COVID-19 Pandemic Readiness:
Let's not reinvent the wheel – European Medical Research Infrastructures are part of the global response

The European Commission led a highly successful[1] round of funding for diagnostics, treatments and vaccines against coronavirus. These resources must be used in the most efficient way possible. The best way is via cross-border, multi-sector and multi-disciplinary research collaboration based on existing networks, to reach a scale of partnerships and coordination that has yet to be achieved during the COVID-19 crisis. Medical Research Infrastructures, EATRIS-ERIC, ECRIN-ERIC and BBMRI-ERIC are international organisations whose purpose is to facilitate and manage such international research collaborations.

Five practical steps to accelerate COVID-19 research

Governments world-wide are walking a tightrope by seeking to limit economic damage with minimum risk to public health and healthcare systems. Research can and should properly inform policymakers and provide both guidance and practical support. The European Commission, national governments and international organisations have the opportunity to take practical steps to guarantee that the resources put together via the Coronavirus Global Response will be used in the most efficient way to achieve its goals as well as to build resilience and improve our readiness to future outbreaks.

<u>Recommendation 1:</u> Avoid small, underpowered studies that will not generate robust, actionable information

As of May 7th, 2020, there are 3,474 clinical studies of COVID-19 underway or completed in the last three months, of which 1,589 are to study treatment-management.[2] While the rapid response to the crisis is heartening, this proliferation of trials raises questions about the risk of

[1] https://ec.europa.eu/commission/presscorner/detail/en/ip_20_797
[2] https://covid-19.cochrane.org/?q=d(2020-02-07:)&pn=1

redundant, underpowered trials, and methodological weaknesses.[3] As a consequence, we risk not only wasting precious time and resources on studies that do not generate usable results, but also generating and publishing unreliable results, with more funds then wasted on follow-on research, with little to no substantial patient benefit. The combination of small-scale clinical studies with harmonised agreement of inclusion, testing and reporting, across institutes and even countries, would solve this underpowering.

Recommendation 2: Fund larger-scale, multi-national and multi-site research

In order to overcome the above-described risk and generate reliable knowledge about the complex behaviour of the human immune response to SARS-CoV-2, both laboratory and clinical research must be designed to enable large numbers of individuals (or preclinical models or biological samples) to be studied under the same conditions. Commonly accepted and agreed biomarkers for multicentre studies are critical. This cannot be undertaken within one hospital or university – in fact, it is unlikely to be possible within a single country in a reasonable timeframe, due to dwindling patient numbers in this phase of the outbreak. In Europe, the only solution is a multi-national research effort, requiring considerable coordination and comprehensive quality management.

Recommendation 3: Ensure that researchers exchange information, protocols, guidelines and reference materials

If smaller studies are designed in isolation, it is very likely that the information generated will not be interoperable with the results of other, similar studies conducted in other regions or institutes. When this happens, the research ends up being duplicative, potentially with little new knowledge being generated compared to those other studies. However, if researchers are encouraged – for instance by making it a criteria for funding – to share their study protocols publicly before execution, adopt standards where these are available, and exchange high-quality biomaterials

[3] Beyond weaknesses in the design or statistical power in some studies, the majority of repurposing trials are conducted as 'open-label', without drug blinding, and some compare injectables with tablets without using double placebo. Many adopt a light trial monitoring plan which may not be compatible with a marketing authorization dossier, or an extension of the indication.

and protocols with other institutions studying similar research questions, then we can increase the likelihood that the information generated can be combined to create more robust results. This approach can increase the knowledge yield for each Euro spent on research.

<u>Recommendation 4:</u> Ensure that studies to be funded have a comprehensive quality management programme

For study results to be robust and reliable, attention must be paid to minimise variability and increase reproducibility. Such sources of error arise in all phases of the research process, including design, execution (e.g. laboratory protocols, use of validated reagents and use of reference materials), and data analysis and reporting.[4] When conducting multi-site studies, the need for centrally coordinated, professional quality assurance is even greater.

