RARE DISEASES

AN OPPORTUNITY FOR PRIMARY CARE

Gerard Nguyen

Primary Care, Cabinet Marcel Monny Lobe, Soisy sous Montmorency France

Hopital Avicenne APHP

Rett Syndrome Europe, AFSR, HUFERDIS (Hungary)

RARE & MANY

- The RD Community success story
- The Lessons Learned
- The State of the Art
- New Landscape of Primary Care Practice
- Facing New Challenges

UNMET NEEDS

- Problems listed by patients (EURORDIS)
  - Lack of access to correct diagnosis
  - Lack of information
  - Lack of scientific knowledge
  - Social consequences
  - Lack of appropriate quality of care
  - Inequities in treatment and care
  - High cost of exsiting drugs and care

IMPACT


Feelings of depression
T: 71% UT: 81%
75%
T: 66% UT: 75%
69%
Feelings of anxiety/stress
T: 84% UT: 89%
86%
T: 81% UT: 82%
82%
Less interaction with friends/family
T: 64% UT: 79%
70%
T: 64% UT: 77%
68%
Isolation from friends/family
T: 63% UT: 68%
65%
T: 53% UT: 66%
57%
Worry about how their health will change in the future
T: 89% UT: 86%
90%
T: 79% UT: 88%
91%
Lack of available information on rare disease caused worry
T: 80% UT: 86%
83%
T: 79% UT: 88%
81%
Felt they had no one to turn to in the medical system for information/support
T: 59% UT: 74%
65%
T: 47% UT: 67%
53%
0
20
40
60
80
100

DIAGNOSIS PROCESS

According to patients surveyed, it takes:

on average **7.6 years in the US**

on average **5.6 years in the UK**
for a patient with a rare disease to receive a proper diagnosis

According to patient/caregiver respondents, in order to get a proper diagnosis, a patient typically visits up to

8 physicians: 4 primary care and 4 specialists

and receives **2** to **3** misdiagnoses

Fabry disease: : average delay of 15 y after clinical presentation

EURORDIS survey : 25 % of respondents (n=5980), 5 to 30 y from onset of symptoms and diagnosis confirmation, 40% reported an initial wrong diagnosis

BARRIERS

Barriers	Percentage of US physician respondents that agreed with statement	Percentage of UK physician respondents that agreed with statement
More difficult to address the needs of a rare disease patient in typical office setting	92%	88%
More office visits are required to diagnose	98%	96%
More office visits needed to adequately address symptoms	92%	88%
Medical professional organizations do not give enough attention to rare diseases	46%	50%
Aren't enough opportunities to network with other physicians who treat rare diseases	54%	62%
Difficult to coordinate with other physicians when managing a patient with a rare disease	76%	88%
Adequate and effective treatments are less available once patient is diagnosed	86%	90%

THE FINANCIAL BURDEN

Assigning a monetary value to the loss in quality of life of $75 000 per QALY, the mean per-patient annual intangible cost of DMD was estimated at between $37 980 and $46 080

	Direct medical costs and informal care	Indirect costs	Intangible costs	Total annual cost per patient	Total costs per year based on prevalence
Germany	42,360	20,770	45,860	109,000	278 058 000
Italy	23,920	18,220	37,980	80,120	154 465 000
UK	54,160	18,700	46,080	118,950	200 478 000
US	54,270	21,550	45,080	120,910	1 217 373 000

