RD-ACTION Workshop Report

‘Exchanging data for virtual care within the ERN Framework’

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Wednesday 28th September -Thursday 29th 2016

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SESSION 1: AIMS OF THE WORKSHOP AND THE RARE DISEASE POLICY CONTEXT

Welcome to the Workshop and Participant Introductions

Victoria Hedley, the Thematic Coordinator for the RD-ACTION Policy & Integration work-package (WP6) welcomed the participants to the workshop. The diversity of the stakeholders present was noted: each of the 24 Applicant Networks was invited to nominate a representative, and in the end 21 potential ERNs were present. The strong European Commission (EC) representation was also highlighted – 10 EC colleagues participated to the workshop, from DG SANTE Unit B3 (Cross Border HealthCare and eHealth), Unit C1 (Programme Management and Diseases), DG Research & Innovation, and the Joint Research Centre. This workshop follows a two-hour meeting between the Board of MS of ERNs (BoMS) and the Applicant Network Coordinators (ANCs). To ensure continuity between the two meetings, the BoMS Discussion Session chairs from the morning, Till and Akaterini, participated to the workshop also. As this is the first JA workshop organised *after* the ERN call, and the topic has particular relevance to patients and public, it was agreed that strong patient participation would be highly advantageous; therefore, in addition to 4 EURORDIS experts, 11 ePAGs joined the workshop. Last but not least, the workshop united experts from RD-ACTION, RD-Connect, Neuromics and Orphanet, to present and stimulate discussions.

Aims of this workshop (Victoria Hedley) (Presentation available **here**)

This workshop topic was selected for the first in this series of workshops, as it is of central importance to the ERN concept – the notion that **expertise** travels as opposed to patients in fact rests upon the ability of **data** to travel, and the most obvious manifestation of this will be the virtual consultations conducted by the Networks. In the RD field, patient data holds huge potential for research as well as for care; however, for this particular workshop, the emphasis will be on sharing data for care (i.e. the topic of registries lies somewhat beyond the scope of this meeting).
After exploring the status quo and the policy background to ERNs -with an aim of identifying accepted standards and resources which the Networks may exploit- the participants will explore several important aspects of virtual consultations. Any mention of sharing or exchanging data demands an analysis of the accompanying ethical, legal and social issues (ELSI), including agreement of the level of consent required in the ERN framework.

Several ANCs whose groups conduct virtual consultations at present will share the experiences and challenges they face, with a view to stimulating discussions on good practices for the organisation and execution of virtual encounters. This will lead to discussions on when and how to 'refer' a patient to the expertise of the ERN itself, as opposed to a member HealthCare Provider (HCP). The final session of the workshop will explore and identify the 'low-hanging fruit' in terms of ways to standardise data to maximise its value. Although the workshop will strive not to stray too far from the agenda and main topic at hand, it is acknowledged that there are many important issues relating to registries, research, guidelines etc. that people will wish to discuss; for this reason, a post-workshop session has been added to the agenda, in which participants are free to raise any topic to support the planning of future workshops.

Overview of this morning's discussions **(Please see the dedicated report[1])**

The EU Rare Disease framework: the context for ERNs (Jaroslaw Waligora)

(Presentation available **here**)

Jaroslaw summarised the watershed moments in European RD policy contributing to the emergence of ERNs, including the 2008 Commission Communication[2] and the 2009 Council Recommendation[3]. The latter made specific recommendations to Member States (MS) relating to centres of expertise and ERNs. The drive for countries to adopt national plans and strategies was outlined, along with another major theme of the Council Recommendation, coding and inventorying; here, Jarek, emphasised the unique role played by Orphanet. The efforts to increase the visibility of RD in Europe through use of the OrphaNumber (and the Orphanet RD Ontology) were demonstrated, with emphasis on the activities of RD-ACTION WP5 (seeking to implement the *Recommendation on Ways to Improve Codification for Rare Diseases in Health Information Systems.*[4]) EU activities in research, registration, and patient empowerment were also presented. The goals of RD-ACTION Policy WP (i.e. the WP organising this workshop) were outlined, to demonstrate how Joint Actions at the EU level support bodies like the EUCERD and Commission Expert Group on Rare Diseases. **These bodies have played a key role in defining the concept of ERNs** (for instance the Addendum[5] to the 2013 EUCERD Recommendations on RD ERNs espoused the model for grouping RD, the influence of which is very visible in the eventual ERN proposals) **and it is important that all RD-related initiatives, including ERNs, take note of and attempt to implement existing Recommendations wherever possible.**

Summary of the ERN Status Quo (Enrique Terol)

(Presentation available **here**)

24 proposals have been submitted, involving 960 expert units in 370 hospitals (some hospitals have up to 15 units participating in ERNs). The proposals involve 25 EU MS plus Norway. With the exception of gynaecological (which is nonetheless included in the future scope of other networks), proposals have been submitted for all CEGRD groupings proposed in the Addendum (as above). The EC eligibility checks have now been conducted, with very few HCPs declared ineligible. The Independent Assessment Body Andalusian Agency for Healthcare Quality (ACSA) is now conducting the technical assessment, with a deadline of 16th November to write a report for the BoMS. The BoMS meets on 16th December and will have the final decision regarding approval of the Networks. The timeline for the CHAFEA-led Grant applications (for coordinator funding, so-called 'glue money') was explained. The outline for the 2017 formal ERN conference in Vilnius (9-10th March) was presented – there will be a KOM for all Networks (although only a limited no. of participants from each will be able to attend – the details are being discussed). Branding and communication plans were also shared: each HCP will bear the basic ERN logo, and each ERN will also have an 'extended' logo which will retain the acronyms selected by the ANCs. The EC is now involved in legal discussions over contracting with the coordinators to authorise use of the official logo.

[1] Available here - http://www.rd-action.eu/european-reference-networks-erns/rd-action-meeting-between-potential-ern-coordinators-and-board-of-member-states/
[2] https://ec.europa.eu/health/ph_threats/non_com/docs/rare_com_en.pdf
[3] http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:C:2009:151:0007:0010:EN:PDF
[4] http://ec.europa.eu/health//sites/health/files/rare_diseases/docs/recommendation_coding_cegrd_en.pdf
[5] http://ec.europa.eu/health//sites/health/files/rare_diseases/docs/20150610_erns_eucerdaddendum_en.pdf

What do we mean by virtual care? Summary of the state of the art across the RD field and beyond (Victoria Hedley)

(Presentation available **here**)

Victoria explained that patients seek care on a cross-border basis for many reasons and under various conditions. Much work has been done over the last decade to prepare the field for emergency cross-border care – the RD-ACTION team is collaborating with key actors and initiatives from the eHealth field involved in propelling these activities, to ensure a degree of harmonisation between the unplanned and planned (i.e. ERN-related) spheres. A select number of achievements of these initiatives (such as MS agreements, legal arrangements, auto-translation assets, and Master Value Catalogues) were summarised. Victoria demonstrated how physicians in the RD and specialised healthcare field seek advice from cross-border colleagues at present – it was emphasised that such discussions *do* happen, out of necessity and a drive to help the patient, but if clinical notes or images etc. need to be shared, this is typically done by email or over the telephone, basically through less-than-ideal channels, devoid of technical or legal safeguards. This should all change with the advent of ERNs, at the heart of which will sit the virtual consultations. These 'virtual consultations' may take various forms; after all, the 24 ERNs are very heterogeneous, and not all will require the same volume or type of virtual encounter. For some fields, it may usually be sufficient to upload clinical summaries and scans/images/x-rays etc. to a shared secure platform, which other experts in the ERN can view in their own time. In some cases, a one-to-one teleconsultation would be most appropriate, perhaps with the patient present. In other cases, the 'virtual tumour board' type of model will be more relevant, in which multiple experts gather in real-time via a live video link, to discuss a number of complex patient cases. Regardless of the method used, ERNs should revolutionise cross-border healthcare for conditions requiring a particular concentration of expertise.

Discussion

In an opening debate following the first few presentations, the group discussed the merits of the OrphaCode and how the advent of ICD 11 will impact its use. The WHO is currently reviewing ICD 11 and, for the first time, a RD Topic Advisory Group (TAG) has been incorporated; however, full implementation will take several years still. Countries incorporating the OrphaCode in their health information systems now will be compatible with the future ICD 11, due to the cross-referencing of terminologies work carried out through the previous and current Joint Action. Participants proposed a need to ensure effective cross-links with the ERICs (European Research Infrastructure Consortium) and other Research Infrastructures, to establish common ground for shared activities. This should include BBMRI, EATRIS, ELIXIR, ECRIN *et. al.*

The current level of interoperability between Europe's ca. 588 RD registries was raised. Although there is little chance of achieving full interoperability in the near future, some progress is perhaps possible in this sphere, at least for new registries, through the provision of specific tools and assets. An ePAG representative emphasised the role that patient organisations can play in creating and populating RD registries, which will be valuable in the ERN framework. Several participants noted that the JRC team building a European Registry for RD Registration has an important function here: participants stressed the need to consolidate what already exists, as if ERNs begin from scratch the field will have lost a lot of time and wasted many resources. Simona Martina, representing the JRC, confirmed that her team is planning another interoperability workshop before the end of 2016, on

the topic of ERNs and registries. As RD-ACTION had also considered organising a workshop on how ERNs can use/integrate registries, it was proposed that the two teams work together on the agenda and goals; in any case, the Joint Action WP6 team will await the outcome of this JRC-led workshop before determining if an additional workshop (possibly with a different emphasis and angle) is necessary.

In the context of the research activities of ERNs, EURORDIS emphasised the importance of reusing tools and resources which have already gained widespread approval and implementation in the global RD research field. For instance, ontologies such as the ORDO and HPO, which will be discussed tomorrow, have already received the *IRDiRC* (International Rare Disease Research Consortium) *Recommended* label.[6] Similarly, tools used in/developed by initiatives such as RD-Connect, E-RARE and the PARENT-JA should be utilised by the Networks, where they can add value. There is now an IRDiRC TaskForce dedicated to Clinical Research Networks, and there should be a clear link to ERNs (the US example should be a useful model here).

Returning to the subject of care, the Group agreed that it will be important to define what we mean by virtual 'care' first of all, as this is not always the same. Different groups in this room will perceive 'care' in different ways – the specialised cancer field is relatively familiar with tumour boards, increasingly virtual as well as in-person, whereas other ERNs emphasise that much of their virtual care will consist of experts analysing images and data to provide a diagnosis, which will not necessarily require a lot of multi-person real-time meetings. Nonetheless, all of these activities come under the umbrella of providing healthcare, and whichever model you use in your ERN, it must be appreciated that the time of experts is very expensive. Therefore, the goal of the next session is to identify ways to optimise the efficiency of these sorts of activities.

