Report of the E-Rare-3 Strategic Workshop on September 20, 2019 in Gdańsk (Poland)

How SHS research can improve health care implementation and everyday life of people living with a rare disease and their families

A preparatory Workshop for Joint Transnational Research Call JTC 2021 in the European Joint Programme on Rare Diseases (EJP RD)

E-Rare-3 Work Package 8/MS 12
Task 8.1.2

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## Abbreviations

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<tr>
<th>Abbreviation</th>
<th>Full Form</th>
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<tr>
<td>CEA</td>
<td>Cost-effectiveness analysis</td>
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<td>DRD</td>
<td>Drugs for rare diseases</td>
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<td>EC</td>
<td>European Commission</td>
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<td>EJP RD</td>
<td>European Joint Programme on Rare Diseases</td>
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<td>ELSI</td>
<td>Ethical, Legal and Social Implications</td>
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<td>ERA-NET</td>
<td>European Research Area Network</td>
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<td>E-Rare</td>
<td>ERA-NET for research programmes on rare diseases</td>
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<td>ERN</td>
<td>European Reference Network</td>
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<td>EU</td>
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<td>H2020</td>
<td>Horizon 2020</td>
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<td>HTA</td>
<td>Health Technology Assessment</td>
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<td>ICER</td>
<td>Incremental cost effectiveness ratio</td>
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<td>IRDiRC</td>
<td>International Rare Diseases Research Consortium</td>
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<td>JPND</td>
<td>Joint Programme - Neurodegenerative Disease research</td>
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<td>JTC</td>
<td>Joint Transnational Call</td>
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<td>MS</td>
<td>Member States</td>
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<td>PAO</td>
<td>Patient advocacy Organisation</td>
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<td>QoL</td>
<td>Quality of Life</td>
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<td>RD</td>
<td>Rare Diseases</td>
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<td>SHS</td>
<td>Social and Human Sciences</td>
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<td>WP</td>
<td>Work package</td>
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Executive Summary

The E-Rare Strategic Workshop was organised on September 20, 2019 in Gdańsk (Poland) to identify topics in the area of Social and Human Sciences (SHS) research that may be suitable for the Joint Transnational Call 2021 in the European Joint Programme on Rare Diseases (EJP RD). This E-Rare Strategic Workshop was part of a week of activities on rare disease research organised by the EJP RD and E-Rare in collaboration with the Medical University Gdańsk.

A working group was set up to prepare the workshop. The composition of this working group consisted of partners of the ERA-NET for research programmes on rare diseases (E-Rare) and of the EJP RD and members of the Working Group on ethical, legal and social implications (ELSI) of the International Rare Diseases Research Consortium (IRDiRC).

A preconference paper was sent to the participants before the Workshop in order to give the participants background information. Invited participants were members of the E-Rare External Advisory Board, (vice)chairs of IRDiRC and the IRDiRC scientific committees, members of the Scientific Evaluation Committee of E-Rare Calls, researchers involved in SHS research, members of the Network Steering Committee of E-Rare and representatives of Patient Advocacy Organisations.

The first session in the E-Rare Workshop was dedicated to the current state of the art of the contribution of SHS to interdisciplinary research for people affected with rare diseases or rare cancers.

The focus of the second session was to discuss what type of transnational research is needed from the perspective of different stakeholders to improve health care implementation and everyday life of people affected with a rare disease.

Subsequently, the participants were divided in six small groups to discuss what kind of SHS research may lead to necessary improvements in health care implementation and daily life. After these discussions, the small groups were united to present the outcomes to each other in a plenary session.

In the last session, the results of a survey for funders were presented in which they could indicate what type of research they are able to fund and whether they would be interested in joining a Call on SHS research for rare diseases and rare cancers. After these survey results, successes, and bottlenecks for transnational SHS research in the field of a specific multisystem rare disorder were presented. Successful measures from the French national SHS research programme on rare diseases were suggested to encourage the collaboration between researchers from different research areas and different countries to have meaningful and multidisciplinary research projects that will contribute to improved health care implementation and everyday life of people affected with a rare disease.

The speakers discussed many projects, initiatives, position papers and scientific literature, which has been collected in the section References in this report.
Main conclusions from the Workshop

- **Many ideas for potential topics** for transnational SHS research for rare diseases on the themes "Improvement of healthcare system" and "Improvement of everyday life" have been collected and are indicated in **session 3, pages 23-24**. From these ideas a final choice has to be made for the EJP RD Call JTC 2021;

- **Several funders have experience** in funding of health related SHS components and are interested to join a transnational call on SHS research;

- **Several challenges** have been identified to prepare a Call on SHS research for rare diseases and/or rare cancers;

- **Measures** have been proposed to encourage transnational and interdisciplinary collaboration between SHS researchers, clinicians, and patient advocacy organisations.
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Introduction and aims of the Workshop

The participants of the workshop in Gdańsk (Poland) were welcomed by Florence Guillot (ANR), coordinator of the ERA-NET for research programmes on rare diseases (E-Rare), on behalf of the Working Group that prepared the Workshop.

Introduction

Sonja van Weely (ZonMw) introduced the background and the aims of the Workshop. The Joint Transnational Calls (JTCs) within the ERA-NET for research programmes on rare diseases (E-Rare, running from 2006-2020) are incorporated in the European Joint Programme on Rare Diseases (EJP RD, running from 2019-2023). In this new 5-year programme, four JTCs have been planned of which the JTC 2021 may focus on transnational Social and Human Sciences (SHS) research for rare diseases and more specifically to socio-economic and health services research for rare diseases and rare cancers.

All E-Rare Calls were dedicated to basic and (pre)clinical research on rare diseases (RD). There were several reasons for not organising a transnational call on SHS research for RDs in the past, e.g. this topic was quite immature for RDs and quite jurisdiction-specific so far. Furthermore, there was difficulty in recognising social sciences and humanities as relevant to clinical practice, health care, and patients' issues in RDs. However, several funding agencies became more interested and/or engaged in transnational calls on SHS research in neurodegenerative diseases in the Joint Programme on Neurodegenerative Diseases. Moreover, a few funding agencies developed national programmes or national calls on SHS research for rare diseases.

Aims

The Strategic Workshop of E-Rare in Gdańsk was dedicated to explore the needs for transnational SHS research for rare diseases with invited stakeholders (clinicians, researchers, representatives of Patient Advocacy Organisations and research funding organisations) to identify topics in the area of SHS research that may be suitable for the JTC 2021 in the EJP RD.

In preparation of the Workshop a survey on funding activities on health-related SHS research was organised and the results of this survey were presented later in the Workshop.

The following list of health-related SHS disciplines for the survey was used (taken from the European Commission (EC) that was adapted from the UNESCO International Standard Classification of Education (ISCED 2011)):

- **Social sciences, business, and law**
  - **Social and behavioural sciences**: economics, sociology, anthropology, demography, geography, psychology, human rights.
  - **Education science**: educational research
  - **Administration**: public and institutional administration, health systems and policy
- **Humanities and the arts**
  - **Humanities**: cultural diversity, linguistics, philosophy, ethics.

A working group consisting of research funding agencies involved in E-Rare and EJP RD, members of the IRDiRC Taskforce on Ethical Legal and Social Implications and the European Alliance of patient organisations (EURORDIS) organised this Workshop.
Sessions

Session 1. Setting the scene
Chair: Virginie Bros-Facer, Scientific director, EURORDIS, France

The three speakers in session 1 discussed the contribution of SHS research in rare diseases and rare cancers from the patient’s perspective and researcher’s perspective.

Durhane Wong-Rieger (President & CEO of the Canadian Organization for Rare Disorders; chair of Rare Disease International, chair of IRDiRC Patient Association Constituent Committee, psychologist by training) gave an overview of the several global aspects of research needed to get insight in the quality of life (QoL) of patients with a rare disease and their family. These aspects are economic and emotional wellness; patient registries, natural history; QoL for patient and impact on wellbeing, care and relationship with his/her family; community services and support; accessing safe, accessible, affordable care and treatment; QoL in clinical trials.

She emphasised that there is anecdotal information from several countries and more for chronic diseases than for rare diseases. In general, there are big gaps in translation and implementation of the rare diseases patients’ needs for services into policies.
Social and Human Sciences (SHS) research for rare diseases is needed to learn something that we did not know and to validate something that is suspected. Linkages among different aspects can be drawn, causative factors identified and underlying or overarching explanatory factors exposed. This kind of research will result in appropriate, effective, and do-able solutions and harness political support for solutions.

For rare diseases in general, the impact on QoL are especially psychosocial aspects (delayed or misdiagnoses, lack of disease knowledge and treatment) and the limited (access to) support. There are also rare diseases’ variable aspects, like limited knowledge and expertise about the rare disease and the comprehensive care requirements.

Durhane Wong-Rieger also mentioned the challenges for applying traditional Health Technology Assessment (HTA) in rare diseases like limited clinical trial data available due to a smaller population, need for novel trial designs, lack of standardized (validated) endpoints (outcome measures), lack of natural history comparative data, lack of validated QoL measures, lack of certainty (long-term evidence of sustainable benefit), lack of comparative therapy (comparison against standard of care problematic), lack of expert knowledge about rare disease, use of standard cost-effectiveness analysis (CEA) and the very high incremental cost effectiveness ratio (ICER).

She emphasised that patients are research partners. The role of a patient can be as individual, as patient community representative, as patient research consultant and as partner/coinvestigator.

Furthermore, Durhane Wong-Rieger mentioned the global initiatives to address exclusion for rare disease patients (see the section References for more information). She concluded that a collaborative approach is necessary for global access to healthcare and therapies for rare disease patients in which alignment of stakeholders’ goals and structured cooperation between researchers, funders, patients, and payers is necessary.
Pauline McCormack (senior lecturer at PEALS (Policy, Ethics & Life Sciences) Research Centre, Newcastle University, UK) elaborated on the question of patient participation in complex research projects from her perspective as researcher with the title “Making spaces and participation places: involvement of patients”. She used the setting of the project RD-Connect, which was funded in the period 2012-2018 by the European Commission, alongside with the two projects NeurOmics and EURenOmics. NeurOmics and EURenOmics generated -omics data and improve diagnosis, care and therapy in neurological and rare renal diseases respectively. RD-Connect developed an infrastructure to facilitate the sharing, systematic integration and analysis of these data. About 100-200 researchers with different expertise in about 50 different countries were involved in these projects.

For the question how to create an environment in which patients can have a meaningful contribution, Pauline McCormack explained that the theory of ‘communities of practice’ (Lave & Wenger 1991) was used. This theory recognises that learning can be a collective activity practiced by those who have the same interests, aims and endeavours, which results in meaningful, on-going dialogue between groups with different backgrounds. In the case of RD-Connect, this opened up space for patient representatives, often volunteers, to introduce meaningful, on-going dialogue between patients/patient representatives and researchers, scientists and clinicians around biobanks, registries and related research.

