Global outbreak research: harmony not hegemony

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To make clinical and biological observations within a timeframe that is likely to benefit patients during disease outbreaks, coordination of global research must match the speed of spread of novel pathogens. Time is short. Circumstances call for international collaboration to understand, treat, and prevent coronavirus disease 2019 (COVID-19).

During previous infectious disease outbreaks, clinical research has often been established on an ad-hoc basis and done in silos, using different methodologies and designs. This approach limits opportunities to compare results, or to combine smaller studies to obtain answers quickly. Thus, perhaps it is self-evident that harmonisation of clinical investigation during outbreaks is desirable. In a meeting of the WHO clinical management research prioritisation group held in January, 2020, harmonised clinical characterisation research was identified as the first priority for COVID-19.

Harmonisation creates opportunities for individual investigators to compare results or collaborate, without applying burdens or obligations. In our experience, the quality and breadth of research is improved by collaborative development and peer review of shared protocols. For example, in the current outbreak, a clinician might design a study to identify risk factors for progression, co-infections, and mechanisms of critical illness. However, clinicians might overlook the need to obtain serum for research groups with the capability to make new assays for seroepidemiology, or peripheral blood mononuclear cells for monoclonal antibody therapeutics during this process. Wide collaboration leads to better, faster science.

Achieving global coordination is difficult enough at the best of times; during a crisis it might seem impossible. But with each new crisis, the same questions arise again and again, and so, the same designs can be used to tackle them. We believe that global harmonisation is possible, at least in the intermittently indispensable field of outbreak research. To achieve such a goal, harmonised investigation needs to be made easier than establishing isolated independent studies, must respect autonomy and sovereignty of investigators, and relinquish normal routes of academic recognition for this work.

To this end, in 2012, a single, standardised generic research protocol was created for clinical characterisation of any emerging infection (the International Severe Acute Respiratory and Emerging Infection Consortium [ISARIC]/WHO Clinical Characterisation Protocol [CCP]), which was the result of many years of international and cross-speciality consensus-building.[1] Since the fundamental research questions in a new outbreak are predictable, the protocol can be established and approved in so-called peacetime, maintained in a hibernating state, then rapidly implemented when required. Carefully designed, flexible biological sampling schedules are included in tiers according to local resources, modular additional studies for specific situations, and scalable case report forms.[1] These tools were released under an open-source licence—ie, anyone can download these materials and use, adapt, or distribute them. Clinical research can feel like it is 95% about filling in forms. We filled in some of the forms, so you don't have to.

In 2016, the ISARIC/WHO CCP was implemented in Brazil in response to the emergence of Zika virus and chikungunya virus in Latin America, facilitating studies of viral shedding and serology.[2] The CCP was also used for the establishment of cohort studies of critically ill patients with Middle East respiratory syndrome.[3] At present, the Uganda Virus Research Institute (Entebbe, Uganda) is using the protocol to study severe acute febrile illness and severe influenza.[4] The value of this approach is becoming apparent in the age of COVID-19. The original reports on clinical findings in COVID-19 used harmonised data collection.[5,6] 46 countries have registered to record clinical data using the ISARIC/WHO CCP Case Report Form and investigators in many countries are planning to use the CCP biological sampling protocol to coordinate studies of transmission, prognostication, pathogenesis, and diagnostics (appendix).

See Online for appendix

Understanding the genetic mechanisms underlying susceptibility[7] might directly advance our understanding of disease mechanisms[8] and possible treatments,[9] but robust studies require recruitment of large numbers of critically ill patients, which requires open, collegiate, and global collaboration. Genetics Of Mortality In Critical Care is an open consortium in which clinicians have been recruiting critically ill patients since 2016. Importantly, this work is led by the clinicians treating the patients, in collaboration with experts in host genetics.

For more on **GenOMICC** see https://genomicc.org

For more on **REMAP-CAP** see https://www.remapcap.org

Operating clinical trials at global scale presents many additional challenges, but even in this domain, substantial progress has been made. Before the COVID-19 pandemic, the critical care community created a highly efficient, randomised, embedded multifactorial adaptive platform trial for community-acquired pneumonia (REMAP-CAP). This single trial was established in 13 countries with the capacity to test new hypotheses quickly. Perhaps most ambitious of all, WHO has developed a global platform—the SOLIDARITY trial[10]—for the evaluation of widely-available interventions to treat COVID-19.

Catastrophes, such as pandemics, drive innovation and lead to marked social change. Within the scientific research community, we believe that perceptions of academic excellence have long undervalued teamwork and collegiality. We hope our colleagues across the world will make use of these tools, either in collaboration or independently, to harmonise clinical research efforts and fulfil the duties of medical science to humanity in the shortest time possible.

We declare no competing interests.

ISARIC clinical characterisation group
clarkdrussell@gmail.com; j.k.baillie@ed.ac.uk

Roslin Institute, University of Edinburgh, Edinburgh EH25 9RG, UK

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