Special Address and Exchange with Dr Andrzej Rys (Health Systems and Medical products and Innovation Directorate DG SANTE)

Dr Andrzej Rys delivered an address to the participants, in which he attested the expertise and enthusiasm of the ERN stakeholder community in driving forwards these plans to make the concept a reality. He informed the group that a contingent of ANCs met with the Commissioner for Health the previous morning, to share some of the challenges and concerns harboured by this community regarding the implementation of successful ERNs. The political interest and will from the European Commission regarding ERNs is particularly notable, and ensuring the success of these Networks is a priority for the Commission. It is also important to strengthen relationships with the MS authorities here, to ensure the lasting impact of these Networks, as healthcare remains after all a MS prerogative. Dr Rys explained some of the steps the EC is taking to support the Networks, but was keen to hear from the Group what *their* main concerns are:

Summary of main concerns highlighted at the invitation of Dr Andrzej Rys

- IT Platform: Several participants stressed that the lack of information on the IT platforms being reviewed and considered under the Tender is a concern. The IT platform will be central to the success -indeed to the operationalisation- of the Networks. The process of selecting the best contactor is not easy: there are many things that need to be incorporated in this platform and people are not operating in a vacuum – for instance, there are assets

[6] http://www.irdirc.org/activities/irdirc-recommended/

already in use by the EC that must be considered. Furthermore, the HCPs typically sit within broader institutions and these wider administrations will be keen to see what sort of IT platform they will be required to install/ link to. Many things need to align for this venture to be successful: **ERNs need a good platform, delivered through a competent contractor, with robust governance and a strong, engaged community to provide input for the effective functioning of the system.**

- **Funding** is, unsurprisingly, another major area of concern for the ERN stakeholders: several ANCs pointed out that there is tremendous spirit and enthusiasm driving these Networks forwards, despite a lack of funding. All ERNs will need coordination funding or 'glue money', not just the top rated Networks. The EC confirmed that it is seeking a means to provide funding for all approved Networks. It would be wise to view ERNs as start-ups: the first challenges will be to demonstrate the added value of these Networks to the world, and the EC is essentially providing seed money here. In 2018 the EC must prepare a report for the European Parliament on the implementation of the CBHC Directive: this means that in 2017 there will be a need to gather information and data. **This report will be a key moment, to demonstrate that the Networks are working and to highlight where greater support or attention is required, with the support of Member States.** This group may need to think creatively in order to identify future sources of additional funding. For instance, there may be scope to utilise the ERASMUS programme to promote the movement of academics and clinicians, especially young academics. The potential European Joint Co-Fund Programme for Rare Diseases offers opportunities to fund some of the research needs associated with ERNs

- **Industry Interactions** The fact that ERNs will seemingly *not* be legal entities was highlighted as a significant barrier to attracting funding, for instance from pharmaceutical companies. The ANCs discussed the possibility of establishing a foundation or similar, to act across all the Networks and make contracts. Dr Rys confirmed that the issue of interactions with industry was a major topic in the BoMS meeting earlier in the week, and that the Board is establishing principles to avoid conflicts of interest. It was emphasised that it is important to view 'interaction with industry' not only as a threat but as an opportunity; indeed, in the RD field, this engagement is essential, for therapy development obviously but also for registries, natural history studies, identifying patient relevant outcomes and study endpoints etc. A balanced approach is necessary, and there are examples of effective Terms of Reference/Industry engagement procedures which could serve as a model here (again, avoiding unnecessary duplication of efforts)

- **Integration of the Networks to health systems -** It will be important to engage the National Contact Points (NCPs) of the CBHC Directive more actively than hitherto, to ensure a seamless process for facilitating the movement of patients when necessary. Furthermore, for patient cases to 'enter' the Networks, the way in which the existing national pathways complement -and expand, where needed- to incorporate the ERNs must be clarified.

- **Compensation** - There are concerns from some ERNs that the time taken to provide virtual consultations and reviews will never be reimbursed, and will continue to fall outside of the CBHD and the social security regulation. Without a route to reimbursement, ERNs may

struggle to dedicate ever-increasing amounts to time to providing expert opinion on patients from other jurisdictions

SESSION 2: VIRTUAL CROSS-BORDER HEALTHCARE IN ACTION

Consent for sharing data cross-border for healthcare (and re-use): impact of the revisions to the Data Protection Regulation (Petra Wilson)

(Presentation available **here**)

Petra introduced the issues around sharing data across borders and the likely levels of consent required for data-sharing in the ERN framework. She specifically focused on the revisions to the General Data Protection Regulation (GDPR) and the key changes people should be aware of. The GDPR is a regulation under EU law, which will enter into force everywhere on 25th May 2018. It is important to note that the Regulation exists to *facilitate* the free movement of personal data within the EU, and that whilst MS are free to add provisions or limitations relating to genetic, biometric or health-related data, these should not hamper the free flow of data. The definition of what constitutes 'health data' is very broad (see Recitation 35). The GDPR makes demands on both data controllers and data processors; for instance, the GDPR demands that a Data Protection Officer be appointed where an organisation's core processing activities require regular and systemic monitoring or where core activities include the processing of sensitive data on a large scale. Data producers and controllers will need to conduct a Privacy Impact Assessment and implement security measures to protect data from loss or any form of unlawful processing.

The definition of consent was emphasised, along with good practices in consenting (such as the importance, if seeking consent, of obtaining consent for *all* the purposes for which the processing is intended.) Petra explained that it *is* possible to legitimately process sensitive personal data *without* obtaining consent, under either:

a) the 'medical care' exemption;[7] or

b) 'public health' grounds (if there is an argument that data processing is necessary for the public health interest and/or scientific research)

Additional important topics such as data portability and the right to be forgotten were highlighted. Petra concluded by presenting a data protection 'checklist' which includes the following: ensuring clarity on the grounds under which an institution can process sensitive data and where these will stand under the GDPR; the importance of following developments at MS level; appointing a Data Protection Officer; if using a consent processes, selecting an appropriate form of consent, etc.

[7] i.e. when the data is necessary for the purposes of preventive or occupational medicine, medical diagnosis, provision of health or social care or treatment, management of health or social care systems and services, under a contract with a health professional or another person subject to professional secrecy under law

The Patient Perspective on sharing data cross-border for care (Matt Johnson and Valentina Bottarelli) (Presentation available **here**)

Key opening messages were delivered, amongst them the following:

- Data is the currency to exchanging knowledge and learning, which drives improvements in outcomes and quality of life for the patient community;
- Data is the key to unlock the potential of ERNs;
- Patient data must be safeguarded, because caring for patients means caring for their data.

The presentation clarified the types of healthcare foreseen in and around an ERN: the ERN will deliver specialist *advice*, and generate and disseminate *knowledge*; the HCPs will deliver the hands-on care. Matt and Valentina outlined the sorts of data that might need to be shared at each stage of the patient's journey 'through' the ERN and during the delivery of care at HCP level.

The team then presented patient perspectives on data sharing, as elicited through projects such as RD-Connect and GCoF (the Genetics Clinic of the Future). Surveys to-date suggest that the level of concern surrounding data-sharing tends to be proportionate to the severity of the disease: the more severe the disease, the lower the level of concern. Besides severity, several other factors may affect patient preferences in this area, including age, culture, disease characteristics and the patients' own experiences. Generally though, data sharing is considered imperative, providing that the following are observed: appropriate consent is obtained; privacy and confidentially are protected; progress resulting from the data-sharing is communicated back to patients; trust is established (particularly through patient representation in governance); and the process to access the data is transparent.

After highlighting four key aspects of data-sharing, the presentation discussed ways of achieving each (whilst also highlighting in parallel the most pertinent sections of the new GDPR). For instance, for 'protection of privacy', safeguards such as ethical review, informed consent and reliable IT solutions were proposed, whilst noting that the new GDPR stipulates safeguards such as pseudonymization and anonymisation. The 'securing consent' section is especially relevant for the discussions of this workshop: the GDPR states that consent must be provided through **clear affirmative action**, must include a 'freely-given, specific, informed and unambiguous' agreement to data processing, must include the right to withdraw at any time, etc. The GDPR also strongly emphasizes the rights of the data subject; for instance, the right to access one's own data, to be informed of the purposes of data processing, to receive a copy of the data in a portable form, and the right to be forgotten. The data processor must show that these rights have been respected.

Discussion: Informed Consent and Data Protection (Chairs Petra Wilson and Jaroslaw Waligora)

It was agreed that one must be very clear in defining the requisite levels of consent for research on the one hand and for care on the other. The Coordinators discussed the likely level of consent needed to conduct different activities. For instance, if seeking to conduct demographic analysis –e.g. ascertaining the number of patients in a particular centre- one could in fact avoid explicit consent by invoking the 'Public Health Interest' exemption. In terms of sharing data in ERNs for care, **in fact it is likely that *legally* this could be covered under the medical care exemption, meaning specific consent is not legally necessary. However, the participants agreed that it would be good ethical practice to <u>always</u> obtain consent in the ERN framework when processing data for care and for research** (each of which will require its own provisos). When it comes to using data for research, the group discussed how broad a consent level might be permissible under the new GDPR, and whether an opt-in or opt-out model of consent would be most appropriate.

It was emphasised that the IT platform for ERNs will provide a certain level of protection here, in terms of tools to consent patients for activities related to the sphere of operations of ERNs: the Tender specifications published in summer 2016 stipulated that the platform:

- (iv) respects European and national legal requirements for data protection and security for health information exchange;
- (viii) registers patient consent for storing and sharing data for treatment (consent form based on a template to be provided by the Commission);
- (ix) registers consent for storing and sharing data for research (consent form based on a template to be provided by the Commission);
- (xi) enforces privacy with role-based user security (patient, health professional, researcher), authentication, identification and authorisation mechanisms to share and store data and information;
- (xii) provides a moderated user-management console with different rights to create and or share and or view data within a single Network or between Networks (e.g. for patients with multiple conditions);

In response to fears from ANCs re. their power to protect data from security breaches, the group was reminded that the IT platform provided to the ERNs will need to demonstrate an ability to share data safely and securely. Thus there should be security by design, built-in from the beginning. Several Coordinators questioned how an ERN could possibly abide by the data protection rules of 28 different countries, as at present what is acceptable in one country is not permitted in another jurisdiction. Petra explained that the existing Directive has hitherto been applied differently in different countries, but that one of the benefits of the new GDPR is that it will -in essence- be applied the same everywhere from March of 2018.

