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Waste in covid-19 clinical trials

The covid-19 pandemic has given rise to a large number of clinical trials evaluating a wide range of therapeutic avenues, but not all are worthwhile.

Chaos and waste. Since spring 2020, experts in health policy and use of medicines have been surprised by the large volume of clinical trials assessing treatments for covid-19 and have been concerned by the poor quality of many of these trials (1). As of late March 2020, clinical trial registries included 201 trials, evaluating 92 products, including drugs and plasma from patients who had recovered from covid-19. One-third of the trials had no clinical endpoint, about half of them planned to include fewer than 100 patients, and two-thirds were not blinded. In other words, there was a high risk that many of the trials would not provide any information that was actually useful in practice (1). As of late June 2020, more than 1000 trials were registered, about 40% of which involved fewer than 100 patients (2,3). Analysts talk about *"disorganization"*, *"chaos"* and "*huge financial resources wasted"* (**a**)(2,4).

Most of the conclusive results have been provided by two trials, which compared a range of treatments in thousands of patients. These were the "Recovery" trial in the United Kingdom and the "Solidarity" trial sponsored by the World Health Organization (WHO) (**b**)(2). This observation points to the need for better coordination of research efforts, to facilitate the initiation of comparative trials which are of the appropriate size to yield decisive and rapid results, rather than a multiplicity of small flawed trials (1-4).

Hydroxychloroquine: misplaced enthusiasm. In late June 2020, more than 100 trials of *hydroxychloroquine* were underway, planned to include a total of more than 100 000 patients (2,3). Yet, by that time, the Recovery and Solidarity trials had already shown that this drug was not effective in treating severe forms of covid-19 (2). This multitude of trials on *hydroxychloroquine* is all the more regrettable since the French study which had sparked worldwide enthusiasm for the drug combines several disqualifying methodological biases (5,6).

These resources – of time, money and patients willing to take part in a trial – would have been better employed in evaluating strategies that received far less attention, including personal protective measures or "lockdowns", which continue to be the subject of much controversy (7).

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a- *This frenzy led to preprints which were to a greater or lesser extent sloppy and biased, and sometimes retracted due to obvious errors, such as the study based on medical record data provided by the Surgisphere Corporation (ref 8).*

b- *The European trial "Discovery", coordinated by France, was meant to include 3200 patients from several European countries, but as of mid-September 2020, only 916 patients had been recruited, including only 30 or so outside France. As of 5 January 2021, its results had still not been published (refs 5,9).*

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