Management and governance structures in the project included patients at different levels and with different purposes to work and learn together (capacity building) and discuss issues: (1) a patient advisory council (patient-patient interaction); (2) a patient and ethics committee (patients- researchers interaction); (3) a management/scientific advisory board included two patients allowing patients to be on the top level of management of projects making strategic decisions; (4) one patient/advocate per work package. Furthermore, workshops of researchers, patients/advocates and external experts met twice per year to provide training and work on issues.

The contacts between patients/advocates and researchers/scientists became more frequent, more detailed and more close after the phase of designing systems and procedures had finished and the phase of making these systems and procedures operational started. In this latter phase the ‘end beneficiary’ (not user) was kept in sight. Focus on dynamic dialogue between researchers and patients developed.

Pauline McCormack concluded that using the theory of communities of practice collaboration between scientists with different background and patients promoted high professional standards, ethical integrity, built trust, and confidence around new developments and technologies.
Rebecca van Kalsbeek (PhD student at Princess Máxima Center for paediatric oncology, Utrecht, The Netherlands) discussed transnational studies on health care implementation, life path studies, social and psychological issues of adult survivors of childhood cancer within the European PanCareFollowUp (PCFU) project.

All of the childhood cancers are rare diseases, due to their low incidence (less than 6 per 100,000 persons per year in the European Union). In the last decennia, the survival of childhood cancers has increased considerably. Unfortunately, it has also become clear that many survivors of childhood cancer have late and chronic adverse effects due to their treatments. These late effects have a very high impact on the health and quality of the lives of patients and family e.g. heart or kidney problems, second tumours, psychosocial problems, cognitive problems and economic problems, resulting in a high societal and economic burden on the system.

Rebecca van Kalsbeek explained that reduction of the late effects of childhood cancer can take place by survivorship care that may consist of prevention, early detection of diseases that are treatable and timely intervention. Survivorship care is performed using evidence-based guidelines/recommendations that are currently in development in international efforts. Most clinics offer survivorship care until the age of 18, but as survivors become adults, they leave the system as there is no adult alternative and become lost-to-follow up. About 30% of the childhood oncology clinics offers survivorship care to adults in Europe.

To improve the implementation of survivorship care, the PanCareFollowUp project was set up and funded by the European Commission for five years from 2019 with 4 million euro. The consortium consists of 14 project partners from 10 countries; the coordinator is Prof. Leontien Kremer (Princess Máxima Center, the Netherlands). The overall aim is to improve the quality of life for survivors of childhood and adolescent cancer by bringing evidence-based, person-centred care to clinical practice in the real world. The project comprises multidisciplinary and multinational efforts with a holistic approach to survivor wellbeing including studies on quality of life and empowerment, physical and psychosocial burden of late effects of childhood cancers and economic burden of survivorship care.

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<th>Outcomes</th>
<th>PCFU Care Intervention</th>
<th>PCFU Lifestyle Intervention</th>
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<td>Implementation</td>
<td>Barriers and facilitators</td>
<td>Barriers and facilitators</td>
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<td>Patient-reported</td>
<td>Empowerment</td>
<td>Achievement of goals</td>
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<td>Health-related quality of life</td>
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<td>Social functioning</td>
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<td>Lifestyle</td>
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<td>Symptoms and outcomes</td>
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<td>Clinical</td>
<td>Number and nature of detected clinical events</td>
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<td>Health economic</td>
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<td>Feasibility</td>
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Two interventions will be investigated: a comprehensive approach to follow-up care (Care Intervention) and an eHealth Lifestyle Intervention. The Care Intervention consists of a pre-visit questionnaire, a clinic visit including potential diagnostic tests, and a follow-up call, after which the survivor received a personal Survivorship Care Plan. A prospective cohort study including 800 survivors in four different European countries will investigate its outcomes. The Life-style Intervention will be an e-health intervention for 60 survivors in The Netherlands. In this intervention, survivors will be coached to reach the lifestyle that they want to change to reduce the burden of the late effects.

A multidisciplinary group of e.g. doctors, nurses, psychologists, ethicists, and survivors is involved in this project. The implementation analyses on the barriers and facilitators will be discussed in focus groups with survivors and health care professionals. The results on empowerment and improvement of quality of life will be provided to e.g. survivor organisations. Another outcome from this project will be recommendations. This project also foresees an implementation study for health care systems.

Session 2. Improvement of health care implementation and everyday life of people affected with a rare disease from different perspectives

Chair: Durhane Wong-Rieger, president & CEO of the Canadian Organization for Rare Disorders; chair of Rare Disease International.

The importance to improve healthcare implementation and everyday life for rare disease patients and their family was discussed by speakers from a different perspective: patient, clinician, industry, and researchers involved in SHS research and health technology assessments.

Perspective of patient

Gábor Pogány (EURORDIS Social Policy Action Group volunteer, and Hungarian Federation of People with Rare and Congenital Diseases Network, Hungary) summarised the challenges for everyday life of families with rare diseases:

- 94% of rare diseases are still incurable – mainly the social care can improve the quality of life.
- The social care system is dealing with the classical handicapped categories and is sometimes not ready for rare diseases patients.
- The majority of social services are connected to ICD (International Classification of Diseases). However, only a few hundreds of rare diseases have a code in the ICD-10; the other thousands of rare diseases do not have an ICD code.
- It is important to provide resources for the sustainability of existing RD specific helplines.
- It is essential to establish so-called resource centres for rare diseases to make integrated care available in countries. However, budget for resource centres is most of the time an issue. A resource centre should be one-stop shop style service specifically designed for people living with rare diseases and their carers. A resource centre is complementary to existing health and social care services and provides holistic services and support, creates a bridge between patients and families and various stakeholders, services and professionals, and contributes to health care, social care, and social support – including rehabilitation, education and employment and works as an information and coordination hub among different sectors. Resource centers may make holistic care a reality for people living with a rare disease.
Only the patient and the patient organization is able to see holistically the entire care system consisting of healthcare, social care, education, employment, etc. Until so far integrated care is needed for rare diseases but occurs only accidentally.

EURORDIS was involved in the EU funded INNOVCare project that had the aim to bridge the gaps between health, social and local services to improve care of people living with rare and complex conditions and to organise a pilot of case management for rare diseases. Studies and assessments included:
- European-wide survey on the socio-economic impact of rare diseases;
- Impact of the intervention according to intervention areas;
- Impact on Quality of Life;
- Cost-benefit of the model (literature reviews, data collection from patients).

The first Europe-wide survey on socio-economic impact of rare diseases was performed via the EURORDIS survey initiative Rare Barometer Voices. This questionnaire in 23 languages involved 3000 rare disease patients and carers from 42 countries and comprised 802 diseases. The qualitative results are written in the report “Juggling care and daily life: The Balancing Act of the Rare Disease Community”.

The results of this survey showed concerning the care pathway:
- For 85% of people living with a rare disease, the disease has impact on several aspects of their health and everyday life;
- Over 65% of people with a rare disease have to visit different health, social and local services in a short period of time...
- ...and 67% feel that these services communicate badly with each other or not at all;
- 3 times more people living with a rare disease and their carers report being unhappy and depressed in comparison to the general population;
- 42 % of patients & carers spend more than 2h/day on illness-related tasks (e.g. hygiene, administration of treatments, helping the people to move); 30 % of carers spend more than 6h/day.

Concerning disability issues:
- More than 7 in 10 have difficulties with daily activities and tasks, with motor/sensorial functioning, with social life/relations;
- More than 5 in 10 have difficulties with personal care activities, controlling behaviour, taking care of finances & everyday administrative tasks;
- More than 4 in 10 have difficulties with communicating with others, understanding, and learning.

Concerning socio-economic impact:
- 7 in 10 people living with a rare disease and their family carers had to reduce or stop professional activity due to the disease;
- The rare disease led to an income decrease for 69%;
- 58 % absence from work over 15 days/year;
- 41 % asked for special leave from work but could not obtain it.

Built on this survey EURORDIS has written recommendations in the EURORDIS Care paper, a position paper of May 2019 with the ambition to have holistic care provided to the 30
million people living with a rare disease in Europe, and their families, by 2030 entitled *Achieving Holistic Person-Centred Care to Leave No One Behind*. A contribution to improve the everyday lives of people living with a rare disease and their families. One of the recommendations in this paper is that socio-economic research in the field of rare diseases should be supported at national and at European level in order to support decision making on health, social and integrated care reforms.

The EURORDIS Care paper supports recommendation 10 of the Commission Expert Group on Rare Diseases from 2016 indicating that support should be provided for research on the topics (1) socio-economic burden; (2) accessibility and appropriateness of healthcare services, including social services; (3) effectiveness and cost-effectiveness of social services and support, as well as rehabilitation and assistive technologies; (4) Innovative care practices in health and social services and their impact on the quality of life of people living with a rare disease.

**In summary**, socio-economic research in the field of rare diseases should be supported at national and at European level in order to support decision making on health, social and integrated care reforms with the following relevant topics from patient perspective, as data are needed to improve care:

- Impact of rare diseases i.e. disability, mental health, socio-economic burden;
- Outcome measures;
- Impact of innovative care practices in health and social services and their impact on the quality of life of people living with RD;
- Care pathways and integrated care: accessibility and appropriateness;
- Effectiveness and cost-effectiveness of healthcare, social care, rehabilitation, and assistive technologies.

**Perspective of clinician**

Birutė Tumienė (on behalf of European Reference Network (ERN) ITHACA, representative of Lithuania in the ERN Board of Member States, National coordinator Orphanet Lithuania, Vilnius University Hospital Santaros Clinics, Centre for Medical Genetics, Lithuania). ERN ITHACA is a patient centred network which meets the needs of those with rare congenital malformation and syndromes with intellectual and other neurodevelopmental disorders.

Birutė Tumienė started her presentation with the acknowledgement of major inequalities for patients due to the remarkably unique rare disease features that needs specific measures that unfortunately are not all in practice:

- **Rare, numerous, heterogeneous.** Consequently, there is limited ability to recognize/ provide care at a primary/ local medical contact point. *Measures: organise care pathways and referral systems, vertical integration, workforce education, tertiary-tertiary care interface, reducing barriers in regionalized healthcare systems.*
- **Heterogeneous multisystem involvement.** Consequently, there is heterogeneity of pathways and multiple contacts with healthcare system. *Measures: organise horizontal integration, multidisciplinary approach, care coordination/case management.*
- **Complexity in diagnostics, treatment, long-term care.** Consequently, there is limited expertise and resources, expensive infrastructures. *Measures: centralization of expertise, infrastructures, and human resources.*
- **Chronic, disabling, childhood-onset in 75%, life-long, complex needs.** Consequently, there are complex and multiple trajectories across systems. *Measures: longitudinal, holistic approach, care coordination/case management, transition of care, patient empowerment, balanced provision of centralized/ decentralized services.*
**Diagnosis**

The mean time for diagnosis of a patient with a rare disease is 5 years because of the unique rare disease features and the odyssey of a patient to get a diagnosis. Many rare disease patients are not yet diagnosed (“stuck in healthcare systems”) and approximately 50% of the rare disease patients are still undiagnosable (syndrome without a name”, SWAN). Measures for these undiagnosed patients are organization of RD care in national systems, direct healthcare – research intersection and EU and international collaboration.