Some of the Networks expressed concern regarding the legal responsibilities that may fall upon coordinating centres once the GDPR comes into force. For instance, will Coordinators be responsible for ensuring that all members HCPs are fulfilling their legal obligations? It was pointed out that not all HCPs have a Data Protection Officer at present. It will be important to clarify whether a HCP is a data *controller* or a data *processor*, under the terms of the new Regulation. If the former, the duties are more formidable. **It was pointed out that, notwithstanding the concerns expressed by the Coordinators, some of the changes and new responsibilities ushered in by the GDPR will apply to *any* centre collecting and processing data after March of 2018, whether connected with an ERN or not.**

In response to the concerns raised over the roles of Coordinating HCPs and their legal responsibilities, the EC advised the ERNs not to become unduly concerned; nonetheless, it was emphasised that **in submitting the ERN proposals, all HCPs confirmed that they indeed adhere to the criteria outlined in the Delegated Decision regarding data protection and the ability to handle and process data in accordance with national rules.** Therefore, this should be expected. It was also emphasised, however, that Coordinators will sign a consortium agreement for their Network, which is currently being drafted by DG Sante: details on 'liability' etc. will need to be very clearly defined in the Consortium Agreement.

The group discussed other possible tools that might be drawn upon at the European level, such as the new Data Protection committee or the European group on Ethics (which was consulted when the article 29 committee drafted eHealth guidance). Furthermore, the GDPR encourages specific codes for research (e.g. the code of conduct for BBMRI); therefore, there is scope for such work to inform the Network operations and alleviate part of the perceived legal and privacy protection burden.

The general consensus was that although HCPs and Coordinators have already agreed that they are able to comply with the criteria defined in the Delegated Acts, nonetheless there is a logical role here for a central body/entity to explore some of the complexities relating to the cross-border sharing of data.

Update – the European Commission has appointed experts to map exactly which aspects of the GDPR will impact upon ERNs, and also to produce a tool-kit of resources for Consenting and ELSI issues.

Examples of rare disease virtual care in action, with a focus on good practices, challenges encountered and lessons learned:

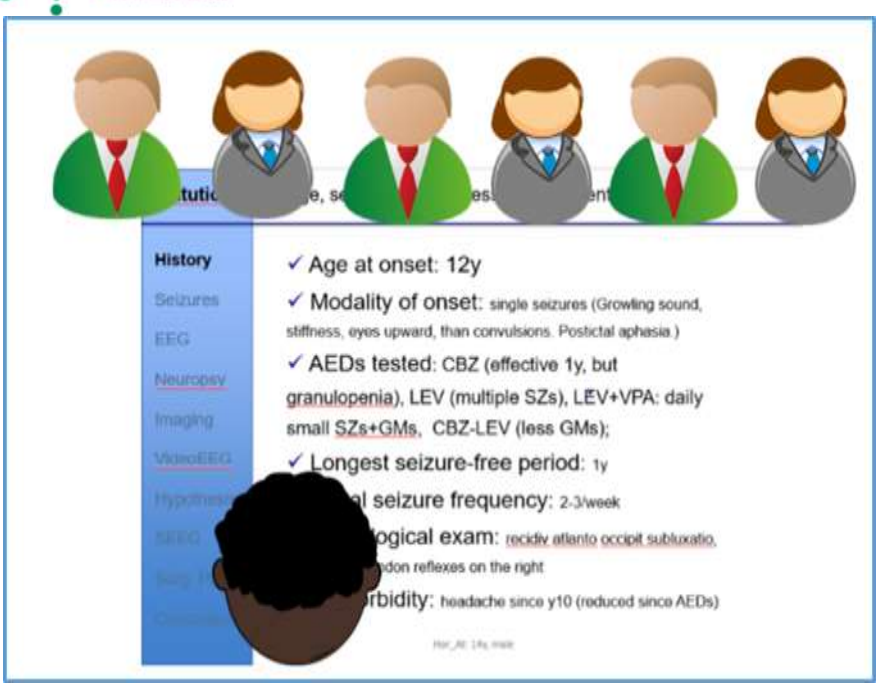
Case Study 1: Virtual care in the field of Paediatric Oncology (Ruth Ladenstein)

The PaedCan ERN is based upon the pilot Network ExPO-r-Net, which defined a network of centres of expertise in paediatric cancer. The group established very specific criteria for their Hubs of Coordination, to ensure they could provide highly specialised interventions when needed, and provide diagnostics etc. Thus far (i.e. as of late September 2016) the network has dealt with 23 cases via this virtual system. In some respects, the concept is very similar to the conventional tumour boards which often take place in hospitals; however, **the ExPO-r-Net team has learned that for the virtual consultations, standardised tools are crucial.**

Case study 2: Virtual care in the field of Rare and Complex epilepsies (Helen Cross)
(Presentation available **here**)

Helen Cross presented the example of the ePilepsy initiative, designed to exchange best practices and promote harmonisation of care in the field of refractory epilepsy and epilepsy surgery. The consortium and the deliverables were explained, amongst them a number of important electronic tools to support the exchange of knowledge and expertise. The most relevant of these in terms of

virtual healthcare is the eCare platform, which enables the execution of epilepsy consultations via the web.

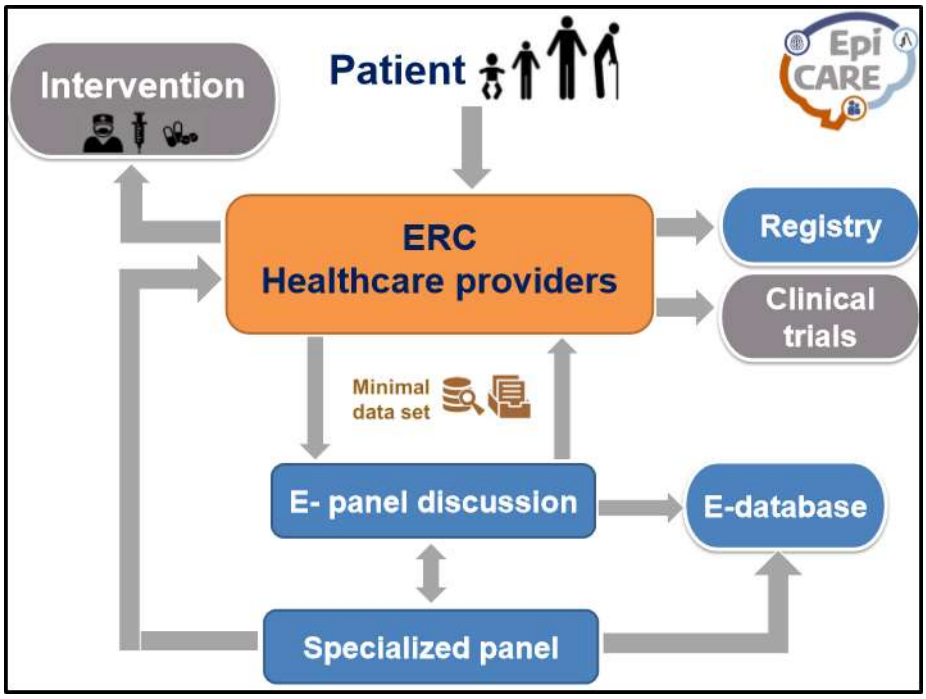


The web-based portal enables doctors treating a patient to receive expert opinions on, for instance, the suitability of that patient for specialised epilepsy surgery. To conduct a pre-surgical evaluation, the doctors need to have a fairly comprehensive set of data about a given patient, including a clinical history, the interictal EEG (and video iictal recording), MRIs etc.

Therefore, the ePilepsy partners agreed a number of data element headings and elements under each, which must be completed before the virtual consultation takes place. For instance, under the 'history' heading, the referring physician must outline family history of seizures; pregnancy history; development, head injuries, age at onset, AEDs tested etc.

A specific process was defined for the MDT discussions: a case is submitted to the coordinator, via an online portal, and a meeting is scheduled, to which all centres are invited (there are approximately 20 centres in the ePilepsy consortium). At present, these virtual meetings take place once a month and last for approximately 2 hours at a time. Typically, 6 patients will be reviewed during each meeting.

Ahead of the meeting, the referring clinician completes the mandatory slide template. During the meeting itself, the lead clinician presents the case, by sharing his/her screen: this way, the data remains local, is not exchanged in any way, and people watch the EEG feed etc. in real-time.



There was a lot of discussion about ethics and consent when commencing the project; ultimately, ePilepsy partners viewed the MDT consultation as another part of the 'healthcare' setting, and additional consent was not

sought. More recently, the network has explored use of an eCRF, to build-up a database of patient case studies. However, completing this data is time-consuming. Helen then presented the expected evolution into Epi-CARE, to demonstrate how HCPs will collect a minimum dataset when wishing to launch an e-panel discussion on a given patient, or convene a specialised panel (the HCPs may also enrol patients to a registry or to clinical trials.)

Lessons learned: there are major advantages to these virtual MDT meetings:

- The patients benefit from expert advice and the local teams then have the option of acknowledging and acting upon the decision (the aim is very much for care to travel, rather than the patients - when the patient does need to travel, this is agreed between the two centres involved, in accordance with official procedures)
- There is also a major educational and training role for people not directly involved in patient care.
- The professionals dialling-in to these virtual consultations are not from general hospitals, they all come from within the expert network of ca. 20 centres.
- Whereas previously, people would get together physically perhaps three times a year, now the experts are able to discuss cases every month.
- However, there are challenges too: not least the fact that there is no reimbursement mechanism for the expert time spent conducting these virtual MDTs.
- It is difficult to schedule meetings, given the workload of the experts involved: typically, the meetings take place between the hours of 5pm and 8pm.
- It is essential to select an appropriate platform: the ePilepsy consortium used GoTo meeting at first, but switched to a more responsive and sophisticated platform hosted by the project coordinators in Lausanne. This is called ACANO, and they find this quite effective and fit-for-purpose in some respects; however, they are not able to store images or videos in the system, although this would be very desirable, as the file sizes are too large.
- **It is important to operate according to agreed procedures, to optimise the efficiency of these meetings. The dataset has been particularly important here (although it can be challenging to get people to complete all elements).**

Case Study 3: Virtual care in the Rare Bone Diseases Field (Luca Sangiorgi)

(Presentation available **here**)

Luca presented the achievements of the European Skeletal Dysplasia Network (ESDN), which uses an integrated multidisciplinary approach to research and diagnostics. Partners use an online case submission tool, which requires comprehensive clinical and radiographic information. The patients are each given ESDN case numbers and the coordinator can follow the diagnostic status of patients attached to named clinicians in the Network. The partner clinicians do not gather virtually in real-time; instead, cases are opened for virtual discussion by a closed posting forum.

