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COVID-19 research in LMICs

We read with interest the Correspondence by Irene Torres and colleagues,¹ and agree that the current scarcity in low-income and middle-income countries (LMICs)

of vaccine to combat the COVID-19 pandemic is a failure of local governments, global solidarity, and multilateral instruments. However, regarding Torres and colleagues' comment that approving placebo-controlled trials in LMICs "sets the wrong precedent because approving such a trial should show that evidence can only be reached with this design",¹ we would like to extend this extremely important discussion. We note an unfruitful divide between the medical and public health communities on how to prioritise resources to address the pandemic; Torres and colleagues' comment feeds this scenario, especially in LMICs. Historically, LMICs are poor generators of their own biomedical research, and this pandemic is no exception (appendix). COVID-19 research produced in LMICs has been weak for reasons such as funding, ethical, and regulatory issues.² Therefore, being able to host and catalyse the local execution of cutting-edge and socially valuable research could have a positive effect in the long term across the fragile health systems of LMICs. This approach would also enable doing other kinds of much-needed research, such as clinical trials on repurposed commonly used drugs, disease surveillance through genomic studies, short-term and long-term effects of COVID-19 on all-cause morbidity and mortality, and policy evaluation studies of implemented strategies in LMICs to contain the COVID-19 pandemic. These efforts should be led by LMIC researchers, who should be given global scientific support.³ As of May 28, 2021, the US Food and Drug Administration and the European Medicines Agency have granted an Emergency Use Authorisation (EUA) to five COVID-19 candidate vaccines.^{4,5} Importantly, regulators issue EUAs on the basis of promising early interim data only; thus long-term safety and effectiveness

monitoring phases are crucial to the final registration or licensure of a candidate vaccine. Furthermore, according to the Declaration of Helsinki (article 33), Council for International Organizations of Medical Sciences (article 5), and WHO Expert Panel, an EUA candidate vaccine cannot yet be considered a gold standard or the best-proven intervention.⁶

We recognise the ethical dilemma about doing blinded, placebo-controlled trials in the middle of having EUA vaccines. Nevertheless, technically speaking, an alternative research design would provide suboptimal evidence and could even delay the accumulation of pivotal data to properly tackle the COVID-19 pandemic. Overall, there are more benefits than drawbacks in promoting COVID-19 research in LMICs, even if using a placebo-controlled trial design. It is key that LMICs should be able to do high-quality clinical trials to be less dependent on high-income countries. Also, doing high-quality clinical trials could lead to important projects of innovation and the transfer of health-related technologies, which would make LMICs increasingly self-sufficient. We must learn from our current national and global failures in tackling the COVID-19 pandemic; otherwise, we will have wasted invaluable lessons learned for the next pandemic.

We declare no competing interests.

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Authors' reply

We thank Ivan Sisa and colleagues for their comments on our Correspondence,¹ but we still worry about the marginalisation of scientific production from low-income and middle-income countries (LMICs). Indeed, these nations usually have scarce public resources to invest in science and, consequently, tend to produce fewer indexed publications compared with high-income countries (HICs). However, such metrics restrict the understanding of academic production to the accrual of articles in English-speaking scientific journals based in HICs and, therefore, to an imperfect appraisal of the impact of their discoveries and the value of the science only in relation to their own realities. Similarly, it is quite short-sighted to assess the scientific power of HICs as the amount of knowledge and products that LMICs adopt and buy from them, rather than as the degree of scientific sovereignty that the latter can develop. Furthermore, reducing the concept of innovation to the unilateral transfer of knowledge from HICs to the rest of the world, where vaccines and medicines are tested

rather than developed, actually contradicts the very purpose of scientific pursuits.

For LMICs to pursue scientific advancement to the same extent as HICs, they would need to dismiss the pluralities of knowledge that make their settings diverse and enriching outside of the laboratory and the clinic. In consequence, LMICs would have to privilege a medicalised version of health and life over other definitions and understandings of health and wellbeing. Even if this path were not pursued, it should not be demanded that LMICs relinquish a key presence on the global stage. Patients, consumers, doctors, and researchers in LMICs should not be required to validate methods and results of trials devised in HICs, without strengthening local capacity in research, technological development, and production of medicines (including vaccines) to become an increasingly equal counterpart across research cycles. Ultimately, appraising scientific innovation in terms of consumable knowledge without regard to local capacities and diverse wellbeing undervalues the importance of scientific sovereignty.

Any collaboration between governments, or academic or public and private institutions, across countries with different levels of income should aim towards scientific sovereignty and, eventually, the dissemination of knowledge in the reverse direction. International instruments, agreements, and funders should ensure there are policies in place to promote equity and to ultimately guarantee egalitarian scientific collaborations. Meanwhile, effective vaccines and medicines that are crucial in dealing with public health problems, when available, should be considered global public goods to be distributed across countries swiftly, in accordance with global solidarity mechanisms.

We declare no competing interests.

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IgG4-related disease and Rosai-Dorfman-Destombes disease

We appreciated reading the expert Seminar on histiocytosis by Jean-François Emile and colleagues.¹ However, we wish to clarify the importance of increased IgG4-positive plasma cells seen in some patients with Rosai-Dorfman-Destombes disease (RDD). First, hyper-IgG4 syndrome is a misnomer; the correct term is IgG4-related disease (IgG4-RD), and RDD should not be considered a subtype of IgG4-RD or vice versa.² Although there are overlapping clinical features between the two conditions (eg, lymphadenopathy, pancreatitis, and hypertrophic pachymeningitis), each disease has distinct clinical features, pathophysiology, and treatment requirements. For example, cutaneous and subcutaneous disease is the most common extranodal presentation of RDD, whereas IgG4-RD rarely involves the skin.

IgG4-RD is so named because of the prominence of IgG4-positive plasma cells in affected tissues and increased IgG4 concentrations in serum. A subset of patients with RDD also



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