Milestone 15

OD4RD2 Whitepaper: Semantic interoperability of data on rare diseases - ORPHAcodes as part of the coding system landscape

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This document represents milestone 15 of the OD4RD2 project, which has received funding from the European Union. The document has been produced by the members of the OD4RD2 - Work Package 4. The OD4RD2 project has been launched in April 2023 for a 33-month period.

More information on the activities of the OD4RD can be found at www.OD4RD.eu

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Executive summary

Rare diseases (RD) represent a major public health issue. The lack of reliable epidemiological data hinders much needed progress in diagnostics and therapy. ORPHAcodes can make RD data collectible, findable and traceable, being currently the only way to identify patients with RD in collected data. Therefore, the use of ORPHAcodes in addition to already used coding systems are recommended by the Public Health Best Practices by the European Commission, among others.

Another advantage of ORPHAcodes is the possibility to directly access additional information on aetiology, diagnostics and treatment options within the Orphanet database. With the establishment of the European Health Data Space (EHDS) for secondary data use ORPHAcodes will become a major driver in RD research. Also, ORPHAcodes are the only coding system that allows to mark suspected RD patients who have not yet received a diagnosis (despite having exhausted all state-of-the-art and available diagnostic options) with a specific code and thereby make them visible in the healthcare system.

The interoperability of data is of growing importance in the health sector. The implementation of ORPHAcodes in national coding systems will have to overcome technical and capacity-related obstacles, and the interoperability with already used coding systems and terminologies is an important question to be answered. To address that need, ORPHAcodes are delivered in a variety of services and tools that can be adapted to the different settings, in particular a specific set of tools are available for automatic mapping to the main terminologies in use for facilitated transcoding. Further to this, ad-hoc solutions have also been created in some European countries to adapt to specific situations.

Regarding the implementation of ORPHAcodes, it is recommended to capture the respective ORPHAcode for patients with rare diseases at the point of care and to enable the inclusion of the ORPHAcode in the consecutive data flow. In case of a joint use of two or more coding systems, it is recommended to link the Orphanet nomenclature of RD to the other coding system(s) in a standardised way and as much as possible, so that at the point of coding, codes from both coding systems can be captured. To avoid future misalignment of the different coding systems, it is recommended to the developers and guardians of the different coding systems used in the disease space, to continue and enhance collaboration on aligning the coding systems and enabling the joint use.

Table of Content

1. Introduction

An estimated 30 M European citizens suffer from a RD and therefore represent a major public health issue [1]. More than 6,000 different RD according to a clinical definition are known [2]. RD are often characterised by a chronic course, reduced life expectancy and significant burden for sufferers and the healthcare system. The lack of reliable epidemiological data hinders progress in diagnostics and therapy, which is particularly needed in the case of RD. Since 89% of all RD have a prevalence of less than 1:1,000,000, the critical amount of data necessary to improve knowledge and action-taking can only be achieved by cumulative data collection in different countries. To aggregate this data, it must be collected in a standardised way. Still RD are poorly represented in most existing medical coding systems in use (Figure 1).

Currently, reimbursement-orientated coding systems are not designed to accurately identify RD - they do not provide specific codes for RD. As a result, exact coding for RD with these coding systems is not possible, which means that the actual number of RD patients cannot be validly collected. Without a detailed-enough coding system, this essential information remains hidden, which not only leaves epidemiological data incomplete, but also means that potential for better patient care, research and management remains unused. Furthermore, coding systems in use in healthcare are not intended to accurately represent the rapid evolution of knowledge in the RD field, or to indicate which disease concepts correspond to RD definitions, or to allow for RD-specific aggregation for secondary use.

To fill this coding gap, the Orphanet nomenclature of RD has been developed as a RD-domain specific coding system, using ORPHAcodes. With coding via ORPHAcodes, RD can finally be documented reliably - more precisely, more transparently and with real added value for everyone involved [3, 4, 5, 6, 7, 8, 9, 10, 11].

