Rare2030

Foresight in Rare Disease Policy

A knowledge-base summary:

POLITICAL & STRATEGIC FRAMEWORKS

RELEVANT TO RARE DISEASES

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1. INTRODUCTION TO THE TOPIC

Since the 1990s, rare diseases have been a policy priority at both European Union (EU) and Member State (MS) level. A number of countries led the way in the decade leading up to the first European legislative text concerning rare diseases (the Orphan Medicinal Product Regulation of 16 December 1999): Sweden, for example, established the first centres of expertise for rare diseases in 1990 and a rare disease database and information centre in 1999. Denmark established an information centre in 1990 and then centres of expertise for rare diseases in 2001. In Italy, a decree on rare diseases came into force in 2001. And in France, Orphanet was established in 1997.

In 2008 and 2009, two landmark policy documents ushered in a major period of change: the Commission Communication on Rare Diseases: Europe's challenges (2008) [679 final] and the Council Recommendation of 8 June 2009 on an action in the field of rare diseases (2009/C 151/02. Throughout the period 2010-2016, two successive Expert Groups for Rare Disease provided a space for MS representatives, patients, Industry, and independent experts to join the European Commission in exploring avenues for cross-country collaboration around many diverse aspects of the broad 'rare disease' topic. These Groups, the EUCERD and the Commission Expert Group on Rare Diseases, were supported in their activities by two dedicated EU Joint Actions: the EUCERD JA and RD-ACTION, and issued 8 sets of topically-oriented Recommendations (see end of document) representing high-level ('soft law') commitments each country would strive to implement.

Besides the Commission Communication of 2008 and the Council Recommendation of 2009, several other key policy documents and frameworks have played a key role in shaping the current rare disease field (see below). In particular, the rise of the European Reference Networks (ERNs) would not have been possible without the Directive on the Application of Patients' Rights in Cross-Border Healthcare (often termed the 'Cross-Border Healthcare Directive') Article 12 of which outlined the Network concept.

There have been several important successes for the European rare disease community in recent years, not least the realisation -after a decade of planning and preparation- *of* the ERNs themselves, which have a particular relevance for the rare disease field. However, there is no longer an expert group for rare diseases, and no Joint Action to allow cross-country discussion and collaboration on the full range of issues beneath the 'rare disease' heading. Since 2019, the European Joint Programme for Rare Disease Research (EJPRD) has operated a Policy Board, which provides a space for multistakeholder debate around research whilst also involving health ministry representatives. New bodies have been established in place of the older Expert groups with broader remits, such as the Steering Group on Health Promotion, Disease Prevention and Management of Non-Communicable Diseases (SGPP), the EU Health Policy Platform, and the Expert Group on Health Information; however, in each of these, 'rare diseases' sits amongst many other health priorities. The ERN Board of MS is a very important stakeholder body, but its mandate specifically centred on ERNs (as opposed to all issues under the RD 'spectrum'.)

In this relative vacuum, it is important that the implementation of past/existing policies is reviewed. In 2014, the Commission published an Implementation Report on both the Council Recommendation of 2009 and

the Commission Communication of 2008. It concluded that "by and large, the objectives of the Communication and the Council Recommendation have been reached" but acknowledged that "there is still a long way to go". The more recent report from the European Court of Auditors, however, highlighted the lack of concerted attention to the broad rare disease framework in Europe since this time ("the Commission has not taken stock of its progress in the implementation of the EU rare disease strategy since 2014").

For further background on the European Policy frameworks for rare diseases, and all of the above, please see the Overview Report for the State of the Art of Rare Disease Activities in Europe.

