code	Group codes allowed	Code Not yet available in the system (but available on orpha.net)	Antecedent of RD history shown?
	Ongoing, Probable, Confirmed, Undetermined /!\ new items starting August (waiting for additional information by BNDMR)	Primary OC and then transcoding to ICD10 through the Mapping file provided in the Nom Pack	HPO, Genes HGNC, OC (groups allowed)	Removed with each new issue. But not retroactively on already registered diagnosis, a QC is carried out whenever data is exploited at the registry level to remove all the inactivated codes	Available	Yes in the Additional Clinical description box	Can be traced in a free text box	No
	Not available, OC is assigned only when the diagnosis is confirmed	ICD10 (primary code used) => OC		No process in place yet	Available but not used yet	Yes however clinicians are advised not to use Group codes		N.A. as the card is delivered only for chronic conditions/well established diagnosis
	Not available	Alpha-ID-SE file as basis for coding tools of the hospital software manufacturers. The ORPHAcodes are aligned to ICD10-GM by the Orphanet DE/BfArM experts	Not available	Removed from the file upon Annual Release of Nom Pack (Differential File)	Available	Yes some are present in the file	No	No
 * (*Veneto Region)	In the Veneto Region Hospitals, Clinicians register confirmed diagnosis (as this is linked to benefits provision). If	Primary OC and then ICD-10 (and OMIM) codes are derived from the Nom Pack. In case of issues, they	ICD10-ICD9-CM-OMIM; OMIM, ATC for drugs; HPO (only for some diseases)	Removed or referred to with each new issue. Changes are traced so each OC has a validity framework.	Available, but we are waiting for the WP7 Jardin SOP procedure to	Group codes are blocked in the system, except for some, that can be recorded in the registry because either		No

	the diagnosis changes over time or is further specified they can record it in the same patient file defining a historical diagnosis pathway.	are solved by medical team of the Registry		In the RD Registry some diagnoses are available although an OC is not assigned yet in the Orphanet nomenclature (ultrarare diseases). A procedure is in place for their inclusion in the RD Registry following an evaluation procedure, although an OC is not assigned yet.	fully implement it	they are quite specific (i.e. ORPHA: 261821 and similar) or they are included in the National official list of RD and/or are historic diagnoses		
	Not available: Doctors register (working) diagnosis and should adjust when more information is collected during the process.	Primary DT (Diagnosis Thesaurus) with alignment to ORPHAcodes, SNOMED CT and ICD-10..	not available in general, local availability possible.	The term in the diagnosis thesaurus and its ID stays the same and the OC linked to it is updated automatically with each new Orphanet Nom pack release	Available, but not yet officially in use (national definition has to be set first).	Yes	Nothing available for such codes.	Yes, in medical history
	Not available. OC inserted ONLY when all investigations have been carried out = definitive diagnosis.	ICD-10 mandatory and coded independently of OC. However, when a patient has been coded with OC, ICD-10 coding of consecutive hospital encounters is guided through the Mapping file.	ICD-10	When accessing the patient file, the clinician is notified and requested to update the OC if it has been inactivated	Available	Yes. However, when a group code is chosen, a warning notification pops up, recommending using a code at disorder or subtype level for confirmed diagnosis	Clinicians are advised to temporarily code with the OC at the classification level above, and update when the newly created OC becomes available.	dedicated box indicates history of RDs coded with OC that are cured

	Not available in the EHR. OC inserted ONLY when all investigations have been carried out (genetic confirmation) = definitive diagnosis. These options will be available in the RD registry	ICD10 mandatory	In the genetic cards OC+ ICD10-OMIM	Procedure under implementation, will be addressed with the next release of the Nom Pack in the National RD Registry	a Standard Procedure is being written for the clinicians , it will be a separate tab in the RD registry	Yes especially for non genetic expert centres, because it is associated for reimbursement & benefits . But advised to use aggregation level	No	No
	Confirmed/Suspected	Primary OC	In some cases, ICD-10, but in general not available	In general, removed once the new release is implemented.	Available	Yes	In most cases it can be traced in a free text	No

Table 1c Data Exploitation

Country	Exploitation tool	OC File used for exploitation	Quality Control of registered data	Numbers, reports, analysis & links reference documents available
 *	Anonymized data in the National RD registry system (BNDMR/piramig). Piramig allows to provide statistics by NRN centre. RD can be linked to other repository i.e système national de données de santé (SNDS), for socio-economical studies	Nom Pack including classifications	Yes by the National RD Registry BNDMR staff. Liaison with clinicians if needed (coherent code vs additional diagnosis descriptors, inactivations….)	1,372 M patient registered in the National RD Registry BNDMR & several publications and analysis https://www.bndmr.fr/publications/nombre-de-cas-par-mr/ / https://www.bndmr.fr/communications-scientifiques/publications-scientifiques/ Data from the BNDMR is also sent to the National Platform which collects, analyses and compares activity reports of Officially designated RD expert centres and RD competence centres with the aim to assess the relevance of allocated to establishments and, where necessary and if necessary, to resize funding more equitably https://www.bndmr.fr/exploiter/donnees-site/piramig/
	Not yet available, work with the excel files – Monthly query will be available	N.A.	N.A.	As of 12/2022 : 10,253 RDPCs having been requested. https://www.backoffice.dgs.pt/upload/DGSv9/ficheiros/i031062.pdf
	Alpha-ID-SE file, ORPHAcodes based on Orphanet nomenclature pack	Alpha-ID-SE file, ORPHAcodes based on partial Orphanet nomenclature pack Flat file	No	Not available
 (Veneto Region)	Veneto Region RD registry: The system provides patients data collection through synthetic clinical records filled on-line by the RD Centres and the other sources of data. It provides indicators to monitor the NP and RD centres activity (including ERN activity), and all the RD activity carried out by Local Health Services. It is linked to other official repository (i.e; Regional /National System of Health data...)	Annual release of Nom Pack & Orphadata files	QC procedures are incorporated in the data input phase (IT system) and performed on the data by the Registry team (MD, Stat, IT).	57 291 Patients registered as of 31.12.2023 https://pubmed.ncbi.nlm.nih.gov/37978388/ https://pubmed.ncbi.nlm.nih.gov/30309015/ https://pubmed.ncbi.nlm.nih.gov/24646171/ https://relazionesanitaria.azero.veneto.it/dettaglio-categorie/64940e9486603e1f50dd86e7 https://www.researchgate.net/publication/377950582_Aging_and_rare_diseases_from_epidemiology_to_a_call_to_action/fulltext/65be3b4c34bbff5ba7eaabc1/Aging-and-rare-diseases-from-epidemiology-to-a-call-to-action.pdf *(in press)*

Country	Exploitation tool	OC File used for exploitation	Quality Control of registered data	Numbers, reports, analysis & links reference documents available
	Online statistics are available for RD registry users including hospital managers and for the regional health authority.			
	ORPHA-viewer: it exploits data registered in the EHR. Future developments: the ability to use the tool for research purposes, policy making, data exchange with ERNs and the national designation of expert centres.	The tool exploits the ORPHAcodes API and can aggregate data and exploit the classification.	No	Not yet available: First figures are expected in second half 2025.
	RD REGISTRY	Nom Pack (Flat file without classifications. Aggregation Level is included)	No	4,600 patients registered in the RD Registry (as of April 2025). Annual report for 2023 available in Norwegian (https://www.oslo-universitetssykehus.no/492073/contentassets/a7626093c2124fcaa8dcda0584af5473/arsrapport-sjeldenregisteret-2023.pdf)
	National Health Funds obtains reports from manually collected data. Soon RD Registry will be available	In the Registry: Nom Pack list of diagnoses from the level of disorders (scroll list) to force assigned at the aggregation level	Team in place who carries out QC	Not yet available
	National RD Registry	Nom Pack	In general, planned, not yet established	3’624 patients registered in the RD Registry (as of March 2025). Annual report not publicly available but further information available from the RD Registry if requested.

Summary of data capture and data flow compared to guidelines.

Guidance documents for ORPHAcoding implementation and exploitation are available [xxi]. Among those, the Standard procedure & guide for coding with ORPHAcodes provides general rules for routine coding with ORPHAcodes together with 6 guidelines in order to achieve internationally standardized data collection [lxii].These guidelines invite to maximize exhaustivity, to use the ORPHAcode alongside other terminologies in use, to prefer primary ORPHAcoding to secondary transcoding and to use the reference mappings provided when transcoding.

In terms of implementation use cases (table 3), we observe a diversity of solutions set up in the different countries according to the characteristic and structure of the existing monitoring systems but also according to on a variety of background elements. The different ORPHAcoding use-cases can be generalised & mapped to the data flow scenarios in ERN hosting HCPs described in the JARDIN project survey, as presented in figs 2 to 5. The compliance to the 6 guidelines presented above is summarised in table 4.