ORPHAcodes are therefore suitable for enabling the consolidation of data on RD at the European level or worldwide. According to the “Recommendation on Ways to Improve Codification for Rare Diseases in Health Information Systems” by the European Commission Expert Group on Rare Diseases, the European member states should consider adding ORPHAcodes to their country’s health information system and explore the feasibility and resources needed to do so [12]. This is also recommended by the Public Health Best Practices by the European Commission Expert Group on Public Health and by the European Health Data Set for RD [13].

Another notable important benefit of the ORPHAcodes is the simple and fast access to extensive knowledge on the corresponding RD via the Orphanet database. In this way, the ORPHAcodes of the various RDs can be used to retrieve specific knowledge, i.e. other data elements, such as genes and phenotypes or best practice guidelines, without additional extensive literature analyses [14].

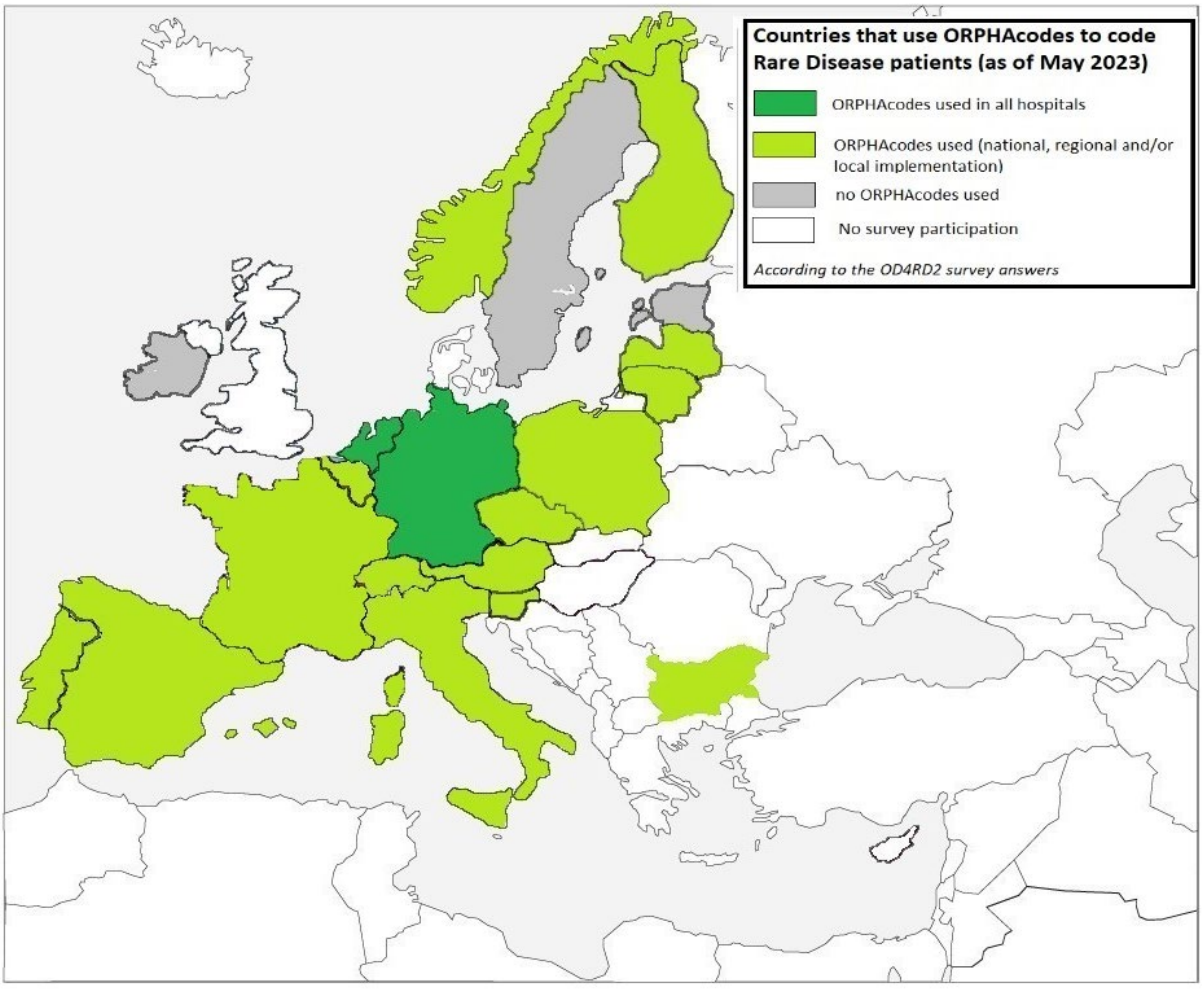

Figure 1: Survey results from the state of play survey within the OD4RD2 project - Usage of ORPHAcodes in countries participating in survey 2023 [15]

To enable a meaningful implementation of ORPHAcodes into national health information systems, some technical aspects should be considered, as well as the interplay with other coding systems in use or in future use. How do we integrate ORPHAcodes into the semantic interoperability landscape in Europe and beyond? How do we bridge the different coding system implementations in countries, systems and use cases?

2. Benefits and Advantages of using ORPHAcodes

To address the integration of ORPHAcodes into a health system, it is crucial to know the reasons why this is important. The usage of ORPHAcodes is a prerequisite for recording exact case numbers of all RD.

ORPHAcodes provide a unique resource on the most recent and scientifically evaluated state of play on coding of RD.

Furthermore, every intervention on the Orphanet nomenclature (i.e. creation or inactivation of an ORPHAcode), is clearly explained in published procedures [16]. Other coding systems, such as ICD or SNOMED CT (Systematized Nomenclature of Medicine Clinical Terms), do not distinct between rare and non-rare diseases.

The ORPHAcode itself provides direct access to additional information on aetiology, diagnostics and treatment options within the Orphanet database. This can help healthcare professionals to treat RD patients and can be of great use in emergency situations. A patient record that includes an ORPHAcode can therefore highlight the need to make use of patient safety measures and provide electronic support in the health care pathway of the respective patient. In this respect, the ORPHAcode can be used as “rarity flag” and therefore as a specific patient safety measure.

