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Hydroxychloroquine Controversies: Clinical Trials, Epistemology, and the Democratization of Science

The claim that anti-malaria drugs, chloroquine and hydroxychloroquine, can cure COVID-19 became a focus of fierce political battles that pitted promoters of these pharmaceuticals, Presidents Bolsonaro and Trump among them, against "medical elites." At the center of these battles are different meanings of effectiveness in medicine, the complex role of randomized clinical trials (RCTs) in proving such effectiveness, the task of medical experts and the state in regulating pharmaceuticals, patients' activism, and the collective production of medical knowledge. This article follows the trajectory of chloroquine and hydroxychloroquine as anti-COVID-19 drugs, focusing on the reception of views of their main scientific promoter, the French infectious disease specialist, Didier Raoult. The surprising career of these drugs, our text proposes, is fundamentally a political event, not in the narrow sense of engaging specific political fractions, but in the much broader sense of the politics of public participation in science. [COVID-19, chloroquine, hydroxychloroquine, randomized clinical trials, AIDS activism]

Introduction

On May 15, 2020, Nelson Teich resigned his position as Brazilian Minister of Health after a mere 29 days in office; one of the main reasons he mentioned for quitting was a disagreement with President Bolsonaro over the generalization in the use of chloroquine (an old anti-malaria drug) to treat COVID-19 (Phillips 2020). Three days later, the president of the United States, Donald Trump, publicly announced that he had started taking a daily dose of the drug on a prophylactic basis, despite the FDA's caution "against use of hydroxychloroquine or chloroquine for COVID-19

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outside of the hospital setting or a clinical trial due to risk of heart rhythm problems" (FDA 2020; Karni and Thomas 2020). One news cycle later, in an article soberly entitled "Jimmy Kimmel Calls Trump a 'Hydroxymoron,'" a *New York Times* journalist commented: "Even a Fox News commentator was alarmed by Trump's revelation that he was taking the antimalarial drug hydroxychloriquine, which the president has promoted as a potential COVID-19 cure, though there is no proof that it works against the coronavirus (and the F.D.A. has issued a safety warning about it)" (Bendix 2020). The key words here are "proof" and "works." Our article attempts to unpack these words in the context of the controversy on the use of chloroquine and hydroxychloroquine as treatment of COVID-19. The preliminary analysis set forth in this article are not based on any original ethnographic research but rather draw insights from engaging with a broad range of documentation: from published biomedical articles to Twitter threads, and the like, read from an historical perspective, and informed by our previous research on the transformation of clinical research and medical statistics since the end of the 19th century.

The coronavirus disease 19 (COVID-19) pandemic is especially scary because of the paucity of effective medical devices to prevent or cure the disease. The sophistication of the genomic analysis of the pathogen that causes it, the SARS-CoV2 virus, and the epidemiological models developed to predict its spread, starkly contrast with the crudeness of the main solution used by governments all around the world to slow its progress: mass quarantine. Unsurprisingly, the pandemic prompted an almost instantaneous international mobilization of medical and public health researchers of unprecedented amplitude looking for solutions to this worldwide calamity. Such solutions, which fall into what Joao Biehl called the pharmaceuticalization of public health, are expected to solve the present sanitary emergency "without people," that is without public debates that may lead to pressures to radically alter the economic and political status quo (Biehl 2007). It is therefore not surprising that technological solutions are strongly favored by the markets. The Dow Jones Index rose sharply on April 30, 2020, with the announcement that the U.S. manufactured drug Remdesivir had a promising effect in the treatment of COVID-19, and then again on May 19, following news of positive preliminary results from an on-going trial of a U.S.-produced anti-COVID-19 vaccine (BBC 2020).

