

# MonitoRare

IX Report on the condition of people living with a rare disease in Italy

## Executive Summary

# UNIAMO

Con il patrocinio di



# orphane.net



## Preface

**Yann Le Cam, Chief Executive Officer, EURORDIS – Rare Diseases Europe**

As citizens and as advocates for public health, it is regrettable that the European Union has not yet adopted a comprehensive public health strategy to improve the well-being of its population. Nevertheless, the EU4Health programme, with a budget ten times higher than its predecessor, has allowed us to address the challenges posed by the COVID-19 pandemic and launch ambitious initiatives for cancer and mental health. In the past year, we have witnessed significant progress in fostering innovation, enhancing access to medicines, modernising health data systems, and embracing new health technologies.

However, despite these advancements, the EU has yet to fully integrate its various health policies, particularly concerning those relating to our rare disease community. The EU and its Member States have embraced the United Nations' Sustainable Development Goals (SDGs) since 2015 and they adopted the UN Resolution on Persons Living with a Rare Disease in 2021, but we have not seen a comprehensive commitment to measurable goals that align with these international standards. There is a missed opportunity to leverage European collaboration for positive change that may be challenging to achieve at the national level alone.

Despite the incomplete and fragmented progress, my hope remains strong, fuelled by the resolute advocacy of our Europe-wide community and national alliances such as ÜNIAMO. Our collective strength will push rare diseases higher on the priority list of EU policymakers in the run-up to, and beyond, the 2024 European elections. The European rare disease community has already made significant strides in securing meaningful policy advancements and elevating rare diseases on the EU's political agenda.

Regarding policy advancements, the European Commission has emphasised the development of new rare disease medicines, leading to proposals to overhaul pharmaceutical legislation.

Efforts are underway to improve the adoption of innovative medical technologies, establish a data exchange ecosystem known as the European Health Data Space, and enhance the use of health data for research, innovation, and policymaking. The European Reference Networks (ERNs), which have connected rare disease clinicians across national borders since 2017, have demonstrated their immense value and will receive increased support from the EU for the next five years. Additionally, coordinated European research initiatives such as the Rare Disease Partnership 2024-2030 and Rare Diseases Clinical Research Networks are set to drive progress at the European level.

On the political agenda, an increasing number of policymakers and institutions have committed themselves to our community's call for a European Action Plan for Rare Diseases, stemming directly from the Rare 2030 foresight study and recommendations published in 2021.

The European Parliament, the European Economic and Social Council, successive Presidencies of the EU Council, and 22 Member States, including Italy, have all aligned themselves with this call. The newly commenced Spanish Presidency of the EU Council has promisingly affirmed that rare diseases will be among its health agenda priorities.

While action on rare diseases cannot solely rely on the EU-level, we also require comprehensive national plans that address the full spectrum of unmet needs for individuals living with rare diseases. In this context, UNIAMO and the Italian rare disease community serve as an exemplary model of how positive change can be achieved at the national level. MonitoRare is a unique evidence tool driving forwards actions and could serve as an example for other countries and at European level. Italy has demonstrated leadership in critical policy areas, such as newborn screening, where it screens for the most genetic conditions in Europe, and Italy recently adopted its National Rare Disease Plan for 2023-2026. UNIAMO has made such advancements possible.

On behalf of EURORDIS and the broader rare disease community in Europe, I eagerly anticipate not only supporting UNIAMO and Italy's advocacy community in enhancing and effectively implementing this National Plan, but also learning from the remarkable and inspiring efforts led by UNIAMO and Italy's rare disease community. Whether at the national or European level, we are undeniably stronger together.

## Introduzione

**Annalisa Scopinaro - President - UNIAMO Federazione Italiana Malattie Rare - Rare Disease Italy**

Ninth edition of MonitoRare, the fifth of this Presidency.

A fundamental Report in the Italian framework, for its specificity and for the peculiarity of the point of view from which the data is analyzed. There are no other similar experiences in the entire European framework.