In addition to the epidemiological knowledge gain which can enhance decision making and statistical reporting [17], the secondary data use of ORPHAcodes enables the identification of expert centres that have already gained extensive experience in the treatment of the respective RD. Experience is a known factor for the quality of treatment. Therefore, the collection of the number of treated RD patients according to the used ORPHAcode can be used to guide specific funding to the relevant expert centres, and by doing so enhance the quality of treatment of the population. As RD patients often require different treatments compared to non-rare disease patients, ORPHAcodes can also be used to adjust funding schemes for disease treatment, like Diagnosis Related Group (DRG) systems.

As the use of ORPHAcodes generates specific markers in patient records, even in the case of very rare diseases, the Europe-wide pooling of data can achieve the numbers of cases that enable epidemiological findings and improvements in diagnostics and therapy. With the establishment of the European Health Data Space (EHDS) for secondary data use, this will become a major driver in RD research, e.g. for Orphan drug research.

ORPHAcodes are the only coding system that allows marking of suspected RD patients who have not yet received a diagnosis (despite having exhausted all state-of-the-art and available diagnostic options) with a specific code and thereby making them visible in the healthcare system [18]. This can make it easier to find those patients in order to re-examine them after new diagnostic methods have been established, or new diseases have been described by medical science, or to contact them for recruitment into new clinical trials that are initiated. With the rising possibilities of genomic research, the use of Artificial Intelligence on big data pools and the development of personalised medicine, this will be a major step towards better diagnostics and care of patients with suspected and diagnosed RD.

3. Problem definition

As digitalisation is moving forward, the interoperability of data is of growing importance in the health sector. Interoperability depends on technical requirements (like standardised interfaces), syntactic annotated data (e.g. use of FHIR) and semantic standardisation. Over the years, different settings, regions and countries have agreed on such standards. With the implementation of cross border data exchange mechanisms, it became clear that these choices do not always align. Multiple coding systems are in use in Europe, and different technical and syntactic standards have been chosen. ORPHAcodes are used by some countries in different settings: e.g. registries, projects, or routine coding.