From September 2003 until the end of 2012, ESDN had 622 users from 45 cases – a total of 1667 patient cases were submitted. The ESDN colleagues use an important ontology tool known as dREAMS, to increase the interoperability of data relevant to radiography.

Luca distinguished between clinical data and a disease registry, emphasising that registries must be designed with respect of their intended purpose(s).[8] Give the major emphasis on diagnostics in ESDN, it is important to participate actively with other centres of expertise, networks and research infrastructures (such as BBMRI and RD-Connect).

Discussion: identifying good practices for virtual consultations (Chairs: T. Voigtländer, M. Johnson and V. Hedley)

The three case studies demonstrated relatively *different* approaches to the provision of virtual care. It is important to consider the numbers of patients expected to be reviewed in virtual consultations under the ERNs, compared to the numbers currently reviewed by the 'pilot' Networks (e.g. 6 per month in the rare and complex epilepsy field, as above) to realistically assess the time commitment of experts here. The two broad approaches to virtual review were clarified:

- ERNs may invoke real-time virtual consultations involving at least 2 HCPs (any fewer and virtual is perhaps less relevant than face-to-face?). Should there be an upper limit?
- ERNs may prefer, in some cases or on some occasions, to use a virtual platform to 'upload' or share or view patient case information, for experts to review in their own time and provide feedback, without a video-based, real-time discussion.

The group was clear that both activities clearly count as virtual healthcare provision: the teams performing online assessments of a patient's haematocrit or using 3D facial scanning tools etc. are doing so in order to try to find a diagnosis and/or recommend appropriate treatment and care. Any future discussions of 'costing' for the services of an ERN should therefore consider these sorts of activities, as well as the real-time virtual consultations, as they all require some level of review of patient information/images/medical data in order to reach an expert opinion.

The participants touched upon the potential for patients to access data held about them in this SaaS platform. It was argued that patient groups need to be able to view data, and indeed ideally will be involved in its generation.[9] The full group of Coordinators was keen to have an opportunity to work with the Platform Provider – especially those with experience of conducting some sort of virtual consultation at present, to ensure that the lessons they have learned can be translated into appropriate solutions in the platform. It was confirmed that the Tenderer is not building a new platform from scratch – they will base their delivery on existing products.

The presenters of the case studies were asked whether they attempt to measure the quality of their consultations at present: this *is* done in the traditional (i.e. face-to-face) tumour boards), and the paediatric cancer group is exploring the translation of this practice to the virtual MDTs. The ePilepsy

[8] This is a particularly important distinction, as noted during the 30th November JRC workshop – see RD-ACTION analysis here: https://www.dropbox.com/s/z6sjfs6pjusr81p/RD-ACTION%20analysis%20of%20the%20key%20issues%20regarding%20ERNs%20and%20Registries%2C%20Dec%202016.docx?dl=0

[9] In fact, this is partially alluded to already, in the SaaS Tender specifications:
"2.5.1. The fixed requirements are that the service (xi) enforces privacy with role-based user security (patient, health professional, researcher), authentication, identification and authorisation mechanisms to share and store data and information;"

group is also beginning to produce formal reports following each consultation. It was apparent that to-date, there has been relatively limited emphasis on ensuring the interoperability of the data shared in the various systems.

Conclusions: Good practices for organising virtual consultations

The workshop participants agreed that, if the number of cases reviewed via an ERN becomes at all significant (which it surely will - for the groups doing this already, numbers are bound to exceed current levels) then **it will be essential for these virtual consultations to be conducted as efficiently as possible. The Group brainstormed several ways to ensure this:**

- **The IT platform must enable the efficient exchange/viewing of data, including large files and video streams**. Interruption to ECG feed or video footage, for instance, will severely hamper the effectiveness of the meetings. X-Rays, MRI scans, CT scans etc. must be high quality images, and should ideally be storable within the platform (something which is not possible in the case studies at present)

- It is important that virtual consultations -especially when real-time- provide the expert teams with **all appropriate data in appropriate forms** for each patient under review, to support discussions on diagnosis, treatment and care. **Organisation upfront pays dividends here, as seen in the case studies. Each ERN will need to agree on the clinical dataset they require for each patient being referred.** The case studies affirmed that when data on a particular patient case is incomplete, the teams go back to the referring doctor to request more information/better quality images etc.

- **Each ERN will need to agree the homogeneity -or lack thereof- across different specialities within its own network scope.** For instance, there may be a logic to agreeing datasets at the level of the subdomain, as opposed to attempting to mandate a single clinical dataset for every patient reviewed in, for instance, a rare endocrinology ERN. Paediatric patients, for a start, will logically require data elements not relevant for adults (e.g. around birth and real-age, in the case of infants, and concerning pubescence for older children, etc.).

- The ERNs will surely consider -especially the larger networks- the level at which there is clinical value in a MDT: for instance, as above it probably makes sense to generally arrange virtual consultations for each sub-domain of a disease-oriented network (e.g. rare inherited neuromuscular or rare peripheral neuropathies). There may be occasions where experts from different subdomains need to be involved, and perhaps different 'transversal groups/working groups' (for instance it may be deemed beneficial to have an expert from a NGS diagnostics group, along with a physiotherapist). **To ensure that people participating in these virtual consultations, especially when real-time, are all in fact needed and their time is being spent wisely, the judgement of the 'screener' or gatekeeper and the person organising the virtual consultation must be second-to-none.** Otherwise, one risks involving many experts for limited input.

- Finally, patients must only 'enter' these virtual care services of the ERN when there is a genuine need to do so (i.e. when the more 'ordinary' causes of the patient's symptoms have been considered and ruled out). A good example is the case of rare anaemias: to ensure that only the more complex, challenging cases are brought to the attention of the ERN in a virtual

consultation, a gatekeeper role is absolutely critical. How ERNs choose to organise this depends upon their disease focus: for some, an online 'tool' to conduct a first screen (e.g. a 'haematocrit measure' or a questionnaire such as the eCare open point) may be appropriate. For others, ERNs may request information to be conveyed to a gatekeeper for 'human' review and a decision made as to whether additional experts should be consulted/whether the patient should be reviewed comprehensively by a dedicated MDT.

In summary, there was significant emphasis not only on carefully selecting the data for clinical reviews but also structuring and standardising it in some way, to enable smoother, more efficient consultations.

Day 2: Thursday 29th September

Discussion on the circumstances under which patients are referred for shared care in the ERN – how do the Networks plan to approach this? (*Chairs: Matt Johnson and Till Voigtländer)*

The previous day's discussions identified the importance of only referring the most complex patient cases for the 'shared care/virtual care' of the ERN itself – not all patients with a rare eye disorder, for instance, would need to become the subject of a consultation in the rare EYE ERN. Therefore, the way in which patients 'enter' the ERN framework, and how these Networks will sit within the existing national landscapes, is of critical importance.

All agreed on a basic premise here: patients should not be contacting ERN coordinators/gatekeepers directly to request 'review' i.e. they should not be self-referring. Nonetheless, ePAG representatives pointed out that, especially in the early years, to help raise awareness of the existence of the ERNs for those who could really benefit from their expertise, it will be important to have fully engaged and expert patients, who know how the systems work and can point their physicians in this direction when required. Websites will need to be informative, to disseminate clear messages. There was a suggestion that it would be logical to highlight on the Orphanet database all centres which are members of an ERN (illustrating which ERN they below to).

To stimulate discussion on how ERN coordinators plan to manage the 'gatekeeper' role and 'receive' patients for care, Victoria displayed three basic scenarios by which patients may enter the ERNs, for discussion:

- We have a doctor based in HCP X, in Finland. HCP X is a member of the rare renal ERN. The doctor has a very complex case, and is unsure how to diagnose the patient accurately or provide optimal care, and therefore he refers this patient to the shared expertise of the rare renal ERN. As a member HCP of the renal Network, his centre will have IT platform access and he will -fairly easily, presumably- be able to launch a request to the coordinator or subgroup lead (or alternative gatekeeper role) to arrange a virtual consultation. Here, the 'pathways' are fairly clear.

- In our second scenario, let us assume we have a doctor from HCP Y in Finland, a centre which is *not* a member of the rare renal ERN. This doctor also has a complex patient with a rare renal condition, of some sort.
    - Should she always 'refer' her patient to HCP X above, as this centre is a full member HCP, and the patient can be referred thence to the ERN (presuming HCP X cannot address the problem)? In this scenario, with whom does the 'responsibility' for entering/uploading information lie, and with whom does responsibility for following/implementing the advice -or not- lie?
    - Or, will this doctor contact the renal ERN's 'gatekeeper' directly, without involving HCP X? If this course is pursued, how does the clinician in HCP Y convey the patient's data to the IT Platform of the ERN?
- If Finland has *no* HCP member in the rare renal ERN, how should Finnish patients with rare renal disorders 'engage' with the ERN when required? In such a scenario, according to the Legal Acts, an 'Affiliated' partner (of one of the 3 types) should have been designated in Finland - so presumably doctors in any Finnish hospital faced with a complex renal patient would refer them to the Affiliated Partner centre which then makes that 'link' with the ERN?

Using these three basic examples as a launching point for discussion, some of the Networks shared their perspectives on how they anticipate patients to enter their ERN for consultation. In the ITHACA group, for instance, the previous experiences with Dyscerne have been illuminating: patients are referred to Dyscerne through a doctor to a clinical geneticist, and THENCE to their specialist team. In the MetabERN, the referrals will depend on the type of disease with which they are dealing. But as a rule of thumb, the ERN should be the last tool/route for making a diagnosis.

As a result of these discussions, the group agreed/highlighted the following *key principles on patient pathways and 'referral' to an ERN:*

- National referrals and pathways are national prerogatives and responsibilities
- Ideally, all European MS will, by now have followed the guidance espoused by the **2009 Council Recommendation on an action in the field of rare Diseases**[10], in particular the call for countries to identify and designate centres with expertise in RD, making this expertise visible in each country. Where this *has* been achieved, an assessment of how the ERNs will complement the existing structures and national networks should be far simpler, because one can assume a certain level of awareness at the national level of the RD expertise already available in-country, making it easier to refer patients from primary and secondary care into specialised tertiary care systems, which will likely be the nearest gateways to the ERNs. If there is a lack of awareness, nationally, of existing RD expertise and gaps, it will be more difficult. If one relies on tertiary service specialists, it is necessary to have a strong baseline knowledge, and not all of the countries seem to have this yet.
- Access to a virtual consultation within any given ERN will clearly be easier in cases where a country has at least one member HCP. In these cases, it is imperative that ERNs strengthen (and in no way supersede or undermine) the national networks and help to streamline the pathways, where there is scope for this. For the countries which do not have members in

[10] http://ec.europa.eu/chafea/documents/health/prague-rd-council-recommendation_en.pdf

particular ERNs, a particular effort will be necessary to avoid *de facto* exclusion of patients to the services of the ERNs when needed - this is why the 'affiliation' concept is so important.