2. CONCEPT OF A NATIONAL PLAN/STRATEGY FOR RARE DISEASES

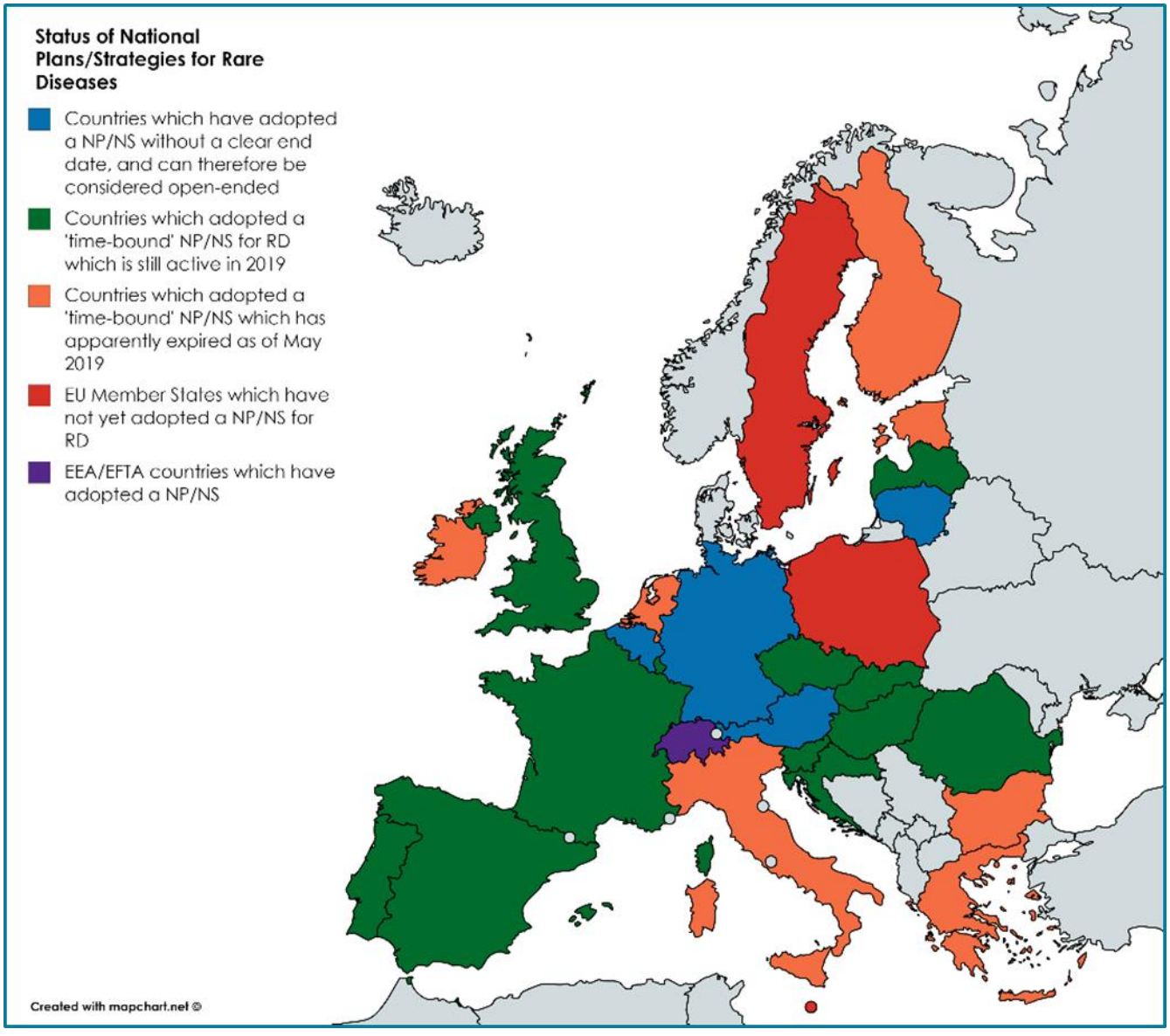
An essential component of political and strategic frameworks for RD is the topic of National Plans or Strategies (henceforth NP/NS). The Council Recommendation of 2009 recommended that MS elaborate and adopt a national plan or strategy for rare diseases "as soon as possible, preferably by the end of 2013 at the latest". This document recommended that these NP/NS should strive "to ensure that patients with rare diseases have access to high-quality care, including diagnostics, treatments, habilitation for those living with the disease and, if possible, effective orphan drugs". They should

- be aimed at "at guiding and structuring relevant actions in the field of rare diseases within the framework of their health and social systems;"
- "take action to integrate current and future initiatives at local, regional and national levels into their plans or strategies for a comprehensive approach;"
- "define a limited number of priority actions within their plans or strategies, with objectives and follow-up mechanisms;"