The presentation of the Report has been accompanied, since last year, by the Convention: a day of debates, insights, meetings, exchanges, launching of issues and drafts of possible solutions. The Federation's activity focuses on what are the concrete actions, implementable in a short time, that can really change the quality of life of people with rare diseases, but without forgetting a broad perspective vision that gives directions to political and institutional activity so that systemic knots can be untied.

The Convention is the living yeast of our advocacy and participation activities.

This year, the "MonitoRare Aperitifs," a happy intuition of Rita Treglia, accompanied the discussions of the Patient Organisations' representatives, who gathered to identify priorities and set up the lineup of urgently needed interventions.

It is difficult to summarize what the Federation is changing in the legislative and political framework, thanks to the synergistic actions of awareness, advocacy, and work at institutional tables. We see the results when our methods are imitated, our ideas replicated without authorship, our demands incorporated into laws, regulations, decrees. The "rare" world is changing because there is a Federation pushing: a reasoned, shared change, unencumbered by individual interests but permeated by collective interests. The unity of purpose can be seen in the adoption of common languages, the repetition of the same concepts, and the push for concrete actions.

If 2021 was the year of Law 175 and the UN Resolution, as well as the approval of the Framework Law on Disability, 2022 was a year of consolidating positions, focusing on urgent issues, and building the next leaps. The work on updating the National Plan was completed in May, with the delivery of the draft to the Minister of Health. The Extended Newborn Screening Group continued its examination of the pathologies to be proposed for the panel update, albeit held back by the change introduced by the budget law, which eliminated, contrary to all European regulations that will soon have to be applied in Italy as well, the need for HTA assessment.



Individual regions have continued the work of structuring the network and consolidating procedures. ERNs are gradually finding their role within a national context, thanks in part to the contributions of the three coordinators in our territory (ERNBond, Metabern and Reconnet).

AIFA has been undergoing a reform, not yet fully implemented, which should optimize the internal flows of the institution. The call for research on rare diseases, provided for in the NPRR, has been issued, and the applications, which were received although with great difficulty due to the stringent conditions set, have been taken up, evaluated and, where appropriate, approved. A sore point of the call was the lack of provision for the active and recognized participation of patient associations.

Discussions and meetings on pharmaceutical strategy revision have increased in Europe, with a focus on updating the Orphan and Pediatric Drug Regulations. But regulations on HTA and Health Data Space, not directly concerning but closely interconnected with rare diseases, have also been the subject of discussion.

The debate was also intense in Italy, with the Federation engaged in institutional meetings also together with Eurordis delegates, to emphasize the unity of the positions of patient representatives.

The second half of the year focused on a series of events that suspended, bubble-like, a range of activities.

The fall of the government with the need for new elections completely changed the political scenario. Taking into account the reform, the number of parliamentarians was reduced, increasing the concentration of attributions in the head of each individual representative.

Uniamo worked with FAVO (the Italian Federation of Voluntary Associations in Oncology) to proceed with the reconstitution of a parliamentary inter-group that would take into account the specificities listed in Law 175: rare diseases and rare cancers.

Thus was born the Parliamentary Intergroup Rare Diseases and Oncohematology, a perfect example of cooperation between political forces and reference associations. At the helm were Orfeo Mazzella (M5S and also spokesperson for the Campano Malattie Rare Disease Forum, with two rare diseases) and Elisabetta Gardini (Forza Italia). At the end of the year, the effort to recompose with respect to the Rare Diseases Intergroup announced by Congresswoman Boschi (Italia Viva) was also great. The harmonization work was crowned with success at the beginning of 2023, during Rare Disease Day, with the reunification of the two intergroups and the labeling of the Parliamentary Intergroup of Rare Diseases and Oncohematological Diseases, together with UNIAMO, FAVO, and AIL.

In this complex political and institutional framework, Uniamo has continued an intense activity, promoting or participating in many discussion tables, building consensus, position papers and in-depth studies. In order to systematize the much work that has been done and to make explicit the positions that the patient community gradually takes on topical issues, we thought of launching an editorial series: the Ephemeredes. The name has three definitions, and each contains an element we felt close to it: the daily record of proceedings, which calls us back to an ideal journey through pathology; the periodic publication, which responds to our wishes; and the table, which provides coordinates, our aspiration and intent in the publication of these booklets. The relative rarity of the use of this term, its feminine connotation, and its originality since the last person to use it was in 1840 for publications of a literary or scientific nature, further convinced us that we were made for each other: federation and ephemera, a community of people with rare disease and a periodical publication that chronicles a journey and tries to guide its course. Thus, during the year we published comments on the European Orphan Drug Regulation, participation of patient representatives in ethics committees, models of caretaking, access to treatment, and the push toward increasingly early diagnosis. In addition, we published the results of two surveys.