The development of the EHDS regulation and the work leading up to it set the stage for discussions on semantic interoperability in Europe. Guidelines on specific domains are in place, like the eHealth Network (eHN) Guideline on Patient Summary [19,20]. Implementing the guidelines in Europe might require changes to the standards chosen by a country or the need for mapping between different settings.

ORPHAcodes are mentioned in the guidelines and are recommended to be used for coding, if a RD is diagnosed. This puts many countries in a position to decide on how to use ORPHAcodes.

In a workshop within the project OD4RD2, the participating countries discussed the issue, and compiled a non-exhaustive list of challenges:

3.1. Technical challenges

For coding of diseases, in many countries the International Classification of Diseases (ICD) and/or SNOMED CT are used. Due to the typically wider scope of ICD-codes as compared to ORPHAcodes, automated data translation (cross-reference of data) from ICD-10 and earlier ICD versions to ORPHAcodes is not possible without major loss of information. Capturing the ORPHAcode at the point of coding would often require a change to the IT-System, adding the respective fields. However, in many countries, IT-systems are in place that are highly complex and are used for multiple purposes (documentation, reimbursement data generation, monitoring, etc.). Changes to these IT-systems are costly and time consuming and often only done if a legal obligation requires the change. Some facilities even lack Electronic Health Record Systems to capture coding, so additional manual coding would be required.

Within the project OD4RD tools to help overcoming technical issues and a helpdesk have been implemented, which can be used and adapted for national implementations.

3.2. Resource challenge – Training and implementation support

Implementing ORPHAcodes into a setting requires a few prerequisites. If the language used in the coding setting is not English, a translation of the Orphanet nomenclature of RD has to be undertaken (if not already provided within the Orphanet nomenclature) and, once in place, requires updating and maintenance.

Training of the persons coding with ORPHAcodes is required as well, and again, if a national language has to be used, a translation of existing training material might be required, or new material needs to be developed. Additionally, training material needs to be catered to the specific coding setting, so available training material from other settings might require adaptation. Once the implementation has started, continuous support of the coders should be provided. Otherwise, untrained use of ORPHAcodes can lead to different use of the Orphanet nomenclature of RD and subsequently to inconsistent data. One of the measures of OD4RD has been the implementation of a national nomenclature hubs network, which allows the national contact points to learn from each other and to share resources (e.g. training material) for supporting the implementation of ORPHAcodes.

Many countries reported that the amount of required resources for this is not clear and often underestimated. To support successful implementation, relevant resources should be available before starting the implementation.

3.3. Coding system interoperability challenge

As the ICD in its ninth (ICD-9) or tenth revision (ICD-10) is in place in many countries, the question of why an additional coding system for RD is needed is frequently asked. As ICD-9 and ICD-10 do not offer sufficient detail, the answer is straightforward: if you want to accurately capture patients with RD in your data and to differentiate RD from non-RD, ICD-10 is not sufficient. The same ICD-10 code may correspond to multiple RD and also include common diseases, thereby making them indistinguishable. If at the point of care data is only coded with ICD-10, it will not be possible to map this data automatically from ICD-10 to ORPHAcodes in a sufficient way, as the detail on the RD is lost in most of the ICD-10 codes. Instead, it is necessary to go back into the documentation, and sometimes to consult the health care professional treating the patient in order to collect the necessary detail to accurately assign the correct ORPHAcode.

Next to the use of ICD, SNOMED CT is a widely used coding system, often the key coding system in electronic health records (EHRs) (Figure 2). As SNOMED CT is more detailed and allows to capture RD more accurately based on a collaboration between INSERM (Institut national de la santé et de la recherche médicale, US-14 Orphanet) and SNOMED International, the same question is not as straightforward to answer in this case. But, as well as ICD, SNOMED CT does not provide for a specific distinction

of rare versus non-rare diseases. If data is captured only using SNOMED CT, the possibility to flag a person as patient suffering from a rare disease or a suspected rare disease is lost. As well there are some limitations to the joint use as not all ORPHAcodes (in particular, but not exclusively, the most granular ones) are fully represented in SNOMED CT. Capturing ORPHAcodes together with SNOMED CT could overcome this problem.