**Treatment**

About 5% of the rare diseases have specific treatments. On one hand, there is an explosive rise of orphan drugs in the Research & Development pipeline. On the other hand, there are also rising costs and return on investment/affordability issues for the EU member states. The fragmentation of common diseases into orphan indications could even give a risk for “reversed” inequity in rare diseases versus common diseases as broader, non-orphan indications may be neglected.

For about 95% of the rare diseases there is only symptomatic treatments available. For these rare diseases there is a basket of lack in basic services, like diagnosis, evidence-based symptomatic treatments, secondary/ tertiary prevention, care pathways, long-term management, care coordination, psychosocial support, and palliative care.

Optimal scenarios/main needs for different stakeholders in the rare diseases area are according to Birutė Tumienė:

**For patients/families:** timely diagnosis, effective treatments, and long-term management; well-organised care, addressing complex needs of patients and families; recognition of the concept of health as ‘a state of (complete) physical, mental, and social wellbeing...’ (WHO, 1948).

**For clinicians (local/regional):** basic education/ information on rare diseases (“red flags”, capabilities to follow long-term management plans) and health system literacy (where, how to refer).

**For clinicians (experts):** well organized health system (clear care pathways, navigation of patients, their data, and funds); reimbursement of all related activities; administrative aid; time and conditions to gain and maintain expertise.
For researchers: facilities and resources for research (registries, biobanks, animal models, etc.).

For health and social care systems: rare disease services that are cost-effective and well integrated into an existing framework; solutions in accordance with the global trends and challenges, like rising costs, increasing demand for competences and skills, innovations, translational research, personalized medicine, information society, IT technologies, patient choice-driven provision of services (consumer-driven rather than supply-driven model), involvement of communities.

Birutė Tumienė also indicated that there should be more recognition for the inequality and human rights in rare diseases by authorities and organisations. She referred to “...availability of health care and services remains low and their quality poor, especially with regard to associated impairments. Rare diseases often attract stigma and discrimination, and many persons living with a rare disease find themselves excluded from participation in employment and from integrating fully and productively into society” - Report of the United Nations High Commissioner for Human Rights, 2019.

Like Gábor Pogány, she also touched upon the problem that rare disease codification, tracking, and monitoring is missing. When there is no visibility of rare diseases in the healthcare system it looks as if there is no problem. The EU funded project RD Action showed that in the ICD 10 codification only 559 specific codes match Orphanet rare disease entities (including groups of diseases). The ICD 11 will have codes for 3718/6164 rare disorders (2015), whereas there are nearly 7000 ORPHA codes. The international medical terminology system SNOMED CT had 38% of ORPHA entities in August 2015.

Solutions for the problems indicated above can be at least partly delivered by national Centers of Excellence and ERNs. There are 24 ERNs for rare diseases with more than 950 Centers of Excellence that oversee 700,000 patients/year. ERNs are a triangle of highly specialised healthcare, research and education and the largest platform for clinical, translational, socioeconomic research in rare and complex diseases. They form economies of speed, scale and scope for multiple tasks like developing and implementing rare disease clinical guidelines, collecting cohorts and data, performing clinical, epidemiological, socioeconomic research, creating curricula for education on rare diseases, monitoring rare diseases for evidence-based policy making, etc. Now 5 ERN registries are operating, and 19 ERN registries are in development resulting in availability of data of 1 million patients in 2022.

Nevertheless, the major challenge is to integrate ERNs and services into the national systems. As an expert panel questioned “What is the use of enormous amounts of expertise if they remain confined to the individual centres participating in the network? These centres must be able to reach all patients in their territories – and in other Member States, if no national reference centre has been established – in order to really make a difference to the care of these patients. Thus, ERNs are effective only in so far as they are inclusive, proactively reaching out to the populations they serve.” – Expert Panel on Effective Ways of Investing in Health (EXPH): Opinion on Application of the ERN model in European cross-border healthcare cooperation outside the rare diseases area, 2018.

Missing points for integration in national systems are (implementation of) innovative services and care provision models; care pathways: organization, navigation of patients/data/funds, fine balance between centralized and decentralized services; a framework of psychosocial
services (respite, resource centers); socioeconomic evaluation of interventions or lack of interventions and data for evidence-based policy making.

As a final point Birutė Tumienė indicated that an important point of attention is wasteful spending in health that may be even more in rare disease care, including

- wasteful clinical care (e.g., preventable adverse events, ineffective or inappropriate care due to lack of specialized knowledge and skills, etc.) and
- operational waste (e.g., inefficient use of expensive infrastructures and human resources due to lack of centralization, duplicated or redundant healthcare services due to poorly developed rare disease care pathways, etc.).

**Figure 1.1. Three categories of waste mapped to actors involved and drivers**

From: Tackling wasteful spending on health © OECD 2017

Examples of literature on wasting of rare diseases care shown in the presentation of Birutė Tumienė are summarized in the section References.

Innovation is a key instrument/solution for achieving sustainable and efficient solutions (either sustaining/evolving or disruptive). "Disruptive innovation" in health care is a type of innovation that creates new networks and new organisations based on a new set of values, involving new players, which makes it possible to health improve outcomes and other valuable goals, such as equity and efficiency. This innovation displaces older systems and ways of doing things." (Expert Panel on Effective Ways of Investing in Health (EXPH)).

Topics for SHS research that Birutė Tumienė would like to propose are the following:

**Innovative services/ care provision models**

- Integrated care, clinical networks, care coordination, case management;
- IT/digital services, eHealth, mHealth, telemedicine …;
- Patient-centeredness, value-based care;
- Patient-empowerment/self management;
- Role and involvement of patient organizations;
- Invoking social media;
**Educational research**
- Workforce education, proper skill mix, teamwork.

**Socioeconomic research**
- Costs of “diagnostic odysseys”, inappropriate, low-quality care, lack of centralization;
- Unwarranted variation in service provision;
- Data-driven modelling of care pathways.

**Perspective of SHS researcher – living the genomic dream**

Pauline McCormack (senior lecturer at PEALS (Policy, Ethics & Life Sciences) Research Centre, Newcastle University, UK) presented the sociology of expectations/sociology of hope, including aspects of bioethics and started with an anecdote.

The biomedical encounter – anecdote. For anyone who is familiar with the challenging of the medical model with the social model, impairment model, critical disability studies might think we are way past the primacy of the medical model especially in rare diseases. Pauline McCormack shared her anecdote from a neurologist who was worried about a young man that the neurologist treated since childhood. The patient stopped attending clinic, and the neurologist could not check his health status and whether he was taking his medicines. The neurologist did not know what to do to convince him of long-term health problems related to non-compliance. Pauline McCormack told the neurologist that young adults are finding independence, transitioning to adulthood, showing risk-taking behaviour, challenging what has so far been normal and questioning whether it’s right for them or not. Thus, there are many possible explanations as to why he is not attending clinic. However, the neurologist said that it was not that complicated, but that he just did not want to take his medicines. This neurologist was confirming and privileging the biomedical approach to this patient with a rare disease, ignoring the social and personal interactions with the young person.

Biomedical-technoscientific approach. A biomedical approach assumes e.g. that the body/person can be reduced to a set of biological components: “the body can be repaired like a machine; thus medicine adopts a mechanical metaphor, presuming doctors can act like engineers to mend that which is dysfunctioning” (Nettleton). Another element at play is the development of technology - “the merits of technological interventions are sometimes overplayed, which results in medicine adopting a technological imperative” (Nettleton).

Role of sociology. Sociology recognises people’s innovative strategies to negotiate living with(in) their bodies in their everyday social lives’ (Zitzelsberger). Sociology challenges expectations of success/normality and seeks deep understanding of people's experiences and relationships with healthcare, new treatments, technologies, and interactions with everyday life.

Genomics – a contemporary example. Pauline McCormack introduced the example of the 100,000 genomes project starting in 2012 and established to sequence 100,000 genomes from around 85,000 patients affected by a rare disease or cancer. The title of Pauline’s presentation came from the Chief Medical Officer “Now we need to welcome the genomic era and start living the genomic dream” (2016).

Pauline McCormack has the opinion that there was a continuing positive message from the start on this 100,000 genomes project saying that there were benefits for the nation (the
promise of better health), benefits for especially rare disease patients (promised diagnosis, treatments and cures), benefits to economy and scientific knowledge and making bold claims (‘changing the way we treat medicine in 21st century’ (Genomics England 2016)). The goal in the UK is taking genomic medicines mainstream into care.

The general public were positive on this new development of sequencing genomes, but rare disease patients were positive with reservations. Genetic Alliance UK asked in a survey what patients thought of the genome sequencing. 87% of the survey responders said that they thought genome sequencing would be helpful to themselves or their child if it were offered to them today and 94% said that they were either “very likely” or “quite likely” to give their consent for sequencing. However, 30% of those said, that consent for this data to be used for research would be dependent on whether or not they had a diagnosis.

The first study on the experience of patients undergoing genome sequencing showed 83% of participants expected utility from the test that would tell them something useful (Lupo 2016). However, in reality the actual utility is between 12-30%. Furthermore, from the expected 100,000 genomes sequences, 5,000 results returned after 7 years. In conclusion, there is a massive expectation of utility that does not meet with reality for rare disease patients.

*Powerful Genetic Imaginary:* An imaginary is a collectively embraced actionable future in which technological change will bring about certain positive, culturally intelligible results’ (Weiner et al 2017). Great expectations for people undergoing genomic sequencing brings a ‘regime of hope’ (Martin 2008, Rose 2007). Those ‘whose very hopes for survival are closely bound up with the materialization of such promises’ (Haase 2017). When we make promises around clinical genomics in particular, we offer those involved a future that in many cases is not possible. The rare disease patients are offered hope that might not be realised.

*The Genomic Dream! – Some problems.* The dominant discourse of genetics in understanding health and disease neglects other factors, like social. There are ways of living well with rare conditions. For example, the holistic care (physio, steroids, cardiac surveillance, social support) made a difference in life expectancy for patients with Duchenne Muscular Dystrophy as it doubled the life expectancy (or more). Although the gene was discovered in 1980, the hope on genomic solutions is still not fulfilled for them.

*Problems with Promises:* Positive language suggests that implementation will be predictable and that is not the case according to Pauline McCormack. E.g. performing research from bench to bedside is rarely linear and is not a simple process. Translation into clinical care introduces complexity and new uncertainties. Therefore, the discrepancy between genetic imaginary and actual experience gives disruption.