In addition to the institutional and more purely advocacy activities, aware of the need for a broad awareness with respect to the issues to be investigated and resolved, we decided to develop for the Rare Disease Day a campaign that would break out of the classic places of confrontation and accompany, in an ideal journey, the patient's journey, throughout the month of February. With the hashtag #ununiamoleforze we branded buses and shelters in Rome and Milan, telling 5 stories exemplifying as many patients and accompanying the inaugurations with events of media impact.

Institutions, Scientific Societies, Patient Associations, Pharmaceutical Companies largely espoused this new concept and distributed the events organized over the 28 days (sometimes beyond), unifying graphics and messages.

I would like to thank, on behalf of myself, the Executive Board, and the entire community of people with rare diseases, those who provided the data that form the basis of this report, those who compiled it, those who took care of the graphics and layout, those who provided the photos that bring it to life, those who worked behind the scenes on a daily basis, and those who supported the final event.

My personal thanks to all those in the Patient Associations who work daily to improve the quality of life for people with rare diseases. The achievements we have made over the years would not have been possible without the individual contributions each of them has made.

The Report is always on my desk, a unique source of compendium of data on rare diseases, an irreplaceable working tool. I hope it will be as useful to you as it is to us.

Have a nice reading.





## Executive Summary

The gradual exit from the state of emergency brought about by the Covid-19 pandemic - officialized at the end of March 2022 in our country - actually coincided with the first steps of the implementation of Law No. 175 of November 10, 2021, "Provisions for the treatment of rare diseases and the support of research and production of orphan medicinal products" which resulted in a decisive progress of the national rare disease network mainly due to the effect:

- of the establishment, by Decree of the Undersecretary of State for Health dated September 16, 2022, of the National Committee for Rare Diseases (CoNaMR) in which the involvement of the most representative sector associations of people with rare diseases at the national (ÜNIAMO) and European (EURORDIS) levels is provided for. The decree also regulates how the CoNaMR, which has a three-year term, is to function, and provides that members may be renewed only once;
- of the approval, after a long gestation period, of the National Rare Diseases Plan 2023-2026 and the document for the "Reorganization of the National Rare Diseases Network" which occurred with the State-Regions Conference Agreement of May 23, 2023, which defines the networks the tasks and functions of the coordination centers, reference centers and centers of excellence participating in the development of the European Reference Networks (ERNs). The Agreement also provides for the allocation of 25 million euros annually for each of the years 2023 and 2024 for the implementation of the NPRD from the resources of the National Health Fund earmarked for the realization of specific objectives of the National Health Plan, pursuant to Article 1, paragraph 34, of Law No. 662 of December 23, 1996, postponing to a subsequent measure the definition of the modalities for the allocation and disbursement of these resources.

Moreover, at the beginning of 2023, 4 additional decrees were issued, provided for, respectively, by paragraphs 5, 7, 11 and 15, of Article 2, of Law no. 3/2018 "Delegation to the Government in the field of clinical trials of medicines as well as provisions for the reorganization of the health professions and for the health management of the Ministry of Health" which will finally allow to unlock the hybrid situation that clinical trials in Italy have experienced in the last 5 years by favoring the final stabilization of the regulatory framework of clinical trials, aligning with Regulation (EU) No 536/2014 of the European Parliament and of the Council on clinical trials of medicinal products for human use that entered into force on January 31, 2022.

In this context, it should also be positively recalled the agreement, recently sanctioned at the State-Regions Conference in the session of April 19, 2023, with respect to the draft decree concerning the definition of the rates of outpatient specialist and prosthetic care, which arrives more than 6 (six!) years after the Prime Ministerial Decree of January 12, 2017 defining and updating the essential levels of care (LEA).