To support countries in this activity, the EUCERD adopted a set of Recommendations on Core Indicators for Rare Disease National Plans and Strategies. The groundwork for this document was led by the EUROPLAN project and the EUCERD Joint Action between 2008 and 2013. The overall objective of the Recommendations was to enable the capturing of relevant data and information on the process of planning, implementing and monitoring of NP/NS. The resulting Core Indicators highlight important components for a robust and comprehensive NP/NS and their adoption was accompanied by a commitment from Member States to regularly collect this information, based around a number of fundamental questions.

3. STATUS QUO OF NATIONAL PLANS/STRATEGIES FOR RARE DISEASE ACROSS EUROPE

The data for the following sections comes from the Resource on the State of the Art of Rare Disease Activities in Europe. Data for a number of countries is awaiting update; **therefore, these figures may change slightly in the coming months.** At Member State level, there is a great heterogeneity in the state of advancement of national policies, plans or strategies for rare diseases. This map below shows the status quo as of **May 2019.**



3.1. Summary of the Status Quo

- 25 European MS have adopted a NP/NS for rare diseases at some stage
- Most countries adopted a NP/NS with a specific chronological span i.e. are time-bound
- Of the 20 MS which adopted time-bound NP/NS at some stage:
    - 1 (Austria) has since become open-ended (see below)
    - The following 7 countries adopted time-bound NP/NS which, as of May 2019, appear to have ***expired*** and not to have been replaced/renewed: **Bulgaria; Estonia** (a RD Development Plan under the main National Health Plan apparently expired in 2017)**; Finland** (though a new plan is pending approval, after the first plan expired in 2017)**; Greece; Ireland; Italy; Netherlands**
    - The NP/NS for the following 12 countries are apparently still active in May 2019: **Croatia; Czech Republic; France; Hungary; Latvia; Luxembourg; Portugal; Romania; Slovak Republic; Slovenia**; **Spain; UK**
- 'Open-ended' NP/NS: The following countries adopted NP/NS which were not time-bound: **Belgium, Cyprus, Denmark, Germany, Lithuania**. A 'new' addition to this category is **Austria** (which adopted a first NP for the years 2014-18 and since the beginning of 2019 extended this on an open-ended basis, with time-frames for specific actions);
- Three EU MS appear not to have adopted a NP/NS by the end of May 2019: **Poland, Malta and Sweden**

In terms of Non-MS EEA countries and Switzerland: Switzerland has also adopted a National Plan for Rare Diseases.

3.2. Implementation of National Plans and Strategies for Rare Diseases

The Resource on the State of the Art of Rare Disease Activities in Europe (SotAR) collects information from all EU MS via a structured questionnaire. This questionnaire is designed to collect the data to which countries committed to provide via the 2013 Recommendations on Core Indicators (see above). Several questions relate not only to the existence of a NP/NS but to the level of support (financial, in particular) behind the plan or strategy, and the existence -and level of functioning- of a dedicated body to oversee the implementation and/or evaluation of the plan.

On the question of **dedicated funding for the NP/NS**:

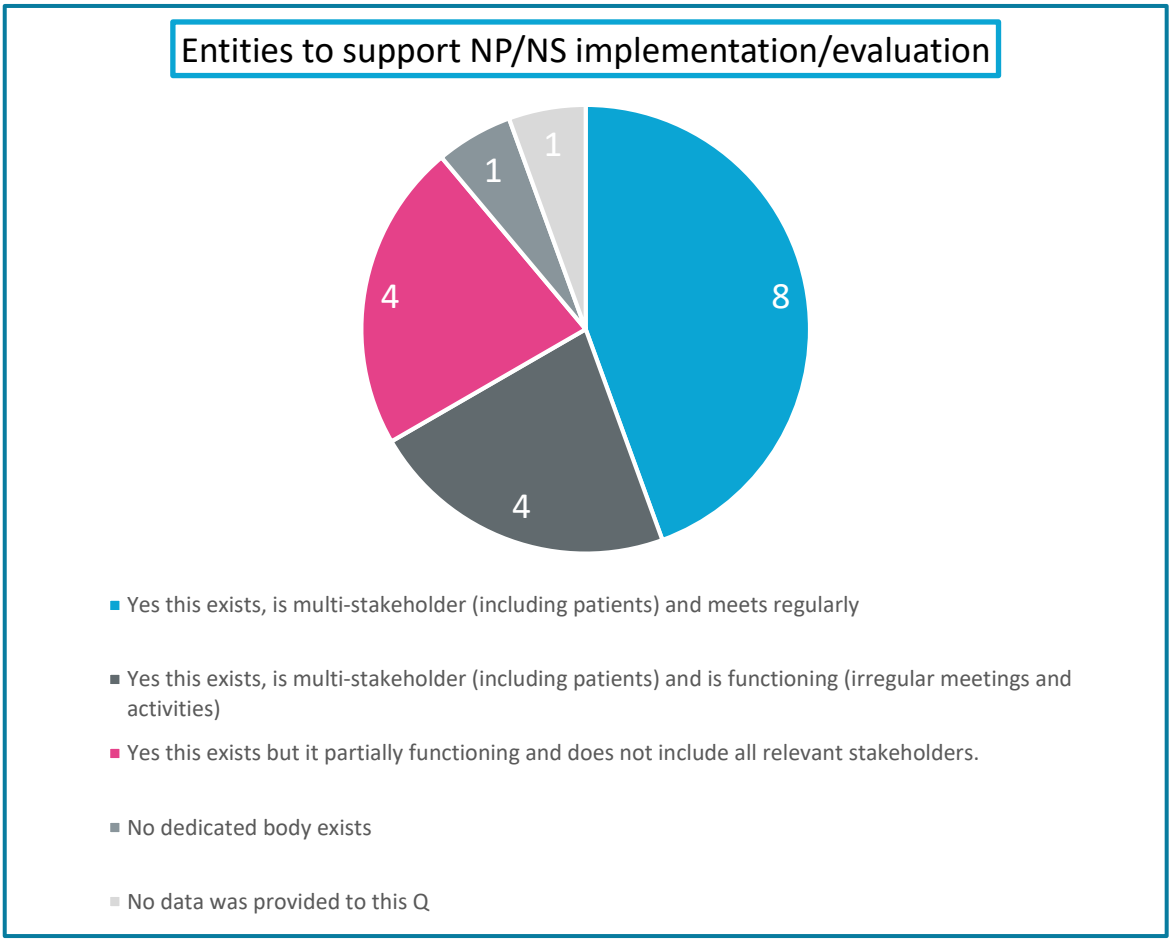
- Many countries noted that funding was available for specific actions mentioned within the NP/NS; however
- Very few countries have dedicated funding set-aside to fund the NP/NS itself, comprehensively:
- Of the 18 EU MS with a still-active NP/NS:

- Only 4 report having dedicated budgets to strategically support the NP/NS implementation:
  - Belgium (stipulated 15M Euros per year)
  - France (funding dedicated to the CoR – no figure provided)
  - Romania (stipulated just over 1.009 Million Euros per year)
  - Slovak Republic (stipulated 240,000 Euros per year)

It is difficult to obtain accurate and unequivocal data on the extent to which countries are investing to support their NP/NS implementation.