*The Trinity of Perspectives leads to the Path of Enlightenment!* Pauline McCormack indicated that we do not understand the everyday expectations. The three-way system of patient/family advocacy, medicine/science and sociology/ethics should be able to get more insight in the complex everyday life of patients with rare diseases.

In the discussion after this presentation there was a clear difference in opinion in the audience: some participants agreed that there was a lot of things to be done before the genetic dream becomes true for patients, e.g. having
enough genetic counsellors to inform patients in the right way and the consequences for treatment for them; other participants (e.g. a clinical geneticist) was convinced that the genetic dream has come true as the new techniques can reveal the genetic diagnosis of a rare disease patient in three weeks.

**Perspective from industry**

**Alexandre Méjat** (Manager International Scientific Affairs, AFM-Téléthon, France) gave the perspective of the patient organisation AFM-Téléthon going into the industry world.

AFM-Téléthon, the French Muscular Dystrophy Association, was created by Yolaine de Kepper, mother of seven children of which four had Duchenne Muscular Dystrophy. She was president of AFM-Téléthon from 1958-1981. AFM-Téléthon organised the first French téléthon in 1987 and is still doing. This French fundraising event is organised in early December with a TV show and many other activities (dancing, sport events, dinners, etc.) raising budget for about 85-90 million euro per year. Of this budget, 60 million euro per year is dedicated to rare disease research since 1987.

The Généthon laboratory was created in 1990 by AFM-Téléthon thanks to Téléthon donations and is dedicated to genomics and gene therapy development. The first efforts of Généthon resulted in 1992 in the human genome first maps. The offering of the first human genome maps to UNESCO was the first step for the Universal Declaration on the Human Genome and Human Rights (1997) in which Article 1 states that *the human genome underlies the fundamental unity of all members of the human family, as well as the recognition of their inherent dignity and diversity*. Alexandre Méjat indicated that in a symbolic sense, genetics is the heritage of humanity and that the human genome should never be patented.

Because what patients needed did not exist, AFM-Téléthon created the Institute de Myologie (1996) and the institute I-Stem (2005). Together with Généthon these institutes form the Institute des Biotherapies. During the years AFM-Téléthon invested from fundamental research to preclinical research up to clinical trials.

Institute de Myologie is expert in muscle sciences, creating clinical trials and validations of outcomes and treatments. This institute created a set of myotools to be able to measure muscle force, muscle function and muscle activity as alternatives to the 6-min walking test that is used in clinical trials thus far.

I-Stem is a stem cell institute that investigates repurposing drugs on stem cell models. Because these drugs have already been investigated for other diseases, some research like
safety profile is already known and toxicology research is already performed. As it appeared difficult to find an industrial partner to fund phase 3 clinical trials, AFM-Téléthon also funds phase 4 (postmarketing) clinical trial for repurposing drugs. Alexandre Méjat indicated that ERNs could play an important role as expert center and in finding patients for these clinical trials.

Généthon Bioprod was created in 2011 for production facility of vectors for human clinical trials for gene therapy and is able to prepare products for clinical trials. This institute is integrated in Yposkesi, a private industrial platform to produce innovative therapies (cell and gene therapy). Yposkesi means “promise” in Greek. AFM-Téléthon and French government are the owners.

The big issue is now how to get innovative therapies available for all. The price for the first gene therapy in 2012 (Glybera; 1 million dollars per patient) appeared to be too high for society and was not acceptable. In addition, other gene therapy products like Zolgensma (a gene therapy for young children with spinal muscular atrophy (SMA) that is approved in the US) will cost about 2.1 million dollar per patient. Many start-up biotechs that develop these therapies are funded by governmental funding or by patient organisations. After big pharmas have bought the biotech companies, they ask for a high price for the innovative therapy product. The high costs for development of these therapies mentioned by the big pharma should be transparent and justified by independent sources. Alexandre Méjat pleaded that a new economic model should be invented that abandons the «profit-only» model to imagine a new pharma-ethical model insuring access to treatments to patients with a concept of «Fair and sustainable price».

Alexander Méjat finished his presentation with a quote on the patient power from Michel Callon: «This power is not synonymous with arbitrary and lonely exercise of authority, let alone revenge. It is an enlightened power that recognizes the irreplaceable contribution of specialists. But it is a power that gives the patients the last word: they are sources of ideas, questions, knowledge and know-how and they are the ultimate object of all the efforts that are made. The patient power is only the other name given to the will to cure.»

**Health Technology Assessment (HTA) Perspective**

Beth Potter (Associate Professor at the School of Epidemiology and Public Health, University of Ottawa, Canada) does not work with an HTA organisation, but her work interacts with HTA. She started her presentation with the scope of interventions for rare diseases that could be considered for HTA, moving beyond the common focus on diagnostic tests and orphan drugs to include surgery (e.g. organ replacement), physical therapy, diet and lifestyle modifications and psychological and educational interventions. Some interventions also operate at the level of the system of care, such as interventions to promote improved access to care (e.g. telemedicine), screening and diagnosis programmes, and interventions related to the organisation and coordination of care.

In addition to the scope of interventions, the scope of relevant outcomes also has to be considered: the “triple aim framework” (Berwick et al, 2008) highlights the relevance of improved clinical and population health, improved health care experiences, and manageable health system impacts, including cost of care.
There is a scarcity of evidence on the effectiveness of interventions for rare diseases. Several sources of gaps in evidence can be identified, including uncertain natural history, clinical heterogeneity, challenges in identifying and measuring the highest priority outcomes, and the small number of patients available to participate in research.

The WHO defines HTA as follows: “Health technology assessment (HTA) refers to the systematic evaluation of properties, effects, and/or impacts of health technology. It is a multidisciplinary process to evaluate the social, economic, organizational, and ethical issues of a health intervention or health technology. The main purpose of conducting an assessment is to inform policy decision making.” The last sentence was emphasised by Beth Potter. She commented that in practice the focus is often on the clinical and cost-effectiveness of interventions, while the other elements in this definition could be particularly relevant for SHS research.

In the rare disease field HTA is frequently performed to inform decisions about drugs for rare diseases (DRD; this term is used in North America; in Europe it is called orphan medicinal products). While randomized trials are considered the gold standard study design to evaluate the efficacy and effectiveness of therapies, they are often challenging to conduct for DRD, so that the evidence base relies more heavily on study designs that are at higher risk of bias. In addition, the frequently high per-patient costs for DRD mean that these therapies often do not meet the cost-effectiveness criteria used in HTA and by policy decision-makers.

Beth Potter noted that HTA organizations, researchers, and policy makers do recognize these challenges as quite critical to address when considering HTA for DRD, with several strategies that have been used in practice. These strategies fall in three broad and overlapping categories: (1) separate HTA processes for DRD, (2) flexible clinical and/or cost-effectiveness criteria within existing HTA processes (or associated policy decision-making processes) and (3) recommendations or funding decisions that incorporate risk sharing or “managed entry agreements” (including evidence generation) between manufacturers and payers. Nevertheless, these strategies are somewhat controversial.

Beth Potter sees important transnational opportunities for SHS research for rare diseases related to HTA. Notably, the budget impact of DRD is high and increasing for health care systems and other payers, including individual patients and their families. Furthermore, there is uncertainty about the evidence and challenges associated with HTA that collectively result in disparate policy decisions about funding and reimbursement across jurisdictions. This uncertainty translates into inequities in access to effective health care for patients living with rare disease.

To reduce these inequities and ensure that interventions are rigorously and appropriately evaluated, Beth Potter suggested that transnational research within three broad areas may be most valuable for HTA in rare disease:

- Research to improve capacity to generate robust clinical effectiveness evidence for DRD;
- Research to improve HTA and policy decision-making processes for DRD;
- Research that emphasizes health system implementation of efficacious DRD.
Her specific suggestions for transnational research for these three broad areas were:

1. **Research to improve capacity to generate robust clinical effectiveness evidence**
   - Alternative study designs to evaluate interventions for rare diseases (e.g., innovative clinical trial designs appropriate for small patient populations);
   - Transnational research infrastructure for evidence generation (e.g., addressing barriers to data sharing to enable multinational studies; facilitating knowledge synthesis through data harmonization and interoperability across studies; creating multinational registries that adhere to established principles regarding governance, data quality, ethical standards).

2. **Research to improve HTA and policy decision making processes for drugs for rare diseases**
   - Patient involvement, including patient-partnered studies (particularly to identify and prioritize outcomes);
   - Studies of approaches to foster earlier and more coordinated collaboration among stakeholders across entire DRD pathway (e.g., “adaptive pathways”);
   - Research to better understand considerations other than clinical and cost-effectiveness (social value judgements) of DRD and how these are incorporated into HTA and policy decision-making.

3. **Emphasis on health system implementation**
   - Evaluations of rare disease therapies that consider health system implementation (e.g. studies to understand “real-world” effectiveness of interventions with demonstrated efficacy; studies of ‘co-interventions’ that could optimize DRD effectiveness and improve quality of life);
   - Studies of health system level interventions that may reduce inequities in access to effective clinical interventions (e.g., health care coordination, telemedicine);
   - Studies that emphasize outcomes related to patient experience.

**Session 3. Interactive session for first identification of ideas for topics for the Call JTC 2021 within the European Joint Programme on Rare Diseases**

*Chairs: Eva Müller-Fries, Scientific Officer at DLR Project Management Agency, Germany and Diana Désir-Parseille, Official in charge of research administration, French Foundation for Rare Diseases, France*

The aim of interactive session was to identify a first selection of ideas for topics for the EJP RD Call JTC 2021.

After introduction of this interactive session by Eva Müller-Fries and after lunch, the audience was divided in six small groups that discussed in parallel the key question for this afternoon: How can SHS research improve health care implementation and everyday life of people living with a rare disease and their families? The challenge in these discussions was to focus on research that is specific for rare diseases.
Each small group consisted of different stakeholders (patients, researchers, clinicians, funders) and included one of the speakers. Eva Müller-Fries and five members of the preparatory working group moderated the discussions in the small groups. In each group, one member was asked to be the rapporteur and to present the main results of the group to the audience in the plenary part of the interactive session.

In the parallel session every participant could point out his/her ideas on important SHS research for specifically rare diseases topics on green cards and put the topics under the header of “Improvement of healthcare implementation” or under the header of ”Improvement of every day life“. The topics were discussed and grouped on yellow papers. If there was time enough, each group made a first prioritisation using red dots.

Results of the interactive session: What SHS research is needed to improve health care implementation and everyday life of people living with a rare disease and their families?

Each rapporteur presented the outcomes of the discussions in the plenary session. Groups came up with several similar or overlapping ideas and topics but also with additional topics. From the presentations of the rapporteurs and the input from the participants that was written on the collected material (green and yellow cards) in the parallel sessions, the following broad range of ideas were identified to improve health care implementation and everyday life of people living with a rare disease and their families.