The path of implementation of Law No. 175 of November 10, 2021, however, remains largely incomplete due to the failure to define the implementing measures of the specific measures to support research on rare diseases and the development of orphan medicinal products and the solidarity fund for the support of the work of care and assistance of people with rare diseases.

To date, moreover, not even the update of the "SNE panel" (Expanded Neonatal Screening) has been carried out, despite the fact that the positive opinion regarding the introduction of SMA (spinal muscular atrophy) was delivered by the Working Group to the Ministry now more than 2 years ago. Not to mention that the predictions for the expansion of expanded newborn screening to neuromuscular diseases of genetic origin, severe congenital immunodeficiencies, and lysosomal storage diseases date from late 2018 (Law No. 145 of December 30, 2018). A hopeful sign on this front comes from the many regions that are now implementing and/or experimenting with newborn screening also for other diseases not included in the current national panel.

For the more punctual aspects, there are once again, numerous insights that emerge from reading the "MonitoRare" report and that lend themselves well to subsequent in-depth analysis. In these first pages we venture with the arduous task of trying to effectively summarize the snapshot of this ninth edition of the report with the sole intent of offering for reflection some elements that, more than others, assume a strategic role for the future of care for people with rare diseases (PcMR) and their families at the international, national and local levels.

Some examples of the strengths of the rare disease system in Italy that the ninth edition of MonitoRare confirms are:

## Drug accessibility

- 8.4 million doses of orphan medicinal products were dispensed in 2021, or just 0.03% of total pharmaceutical consumption;
- spending on orphan medicinal products in 2021 was €1,535 million, accounting for 6.4 percent of total pharmaceutical spending;
- the number of treatments for rare diseases included in the list of Law No. 648/1996 increased from 31 in 2018 to 45 in 2022 (there were just 13 in 2012);
- the number of people with rare diseases who have benefited from the AIFA fund (referred to in Law No. 326/2003, Art. 48) drops to 229 in 2022, after witnessing an exponential increase in previous years, from 20 people in 2016 to 1,361 in 2020;
- as many as 8 of the 16 Advanced Therapy Medicinal Products (ATMPs) with European approval (figure updated to May 2022), are currently reimbursed in Italy (the same number as in France and 2 less than Germany and England), while 3 ATMPs are under evaluation; another 3 ATMPs in Italy have not yet begun the evaluation process for requesting reimbursement and finally 2 ATMPs have not been granted reimbursability.

## Access to information

- 16 Regions/PPAAs have an institutional information system specifically dedicated to rare diseases: more than 8,000 PcMRs with whom they came into contact in 2022, to which should be added the more than 2,500 PcMRs who came into contact with the Rare Disease Hotline of the National Center for Rare Diseases of the Istituto Superiore di Sanità (CNMR-ISS).

## Training

- the number of CME courses dedicated to rare diseases settles at 74 in 2022 (of which 14, 20%, with the presence of a Uniamo representative among the speakers), trend steadily increasing (it was 49 in 2021); there is a positive return to in-person training;

## Newborn screening and clinical laboratories

- at the end of 2022, the expanded neonatal screening program is active in all regions/autonomous provinces. There is also increasing homogenization of the number of diseases included in screening panels at the regional level;
- the DPCM January 12, 2017 "Definition and update of essential levels of care" in Art. 38 guarantees all newborns the necessary services for the early diagnosis of congenital deafness and congenital cataract. By the end of 2022, newborn hearing screening is active throughout the country. Similarly, neonatal ophthalmological screening is active throughout the country with the exception of two regions (in one region it is not active, in another it is being implemented);
- constant growth in the last five years in the number of rare diseases tested in Italian clinical laboratories considered in the Orphanet database, which, in the face of substantial stability in the number of laboratories, increase by almost 800 within 5 years: from 1,999 in 2018 to 2,786 in 2022.

