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COVID-19 Network: the response of an Italian Reference Institute to research challenges about a new pandemia

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To the Editor,

on February 21st, 2020, the first case of SARS-CoV-2 transmission within the Italian borders, with no apparent link with imported cases, was reported (1). The number of confirmed infections has therefore multiplied, and Italy is currently the second European country by number of recorded cases, with Lombardy, the most affected region (2). The regional health service has been reorganized, and COVID-19 units have rapidly been developed in most regional hospitals (3). COVID-19 outbreak also represents a significant challenge for the organization of translational research activity in a coordinated and multi-disciplinary approach.

Founded in the XV century, the Ospedale Maggiore Policlinico in Milan, Italy, is one of the leading Italian hospital in clinical and research activities with 900 beds and 36,000 hospitalization per year. Notably, it hosts units for clinical follow up and translational research in pulmonary, haematological, infectious diseases, as well as a national reference centre for Extracorporeal membrane Oxygenation (ECMO). From 21st February 2020, to cope with the COVID-19 emergency, the organization of the Hospital has been quickly modified and four different pavilions have been entirely dedicated to the management of COVID-19 patients to accommodate 350 patients of which 50 in ICUs.

In the ongoing COVID-19 pandemic, the central research governance of the Ospedale Maggiore Policlinico has faced several challenges arising from: (i) the emergence of many study proposals from different research groups, on the same patients; (ii) the need to coordinate ethical questions in the absence of standardized procedures and approved treatments; (iii) the need to collect biospecimens of interest for basic science and translational research projects; (iv) the need to divert staff from their normal research routines to COVID-19 focused projects, consistent with public health goals.

Thus, our first action was to rapidly establish a COVID19 Research Steering Committee with the aims to guide Institutional research activities.
Subsequently, an Institutional Coronavirus Registry ("COVID-19 Network"), was established to answer present and future research questions regarding the epidemiology and clinical presentation/evolution of this disease (4) and set up a biobank of biological samples for translational studies (EC approval nr. 241_2020, 17th March 2020). Funding for the bio-banking activity was provided by Scientific Direction to the POLI-MI biobank, the Hospital central facility for collection, conservation and assignment of biological material.

Aims of the registry are to: a) describe the epidemiological and clinical characteristics of patients admitted to the COVID-19 units; b) describe diagnostic and therapeutic interventions; c) evaluate the short- and long-term clinical outcomes and prognostic factors; d) allow subgroup analyses of specific patients’ groups. Moreover, biological samples (plasma, PBMCs and stool) are collected at time of diagnosis and at several timepoints and stored for future investigations.

The registry includes all consecutive adults (aged 18 years or older) with a positive RT-PCR for SARS-CoV-2 at the time of admission to the Policlinico Hospital, with more than 800 patients expected to be enrolled.

The response of our Hospital to COVID-19 outbreak was fast and well-structured in order to guide Institutional research activity on COVID19 in an integrated and multi-disciplinary basis. To this end, beyond the medical staff, 15 data managers, 1 biostatistician and 1 ethics were involved in this activity. So far, 103 studies in several patients’ groups are in different stages of development, among these 58 are observational, 19 non-pharmacological interventional and 6 pharmacological interventional studies. The Ethical Committee meets on a daily basis to rapidly assess the scientific and ethical value of studies. Moreover, we have opened the Registry to several Regional and National centers to allow collection of data also for centers with limited research resources, and to create a Network of different hospital units. To date, more than 984 patients overall have been enrolled (641 observed at the coordinating centre, Policlinico Hospital), and more than 1000 biological samples have been stored. Moreover, researchers from this study group already produced 112 papers on COVID-19 (currently in press or already published).
The COVID-19 network will also provide a platform for future national and international multicenter studies and investigator-initiated satellite projects: we are planning not only epidemiological studies, but also precision medicine studies with a multidisciplinary approach, including immunology, virology, and omics approaches. To the best of our knowledge, only 3 others multi-centric registries are currently ongoing at a National level, focused on neonates, children and intensive-care units.

Evaluating our experience as Reference Hospital facing COVID-19 epidemic, we think that the tools that have facilitated research activities have been: (i) strong leadership in different disciplines which proved fundamental in the management of COVID-19 patients; (ii) IT resources, such as RedCap, i2b2, tele-conferencing systems; (iii) coordination between different research units; (iv) involvement of data manager and technical personnel dedicated to data collection, sample collection, processing and storage; v) collaboration with others Research Institutes and clinical centers; vi) strong motivation and altruism of both clinical, research and support staff.

On the other hand, administrative issues linked to documents generation and approval often acted as barriers. Furthermore, limited data available in clinical electronic records required large human resources (data managers) to input high-granularity data. Finally, conducting interventional pharmacological studies proved difficult, owing to the limited preclinical and clinical data on many proposed drugs, and to centralization at national level of drug trials.

To fully exploit the potential of our registry, data sharing will be crucial: consistently with similar initiatives at the national and international level, our data will be available for projects proposed by basic and clinical research groups worldwide.
1 Transparency declaration

COMPETING INTERESTS: The authors have no competing interests to disclose.

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3 References