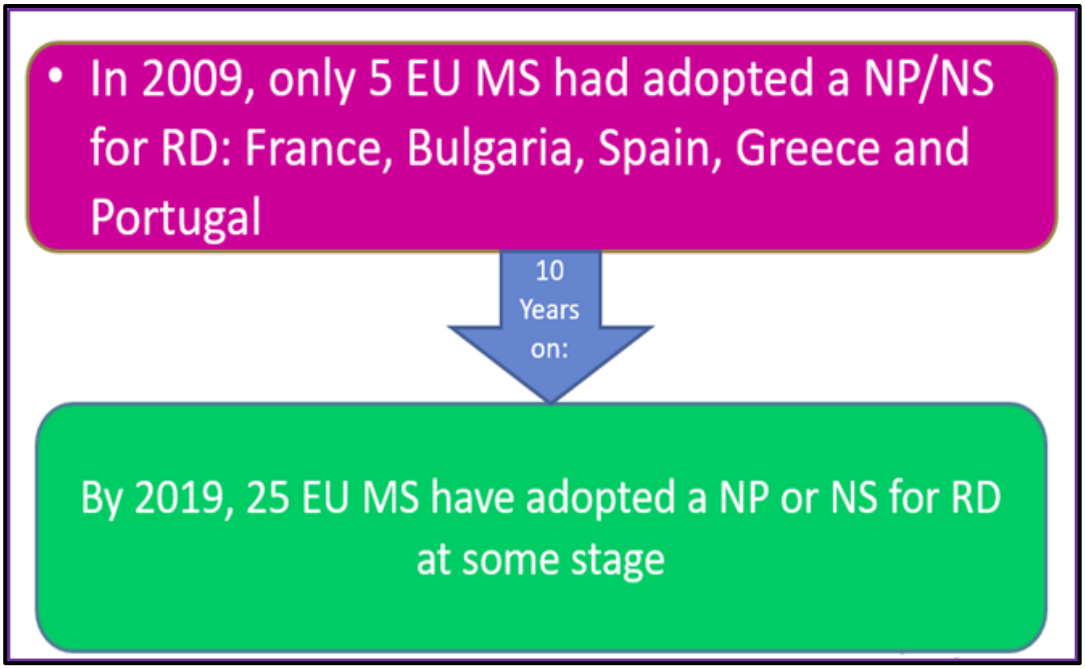
The EUCERD Recommendations on Core Indicators for Rare Disease National Plans and Strategies place emphasis on the need for a **dedicated multistakeholder body to support NP/NS activities**. The precise function of such a body depends upon the level of maturity of the national activities, but could include the following: shaping the development of a NP/NS (i.e. overseeing the drafting process); overseeing the NP/NS implementation, once adopted; and evaluating existing or past NP/NS to support the generation of new Plans or Strategies.

The Core Indicators, whilst not delving into the granularity of possible roles for such a body, nonetheless emphasise that such entities should be multistakeholder (including patients, as well as policy-makers, academics, clinicians, and other relevant experts) and be *functional* as opposed to a 'token' body (e.g. should meet regularly). The figure below shows the status quo in the 18 MS with **currently-active** NP/NS:



3.3. Evolution of national plans and strategies for rare diseases – European trends over the past decade

- As of 2009, 5 EU MS (Bulgaria, France Greece, Portugal and Spain) had adopted a national plan/strategy for rare diseases.
- By 2019, 25 EU MS had adopted a national plan/strategy for rare disease at some stage; this increases to 26 if one includes all EEA countries and Switzerland
- France is now in its 3rd National Plan



However: the number of expired NP/NS which have yet to be renewed is slowly increasing: as of July 2018, 6 time-bound plans had expired without replacements (and this included Austria and Lithuania, both of which are now classed as open-ended), whereas currently the figure is 7. Only 2 NP/NS for which a set time period was established appear to reach beyond 2020 (Luxembourg and France). It is often the case that evaluating and renewing NP/NS is a lengthy process, leaving countries without active plans or strategies for extended periods of time. **At this crucial juncture, it is imperative that a renewed focus is placed on the National Plans and Strategies for Rare Diseases in Europe**, in order to:

a) evaluate the extent to which existing NP/NS have actually been implemented in European countries;

b) encourage countries to adopt their 2nd and 3rd NP/NS, to maintain the much-needed national focus and momentum on rare diseases; and
c) define the key objectives and content for this next generation of NP/NS, by identifying good practices which have yielded results in particular countries/regions, assessing their transferability to other countries/situations, and agreeing new issues and topics which should be addressed via robust Plans and Strategies for the coming years.