## The quality and coverage of surveillance systems

- coverage of regional rare disease registries (RRMRs) increases: the estimated population prevalence of people included in RRMRs as of Dec. 31, 2021 rises to 0.74% (0.84% in under-18s) from 0.30% in the first edition of the MonitoRare Report in 2015;
- the data contained in the RRMRs are for all rare diseases listed in Annex 7 of the DPCM 12.01.2017: based on the more than 425,000 PcMRs recorded in the RRMRs at the end of 2021 (+ 48. 000 units compared to the previous year) the most prevalent group is diseases of the central and peripheral nervous system (15.5%), followed by the group of congenital malformations, chromosomopathies, and genetic syndromes (14.6%), then diseases of the blood and hematopoietic organs (12.8%); all other groups of diseases register a percentage weight on the total of less than 10%.
- **The differences by age are very significant: in children/youth, 40 percent of rare diseases are ascribable to the group of "Congenital malformations, chromosomopathies and genetic syndromes"**, the percentage weight of which decreases to less than 9 percent in adults for whom the modal class turns out, on the other hand, to be the group of "Diseases of the central and peripheral nervous system" (slightly less than 18 percent);
- 1 in 5 of those included in RRMRs with a rare disease is under 18 years of age;
- the phenomenon of health mobility is relevant: the estimated mobility on the data of RRMs is 15% in the overall population and reaches more than 17.8% in minors;



- based on the data currently entered in RRMRs, the number of people with an exempt rare disease in our country is expected to reach more than 530,000;
- according to the most recent studies, the prevalence of rare diseases would be between 3.5% and 5.9% of the population worldwide: the total number of people with rare diseases in Italy would consequently be between 2.1 and 3.5 million, a figure far higher than that of exempt PcMRs alone.

## Research

- growing weight of authorized clinical trials on rare diseases in total clinical trials: from 31.5 percent in 2018 to 35.3 percent in 2022. Authorized clinical trials on rare diseases in 2022 will stand at 230 after the previous year's increase (there were 260 in 2021);
- in 2022, clinical trials on rare diseases in Phase I and II are well above the threshold of 50% of the total (56.9%);
- slightly increasing the weight of active ingredients of biological/biotechnological nature, accounting for 38.1% of the total of clinical trials on rare diseases compared with the previous year (28.7% in 2020). More prevalent in rare disease clinical trials are ATMPs (8.7 percent vs. 3.8 percent), which is a definite upswing from the previous year;
- the number of research projects on rare diseases with the presence of Italian research groups grows - rising from 900 in 2018 to 1,094 in 2022 - but, in percentage terms, the figure confirms the decreasing trend of the previous five years.
- The number of participating centers, the number of people involved and the number of diagnoses refined by the various programs implemented for undiagnosed diseases increase.

## The quality of reference centers

- there are 235 centers of reference for rare diseases identified by regions/PAAAs (4 per 1 million inhabitants); 84 of these are part of at least one ERN (there were 66 until the end of 2021);
- Italy remains in first place in terms of the number of health care providers (HCPs) who are members of ERNs even after the enlargement call, the outcomes of which were announced at the end of 2021: 332 out of about 1,500 (more than 1 in 5 as before), and Italian HCPs are present in all ERNs like France, the Netherlands, and Belgium). The median figure for the presence of Italian HCPs in ERNs is 14 (it was 6 at the end of 2020);

- with regard to cross-border health care, Italy is characterized by a significantly higher level of active mobility: there were 14,604 incoming patients in 2021 (an average of about 9,400 per year over the period 2017-2021) compared to passive mobility (outgoing patients, about 170 per year over the period);
- during 2022, 12 more Diagnostic Therapeutic Care approved by regions/PAs bringing the total number to more than 340 PDTAs defined at the end of 2022.

## **The active participation of people with rare diseases and their association representatives**

- the number of Italian associations of people with rare diseases rises to 718 (1.2 per 100,000 inhabitants);
- 15 regions/PAAAs reporting that they provide for the presence of representatives of associations of people with rare diseases in regional-level participatory bodies on rare diseases;
- 3 representatives of people with rare disease are members of the "Coordination Center on Neonatal Screening" provided for in Article 3 of Law No. 167 of August 19, 2016 "Provisions on mandatory neonatal diagnostic tests for the prevention and treatment of hereditary metabolic diseases";
- one representative of people with rare disease is a member of the national coordination center of territorial ethics committees provided for by Law No. 3 of January 11, 2018 "Delegation to the Government on clinical trials of medicines as well as provisions for the reorganization of health professions and for the health management of the Ministry of Health"
- one representative of people with rare disease is included among the members of the SNE Working Group;
- two representatives of people with rare diseases are included among the members of the National Committee for Rare Diseases.

