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The value of open-source clinical science in pandemic response: lessons from ISARIC



The International Severe Acute Respiratory and Emerging Infection Consortium (ISARIC) is a global federation of clinical research networks that work collaboratively to prevent illness and deaths from infectious disease outbreaks. In 2014, we proposed that effective and timely research during outbreaks of emerging infections would benefit from pre-prepared research tools, global collaboration, and research-ready clinical networks.¹ After applying this research model to several outbreaks, and particularly the COVID-19 pandemic, we can now explore what has been achieved to date.

ISARIC launched the Clinical Characterisation Protocol (CCP), in collaboration with WHO in 2012.¹ A key aim was to avoid delays in initiating research, such as those seen during the 2009–10 influenza A H1N1pdm09 pandemic and other outbreaks.² The CCP and associated case report forms (CRFs) were the first steps towards global, harmonised clinical datasets to create frameworks for characterising current and potential future emerging infectious diseases. These adaptable research tools were developed and shared early in the COVID-19 pandemic by ISARIC³ to prepare the health community for outbreak research.

After receiving approvals from the WHO Ethics Committee in 2013 (RPC571 and RPC572, 25/04/2013), the CCP was implemented in various settings (appendix p 2). This broad uptake of the CCP, and the development

of tools to support its implementation for various diseases and contexts, meant that ISARIC partners were primed for a rapid response when COVID-19 emerged and spread in 2020. Working with WHO, ISARIC used early reports from Wuhan, China, to inform the adaptation of the CRF. On Jan 24, 2020, when less than 1000 COVID-19 cases had been reported globally, the ISARIC-WHO COVID-19 CRF was launched and made available globally.³ ISARIC provided a data management platform, using REDCap, to collect and store data for institutions that lacked available resources or necessary infrastructure. Rapid access to the CRFs enabled collection of critical data for early characterisation of the disease in hospitalised patients, first in Wuhan,⁴ and then globally.^{5–8} Institutions that chose to use the CRF and database simultaneously, collected data for local analyses and also contributed data for aggregated international analyses. As the COVID-19 pandemic progressed and an increasing number of institutions contributed data, the research benefits of a large, aggregated dataset also increased. To disseminate this knowledge, ISARIC and international collaborators issued the first online report analysing risk factors, symptoms, treatments, and outcomes of patients with COVID-19 in March, 2020.⁹

As of July, 2021, 1651 sites in 57 countries have contributed data from 516 689 individuals with COVID-19 (appendix p 1),¹⁰ including 272 759 individuals

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See Online for appendix

For the ISARIC clinical data reports see <https://isaric.org/research/covid-19-clinical-research-resources/evidence-reports/>

from low-income and middle-income countries (as defined by the Organisation for Economic Co-operation and Development). These data have informed a publicly available, regularly updated, clinical data report, with the aim of accelerating a collective understanding of COVID-19 globally. The data series have been published frequently on medrxiv.org, to help inform the development of policies and clinical management guidelines. Through the collaborative platform, analyses are underway for over 20 studies.

This approach has enabled global collaborators to produce highly relevant outputs during a novel pandemic. Research preparedness helped avoid or minimise well known bottlenecks, including protocol development, database set-up, contractual agreements, funding applications, and ethics and regulatory approvals. Additionally, the open-access research tools enabled the standardised collection of high-quality data, for ease of aggregation and harmonisation. Bringing together a global community in a common data platform fosters a sense of solidarity and community, which is valued by collaborators and contributors (appendix p 3).

Coordinating research efforts during an evolving pandemic, across more than 1600 institutions, is a significant undertaking and requires efficient systems to track and acknowledge contributors. Promoting local ownership of data and research strategy requires provision of support to institutions with varying resource levels. The burden of data collection on health-care workers, who are already facing considerable pressures, must be balanced with efficient systems to deliver high-calibre science that will inform and improve patient care. By supporting research groups with tools that are standardised but flexible, ISARIC has delivered an adaptive, observational infrastructure that enables

the generation, collection, analysis, and dissemination of important knowledge during a pandemic. The success of ISARIC highlights the fundamental importance of investment in research preparedness by health-care systems, funders, and government organisations. Our COVID-19 experience has shown that a global collaborative approach, based on research readiness in a peer-to-peer network, is achievable and effective. If this approach can be developed and maintained for future epidemic and pandemic research responses, the benefits should be even greater.

Members of the ISARIC Clinical Characterisation Group and their declaration of interests statements are listed in the appendix (pp 4–9, 11–14).

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Long-term consequences of the misuse of ivermectin data

Ivermectin is an oral anti-infective medicine that is integral to neglected tropical disease programmes. It is safe and effective for the treatment and control of lymphatic filariasis, scabies, and onchocerciasis, sometimes as part of a mass drug administration, as recognised in the WHO road map for neglected tropical diseases 2021–30.¹ The WHO essential medicines list provides recommendations for minimum medicine

needs for a basic health-care system, which includes ivermectin as an anthelmintic, antifilarial, and anti-ectoparasitic treatment.²

There has been a groundswell of opinion across several countries that ivermectin might be useful in reducing the symptoms of and mortality due to COVID-19, with many citing meta-analyses that infer positive effects,³ however, these conclusions appear to be unreliable. On

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For the French translation of the Comment see Online for appendix 1

For the Spanish translation of the Comment see Online for appendix 2