The ICD has undergone a thorough revision and was released in its eleventh revision (ICD-11). More granularity has been added and the coding of RDs is more accurate with ICD-11. In the most recent releases of ICD-11 (2024-01, 2025-01) ORPHAcodes of the disorder level have 15,3% exact matches to an ICD-11-MMS concept (MMS code), 45,48% matches to index terms of ICD-11 and 60,78% overall coverage of URIs of ICD-11 (foundation concept, exact and index matches) [21]. Countries are starting to plan for the implementation of ICD-11 and again are faced with the question of how and why to use the ORPHAcodes together with ICD-11.

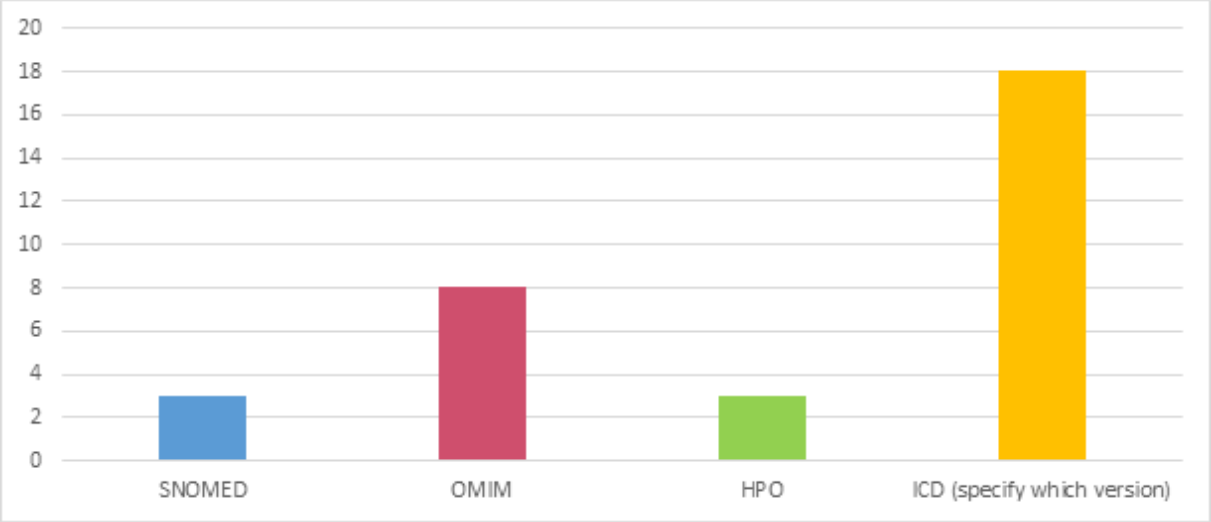

Figure 2: Survey results from the state of play survey within the OD4RD2 project - joint use of ORPHAcodes with other coding systems

To answer these questions in a way that is addressing all country needs, cater to all use cases and not add to the burden of coders, administrators and users of data is difficult, but crucial. An attempt to answer this question is given in the section “Proposed solution, conclusion and recommendations for action” of this paper.

4. Intermediate solutions in some countries

As countries are facing these challenges, some intermediate solutions have been put in place, which can help to refine a recommended way forward. In the OD4RD2-project these solutions have been shared between countries, and “lessons learned” reports helped the project partners to approach the issue.

It was reported that advocating for the use of ORPHAcodes (see also section Benefits and advantages) to decision makers is essential to generate openness for inclusion of ORPHAcodes at the point of decision making. Some countries reported, that depending on the technical possibilities and the necessary implementation effort in the respective IT system, it may make sense to initially set up a way to capture an ORPHAcode with a free comment field. However, this was noted to be a workaround and could help to show the benefits of the use of ORPHAcodes from data collected in that IT-system. It is not fit for long term use and does require substantial resources and training of coders to guarantee harmonised data capture.

