Haut Conseil de la Santé Publique

High Council for Public Health

Assessment of National Rare Diseases Plan 2005-2008

Synthesis - April 2009

Rare diseases: a real public health problem justifying the need for a Plan

Four years was not enough to meet all the targets announced. As the qualitative survey shows, social recognition is essential in the eyes of the patients and a public health plan, albeit symbolic, is the mark of social recognition.

The illnesses in question are rare but numerous with vast needs. At least 7000 rare diseases have been described so far and new pathologies are identified on a regular basis. Furthermore, 20 to 40% of patients monitored by benchmark centres have still not been diagnosed because many rare diseases still have to be identified.
This is therefore an important and many-sided problem (obviously raising the question of training and information) affecting a significant part of the population. The low prevalence of each illness leads to specific difficulties for the patients and their families and raises specific questions in terms of medical research and organising the care system. For these different reasons, implementation of a focussed policy equipped with new means would be a pertinent choice.

The assessment confirms the relevance of the Plan's aims and actions

The Plan has been set up around ten strands that all seem to be relevant. No-one questioned by the Evaluation Committee (Comité d'Evaluation, Codev) has questioned the Plan's aims or the main action lines set to attain them. This overall positive feeling about the Plan's direction does not exclude critics on certain aspects of its implementation.

For the more important strands (access to care, research, information for patients and doctors, etc.), programmed actions have demonstrated that they are adapted to meeting the Plan's aims but work must be sustained in the long term if we do not want to risk losing any gains from the first Plan. On the contrary, delays seen in implementing some of the ten strands (epidemiology, training professionals, organising screening) are partly explained by the fact that the corresponding actions were poorly focussed or that the means envisaged to implement them lack accuracy. The proposals made strand by strand aim to reformulate the corresponding action strategies.

Over-fragmented steering

Plan steering is one of its weaknesses. The Directorate for Hospitalization and Organization of Care (Direction de l'hospitalisation et de l'organisation des soins, DHOS) and the Directorate General for Health (Direction générale de la santé, DGS) have jointly run steering where the DHOS has specifically tackled the benchmark centres system and the DGS covered information for the public and professionals as well as relations with agencies and

institutions helping to implement the Plan: National Institute for Public Health Surveillance (Institut National de Veille Sanitaire, InVS), French National Authority for Health (Haute Autorité de santé, HAS), National Health Insurance Fund for Salaried Workers (Caisse nationale d'Assurance Maladie des Travailleurs Salariés, CnamTS).
For Codev, this fragmentation of responsibilities was detrimental, along with the weakness of human and financial resources mobilised for administrative monitoring.

Institutional players from different ministries, agencies or independent authorities are not involved in coordinating actions.

Alternate presidency of the Plan Monitoring Committee, switching between the DGS and the DHOS, leads to a lack of effectiveness for this authority. DGS-DHOS joint steering has been demonstrated to drag it down and present difficulties in terms of communicating and maintaining an overall view of the Plan's dynamics.

The Plan Monitoring Committee has only met three times and has not delivered a summary report. Due to its composition, its operation and the resources made available to it, it was difficult for it to assume operational monitoring on all the Plan's strands. Steering remained fragmented which partly explains the lack of monitoring and support for the Plan's actions as they came across implementation problems (epidemiology, screening, training professionals, social support).

Another harmful consequence of this situation was the difficulty for Codev to bring together data on implementing the Plan required for its assessment, in the particular absence of results indicators, instrument panels and reports from the DHOS-DGS Monitoring Committee.

Only the National Consulting Labelling Committee worked satisfactorily, running constant partnership work between the different participants involved, including associations.

Spending generally matches commitments

The National Rare Diseases Plan (Plan national maladies rares, PNMr) posted extra expenses amounting to 108.46 million Euros for the period 2005-2008[1]. Out of this amount, 40 million was assigned to financing benchmark centres (creating jobs for doctors and paramedical staff), 43.1 million went to financing research (of which 22.5 million went to the Hospital Clinical Research Programme) and 20 million went to developing screening and diagnostic tests. Codev investigations reveal that these commitments were globally respected, at least for the most important actions. The most significant deviations from the commitments involve strand 1 (epidemiology) and 3 (information) ("annexe 10", page 162).