With the first announcement of COVID-19 epidemics, clinicians embarked on a frantic search for an effective treatment for SARS-CoV2, especially important because mass production of a safe vaccine may be a slow and uncertain process. Yet, as the first claims regarding the effectiveness of various molecules started to hit the news, discussions about the rules that had been guiding the organization of clinical research for decades grew heated. Not only was the need to randomize the allocation of participants to treatment and control groups in clinical trials contested; even the need for a *control group*, seen as essential when providing a proof of efficacy of a given therapy, was questioned. This debate quickly centered on the therapeutic value of an old anti-malaria drug, chloroquine, and its newer, and potentially less toxic derivative, hydroxychloroquine. Then it promptly turned into a controversy on what counts as evidence of effectiveness of a treatment.

Discussions on regimens of proof in clinical medicine, the value of randomized clinical trials (RCTs), and the authority of experts also evolved into debates on the role of lay public in decision-making that concerns them directly. To social scientists

with an interest in the history of clinical research and medical statistics, these debates carried a definite air of *déjà vu* about them, especially perhaps to those of us with any knowledge of the French context. This is because the international career of the hydroxychloroquine treatment against COVID-19 started in France and unfolded in the background of a long history of French medical controversies. These pitted an initially tiny minority who defended the superiority of statistical evidence against those who believed in the pre-eminence of the uncommunicable knowledge of the experienced clinician (Lawrence 1985). In the controversy over the therapeutics of COVID-19, the debate acquired an additional hue. Adversaries of the relatively newly acquired consensus that favored RCTs as proof of efficacy of a medical intervention mobilized the notion of democratization of scientific knowledge to legitimate the use of a treatment that, they claimed, was strongly supported both by the general public and rank and file medical practitioners who jointly rebel against the tyranny of medical elites (Raoult 2020c, 2020e).

In this article, we use the chloroquine/hydroxychloroquine controversy as a window on conflicting claims of authority in contemporary medicine—statistical objectivity vs. charismatic subjectivities, or activism vs. official experts. The production of medical knowledge carries a unique emotional load because its applications radically modify individual and social bodies. The chloroquine/hydrochloroquine dispute, we argue, goes well beyond entertaining stories about colorful doctors, headstrong political leaders, and their faithful followers and fierce adversaries. At its center is a vital political issue: Who is entitled to participate in the shaping and validation of new medical knowledge and practices?

The Amazing Planetary Career of Two Somewhat Modest Drugs

Even keeping in mind the desirability of wonder drugs in times of epidemics, the present worldwide craze for chloroquine (a well-known, fairly dated antimalaria drug), and, more often, hydroxycholoquine (used today mainly to treat auto-immune diseases, such as lupus and rheumatoid arthritis) is puzzling in many ways. One of the main objects of bewilderment is the role played by Professor Didier Raoult, a French microbiologist and figurehead of *Méditerranée Infection* (a medical-cum research center based in Marseille) in super-spreading this vogue. Although not the first physician to advocate the use of chloroquine in the treatment of COVID-19 patients—Chinese experts were promoting it in early February 2020—Raoult was instrumental in widening the attention from chloroquine to the less toxic hydroxycholoquine and quickly became a prominent if polarizing figure in France, at a time when the number of admissions in intensive care units and the death rate were starting to spike.

An accelerated pre-publication of a non-randomized hydroxychloroquine clinical trial by Raoult and his collaborators—as shown by Gautret et al., the article received on March 16, 2020, was accepted a day later through a fast track and uploaded online on March 20—immediately created considerable buzz because, according to its authors, it had shown that patients who had received the molecule were cured in six days (Gautret et al. 2020). Raoult promptly gained national and worldwide fame, first through his highly popular YouTube channel (some of his video posts, in French, have been watched over one and a half million times), then,

decisively, thanks to the campaigns in favor of chloroquine and hydroxycholoquine launched at the same time by French anYoud U.S.-based supporters. In France, a highly successful petition in favor of the administration of hydroxychloroquine in the treatment of COVID-19 was instigated by a former minister of health, Philippe Douste-Blazy (Payet 2020), while President Macron, perhaps impressed by popularity of hydrochloroquine, traveled to Marseille April 8, 2020, to visit Raoult's laboratory (Sciama 2020).