EUCERD

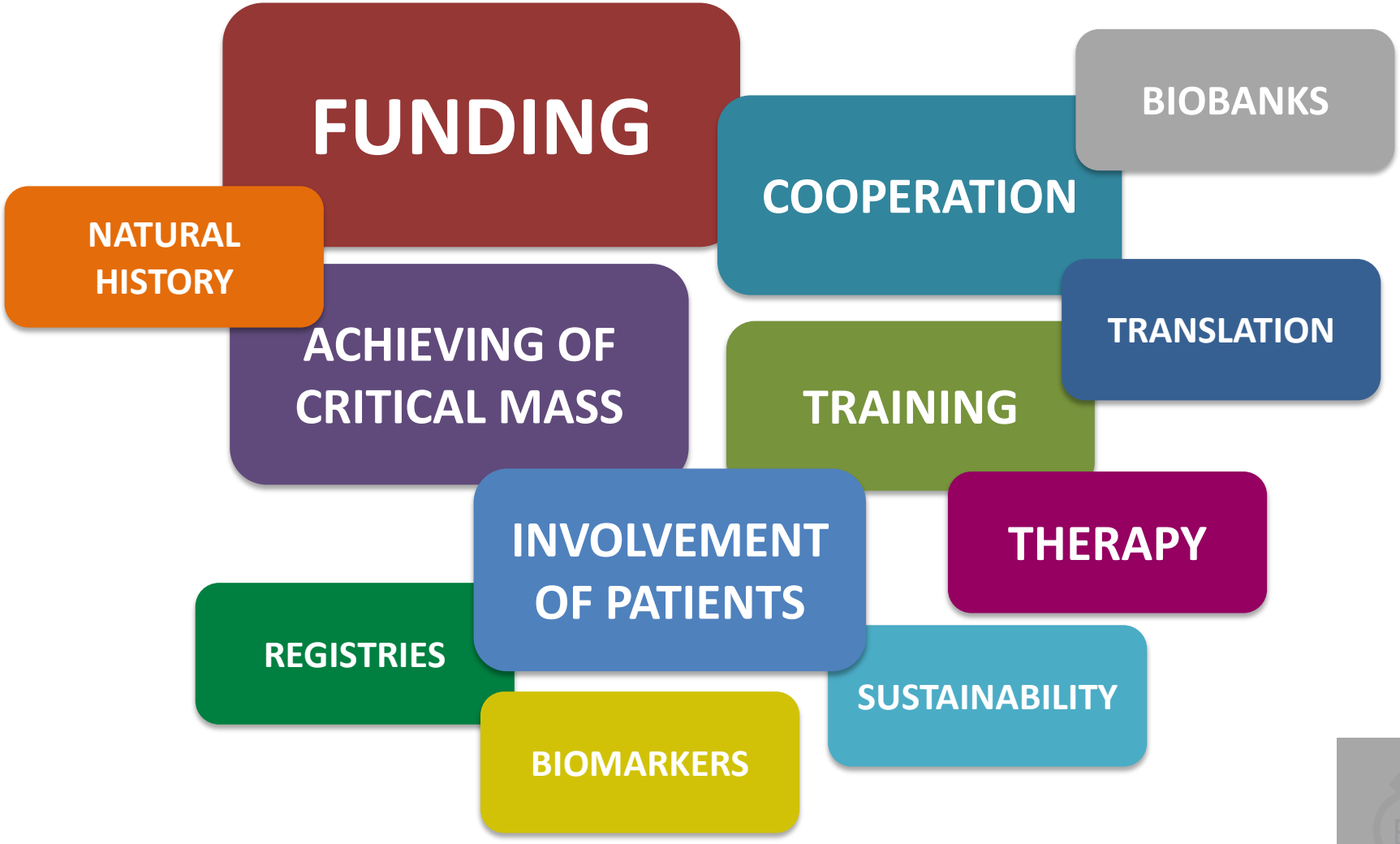
RARE & MANY

- Rare
  - 1/1200 in the US
  - 1/2000 in the EU
  - 1/2500 in Japan
- Many
  - 7000 diseases
  - 8% of the population , 25 M in the US
  - 6-8% and 30 M in Europe

RARE & MANY = COLLABORATION

- Respond to patients' expectations
- Mobilisation of critical mass of expertise and resources
- Avoid overlap
- Deliver new cures and diagnoses
- Bridging gaps
- Collective intelligence
- Gathering all stakeholders***

RESEARCH ISSUES



EU FUNDING

Over two decades of investment in the area

47 projects

€ 64 million

7th EU Research Framework Programme (2007-2013):

59 projects

€ 230 million

- **Over € 620 million invested in close to 120 collaborative projects**
- **Plus more than 100 individual fellowships, grants and training networks**

~120 projects

>€ 620 million

EU funded collaborative research in rare diseases

- Europe wide studies of natural history and pathophysiology
- In vitro/in vivo models
- Registries & bio-banks
- Identification of biomarkers
- Clinical trials methodologies for small populations
- -omics for rare diseases and linking data
- Development of preventive, diagnostic and therapeutic interventions

Research and Innovation

SEVENTH FRAMEWORK PROGRAMME

WORLDWIDE COLLABORATION

Exploratory Workshop Reykjavik

Launch Washington

Scientific Committees

Working Groups

IRDiRC 2013 Conference

3000 diagnostics

6000 diagnostics

2010 2011 2012 2013 2015 2020

Support- IRDiRC Scientific Secretariat

50 new applications for market authorisation

200 new applications for market authorisation

Research and Innovation

E RARE 3: COLLABORATION INFRASTRUCTURES

EUROPEAN RESEARCH INFRASTRUCTURES:

BIOBANKS, CLINICAL TRIALS, TRANSLATIONAL MEDICINE, MOLECULE SCREENING, MOUSE MODELS

- Facilitated access
- Exchange of best practices
- Models for sustainability
- Communication & training