4. WHAT OTHER POLICY AREAS INFLUENCE RARE DISEASES AND RARE-DISEASE POLICY-MAKING?

Rare disease policy-making lies at the crossroads of a multitude of policy areas, rendering the development of comprehensive policies challenging. Due to the diverse nature of conditions included under the RD definition, many policies and programmes include rare diseases. For example, RD are present in cancer policies as rare cancers belong to both categories (31): indeed, for the area of rare cancers, the main challenge is to ensure that rare cancers do not fall between the two stools of 'rare diseases' and 'cancers'. Following on from the 2009 *Commission Communication on an action against cancer*, the European Partnership on an action against cancer (EPAAC), worked to raise awareness of the challenges faced by rare cancers and to insist on the need for tailored policies. The work on rare cancer policy has continued under the Joint Action on Rare Cancers (2016) which, amongst other work streams, strives to build a coherent policy framework for the management of rare cancers in Europe, and notably structures its work around the two rare-cancer focused European Reference Networks (ERN EURACAN, ERN PaedCan). The global effort towards universal healthcare is also a major influential factor for rare disease policy and the emphasis on equity, quality, responsiveness, efficiency, resilience should very likely contribute to a better inclusion of rare diseases in national health policy planning (cf. UHC2030).

A number of disability policies also include rare diseases and shape part of the rare disease political framework (33); for example, the European Union disability policy includes measures for rare disabilities (EURORDIS 2011). Genomic and precision medicine programmes and initiatives (2; 3; 18) are also policy areas of interest to rare diseases. In addition, the specificities of rare diseases, implying the need for exchange of information and innovative data management/discovery techniques, make eHealth policies and the legislation around the use of artificial intelligence for medical and healthcare purposes, critical. This is particularly important as regards to the development of tools and services that have a high potential of promoting rare disease research, care and treatment opportunities (8).

In addition, the quality of healthcare and policy actions for rare diseases is clearly linked to the global and national economic context and larger economic policies, and thus is significantly influenced by budget

constraints, which might act as a hurdle to rare disease policy development (9; 10). In the future, we are sure to see a mutual influence and interaction between rare disease policy and the UN Sustainable Development Goals, which are both concerned with ensuring that no citizen of the world is left behind.

(For a schema showing adoption schedule for EU MS, please see page 11);

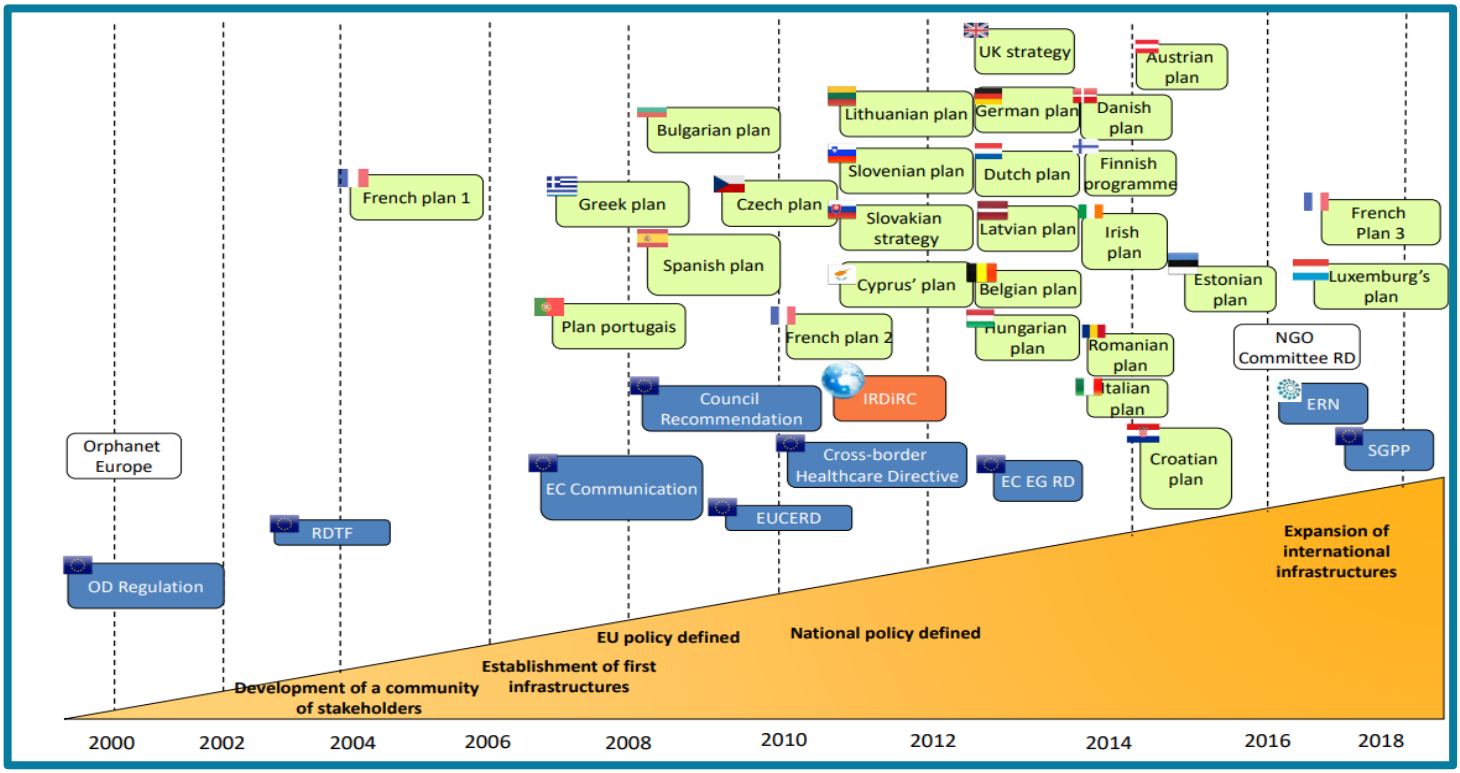
5. RESULTS OF THE RARE 2030 LITERATURE REVIEW