In the United States, Georgy Rigano, U.S. lawyer and Fox News collaborator, uploaded a Google document praising the new therapy for COVID-19. This document became rapidly popular among Silicon Valley entrepreneurs. Raoult then authorized Rigano to share his results on Twitter before they were officially published. On March 16, 2020, Elon Musk, the CEO of Tesla, tweeted a link to this document to his nearly 33 million followers, an especially efficient promotion avenue. Rigano also publicized Raoul's study on Laura Ingraham's show on Fox News; Ingraham became then an enthusiastic supporter of hydroxychloroquine. Later Raoult appeared on Doctor Oz's Fox News program, another important avenue of publicity for hydroxychloroquine (Sayare 2020; Wong 2020). The new therapy continued to be promoted by a plethora of Fox News hosts, before being enthusiastically endorsed by Presidents Trump and Bolsonaro (Baker et al. 2020; Henrique 2020)

In both international and French medical arenas, however, Raoult's promotion of hydroxychloroquine was heavily criticized; in France, known infectious disease specialists such as professors Jean Michel Molina, Karine Lescombe, Christine Rouzieux, and Philippe Ravaud were thoroughly critical of him. The fast-growing controversy centered mostly on the methodological choices made by the French team: the lack of randomization, and even of a properly constituted control group. In the original article by Raoult et al., the study was described as "a single arm protocol"; the control group was made up of patients hospitalized in the Marseille area, who seemed to differ significantly from the "hydroxychloroquine group." On April 3, 2020, the International Society of Antimicrobial Chemotherapy (ISAC), which had initially fast tracked the publication of the article by Raoult and his collaborators in its house journal, went to the rather extraordinary length of publicly stating that "the article [did] not meet the Society's expected standard, especially relating to the lack of better explanations of the inclusion criteria and the triage of patients to ensure patient safety" (ISAC 2020). ISAC representatives blamed an unnamed "Associate Editor" for publishing the article without realizing that its authors "had excluded data from patients who were not responding well to treatment," and firmly maintained that, although one of the authors of the article—Jean-Marc Rolain—was also the editor-in-chief of the journal, "he had no involvement in the peer review of the manuscript" (France 24 News 2020).

Regimes of Proof: "Caring Physicians" versus "Cold-blooded Methodologists"

The severe criticisms of hydroxychloroquine treatment cut little ice with Raoult, who swiftly counter-attacked with a series of videos, interviews, and an opinion column in France's most influential newspaper, *Le Monde*. In this article, he denounced the nefarious role of what he called "methodology maniacs," in the bureaucratization

of clinical research, and the consecutive forgetfulness of the physician's first duty: to save lives (Raoult 2020a).

Emotionally detached methodologists versus clinically oriented medical humanists. … At first glance, the controversy seemed to rerun an all-too-familiar theme in the history of medicine, especially in the French context, where clinicians long resisted the growing influence of statistics in medicine. One detail, though, proved altogether surprising and interesting, namely Raoult's insistence that his outstanding medical science stemmed from his command of epistemology and the history of medicine. At the center of the ongoing controversy on the use of chloroquine and hydroxychloroquine to treat COVID-19 is the almost-two-centuries-long discussion on the right way to prove therapeutic effectiveness. Critics of Raoult's study maintained that, because of the high spontaneous recovery rate of the disease (about 80–85%), only a large-scale randomized trial could provide scientific evidence of clinical efficacy (Cascella et al. 2020). Raoult and many of his supporters, for their part, objected to what they saw as a sterile approach promoted by methodology-obsessed purists with an agenda that could only delay the administration of the much-needed drug to suffering patients. Since the 1820s, when P. C. A. Louis undertook his pioneer comparative evaluation of bloodletting, opponents of clinical trials have championed clinical intuition against statistical protocols, the irreducible idiosyncrasy of each and every medical case against the law of large numbers, etc. In his *Le Monde* article and an interview posted on site of the Marseille Institute of Institute Méditerranée Infection, April 22, 2020, Raoult, too, drew heavily on this repertoire (Raoult 2020a, 2020d).