Also to be recorded positively is the fact that, as of the end of 2022, there are 16 regions/PAAAs that have included the topic of rare diseases within the general health planning tools (in force or in the process of approval in 2022) or that have defined a Regional Rare Disease Plan.

The other side of the coin is represented by the critical issues, some of which are also mentioned above, that persist, such as the long lead times for implementation of measures related to people with rare diseases and the territorial inhomogeneities in access to health, social and social services of which are exemplified by:

- the inhomogeneity in the geographic distribution of Italian hospitals participating in ERNs: 7 Regions/PPAAs have no centers participating in ERNs and 2/3 of the hospitals participating in at least one ERN are located in northern regions. This is also not irrelevant in light of the document reorganizing the National Rare Disease Network and the potential role within it of the so-called "centers of excellence" (the reference centers participating in ERNs);
- The uneven geographic distribution of centers eligible to prescribe advanced therapies (ATMPs);
- the problem of lack of affordability of ATMPs that seriously jeopardizes, for people with rare and ultra-rare diseases, access to treatments that have proven to be of enormous clinical benefit;
- the difficulty of access to care as evidenced by the data on health mobility, especially of children with exempt rare disease highlighted by RMRs
- the still incomplete activation of expanded newborn screening as per Law No. 167/2016 and the failure to update the panel of diseases to be included;
- the failure to define the implementation measures of the specific measures to support research on rare diseases and the development of orphan medicinal products and the solidarity fund for the support of the work of care and assistance of people with rare diseases provided by Law No. 175/2021;
- the failure to define the Diagnostic Therapeutic Care Pathways of people with rare diseases in some territories and the diversity of models adopted for definition;
- the still partial coverage of the entire population of people with rare diseases exempt from some of the Regional Rare Disease Registries.

The intervening recent approval of the National Plan for Rare Diseases 2023 - 2026, mentioned above, represents, on the one hand, an important milestone (also due to the attention devoted much more extensively than in the previous plan to the issue of treatments, pharmacological and otherwise), long awaited by the community of PcMRs, but at the same time it represents a new starting point that now requires to be declined operationally by identifying the system of responsibilities, the timeframe for implementation, the necessary resources and the expected results from "MonitoRare" over time.





## Conclusions

These past few years have seen an acceleration on many issues pertaining to rare diseases. After a long period of building and planning, we have come to achieve a number of goals that have imprinted further change on the system. This change must, in the coming years, lead to a grounding that truly impacts the daily lives of people with rare diseases.

On the one hand, we have a Plan, recently dismissed by the State-Regions Conference; a law; extensive neonatal screening which is an European excellence; the highest number of HCPs members of ERNs in Europe; a network built thanks to a ministerial decree and revised together with the NPRD update; approved treatments in numbers equal to the European average. On the other hand, some people with rare diseases complain of a lack of early diagnosis, difficulties in continuous and structured care, especially in transition, a lack of services capable of supporting the needs of families, progressive impoverishment due to rising expenses, lack of recognition of social benefits, scarcity of research on less pharmacologically attractive diseases, and difficulties in finding information, including on research and clinical trials; this is compounded by a jagged picture on the provision of LEPs- Essential level of social services , on which there is still no national guidance, as well as little attention to the peculiarities of work and school placement.

Some of these problems reported by families could be solved with a different organizational arrangement that is more attentive and close to the needs of families. The introduction, for example, of some simplifications during the COVID (online Therapeutic Plan approval, dematerialized prescription, teleconsultations) as well as some simplifications at work (the granting of smart working for frail people was one of the examples) were welcomed with a sigh of relief: it is a pity that many of these measures were not given continuity and therefore what was "granted" was in most cases withdrawn.