**Improvement of healthcare implementation**

- **Identification of barriers and facilitators** and comparison/mapping of cost-effective and useful social and health care best practices between countries and with different stakeholders (healthcare professionals, patients, policy makers, nurses, etc.); assessment of social equity for rare diseases; improvement of communication with all stakeholders; access of policies and access to services;
- **Health economic research** like policies on costs of treatment, evaluation of parameters for assessment of price of therapies; value of care and effective therapies evaluation; ethics perspective on drug development;
- **Socioeconomic research** on all aspects (interventions/lack of interventions; social care burden; out-of-pocket payments; impact on family);
- Find ways to recognise the value of rare disease patients to the society (participation in society);
- **Integrated care** including innovative services/care provision models; care pathways; transition of care of childhood into adulthood;
- **Diagnosis** - Bottlenecks and limiting factors hindering access to available diagnostic tools/diagnostic delays/criteria for implementation of neonatal screening;
- **Therapy** - Implementation of results from clinical trials with e.g. repurposed drugs in clinical practice;
- **Data Use registries**: ethical aspects (not only on genetic data), patients involvement, holistic registries (including medical data, school, work etc.);
- **Educational needs** for professionals (skills, etc.);
• **Encourage transnational cooperation**, in which more advanced countries will provide guidance to the others in building ‘the basis’, which can boost some immediate but also future improvements both to the benefit of patients and to SHS research.

**Improvement of everyday life**

- **Psychological burden**: financial/economic burden, impact on family relations (care givers and non-care givers), including school integration and impact on siblings, stress anxiety;
- **Patient engagement** in value-based care, in patient-centred care;
- **Quality of life of survivors** of rare cancers and of rare disease patients with an effective therapy (identifying themselves not being a patient anymore);
- **Our identity in a social sense** (what makes us similar and diverse), national preferences;
- Establish the right tools to assess effect of treatment/PROMs (Patient Reported Outcome Measures) that are effective, reproducible, innovative;
- Transnational measurements and improvement of **well-being through non-medical/non-pharmacological intervention**;
- Innovative **digital technology** (e.g. E-health, communication purposes, access to tools, access to holistic care) and innovative use.

This broad range of ideas for topics will be used to determine the focus of the EJP RD Joint Transnational Call JTC 2021 taking also into consideration what kind of topics are possible to finance for the funders that will take part in this Call.

Two suggestions were given for organising the Call. The involvement of early career investigators in interdisciplinary SHS research should be recommended in the Call. The second comment was that patient involvement should be part of the criteria for evaluation of the research projects in this Call on SHS research.

**Session 4. Feasibilities, advantages, and bottlenecks of transnational health-related SHS research**

*Chairs: Russell Wheeler, Patient Advocate at ERN-EYE and Leber’s Hereditary Optic Neuropathy Society UK and Ralph Schuster (Scientific Officer at DLR Project Management Agency, Germany)*

In this session the outcomes of the survey of funding agencies on funded health-related SHS research were discussed next to successes and bottlenecks for transnational SHS research and measures to facilitate researchers from different areas to collaborate.

**Feasibilities**

*Sonja van Weely* (Senior Programme manager, ZonMw, The Netherlands) presented the outcomes of a survey for funders on funded health-related SHS research. The reason for sending a survey was that all E-Rare Calls and the first two Calls in the EJP RD were/will be dedicated to basic and (pre)clinical research on rare diseases. If there would be a call in the EJP RD dedicated to SHS research, the information should be gathered whether funders are able to fund SHS research for rare diseases and whether they are interested to do so.
The working group that prepared the workshop also prepared the survey questions. The definition of health-related SHS research and the definitions of rare diseases and rare cancers was the same as used for the Workshop (see the Section Introduction and Aims). The survey was sent to funders involved in the programmes for rare diseases E-Rare and/or EJP RD, funders that are member of IRDiRC, funders involved in the Joint Programme on Neurodegenerative Diseases Call JTC 2018 on SHS research, and funders involved in ERA-Nets HERA (humanities) and NORFACE (social and behavioural sciences) through the coordinators of these two ERA-Nets. In total 74 different funding organisations from 33 countries received the survey: Europe/European associated countries (58 funders), Australia (2 funders), Canada (4 funders), Japan (2 funders), US (8 funders). The period for sending the survey and collecting the answers was July-August 2019.

Out of the 74 funders, 33 responded (45%). The survey was completed by 30 funders, sometimes with additional e-mails to explain their responses. These 30 funders were located in Europe/European associated countries (22 from 17 countries), Canada (3 funders), Japan (1 funder), USA (4 funders). Funders from 3 different countries in Europe send their short information via e-mail.

Main answers in survey

A. Currently two funders have specific national funding calls or programmes on health-related SHS research specific to rare diseases.

1. The French Fondation Maladies Rare (FFRD): has the Action “Improving patients’ life path” from 2013 that is still going on. They have completed six calls; one call is going on in September 2019. In the six Calls 39 projects were funded in three research topics:
   - Activity limitations, compensation strategies and needs for support;
   - Social involvement;
   - Ethics and human rights.

One of the eligibility criteria was that the project should involve SHS researchers, clinicians and patient’s organisations. The 2-year-research projects costs max 100k€ and included personnel costs, running costs, travel costs, equipment, and services. More detailed information on this Action was given in the presentation of Laura Benkemoun.

2. The Canadian Institute for Health Research – Institute of Genetics (CIHR-IG) developed a Knowledge Synthesis Grant funding opportunity to support research on the socio-economic burden of inherited (rare) diseases. In the context of this funding opportunity, patient is "an overarching term inclusive of individuals with personal experience of a health issue and informal caregivers, including parents and family, friends, and members of support organizations (e.g. patients’ associations)."
B. Seventeen funders (57%) indicated to have national funding calls or programmes on health-related SHS research that are not specific for rare diseases and/or rare cancers. 12 out of these 17 funders (71%) mentioned several different programmes on health-related SHS research. Examples of these programmes are:

- Programmes on palliative care;
- Programmes on ethical, legal and social implications of genomic research or on digitalisation;
- Dissemination and implementation research in health (overcoming barriers in adopting, adaptation, integration, scale-up and sustainability of evidence-based interventions, tools, policies and guidelines);
- Patient oriented research and patient oriented research impact assessment;
- Model registries for care/health services research.

C. Thirteen out of 30 (43%) funders indicated to have health-related SHS component elements in current programmes. In the question, the following examples of SHS components were mentioned: patient involvement, health technology assessment/cost-effectiveness studies, socio-economic aspects including burden of a disease, quality of life.

Nine of the 13 funders have also a specific SHS programme or Call; the other four funding organisations have general programmes in which health-related SHS elements may be funded. Examples of these health-related elements in general programmes:

- Clinical trials with high relevance for patient care;
- Genomics and precision health;
- Patients well-being;
- Research programme on visual impairments.

D. Twelve out of 30 funders (40%) indicated to be involved in bi- or multinational Calls on health-related SHS research or with a module on SHS-research. Examples of these calls that were mentioned:

**Multinational Calls**

- Neuron JTC 2017 (ELSA of Neurosciences);
- JPND JTC 2018 (Health and Social Care for neurodegenerative diseases);
- ERAPerMed JTC 2019 (Personalised Medicines) and Neuron JTC 2018, each with a component dedicated to SHS aspects;
Trans-Atlantic Platform Social Sciences and humanities.

In the EU Joint Programme - Neurodegenerative Disease Research (JPND) 2018 Joint Call on Health and Social Care Research and Innovation the research area that were included were (1) Care pathways, (2) Factors influencing progression and prognosis of disease; (3) Outcome measures; (4) Palliative Care; (5) Cost-effectiveness, affordability and overall effectiveness of interventions and (6) Supporting Technologies.

Bi-national Calls or programmes
- France - German
- Canada - USA
- Turkey - Korea / Turkey - France / Turkey - Russia

E. On the question whether funders expected local challenges for getting health-related SHS research funded, the answers are shown in the following table.

<table>
<thead>
<tr>
<th>Item</th>
<th>Total responses</th>
<th>Yes</th>
<th>No</th>
<th>N/A</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Interest of researchers?</td>
<td>30</td>
<td>9</td>
<td>18</td>
<td>3</td>
<td>• Small number of researchers interested</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>• Networking of SHS researchers and RD clinical researchers needed</td>
</tr>
<tr>
<td>Review process?</td>
<td>30</td>
<td>4</td>
<td>23</td>
<td>3</td>
<td>• Difficulties finding evaluators</td>
</tr>
<tr>
<td>Other challenges?</td>
<td>30</td>
<td>9</td>
<td>18</td>
<td>3</td>
<td>• Differences in health systems</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>• Differences in national regulations and ethical considerations</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>• Policy makers not enough involved</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>• Topic may not be highly prioritised</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>• Finding budget</td>
</tr>
</tbody>
</table>

F. Do funders have the possibility to join and are they are interested to join the SHS Call for rare diseases and/or rare cancers (EJP RD JTC 2021)? The answers are summarised in the table below.

<table>
<thead>
<tr>
<th>Question</th>
<th>Total responses</th>
<th>Yes</th>
<th>No</th>
<th>N/A</th>
</tr>
</thead>
<tbody>
<tr>
<td>Possible for your funding organisation to join?</td>
<td>30</td>
<td>20*</td>
<td>4</td>
<td>6</td>
</tr>
<tr>
<td>Interested to join?</td>
<td>30</td>
<td>19*</td>
<td>2</td>
<td>9</td>
</tr>
</tbody>
</table>

Several funders that indicated "yes" for both questions commented that in July/August 2019 it was too early to commit (a vague yes, it is now only an expression of interest, etc.). Funders also commented that more information was needed on the topics within the SHS research. Furthermore, some funders indicated that their Review Board or Presidium has to decide to join or joining this Call was dependent on availability of the funds. US funders and the Japanese funders indicated that they were interested but foresaw difficulties in joining the Call. For the US, this is a complex process due to US Federal Regulations; for Japan, it is complex due to the different fiscal years in Europe and Japan.

G1. On the question whether there were restrictions in topics to be chosen, only 3 funders responded, each with a different comment: the topics should not be too specific due to the
small research community in this field, one funding organisation indicated that it cannot fund patient involvement, and one funder thought that the topics should focus on health and not on humanities.

G2. Four funders indicated that a scientific hypothesis/objectives/research question is needed, or an innovation aspect clearly included to be able to fund a project – for some this is also needed because they only fund fundamental and/or exploratory research of high scientific level.

Conclusions

Sonja van Weely concluded that

- Many funders (70%) that responded to the survey have national programmes, calls or possibilities to grant health-related SHS research.
- Quite some funders (40%) collaborate in a bi-national or multi-national way to fund health-related SHS research.
- Two funding organisations (7%) have a dedicated programme on SHS research for rare diseases.
- Many funding organisations (63%) are interested in a multi-national collaboration to fund SHS research for rare diseases.
- Some funding organisations (13%) indicate that a scientific hypothesis/objectives/research question is needed, or an innovation aspect clearly included being able to fund a project.
- One of the suggestions in the survey was that it would be worthwhile to organise a networking event for SHS researchers and rare diseases clinical researchers.