<u>Recommendation 5:</u> Utilise professional international organisations to facilitate and manage cross-border research collaborations

Beyond excellent and robust science, cross-border research collaborations require professional guidance and operational management. Navigating the legal landscape, ensuring regulatory compliance, assuring patients and authorities of adequate privacy, ethics and confidentiality, facilitating effective public-private cooperation, and managing cross-national quality frameworks require dedicated and professional capacity. Single institutions acting as study coordinators do not have the capacity and expertise to roll out a multi-national study; however, through the ESFRI medical research infrastructures[5] - EATRIS-ERIC, ECRIN-ERIC and BBMRI-ERIC – there are international organisations available whose purpose is to facilitate and manage such international research collaborations. They provide access to multi-national research facilities and resources, operating under harmonised conditions and highest quality standards, supported by central coordination offices that are composed of experts covering all the areas mentioned above.

[4] Freedman LP, Cockburn IM, Simcoe TS (2015) The Economics of Reproducibility in Preclinical Research. PLoS Biol 13(6): e1002165. https://doi.org/10.1371/journal.pbio.1002165
[5] https://eatris.eu/insights/bbmri-ecrin-and-eatris-join-forces-to-offer-covid-19-fast-response-service/

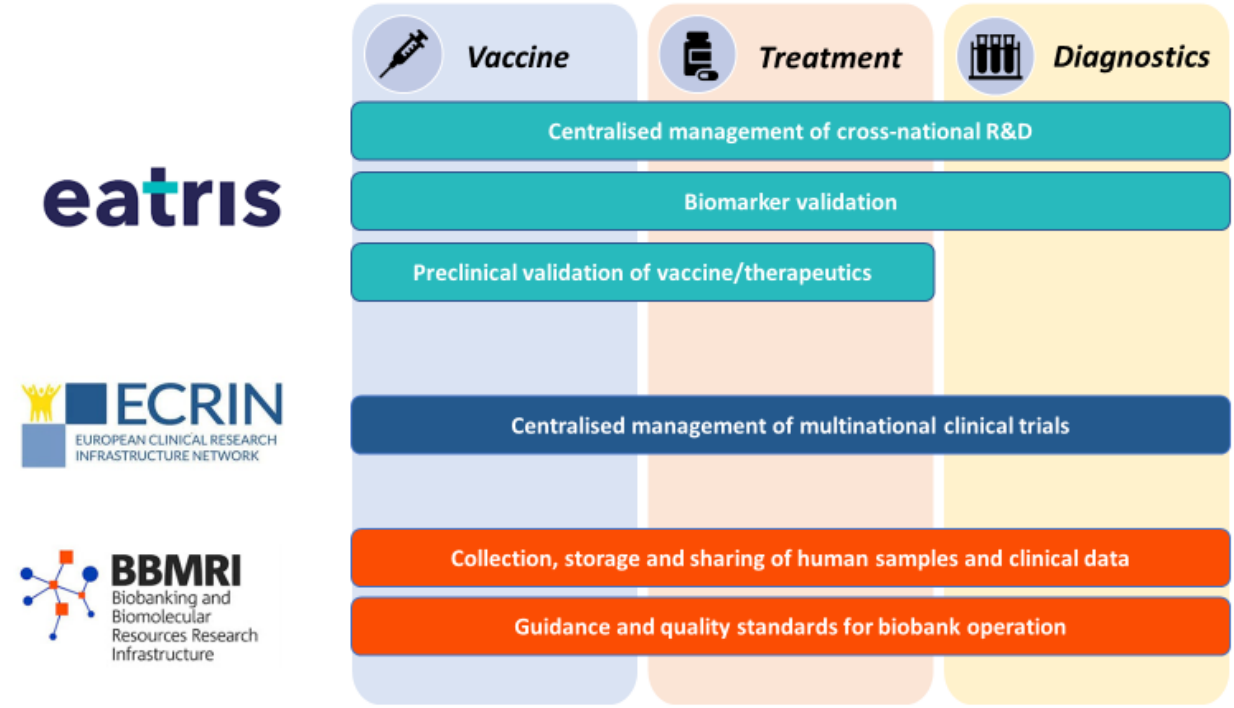

Figure 1: Overview of the Medical Research Infrastructures' assets to support COVID-19 research