As we explained previously, contrary to what Raoult claimed, the introduction of randomized trials in medicine was not the result of an alliance between statisticians and methodologists working for the pharmaceutical industry, but rather started as a medical reform movement led by clinicians appalled by the negative consequences for patients, especially the more vulnerable ones, of ego battles among senior physicians, and clashes between therapeutic schools of thought (Berlivet and Löwy 2020). For all their connotations of detached, objective, technocratic (and hence allegedly apolitical) methods, RCTs were actually crafted and promoted by a mix of clinicians and medical statisticians with a clear progressive, often left-wing, political agenda. Major Greenwood and Austin Bradford Hill, who undertook to revamp clinical research methodologies in interwar Britain, both associated themselves with social medicine—the former was a founding member of the Socialist Medical Association, whereas the latter had a social–liberal leaning and developed a keen interest in occupational health (Armitage 2003). Hill famously designed the two 1946 RCTs organized by the Medical Research Council to assess, respectively, the effectiveness of a whooping cough vaccine (MRC 1951) and the streptomycin treatment of pulmonary tuberculosis (Doll 1992; MRC 1948), with the aim of neutralizing conscious and unconscious biases in the evaluation of the effectiveness of medical interventions. Three years before, Philip D'Arcy Hart and Joan Faulkner, a socialist and a communist respectively, had masterminded a properly controlled trial (though not randomized) to assess the effects of an antibiotic, patulin, on the course of common colds (Chalmers and Clarke 2004).

In the following decades, a growing community of clinical researchers with a background in medicine or/and statistics effectively adapted to the medical context

an experimental design initially devised by R. A. Fisher between 1925 and 1935. Archibald (Archie) Cochrane, whose fight to improve the quality of study design inspired evidence-based medicine pioneers (the Cochrane Collaboration, established in 1993 at the instigation of Iain Chalmers, is named after him), was also a socialist physician who volunteered to serve in the health services of the Spanish Republican Army during the Spanish Civil War. Even if politics did not play the same part in shaping the professional career of the North American precursors of clinical epidemiology, key figures such David Sackett did not exactly side with the medical establishment—nor any other kind of establishment. It is beyond doubt that these original reformist inclinations faded away with time, as routine took a toll. Physician and epidemiologist John P. A. Ioannidis summarized it angrily: "As EBM became more influential, it was also hijacked to serve agendas different from what it originally aimed for. Influential randomized trials are largely done by and for the benefit of the industry" (Ioannidis 2016: 82). However, what the demand by an increasing number of patient organizations, starting with the HIV/AIDS activists of the 1980, to be involved in the organization of clinical experiments underlines, is the centrality of modern clinical trials in the collective production of medical knowledge—even, or especially, during a public health crisis. As Harry Marks reminded us in an article tellingly subtitled "Why RA Fisher Is Important": "In the absence of a randomized experiment to provide a valid estimate of probability, one was left in the hands of 'scientific authorities' with less leverage to discuss their viewpoint" (Marks 2003: 933).

Chloroquine and Epistemology

Raoult and other promoters of chloroquine and/or hydroxychloroquine explain that these promising treatments are (1) cheap and (2) harmless, since they are already being used by millions of patients suffering from different conditions—therefore, there is nothing to lose by trying them out. Moreover, the innocuity argument of hydroxychloroquine became increasingly prominent in Raoult's argumentation: Facing a health emergency, it was the physician's duty to try a safe and potentially efficient drug (Raoult 2020d; Sayare 2020). Facing increasing criticism of his clinical studies, as well as reports that chloroquine and hydroxychloroquine were not as innocuous as he claimed, since preliminary reports pointed to potential toxicity of these compounds in COVID-19 patients (e.g., Borba et al. 2020; Magagnoli et al. 2020), Raoult developed a second, interesting line of argument. He attempted to prevail by linking the (alleged) superiority of his approach to his command of epistemology and medical history. It quickly became a key trope of his public interventions. Thus, in an interview aired on French Radio Classique on April 1, 2020, he claimed that:

> I am an epistemologist, that is a specialist of the science of science. History of infectious diseases teaches us that this method [randomized clinical trials] was practically never used to demonstrate the effectiveness of a new treatment. […] Large scale clinical trials were promoted by the pharmaceutical industry, then everybody confused this approach with science. (Raoult 2020b)

What we found interesting in this statement is clearly not the claim that randomized clinical trials had little to no impact on the search for treatments against infectious diseases—a bizarre assertion considering the iconic status of the pioneer streptomycin trial of 1946, the trials of antiretroviral drugs in HIV infected patients, and many other randomized trials. Rather, what was interesting was Raoult's attempt to turn the philosophy of science into an instrument of power, to prevail in a medical controversy at the beginning of the 21st century. This argument may be linked with a French tradition of cultivated physicians who aspired to become, and sometimes indeed became, public intellectuals. In this case, however, Raoult employed it to differentiate himself from his, allegedly less sophisticated critics, too easily fascinated by mere methodology and mathematical formulas. Raoult's definition of epistemology as "the science of science" seems especially revealing here—as if the philosophy of science was some kind of meta-knowledge that could provide the trained philosopher with an upper hand over the non-initiated. Those who criticized his clinical experiments, Raoult claimed in an interview aired on Radio Classique, on April 17, 2020, were simply not familiar with the teaching of Karl Popper, Thomas Kuhn, and Paul Feyerabend, who had shown that science is never static, and that—consequently—research methods are bound to be outdated sooner or later. This was precisely what had happened to randomized clinical trials: Science had moved to a very different place, and the growing strings of unfair attacks leveled at his clinical trials of hydroxychloroquine merely revealed the depth of epistemological ignorance on the part of his detractors (Raoult 2020c).

Science and Democracy: Unauthorized Drugs, Experts, and Activists

While Raoult claimed that the essential superiority of his approach came from the combination of his profound clinical knowledge with his mastering of epistemology and history of science, his collaborator, Yanis Roussel—the architect of the highly successful campaign in favor of hydroxychloroquine therapy in the social media—proposed a somewhat different and potentially more persuasive argument. The popular pressure for widespread use of hydroxychloroquine to treat COVID-19 despite experts' objections, Roussel argued, denoted a profound aspiration to democratize science. Politicians aspire to ground their interventions in scientific consensus, forgetting that the scientific establishment, too, tends to be conservative, and that all too often scientific progress has to be fought for. In this perspective, the extension of the battleground to the Twittersphere was welcome news indeed: By sharing Raoult's 28-page-long original article tens of thousand times (recall that it was linked with Elton Musk's tweet account), the general public was successfully democratizing scientific knowledge. (Roussel 2020). As a matter of fact, Raoult and Roussel argued, the public's request that the randomized clinical trials stage be dropped merely repeated similar demands by AIDS activists, back in the 1980s and 1990s. And here comes out another crucial trope of Roussel's and Raoult's discourse, namely that their critique of medical research is consonant with that of AIDS activists—but are they?

In the late 1980s and early 1990s, AIDS activists in the United States and elsewhere strongly criticized the rules that regulated the organization of clinical trials for new therapies. ACT-UP (AIDS Coalition to Unleash Power) staged dramatic

demonstrations against organizations such as the Food and Drug Administration, and the National Institute of Allergy and Infectious Diseases (NIAID). "Red tape kills," their slogan read. Crucially, however, randomized clinical trials were never dropped altogether, but rather did the medical and administrative elites, in many different countries, yielded to the activists' demand, and started to include them in the discussions over the organization of new clinical trials. This, in turn, resulted in important changes in the rules that previously governed such trials, with the development of fast-track clinical trials; the legalization of patients' compassionate access to off-label drugs; the abandonment of the principle that patients who had already received any drug ought to be excluded from trials; the elimination of trials against placebo; and, above all, the routine inclusion of patients' representatives in the planning of clinical trials (France 2016).