Loans made available for the benchmark centres essentially correspond to the commitments undertaken. This created 400 to 500 jobs. However, several line loss mechanisms were able to intervene, linked particularly to measures to return loss-making health establishments to a well-balanced situation. It is best to observe that current conditions for executing hospital budgets make it difficult to shelter loans, even when they are subject to explicit political decisions. The deviations inferred between the commitments and what actually was carried out are actually limited, but the existence of mechanisms to erode flourishing loans has undermined confidence and enthusiasm from the coordinators of benchmark centres and raises the question of durability for these centres' resources. In this respect, Codev reveals that certain jobs (clinical research assistants, social workers, psychologists) are too often unstable.

[1] Spending on orphan drugs was estimated by the AFSSAPS to be 450 million Euros in 2007

Lack of data on the Plan's overall cost

The figures summarised in the preceding paragraph only provide one part of the information required to produce a financial balance for the Plan's implementation. Firstly, one part of the spending displayed actually corresponded to pre-existing actions. Next, Codev did not know if public money contributions made an impact on other financing. Charity financing remains more significant than public financing.

Finally, and this is the essential point, these amounts only retrace the spending written up in the State budget. The majority of public spending to tackle rare diseases is made up of health insurance repayments, particularly in terms of orphan drugs, most of which predate the Plan. Setting up the benchmark centres has presumably been able to reduce misdiagnosis, thereby avoiding useless consultations and examinations. Whatever the circumstances, it must be admitted that it is not possible to even approximately assess the impact of a policy such as PNMr on public finances.

Undeniable improvement in caring for patients but there is a still a way to go

The associations and professionals hold a very positive opinion of the benchmark centre system as essential for improving patients' medical care.
The work done on doctor and public information, particularly thanks to Orphanet (the portal for rare diseases and orphan drugs), has helped to improve access to adapted care. However, it is not possible to measure the breadth of this progress, due to lack of indicators.

Statements compiled by the qualitative patient survey reveal that family misdiagnosis remains considerable. The first contact for families and patients remains the GP, who too often is helpless. It is impossible for them to know about all rare diseases and even more difficult to make a diagnosis. It is not clear whether all GPs react by using Orphanet or know how to get the best from it. Specialists often have a fragmented, "organ-specific" view of symptomology that does not always allow them to come up with rare diseases (as they are often cross-discipline). Finally, although Codev information is not complete on this point, it seems that progress made in terms of patients' social support is unequal and overall deficient. More generally, the patient survey highlights persistent difficulties in their daily lives.

Inequalities in repayment for services that raise fairness issues

If progress has been seen in medical care, particularly through the benchmark centres, difficulties remain in terms of social issues and health insurance. Detailed analysis of how strand 2 ("recognise the specific nature of rare diseases") was implemented demonstrates that refunding certain services (transport costs, drugs other than orphan drugs) is too often attributed to local decisions made by health insurance funds. For the patients, this often means that they have to turn down some care or services or pay high co-payment costs. There are geographical inequalities in the face of the Plan's fairness target.

General conclusions: justified effort, progress to be consolidated, deficiencies and concerns...

The effort is justified

Taking into account the uncertainties given above, it is impossible to get an accurate view of the Plan's cost and its results obtained in terms of fairness, public health and collective well-being. *A fortiori,* it is not possible either to answer Codev's question on the validity of the

consented effort concerning the overall problem of health spending: "What judgement can we make about the Plan from the point of view of assigning public resources? Has mobilisation around the Plan affected other public health priorities?"

Nevertheless, Codev believes that it is possible to give an indirect, careful and "qualitative" answer to these questions by highlighting that the Plan follows a progress dynamic for the whole health system, both in terms of organising care and research concepts and methodologies. The aim to do everything possible for any health problem, regardless of its rarity, still lacks a medical response although this is strongly demanded by our society. Mobilising associations and other players in the Plan around this target shows its social legitimacy and therefore its relevance.