Conclusion

As strong supporters of a European research culture of quality standards and reproducibility, we stress the need for the development of cross-border policies that specifically focus on facilitating highly coordinated, standardised research that is underpinned by a strong quality framework. Such an approach is essential to develop robust findings and translate these rapidly into preventive and therapy interventions. **This is why we call for a high level of coordination of the research to be conducted, encouraging the best use of Medical Research Infrastructures such as EATRIS-ERIC, ECRIN-ERIC and BBMRI-ERIC in forthcoming national, European and global calls and action plans.** In doing so, we have the opportunity for an improved management of the transnational clinical challenges of the SARS-CoV-2 infection, as well as future pandemics, and subsequently develop effective therapeutic interventions and preventive vaccines.

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ABOUT US

BBMRI (Biobanking and BioMolecular resources Research Infrastructure)

BBMRI-ERIC is a European Research Infrastructure for biobanking that brings together all the main players from the biobanking field (researchers, biobankers, industry, and patient advocacy) to boost biomedical research. BBMRI offers quality management services, support with ethical, legal and societal issues, and a number of online tools and software solutions for biobankers and researchers. Ultimately, the goal of BBMRI is to make new treatments possible.

Hosting one of the world's largest catalogues of human samples (such as blood, tissues, cells or DNA) and associated clinical and research data, BBMRI-ERIC connects more than 600 biobanks from 20 EU countries and 1 international organization. Its mission is to facilitate research on human samples for personalised medicine, while keeping the highest scientific standards and, most importantly, preserving patients and citizens' privacy. BBMRI-ERIC provides services to academia and industry to develop better treatments, test diagnostic tools and advance biomedical research. BBMRI-ERIC is composed of 21 national nodes that support biobanking at the local level, and a European headquarter based in Graz, Austria. http://www.bbmri-eric.eu – contact: francesco.florindi@bbmri-eric.eu

EATRIS (European Research Infrastructure for Translational Medicine)

EATRIS aims to accelerate the translation of promising discoveries into patient benefit. EATRIS helps academia and industry decrease risk to their drug, vaccine or diagnostic development programme and increase their potential to reach patients. EATRIS provides fast, tailored access to cutting-edge enabling technologies and expertise in translational research, focusing on preclinical and early clinical development of drugs, vaccines and diagnostics. Via our central hub in Amsterdam, users can access the vast array of clinical expertise and high-end facilities that are available within 105 top-tier academic centres across 13 countries in Europe. Solutions are provided in the fields of advanced therapy medicinal products, biomarkers, imaging and tracing, small molecules and vaccines. https://eatris.eu/ - contact: annecharlottefauvel@eatris.eu

ECRIN (European Clinical Research Infrastructure Network)

ECRIN is a not-for-profit intergovernmental organisation that supports the planning, set-up and management conduct of multinational clinical trials in Europe. As of 2013, ECRIN has the legal status of a European Research Infrastructure Consortium (ERIC). ECRIN provides a means to access patients and medical expertise throughout Europe and overcome the above challenges by offering researchers support to prepare and implement multinational trials. Support areas include advice, preparation of applications for funding, protocol evaluation, trial management, quality assurance and more. ECRIN offers investigators the tools they need to address regulatory and ethical issues, to measure outcomes and to assess risk. These tools are critical for project success, especially when operating in a multi-country context where local legislation and requirements can vary greatly. ECRIN provides consultancy and management services to more than 30 40 multinational trials, with an average of seven countries per trial. http://www.ecrin.org – contact: christine.kubiak@ecrin.org