Addressing challenges to multi-country collaboration models for rare diseases

Rare diseases, defined as conditions affecting no more than one person in 2,000, collectively impact an estimated 30-35 million EU citizens. Since patient volume is a core parameter for advancing innovative diagnostics and healthcare interventions, this is, per definition, a limiting factor in the study of rare diseases. This slows research and recruitment to clinical trials. Consequently, survival rates for rare disease patients trail behind those of more prevalent medical disorders. As a rare disease prototype, the cure rates for childhood cancers have significantly improved in recent decades, but cancer now accounts for 20% of all childhood deaths after infancy compared to only 11% in the 1960s, as death from more common diseases has become rarer.

Currently, real-time sharing of primary health data is feasible and routine within individual rare disease healthcare centres. However, similar primary health data sharing between rare disease centres within and across EU Member States to address clinical needs and improve health outcomes can be technically troublesome and even legally impossible, posing a critical barrier to improving rare disease healthcare.

Focusing on childhood cancer as a prototype for rare diseases, the study addresses the rare disease volume challenge by (i) reviewing existing cooperative structures and identifying legal barriers to extensive, real-time, multi-country primary health data sharing, (ii) exploring attitudes to such data sharing among rare disease patients/parents and health professionals, and (iii) presenting six policy options conducive to more in-depth multi-country collaboration between centres responsible for treating rare diseases.

The report presents six policy options for establishing multi-country rare disease ecosystems. Policy option 0 is the baseline. Policy option 1 is close to the current European Reference Network (ERN) structure and involves pseudoanonymised cross-country data sharing between a limited number of health centres with predefined standards for which data to share. Policy option 2 involves sharing complete (in practice secondary) medical files within the rare disease ecosystem. Policy 3 involves sharing complete medical files in a pseudonymised form in real time. Policy option 4 involves sharing data in real time without pseudonymising the data and thereby allowing external health professionals to interact directly with the patients. Policy option 5 would give the EU and Member States a role in providing a central body to facilitate, supervise and monitor the multi-country rare disease ecosystems. Policy option 6 involves funding to develop and support multi-country rare disease ecosystems.

ERNs and multi-country rare disease ecosystems could be seen as complementary platforms to address rare diseases. The rare disease ecosystems could strengthen networking at all levels, and may function as an alternative to the centralisation efforts that have so far characterised rare disease healthcare.
Policy option 1: Pseudonymised data sharing with selected experts to improve clinical practice

This option could potentially be covered by ERNs and the European Health Data Space (EHDS) once fully implemented. It promotes the sharing of rare disease patients' pseudonymised healthcare data among named health professionals within a rare disease ecosystem. Data would be restricted in type (text excerpt, biochemical results, images, etc) and in time (selected time period). Each update of a patient's pseudonymised health data would require their consent. The main difference from the current ERN system is that data would be shared for all patients or medical issues that fulfill preset criteria. For chronic rare diseases that are not life-threatening, option 1 would cover most ecosystem needs. The current individual ERNs could be expanded to encompass well-defined rare disease ecosystems that fall within the disease target of the ERN. Accordingly, an ERN would include not just one but multiple ecosystems. Health professionals within each ecosystem would increase their expertise in diagnostics, clinical care, and/or research through access to a larger volume of patient data.

Policy option 2: Sharing complete medical files within a rare disease data ecosystem to improve clinical practice

This policy is a moderate expansion of policy option 1, where patients or legal guardians give consent to the sharing of their full medical file, albeit pseudonymised, to improve clinical care. This option could potentially be covered by ERNs and the EHDS, once fully implemented, if the consent process included specifications on data, the involved rare disease centres and named health professionals within the individual rare disease ecosystem that could access the health data.

Policy option 3: Sharing complete medical files in real time to improve clinical practice and for individual case discussion

With this option, the pseudonymised files would be continuously updated in real-time. Contrary to options 1 and 2, each patient would provide consent only once, typically at the time of diagnosis. The health professionals within an ecosystem would have continuous access to the health data on all patients in the ecosystem, which could improve their expertise. This option would allow the health professionals involved to discuss healthcare issues requiring immediate action in real time with other experts. This policy would require an EHDS infrastructure that ensured continuous real-time data updates and access, albeit with pseudonymisation for all patients in the rare disease ecosystem.