BBMRI
Biobanking and Biomolecular Resources Research Infrastructure

ECRIN
EUROPEAN CLINICAL RESEARCH INFRASTRUCTURES NETWORK

EATRIS
European Infrastructure for Translational Medicine

EU-OPENSCREEN
Chemical keys for life's locks

INFRAFRONTIER
mouse disease models

EUCERD Joint Action

2014 REPORT ON THE STATE OF THE ART OF RARE DISEASE ACTIVITIES IN EUROPE

PART I: OVERVIEW OF RARE DISEASE ACTIVITIES IN EUROPE

2014 REPORT ON THE STATE OF THE ART OF RARE DISEASE ACTIVITIES IN EUROPE

PART IV: EUROPEAN MEDICINES AGENCY ACTIVITIES AND OTHER EUROPEAN ACTIVITIES IN THE FIELD OF RARE DISEASES

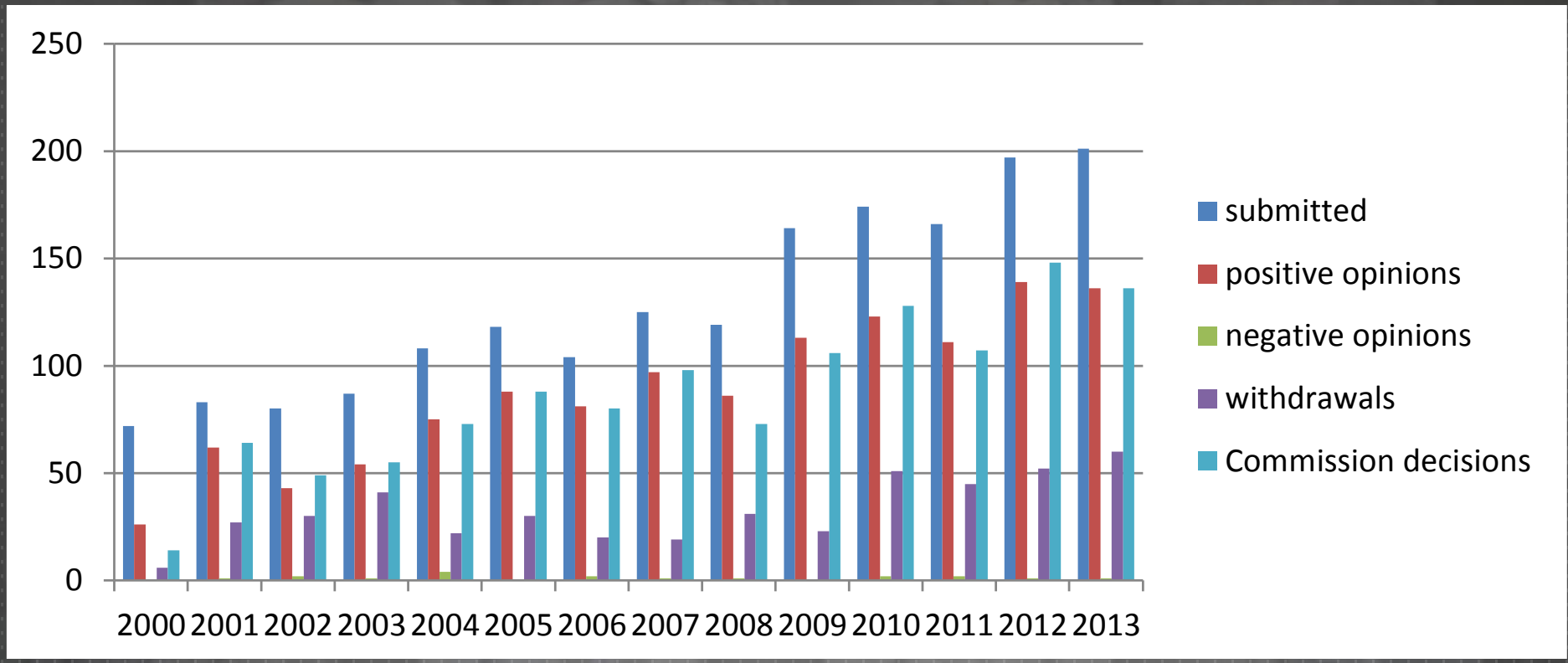
EUCERD Joint Action

ON THE STATE OF THE ART
EASE ACTIVITIES IN EUROPE

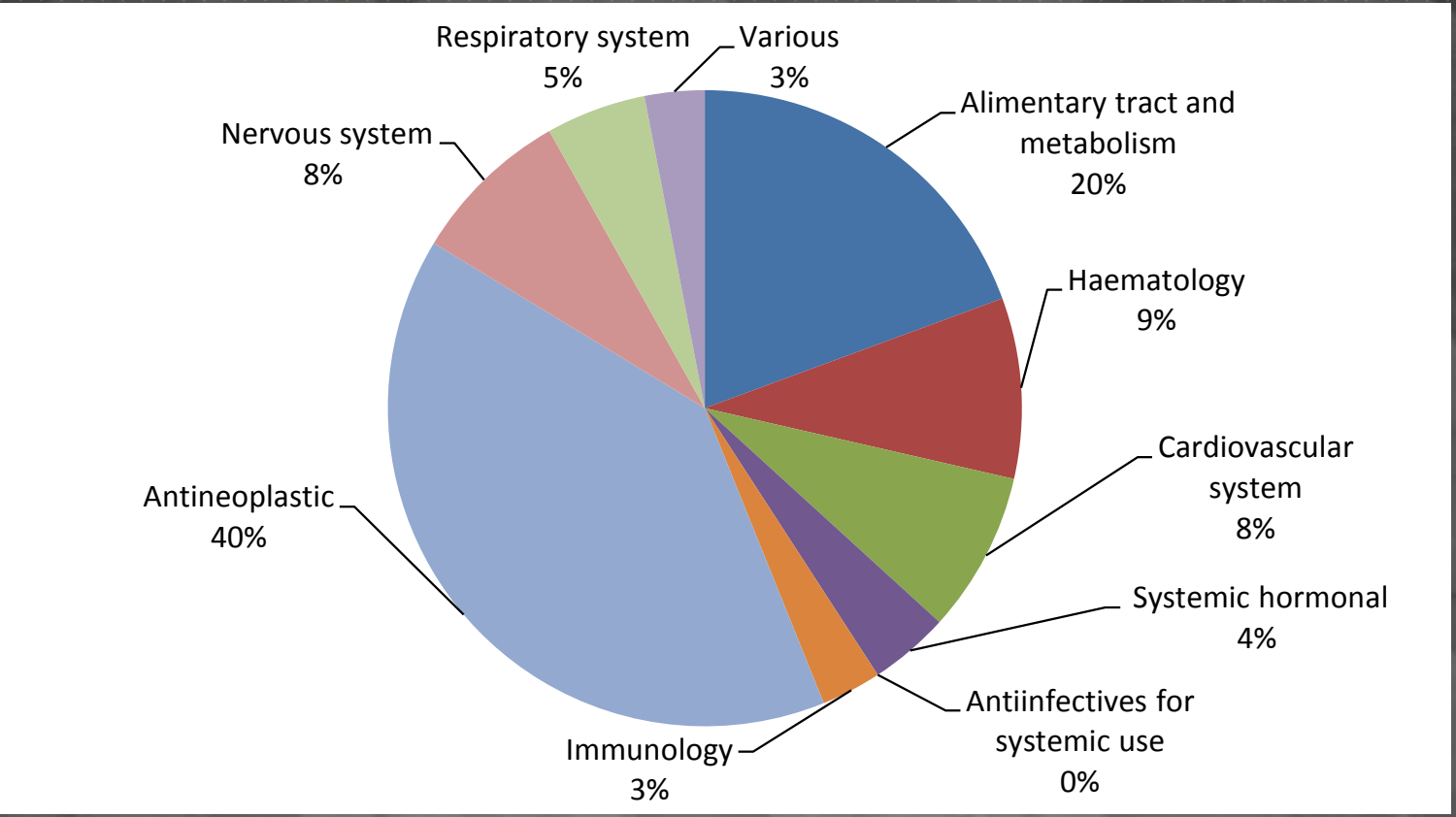
PART II: KEY DEVELOPMENTS IN THE FIELD OF RARE DISEASES IN EUROPE IN 2013

EU RD ACTIVITY

ORPHAN DRUG: STATUS DESIGNATION



OD POSITIVE OPINION BY THERAPEUTIC AREA



PATIENT TRAINING

EURORDIS

EURORDIS in brief

EURORDIS is a patient-driven alliance of patient organisations and individuals active in the field of rare diseases

EURORDIS' mission is *"to build a strong pan-European community of patient organisations and people living with rare diseases, to be their voice at the European level, and – directly or indirectly – to fight against the impact of rare diseases on their lives"*

Today, EURORDIS has 423 member organisations in 43 countries, of which 29 are European Member States and represents more than 1000 different rare diseases.

EURORDIS and Orphan Drug Development

EURORDIS played a front-line advocacy role in obtaining the EU Regulation on Orphan Drugs (1999), some key measures for patients in Revision of EU Pharmaceutical legislation (2003), EU Regulation on Paediatric Use of Medicines (2006) and the EU Regulation on Advanced Therapies (2007).

Since 2000, EURORDIS officially represents the 30 million rare disease patients at the European Medicines Agency (EMA) as members of various committees and working parties responsible for different regulatory steps of orphan drug development.

EURORDIS is also active in improving quality of information on and access to therapies for rare diseases.

ORGANISERS

Dr. Fabrizia Bignami
Therapeutic Development Director

Dr. Maria Mavris
Drug Development Programme Manager
Email: maria.mavris@eurordis.org
Tel: +33 1 56 53 52 19

EURORDIS
Rare Diseases Europe

EURORDIS SUMMER SCHOOL 2010

2008

2009

EURORDIS Summer School in Regulatory Affairs and Health Technology Assessment (HTA) for Advanced Patient Advocates

