ECRIN’s and the SCTO’s roles as COVID-19 fosters innovation and catalyses cooperation amongst European clinical research actors

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Uncoordinated and fragmented research activities were the scientific community’s early reactions to the COVID-19 pandemic, with researchers planning and running many small stand?alone trials or observational studies of single?agent uses. In this article, we discuss actions that were taken by the European Clinical Research Infrastructure Network (ECRIN) and its national partner the Swiss Clinical Trial Organisation (SCTO) to address the issue of uncoordinated clinical research.

A lack of clinical research coordination in the race for COVID-19 solutions

One of the key instruments for addressing the COVID-19 outbreak is clinical research. At present, this includes clinical trials on drug repurposing and vaccines; in the future, it will focus on trials evaluating innovative treatments with novel designs. The clinical research community has shown tremendous activity over the past year and has initiated many repurposing trials supported by national and international funds.[1] It turns out that similar trials, addressing the same questions, are frequently run in parallel in multiple countries. This wastes time and resources that would be better used in well-designed multinational trials, and it raises ethical questions in respect of patients volunteering to participate. It turns out that similar trials, addressing the same questions, are frequently run in parallel in multiple countries. This wastes time and resources that would be better used in well-designed multinational trials, and it raises ethical questions in respect of patients volunteering to participate.

Understandably, better coordination at the international level helps to avoid the fragmentation of clinical research capacity and leads to faster and more robust results. The world has reacted to the COVID-19 pandemic with calls for funding to accelerate research,[2] initiatives for coalitions for preparedness, the pursuit of cooperation across continents,[3] and – let us not forget – efforts to fast-track trial authorisation and publication as well as increase the transparency of research results.

ECRIN’s COVID-19 task force

In March 2020, ECRIN established a COVID-19 task force with its national partners to ensure the

preparedness of clinical trial units (CTUs) for COVID-19 trials and to combine and coordinate national initiatives to promote multinational rather than national trials. The task force continues to meet regularly and relies on actions carried out by members of ECRIN's national networks. Its efforts include networking with national funders, sponsors-investigators, and CTUs.

In addition, ECRIN launched the Clinical Research Metadata Repository to enable quick access to COVID-19 clinical research information and related data objects.[4] ECRIN's COVID-19 task force continues to update clinical trials literature reviews, COVID-19 funding calls, and databases on regulatory and ethical requirements, data protection, and fast-track approvals across Europe. Further outreach includes participating in the EU COVID-19 data hub operated by the European Molecular Biology Laboratory's European Bioinformatics Institute (EMBL-EBI) and assisting with the development of a COVID-19 clinical trial patient-level data-sharing platform (the European Open Science Cloud's EOSC-Life) that is compliant with the EU's General Data Protection Regulation (GDPR).

In the first half of 2020, hundreds of clinical trials were being conducted across Europe at the national level to test potential treatments of SARS-CoV-2; however, there was a marked absence of multinational clinical trials – except for the World Health Organization's (WHO's) Solidarity trial. ECRIN contacted the European Commission and promoted the idea of developing multinational, multi-arm platform trials to rapidly recruit patients and test multiple treatment options (see Box 1). This led to the EU-RESPONSE project, which is funded by the European Union and coordinated by the French National Institute for Health and Medical Research (INSERM).

EU-RESPONSE project

In April 2020, the European Commission committed to developing instruments to help European countries and clinical researchers join forces, in particular by setting up a pan-European network for COVID-19 clinical trials to foster collaboration and coordination. In partnership with academic clinical research institutions across Europe, EU-RESPONSE (EUropean RESearch and Preparedness netwOrk for pandemics and emerging iNfectious diseaSEs) was approved for funding in July 2020 with funds from the European Commission's Horizon 2020 programme. The central activity in this network is the promotion of COVID-19 trial platforms in Europe that cover the various steps of disease progression. There is a growing consensus that multi-arm, multinational, adaptive platform trials[5] represent the most appropriate solution to test multiple interventions for a given medical condition and for disease outbreaks.[6]

EU-RESPONSE allows for the European expansion of ongoing studies, for example the DisCoVeRy and Solidarity trials, and the further expansion to many other European countries. Additionally, EU-RESPONSE allows a new multinational European adaptive platform trial to be built. This will be a flexible platform, providing a modular trial network that will enable most, if not all, European hospitals to participate at their preferred level of commitment. Hospitals will be able to run repurposing trials, assess combination strategies, and evaluate the efficacy and safety of new compounds on COVID-19.

The EU-RESPONSE project also includes a coordination module, led by ECRIN, with other EU-funded projects such as RECOVER and REMAP-CAP. This ensures complementarity and cooperation across all large European COVID-19 trials and improves their capacity to answer the needs of society through dialogue with the European Medicines Agency (EMA), national competent authorities, health technology assessment (HTA) networks, and industry partners. ECRIN will play a key role in reaching the objectives of the EU-RESPONSE project, and EU-RESPONSE complements the other tools available at ECRIN to help clinical researchers and national infrastructures in the battle against COVID-19.

The SCTO's contributions to research activities related to COVID-19

The EU-RESPONSE consortium brings together 21 partners from 13 EU countries, Norway, Switzerland, and Turkey. The SCTO is the project partner for Switzerland with observer status in ECRIN and plays a role in the realisation of the project's key objectives. The SCTO contributes to the project with expertise from its CTU network and with advice on trial design and protocol development, with statistical expertise, and with site support for the conduct of clinical trials. With its expertise in coordinating the WHO's Solidarity trial at 17 clinical sites in Switzerland, the SCTO's CTU network is in an excellent position. Moreover, the network is well-prepared to efficiently contribute to EU-RESPONSE and assure a smooth transition from current trials to upcoming EU-RESPONSE trials.

In addition to its participation in the EU-RESPONSE project, the SCTO's CTU network is actively supporting research activities related to the COVID-19 outbreak at CTU institutions. All CTUs in the network are either implementing changes for studies that are already underway, participating in COVID-19 tenders, or starting or supporting the performance of such studies.

BOX 1: WHAT ARE PLATFORM TRIALS?

Platform trials are a new type of clinical trial in which multiple interventions can be evaluated simultaneously against a common control group within a single master protocol. Platform trials are an extension of adaptive, multi-arm, multistage trial designs that allow for the evaluation of multiple interventions using interim evaluations and the addition of new interventions during a trial. Platform trials offer the flexibility of dropping ineffective arms early based on interim data and allow for the possibility of introducing new arms into a trial.

Based on a master protocol and subsequent amendments that open or close sub-protocols, platform trials allow continuous recruitment, randomisation, and the investigation of patients. Repurposed drugs, as well as new treatments or vaccines, can be tested without wasting time for trial approval and setup because just an amendment is needed. A common control arm lowers the number of patients who need to be recruited.

1. Janiaud P et al. (2020) The worldwide clinical trial research response to the COVID-19 pandemic – the first 100 days [version 2; peer review: 2 approved] F1000Research 9:1193. doi.org/10.12688/f1000research.26707.2
2. See the EMA's press release from 19 March 2020 calling for pooling research resources.
3. See the EMA's press release from 15 May 2020 on the need for international coordination to encourage large, relevant COVID-19 clinical trials.
4. The Clinical Research Metadata Repository provides information on many other disease areas as well.
5. Woodcock J and LaVange LM (2017) Master protocols to study multiple therapies, multiple diseases, or both. New England Journal of Medicine 377:62-70
6. Dean NE et al. (2020) Creating a framework for conducting randomized clinical trials during disease outbreaks. New England Journal of Medicine 382:14