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Letter to the Editor

## Response of an Italian reference institute to research challenges regarding a new pandemic: COVID-19 network

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On 12 February 2020, the first case was reported of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) transmission within Italy's borders with no apparent link to imported cases [1]. The number of confirmed infections has therefore multiplied, and Italy currently has the second highest number of recorded cases in a European country, with Lombardy the most affected region [2]. The regional health service has been reorganized, and coronavirus disease 2019 (COVID-19) units have rapidly been developed in most regional hospitals [3]. The COVID-19 outbreak represents a significant challenge for organizing translational research activity using a coordinated and multidisciplinary approach.

Founded in the 14th 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, haematologic and infectious diseases, as well as a national reference centre for extracorporeal membrane oxygenation. From 21 February 2020, to cope with the COVID-19 emergency, the hospital's organization was quickly modified,

with the installation of four different pavilions entirely dedicated to the management of COVID-19 patients to accommodate 350 patients, of which 50 are in intensive care units.

In the ongoing COVID-19 pandemic, the central research governance of the Ospedale Maggiore Policlinico has faced several challenges arising from: (a) the emergence of many study proposals from different research groups on the same patients; (b) the need to coordinate ethical questions in the absence of standardized procedures and approved treatments; (c) the need to collect bio-specimens of interest for basic science and translational research projects; and (d) 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 COVID-19 research steering committee with the aim of guiding institutional research activities.

Subsequently, an institutional coronavirus registry known as the COVID-19 Network was established to answer present and future research questions regarding the epidemiology and clinical presentation/evolution of this disease [4] and to set up a biobank of biological samples for translational studies (EC approval 241\_2020, 17 March 2020). Funding for the biobanking activity was provided by scientific direction to the POLI-MI biobank, the hospital central facility for collection, conservation and assignment of biological material.

The aims of the registry are to: (a) describe the epidemiologic 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; and (d) allow subgroup analyses of specific patients' groups. Moreover, biological samples (plasma, peripheral blood mononuclear cells and stool) are collected at the time of diagnosis and at several time points, and stored for future investigations.

The registry includes all consecutive adults (aged 18 years or older) with a positive RT-PCR result 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 COVID-19 on an integrated and multidisciplinary basis. To this end, beyond the medical staff, 15 data managers, one biostatistician and one ethicist were involved in this activity. So far, 103 studies in several patient groups are in different stages of development; among these, 58 are observational, 19 non-pharmacologic interventional and 6 pharmacologic interventional studies. The ethics committee meets daily to assess the scientific and ethical value of the studies. Moreover, we have opened the registry to several regional and national centres to allow collection of data for centres 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, Ospedale Maggiore Policlinico), and more than 1000 biological samples have been stored. Moreover, researchers from this study group have produced 112 research articles on COVID-19 (currently in press or already published).

The COVID-19 Network will also provide a platform for future national and international multicentre studies and investigator-initiated satellite projects. We plan not only epidemiologic studies but also precision medicine studies with a multidisciplinary approach, including immunology, virology and omics approaches. To our knowledge, only three other multicentre registries are currently ongoing at a national level, focused on neonates, children and intensive care units.

On the one hand, in evaluating our experience as a reference hospital facing the COVID-19 epidemic, we think that the tools that have facilitated research activities have been: (1) strong leadership in different disciplines, which proved fundamental in the management of COVID-19 patients; (b) IT resources, such as RedCap, i2b2 and teleconferencing systems; (3) coordination between different research units; (4) involvement of data managers and technical personnel dedicated to data collection, sample collection, processing and storage; (5) collaboration with other research institutes and clinical centres; and (6) strong motivation and altruism of clinical, research and support staff.

On the other hand, administrative issues linked to document generation and approval often acted as barriers. Furthermore, the limited data available in the clinical electronic records required a lot of human labor (data managers) to input highly granular data. Finally, conducting interventional pharmacologic studies proved difficult because of the limited preclinical and clinical data on many proposed drugs and because of the national-level centralization of drug trials.

To fully exploit the potential of our registry, data sharing will be crucial. Like similar initiatives at the national and international levels, our data will be available for projects proposed by basic and clinical research groups worldwide.

### Transparency declaration

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