Executive Agency for Health and Consumers
AFM
Fundació Doctor Robert UAB
Inserm

www.eurordis.org

EUPATI

European Patients Academy on Therapeutic Innovation

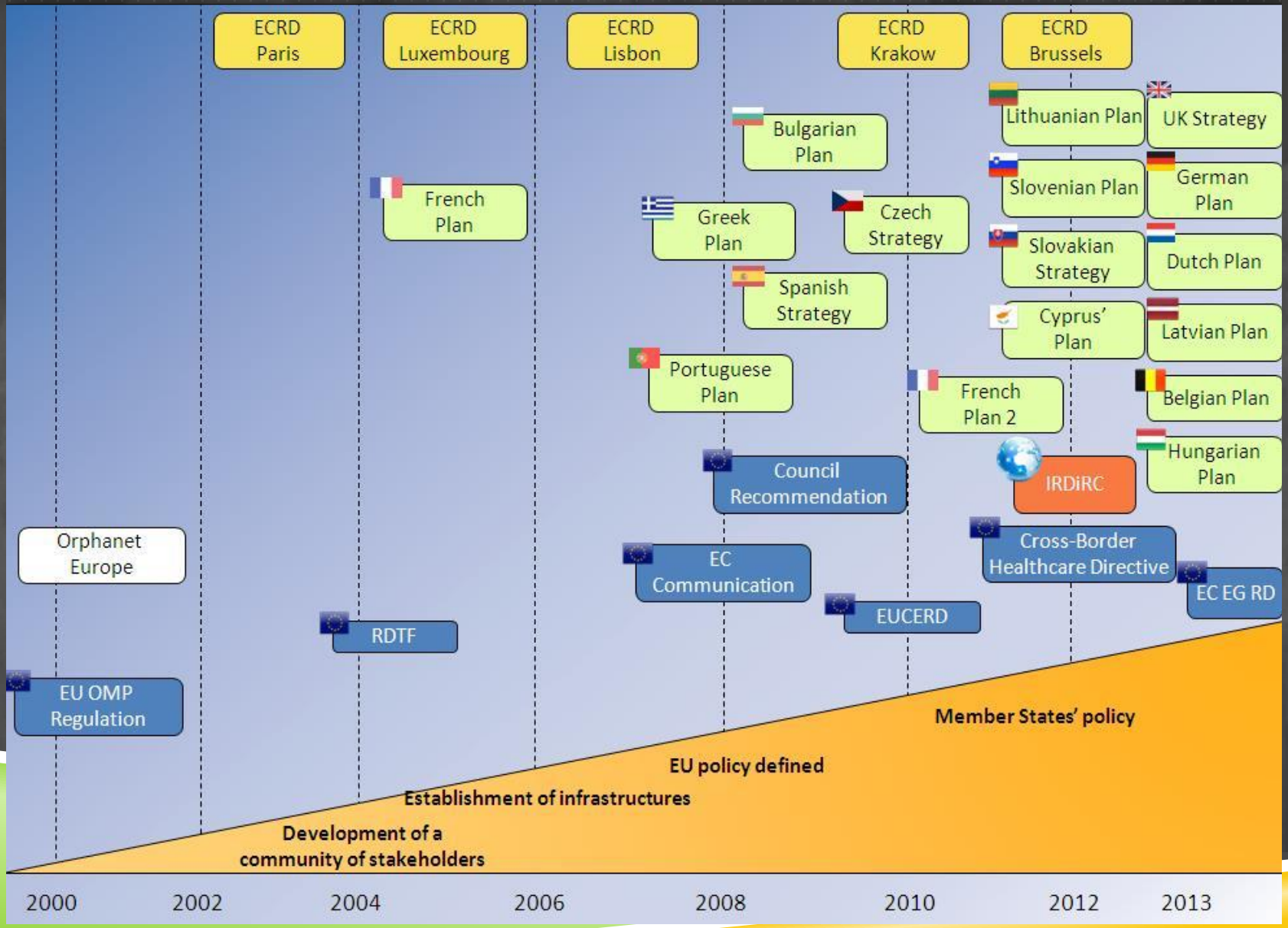
Web:

www.patientsacademy.eu

Twitter: @eupatients

as well as:

NATIONAL RD PLANS



SOCIAL HEALTH

Every year, 28% of the PLWRD needed the assistance of a social worker.

92% of PLWRD consider that «informing patients about their rights and guiding them towards social services, schools, leisure activities or vocational guidance» is necessary

Social assistance services respond inadequately to the expectations and needs of PLWRD

On average, 16% of PLWRD (up to 24% for the low income group) were forced to move house because of their disease;

EURORDIS Survey

FRANCE RD NATIONAL PLAN (I)

131 National centres of expertise were designated in University hospitals (2005-2007), then 500 centres of competence in regional hospitals organised in disease specific networks linked to the centres of expertise (2007-2008)

Missions of the centres of expertise (« centres de référence » in French) :

- Improve diagnosis, organise pluridisciplinary care from birth to end of life
- Expertise and second opinion
- Research, epidemiological surveillance and clinical trials
- Production of National protocols for diagnosis and care, participation in European guidelines if possible
- Information and training of health and social professionals, patients and their family,
- **Coordination with provision of primary care, medical and social care**

During the 1st Plan, two pilot networks in the field of social services were launched by centres of expertises in the regions of Pays de la Loire and Languedoc Roussillon, as well as a few other initiatives in other regions, (in particular therapeutic education programmes).

C. Nourissier

FRANCE RD NATIONAL PLAN (2)

1. Creation of about 25 disease specific networks

- Composition : all stakeholders - centres of expertise, diagnosis and research laboratories, patient associations, **social professionals**, care networks -
- Aim : strengthen them, share ressources and tools, and cover all rare diseases and patients with unclear diagnosis in the long term :
- Missions: to reduce diagnostic delay for all diseases, including the very rare, improve legibility of the health care system for all, develop continuity of medical care, diagnostic and therapeutic innovation, basic, clinical and translational research and **social care**.
- call for proposals in 2013, 15 networks already identified. Governance and coordination shall be supported by the Ministry of Health in 2014.