More discussion will be needed whether rare cancers will be included in this Call. In the survey, four funders mentioned that they cannot fund rare cancer research; two funders mentioned that in their country cancer charities are present that should join the Call in case rare cancers would be included in this call. One funder had the opinion that rare cancers should not be included in this Call. On the other hand, in a subgroup during the interactive session 3 it was stated that for researchers from relatively small countries it would be beneficial to include rare cancers in the call as a broader topic increases the chance for these researchers to find a thematic overlap. Inclusion of rare cancers could also simultaneously solve concerns about too little interest in the SHS call and the pressure on EJP RD to include the rare cancers into its scope.

Successes and bottlenecks

Nathalie Angeard (Lecturer Neurosciences, Paris Descartes University, Memory, Brain & Cognition Lab Université de Paris; Centre de Référence Paris Est des Pathologies Neuromusculaires, Institut de Myologie, Hôpital de la Pitié-Salpêtrière, France) elaborated on examples of SHS research with a focus on Myotonic Dystrophy type 1 (DM1) and in the context of international collaboration.

SHS research on Myotonic Dystrophy (DM1)

DM1 is a severe and multisystem rare disease. It is the most prevalent neuromuscular genetic disease. The estimated prevalence is 10 per 100,000 people affected in European populations. DM1 is one of the most variable human diseases with complex, multi-systemic, and progressively worsening symptoms. The main muscle symptoms are distal to proximal muscle weakness and myotonia. Pulmonary and cardiac functions are also
impaired with sudden death from cardiac complications being a significant cause of fatality. Other prominent clinical features are cataracts, cognitive and intellectual deficits, endocrine abnormalities, and gastrointestinal related symptoms. Excessive daytime sleepiness and psychiatric symptoms might lead to restricted social participation and quality of life can be seriously impaired.

DM1 is not only a neuromuscular disease but also a brain disorder. Dysfunction of the central nervous system is a common feature in a substantial proportion of patients with DM1. The severity of cognitive impairments appears to depend on the age of onset of the disease and highly variable from subtle cognitive deficits to intellectual disability.

CNS symptoms in the different forms of DM1

Preliminary observations on DM1 psychological/cognitive related symptoms have shown weaknesses in several psychological domains (e.g. cognition, processing and/or comprehension of emotion, interpersonal relationships), increase in difficulties related to fatigue symptoms, excessive daytime sleepiness, and chronic pain. Furthermore, there is a reciprocal influence between the difficulties, e.g. attentional processes are influenced by excessive daytime sleepiness.

DM1 is a neurodevelopmental disorder ranging from severe/mild intellectual disability within the most severe (congenital) phenotype to subnormal intelligence and specific cognitive impairment in the childhood or juvenile forms of DM1, learning disabilities (dyslexia and/or dyspraxia), attention / executive functions impairment, social cognition vulnerability, and ADHD and/or Autism Spectrum Disorder comorbidity. Research on the social cognition vulnerability in the childhood form of DM1 has shown that impaired emotional recognition skills and low scores in Theory of Mind tasks appeared to be influenced by demographic, genetic and environmental factors i.e. sex of the patient, number of CTG repeat size and mode of transmission (maternal or paternal).

DM1 is also a neurodegenerative disorder with first signs of impairment in social recognition, then in executive functions, decision-making and memory in the late stage. Nathalie Angeard showed results that decision-making in DM1 patients is associated with emotional sensitivity to immediate prospect but with insensitivity to future consequences.

Successes of transnational collaboration

The collaboration on the central nervous system (CNS) of DM1 started with a European Workshop that focused on CNS dysfunction in DM1 and was organised in 2011 and updated in 2012, 2013, 2014 (supported by the Marigold foundation) making consensus reports on several aspects of DM1. These European Workshops developed into an international collaborative network in 2016 (supported by the Myotonic Dystrophy Fundation). In this network 60 clinicians from Europe, Canada & United States are present. Two guidelines were published with specific recommendations on neuropsychiatric management in adults with DM1 and on neurodevelopmental and psychological management in paediatric forms.
of DM1. These guidelines have been translated in several languages to be able to be used in several countries.

Nathalie Angeard introduced advantages and some bottlenecks in transnational collaboration.

**Advantages of transnational collaboration**

In the international network, several SHS university teams with good expertise in the domain collaborate. The studies are carried out in close collaboration with patient associations (AFM, MDF). There is support for national registries on DM1 (DM-Scope in France) and the DM registry is a useful platform to promote DM research. An international registry for DM1 is in progress.

**Bottlenecks**

In the international network, there is a lack of homogeneous cohorts with the same phenotypic classification criteria. There are multiple national clinical practices guidelines, psychological or cognitive support recommendations and these have to harmonised. There is also a lack of harmonization in ethics and biomedical legal issues and a variability of psychological or cognitive assessment tools. Furthermore, there is heterogeneity in national funding.

**The next step – a Europe wide project**

A European collaborative neuropsychological network in DM1 (ECON-DM1) is being set up with French, Swedish, Spanish, Italian and Serbian academic teams to prevent cognitive and social emotional progressive impairments. A cross-sectional study with a translational perspective from micro (brain and biomarkers) to macrogenetic (social cognition) levels with innovative tools will be implemented. Also, non-profit organizations and DM1 or NMN national registries (French, Italian) will join.

**Measures**

Laura Benkemoun (National joint responsibility for SHS programs, East Regional Manager, French Foundation for Rare Diseases (FFRD), France) presented some key points of the French SHS Calls, measures to facilitate researchers from different areas to collaborate and a strategy for dissemination/communication of the topics in Call EJP RD JTC 2021.

She introduced the FFRD Annual Call – Improving patients’ lives, a French national Call on SHS research. Six calls for proposals were closed (2013-2018) and the seventh call was ongoing in September 2019. The FFRD received 296 proposals in the six calls that resulted in 39 funded projects. In these projects 120 teams, 250 experts and 50 PAOs were involved. For the six calls 3.1 million euro was allocated and this budget came from CNSA.
(Caisse Nationale de Solidarite pour l’autonomie), IRCEM (fondation d’entreprise) and Ministère des affaires sociales et de la santé de France.

The funded projects cover a wide variety of SHS domains and rare diseases medical domains (see the two figures below) and are all dedicated to improving patient’s lives, either in patient’s care pathway or in everyday life.

The main themes to improve patient’s care pathway were:
- Predictive aspects of diagnosis (4 projects);
- Diagnosis announcement (3 projects);
- Better understanding of rare disease for better care (5 projects);
- Knowledge sharing (3 projects);
- Economic burden (1 project).

The main themes to improve everyday life were:
- Childhood-parenthood transition (3 projects);
- gender studies/identities (1 project);
- parenthood/family life (1 project);
- Social interactions/development and socialization (7 projects);
- Education/school interactions (3 projects);
- Employment/professional life (2 projects);
- Quality of life (6 projects).

**SHS domains investigated in the funded projects**

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<td>Psychology</td>
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<td>Learning sciences</td>
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**Medical domains investigated in the funded projects**

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<td>Autoimmune diseases</td>
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<td>Others</td>
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<td>Neuromuscular</td>
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<td>Endocrinology</td>
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<td>Dermatology</td>
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<td>Pulmonology</td>
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<td>Rare cancers</td>
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</table>
Measures to facilitate researchers from different areas to collaborate – Key features of national experience of FFRD

The start of these national calls for SHS research on rare diseases was a unique opportunity in France. A dedicated internal team of FFRD of seven regional managers were in close connection with research teams, helping to find the right expertise if needed. An important eligibility criterion is that each project must involve at least one SHS researcher, one clinician and one PAO (Patient Advocacy Organisation) having mutual recognition - the winning trio! Another criterion was that every project funded should address the real problematics of a patient.

All stakeholders were represented in the working group preparing the calls and in the Selection Committee for selecting the applications: rare disease clinicians, experts in SHS research, patient organizations’ representatives and funders. In October 2016 a scientific workshop has been organised in Paris to facilitate networking to foster new projects. 250 attendees attended this workshop.

Measures to facilitate researchers from different areas to collaborate internationally – Proposals

It will also be a unique opportunity to organise the first SHS Call on rare diseases in Europe. Laura Benkemoun launched the proposal to organise junior/young scientist application tracks to get them more involved in the interdisciplinary SHS research for rare diseases.

She gave some proposals for measures based on the French national experience. An important eligibility criterion should be the winning trio. Each project should involve at least one SHS researcher, one clinician from a rare disease reference center and one representative of a relevant PAO.

All stakeholders should be represented in the working group for preparation of the Call text and in the Selection Committee - bringing together RD clinicians, experts in SHS research, patient organizations’ representatives from every country involved in this specific EJP RD Call.

Matchmaker support may be needed to give different stakeholders the opportunity to network. Possibilities for such matchmaker support may be:

- Networking event(s) (workshop, webinar...);
- Matchmaking tools (EJP Partner Finding Tool, E-Rare module, Net4Society Research Directory, Triple platform, online tool...).

Strategy for dissemination / communication of topics – Key features national experience of FFRD

Laura Benkemoun indicated that several elements are important for dissemination and communication of the SHS topics in the national calls:

- Early detection: 7 regional managers detected the existing expertises in the field, raising research team awareness on rare disease problems and SHS call opportunities;
- Early dissemination to allow matchmaking and a wide coverage as matchmaking can be time-consuming. The dissemination phase started about 4 months before the opening of these SHS calls;
- Wide coverage: every network was requested to disseminate the information on the SHS call:
  - Rare disease networks: clinicians, hospital’s scientific directors, RD national networks and reference centers...;
SHS networks: SHS researchers, university’s VP of research, national alliance for SHS (Athena), national support structures for SHS (MSH)…;
PAO networks: Alliance maladies rares, national PAOs…;
Funder’s network: CNRS, Inserm, ANR…;
Members of former funded projects.

Strategy for dissemination / communication of topics – Proposals for international call

In analogy with the national calls on SHS, Laura Benkemoun proposed the same three elements of dissemination and communication for the EJP RD JTC 2021 Call:

- Early detection: inclusive, innovative and reflective society’s national contact points (Net4Society1) or networks from the European Alliance for the Social Sciences and the Humanities (EASSH) could help identifying experts in the field, raising research team awareness on rare disease problematics and SHS call opportunities;
- Early dissemination: a pre-announcement and/or white paper could be written to attract attention on this international call;
- Wide coverage: every national and international network should be requested to disseminate this call:
  - Rare diseases networks: clinicians, hospital’s scientific directors, rare disease national networks and reference centers, European Reference Networks…;
  - SHS networks: SHS researchers, university’s VP of research and Europe units (League of European Research Universities (LERU)…), national and international alliances for SHS (EASSH), national and international support structures for SHS (National Contact points, MSH)…;
  - PAO networks (Eurordis, International alliances and networks…);
  - European funder’s networks;
  - Members of former national and international funded projects.