5.1. Observed trends in Europe

Firstly, the most striking trend at the European level is the **emergence of rare diseases as a concept** (13), and the **official recognition of the challenges in the field of rare diseases**, leading to the **development of a European policy framework with an impact on the emergence of rare disease policies in Member States**. Indeed, the first legislative text in the field of RD, the Orphan Medicinal Product Regulation of 1999, was followed by the creation of the Rare Disease Task Force in 2004 and the multi-stakeholder drafting of the two first keystone documents at European level: the Commission Communication in 2008 and the Council Recommendation in 2009. These texts, and the policy support mechanisms provided in the form of the EUCERD/Commission Expert Group on RD and associated Joint Actions, have proven to be critical in e**nhancing policy change and the adoption of RD legislation at EU and Member State level** (20; 21).

They have **provided the rare disease field with increased visibility**, the assurance of support and guidance at the EU level, and a basis for cooperation. Furthermore, the **European Commission has actively shaped the policy field** and the implementation of legislation by maintaining, and even increasing, the priority level of the issue over the years (21,28) and through its active **financial and administrative support of projects dedicated to the advancement of RD research, information and structuration of networks**. Some authors even mention a process of harmonisation taking place and **a certain relative policy coherence** in the region with common definitions and legislations as well as **transnational actions** (16; 30). The European Commission has also contributed to the **structuration of rare disease research policy** via its EU Framework Programme for Research and Innovation. Indeed, under the Seventh Framework Programme for research, from 2007 to 2013, €620 million was allocated to over 120 collaborative research projects on rare diseases, and the EU commitment on this path continues with the Horizon 2020 programme (5; 7). This trend continued with **European support to the International Rare Disease Research Consortium and its ambitious goals** (from 2012) with the support of the EC and the NIH.

Nevertheless, despite this relative unity, **differences exist between Member States and some are further ahead of others in terms of national implementation of rare disease legislation** (21; 28). For instance, **France is often cited as a model,** having adopted the first comprehensive national plan for rare diseases in the world in 2004; today, France is implementing its third national plan and is seen as an instrumental actor and a leading figure for European policy on this matter (5; 17; 28; 30). This suggests the existence of a **trend of rare disease policy emerging as the result of exchange of experiences at national level, notably through a certain number of fora at European level**, such as the Rare Disease Task Force, the European Union Committee of Experts on Rare Diseases, the Commission Expert Group on Rare Diseases, and the current Steering Group on Prevention and Promotion of Health. The supportive role of the EC has facilitated this trend, as has the **willingness of stakeholders, including national competent authorities, to share experiences**.