C. Nourissier

FRANCE RD NATIONAL PLAN (2)

AnDDI-Rare developmental anomalies and malformations
CARDIOGEN transmitted heart diseases
DEFI SCIENCE (Challenge for Science) brain development diseases and intellectual disabilities
FAI2R rare auto-immunes and auto-inflammatory diseases
FILFOIE rare liver diseases
FILNEMUS neuromuscular diseases
FIMARAD rare dermatological diseases
FIRENDO rare endocrine diseases
G2M rare hereditary diseases of metabolic origin
MARIH immuno-hématologic rare diseases
MCGRE rare diseases of red cells and of erythropoïesis
MUCO cystic fibrosis and CFTR anomalies
ORKID rare kidney diseases
RESPIFIL rare respiratory diseases
SENSGENE rare sensory diseases
SLA amyotrophic lateral sclerosis

C. Nourissier

RARE & MANY = COLLABORATION

- Respond to patients' expectations
- Mobilisation of critical mass of expertise and resources
- Avoid overlap
- Deliver new cures and diagnoses
- Bridging gaps
- Collective intelligence
- Gathering all stakeholders***

PRIMARY CARE ACTORS ?

NEW LANDSCAPE OF PRIMARY CARE

- Re-appraisal
  - Role and Responsability
- Rebuilding the ecosystem
- Re-positionning
  - Front Line
  - Go-between actor

PRIMARY CARE

- Front line
- Management of undifferentiated problems in unselected patients
- Management of common problems in common patients
- And …extraordinary, complex cases in ordinary practice…
- "Narrative Medicine" Centered approach
  - Story telling, anecdotes
  - Diagnosis delivery, annoucement
  - Decision making
  - …in Real life…

PRIMARY CARE

- 12,7% patients with RD
- The first to identify the problem in 89%
- To establish the definitive diagnosis in 54%
- To provide acute care for the problem in 56% and continuing care in 76%
- …care for the patients through their final illnesses in 17%...
- …sought consultation from specialists for 85%

- W Philips, 2004

DIAGNOSIS PROCESS IN PRIMARY CARE

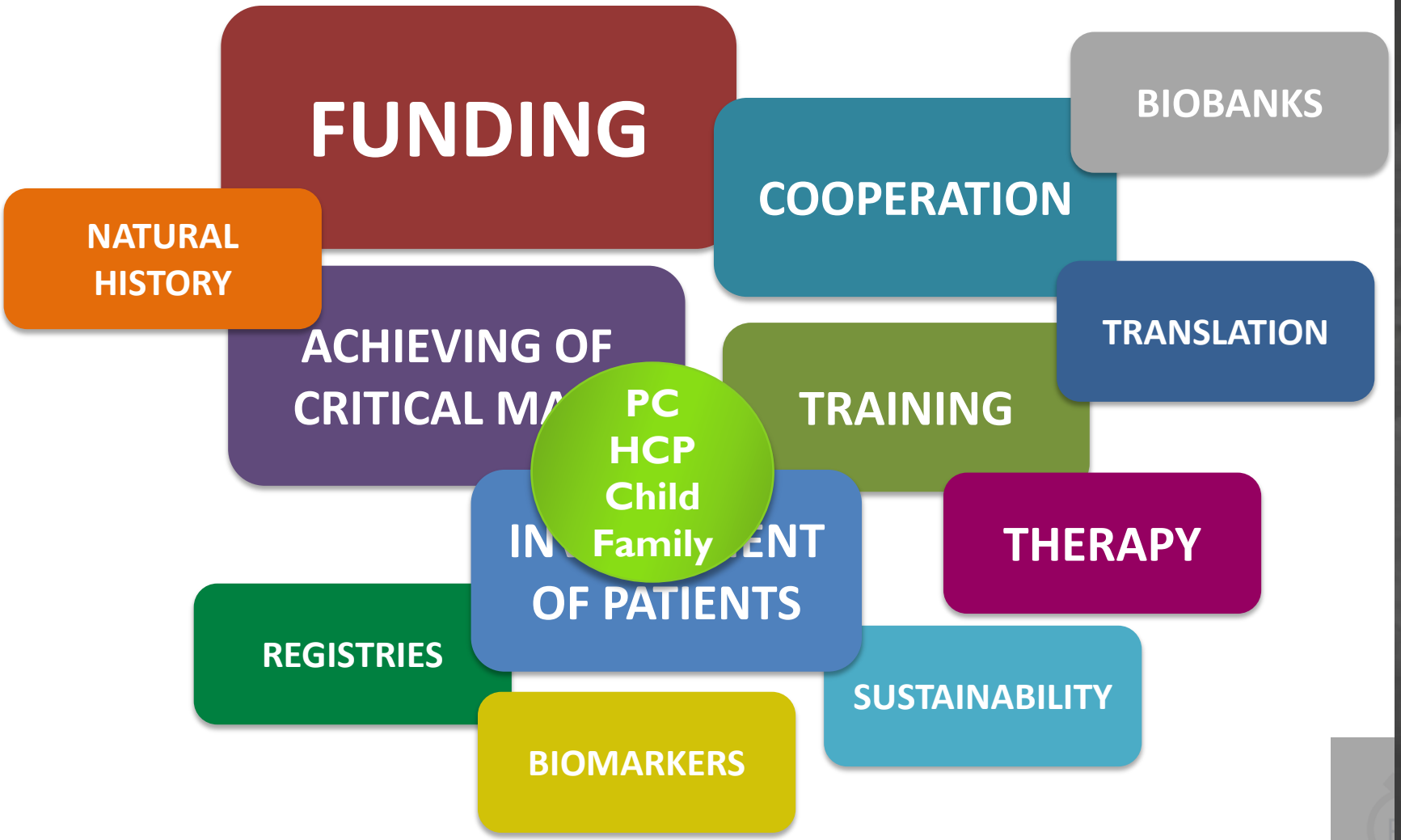
- I suspect something wrong….