The Plan has made it easier to set up an environment where vitality is the gauge of future progress. It has permitted setting up networks for teams that were not likely to meet each other and it has urged existing teams to structure themselves better. This has thereby created a section of professional and association networks with dynamism proven by French leadership in this field. Furthermore, the effort made concerning rare diseases can be a source of progress for the whole care system as it sets up ways of coordinating and sharing skills that can be applied to other fields. Progress in research on rare diseases has benefited other aspects of human pathology.

Progress should be consolidated
The innovating nature of the solutions developed within the framework of the Plan raise the question of how long they will last. At a time of significant financial difficulties, there is a major risk of questioning structures for which the operating methods have not been sufficiently consolidated, and work methods that are, as yet, poorly anchored within health system routines. This concern particularly involves the benchmark centres, Orphanet and financing research. It must be taken into account as a priority in the next PNMr.

Deficiencies and concerns
Little progress has been made in terms of epidemiology, due to lack of means and adapted organisation.
The screening strand is slowed down at different levels and there is a certain delay in France despite the French system's overall progress in the field of rare diseases.
Tackling different services causes inequalities. We still do not know if the device organised by article 56 of the social security funding act project (Projet de loi de financement de la Sécurité sociale, PLFSS) and by implementing the rare diseases cell within the CnamTS will be enough to tackle them.
The partnership between the benchmark centres and the Departmental Home for Disabled Persons (Maison départementale des personnes handicapées MDPH) has yet to show any results and the question of the MDPH located in departments and regions with no benchmark centre has not been resolved. There are also inequalities in terms of social care for handicaps linked to rare diseases.

Recommendations

These transverse recommendations must be articulated with the proposals that appear, strand by strand, in the report's balance section.
The central recommendation is to include rare diseases in long term programming and draw up a second Plan (PNMr 2).
PNMr 2 must improve not only its steering, but also its content, taking on board the assessment's conclusions.

Steering and monitoring

Real policy monitoring must be assured for the whole duration of the Plan. It is necessary to maintain national steering for the Plan even if the "Hospital, Patients, Health and Territories" law is likely to give accumulated power to the regions in terms of health and social organisation.
To be effective, the Plan steering structure must have the means and be given clearly stated political legitimacy and coordination authority. The following architecture might be proposed:
● Strategic steering of the Plan assured by one person (or a light project structure) with inter-ministerial authority, located within the Health Ministry. Administrative and financial monitoring would also be assured there.
● A steering committee would be set up, comprising doctors, researchers, associates and administrators appointed for five years (six to ten people). This committee would be in charge of making proposals to improve the Plan's implementation conditions.
● The steering committee would comprise work groups on specific matters and groups of experts in charge, in liaison with the HaS, of assessing the activity of the benchmark centres and their partners in situ (see strand 6).
● A monitoring committee, comprising representatives from different public or private institutions in charge of the Plan (Ministers, State agencies, Orphanet, the GIS-Institute for rare diseases (Groupement d'intérêt scientifique maladies rares, GIS-Institut des maladies rares) associations, manufacturers, representatives from the European Union, national federation for benchmark centres). They would meet every year to examine annual reports from the steering committee and give an opinion on this basis.
● Administrative and financial monitoring should be assured in the future, strand by strand, with annual publication of official monitoring reports.

Monitoring and assessment indicators

Monitoring indicators for the next Plan should be defined by the committee drawing up the Plan, in partnership with the High Council for Public Health (Haut Conseil de la Santé publique, HCSP).

Four major categories of indicators might be proposed.

1. Care activities. Due to the great disparity of the pathologies and therapeutic progress, classic activity indicators are not appropriate.
2. Procedure indicators. Procedure assessment is currently limited to the benchmark centres, involving very time consuming questionnaires. These questionnaires should be withdrawn or simplified. In liaison with administration study services, the steering committee should establish a survey grid adapted to the specific nature of rare diseases.
3. Efficacy. Efficacy indicators depend on progress in epidemiology and collecting data on the social aspects of the cover and standard of living. Studies on human and social sciences will also be required.
4. Cost. Codev has not been able to reconstitute an accurate financial balance for the Plan. This monitoring is required by Plan steering and assessment, even if it currently seems almost impossible to analyse cost/benefit ratios for the financed actions.