One can already start to picture how flimsy the parallel between social network mobilizations in favor of immediate access to (hydroxy)chloroquine and the extensive work undertaken some 30 years ago by AIDS activists to reform clinical research is. It is not just that COVID-19 is an acute disease—which evolves very rapidly, but, on the other hand, is only lethal, or even severe in a limited number of cases—whereas AIDS is a chronic condition—with an average survival time that was initially about 18 months from the appearance of the first symptoms. Or that the stigma associated with Sars-CoV-2 (when observed) is not of the same kind as the one associated with HIV infection. It is above all because the two cases vary widely when it comes to the approach to scientific evidence, clinical experiments, and collaborative scientific practices.

It is true that, in the 1980s and early 1990s, some AIDS patients attempted by all possible means to get access to potential therapies. They formed organizations such as the Dallas Buyers Club, depicted in the eponymous 2013 film, that smuggled a series of unproven treatments; set up unofficial, community-based trials of these illicit drugs; and avidly read *AIDS Treatment News*, a publication that centralized and shared information on potential AIDS cures. Gradually, however, AIDS activists realized that the only treatments that displayed a curative effect, however modest, were those developed by the pharmaceutical industry. Accordingly, they became increasingly interested in all aspects of drug testing. In the late 1980s, members of the ACT-UP affiliated Treatment and Action Group (TAG) joined the AIDS Clinical Trials Group of NIAID (Epstein 1995). NIAD's director, Dr. Antony Fauci, was initially reluctant to involve TAG activists in the planning of clinical trials but ended up welcoming them (Shulman 2003). In France, the inter-organizational group TRT5 was established in 1992 by 10 or so AIDS organizations to provide collective expertise on therapeutics and clinical research to the whole community (Barbot 2002; TRT5 2020). Through their (cautious) collaboration with NIAID or other medical research organizations all around the world, AIDS activists gradually acquired the expertise they needed to be able to engage with clinicians and scientists and get heard. Having progressively learned enough virology, biochemistry, immunology, epidemiology, and statistics—often with the help of understanding professionals—they were able to bring important innovations to the design of drug trials. At the same time, medical researchers and public health officials increasingly understood the practical advantages of working with patient organizations.

Becoming Stakeholders in Clinical Research Takes Time and Efforts

The process of integration of patients' representatives into instances in charge of organizing the experimental trial of new drugs was by no means smooth and conflict free; in the end, however, activists who had once angrily protested against the shortcoming of official science turned into influential protagonists of clinical research, and effectively challenged the traditional hierarchical relationship between experts and lay persons in the process (Löwy 2000). Their role became even more crucial in the mid-1990s during the organization of various clinical trials that aimed to assess the effectiveness of triple-drugs therapy—a turning point in the therapeutic approach to AIDS. Clinical trials of anti-retroviral compounds adopted many of the changes proposed by AIDS activists, who, in turn, accepted the basic tenants of randomized clinical trials, therefore recognizing the centrality of methodologically sound approaches for establishing both the safety and effectiveness of therapeutic agents. In parallel, researchers in charge of planning and implementing these trials, who were initially wary of working with patients' spokespersons (a hindrance they only tolerated for political reasons), realized first hand that such collaborations not only facilitated the recruitment of patients into clinical trials by making them more user-friendly, but also, and more crucially, improved the effectiveness of these trials by reducing the gap between the purified universe of clinical experimentation and the real-life uses of new drugs, with its often unforeseen consequences (Epstein 1996).

One of the conclusions that were often drawn from this history by medical commentators and patient representatives alike was that there was no need to be intimidated by experts: Everybody could become one, if need be. This has some truth to it—though it is important to remember the amount of time and efforts invested by patients' representatives in the process. Lessons learned during the AIDS epidemics paved the way to other collaborations between medical researchers and users of health care. Any such collaboration relies, however, on the slow transformation of users into competent counter-experts, able to critically evaluate the views of professionals. By contrast, in the story around chloroquine and hydroxychloroquine, the general public was invited to endorse at once the seductive rhetoric of a charismatic doctor (Viktorovitch 2020).