- And consult the literature: 12.3%
- And consult experts to help me: 23.1%
- And refer to experts to make the diagnosis: 64.6%

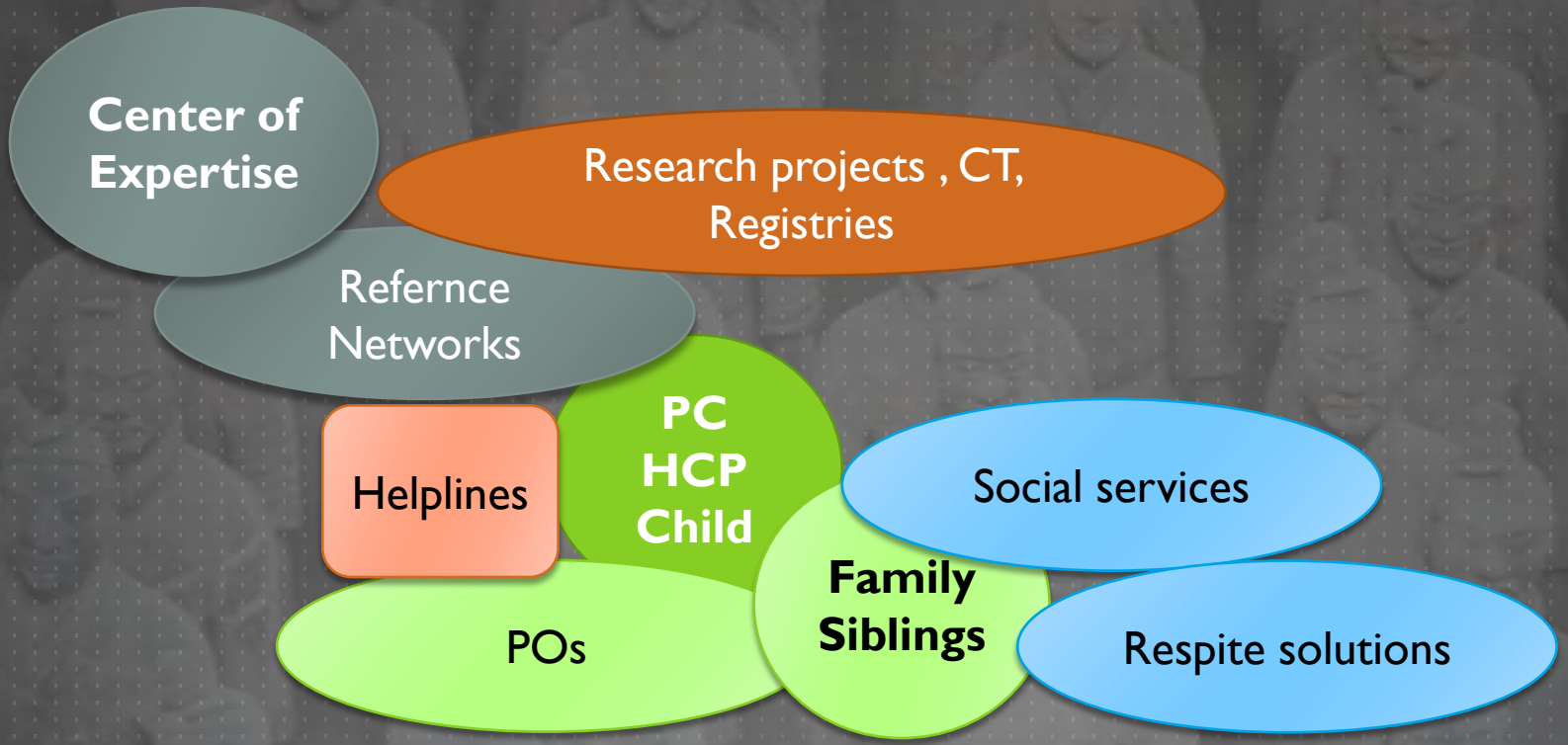
ASPECTS OF DIAGNOSIS

- Atypical presentation
- Non specific symptoms
- Co-morbidity +++
- Very rare conditions
- Life threatening
- Family burden
- “first time” features
- “something wrong”

