MonitoRare Report 2020

Executive Summary

2019 opened positively for the community of people with rare diseases with the announcement, in the second half of February, by the then Minister of Health Giulia Grillo, of the establishment of a working group, in which RD community representation was also envisaged recognizing this fundamental role of advocacy to UNIAMO, for the elaboration of the second National Plan for Rare Diseases.


Among the tasks entrusted to the Working Group also the identification of indicators and tools for monitoring of the actions envisaged by the NPRD itself, also with a view to verifying the NPRD 2013-2016. The working group was also entrusted with the function of carrying out the tasks of coordination and monitoring of the previous Coordination and Monitoring Body for the development of ERNs (Ministerial Decree 27.07.2015 referred to in Art. 13 paragraph 2 of Legislative Decree 4/3/2014 no. 38) that expired in 2018 and in which, up to that moment, the representatives of the people with rare disease were not involved.

More than a year later, however, there is still no tangible evidence of the results of this work: to date, in fact, there is still no evaluation of the 2013-2016 NPRD, regardless of what UNIAMO has done in recent years through the Monitorare report and there is still no trace of the new national planning, even if it must be taken into account that the epidemiological emergency from COVID-19 also led to the interruption of the workgroup’s activities.

However, not everything has stood still: on the legislative side, in fact, the discussion of the draft law on rare diseases entitled “Regulations for the support of research and production of orphan medicinal products and care of rare diseases. C. 164 Paolo Russo, C. 1317 Bologna, C. 1666 De Filippo, C. 1907 Bellucci and C. 2272 Panizzut " is still ongoing.

In terms of newborn screening, it should be positively mentioned the enlargement to neuromuscular diseases of genetic origin, severe congenital immunodeficiencies and lysosomal storage diseases occurred with the 2019 Budget Law with an endowment of an additional 4 million euros. Furthermore, in February 2020, the so-called Noja amendment intervened, during the conversion of the Milleproroghe Law Decree
of 30 December 2019 which, by amending Law no. 167/2016 established a specific deadline (end of June 2020) by which the Ministry of Health should have completed the process of revision and expansion of the panel of diagnosable diseases through screening and provides for an increase in funds equal to 2 million euros for the year 2020 and further 2 million for the 2021 for early diagnosis through screening.

The progressive implementation of regional systems for extended neonatal screening (ENS) of hereditary metabolic diseases as regulated by Law no. 167/2016 and subsequent amendments and by the Decree of the Ministry of Health of 13 October 2016 "Provisions for the start of newborn screening for the early diagnosis of hereditary metabolic diseases" was one of the main areas of commitment of the Regions / PPAA which found in the Coordination Center on neonatal screening, an effective place and system growth tool that made possible that at the end of 2019 the regional ENS program is in the process of being finalized also in the last 3 Regions that had not yet activated it. In Lazio and Tuscany, in particular, a pilot program has started for the enlargement of the ENS to the SMA (Spinal muscular atrophy) since the second half of 2019.

The national ENS program represents a flagship of the Italian rare diseases network as the updated data on the comparison with the other Member States of the European Union confirm. Other strengths of the national rare diseases network are represented by the organizational model of the regional networks of rare diseases, in accordance with the national policy, and the excellence of various centers of expertise also confirmed by the data on participation in the European Reference Networks; the treatment accessibility also through the different paths defined over time; the surveillance and monitoring system implemented on a regional / interregional and national basis and the existence of multiple institutional reference helplines for rare diseases.

For the more specific aspects, this year too there are many "food for thought" emerging from the reading of the “MonitoRare” report leading to subsequent in-depth analyzes. In these first pages, we grapple with the arduous task of trying to effectively summarize the photography of this sixth edition of the report: we try with the sole intention of offering to our reflection some elements which, more than others, assume a strategic role for the future of care for people with rare disease (PLWRD) and their families internationally, nationally and locally.

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

- Treatment accessibility
- the total number of orphan medicinal products available in Italy at the end of 2018 was 109 (out of 135 authorized by the EMA). There were 17 new authorizations by AIFA in 2018, a slight increase compared to the average figure for the three-year period 2015-2017 (equal to 15);

- consumption of orphan medicinal products (OMP), from 2014 to 2018, increased by 43.5% in absolute terms and by 66.6% in relative terms on the total consumption of medicines;

- expenditure on orphan medicinal products increased from € 1,060 million in 2014 to € 1,781 million in 2018 (+ 68.0%): in the same period of time the incidence of expenditure for orphan medicinal products on the total pharmaceutical expenditure rose from 5.3% to 8.1% (+ 52.5%);

- the number of treatments for rare diseases included in the list of Law 648/1996 increased from 13 in 2012 to 29 in 2019;

- requests for access to the AIFA fund (pursuant to Law 326/2003, Art. 48) increase exponentially from 82 in 2017 to 991 in 2019 (they were just 20 in 2016), with an approval rate for requests rising from 65.1% in 2017 to 79.4% in 2019 (the number of beneficiaries rises to 1,751 including also rare cancers).