Many countries pointed out that it is crucial when implementing ORPHAcodes to take care to minimise or avoid additional coding effort for the coders. Putting additional burden on the coders will create resistance and raise the cost of implementation. Therefore, it would be optimal, if the associated codes (e.g. ICD-10 and ORPHAcodes) were provided automatically by the hospital software when a disease diagnosis is selected. This also ensures that RDs are coded consistently, and that errors are avoided when selecting ORPHAcodes. Putting this mechanism in place requires a central point where the association of the codes is maintained and provided. Orphanet is providing such linkage, but due to some country-specific modifications of ICD-10 or national requirements additional work might be necessary in such a central point. An example for such implementation can be seen in Germany [22,23,24], Spain [7] and the Netherlands.

Storing ORPHAcodes not only for the respective treatment case but also in the patient health record can also reduce the coding effort and, in addition, serve as valuable information for the treating physicians. This way the ORPHAcode will “accompany” a patient on their patient journey and will allow health care professionals to easily extract relevant information on the specific RD from Orphanet using the ORPHAcode.

Expert centres can assist with advocating and training on the use of ORPHAcodes. On the one hand they have research interests, and - in case of Europe - ERN registries to populate with data. On the other hand, they are domain experts and can help to point out challenges and benefits at local level and to find practical solutions. Therefore, involving expert centres in the implementation roadmap is seen as beneficial and desirable in the OD4RD2-project.

Even though these initial solutions are possible steps towards ORPHAcode implementation, a wider and more harmonised approach seems to be helpful and desired by the participants of the project. Especially the coding system interoperability challenge seems crucial and would benefit from guidance.

5. Proposed solution, conclusion and recommendations for action

5.1. Proposed solution

The need for ORPHAcodes is clearly documented. The recommendation on ways to improve codification for RD in health information systems was adopted by the Commission Expert Group on Rare Diseases (CEGRD) in 2014, ORPHAcodes have been recognized as best practice by the European Commission since 2017, and the implementation of the EHDS regulation will require to use ORPHAcodes in electronic health records. Therefore, it is essential to start implementing ORPHAcodes into national health systems now. In order to avoid additional burden for health care professionals, smart solutions need to be in place. Lessons learned from the implementation survey within OD4RD and from a workshop on this issue indicated, that a linked implementation of ORPHAcodes with other coding systems that are already in place is key to success.

If the coding system in use is not as detailed as the Orphanet nomenclature of RD, a mechanism linking the two coding systems through the disease name is a solution. An example is the joint implementation of ICD-10 and ORPHAcodes in Germany. Another example of minimising the additional coding burden through coding system linkage, is the Norwegian implementation in which the ORPHAcode follows the patient rather than being linked to a specific hospital encounter. When an ORPHAcode is assigned to a patient, ICD-10 coding of subsequent hospital encounters for which the RD was either the reason, or relevant, for the encounter is guided by means of the ORPHAcode-ICD-10 alignment.

Discussions showed that it is crucial to capture the ORPHAcode at the time of data capture at the point of care or at the initial coding of the detailed clinical documentation. Adding ORPHAcodes to the dataset at a later time based only on the previous coding with the less detailed coding system is not possible, will result in significant loss of information, or will create extra burden for coders. Therefore, it is recommended to capture the ORPHAcode directly and to implement the necessary field(s) in all coding related IT-systems. Likewise, the ORPHAcode should also be available in the data flow after the point of coding to enable secondary data use on specific scientific questions on RDs with ORPHAcodes.

Even if the coding system in use is of the same detail for some diseases as the ORPHAcodes - like up to a certain degree SNOMED CT and ICD-11 are - it is recommended to link them in the IT-implementation so that they can be used together in the process of coding. This can be done on the basis of the disease name as well as on a concept-to-concept link where possible between the two coding systems in place, for example, by using the curated mapping files provided together with the ORPHAcodes. Whether the terminologies are completely linked or not at the point of coding, it is recommended to include the ORPHAcode aside the generic coding system

in use, to avoid later transcoding efforts and inaccuracy in detecting RD patients if done afterwards. Then, to tackle the interoperability challenge, Orphanet mappings can be used to transcode ORPHAcodes in the generic terminology when needed for other use cases.