PRIMARY CARE ISSUES



RD PRIMARY CARE ECOSYSTEM



LESSONS LEARNED: NEW CHALLENGES

Patient social media, communities on line

Telemedicine, e patient, patient 2.0

Advanced Therapy, Gene therapy

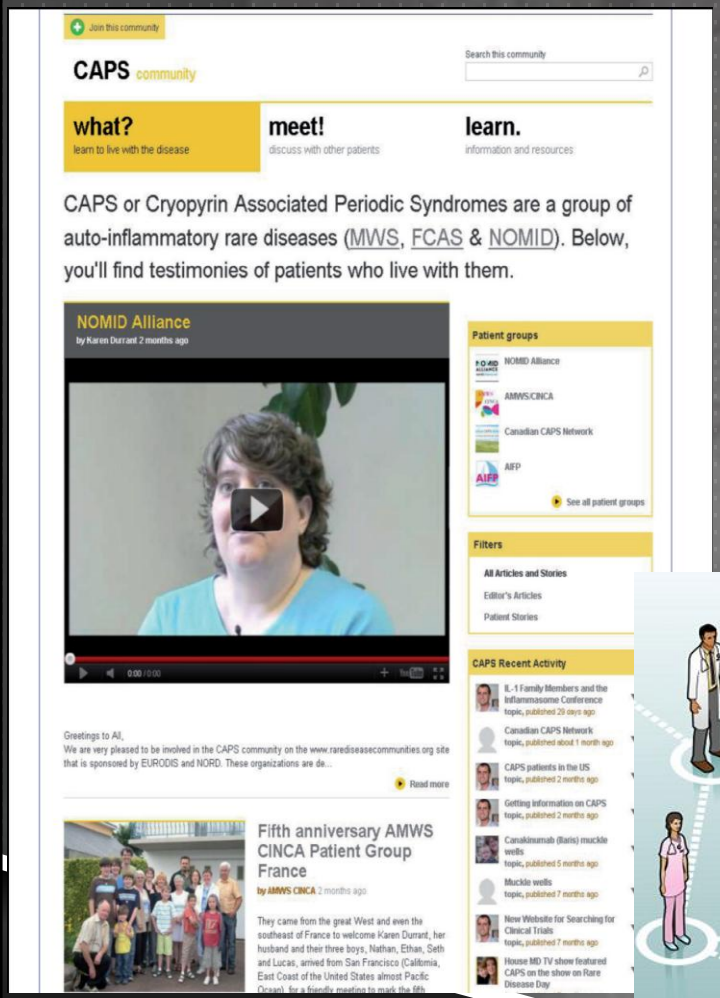
Consequences of fast track drug development process

Personalised Medicine

Big data

PERSPECTIVES…
THE CHILDREN WORLD

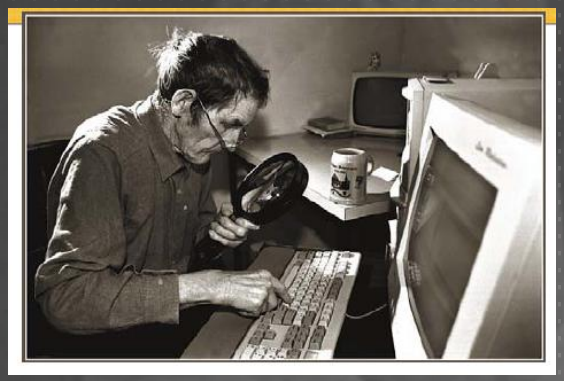
MULTIMEDIA PATIENT SOCIAL NETWORKS….



What is Social Media ?

- "…**social media collaboration, interaction**
- and **sharing** –**web 2.0** video… some popular tools are **blogs**, **wikis**, **Twitter** and …?"

New practices: information search



Orphanet
Eucerd
Irdirc
Horizon 2020
EMA PDCO, COMP
EudraCT
Eurordis
…

I have a RD X
With a mutation XYZ
Under a OD

- MA under control
-PMS
-RMP
- Registries (Drug and Disease)
-ATU
-Off label
- FB : shortage soon
- Care protocol
- Biomarker follow
- Reimbursement protocol
- Informed consent
- Data privacy
- Transborder directive
- Reference network

RD AN OPPORTUNITY FOR PRIMARY CARE

- Lessons learned from RD Community activism and activities
  - How to manage complex situations
  - How to step in the future
  - How to move from "disease centered" to "patient centered" care
  - How to innovate (tools, practices, drug development and drug access, rpicing, HTA…)
  - How to implement Quality of practice (COI)

HCP : Gardianship of Patient Centered Care & Ethics of Care

CONCLUSION: A CALL TO ACTION

- An empowerment program
  - Training: RD intensive course
  - Research in primary care
  - Becoming active stakeholders in CE, Refernce Networks
  - Implementing information platform
  - Taking part in registries, surveys
  - Participating in calls for experts and calls for projects
  - To advocate
    - Added value of care
    - For inclusion of "primary care" in research program (Horizon 2020)
    - For new organisation of primary care integrating "case manager"