Laura Benkemoun concluded that the experience of the FFRD, being the Call secretariat of the EJP RD JTC 2021, could be used for the preparation of this international Call and that she was happy to discuss the proposed actions with the public.

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1 Net4Society is the international network of National Contact Points for the Societal Challenge 6 (“Europe in a changing world: inclusive, innovative and reflective societies”) in Horizon 2020. National Contact Points (NCPs) are set up to guide researchers in their quest for securing EU funding.
Conclusions

The invited speakers touched many issues from their perspective as patient, researcher, clinician, patient organisation getting into industry, and funder. Lively discussions took place. Many recommendations, reports and references were shared, that are compiled in the separate section References. All participants agreed that SHS research for rare diseases is needed and they came forward with many ideas for potential topics for transnational SHS research on the themes “Improvement of healthcare system” and “Improvement of everyday life”.

The results from the survey for funders in 2019 showed that several funders have experience with SHS elements in their national programmes; only two funders have a specific national programme or Call on SHS research for rare diseases. Several funders involved in EJP RD have taken part in the transnational Call on SHS research in the Joint Programme on Neurodegenerative Diseases.

Challenges have also been mentioned in the Workshop:

- Choice of the final topic(s) for the transnational call
  - Some potential topics mentioned may not be suitable for transnational research;
  - The heterogeneity in national clinical practices, guidelines, recommendations have to be taken into account;
  - There is lack of harmonization concerning ethics and biomedical legal issues across countries.
- Transnational and interdisciplinary collaboration between SHS researchers, clinicians and patients/patients representatives is a requisite in a Call for SHS research for rare diseases. Therefore, measures are needed like e.g. early detection of interested partners and offering matchmaker support / matchmakers tools;
- Choice whether rare cancers should be included in the SHS Call next to rare diseases;
- Early and wide dissemination of the Call text for SHS research for rare diseases for applicants is needed;
- Reflection of the duration of the projects is needed. E-Rare and EJP RD have funded 3-year projects until so far. However, the duration of SHS research may have to be different dependent on the topic(s) (1-2 years?);
- Reflection from funders on the national budget needed for a research project in this specific call on SHS research;
- Multistakeholder evaluation of the applied (pre)proposals is needed.

The next steps are to compile all the information of the Workshop in a report, to make choices on the topics for EJP RD JTC 2021 and requirements for the research projects and disseminate this information as early as possible. Possibilities should be investigated to offer matchmaker support for creation of transnational and interdisciplinary consortia that will apply in the Call on SHS research.
Acknowledgements

We are very grateful to all speakers and chairs in this Workshop who did a great job in setting the scene for the needs of SHS research for rare diseases and keeping the time. We would like to thank all participants for their active contribution in the Workshop. A special thanks to all members of the Working Group that prepared the survey for funders and the programme for this Workshop and invited the speakers. We would also like to thank Eva Müller-Fries, Matthias von Witsch and Ralph Schuster for their preparation of the interactive session. We thank the representatives of the funding agencies for completing the survey. Furthermore, we are very grateful for the help of the coordination of the EJP RD for organising the location of the Medical University Gdańsk and the pleasant cooperation with the representatives of the Medical University of Gdańsk.
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Taskforce IRDiRC FCC on ELSI


Presentation Durhane Wong-Rieger

United Nations General Assembly. Resolution adopted by the General Assembly on 10 October 2019. Political declaration of the high-level meeting on universal health coverage…… item 34 includes rare diseases: https://undocs.org/en/A/RES/74/2

World Health Organization. WHO-RDI Memorandum of Understanding on Rare Diseases

Asia-Pacific Economic Cooperation. APEC Rare Disease Network

Global Commission to End Diagnostic Odyssey for Children with Rare Diseases. Global Commission Year One Report

Presentations Pauline Mc Cormack

McCormack P et al. ‘You should at least ask’. The expectations, hopes and fears of rare disease patients on large-scale data and biomaterial sharing for genomics research. European Journal of Human Genetics 24,1403-1408 (2016)


RD-Connect: https://rd-connect.eu/

EUReNOMics: https://www.eurenomics.eu/

NeurOmics: https://rd-neuromics.eu/

Presentation Rebecca van Kalsbeek


Rare care project with information on incidence on rare cancers: http://www.rarecare.eu/rarecancers/rarecancers.asp

PanCareFollowUp: http://pancarefollowup.eu/

**Presentation Gábor Pogány**


EURORDIS. 2017. Juggling care and daily life: The balancing act of the rare disease community. Survey performed via EURORDIS survey initiative Rare Barometer Voices

EU Joint Programme - Neurodegenerative Disease Research (JPND) 2018 Joint Call on Health and Social Care Research and Innovation. Full Call text and funded projects

**Presentation Birutė Tumienė**


RD Action – data and policies for rare diseases; http://www.rd-action.eu/

*Inequities and human rights in rare diseases*


Rare diseases: a major unmet medical need, 2017

European Pillar of Social Rights, 2017

European Disability Strategy 2010-2020: a Renewed Commitment to a Barrier-Free Europe, 2010

Tokyo Declaration on Universal Health Coverage: All Together to Accelerate Progress towards UHC, 2017

Communication On effective, accessible and resilient health systems, 2014
Communication On enabling the digital transformation of health and care in the Digital Single Market: empowering citizens and building a healthier society, 2018


Expert Panel on Effective Ways of Investing in Health (EXPH): Opinion on Application of the ERN model in European cross-border healthcare cooperation outside the rare diseases area, 2018

Tackling wasteful spending on health, OECD, 2017

Wasteful spending in the care of sarcoma patients


Wasteful spending in other rare diseases


Presentation Alexandre Mejat

Presentation Beth Potter

World Health Organization. Health technology assessment

Kanters TA et al. Systematic review of available evidence on 11 high-priced inpatient orphan drugs. Orphanet J Rare Dis 8, 124 (2013)


Morel T et al. Reconciling uncertainty of costs and outcomes with the need for access to orphan medicinal products: a comparative study of managed entry agreements across seven European countries. Orphanet Journal of Rare Diseases 8,198 (2013)

Tingley K et al., Using a meta-narrative literature review and focus groups with key stakeholders to identify perceived challenges and solutions for generating robust evidence on the effectiveness of treatments for rare diseases. Orphanet J Rare Diseases 13, 104 (2018)

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Jansen-van der Weide MC et al. Rare disease registries: potential applications towards impact on development of new drug treatments. Orphanet J Rare Dis 13:154 (2018)


Eight principles of patient-centered care: Picker Institute

Presentation Nathalie Angeard


Angeard N. et al. A new window on neurocognitive dysfunction in the childhood form of myotonic dystrophy type 1 (DM1). Neuromuscul Disord. 21(7), 468-476 (2011)


Labayru G et al. Social cognition in myotonic dystrophy type 1: Specific or secondary impairment? PloS one, 13(9), e0204227 (2018)


Meola G et al. Executive dysfunction and avoidant personality trait in myotonic dystrophy type 1 (DM-1) and in proximal myotonic myopathy (PROMM/DM-2). Neuromuscul Disord. 13(10), 813-821 (2003)


**Presentation Laura Benkemoun**

Information on the Action

Funded projects including the SHS research projects

*Matchmaker tools mentioned by Laura Benkemoun*

Net4Society Research Directory

Triple platform
Annexes

A. Working group preparing the E-Rare Strategic Workshop
B. Programme
C. List of participants
D. Preconference paper
## A. Working group preparing the E-Rare Strategic Workshop

<table>
<thead>
<tr>
<th>Name</th>
<th>Organisation</th>
<th>Country</th>
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<tbody>
<tr>
<td>Sonja van Weely</td>
<td>ZonMw (Chair)</td>
<td>The Netherlands</td>
</tr>
<tr>
<td>Etienne Richer</td>
<td>CIHR</td>
<td>Canada</td>
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<tr>
<td>Ralph Schuster</td>
<td>PT-DLR</td>
<td>Germany</td>
</tr>
<tr>
<td>Virginie Bros-Facer</td>
<td>Eurordis</td>
<td>France</td>
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<tr>
<td>Diana Désir- Parseille</td>
<td>FFRD</td>
<td>France</td>
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<tr>
<td>Laura Benkemoun</td>
<td>FFRD</td>
<td>France</td>
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<tr>
<td>Florence Guillot</td>
<td>ANR</td>
<td>France</td>
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*In collaboration with Taskforce IRDiRC FCC on ELSI*

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<tr>
<td>Adam Hartman</td>
<td>NIH/NINDS (Leader)</td>
<td>USA</td>
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<tr>
<td>Melissa Parisi</td>
<td>NIH/NICHD</td>
<td>USA</td>
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<tr>
<td>Nicole Lockhart</td>
<td>NIH/NHGRI Div. Genomics and Society</td>
<td>USA</td>
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*and EJP RD/IRDiRC coordination unit*

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<tr>
<td>Daria Julkowska</td>
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<td>Juliane Halftermeyer</td>
<td>INSERM Transfert</td>
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<tr>
<td>Carla d'Angelo</td>
<td>INSERM</td>
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B. Programme

Plenary sessions

08.30-09.00
Registration

09.00-09.15
Welcome
Dr. Florence Guillot, coördinator of ERA-Net E-Rare 3. ANR, France

Goals of the workshop
Dr. Sonja van Weely, chair of the preparatory Working Group, ZonMw, The Netherlands

Session 1. Setting the scene
Chair: Dr. Virginie Bros-Facer, Scientific director, EURORDIS, France

09.15-09.30
1.1 Contribution of SHS research to improve health care implementation and everyday life of people living with a rare disease and their families from patients’ perspective
Dr. Durhane Wong-Rieger, President & CEO of the Canadian Organization for Rare Disorders; chair of IRDiRC Patient Association Constituent Committee

09.30-09.45
1.2 Contribution of SHS to interdisciplinary research on rare diseases from researchers’ perspective
Dr. Pauline McCormack, senior lecturer at PEALS (Policy, Ethics & Life Sciences) Research Centre, Newcastle University, UK

09.45-10.00
1.3 Contribution of SHS to interdisciplinary research on cancer:
Transnational studies on health care implementation, life path studies, social and psychological issues of adult survivors of childhood cancer within the PanCareFollowUp project
Rebecca van Kalsbeek MD, Princess Máxima Center for pediatric oncology, Utrecht, The Netherlands

10.00-10.30
1.4 General Q&A

Coffee break
Session 2: improvement of health care implementation and everyday life of people affected with a rare disease from different perspectives  
Chair: Dr. Durhane Wong-Rieger

11.00-11.20  2.1 Perspective of patient  
Dr. Gábor Pogány, EURORDIS Social Policy Action Group volunteer, and Hungarian Federation of People with Rare and Congenital Diseases Network, Hungary