There is a need for the specificity of rare diseases to be increasingly understood and protected; there is also a need for words to be followed by deeds. Families have daily and immediate needs; they cannot always be told that changes take time. The costs to be incurred to ensure a decent life for people with rare diseases impoverish households day after day; this also leads to psychological issues (depression, anxiety, anger) that greatly impact families. Last year's conclusions are, unfortunately, still dramatically true, as both Istat data and our surveys show.

Law 175 talks about quality evaluation of centers. We should give an award to all those doctors and clinicians whose humanity overcomes procedural pitfalls while remaining humane and compensating for bureaucratic difficulties with their empathy. We are grateful to them, as toward all those who strive every day to ensure our services and care. But at the same time we feel the need to see procedures innovated that aggravate daily difficulties, aiming for greater integration at all levels, avoiding rounds and peregrinations from office to office.

The most felt problems are those that impact the gray area that exists between health care and social support. The separation of responsibilities between the Ministry of Health and the Ministry of Labor and Social Policy, with funds that cannot be integrated but above all with a lack of structured interchanges, does not help the construction of a support network around families.

This is one of the most heartfelt challenges for families.

Then, of course, the big issues remain.

We need research: we need careful policies to give tax relief, such as those provided by L. 175 but still not implemented and such as those planned with the revision of the European Regulation. But also improved knowledge of lines of research and also of "failures," optimization of dedicated resources, transparency on results achieved. Research should result in clinical trials, which also ensure early access for many patients without other hope and should be facilitated-as the reform regarding Ethics Committees is trying to do. We have put a lot of effort in recent months to ensure that patient representatives sit on the Committees who can make explicit what the community feels are indispensable needs. Not in all cases have our suggestions on the criteria for representation been taken up, but some steps in this direction have been taken, and we especially thank Regione Lombardia for giving us a way to work with the various representatives on this.

There is a need for early diagnosis. The diagnostic pathway is still too long, exceeding an average of 4 years. Expanded newborn screening, omics techniques, training in diagnostic suspicion: these are just some of the many ways through which early diagnosis can be achieved.

In this area, too, there are many obstacles yet to be overcome: very long times for inclusion in the SNE-extended newborn screening panel; lack of provision in LEAs - Essential Levels of Assistance and therefore in the rates of laboratory tests necessary for diagnosis; need for certified and accurate laboratories; scarcity of physicians able to interpret genomic investigations correctly; lack of specific preparation and overview in many physicians and specialists, who refer patients from one point to another without trying to see the complex of symptoms with the support of several colleagues. A separate note for people who are stationed in this system for very long years without finding a way out: there is a need to optimize everyone's efforts, with a common and shared program that can guarantee a point of access, a multiprofessional vision, specific examinations and the return of a diagnostic suspicion in fair and acceptable time. At the European level, the focus on early diagnosis and non-diagnosis is very high.

In all this, we must not lose sight of the ethical issue: changes in diagnostic possibilities, major scientific advances, are reaching degrees and specifics not foreseeable until recently. Careful discussion must be had about the pros and cons of each choice, especially for diseases with onset (certain or probable) in adulthood. Critical thinking needs to be solicited; we have begun, with Telethon, to start putting some pieces in place as part of the RINGS project. But a long way still needs to be done. Also crucial in these issues is the role of information, which is often "disinformation" instead. These are issues that require to be handled like depleted uranium, not thrown on the front page with approximations that are embarrassing to insiders, but gripping to the public. Covid should have taught us something in this regard.

When therapies are approved, there is a need for them to get as quickly as possible to patient availability. The system is very complex, but everyone can do his or her part to make the process faster: by composing increasingly complete dossiers, by providing administrative pathways before there is final approval (even the National Plan talks about Horizon Scanning), by facilitating with careful planning the inclusion in the Regional Repository, by facilitating the purchasing pathway of the centers where they exist. So many little pieces that must work in unison, sometimes in parallel and sometimes in sequence, like the mechanisms of a precision clock.