- If a broad awareness of the ERN concept is lacking in any given health system, the impact of the Networks can only ever be minimal. A major communication effort will be needed, in each country, and ERNs will need to be carefully 'marketed', to truly become the next frontier in specialised care.

SESSION 3: ADDING VALUE TO RARE DISEASE DATA

The State of the Art in Coding Rare Diseases (Ana Rath and Remy Choquet)

(Presentations available **here** and **here**)

Ana and Remy summarised the concept of the OrphaCode -and its ontology, the Orphanet Rare Disease Ontology (ORDO)- and how it is linked to mainstream coding systems. Improved codification of RD is cited as a priority in the 2009 *Council Recommendation on an action in the field of rare diseases*. There are myriad important reasons to embed an accurate and granular coding system capable of distinguishing between individual rare diseases – the most obvious being the ability to generate robust epidemiological data (without an accurate coding system it is impossible to count how many patients are living in any given country and where they are based, meaning service planning is difficult) There is a clear need to 'construct' the natural history of a rare disease (i.e. to understand the natural course of development and prognosis for patients and families) and to identify patients accurately for appropriate clinical research. All of this demands a common language to allow for data sharing, to serve both care and research purposes.

Orphanet has a dedicated coding nomenclature. Each disease is given a unique and stable number, known as the ORPHA Number. Each of these numbers is given a preferred term and all known synonyms and are mapped to OMIM, to ICD10, UMLS, SNOMED-CT, MeSH and MedDRA (where corresponding codes exist) and are also translated to numerous languages. The process by which new codes are created/revised was explained, along with the origins of the ontology form of the Orphanet nomenclature, the ORDO (an ontology is essentially a machine-readable version of the coding system, allowing the positioning of a disease within a 'tree and branch' structure.[11]) The ORDO has the accuracy and sensitivity to capture the interrelatedness of diseases.

The preferential status of Orphanet nomenclature for the RD field has been confirmed at European and MS level by the approval in 2015 of a set of *Recommendations on Coding Rare Diseases in Health Information Systems*[12] which advocate use of the OrphaCode. More recently, IRDiRC –the International Rare Disease Research Consortium- awarded the ORDO the 'IRDiRC

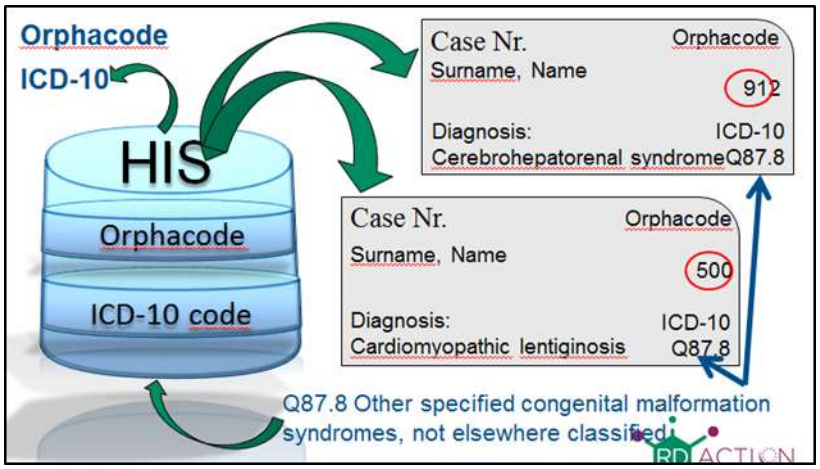
[11] For instance, a condition like Limb-Girdle Muscular Dystrophy 2a (LGMD 2a) is a distinct sub-type under the heading of 'Limb-Girdle Muscular Dystrophy' (the 'Disorder') which in turn sits under the broader heading of 'Muscular Dystrophies' (i.e. the 'Group of Disorders') which itself sits under the yet broader heading of 'Neuromuscular Diseases' (i.e. the 'system anomaly'). It is important to know that LGMD2a belongs to this nest of conditions, but is nonetheless distinct from other subtypes (e.g. 2f) which may have very different phenotypes/clinical presentations.

[12] http://ec.europa.eu/health//sites/health/files/rare_diseases/docs/recommendation_coding_cegrd_en.pdf

Recommended' label, thus singling it out as a high quality resource of particular relevance to the rare disease field.

Remy Choquet provided insights from a national (France) user perspective. The value of any data is determined not only by the box we put it in, but by the ability to interpret that data *outside* of that box. The most granular and sensitive system for coding RD, the OrphaCode is not yet used widely in health systems, and this has implications, as Remy demonstrated. ICD 10, the latest version of the International Classification of Disease coding system, only contains dedicated codes for several hundred of the ca 8000 separate rare diseases, around 3%.[13] SNOMED-CT now covers ca 38% of the rare diseases inventoried in Orphanet.

RD experts have contributed substantially to the latest version of the ICD, ICD 11, since 2009: 5000 RD have been included. Remy demonstrated why the OrphaCode is so important, using the example of two separate and very different conditions. Cerebrohepatorenal syndrome and Cardiomyopathic lentiginosis will both be classified under ICD 10 using one single code, Q87.8, which stands for 'Other specified congenital malformation syndromes, not elsewhere classified'. Clearly this is a rather vague, 'catch-all' heading. The Orphanet nomenclature, however, allocates two different codes (912 and 500 respectively). **This is crucial, if one wishes to know the number of patients living with each condition in a given population, and in order to explore the symptoms associated with each condition** etc.



A fallback option when there is no appropriate code in a system like ICD 10 is to deem a patient 'unlabeled' which is also problematic - there are after all two types of truly undiagnosed patients: the patients with a disease for which a genetic diagnosis *exists*, but who have not yet been identified as having that particular condition; and patients who are undiagnosed because science *has* no current diagnosis for their condition. It is important to remember that no coding system is comprehensive, as where there is no diagnosis there is of course no code.

It is not always easy for hospitals to incorporate the Orphacode alongside their mainstream systems (such as ICD and SNOMED-CT); therefore as part of RD-ACTION's focus on implementing the Recommendations[14] the teams in WP5 are creating practical instructions for hospitals on how to use the codes.[15] The full suite of tools will allow providers to pick and choose what they use.

[13] Ségolène Aymé, Bertrand Bellet and Ana Rath. 'Rare diseases in ICD11: making rare diseases visible in health information systems through appropriate coding' *Orphanet Journal of Rare Diseases* (2015) 10:35

[14] The Recommendations state that "Member States should consider adding Orphacodes to their country's health information system and explore the feasibility and resources needed to do so…"

[15] http://www.rd-action.eu/

The benefits of harmonising practices in capturing clinical (phenotypic) data for care and research in rare diseases (Ana Rath)

(Presentation available **here**)

The ability to capture the in-depth clinical description of patients is very important for many rare conditions; indeed, it is often the key to achieving a diagnosis when genetic testing or sequencing alone is insufficient. Furthermore, this 'deep phenotyping' approach is also important for understanding the symptoms associated with each genetic anomaly/disorder and the natural development of symptoms over time. This is especially important in diseases which have more than one genetic 'form', as often what is ostensibly a single condition manifests very differently, resulting in patients with drastically different phenotypes (a good example would be Niemann Pick Disease Types A and B). The problem is that physicians and healthcare professionals traditionally describe the same clinical feature in different ways, thus it is very valuable to have agreement on how these terms are used. In this day and age of electronic data sharing, it is necessary to use a particularly robust ontology, to ensure that IT systems can understand that terms such as 'long narrow head', scaphocephaly, and dolichocephaly actually all mean the same thing.

The Human Phenotype Ontology has been deemed particularly appropriate for use in the rare disease field; for instance, it was awarded the 'IRDiRC Recommended' label.[16] This preferential status is largely due to the efforts undertaken in recent years to align clinical descriptions appearing in Orphanet (symptoms associated with each condition are listed in the inventory) with phenotypic terms in HPO. Furthermore, a number of disease areas have worked closely with the HPO developers to tailor the ontology to be optimally useful for their field. HPO now includes layperson synonyms too, which is very helpful. The tools utilising and building upon the HPO are improving all the time; for instance, Ana presented a new resource, PhenoPackets.

Case Study: Practical Advice on agreeing harmonised phenotypic datasets for care and research: example and discussion of the steps needed to agree this (Holm Graessner)

(Presentation available **here**)

Several communities (e.g. rare neuromuscular) have taken steps to tailor the HPO to serve their needs. This has particularly been the case in the research field, and Holm presented his experiences in the NeurOmics project (Integrated European Project on Omics Research of Rare Neuromuscular and Neurodegenerative Diseases). The overall goal of NeurOmics (http://rd-neuromics.eu) is to improve diagnosis, care and therapy for patients and facilitate clinical trials. One major focus is to combine various types of data from the patients visiting partner centres who either lacked a diagnosis altogether or else had a confirmed *genetic* diagnosis but exhibited an unusual phenotypic presentation. Specifically, the partners sought to link genomic data (from the sequencing of the patient's whole exome or whole genome) with detailed clinical ('phenotypic') data.

[16] The term has now been changed to 'IRDiRC Recognized Resources' http://www.irdirc.org/activities/irdirc-recognized-resources/

The ability to link these two data types is particularly important for patients without a clear diagnosis, as researchers can determine whether mutations in any candidate genes (identified via the sequencing and subsequent analysis) are associated with the observed phenotypic profile. The project partners agreed with the 'sister' initiative, RD-Connect (which has built a dedicated platform for this data linkage) that they would use the HPO to capture all their phenotypic information on patients whose exomes (and later genomes) were sequenced under NeurOmics.