Policy option 4: Sharing real-time medical data with direct access to patients for delivery of care

This is very similar to option 3, but the medical data would not be pseudonymised. The rare disease experts within the ecosystem would have access to the full (in practice a secondary) medical file in real time, and the external experts would be able to interact directly online with patients when sharing a common language or facilitated by a machine translation interface, providing both the patient or legal guardians and the rare disease institution had consented to this. The machine translation would require ownership of translated data to remain with the original healthcare centre and to be processed transparently in line with EU law. The attending physician would always be present in such conversations/interviews between patients and external experts to ensure transparency of the advice and therapeutic options. Contracts between the ecosystem healthcare institutions could include a section highlighting the fact that liability remained with the treating health centre.
Policy option 5: EU organisation for rare disease data ecosystems

A central EU body for multi-country rare disease data ecosystems could function as an add-on to the four policy options above. The body’s main tasks would be to develop and supervise the infrastructure and standards to implement rare disease data ecosystems. This would mean:

- developing regulations and guidelines for establishing the rare disease ecosystems;
- building, facilitating and offering rare disease expertise by establishing the necessary infrastructure, including technical, legal, and inter-centre contracts;
- establishing a central health data governing structure within the EHDS with clear and transparent standards for data encryption, upload, storage, access and deletion.
- establishing a governance board similar (or identical) to the current Board of Member States (BoMS) to supervise the rare disease ecosystems. The BoMS could clarify and assist in necessary adjustments of national legal regulations to allow participation in multi-country rare disease ecosystems;
- establishing standards for the cross-country consent process, similar to – though more detailed than – the current ERN system. This should clarify the purpose of the data sharing and the actors involved within the rare disease ecosystem.

Policy option 6: Funding opportunities for rare disease data ecosystems

The policy options presented above represent a novel EU healthcare collaboration model that calls for joint action between the European Commission and Member States to provide the resources and funding needed to support the following five main areas.

- Legal descriptions and EU standards for inter-centre contracts, consent procedures and clarification of ownership of machine translation of medical data
- Standards for data capture, data hosting, data security and data access
- Organisational standards for multi-country rare disease healthcare ecosystems
- Building, sustaining, and governing of multi-country rare disease healthcare ecosystems
- Support for the day-to-day coordination activities and monitoring of patient outcomes within a rare disease ecosystem.

The actual EU and Member State costs associated with options 1 to 4 are not addressed in this report, but there is a need to provide EU funding opportunities for childhood cancer and other rare disease healthcare centres, to pilot and evaluate multi-country rare disease healthcare ecosystems. Importantly, the building of multi-country rare disease ecosystems may not only reduce health inequalities, including childhood cancer survival rates, within and across Member States, but may actually save both lives and costs by improving the quality of healthcare and reducing the risk of treatment failures, e.g. for childhood cancer, where treatment of relapses is far more costly than first-line therapy.
This document is based on the STOA study 'Addressing challenges to multi-country collaboration models for rare diseases'. The study was written by M.D. DMSci Kjeld Schmiegelow, University of Copenhagen, Denmark, as principal investigator of the study; Professor Dr. Uir. Dr. Rer. Med. Karsten Fehn, Fehn Legal, Düsseldorf, Germany; Lawyer Daniel Westman, Company Daniel Westman, Stockholm, Sweden; Associate Professor PhD M. Anthrop. Ignasi Clemente Pesudo, Barcelona, Spain; Parents' representative Dana Atanasovska, Zagreb, Croatia; and Cand. Soc. Naja Vucina Pedersen (coordinating study administrator) at the request of the Panel for the Future of Science and Technology (STOA), and managed by the Scientific Foresight Unit, within the Directorate General for Parliamentary Research Services (EPRS), European Parliament. STOA administrator responsible: Luisa Antunes, Scientific Foresight Unit (STOA).

DISCLAIMER AND COPYRIGHT

This document is prepared for, and addressed to, the Members and staff of the European Parliament as background material to assist them in their parliamentary work. The content of the document is the sole responsibility of its author(s) and any opinions expressed herein should not be taken to represent an official position of the Parliament.

Reproduction and translation for non-commercial purposes are authorised, provided the source is acknowledged and the European Parliament is given prior notice and sent a copy.

© European Union, 2024.

stoa@ep.europa.eu (contact)
http://www.europarl.europa.eu/stoa/ (STOA website)
www.europarl.europa.eu/thinktank (internet)
http://epthinktank.eu (blog)