Moreover, over the years more space has been allocated for the **involvement of rare disease patients and advocacy groups in policy decision-making**. Local stakeholders are cited and recognised as key players and **drivers for the implementation of policies** (22). Indeed, the role of patients and patient advocates in the political and economic system over time has evolved (35) and they were increasingly included in strategic, multi-stakeholder committees and expert groups such as the RDTF, EUCERD, and Commission Expert Group on RD (12; 19; 21). Their role is gradually becoming more central to the decision-making process, **making the patient voice integral to the policy-making process** (1). This has ultimately led some advocates to play the role of broker between patient organisations, national and supranational structures, the media and health services (35).

5.2. Observed trends at the global level

For a summary of national -and regional- policy frameworks beyond Europe, see the 2018 Overview Report for the State of the Art of Rare Disease Activities in Europe **(pages 23-45).**

When examining supranational bodies and their approach to rare diseases, one can note the **growing interest and official recognition of the challenges posed by rare diseases,** which are now included in the **health priorities of global entities such** as the WHO. Examples include the recent mention of rare diseases at the 71st World Health Forum and the **establishment of a NGO Committee for Rare Diseases at the United Nations**. Moreover, **actors in regions such as Latin America and Asia-Pacific are currently in the process of developing their national and regional frameworks,** exchanging experiences in the process. Nevertheless, regions like Russia or Africa lag behind even within the more cohesive regions, thus a **discrepancy regarding rare disease definitions and implementation of policies is observable** (16; 21; 26).

On a global scale, some authors also highlight the trend of the **emergence of collaborative networks** in the last ten years. Such **organisational models tend to embrace a wide range of stakeholders** such as decision-makers, healthcare professionals, patient organisations and private entities such as biopharmaceutical laboratories. This multidisciplinary approach allowing a variety of perspectives to meet has gained momentum recently and seems to **garner support as a means to inform policy-making.** In addition to such horizontal networking, a **vertical form of networking** has been highlighted, with links made between players at the local, regional, national and supranational level (15).

Linked to such phenomena is the fact that **organisations have displayed a tendency to unify and gain an international dimension in order to increase their influence at the international level** (5). Indeed, it is stated that the **specificities of rare disease policy require actions at the highest institutional level** and a maximum level of international cooperation in order to set the agenda and promote action in the field (6). There seems to be a growing emphasis on *regional* collaboration, as evidenced by transnational initiatives, which help to promote the case for rare diseases in areas such as the Asia-Pacific region (16; 36).

A pertinent element of rare disease planning, particularly with reference to national plans, is the attention paid to the **sustainability of the policies and systems elaborated and adopted**. Not only does the model need to ensure equity, fairness and accessibility for all, but the plan/strategy/policy must be manageable, to put as little constraint on the budget as possible and guarantee its resilience over time (see above) (9; 10).

Finally, the **importance of societal values** when devising rare disease policy is evident from the literature. This type of discourse shifts the balance to the population's rather than the policy-makers' preferences and embraces the citizens' perspective and priorities for health decisions (Shirizzo et al; 25). It leads to distinctive results regarding priority rankings and has significant consequences for rare disease policy-making.

REFERENCES FROM THE RARE DISEASE FIELD LITERATURE REVIEW

FULL LIST OF ARTICLES / PUBLICATIONS FOUND IN THE LITERATURE REVIEW:

- https://docs.google.com/spreadsheets/d/1SRXASsFiD9sdQz286SVo860XdTpGaOIncyjIhGphULI/edit?usp=sharing

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Rare2030

Foresight in Rare Disease Policy

The health of 30 million people living with a rare disease in Europe should not be left to luck or chance. The Rare 2030 foresight study prepares a better future for people living with a rare disease in Europe by gathering the input of a large group of patients, practitioners and key opinion leaders to propose policy recommendations.

Since the adoption of the Council Recommendation on European Action in the field of Rare Diseases in 2009, the European Union has fostered tremendous progress to improve the lives of people living with rare diseases. Rare2030 will guide a reflection on rare disease policy in Europe through the next ten years and beyond.

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