Therapies, to date available for only 5 percent of diseases, are not enough. For those who have none, we need habilitative and rehabilitative treatments that go beyond the logic of "blocks" of 10, 20, designed for those with temporary pathologies. What is needed is an intake that we call "holistic," which encompasses the whole path of the person and goes beyond the ability of each person to be able or not to find the best paths, and then accompanies in the various stages with strong support and coordination between offices that avoids too many turns, as we wrote above. Psychological support should become the practice, both at the time of diagnosis and in the stages of the bumpy road thereafter. But we need to have a stroboscopic view, thinking about the issues of access and attendance at school (for those who have therapies and not a nurse, a cognitive disability and not a support teacher, physical needs and not a personal caregiver), the real possibility of access to a job (last year we published our position on this issue, with proposals for improving Law 68), the needs of a caregiver too often confined at home or relegated to caregiving with no options.

We ask for special attention to a topic that is very important to us, which has also been included in the National Plan: palliative care. Fundamental to accompany to an improvement in the quality of life of many people and children with rare diseases, still to be fully developed at the territorial level and to be untied from the common meaning related to an end of life.

We need institutional information, from scientific sources, accessible and cross-cutting. We also need training, everyone: from patient representatives, to be increasingly incisive at the tables in which they are involved; to clinicians, to improve diagnosis and care; to researchers, to finalize research to concrete needs; to representatives of institutions, to understand the complexity of the problems and find administrative solutions; and to all health, social, and social workers who impact with people with rare diseases, to ensure the best possible care.



Much has been done, much more remains to be done.

As always, the Federation will do its part, putting together pieces of which this Report is an important example, serving as a support and stimulus to the reasoning we will all do together.

And as usual, the Report is dedicated both to all people with a rare disease and to the many people and their families who prove every day, by their lives and their work within the Associations, that a rare disease breaking into our daily lives is one of the many opportunities that life gives us to improve this world and make it more equitable and just for all.

Ad maiora



## THE INDEX OF THE REPORT

PREFACE

INTRODUCTION

EXECUTIVE SUMMARY

THE WORKING METHODOLOGY OF THE NINTH REPORT

### A. RARE DISEASES: A SYSTEM CHALLENGE

1. The resource node in support of people with rare diseases: from financing the national health system to social funds and social health
2. The Italian regulatory framework in the European context
3. People with rare diseases in Italy

### B. THE ITALIAN PANORAMA

1. Prevention and diagnosis
2. Follow up and patient journey
3. Treatments
4. Research
5. Training
6. Information
7. Empowerment of associations

CONCLUSIONS

BIBLIOGRAPHY

LIST OF ACRONYMS AND ACRONYMS USED

ASSOCIATIONS AFFILIATED TO UNIAMO

PHOTO PROJECT "RARE LIVES"

THANKS

Number of pages: 436

## THE INSTITUTIONS INVOLVED

**The MonitoRare Report was created with the contribution of data from:**

**The regional coordinators for rare diseases** (Abruzzo, Basilicata, Campania, Emilia-Romagna, Friuli-Venezia Giulia, Lazio, Liguria, Lombardy, Marche, Molise, PA Bolzano, PA Trento, Piedmont, Puglia, Sardinia, Sicily, Tuscany, Valle of Aosta, Veneto)

**Superior Institute of Health** - National Center for Rare Diseases

**AIFA** - Italian Medicines Agency

**Ministry of Education and Merit** - IV Disability Office. Hospital school and home schooling. Integration of foreign students - Directorate-General for students, integration and participation

**Ministry of Health** - Office 2 Recognition and confirmation by IRCCS - General Directorate of Research and Innovation in Healthcare

**BBMRI.it** - Biobanking and BioMolecular resources Research Infrastructure Italy

**Telethon Foundation**

**Orphanet Italy**

**Military Pharmaceutical Chemical Institute** - AID Defense Industries Agency Production Unit

**Simmesn** - Italian Society for the Study of Hereditary Metabolic Diseases and Neonatal Screening

**SIPPED** - Italian Society of Pediatric Psychology



**ÜNIAMO**  
Federazione Italiana Malattie Rare

Via Nomentana, 133  
00161 Roma  
[www.uniamo.org](http://www.uniamo.org)  
[segreteria@uniamo.org](mailto:segreteria@uniamo.org)

Dona il 5x1000  
C.F. 92067090495  
IT53M0306909606100000010339