11.20-11.40  2.2 Perspective of clinician (ERN representative)  
Dr. Birute Tumiene, on behalf of ERN ITHACA, Vilnius University Hospital Santaros Clinics, Centre for Medical Genetics, Lithuania

11.40-12.00  2.3 Perspective of SHS researcher  
Dr. Pauline McCormack, senior lecturer at PEALS (Policy, Ethics & Life Sciences) Research Centre, Newcastle University, UK

12.00-12.20  2.4 Perspective from industry  
Dr. Alexandre Méjat, Manager International Scientific Affairs, AFM-Téléthon, France

12.20-12.40  2.5 Perspective from HTA  
Dr. Beth Potter, Associate Professor at the School of Epidemiology and Public Health, University of Ottawa, Canada

12.40-12.50  2.6 General Q&A

12.50-13.00  Introduction Session 3  
Dr. Eva Müller-Fries, Scientific Officer at DLR Project Management Agency, Germany

Lunch

Session 3

14.00-15.00  3.1 Interactive session  
The audience will be divided in groups to create ideas for the Call JTC 2021. Each group will be supported by a facilitator (member of the preparatory Working group)

Coffee
Plenary sessions

15.30-16.00  **3.2 Outcomes of the Interactive session 3.1: First identification of ideas for topic(s) for the Call 2021 within EJP RD, presented by rapporteurs of each group**
Chairs: Dr. Eva Müller-Fries, Scientific Officer at DLR Project Management Agency, Germany, and Mrs Diana Désir-Parseille, Official in charge of research administration, French Foundation for Rare Diseases, France

Session 4: Feasibilities, advantages, and bottlenecks of transnational health-related SHS research
Chairs: Russell Wheeler BSc, Patient Advocate at ERN-EYE and Leber's Hereditary Optic Neuropathy Society UK, and Dr. Ralph Schuster (Scientific Officer at DLR Project Management Agency, Germany)

16.00-16.15  **4.1 Outcomes of survey of funding agencies on funded health-related SHS research**
Dr. Sonja van Weely, Senior Programme manager, ZonMw, The Netherlands

16.15-16.30  **4.2 Successes and bottlenecks for transnational SHS research**
Dr. Nathalie Angeard, Lecturer Neurosciences, Paris Descartes University, France

16.30-16.45  **4.3 Measures to facilitate researchers from different areas to collaborate and strategy for dissemination/communication of topic of Call JTC 2021**
Dr. Laura Benkemoun, East Regional Manager, French Foundation for Rare Diseases, France

16.45-17.15  **4.4 Reflections from speakers session 1 and 2 and audience**

17.15-17.30  **Conclusions/Wrap up**
Mrs Diana Désir-Parseille and Dr. Laura Benkemoun, French Foundation for Rare Diseases, France, and Sonja van Weely, ZonMw, The Netherlands

17.30  **End of the Workshop**
## C. Participants

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D. Preconference paper

Preconference paper
E-Rare Strategic Workshop on September 20, 2019
Gdansk (Poland))

How SHS research can improve health care implementation and everyday life of people living with a rare disease and their families

Aim of the E-Rare Strategic Workshop

The aim of the E-Rare Strategic Workshop on Social and Human Sciences (SHS) research is to identify topics in the area of SHS research that may be suitable for the Joint Transnational Call 2021 in the European Joint Programme on Rare Diseases.

Proposed outcomes of this Workshop

- **Topics** within the research field of SHS that have added value for people with a rare disease;
- The proposed topics should be of interest for several countries as the projects will be funded **transnationally** in the European Joint Programme on Rare Diseases;
- Recommendations for the best ways to **bring together researchers from different areas**.

Outline of the Workshop

The first session is dedicated to the **current state of the art** of the contribution of SHS to interdisciplinary research for people affected with rare diseases or rare cancers. Speakers will present examples of interdisciplinary research in this field.

The focus of the second session is to discuss what type of transnational research is needed from the **perspective of different stakeholders** to improve health care implementation and everyday life of people affected with a rare disease.

The third session is an interactive session where **potential topics** will be discussed in small groups for the Joint Transnational Call 2021 that may lead to necessary improvements in health care implementation and daily life.

In the fourth session, the outcomes of the third session will be further refined: what **type of research** is possible to fund for interested funding agencies, is **transnational funding a real added value** for the proposed topics and how can we facilitate **collaboration between researchers** from different areas to have meaningful and multidisciplinary research projects that will contribute to improved health care implementation and everyday life of people affected with a rare disease?

Survey for interested funding organisations

A survey was prepared to gain further insight whether funding organisations are interested to fund health-related SHS research (nationally and internationally) and which potential topics within SHS can be funded or cannot be funded. In this survey, the following list of health-related SHS disciplines for this specific call has been used (taken from the European Commission (EC) that was adapted from the UNESCO International Standard Classification of Education (ISCED 2011)): 
• **Social sciences, business and law**
  - **Social and behavioral sciences:** economics, sociology, anthropology, demography, geography, psychology, human rights.
  - **Education science:** educational research
  - **Administration:** public and institutional administration, health systems and policy

• **Humanities and the arts**
  - **Humanities:** cultural diversity, linguistics, philosophy, ethics.

The survey has been answered by 30 funding organisations in Europe, Canada, USA and Japan in the period July-August 2019. Of the funding organisations that completed the survey 70% have national programmes, calls or possibilities to grant health-related SHS research. Two funding organisations have a dedicated programme on SHS research for rare diseases. Many funding organisations (63%) are interested in a multi-national collaboration to fund SHS research for rare diseases. Some funding agencies (13%) have indicated that a scientific hypothesis/objectives/research question or an innovation aspect have to be clearly included in a project to be able to fund a project. More discussion is needed whether such a Call should be focused on rare diseases with or without rare cancers included.

**Background information for the E-Rare Workshop**

**Rare diseases (RD)**

Rare diseases are life threatening or chronically debilitating conditions from which fewer than five affected persons per 10,000 citizens in the European Union (EU) suffer\(^2\). It is estimated that more than 7,000 different RDs exist, affecting between 6% and 8% of the population in the course of their lives. For rare cancers the definition as proposed by the Surveillance of Rare Cancers in Europe (RARECARE) project is that cancers are rare for which the number of newly-diagnosed cases are less than 6 per 100,000 persons per year.

Research on RD remains scarce and scattered throughout the world. This scarcity of research translates into delayed diagnosis, few medicinal products, little knowledge on rare diseases and their consequences for patients in daily life. This lack of know-how of these aspects results in difficulties in access of multidisciplinary medical, social, and local care that people with a rare complex disease so often need. Therefore, RDs are a prime example of a research area that strongly profits from coordinated research on a European and international scale.

**SHS research for RDs**

In April 2016 the European Commission Expert Group on Rare Diseases (adopted new recommendations to the European Commission and Member States (MS) on how to support the incorporation of RDs into social services and policies. The 10\(^{th}\) recommendation is on socio-economic research: Socio-economic research in the field of RD care provision/organisation should be supported both at MS level and at European Union level. Support should be provided for research on the following topics:

\(^2\) Other continents use slightly different definitions for rare diseases.
• Socio-economic burden of RD;
• Accessibility and appropriateness of healthcare services, including social services, for people living with a RD and their families;
• Effectiveness and cost-effectiveness of social services and support, as well as rehabilitation and assistive technologies for people with a RD;
• Innovative care practices in health and social services and their impact on the quality of life of people living with RD.

In the programme Horizon 2020 of the European Commission (EC), the social sciences and humanities have been given an enhanced role as a cross-cutting issue aimed at improving the assessment of and response to complex societal issues. This type of research could provide the social and economic analysis necessary for improving a patient’s life and/or reforming public health systems.

European programmes on rare diseases research: E-Rare and European Joint Programme on Rare Diseases (EJP RD)

E-Rare, the ERA-Net for Research Programmes on Rare Diseases (www.erare.eu) was built to link responsible funding organizations and ministries, to combine the scarce resources for RD research and thus enable the participation of many researchers to transnational projects via Joint Transnational Calls (JTCs). The ten calls performed in the E-Rare-1 (2006-2010), E-Rare-2 (2010-2014) and E-Rare-3 (2014-2019) programmes have shown that funding of projects on RD research in a coordinated way is clearly possible and needed. In the last 10 years E-Rare has created a sustainable network of RD research funders. Moreover, there was significant interest for collaboration between RD researchers in Europe, resulting in 130 funded projects with a total budget of about M€115.

From 2019 the E-Rare activities are integrated in the new programme within Horizon 2020: European Joint Programme on Rare Diseases (EJP RD; http://ejprarediseases.org/). This programme brings more than 130 institutions from 35 countries together and has two major objectives: (i) To improve the integration, the efficacy, the production and the social impact of research on RD through the development, demonstration and promotion of Europe/world-wide sharing of research and clinical data, materials, processes, knowledge and know-how; (ii) To implement and further develop an efficient model of financial support for all types of research on RD (fundamental, clinical, epidemiological, social, economic, health service) coupled with accelerated exploitation of research results for benefit of patients. The EJP RD follows the policies and guidelines of the International Rare Diseases Research Consortium (IRDiRC). The budget for this programme is over €100 million, of which €55 million will come from EU’s research and innovation programme Horizon 2020.

Within Pillar 1 (Funding of research) four Joint Transnational Calls (JTCs) have been planned; the JTC 2021 may focus on SHS research for rare diseases.

E-Rare Strategic Workshop on SHS research

All E-Rare Calls were dedicated to basic and (pre)clinical research on RD. Therefore, the exploration of organising the JTC 2021 on transnational SHS research needs additional preparation before this call may be opened at the end of the year 2020. The current E-Rare Workshop is one of the final activities of E-Rare 3 to prepare the possibility of focussing the JTC 2021 on SHS research on RD in the EJP RD. A working group consisting of research funding agencies involved in E-Rare and EJP RD, members of the IRDiRC
There were several reasons for not organising a transnational call on SHS research for RDs in the past, e.g. this topic was quite immature for RDs and quite jurisdiction-specific so far. Furthermore, there was difficulty in recognising social sciences and humanities as relevant to clinical practice, health care, and patients' issues in RDs.

Some recent experiences and initiatives (both national and international) on funding of this type of research for RDs have encouraged the community of funding agencies to plan a transnational call on SHS research in the EJP RD. The French Foundation on Rare Diseases (FFRD) has national experience with this topic and will be the Joint Call Secretariat of the JTC 2021. Early considerations within members of the group of funders resulted in the suggestion that JTC 2021 may focus on social, economic, and health services research for RDs with the aim to propose improvements to the daily life of the RD patient, as well as appropriate implementation of improvements in healthcare for RDs in general. The E-Rare Strategic Workshop aims to elaborate on this further and select final topics within SHS research that are needed by people with a RD and that are within the capacities of interested funding agencies.