	Guideleine 1 - Several tools and strategies could be set at MS level to produce data or statistics for RD, nevertheless each country should set this strategy accordingly to a standard principle of maximizing exhaustiveness as well as possible re-use of existing data collections	Guideline 2 - Code the data in a way that the reporting can compile to the granularity of the international recommended list of ORPHAcodes (MF-granularity). If no further national needs for reporting are necessary, use the codes from the MF directly	Guideline 3 - Whenever possible capture the diagnostic assertion for all RD cases. Use the Options	Guideline 4 - Update your coding resource according to the internationally agreed cycle in order to have the most recent coding file and to ensure comparability.	Guideline 5 - Keep track, for each patient file, of the different ORPHAcodes and associated versions that were used to describe the patient's diagnostic pathway.	If ORPHAcodes are used together with another national coding system for morbidity coding, the two systems should be linked in a standardized way to ensure that code combinations are standardized and the coding effort for the user is minimized
Direct ORPHAcoding	Yes	Yes	Possible but depending on the strategy in place	Possible but depending on the strategy in place	Possible but depending on the strategy in place	Yes OC=>GC
Transcoding for reference list	Depending on final content of reference List => **additional strategy should be in place**	Depending on the strategy in place	Possible but depending on the strategy in place	Possible but depending on the strategy in place	Possible but depending on the strategy in place	Yes , but depending on the strategy not ALL the disorder level RD are covered
Secondary Transcoding A (ahead of National Collection data System	**Secondary transcoding from a GT =>OC does not allow to cover 100% of the disorder level*=> additional strategy should be in place**	**=> additional strategy should be in place to cover ALL disorder level**	Possible but depending on the strategy in place	Possible but depending on the strategy in place	Possible but depending on the strategy in place	Yes but GC=>OC **=> additional strategy should be in place to cover ALL disorder level**
Secondary Transcoding B (At the Registry level)	**Secondary transcoding from a GT =>OC does not allow to cover 100% of the disorder level*=> additional strategy should be in place**	**=> additional strategy should be in place to cover ALL disorder level**	Possible but depending on the strategy in place	Possible but depending on the strategy in place	Possible but Depending on the strategy in place	Yes but GC=>OC **=> additional strategy should be in place to cover ALL disorder level**

Table 4: Compliance of each implementation use-case with the 6 guidelines of the Standard procedure & guide for coding with ORPHAcodes (GC= general code & OC=ORPHAcode)

* not all RD diagnosis are present in generic terminologies and some of the generic codes are aligned with more than one ORPHAcodes because they are less granular (see paragraph below)

Primary ORPHAcoding Use case

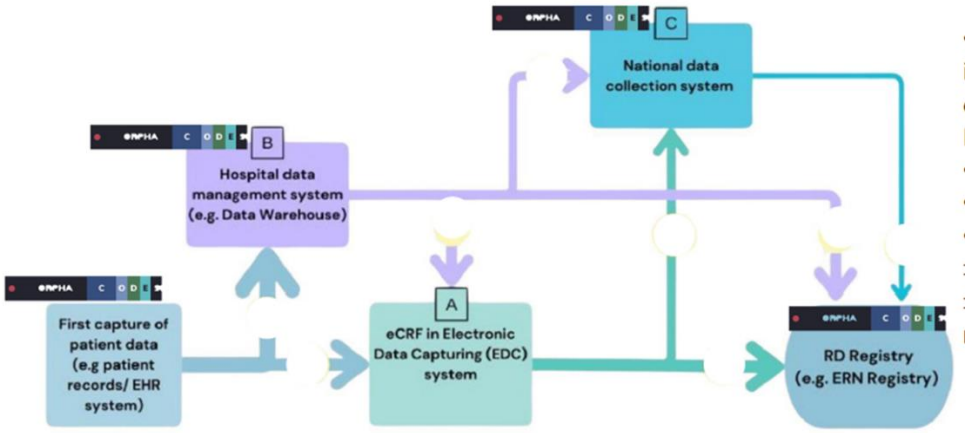

Fig.2 Primary ORPHAcoding Use case

Direct implementation of the ORPHAcodes in the EHR (with possible automatic retrieve of the ICD10 code) allows for the visibility of all RD diagnosis, including undiagnosed as well as precise and accurate RD coding (if the complete Nomenclature Pack info is implemented and annually updated). This enables to contribute to complete epidemiological data, for the healthcare systems to have the potential capacity to address all the specific and often vital needs of all RD patients as well as health planning potentially for ALL RD. Furthermore, it allows to provide electronic support in the health care pathway of the patient thanks to Orphanet Knowledge linked to ORPHAcodes. This strategy well eases the production of RD-related indicators and the possibility of healthcare monitoring regarding a given RD or a group of RD, or RD as a whole.

Transcoding use case: Ahead of the EHR coding/reference list

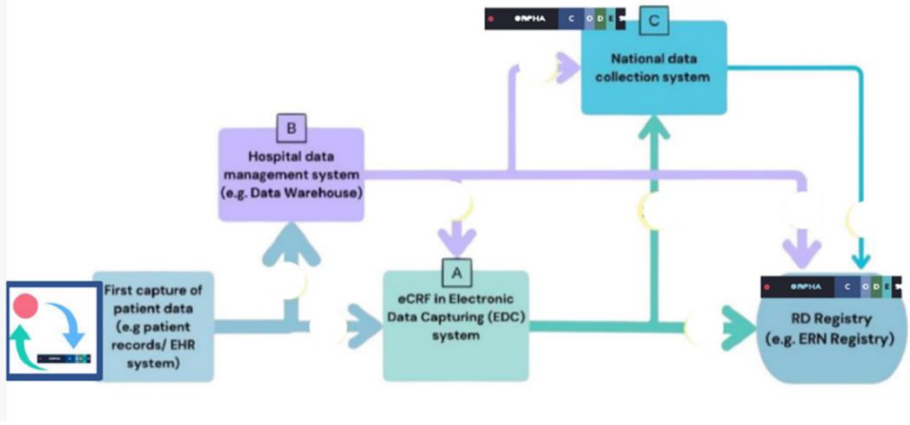

Fig3 Transcoding use case: Ahead of the EHR coding/reference list

The transcoding effort is carried out ahead of first capture of patient data, generating a reference list for which automatic transcoding is possible thanks to the Orphanet mapping files and/or additional local mapping files. This exercise requires additional effort in terms of creation and validation of the reference list, which often do not contain all the disorder level entities. In particular, this strategy may not allow to identify undiagnosed patients. To reach exhaustiveness of epidemiological data, an additional strategy should be in place to trace the RD diagnosis which are not present in the reference list and therefore not recorded at the level EHR. The loss of information at the point of care could result in an impaired capacity of healthcare systems to address all the specific and often vitals needs of RD patients as well as inadequate health planning for the therefore non-identified rare diseases, as well as limited healthcare monitoring in regard to a given RD or a group of RD, or RD as a whole.

Secondary transcoding use case A: ahead of National Collection data System

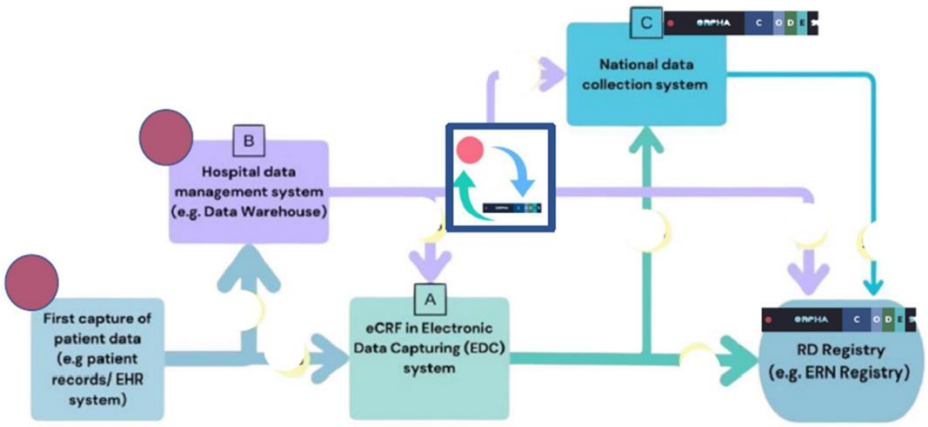

Fig 4 Secondary Transcoding use case A: ahead of National Collection data System

The transcoding effort is carried out ahead of data entry in the National Data collection System, although automatic transcoding is possible thanks to the Orphanet mapping files, this implies retrieval of generic terminologies diagnosis from the EHR in which not all RD diagnosis are traced (in particular often undiagnosed are not traced via a code) [info on alignments: https://github.com/OD4RD/Main-Help-Desk/wiki/5.-Alignements-with-other-terminologies]. To reach complete epidemiological data, an additional strategy should be in place to ensure that all the disorder level ORPHAcodes are identified and be able to trace the RD diagnosis which are not present in generic terminologies as well as for the generic codes that are less granular than ORPHAcodes and therefore which are aligned with more than one ORPHAcodes. The loss of information at the point of care could result in an impaired capacity of healthcare systems to address all the specific and often vitals needs of RD patients as well as probable inadequate health planning for the non-traced diseases; in particular, it does not allow the portability of RD diagnosis across the patient's care pathway, impairing continuity of care. As a consequence, there is limited healthcare monitoring in regard to a given RD or a group of RD, or RD as a whole.