To standardise this process, the partners agreed some **generic** information, to be collected across all ten groups of Neuromuscular and Neurodegenerative conditions within the focus of the project (e.g. ataxias, hereditary spastic paraplegias, Huntington's Disease etc.): in addition, it was necessary to agree core **clinical** data items for each patient 'enrolled' in the NeurOmics project. In each of the ten groups, the experts determined the clinical terms of greatest relevance to their patients, and efforts were made to align these terms -and all the possible synonyms people might use- with the official HPO terms. As an example, terms such as 'swallowing problems' or 'swallowing difficulties' were both matched to 'dysphagia'. As this was to be a structured dataset of information to be captured for every patient with, for example, a form of Ataxia, it was agreed at the project coordination level that a particular 'tool', built upon and powered by HPO, would be used: PhenoTips.[17]

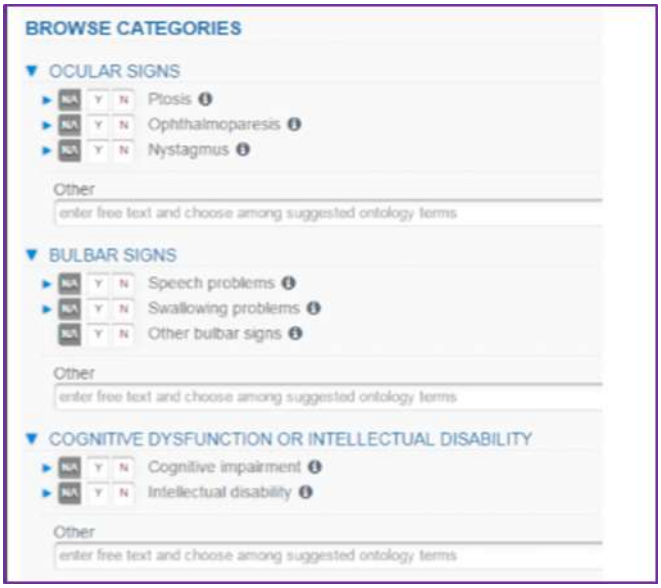
GENERIC CORE DATA				
Individual code				
Gender	Male	Female		
Ethnic origin	Father *(Drop down menu with countries)*	Mother *(Drop down menu with countries)*		
Clinical status	Affected	Unaffected	Undetermined	
Other relatives affected	Yes	No	If yes, give number	Unknown
Other relatives included in this study	Yes	No	If yes, give number	
Relative code	*(The next 3 rows may need to be repeated several times depending on numbers of relatives included in the study)*			
Relation to individual	*(Drop down menu here with all possible relationships)*			
Relative's clinical status	Affected	Unaffected	Undetermined	
Inheritance	Sporadic	Recessive	Dominant	X linked
Consanguinity	Yes	No	Unknown	
Disease course	Static	Progressive	Fluctuating	Episodic
Age at onset	Years:	Months:		

Each disease strand (10 in this case[18]) thus carried out this brainstorming process to agree the most important clinical features, and cross-mapped the different ways in which they described them, resulting in a tailored dataset for the NeurOmics focal conditions; typically, this was achieved through a combination of advance preparation and a one-day workshop to confirm the datasets. The number of clinical terms selected by each of the disease areas varied, with the largest number of terms (111) selected by the Spinal Muscular Atrophy group.

This knowledge-generation and terminology mapping activity was very useful, both for the clinicians/researchers but also in terms of enriching and enhancing the utility of the central HPO resource. For instance, the HPO already contained a clinical symptom coded as 'amyotrophy' but the experts explained that they required a more specific term, namely atrophy, to be made available (because atrophy is not always amyotrophy), and this was duly incorporated to the main ontology for future use. Similarly, whereas the HPO originally had a code for 'tube feeding in infancy', the patients NeurOmics encountered sometimes began tube feeding only in teenage or adult years, and this also was revised. It was recognised at the outset that in some diseases, clinicians will need to

[17] https://phenotips.org/
[18] http://rd-neuromics.eu/diseases/

capture information on a particular scale, requiring unique data fields not previously in the HPO. For instance, the Huntington's Disease researchers needed to record the patient's position on the Unified Huntington's Disease Rating Scale (UHDRS) and data relating to functioning, which the PhenoTips forms were able to incorporate.



Once the terms were agreed, the HPO team could then 'embed' the tailored dataset for each of the ten areas in a bespoke 'instance' (i.e. specific online version) of PhenoTips. Each instance was harmonised to the others, however, meaning the SMA physicians recorded 'muscle weakness' in the same way as the other 9 areas (in fact, there was substantial overlap between the terms selected by the 10 groups).

PhenoTips thus became the web-based medium through which the clinicians provided the phenotypic data on each patient. Each time the physician logs-in, the system prompts them to complete the agreed fields and select 'yes', 'no' or 'other' to indicate if a symptom is present or not. There is also an option to add extra clinical features, where relevant, even if outside of the agreed mandatory set.

Once one has collected all of this data, Holm explained how it can be used. One can search for patients with particular features, diagnoses, disease histories etc. (so for instance you can search for all patients with sleep apnoea). In the case of NeurOmics patients who are given a diagnosis/a more accurate diagnosis through this process of data integration, the diagnosis will always be confirmed through gold-standard techniques before being relayed to the patients. Where a diagnosis has not yet been forthcoming, the data will support research in solving the unsolved cases. **The data only holds this potential, however, because of the preparatory work in optimising the HPO and the partners agreeing to use this Ontology for the clinical descriptions across all related initiatives.**

Global efforts to agree a Patient Unique Identifier for the rare disease field: current progress and what ERNs need to do to synergise (Rachel Thompson)

(Presentation available **here**)

Rachel explained that, despite the theoretical division between care and research, in the RD field there is often substantial overlap in practice. ERNs are particularly relevant here, given the research requirements. In demonstrating the state of the art in data sharing for RD, Rachel introduced the RD-Connect initiative. RD-Connect is a 6 year (2012-2018) initiative funded under FP7, dedicated first and foremost to overcoming data silos and making data *usable* and *reusable*. Data is here defined broadly (e.g. phenotype data, genomics data (from WES or WGS), clinical trial data, natural history data, biosamples, etc.), to support many forms of RD research: gene and modifier discovery; genotype-phenotype correlation; patient trial recruitment; increased number of biosamples for research etc. The traditional barriers to data sharing were summarised.

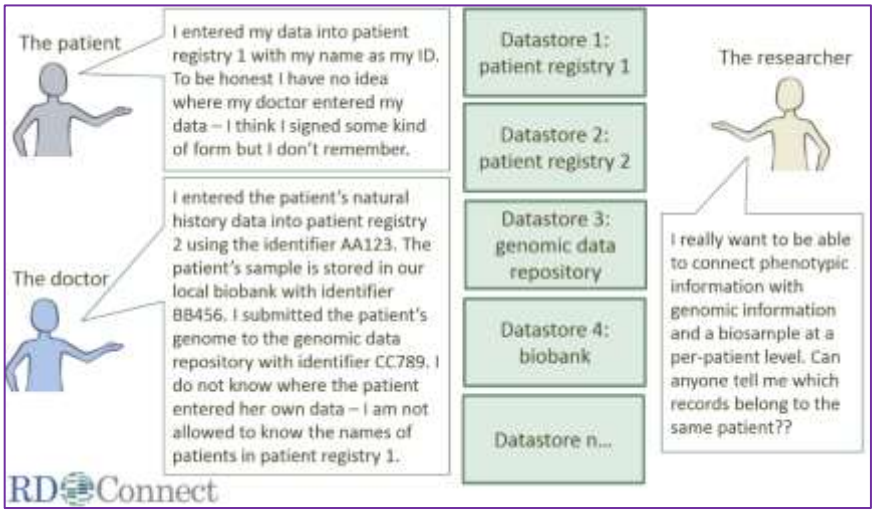
Harmonisation in phenotypic data is more valuable than ever, to support diagnoses and a greater understanding of diseases and clinical outcome measures. Because data today is usually collected and shared electronically, clinical information must be captured in a 'computable' form. In these respects, the concept of FAIR data is growing in prominence. FAIR is basically a set of principles[19] for data and metadata (metadata are data *about* data):

- ✓ Findable - (meta)data is uniquely and persistently identifiable. Should have basic machine readable descriptive metadata.
- ✓ Accessible - data is reachable and accessible by humans and machines using standard formats and protocols.
- ✓ Interoperable - (meta)data is machine readable and annotated with resolvable vocabularies/ontologies.
- ✓ Reusable - (meta)data is sufficiently well-described to allow (semi)automated integration with other compatible data sources.

FAIR principles are there to help data generators to prepare their data from the beginning ('at source') for interoperable use and analysis across different resources. The consequences of *not* doing this are vastly wasted resources and wasted person months for researchers wishing to pool datasets which were not designed to be sharable. There will *always* be some additional work -this is not a 'quick fix' but a *quicker* fix'- but developers estimate that each time you try to align two independent and 'non-FAIR' datasets into a state where you can compare and analyse the data, it takes 6 months, whereas if the data is linkable at source, this can be done in 1 month.

Rachel explained the concept of ontologies: ontologies are a way to make data 'computer accessible', i.e. for IT systems to understand how data items relate to each other or do *not* relate (e.g. to know that item A in registry 1 means the same thing as item B in registry 2, and is similar to but not quite the same as item C in registry 3). There is consensus in the RD field on the appropriateness of HPO for phenotypic descriptions and ORDO for naming diseases. However, she emphasised that each of these is purpose-specific, to an extent: even these two ontologies have limitations, thus ontologies can be perfect for certain uses and need tailoring or adaptation for another.

Rachel summarised the way in which data enters and moves through the RD-Connect platform, and illustrated examples of new pathogenic genes discovered through use of the platform to-date. In the final part of her presentation, Rachel explained the concept of the 'GUID' or Global Unique Identifier. This is essentially a means for the research community to know that data pseudonymised in one registry relates to the same patient as data



[19] http://www.nature.com/articles/sdata201618

from another source, whether this other source be another (unconnected) registry, a natural history study, a biosample from that patient, etc. This is very important, as oftentimes a more comprehensive picture of the patient's condition (or suspected condition) can emerge through pooling this data. Similarly, researchers may need to find a biosample from the patient, to further test a hypothesis. The problem of course is that data repositories cannot store identifiable data bearing the patient's personal information. It IS possible however, to pseudonymise the patient's identity by using a code of sorts, which could not be deciphered with human logic. To truly allow the possibility of linking data from the same patient when collected and stored by different actors, it is necessary to have a means of constructing an identifier in such a way that each patient will always receive the *same* identifier, or a linkable identifier, no matter who requests that identifier. Different identifiers were outlined, namely the GUID/PUID (Patient Unique Identifier), the RD-ID (which is a PUID for RD) and the HD-ID (an identifier used specifically in the Huntington's Diseases field).

The GUID/PUID concept works on the following principles: to generate an identifier that will serve the purpose of linking pseudonymised data, it is necessary for the data source to collect particular items of personally identifiable information (PII), in a certain way - at present, there is reasonably good consensus on what these should be these: first, middle and surname as per birth certificate, date of birth, and city of birth as per birth certificate. Under one possible scenario, this PII is converted into a "one-way hash" (a string of code that does not contain identifying information), and the hash is sent to a central server, which returns a GUID for that participant. The GUID will be new if it has never seen that hash before, but if it has encountered that hash, it will return an existing GUID (i.e. one created uniquely for that particular participant). Rachel emphasised that extensive patient consultations had been carried out in RD-Connect here, to explore patient perspectives on this approach.

