Pan-European Disease-Specific Investigation Networks Workshop Report.

On October 1, ECRIN and a selection of its national partners hosted a workshop dedicated to the development of Pan-European Disease-Specific Investigation Networks, which took place in Brussels.

There has recently been a clear call for more multinational clinical trials in Europe, a fact highlighted in both the Draghi and Letta reports. To address this issue, Europe's Life Science Strategy 2030 includes the preparation of a Clinical Research Investment Plan which aims to facilitate the funding mechanisms for multinational trials, boost the conduct of multinational clinical trials and to strengthen infrastructures in the field of clinical research. The workshop aimed to discuss the features and utility of Europe-wide disease-specific investigation networks that would serve to increase patient recruitment and investigation for both investigator-initiated and industry-sponsored trials, and act as a complementary mechanism to the existing disease-agnostic research infrastructures such as ECRIN, where the central node provides generic multinational trial management services to the study sponsor through the coordination of local / national CTUs. In addition, investigation networks would provide disease intelligence; facilitate recruitment and investigation; and foster patient and public involvement.

To better understand the current situation, examples of national disease-specific investigation networks, including FCRIN4MS (FR), ANEST-ICU & PALLCARE (CZ), ICC CTN (IE), Strokelink (FR), were presented with a focus on the network objectives, structure, scientific output and economic model, along with their existing efforts to go beyond borders. The national coordination of investigator networks from France, Ireland, Czechia and Australia[1] also described the fundamental organisational and strategic blocks that shape the national structuring activities. In the afternoon, two round tables with representatives from networks, the European Commission,

[1] Australian Clinical Trial Alliance (ACTA), https://clinicaltrialsalliance.org.au

funders, industry, and HTAs discussed the characteristics, selection, funding and governance for future pan-European investigation networks.

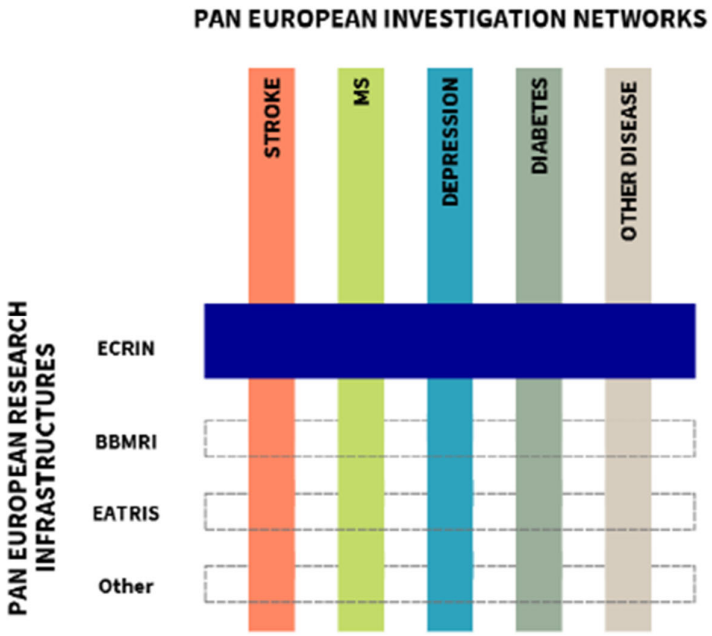
To avoid duplication and fragmentation, a model that would fit within a matrix of current research infrastructures (Figure 1), and the disease networks was discussed. Three potential versions – which are not mutually exclusive - were proposed at the start of the day for the creation of Pan-European disease-specific investigation networks:

1. Build new disease-specific networks from scratch

2. Take advantage of existing national disease-specific networks and expand across Europe

3. Unite existing national disease-specific networks working on the same disease across Europe.

Fig 1: Complementarity and coordination of disease-specific pan-European investigation networks and disease-agnostic pan-European research infrastructures



Throughout the course of the day, the different models, their strengths and their weaknesses were discussed. What was made clear through the discussions is that, where at the national level there is homogeneity in the investigator network structure, at the European level there is greater heterogeneity, lack of connection, collaboration and limited awareness. It was also highlighted by those who have worked at the

European level that the cross-border experience is beneficial to the national investigator networks. It enables them to grow their knowledge base with complementary focuses, allowing for better coverage and greater impact for the patients.

Disease-specific networks characteristics

During the discussions of the workshop, participants highlighted three characteristics as key elements to include in, or link directly to, investigational disease-specific networks: medical intelligence, patient involvement, and clinical trial readiness and performance.