It is important to make sure that in the coded data the ORPHAcode is included in subsequent data flow to fulfil requirements of the EHDS regulations.

Already the developers and guardians of the major coding systems like ICD-11, SNOMED CT and ORPHAcodes have initiated joined projects to enable this concept-to-concept linkages. It is crucial to continue these collaborations and to try to align these major coding systems as much as possible, even though a 100% alignment does not seem to be achievable and most of all maintainable, if the systems are maintained separately. A recent announcement from WHO and SNOMED International on a planned collaboration to align ICD-11 and SNOMED CT states “This collaboration aims to facilitate a seamless data conversion and linkages for users of both ICD-11 and SNOMED CT towards a robust and interoperable health data ecosystem. […] Linking ICD-11 and SNOMED CT will enable the effective use of health data – ultimately saving lives” [25]. As the ORPHAcodes already align with both of these coding systems through collaborations, the hope is that this will provide benefits for patients with RD and help to save lives in this population.

5.2. Recommendations for action

Based on these considerations, the following recommendations for action can be given.

1. It is recommended to capture the respective ORPHAcode for patients with RD at the point of care and to enable the inclusion of the ORPHAcode in the consecutive data flow.
2. In case of a joint use of two or more coding systems, it is recommended to link the Orphanet nomenclature of RD to the other coding system(s) as much as possible and using standardized, curated mappings so that at the point of coding, codes from both coding systems can be captured.
3. To avoid future misalignment of the different coding systems, it is recommended to the developers and guardians of the different coding systems used in the disease space to continue and enhance collaboration on aligning the coding systems and enabling the joint use.

6. Sources and references

[1] Wakap, S.N. et.al.: Estimating cumulative point prevalence of rare diseases: analysis of the Orphanet database. European Journal of Human Genetics, 2020, 28, 165-173 https://www.nature.com/articles/s41431-019-0508-0

[2] Wang, C.M. et.al.: Operational description of rare diseases: a reference to improve the recognition and visibility of rare diseases. Orphanet Journal of Rare Diseases, 2024, 19, Article number 334 https://ojrd.biomedcentral.com/articles/10.1186/s13023-024-03322-7

[3] Mazzucato, M. et.al.: ORPHAcodes use for the coding of rare diseases: comparison of the accuracy and cross-country comparability. Orphanet Journal of Rare Diseases, 2023, 18, Article No. 267 https://ojrd.biomedcentral.com/articles/10.1186/s13023-023-02864-6

[4] Pichon, T.net.al.: Overview of patients' cohorts in the French National rare disease registry. Orphanet Journal of Rare Diseases, 2023, 18, Article No. 176 https://ojrd.biomedcentral.com/articles/10.1186/s13023-023-02725-2

[5] Gunne, E. et.al.: A retrospective review of the contribution of rare diseases to paediatric mortality in Ireland. Orphanet Journal of Rare Diseases, 2020, Nov. 4, 15(1), 311. https://pubmed.ncbi.nlm.nih.gov/33148291/

[6] Chiu, A.T.G. et.al.: Healthcare burden of rare diseases in Hong Kong – adopting ORPHAcodes in ICD-10 based healthcare administrative datasets. Orphanet Journal of Rare Diseases, 2018, 13, Article No. 147 https://ojrd.biomedcentral.com/articles/10.1186/s13023-018-0892-5

[7] Rico, J. et.al.: The interoperability between the Spanish version of the International Classification of Diseases and ORPHAcodes: towards better identification of rare diseases. Orphanet Journal of Rare Diseases, 2021, 16, Article No. 121 https://ojrd.biomedcentral.com/articles/10.1186/s13023-021-01763-y

[8] Walker, C.E. et.al.: The collective impact of rare diseases in Western Australia: an estimate using a population-based cohort. Genet Med., 2017, May 19(5): 546-552 https://pubmed.ncbi.nlm.nih.gov/27657686/