A Joint task force has been convened under the auspices of the IRDiRC and the Global Alliance for Genomics and Health (GA4GH) which is due to return its findings and proposals here at the end of the year. http://www.irdirc.org/activities/currentactivities/participant-unique-identifiers.

Discussion: guiding principles and good practices for standardising RD data (Chairs A. Rath and V. Hedley) (Presentation available **here**)

There was broad discussion on how the ERNs might recognise which 'tools' (such as the Phenomizer[20], for instance) are genuinely useful and have 'staying power'. Participants pointed out that sometimes there are several similar tools available, and questioned whether it was desirable/feasible for all the ERNs to harmonise the tools they use. It was agreed that one should exercise caution in embracing any particular tool or 'instance' of a standard; **however, if we want to optimise the interoperability of data in the ERN framework -and by extension, the wider RD field- it is necessary to agree the core standards, where these have reached a sufficient level of maturity and acceptance and will not 'disappear'.** Orphacode and HPO have been endorsed in this way, although their effective usage requires forethought and preparation, if one wishes to harness their full potential for enriching the data. In attempting to agree good practices between the ERNs, the goal is not to *enforce* one entity or another. ERN communities must decide themselves what they do

[20] http://compbio.charite.de/phenomizer/

with their data and where they deposit it etc. (e.g. if they wish to use particular variant-calling platforms); rather, **this debate is about enhancing the discoverability and reusability of that data.**

In the course of these discussions, several ERN coordinators identified a need to agree a means of coding not just diseases, but also therapeutics and medical devices, for instance – this is very important, and all ERNs were encouraged to share key standards and ontologies of particular relevance to their field with the RD-ACTION organisers.

The group discussed various issues around sharing/exchanging data. Rachel explained that the RD-Connect ELSI research[21] highlights the fact that patients have the right to *expect* researchers to share data, under appropriate conditions, and this does not mean waiting until publications are released. **To do this requires changes in the way in which data is collected and stored.** Again, it was emphasised that gathering robust phenotypic data may require some tailoring of the HPO within specific disease communities: some of the things people will wish to capture are not really 'phenotypes' e.g. wheelchair use. Therefore, effort upfront is required, but the message is that this will pay dividends.

There was lively discussion as to the *types* of data that will be shared in the ERN framework, and this included a 'diversion' into the topic of registries. An important issue here of course is how one actually *defines* the ERN framework. Most people agree that the ERNs will offer an unprecedented opportunity to increase the proportion of RD patients enrolled -or offered the *chance* to enrol- in appropriate, quality-assured registries. Whether these are somehow embedded in the ERN IT Platform, or sit outside of it (e.g. existing robust registries, or new ones that may be established) ERNs will surely encourage increased patient registration. As few registries are able to fulfil multiple purposes effectively, teams will need to consider what *sort* of registries they wish to enrol patients to, and where these sit. Alongside this, there is the highly relevant issue of what data the SaaS for a clinical patient management system will retain, and what this will be useful *for*. The Tender is clear: data will be shareable for virtual care, and will be pseudonymised and retained for re-use: the specifications demand that the service:

> "(xiv) encrypts and stores the data;
>
> (xv) pseudonymises patient data for sharing, use in clinical decision making tools, protocols, guidelines, case library or research;
>
> (xvi) hosts the data storage within EU borders and ensures that the hosting is single-tenant with stable, fast and easy data storage and retrieval, back-up and recovery;"

A key question, then, is what data one wishes to collect during virtual care encounters, knowing it will be available later for secondary purposes. One must balance the utility of the data stored in that platform against the efforts required to collect the data.

How the ERN platform will interact -or not- with *other* types of data seemed much clearer; for instance, it will surely *not* be possible to store raw WES or WGS data in the SaaS! One must envisage

[21] http://rd-connect.eu/platform/ethics/

'safe havens' equipped to store such raw data, such as the European Genome Phenome Archive (which is used as the raw data repository in RD-Connect.)

Several coordinators emphasised the need to provide for undiagnosed patients, and participants discussed how to 'code' such patients using OrphaCode. The group appreciated the importance of agreeing a common means of pseudonymizing patients in the ERN framework: this is a crucial issue, particularly as we move towards ever-greater reliance on eHealth. **If a set of PII has been agreed as the basis for generating a common means of linking data whilst preserving privacy (e.g. via a GUID–like system) then the ERNs should, logically, include these elements in any common dataset agreed for virtual consultations in the ERNs (and indeed, for any patient registration connected with each ERN).** Beyond this, one will need to consider if there are any *clinical* items that would be essential for all ERNs to collect, or if this will be too different from one Network to another (participants proposed there is more relevance to agreeing common data elements for certain types of *registries*, as opposed to clinical case report forms).

In response to a question about how to encourage MS to use the OrphaCode in their HIS, it was emphasised that the JA (RD-ACTION WP5) is attempting to provide as much hands-on support to countries as possible, to help them fulfil the Recommendations on coding for rare diseases. Once again, it was noted that ERNs have a unique potential to propel many of these initiatives into the mainstream, and optimise the way in which **data is collected and stored: ERNs, sitting at the crossroads between care and research and in a sense 'beginning from scratch', are a perfect ecosystem in which to 'get things right'.**

Summary of the 'Tool-Kit' resources to be finalised post-workshop and next steps: (A. Rath and V. Hedley)

In summarising the workshop, Ana and Victoria made the following points:

- The ability to share and pool data is essential in the RD field, and in all fields requiring a specific concentration of expertise: only through data congregation can one attain a critical mass, which generates knowledge and drives forwards improvements in healthcare
- Additional legal support from the European Commission would be invaluable, relating to obligations of ERNs concerning data handling under the new GDPR[22]
- In legal terms, it is probably possible for patients to receive virtual care/ a virtual consultation in an ERN *without* providing explicit consent; however, the group was unanimous that informed consent should always be obtained, as a 'best practice'
- RD-ACTION will assemble papers which address relevant ELSI issues for rare disease data (research papers) and will also assemble as many sample IC forms as possible, for conveyance to the EC teams delivering the final Consent forms for the ERNs
- Use of agreed ontologies such as the ORDO and the HPO adds value to data, especially in terms of the **reusability** of that data – standards which exist already and have gained a certain level of 'acceptance' in the wider RD and specialised healthcare field should be

[22] Several Tenders have subsequently been awarded, to address this important area:
- Tender SANTE/2016/B3/053: Analysis on the Impact of EU legislation on the operation of ERNs
- Tender SANTE/2016/B3/061: Informed consent for European Reference Networks implementation

promoted in the ERN framework, to enhance the value of the data which is collected, exchanged, and retained.

- In recommending standards for use with ERN-related data, it is important to note that the process is not unidirectional: what other standards should be embraced, which are used widely in the RD and/or specialised healthcare/ technology field and have been proven to enhance the utility of information/data (e.g. standards around coding medical devices)?
- There are practical questions from this audience on how one actually ***uses*** these different ontologies (e.g. how to use the OrphaCode and make it most useful for a particular disease area) and what they can do to enhance the work of ERNs. It would be useful to arrange a more hands-on demonstration for some of these tools, to explore what needs to be in place, how one can use Orphanet Nomenclature, HPO, Identifiers etc. to add value to the data and increase its interoperability through FAIR approaches, for instance.
- **It would be logical to produce a list of consensus recommendations on standardising data in ERNs, along the lines of:**
    - ERNs should prioritise use of OrphaCode because of x, y and z
    - ERNs should prioritise use of HPO as the best RD-sensitive standard for phenotyping, because of z, y and z
    - ERNs should collect the PII necessary to generate a GUID or similar, as a minimum, from all patients referred for virtual shared care in the ERN and indeed from all patients enrolled to registries.
    - As above, which other standards should be recommended (e.g. OMIM for genes? Lab standards?)
    - Is it also possible to agree on some core statements, such as 'Data should not be collected, used for 'direct' care and then destroyed, unless the patient wishes this'
- To have maximum impact, it is essential that the good practices recommended by this Group are actually *incorporated* to the SaaS for a clinical patient management platform – how do we achieve this?
- The ERN community can –hopefully- agree the ***way*** in which data is captured (i.e. agree the standards used, e.g. Orphacode). Would there be any benefit in attempting to agree a model Case Report Form (CRF)/template, with common data elements, **for the virtual consultations**, or would these differ too much across the ERNs? It is likely that it would not be feasible or meaningful to try to agree *clinical* data elements for collection in virtual consultations across all ERNs; however, this workshop has suggested **that there should be homogeneity in the demographic data (the PII).**
- It is necessary to think carefully about how CRFs –such as will be shared for virtual care- differ from **registries**, and perhaps begin discussions on what the best practices would be for enrolling patients of the ERN in registries (again, do ERNs routinely offer enrolment to patients seen in virtual MDTs, or expand this to all who come to the HCP?)

Post Workshop Meeting

The presentation from Iiro Eerola, DG RTD, is available here:

Post-script: ePAG Representative Feedback on RD Action Workshop on Virtual Data Sharing:

ePAG representatives much appreciated the opportunity to receive ePAG fellowships to attend the RD Action workshop and emphasized the importance for patient representatives to be included in ERN stakeholder meetings to better understand the whole ERN picture including challenges faced by MS, EC and network coordinators. This provides representatives with the opportunity to provide support ERNs and provide solutions as equal partners.

Overall, ePAG representatives found that the range of topics discussed during the workshop was pertinent and interesting. They found it very useful listen to the views of a variety of different experts. Recurring feedback included the critical issue of funding of ERN activities and the contradiction between the main goal of ERNs which is health care and the main source of grants which is research. The main concern seems to be the sharing of data while keeping ethical priorities in mind. Patient access for ERNs is considered important. Many patients are well informed and capable of understanding the details. However, if a patient experience challenges with the online system i.e. uploading documents it was suggested that general practitioner access could be considered as a solution. In addition, it was suggested that if all member states coded, registers would not be needed to know how many patients there are with any particular disease. Patient access to registers is seen as key.

Further, ePAG representatives find it important to further develop and communicate the role of ePAG representatives and how they can contribute to the work of ERNs to clinical leads.

In terms of organising the ePAGs, it was mentioned that it would be important to include alternates for ePAG representative and to add patient representatives for each disease, theme and member state for each ERN to the ePAGs.