-Access to information

- 18 Regions / PPAAs have an institutional information system dedicated to rare diseases, 16 of which in the form of a structured telephone helpline (over 11,000 PLWRD with which they came into contact in 2019). Recently also the Service of Listening, Information and Guidance on rare diseases of UNIAMO has joined the European Network of Rare Diseases Help-lines which includes 25 help-line services at European level, adding to the Rare Diseases Help-line of the National Rare Diseases Center of the National Institute of Health (CNMR-ISS), to the Coordination of rare diseases in the Veneto Region and the other two help lines that joined the network in 2018, namely the Rare Disease Listening Center of the Tuscany Region and the Listening Center for rare diseases in Piedmont and Valle d’Aosta;

- At the beginning of 2020 the new inter-institutional portal was launched - www.malattierare.gov.it - result of a great collaboration between the Ministry of Health and National Institute of Health and set up with the economic support of the Ministry of Economy and Finance and the technical support of the State Printing Office and Mint which in the recent emergency from COVID-19 has already proved to be one of the most used sites for the search for information by people living with rare disease.

-Education and training

1 2019 data not available yet
17 Regions / PPAA have included the topic of rare diseases in the contents of the regional / provincial CME training;

17 PPAA Regions have included the topic of rare diseases in the training plans of the local Health Authorities of the region / PA;

the number of training events dedicated to rare diseases is growing. The number of CME courses dedicated to rare diseases reaches 73 in 2019 from 67 in 2018 (there were on average forty in the previous 3 years) of which 6 in FAD mode -distance learning, keywords: rare disease / s ;

-Newborn screening and clinical laboratories

in the five-year period 2014-2018 there is a marked growth in coverage of extended neonatal screening for hereditary metabolic diseases, increased by more than 50 percentage points (from 43.1% in 2014 to 98.3% in 2018), even though the number of pathologies present in the screening panel in the different Regions still present some differences due to the different degree of activation on the subject prior to Law no. 167/2016 as well as for the different speed of implementation of the provisions of the new legislation;

constant growth in the last five years in the number of rare diseases tested in Italian clinical laboratories included in the Orphanet database which, in the face of substantial stability in the number of laboratories, almost doubling: from 1,165 in 2014 to 2,282 in 2019 (+ 95.9%);

-The quality and coverage of surveillance systems

the coverage of the regional registers of rare diseases (RRRD) increases: the estimated prevalence on the population of the people included in the RRRD as of 31.12.2019 rises to 0.61% (0.72% in minors under 18) from 0.30% of MonitoRare 2015

for the first time, the data relate to all the rare diseases referred to in Annex 7 of the Prime Ministry Decree DPCM of 12.01.2017: based on the over 345,000 PLWRD registered in the RRRDs at the end of 2019 (+ 35,000 units compared to the previous year ) the most present group is that of diseases of the central and peripheral nervous system (16%), followed by the group of congenital malformations, chromosomopathies and generic syndromes (14%), then diseases of the blood and hematopoietic organs (13%); then diseases of the visual apparatus (10%), metabolism (8%), the osteo-muscular system and connective tissue (7%) and blood circulatory system (6%). The other groups of pathologies do not exceed the 5% threshold;

Based on RRRDs data, the number of people with rare disease exemption in our country could exceed 600,000 units with an estimated prevalence of 1.0% of the population;

1 in 5 people with the disease is under the age of 18;
the differences in age are very significant: in children / young people almost 40% of rare diseases are attributable to the group of “Congenital malformations, chromosomopathies and genetic syndromes”, whose percentage weight is reduced to less than 10% in adults for whom the modal class is instead the group of “Central and peripheral nervous system diseases” (almost 20%);

research

- the weight of authorized clinical trials on rare diseases on the total of clinical trials still increases: from 20.0% in 2013 to 32.1% in 2019 (+2% compared to 2018), a figure made even more significant by the fact that in the last year there was a further increase in the absolute number of studies (216 in 2019 compared to 117 in 2013);

- practically 6 out of 10 clinical trials related to rare diseases (58.3%) in 2019 relate to Phase I or II studies (48.9% in 2018);

- the weight of the biological / bio-technological active substances slightly increases, they represent 31.5% of the total number of clinical trials on rare diseases in 2019 (compared to 29.4% in 2018), while active substances of a chemical nature settle at 59.2% (compared to 58.5% in 2018);

- the downward trend of the presence of Italian research groups in the projects related to rare diseases included in the Orphanet platform continues: 13.6% in 2019 (compared to 15.8% in 2018);

- 380 the current research projects on rare diseases conducted by Institutes for Hospitalization, Health Care and Research (IRCCS) in 2019 (12.6% of the total, up from the previous year) for a value of over 15 million euro (13.5% of the total, up from the previous year);