The strengths to consolidate

At the end of this assessment, a rather more positive response can be given to three essential questions:

- Are patients better cared for than before the Plan?
- Do information and training shed more light on rare diseases?
- Has research, and particularly its therapeutic implications, progressed?

The main issue for the PNMR 2 lies in confirming this progress, which implies consolidating three main milestones in the first Plan: the benchmark centres, Orphanet and the Hospital Clinical Research Program (Programme hospitalier de recherche clinique, PHRC)-GIS-Institut system for rare diseases.

Benchmark Centres

If we cannot stand far enough back to answer the first question in quantitative terms of improving the duration and standard of living, it is clear that the benchmark centres have been a source of considerable progress in the quality and homogenisation of the care. This original structure is still fragile because it has not established a place for itself among current directions in terms of reorganising hospitals. This is also seen in the difficulties found by numerous benchmark centres with hospital directors, or even with health complex managers. Their adapted “activity-based-pricing” (Tarification à l’activité, T2A) financing, in compliance with the commitment made, has not always seen the light of day. Their operating conditions depend on their acceptance by the hospital structure which depends on the place. They must be preserved whilst also permitting dynamism for their teams to express themselves in the long term, keep the necessary flexibility to adapt them to the teams' knowledge evolutions and paste over any unexpected cracks, such as misunderstandings and malfunctions due to the designation of the skills centres (see strand 6).

Codev recommends:
- thinking about the status of the benchmark centres within the public health system;
- an overhaul for the procedures and their assessment criteria;
- financing distribution taking into account these assessments and the capacity of benchmark centres to share their means and fill up their different assignments.

Orphanet

The growing worldwide success of Orphanet among doctors, students, patients and the general public plus the large number of services proposed mask great human, financial and institutional fragility. This is not a problem that can be solved by providing an extra worker or support from a national institution.
Durability and development must be assured for this tool with international bearing which would be hard to live with today. The future of Orphanet puts into play the whole international "rare diseases" system and exceeds the framework of France. An international association solution might be envisaged.

Codev recommends that a work group (including representation from the European Community and the WHO) assigned to redefine the needs and the status of the device on a national and European scale. This group should be set up urgently.

Research and therapeutic progress

Due to its specific constraints, research in the field of rare diseases must benefit from a real incentives policy with clearly flourishing financing. This incentive policy also needs financing

for structuring actions. Therapeutic research on rare diseases and its industrial extensions stretch beyond a single country and public powers. European collaboration must be structured for public and industrial research and to develop the interface between these two poles.
Codev recommends:

- fast research into an operating model adapted to European therapeutic research putting joint projects into play between public operators and industry;
- reinstituting calls for projects that are specific to rare diseases;
- planning specific budgets to improve access to the latest technologies (sequencing, murine models, etc.) and incentives for young researchers and bio-IT technicians;
- increasing all the necessary incentive actions to develop networks and interfaces; clinic/research; public/industry/poles competitiveness labs; transnational and specifically European grid;
- bringing together funding and demands regarding orphan drugs on a European scale;
- facilitating any action permitting care for patients across Europe;
- studying the creation of a coordination and action committee on rare diseases assuring permanent liaison with the general European Commission boards involved.

Deficiencies to be compensated

Certain deficiencies in the Plan are explained by a clear lack of means, participants, incentives or even prior thought. To alleviate this, the Codev recommends:

- implementing adapted epidemiology tools[2], encouraging the constitution of cohorts, their longitudinal monitoring, their clinical and biological exploitation;
- radically reviewing the policy for screening rare diseases in all its aspects;
- ending the heterogeneous care depending on funds and assuring national equality, even in overseas regions. There must be dialogue between the steering committee and the health insurance system;
- structuring for rare diseases regional coordination of departmental centres for handicapped people, interfacing with benchmark centres;
- developing communication, not only on rare diseases but also on the Plan and its participants.

[2] This idea of a tool actually recovers three different levels of carrying out the epidemiological work: the tool-software used to collect data; a consensus on a common assembly of this data; methodological help for clinic technicians to design and set up databases.