AGENDA: RD-ACTION Workshop 'Exchanging data for virtual care within the ERN Framework'

28th-29th September 2016 Brussels

Thon Hotel EU, Rue de la Loi 75, B-1040 Brussels

Aim of the Workshop:
The overall aim of the workshop is **to generate and agree guidance and good practices for ERNs to collect and share data for care within the framework of ERNs**

Context and Overall Objectives:
Ethos of RD-ACTION workshops: A key objective of the RD-ACTION Policy WP workplan is to continue to provide support to the rare disease community in conceptualising, implementing and evolving robust ERNs capable of meeting the needs and expectations of people living and working with conditions requiring a specific concentration of expertise. As the 1st ERNs are established and evolve, shared consensus guidance is important to support the Networks but also to ensure a baseline compatibility and interoperability (at various levels) between the ERNs.

ERNs are first and foremost dedicated to care. Once established, and connected by a dedicated IT platform, the Networks will support the exchange of knowledge and expertise between healthcare providers operating at the top of their game. It is important to emphasise that wherever possible (and appropriate), expertise will travel rather than the patients themselves. In practice, this will entail a significant degree of virtual healthcare provision. 24 proposals were submitted to DG SANTE in 2016 and of these, only a few conduct significant, formal eHealth-enabled consultations at present. Nonetheless, other applicants will have experiences and knowledge to share on this point, and it is vital that collectively the ERNs appreciate the state of the art in terms of interoperability in data collection, standardisation, sharing, storage and reuse (including the standards recommended by the EUCERD and Commission Expert Group on RD as well as the latest progress in initiatives such as IRDiRC, RD-Connect, HIPBI, Global Alliance for Genomics and Health etc.).
This workshop will allow the Applicant Network Coordinators and other key stakeholders to pool experiences and good practices and identify ways to approach data-sharing in ERNs, to add value to the planned approaches.

Specific Objectives:

- ***To define more clearly the different types of cross-border care encounter ERNs may involve and how to set-up and execute virtual encounters***
- ***To share the state of the art of coding rare diseases and harmonising phenotypes and explore how this can be used to add value to care provision within ERNs***
- ***To identify and agree good practices in order to optimise the collection and sharing of data for care within the ERN framework via a 'Tool-Kit' of resources***

Expected Outputs of the Workshop:

- **Workshop report, complete with PwPs of all presentations –(output of sessions 1-3)**
- **'Tool Kit' resources:**
  - **Practical suggestions regarding the organisation of virtual consultations (output of session 2)**
  - **A collection of example case report forms and consent forms for rare diseases, for possible use within the ERNs (output of session 2)**
  - **Guiding Principles for standardising data for care in the RD framework (output of session 3)**

Suggested Reading for Participants:
(Documents will be uploaded to a shared folder, before 26th at the latest) https://www.dropbox.com/sh/a7mo0c3ntdlqs27/AAB5QtnUMQCQF1o6Z_Lovfsva?dl=0 :

- What do coordinators require from an ERN ICT platform?
- Descriptive Document for ERN ICT platform (SaaS for a patient clinical management system) as published June 2016 (**pages 10-12** which list the Requirements for the SaaS)
- 'Implementation report Health and Consumers on the Commission Communication on Rare Diseases: Europe's challenges and Council Recommendation of 8 June 2009 on an action in the field of rare diseases' (2014)

AGENDA

DAY 1: WEDNESDAY 28TH SEPTEMBER Begins at 11.30

Session 1: Aims of the workshop and the rare disease policy context

11:30- 11:45: Welcome to the Workshop and Participant Introductions

11:45-11:55: Summary of the ERN Status Quo (Enrique Terol)

11:55-12:10: Overview of this morning's discussions (Chairs from pre-workshop meeting)

12:10-12:20: Aims of this workshop and anticipated outputs (Victoria Hedley)

12:20-12:40: The EU Rare Disease framework: the context for ERNs (Jaroslaw Waligora)

12:40-13:10: What do we mean by virtual care? Summary of the state of the art across the RD field and beyond (Victoria Hedley) (Followed by Questions and Discussions)

13:10-14:00 Lunch (provided for participants in the hotel restaurant)

14:00-14:40: Special Address and Exchange with Mr Andrzej Rys (Health Systems and Medical products and Innovation Directorate DG SANTE)

Session 2: Virtual cross-border healthcare in action

14:40-15:00: Consent for sharing data cross-border for healthcare (and re-use): impact of the revisions to the Data Protection Regulation (Petra Wilson)

15:00-15:15: The Patient Perspective on sharing data cross-border for care (Matt Johnson and Valentina Bottarelli)

15:15-16:00: Discussion Session: what should be included in a model/shared consent form for all ERNs?

16:00 Coffee Break

16:30-17:15: Examples of rare disease virtual care in action, with a focus on good practices, challenges encountered and lessons learned

- example from paediatric oncology (Ruth Ladenstein)
- example from rare and complex epilepsies (Helen Cross)
- example from rare bone (Luca Sangiorgi)

17:15-18:15: Q&A and Discussion: good practices for virtual consultations (*Chairs: T. Voigtländer, M. Johnson and V.Hedley)*

Day 1 ends 18:15

DAY 2: THURSDAY 29TH SEPTEMBER

9:00 Overview of Day 1 (V Hedley)

09:10-09:45 Discussion on the circumstances under which patients are referred for shared care in the ERN – how do the Networks plan to approach this? (*Chairs: Matt Johnson and Till Voigtländer)*

Session 3: Adding value to rare disease data

9:45- 10:30 State of the Art in coding rare diseases (Ana Rath and Remy Choquet) (followed by Q&A)

10:30-11:00 The benefits of harmonising practices in capturing clinical (phenotypic) data for care and research in rare diseases (Ana Rath) (followed by Q&A)

11:00 (Coffee Break)

11:30-12:00 Global efforts to agree a Patient Unique Identifier for the rare disease field: current progress and what ERNs need to do to synergise: (Rachel Thompson)

12:00-12:20: Case Study: Practical Advice on agreeing harmonised phenotypic datasets for care and research: example and discussion of the steps needed to agree this (Holm Graessner)

12:20-13:00: Discussion: guiding principles and good practices for standardising RD data (*Chairs A. Rath and V. Hedley*)

13:00 -14:00 Lunch (provided for participants in the hotel restaurant)

14:00-14:50 Summary of the 'Tool-Kit' resources to be finalised post-workshop and next steps: (A. Rath and V. Hedley)

POST-WORKSHOP MEETING: From virtual care to research and future workshops

14:50 Presentation from DG Research & Innovation '***ERNs and the future of research in the area of rare diseases***' (Iiro Eerola) – followed by discussion on research priorities

15:20 Collective brainstorm on the content of future RD-ACTION ERN-related workshops and additional necessary meetings

16:00 Workshop ends

PARTICIPANT LIST

Applicant Network Coordinators (or their representatives)

PARTICIPANT NAME	APPLICANT THEMATIC GROUPING REPRESENTED
Michelle Battye	Rare Urogenital Diseases
Melanie Brunhofer	Paediatric Cancer
Helen Cross	Rare & Complex Epilepsies
Françoise Ducimetière	Solid and Rare Cancers
Sofia Douzgou	Rare Malformations and Developmental Anomalies and Rare Intellectual Disabilities.
Pierre Fenaux	Rare Haematological Diseases
Holm Graessner	Rare Neurological Diseases
Nicoline Hoogebrugge	Genetic Tumour Risk Syndromes (GENTURIS)
Marine Hurard	Rare Multisystemic Vascular Diseases
Ruth Ladenstein	Paediatric Cancer
Dorothée Leroux	Rare Eye Diseases
Eduardo Lopez Granados	Transplantation (SOT & HSCT) in Children
Maria Madrigal Montero	Rare Immunological and Autoinflammatory Diseases
Maria Manu	Rare Haematological Diseases
Alberto Pereira Day 2 (Faisal Ahmed for Day 1)	Rare Endocrine Diseases
Luca Sangiorgi	Rare Bone Diseases
Georgia Sarquella-Brugada	Rare Cardiac Diseases
Maurizio Scarpa	Rare Hereditary Metabolic Diseases
Franz Schaefer	Rare Renal Diseases
Christoph Schramm	Rare Hepatic Diseases
Andoni Urtizberea	Rare Neuromuscular Diseases
Thomas Wagner (Stephanie Chauvet Day2)	Rare Pulmonary Diseases
Rene Wijnen	Rare Gastrointestinal Diseases

ePAG (European Patient Advocacy Group) Representatives

PARTICIPANT NAME	ePAG REPRESENTED
Tobias Arndt	ePAG Rare Malformations/ Developmental Anomalies/ Rare Intellectual Disabilities
Lut de Baere	ePAG Rare Hereditary Metabolic Disorders
Cosmoferruccio De Stefano	ePAG Rare Multi-systemic Vascular Diseases
Paolo Federici	ePAG Rare Multi-systemic Vascular Diseases
Marleen Kaatee	ePAG Rare Hepatic Diseases

Mary Kearney	ePAG Rare Neurological Diseases
Diana Marinello	ePAG Rare Immunological & Auto Inflammatory Diseases
Gabor Pogany	ePAG Rare Malformations/ Developmental Anomalies/ Rare Intellectual Disabilities
Marianne Rivière	ePAG Rare Connective Tissue and Musculoskeletal Diseases
Jose Willemse	ePAG Rare Hepatic Diseases

European Commission Representatives

PARTICIPANT NAME	AFFILIATION
Anna Carta	DG SANTE B3 (Cross-border Health Care and eHealth)
Jiro Eerola	DG Research & Innovation
Caroline Hager	DG SANTE B3 (Cross-border Health Care and eHealth)
Markus Kalliola	DG SANTE A4 (Information Systems)
Hélène Le Borgne	DG SANTE B3 (Cross-border Health Care and eHealth)
Sevala Malkic	DG SANTE B3 (Cross-border Health Care and eHealth)
Antti Maunu	DG SANTE
Andrzej Rys	Health Systems and Medical products and Innovation Directorate DG SANTE
Enrique Terol	DG SANTE B3 (Cross-border Health Care and eHealth)
Jaroslaw Waligora	DG SANTE C1 (Health programme and chronic diseases)

Board of Members States Representatives

PARTICIPANT NAME	AFFILIATION
Birute Tumiene	Board of Member States Representative for Lithuania
Till Voigtländer	Board of Member States Representative for Austria and Chair of the Board of Member States

Project Representatives and additional ERN experts

PARTICIPANT NAME	AFFILIATION
Valentina Bottarelli	RD-ACTION/ EURORDIS
Virginie Bros-Facer	EURORDIS/RD-Connect
Adela Cañete	Expo-R-Net
Remy Choquet	RD-ACTION
Victoria Hedley	RD-ACTION
Matt Johnson	RD-ACTION/ EURORDIS
Yann le Cam	RD-ACTION/ EURORDIS
Ana Rath	Orphanet/RD-ACTION
Rachel Thompson	RD-Connect
Petra Wilson	IBSG and several eHealth initiatives