- 7.7 million euros (16.3% of the total) the resources of targeted health research invested in projects for rare diseases (an increase compared to the previous year);

- the number of participating centers, the number of people involved and the number of diagnoses improved by the various programs implemented for undiagnosed diseases increase

- 7 of the 12 projects funded by the AIFA 2017 call for independent research are related to rare diseases (58.3%). For the 2018 call, 105 projects were submitted, of which 74 on rare diseases (70.5%) 53 of which were admitted to the evaluation phase by international auditors (out of 68; 77.9%);

-the quality of the centers of competence

- there are 221 centers of reference for rare diseases identified by Regions / PPAA (3.7 per 1 million inhabitants);
Italy ranks first in terms of number of health care providers (HCPs) members of ERNs (European Reference Networks): 189 out of 953 (19.8%) and Italian HCPs are present in all ERNs except one (only France, Holland and Belgium are present in all 24 ERNs). On average there are 6 Italian HCPs for each ERN;

over 240 Diagnostic Therapeutic and Care Paths defined at the end of 2019.

- The active participation of people with rare diseases and their associative representatives
  - the number of Italian organisations of people with rare disease rises to 615 (1 per 100,000 inhabitants).
  - The joint work promoted by UNIAMO with patient organisations and sector institutions led in 2019 to the development of two important reference documents for PCMR:
    - a position paper on extended newborn screening;
    - a position paper on institutional help lines for rare diseases.
  - as mentioned above, a representative of people with rare disease has been identified among the members of the new Working Group in charge of the updating of the NPRD Rare Disease National Plan and which also takes on the role of the Coordination and Monitoring Body for the development of ERNs;
  - 17 the Regions / PPAA which provide for the presence of representatives of RD POs in the participating bodies at regional level;
  - Increase in the number of people involved in the 24 European patient advocacy groups (ePAGs) and the participation of representatives of Italian PLWRD: in 2019 they were 50 out of 306 overall (16.3%) compared to 36 out of 263 (13.7%) in the previous year; it also increases the number of ePAGs in which there is at least an Italian representative (20 of 24, 83.3% vs. 66.7% the previous year);
  - the “ePAG Italy” coordination group was created, with the support of the UNIAMO Federation, which brings together 46 representatives of the Italian PLWRD in the ePAGs;
  - 3 representatives of people with rare disease are members of the "Coordination Center on newborn screening" provided for by art. 3 of Law no. 167 of 19 August 2016 "Provisions regarding mandatory neonatal diagnostic tests for the prevention and treatment of hereditary metabolic diseases";
a representative of people living with rare disease is member of the national coordination center of the territorial ethics committees provided for by Law 11 January 2018, n. 3 “Delegation to the Government for 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”.

It should also be noted that, at the end of 2019, 16 Regions / PPAA have included the topic of rare diseases in the general health planning tools (in force or in the process of being approved in 2019) or have defined a Regional Rare Disease Plan.

The effort made by the National Social Security Institute (INPS) deserves a mention in itself focusing on the adequate assessment of the complexity of rare diseases in the commission for the recognition of civil disability. The positive impact of the guidelines and technical-scientific communications drawn up on the subject by INPS - several of which in recent years - is evident from the data relating to the recognition of civil disability for rare diseases in the 2015-2019 period. There are over 15,000 civil disability recognitions (attendance allowance, disability allowance, invalidity pension, accompanying allowance) occurred in the five-year period for the 16 rare diseases considered with an average of just under 3,050 cases per year. The health recognition for rare diseases in the period 2014-2018 represented on average 0.40% of the total.

The other side of the coin is represented by persistent criticalities, such as territorial inhomogeneities in access to health, socio-health and social services of which they are examples:

- the inequalities in the geographical distribution of Italian hospitals participating in ERNs: 8 Regions / PPAAs have no center participating in ERNs and 66.7% (n = 44) of hospitals participating in at least one ERN are located in the northern regions, the 19.7% (n = 13) in the center and just 13.6% (n = 9) in the south;
- the still incomplete activation of the extended newborn screening pursuant to Law no. 167/2016;
- the different degree of regulation of the administration of pharmacological and non-pharmacological therapies in schools subject to specific discipline in 10 Regions / PPAA;
- the lack of respite programs at competent non-hospital inpatient structures for people with rare disease planned or in progress only in 11 Regions / PPAA;
- the lack of definition of the Diagnostic Therapeutic Assistance Pathways of people with rare disease in some territories and the diversity of the models adopted for the definition;
- the lack of adoption of managerial and administrative solutions aimed at evaluating the feasibility of remuneration methods that consider the complexity of the care management of the person with rare disease in the hospital and territorial setting;
- the lack of adoption of the necessary administrative tools to assess the effectiveness, recognize and ensure adequate remuneration of remote consultancy services by the hospitals / centers of expertise.