Secondary transcoding use case B: At the Registry level

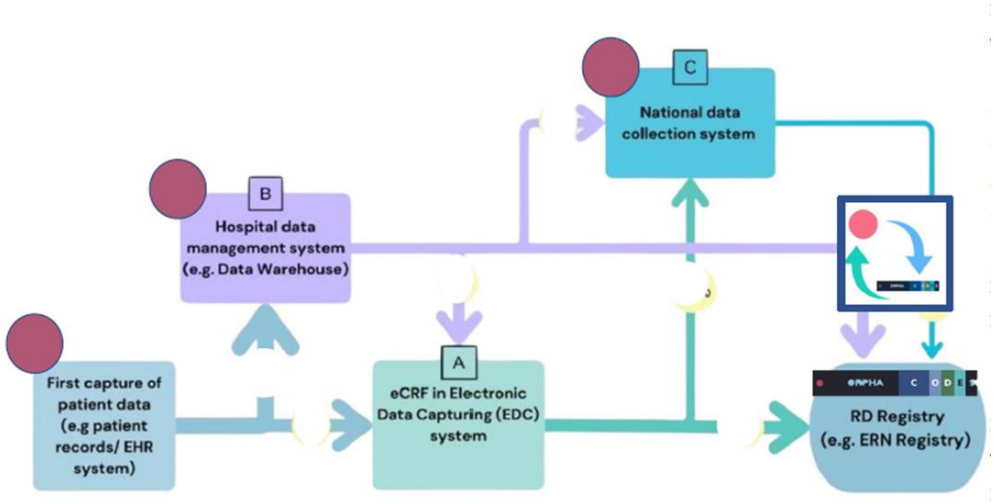

Fig5 ***Secondary Transcoding use case B: At the Registry level***

The transcoding effort is carried out ahead of data entry in the registry, although automatic transcoding is possible thanks to the Orphanet mapping files, or thanks to local mapping files. This implies retrieval of generic terminologies diagnosis from the EHR in which not all RD diagnosis are traced (in particular often undiagnosed are not traced via a code). To reach complete epidemiological data, an additional strategy should be in place to (to ensure that all the disorder level ORPHAcodes are identified) by tracing the RD diagnosis which are not present in generic terminologies as well as for the generic codes which are aligned with more than one ORPHAcodes because they are less granular. The loss of information at the point of care could result in an impaired capacity of healthcare systems to address all the specific and often vitals needs of RD patients as well as probable inadequate health planning for the non-traced diseases; in particular, it does not allow the portability of RD diagnosis across the patient's care pathway, impairing continuity of care. As a consequence, there is limited healthcare monitoring in regard to a given RD or a group of RD, or RD as a whole.

2) Users' feedback

Users' surveys around ORPHAcodes use have been carried out by the OD4RD2 project by contacting in the national language the ERN centres of the national Health Care Prociders (see below) and in English by the JARDIN joint action (see below). When considering these results, one should keep in mind the generic limitations of such investigation tool (i.e. inconsistent or inaccurate responses due to different interpretation if questions, Sample bias (actual respondents could not be the initial target). These surveys are to be considered as complementary approaches as addressed in a large extent to the same recipients, ERN centres in HCPs, when same countries are covered, however they were (i) not necessarily answered

by the same respondent, (ii) questions were not formulated the same way and (iii) not in national language as of JARDIN survey, potentially impacting the responders' interpretation of the question and therefore survey results. In some cases where the answers received were incoherent when compared to the known national situation, it was possible to re-contact the participants to better understand their answer and analysis of these cases indicated some problems in the question design for both surveys. Response rates were comparable, and globally rather low, with 37% for the OD4RD2 survey (table 5) and 33% for the ORPHAcoding related question in the JARDIN Survey. In terms of MS coverage, it represents 15 countries for the OD4RD2 survey and 27 countries for the JARDIN survey (all the countries surveyed by OD4RD provided also answers to the JARDIN survey). Analysis of the distribution of answers by ERN was carried out only in the OD4RD2 survey but not in JARDIN survey.

OD4RD2 National ERN centres survey

A survey to evaluate the 2024 situation of ORPHAcodes usage by health care providers (HCPs) linked to ERNs in countries participating in OD4RD2 has been carried out.
Countries where the survey was launched were Austria, Belgium, Bulgaria, Germany, Spain, Ireland, Italy, Finland, Lithuania, Latvia, the Netherlands (only Radboudumc (RUMC)), Norway, Poland, Portugal and Sweden. Each Orphanet Nomenclature Hub has provided a report which describes in detail the methodology used and the preliminary results are presented.

A) Data analysis was performed by compiling 15 survey reports even though some information was missing in some reports.
B) Analysis by ERN was performed by 11 National Hubs: Austria, Belgium, Germany, Italy, Finland, the Netherlands, Norway, Portugal, Poland, Spain, Sweden

Info	Countries having provided this info	Total	
Reports received	16		
# ERN units contacted	15	1447	Ranging from 629 to 8 according to the country*
Unit Answers received	16	544	
Answer rate		58%	Ranging from 88% to 61% according to the country
Mean coverage of country ERN (at least 1 unit per ERN and per country)	16	85%	Ranging from 100% to 61% according to the country

Table. 5 2024 ERN survey carried out by the Network of Orphanet Nomenclature National Hubs
*In the Orphanet Knowledge base 1523 ERN units are registered overall for these countries, representing 95% contact coverage in the survey. It must be noted that 1 country has not provided information of the numbers of units contacted and that the Netherlands decided to contact only the units present at Radboudumc (RUMC)

Full results, numbers of answers by country and by ERN with complete methodology are available here: https://od4rd.eu/03-deliverables/OD4RD2_ERN-

Survey_11QC%20analysis_VF.pdf [lxiii]. For country reports: please contact your Orphanet Nomenclature National Hub.

A) Results show that "at least" ~30% of all the centres provide data to the ERN coordination (Q1: Do you provide RD patient data to the ERN coordination?; please refer to the full report); and Q2 (What codification system do you use for that purpose?) that shows that at least 18% use ORPHAcodes for this purpose (either alone or coupled with another system) (fig.6), a by country analysis has been performed (fig 7). Respondents which confirm to use ORPHAcodes to send data to ERN coordination, could specify in Q5 if they used ORPHAcodes for annual monitoring, 5-year evaluation, registries or other (fig.8). When considering only the respondents' answers, half of them used ORPHAcodes directly (Q6. Do you codify directly with ORPHAcodes or do you establish the correspondence *a posteriori*?)(fig.9).

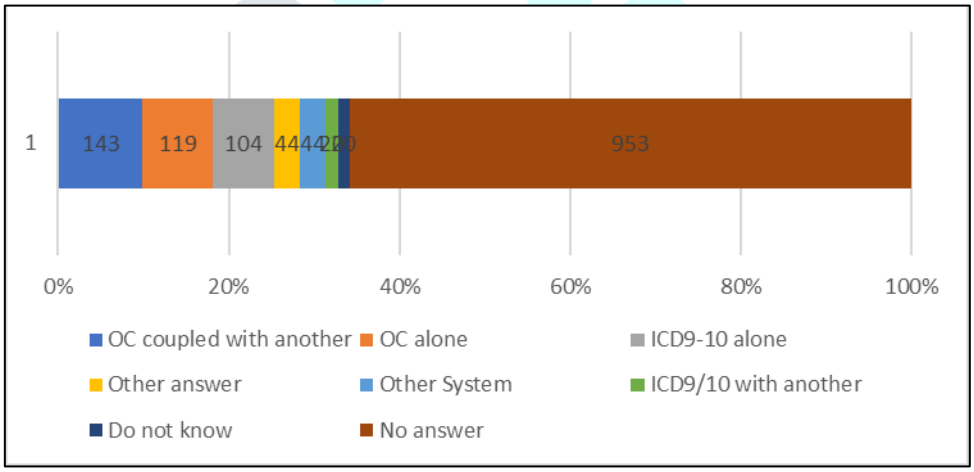

Fig.6. Q2: What Codification System do you use for providing RD patient data to the ERN coordination