1. The first characteristic of these networks is their **disease expertise** (when relevant, working in close collaboration with scientific societies and patient associations). The disease intelligence within the network enables prioritisation of the **research questions** and the capacity to contribute to the protocol design and selection of outcomes.

2. The networks must be built around patient needs with patient and public involvement. Moreover, the research questions from the disease experts **must benefit patients**, improve the level of care and the equity in accessing it, improve quality of life and reduce morbidity, and ease their access to the studies. Trial services should focus on **patient-facing activities (recruitment and investigation**) for either industry-sponsored or investigator-initiated trials.

3. Trial readiness/competence depends on networks being developed **by and with motivated individuals**, with a strong emphasis on collaboration and trust. **A coordinating node** could help organise and streamline trial support and services, while promoting shared standards and methods, monitoring performance, and centralising access. Investigation sites should be selected according to objective quality and performance criteria. Networks should therefore be flexible and able to connect to any sponsor, CTU or CRO. High-quality, **disease-specific, patient-facing trial services** provided by the investigation network must be complementary to trial management services provided by CROs or CTUs. To prevent duplication and fragmentation, strong coordination should be established to distribute roles and responsibilities between disease-agnostic trial management service providers and disease-specific investigation networks.

Building sustainable networks with measured impact

Beyond the need for core criteria to develop the disease-specific networks, the point of sustainability and visible impact of investigational networks was considered.

• Project management experience is essential to build successful disease-specific networks, and full-time dedicated staff to support each disease-specific network's activities is an essential component for success.

• Investigation networks could be seen as a cost-effective investment, as presented by the Australian Clinical Trial Alliance (ACTA), it is important to be able to show their return on investment at the EU level. Such measurement requires establishing a baseline when fledgling investigational networks are initially funded and then tracking growth with, where possible, not only an evaluation at the end of their initial funding period but also continued monitoring with indicators for improving pre-identified weaknesses. Impartial, independent experts must carry out this evaluation, which could be accompanied by an ROI analysis[2] by health economists to assess the health innovation value/socio-economic impact. The need to develop metrics to evidence competitiveness was also mentioned as important. Sustainability means a transition to a valid and self-sufficient business model for the networks. It was mentioned that sustainability is not something the investigation networks should consider at the end of their initial funding period; it should rather be considered and built into their initial request for funding, which should contain appropriate KPIs and impact metrics.

There will not be a one-size-fits-all solution.

The objectives that are set out for the pan-European disease-specific investigation networks will, to a certain extent, dictate some elements of the direction, but flexibility can be built into the structure in order to enable the different needs to be met.

• Disease selection can be both bottom-up (based on rather open-ended calls) and top-down (from the HTAs and public health needs, or patient expectations).

• There should be different service offerings for commercial sponsors (including site readiness) and non-commercial sponsors (including work with the larger community and sites that also have a more representative population).

The model proposed by ECRIN

Many of the core elements of the model are described above. There was consensus among participants that a matrix approach could fit quite well with the needs of disease-specific investigator networks and could be either the expansion of a strong existing national network or the coming together of existing similarly oriented networks. The disease-specific investigator network would focus on the research

[2] See https://clinicaltrialsalliance.org.au/wp-content/uploads/2021/11/Assessing-the-impact-of-clinical-trials-V2.pdf

question, the patient recruitment and the investigation, while a centralised coordination node could take on many of the cross-cutting activities including communications, training, quality management, and sharing best practices. The coordination node for the investigational networks could map site capacities and expertise. ECRIN could play the role of the coordinating node, offering the cross-cutting services alongside its clinical study coordination to academics and SMEs as per its mandate, but industry could also work directly, or through CROs, with investigation networks. Strong coordination and governance mechanisms should therefore be proposed to ensure full complementarity between the disease-agnostic and disease-specific investigation networks.

There was little interest in starting from scratch but quite a lot in seeing how existing networks could be sustained at the national level and united under a Pan-European, or even global, investigational network.

The model also needs to anticipate the current changing landscape of clinical studies and ensure that the investigational networks will fit in well beyond the short term. This type of element could be considered a cross-cutting question to be taken on by coordination with the input of the different investigation networks.

Most importantly, the model to be developed must require minimal resources; if seed funding can be provided, the disease-specific networks should also look for complementary funding, whether from their institutions (universities/hospitals), or charities, industry, etc. Moreover, by centralising disease-agnostic activities that need not be duplicated across the investigational networks, cost savings will be built into the model, while also avoiding fragmentation of tools and standards across disease areas and medical disciplines.