[9] Scanlon, P. et.al.: Measuring the impact of rare diseases in Tasmania, Australia. Orphanet Journal of Rare Diseases, 2024, 19, Article No. 399 https://ojrd.biomedcentral.com/articles/10.1186/s13023-024-03343-2

[10] Navarrete-Opazo, A.A. et.al.: Can you hear us now? The impact of health-care utilization by rare disease patients in the United States. Genetics in Medicine, 2021, 23, 2194-2201. https://www.nature.com/articles/s41436-021-01241-7

[11] Mazzucato, M. et.al.: Estimating mortality in rare diseases using a population-based registry, 2002 through 2019. Orphanet Journal of Rare Diseases, 2023, 18, Article No. 362 https://ojrd.biomedcentral.com/articles/10.1186/s13023-023-02944-7

[12] Recommendation on Ways to Improve Codification for Rare Diseases in Health Information Systems, adopted at the 3rd meeting of the Commission Expert Group on Rare Diseases. Adopted at the 3rd meeting of the Commission Expert Group on Rare Diseases, 12-13 November 2014

[13] Best practice: https://webgate.ec.europa.eu/dyna/bp-portal/transfered last accessed on March 31th, 2025

[14] https://od4rd.eu/communication-material/OD4RD2_Use-Cases_OC-Implementation-DE-FR-NL-NO_2024.pdf

[15] OD4RD2 Deliverable 4.1: State of Play Survey.http://od4rd.eu/03-deliverables/D4.1_OD4RD2_state-of-play-survey_final.pdf

[16] Orphanet procedures. https://www.orpha.net/en/other-information/procedures

[17] The Federal Joint Committee: Regelungen des Gemeinsamen Bundesausschusses zur Konkretisierung der besonderen Aufgaben von Zentren und Schwerpunkten gemäß §136c Absatz 5 SGB V (Zentrums-Regelungen), 2019, 2024. https://www.g-ba.de/downloads/62-492-3498/Z-R_2024-04-18_iK-2024-07-05.pdf

[18] Angin, C. et.al.: Coding undiagnosed rare disease patients in health information systems: recommendations from the RD-CODE project. Orphanet Journal of Rare Diseases, 2024, 19, Article No. 28. https://ojrd.biomedcentral.com/articles/10.1186/s13023-024-03030-2

[19] European commission, Directorate-General for Health and Food Safety: eHN Guideline on Patient Summary (2024) https://health.ec.europa.eu/publications/ehn-guideline-patient-summary_en

[20] eHealth Network Secretariat: Common Semantic Strategy for health in the European Union – eHAction (2019) https://health.ec.europa.eu/document/download/1b35a8ec-98cd-4307-8cd6-0e552d9f8354_en?https://health.ec.europa.eu/document/download/1b35a8ec-98cd-4307-8cd6-0e552d9f8354_en?filename=ev_20190611_co241_en.pdf

[21] Orphanet alignment release, December 2024. https://www.orphadata.com/alignments/

[22] Alpha-ID - an identification number for diagnoses. https://www.bfarm.de/EN/Code-systems/Terminologies/Alpha-ID-SE/_node.html last accessed on March 27th, 2025

[23] Martin,T. et.al.: Seltene Erkrankungen in den Daten sichtbar machen – Kodierung. Bundesgesundheitsblatt Gesundheitsforschung Gesundheitsschutz, 2022, 65(11), 1133-1142 https://pmc.ncbi.nlm.nih.gov/articles/PMC9636302/

[24] Marx,M.M., Dulas,F.M., Schumacher,K.M.: Improving the visibility of rare diseases in health care systems by specific routine coding. Bundesgesundheitsblatt Gesundheitsforschung Gesundheitsschutz, 2017, 60(5):532-536 https://pubmed.ncbi.nlm.nih.gov/28349172/

[25] https://www.who.int/news/item/22-10-2024-who-explores-collaboration-with-snomed-international-for-linkage-between-icd-11-and-snomed-ct last accessed on March 27th, 2025