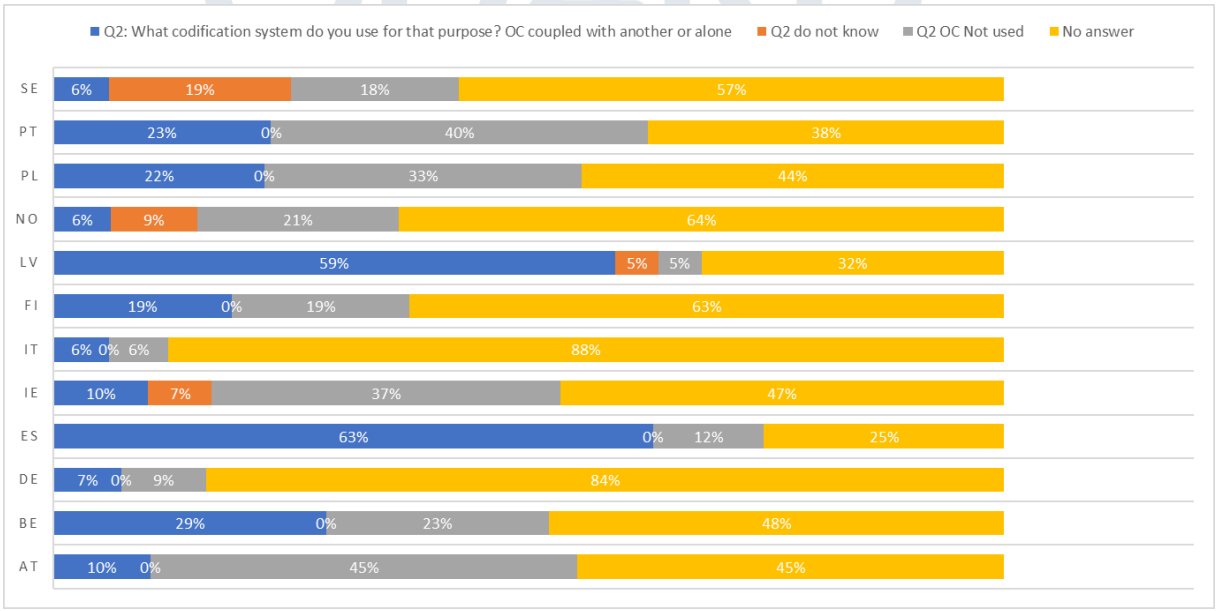

Fig.7. What codification system do you use for that purpose by country and pooling answers ORPHAcodes vs no ORPHAcodes (answers= 487)

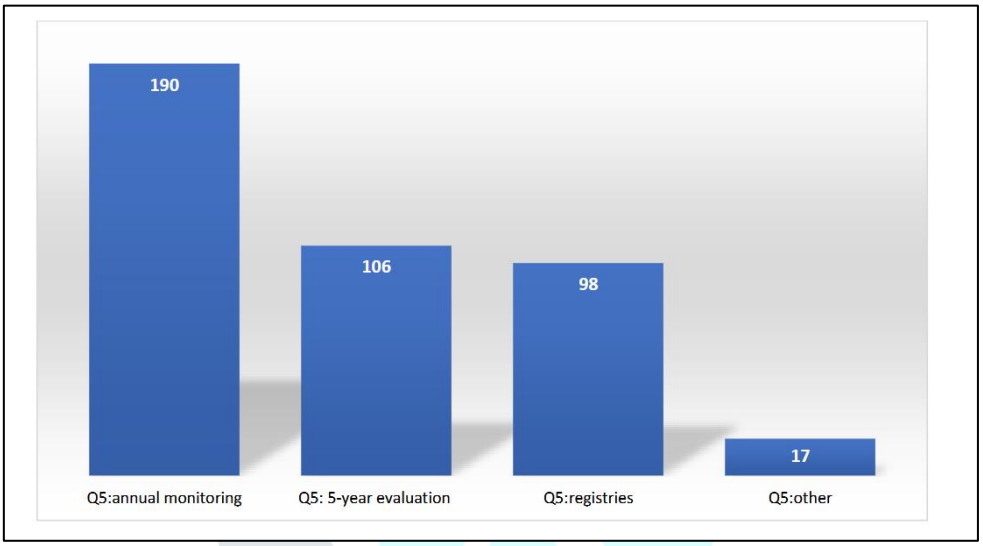

Fig.8 If you use ORPHAcodes to send data to ERN coordination , do you use them for : (multiple choice answer)

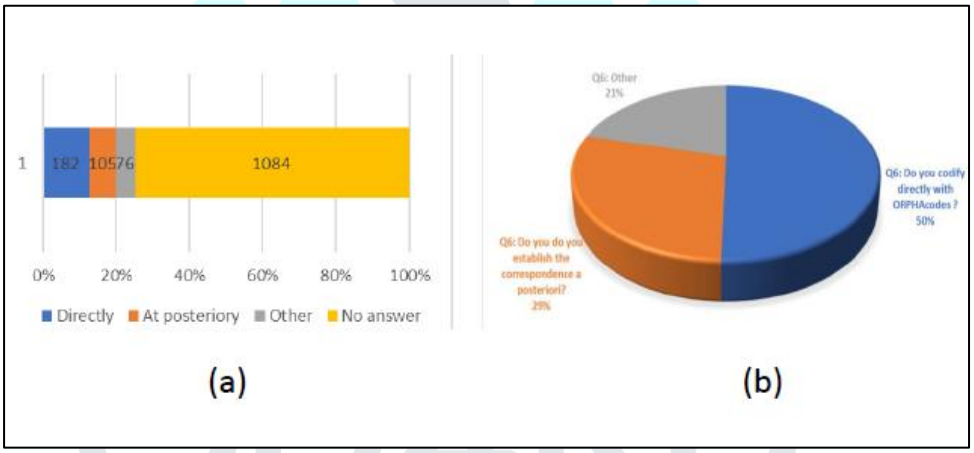

Fig.9 (a) Do you codifywith ORPHAcodes directly or at posteriori (b) Focus on those having answered (363)

An open question aimed at understanding the main reason for not using ORPHAcodes was also present in the survey. Answers for this question were variable according to the users, but they have been categorized by theme and the results show that the main reasons for not using ORPHAcodes are (in decreasing importance order):

- Unavailability of ORPHAcode in Health Electronic Records
- ORPHAcode use not being mandatory
- Lack of time/resources
- ORPHAcodes not suitable
- Lack of knowledge

B) Analysis by ERN was performed. In table 6 are presented the answers received in terms of overall percentage of coverage of centres by ERN for the 11 countries considered (Austria, Belgium, Germany, Italy, Finland, the Netherlands, Norway, Portugal, Poland, Spain, Sweden). *i.e ENDO-ERN answers covered 46% of the ENDO centres present in the 11 countries for which this analysis was performed.*
N.B. Figure 10-11-12 present only the results of the respondents without including the percentage of centres having not answered.

ERN	Centres Answers percentage
Endo-ERN: European Reference Network on Rare Endocrine Conditions	46%
EpiCARE: European Reference Network for Rare and Complex Epilepsies	67%
ERKNet: European Rare Kidney Diseases Reference Network	27%
ERN CRANIO: European Reference Network on Rare craniofacial anomalies and ENT disorders	57%
ERN GENTURIS: European Reference Network on GENetic TUmour RIsk Syndromes	35%
ERN GUARD-HEART : Gateway to Uncommon And Rare Diseases of the HEART	35%
ERN PaedCan: European Reference Network for Paediatric Cancer (haemato-oncology)	26%
ERN RARE-LIVER: European Reference Network on Rare Hepatological Diseases	46%
ERN ReCONNET: European Reference Network on Rare and Complex Connective Tissue and Musculoskeletal Diseases	25%
ERN RITA: Rare Immunodeficiency, Autoinflammatory and Autoimmune Diseases Network	28%
ERN TRANSPLANT-CHILD: European Reference Network on Transplantation in Children (incl. HSCT, heart, kidney, liver, intestinal, lung and multiorgan)	36%
ERN-BOND: European Reference Network on Rare Bone Disorders	40%
ERN-EYE: European Reference Network on Rare Eye Diseases	41%
ERNICA: European Reference Network for rare Inherited and Congenital Anomalies	57%
ERN-LUNG: European Reference Network on rare respiratory diseases	30%
ERN-RND : European Reference Network on Rare Neurological Diseases	29%
ERN-Skin: European Reference Network on Rare and Undiagnosed Skin Disorders	20%
EURACAN: European Reference Network on Rare Adult Cancers (solid tumors)	24%
EuroBloodNet: European Reference Network on Rare Hematological Diseases	33%
eUROGEN: European Reference Network on urogenital diseases and conditions	46%
EURO-NMD: European Reference Network for Rare Neuromuscular Diseases	46%
ITHACA: European Reference Network for Rare Malformation Syndromes, Intellectual and Other Neurodevelopmental Disorders	33%
MetabERN: European Reference Network for Rare Hereditary Metabolic Disorders	49%
VASCERN: European Reference Network on Rare Multisystemic Vascular Diseases	39%
Total general	37%

Table 6. Percentage of answers coverage of centres by ERN in the 11 countries.

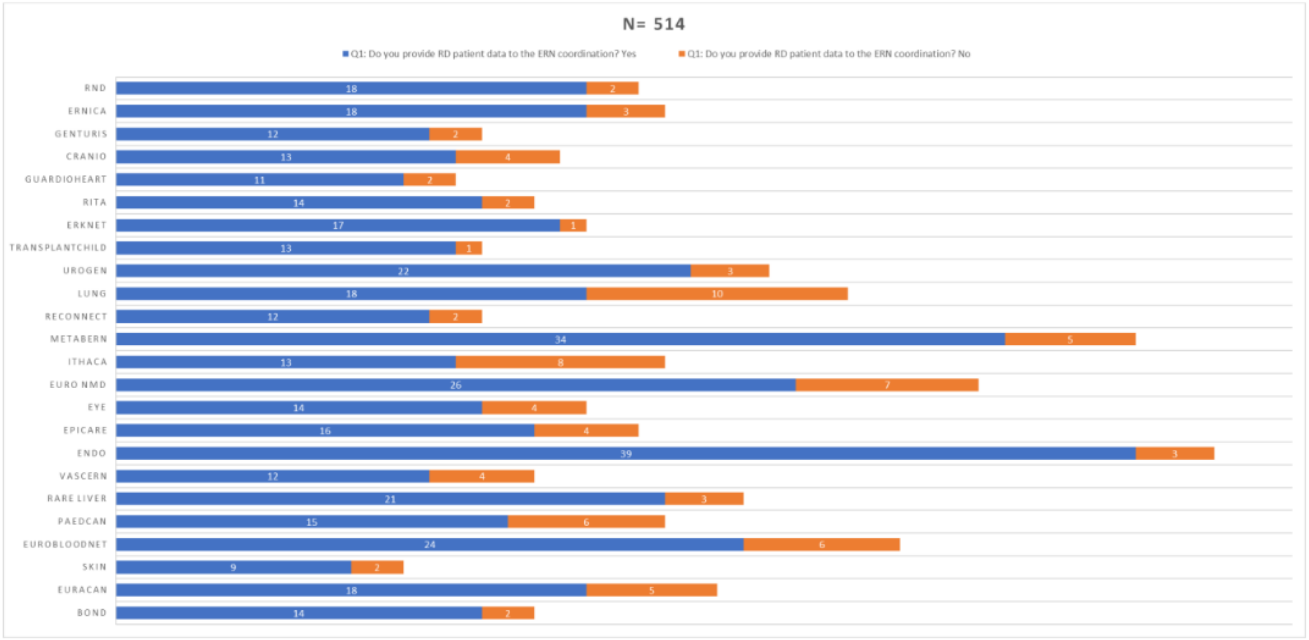

Fig.10 Do you provide Data to ERN coordination (n=514)

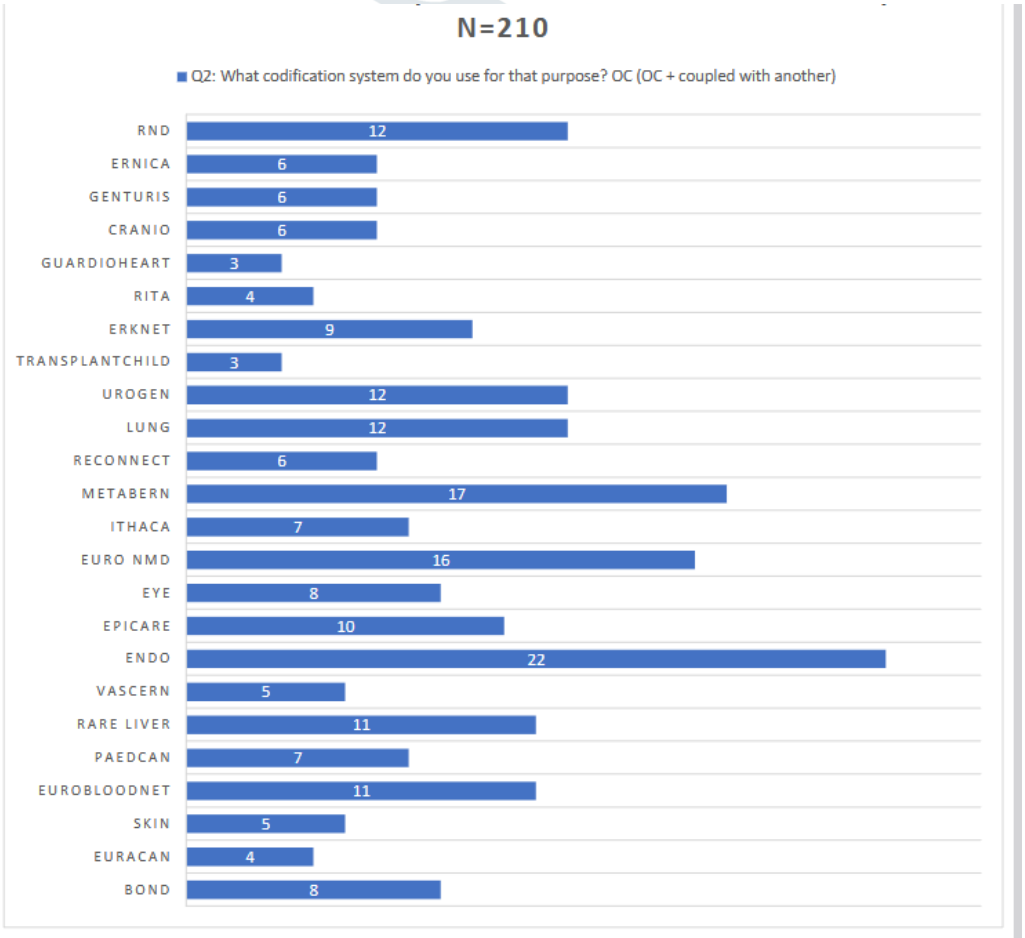

Fig.11 What Codification System do you use for what system: pooling of answers selection "ORPHAcodes" & "ORPHAcodes coupled with another system".(n=210)

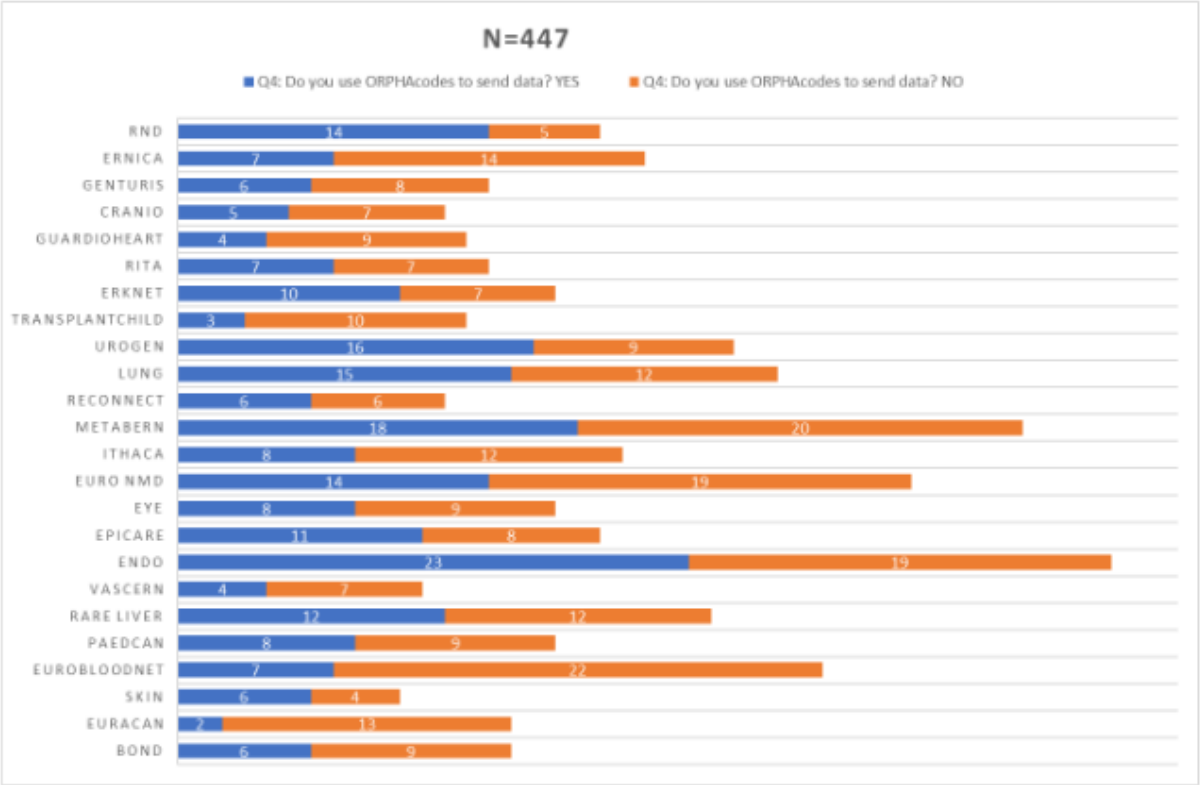

Fig.12 Do you use ORPHAcodes to send data (n= 447)

JARDIN survey Results concerning ORPHACodes [lxiv]

As part of the JARDIN Joint Action, a series of surveys were conducted to better understand the barriers that exist in the journey of rare disease health data; from its first capture in the clinical setting to its final destination into a patient registry. The surveys were tailored to the targeted respondents, who were divided into three groups

1. **Health Care Provider (HCP) Unit Leads:** Clinicians responsible for leading ERN units and for entering data into patient registries
2. **IT Support:** Staff familiar with the current IT infrastructure of HCPs, such as IT experts, data managers, or data stewards
3. **National Authority IT Experts:** Individuals responsible for promoting and developing legal frameworks for data digitalisation

The surveys were sent to participants in all 27 EU Member States and Norway, and covered six major areas concerning rare disease health data, namely:

1. **General Information**: Questions to collect respondents' demographic information.
2. **First Capture of Rare Disease Patient Data**: Questions focused on understanding how patient information is initially captured in each institute, the information systems used for this purpose, and the standards used for describing and structuring data.
3. **Data Flow**: Questions to explore which systems are in place to store and manage patient data from its first capture until its insertion into a rare disease registry. The movement

of data between these systems and to what extent this process is automated was also evaluated.

4. **Rare Disease Patient Registries:** Questions examining the level of participation by HCP units in various rare disease registries and the challenges faced when entering data into these registries.
5. **Data Sharing**: Questions investigating the barriers involved in obtaining ethical and legal approval to share data for secondary uses, such as research.
6. **Data FAIRness**: Questions evaluating the respondents' familiarity with FAIR (Findable, Accessible, Interoperable, Reusable) data principles and the implementation status of FAIR-enabling practices

For full results of the JARDIN survey, please refer to the JARDIN deliverable.

Given that ORPHAcodes are invaluable in identifiying and providing visibility to rare disease patients, one such barrier analysed was the use of ORPHAcodes in HCP Institutions. The question 'Are you using ORPHAcodes in your institution' was included in Section 2 (First Capture of Rare Disease Patient Data) of the survey that was sent to HCP Unit Leads.

The responses (shown in Fig. 13A) highlight that the use of ORPHAcodes is highly variable across the EU member states, with 52% of the 457 responses being affirmative. Whilst countries such as Finland, Latvia, and the Czech Republic reported use rates of 100% for the ORPHAcodes, others such as Ireland and Croatia demonstrated no usage. Interestingly, countries in which there is a national or regional policy to enforce the implementation of ORPHAcodes into Health Information Systems – such as in France (61%), Germany (62%), and the Netherlands (66%) – reported lower than anticipated ORPHAcode adoption rates.

(It is important to note, however, that the non-response rate to this question was relatively high and may lead to skewing or misinterpretation of the results. Fig 13B showcases the same information as Fig. 13A, however includes the 'No Response' outcome as part of the graphic. It can now be seen that the overall use of ORPHACodes amongst the respondents drops to 17%, with 67% of the 1382 total European HCP Units not responding. This highlights that further investigation is needed to truly understand the rates of ORPHAcode implementation across European HCPs).

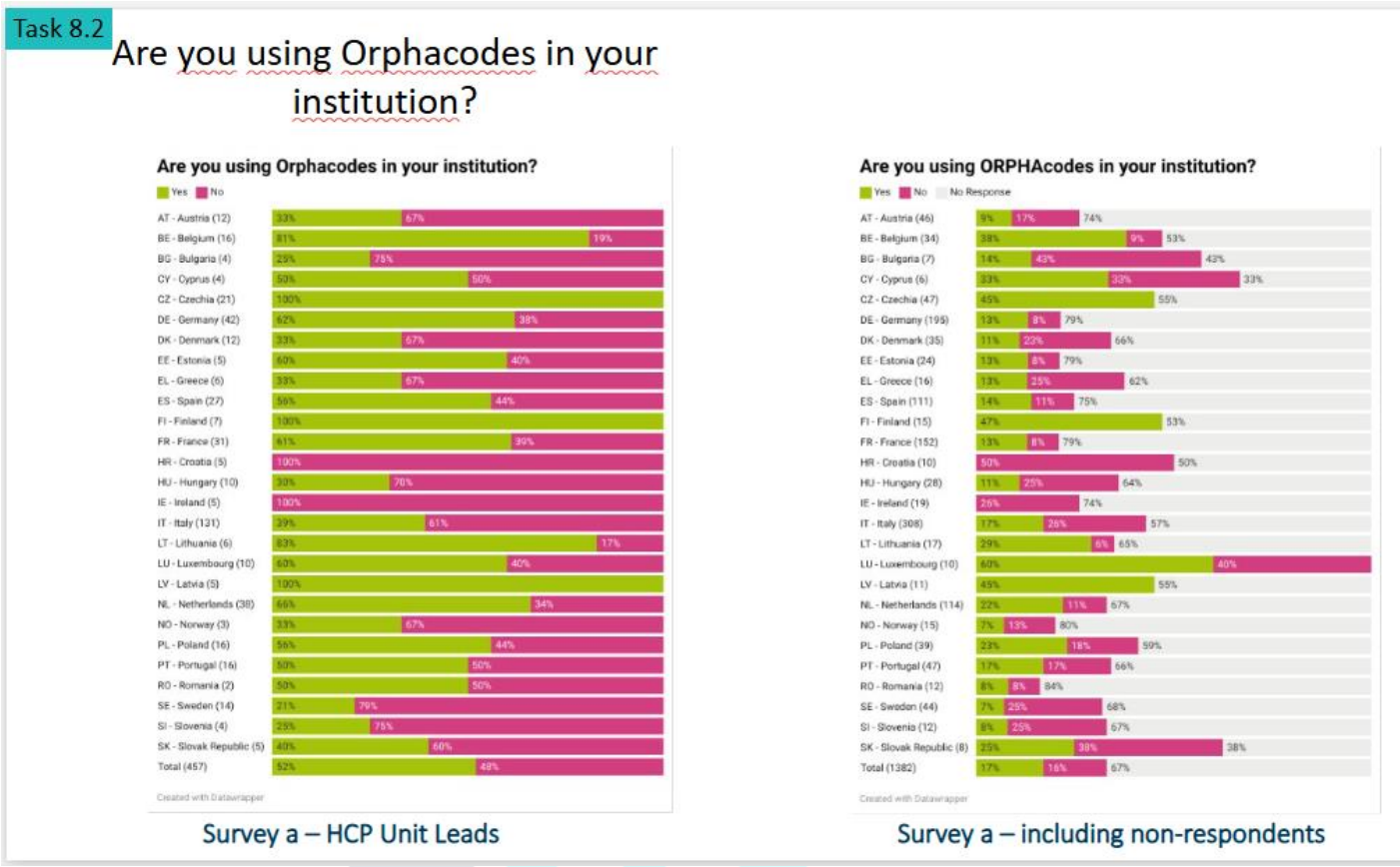

Fig. 13 Survey A address to the HCP Unit leads: Are you using ORPHAcodes in your Institution

3) Available Studies

The literature was surveyed to inventory the available studies that use ORPHAcodes to identify the RD population for their analysis (table 7) when the study also explicitly cite the benefits of ORPHAcoding, it was indicated. The table below presents each study with title/authors and PubMed reference information, whether the ORPHAcoding was direct or at posteriori, whether the ORPHA classification system, or another Orphanet dataset, was exploited for the analysis and the citation on the ORPHAcodes added value, if applicable:

Ref	OCing direct or at posteriori	ORPHA classification or Other Orphanet datasets exploited for the analysis	Paper Citation on the OC added value
ORPHAcodes use for the coding of rare diseases: comparison of the accuracy and cross country comparability. Mazzucato M, 2023. doi: 10.1186/s13023-023-02864-6. PMID: 37667299 [vii]	Direct	yes	ORPHAcodes improve visibility of RD in health information systems. Notably, ORPHAcodes use allows to improved capture of ultra-rare diseases, which are under-represented in ICD-10. With regards to the comparison of

Ref	OCing direct or at posteriori	ORPHA classification or Other Orphanet datasets exploited for the analysis	Paper Citation on the OC added value
			ORPHAcodes to ICD-10 codes: 83.4% of the ORPHAcodes used described their disease associated entity more precisely than the corresponding ICD-10 code. "ORPHAcodes were found to be a versatile resource for the coding of RD, able to assure easiness of use and inter-country comparability across population and hospital databases"
Mazzucato M, Estimating mortality in rare diseases using a population-based registry, 2023 doi: 10.1186/s13023-023-02944-7. Erratum in: Orphanet J Rare Dis. 2024 Feb 6;19(1):43. doi: 10.1186/s13023-024-03051-x. PMID: 37978388; PMCID: PMC10655462 [viii]	Direct	yes	Thanks to the use of ORPHAcodes : highlight the impact on patient survival of specific subgroups of diseases within broader categories, as is the case of lysosomal storage diseases. Although in some cases neonatal screening policies include these diseases, and despite the availability of innovative treatments, it is important to report that affected patients still experience reduced survival. Moreover, as diagnoses are recorded based on the use of ORPHAcodes, a specific RD coding resource, the level of diagnostic detail is higher than that available from studies based on data from an administrative database. In addition, unlike other studies in which ORPHAcodes have been attributed to RD patients starting from ICD codes and reviewing health records, =>in the present study they are assigned at the point of diagnosis/care by RD experts, reducing potential codification biases. RD share many characteristics but are rarely studied as a category.

Ref	OCing direct or at posteriori	ORPHA classification or Other Orphanet datasets exploited for the analysis	Paper Citation on the OC added value
			RD patients experience higher mortality rates compared to the general population. Further research is needed to understand the mechanisms determining mortality in RD patients and especially in subgroups presenting higher death rates. =>The use of a RD specific coding resource such as ORPHAcodes can better identify these diseases as a distinct, although composite category allowing their associated burden to be estimated. This could serve as the basis to develop further targeted healthcare policies to tackle the needs of the most vulnerable groups of patients among the RD population.
Pichon T, BNDMR infrastructure team. Overview of patients' cohorts in the French National rare disease registry. 2023 doi: 10.1186/s13023-023-02725-2. PMID: 37400917; PMCID: PMC10318625 [ix]	Direct, In France, the National Rare Disease Registry (BNDMR). This database collects a minimum data set including diagnosis coded using the Orphanet nomenclature (ORPHAcodes)	Yes and epidemiological dataset	N.A.
A retrospective review of the contribution of rare diseases to paediatric mortality in Ireland. Gunne E, 2020 doi: 10.1186/s13023-020-01574-7. PMID: 33148291 [x]	**Retrospective/transcoding ICD10**=> Review of ICD-10 codes and narrative descriptions from death registration was undertaken to identify RD cases. RD cases were assigned an ORPHAcode	yes	A comparison was undertaken of the RD cases identified in this study versus the number of RD cases identified if only the ICD-10 coding was used. Use of the ICD-10 code in isolation of the narrative record identified only 42% rare disease cases, meaning that ORPHAcodes use would have been required to capture 58% of RD cases. [Mortality coding using ICD-10 codes identified 42% of rare disease cases with the remainder identified using death certificate narrative records] Rare disease patients occupied 87% of bed days used by children < 15 years who

Ref	OCing direct or at posteriori	ORPHA classification or Other Orphanet datasets exploited for the analysis	Paper Citation on the OC added value
			died during hospitalisation from January 2015 to December 2016. Addition of ORPHAcodes to eHealth records would allow RD cases to be reported and costed easily
Healthcare burden of rare diseases in Hong Kong – adopting ORPHAcodes in ICD-10 based healthcare administrative datasets. Chiu ATG, 2018 doi: 10.1186/s13023-018-0892-5. PMID: 30153866 [xi]	**Retrospective/transcoding ICD10=>** We extracted admission records of all patients coded with one or more of the 1084 ICD-10 codes cross referenced with 467 ORPHAcodes during the study period	yes	Cross-referencing between ICD-10 and ORPHAcodes may be adopted in different healthcare datasets for international comparison. Despite differences in the prevalence of individual disease, the disparity between rare disease prevalence (1.5%) and associated inpatient cost (4.3%) in Hong Kong reflects the importance of rare diseases in healthcare policies
The interoperability between the Spanish version of the International Classification of Diseases and ORPHAcodes: towards better identification of rare diseases. Rico J, 2021 Mar 9;16(1):121. doi: 10.1186/s13023-021-01763-y. PMID: 33750434 [xii]	OC-ICD10=> ICD10 ES	yes	ICD-10-ES codes have not enough specificity to identify rare diseases. Direct mapping between ICD and ORPHAcodes or the integration of ORPHAcodes at the healthcare system for diagnoses codification would enable better detection and epidemiological analysis of rare diseases.
Walker CE, The collective impact of rare diseases in Western Australia: an estimate using a population-based cohort. 2017 May; doi: 10.1038/gim.2016.143. Epub 2016 Sep 22. PMID: 27657686; PMCID: PMC5440569 [xiii]	Retrospective transcoding ICD10/OC => ICD10 AU	yes	OC used to identify the RD population. Health-data systems may consider earlier incorporation of ORPHAcodes into data collections so that as ICD-11 is introduced into health-data collections, there will be the capacity to continue to effectively record and report local RD data.
Scanlon P, Measuring the impact of rare diseases in Tasmania, Australia. 2024 doi: 10.1186/s13023-024-03343-2. PMID: 39468681; PMCID: PMC11514960 [xiv]	Transcoding ICD10 AM=> OC.	Yes	N.A.
Navarrete-Opazo AA, Can you hear us now? The impact of health-care utilization by rare disease patients in the United States. 2021 doi: 10.1038/s41436-021-01241-7. Epub 2021	Transcoding, The ICD-10 =>OC	Not indicated	N.A.

Ref	OCing direct or at posteriori	ORPHA classification or Other Orphanet datasets exploited for the analysis	Paper Citation on the OC added value
Jun 28. PMID: 34183788; PMCID: PMC8553605 [xv]			
Chung CCY, Hospital mortality in patients with rare diseases during pandemics: lessons learnt from the COVID-19 and SARS pandemics. 2021 doi: 10.1186/s13023-021-01994-z. PMID: 34384469; PMCID: PMC8358899 [xvi]	Transcoding : ICD10=>OC	Not indicated	N.A
Strashny A, Alford J, Rappole C, Santo L. The National Hospital Care Survey Is a Unique Source of Data on Rare Diseases. Value Health. 2022 Nov;25(11):1814-1817. doi: 10.1016/j.jval.2022.04.1734. Epub 2022 May 30. PMID: 35654662; PMCID: PMC9708926. [xvii]	Transcoding ICD1O=> OC.	Not indicated	N.A.
Walter AL, Baty F, Rassouli F, Bilz S, Brutsche MH. Diagnostic precision and identification of rare diseases is dependent on distance of residence relative to tertiary medical facilities. Orphanet J Rare Dis. 2021 Mar 22;16(1):131. doi: 10.1186/s13023-021-01769-6. PMID: 33745447; PMCID: PMC7983389. [xviii]	Transcoding ICD10=> OC.	Not indicated	N.A.
Friedlander L, Choquet R, Galliani E, de Chalendar M, Messiaen C, Ruel A, Vazquez MP, Berdal A, Alberti C, De La Dure Molla M. Management of rare diseases of the Head, Neck and Teeth: results of a French population-based prospective 8-year study. Orphanet J Rare Dis. 2017 May 19;12(1):94. doi: 10.1186/s13023-017-0650-0. PMID: 28526043; PMCID: PMC5437557. [xix]	Direct, Centres of expertise for rare diseases record a minimum data set on their clinical cases, using a list of rare Head, Neck and Teeth diseases established in 2006. The present analysis focuses on 2008 to 2015 data based on the Orphanet nomenclature.	Yes, *Orphanet Report Series - Prevalence of rare diseases: Bibliographic data - November 2016*	N.A.
Baxter MF, Surfacing undiagnosed disease: consideration, counting and coding. 2023 doi: 10.3389/fped.2023.1283880 . PMID: 38027298; PMCID: PMC10646190 [xx]	N.A. Review	N.A. Review	From a RD perspective for a universal classification to be used during the diagnostic process it will require time to be developed and subsequently implemented in health systems. Whilst this is occurring, one interim approach is to adapt the use of existing e.g., ICD-10, or incoming e.g., ICD-11 coding, approaches combined with elements from the Orphanet nomenclature
Mazzucato M, A population-based registry as a source of health indicators for rare diseases: the ten-year experience of the Veneto Region's rare diseases registry. 2014	Direct.	Yes and epidemiological dataset	N.A.

Ref	OCing direct or at posteriori	ORPHA classification or Other Orphanet datasets exploited for the analysis	Paper Citation on the OC added value
doi: 10.1186/1750-1172-9-37. PMID: 24646171; PMCID: PMC4000007 [xxi]			
Pieroni F, The Tuscany Regional Network for rare diseases: from European Reference Networks' experience to registry based organisation and management model for rare diseases. 2023 doi: 10.1186/s13023-023-02947-4. PMID: 37833795 PMCID: PMC10576286 [xxii]	Direct , OC used in registry	Not indicated	N.A.
Thygesen JH, Zhang H, Issa H, Wu J, Hama T, Phiho-Gomes AC, Groza T, Khalid S, Lumbers TR, Hocaoglu M, Khunti K, Priedon R, Banerjee A, Pontikos N, Tomlinson C, Torralbo A, Taylor P, Sudlow C, Denaxas S, Hemingway H, Wu H; CVD-COVID-UK/COVID-IMPACT Consortium. Prevalence and demographics of 331 rare diseases and associated COVID-19-related mortality among 58 million individuals: a nationwide retrospective observational study. Lancet Digit Health. 2025 Feb;7(2):e145-e156. doi: 10.1016/S2589-7500(24)00253-X. PMID: 39890245.	Transcoding ICD10=> OC.		

Table 7. Studies that use ORPHAcodes to identify the RD population for their analysis (1) study with title/authors and PubMed reference information, (2) whether the ORPHAcoding was direct or at posteriori, (3) whether the ORPHA classification system, or another Orphanet dataset was exploited for the analysis and (4) and the citation on the ORPHAcodes added value if applicable):

Annexes

Annex 1: Available Resources/tools

The Orphanet Nomenclature (ORPHAcodes) is accessible via the Orphanet website (search by disease) or via the www.orphacodes.org [lxv] the one stop shop for all the available resources and tools related to ORPHAcodes, including all the computable information necessary to achieve implementation of ORPHAcodes in health information systems.
ORPHAcodes files are available via the CC BY 4.0 licence (*https://creativecommons.org/licenses/by/4.0/*).

From this website can be downloaded:

- The **Orphanet nomenclature pack:** it compiles various files which provide the computable information necessary to achieve implementation of ORPHAcodes in health information systems and ensures easier and accurate coding. (xml, excel). These files are updated every year in July to reflect the evolution of knowledge and differentials are provided to ensure traceability*.
- The **ORPHAcodes API**: it facilitates the informatic access to the nomenclature pack data and allow flexible implementation into the various IT systems in use in the different countries and/or settings.

** As per recommendation of the RD-ACTION working group for routine maintenance of codification*

Alos accessible from this website are the additional human readable tools which have been developed by Orphanet in order to ease the coding work:

- **The ORPHAcodes Classifications browser** a tool dedicated to browse the Orphanet classifications; it allows searching for clinical entities by ORPHAcode.
- **ORPHAcodes Mappings browser** : a tool that facilitates transcoding by allowing users to search for rare clinical entities and displaying the corresponding mappings in aligned generic medical and genetic terminologies.
- **ORPHAcode Dataviz tool :** a tool that allows visualization of scientific data and classification information associated to rare diseases in a user friendly format.

Furthermore an ORPHAcodes Helpdesk, developed & maintained by Orphanet thanks to the OD4RD project, is available: https://github.com/OD4RD/Main-Help-Desk. This helpdesk is dedicated to answering questions related to the Orphanet nomenclature content and/or the implementation of ORPHAcodes in Health Information Systems or other systems. It is possible to post issues in your language if an Orphanet Nomenclature National Hub is present in your country[4]. Issues addressed to the coordinating team should be written in English.

[4] https://od4rd.eu/02-partners

This online ticketing system allows requests & feedback from local users to be stored, tracked and made available to others interested users. Also, complex demands received by the Orphanet Nomenclature National Hubs can be easily streamlined to the Orphanet Coordinating team. Regular meetings between the Orphanet Coordinating team and the Orphanet Nomenclature National Hubs are held in order to discuss complex demands, to share best practices and find standard solutions to common problems.

To provide a sustainable and homogeneous, standardised support, a 'Questions and Answers' section within the GitHub has been developed based on users' questions: https://github.com/OD4RD/Main-Help-Desk/wiki. It provides standardised and generalised answers among 10 main topics:

- Alignments with other terminologies
- Good practice guidelines on Orphanet Nomenclature
- education and communication
- epidemiology of RD
- ORPHAcodes and nomenclature
- Orphanet classification
- Orphanet tools
- Technical issues
- Guidance documents for ORPHAcoding implementation and exploitation

Annex 3: Funding Projects

For ORPHAcodes production

This nomenclature and classification system have been developed and maintained thanks to Inserm support since 2007 as well as European support since the recognition as a priority, in the Council Recommendation of June 8th 2009 on an action in the field of RD, of the improvement in codification of RD. (RD-PORTAL S12305098-2006119; RD-PORTAL2 S12324970-20091215; ORPHANET EUROPE JOINT ACTION 20102206; EUCERD Joint Action 2011 22 01; ORPHANET OPERATING GRANT 20133305; RD-ACTION JOINT ACTION 677024; ORPHANETWORK FIRECT GRANT 831390; RD-CODE 826607; OD4RD 101070531; OD4RD2 101110100).

For ORPHAcodes implementation

From 2015 to 2018, support for the large number of Member States who expressed their interest in using ORPHAcodes (as a complement to existing coding systems) was provided via a dedicated & mulit-stakeholder working group (**work package 5 (WP5)) of the Joint Action for rare diseases RD-ACTION**)[lxvi]. This working group has notably produced information resources, guidelines and recommendations on ORPHAcoding.

Following the recognition of the Steering Group on Promotion and Prevention (SGPP) of ORPHAcodes as best practice, **the RD-CODE project** [lxvii], co-funded by the Third Health Programme, run from 2019 to 2021. The objective of this project coordinated by Orphanet-Inserm, was to support 4 Member States in improving gathering information on rare diseases by demonstrating real-world implementation in different settings, to guide other countries in the future. The project delivered tools, support services, information resources, guidelines and recommendations according to real-world use of ORPHAcodes so as to guarantee the appropriate use of these coding resources allowing comparability across countries and settings [lx]. Also, a new ORPHAcode to capture remaining undiagnosed patients after full investigation was made available to ensure the visibility of this important group of patients and facilitate their recruitment in clinical trials [v].

The experience from the RD-CODE project, showed that the real-life implementation in health information systems is challenging due to the heterogeneity of coding systems, practices, and tools and that local support in local language for coders and technical teams is necessary to achieve proper implementation in compliance with good practice guidelines for coding resulting in increased data quality and comparability. Thus in 2022 the **OD4RD pilot project**, coordinated by Inserm and cofounded by EU4health, was launched to tackle the invisibility of rare diseases in European member states' health systems, to promote harmonisation of practice and to facilitate generation of standardised interoperable data around RD. In 2023 it was renewed with the 3year **OD4RD2 project** coordinated by Orphanet-Inserm and co-funded by EU4Health[5]. The project produces and maintains the ORPHAcodes, in collaboration with ERNs and experts, to fit the real life coders'needs [lxviii], [lxix], [lxx], [lxxi]. ORPHAcodes are made available with genetic annotations, definitions and transcoding information in order to facilitate the coding work & reduce its burden but also to allow further analysis. Finally, they are delivered in different formats, adaptable to the different settings & systems [6].

The project also provides coordinated support for ORPHAcodes implementation in Health Information Systems of 19-member states' Hospitals hosting ERNs thanks to the growing Network of Orphanet National Nomenclature Hubs which provide a homogeneous, standardised (in terms of quality & practice) and tailored support. Their "lesson learned" are delivered via a dedicated report [lxxii] and feed the Frequently asked section of the central Helpdesk [lxxiii]; which is accessible to the wider community and can guide any other country who plans to implement ORPHAcodes in the future.

The impact of the work of this coordinated network ultimately contributes to facilitating obtention of RD exploitable data at the Member States (MS) level in order to be able to also understand the situation at the EU level (=reinforce the national level to add European value).

The recently started **JARDIN Joint Action** (2024-2027), which is contributing[lxxiv]

- to further investigate the current implementation status of ORPHAcodes in the 27 MS plus Norway
- to cross link with the OD4RD project in providing support for ORPHAcodes implementation in the MS where the OD4RD network is not active

[5] www.od4rd.eu
[6] www.orphacodes.org

- to provide real-life demonstration of the benefits of using ORPHAcodes versus generic terminologies for the RD diagnosis coding and to re-use data for policy making decisions, ERN monitoring, about ERNs activities and hospital performances, allowing also to assess ERNs' added value for hospitals and national health systems.

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