After the development of efficient treatments for AIDS, the focus of intervention of activists involved in clinical trials shifted from the participation in organization of clinical trials to securing access to anti-retroviral drugs, especially for vulnerable populations both in the North and in the South. Groups such as ACT-UP became involved in struggles with drug companies over the pricing of retroviral drugs and the access of deprived populations, especially in the developing world, to vital drugs. In Brazil, ABIA (*Associação Brasileira Interdisciplinar de AIDS*, founded by sociologist Herbert José de Sousa-Betinho) and other AIDS organizations played a key role in shaping the federal government's exemplary policy granting free access to antiretroviral drugs (Bastos 2008). The AIDS crisis also intensified the debates about the testing of new drugs in developing countries, including Eastern Europe and Latin American countries that have reached an intermediary level of economic development, such as Poland and Brazil (Petryna 2009). These discussions, especially when they dealt with clinical experimentation in Africa, usually focused on ethical issues: informed consent, trials against placebos, or the protection of local

populations against economic exploitation (Angell 1997; Emanuel et al. 2004; Shapiro and Meslin 2001; Varmus and Sather 1997).

The thorny issue of the relationship between researchers based "in the North" and experimental subjects living "in the South," was frequently reduced to the sole question of community participation, a vague term that, too often, boiled down to the need for involving local elites in the organization of clinical trials. However, affluent community leaders do not necessary defend the interests of the poor; elders do not always wish to help the young; male chiefs are not necessarily attentive to the interests of women; and prominent local medical researchers may be tempted to privilege the advancement of their career over safeguarding the health of the vulnerable. The inclusion of community representatives in the organization of a clinical trial does not necessarily protect the interests of people directly affected by the experiment.

Nevertheless, there were situated efforts to involve concerned populations in the organization of some clinical trials: For example, activists who promoted clinical trials of anti-HIV microbicides—locally applied substances meant to protect women from HIV infection—paid real attention to the views of the women enrolled in these trials (Heise and Wood 2005; Heise et al. 2005). Besides, it would be a mistake to picture the populations in the South as a purely passive, powerless agent on the medical stage. In a recent opinion column, Fred Eboko reminded us pointedly that institutional review boards had been established in pretty much every African country, and that only a minority of clinical trials in 2018 took place outside North America and Europe (Eboko 2020). If anything, Africa's virtual absence from the clinical trials map is a major problem rather than a blessing (Wasunna 2020).

From AIDS to COVID-19 Therapies

Recently, AIDS activists joined the debate on clinical trials of COVID-19 therapies. From 2011 on, these activists have expanded their goal to securing general access to pre-exposure chemoprophylaxis (PrEP), that is the protection from HIV infection through prophylactic use of anti-retroviral drugs. The most prominent among these is Tenefovir, which is sold by Gilead Ltd (Abdool-Karim et al. 2010; Krakower and Mayer 2011). Campaigners from TAG, in alliance with a new group called PrEP4All Collaboration, which promotes the diffusion of PrEP, attempted to break Gilead's patent on Tenovir, to make the drug more accessible (Break the Patent 2018; Terry 2019). In early 2020, Gilead researchers suggested that another of their drugs, remdesivir, might be used to treat COVID-19, and quickly received generous federal funding to test this possibility (Kolata 2020). In his video of April 22, 2020, Raoult strongly criticized remdesivir trials. The safety of hydroxychloroquine, he stressed, is attested by the fact that it is used by millions of patients worldwide. In the midst of a pandemic, he continued, there was a moral imperative to propose a safe and promising treatment to patients without waiting months for results of a randomized clinical trial, which may arrive only when the epidemics will be on the wane. Instead, experts push a molecule, remedsivir, which was never used in humans, and whose main advantage is to generate fat profits for the pharmaceutical industry. He added that publications about this molecule in leading medical journals are directly written by the industry representatives, a claim that probably alludes to the fact that

the corresponding author of the *New England Medical Journal* article on remdesivir, published online April 10, 2020, is Diana Brainard from Gilead Sciences (Grein et al. 2020; Raoult 2020d, 2020e).

In April 29, *Lancet Infectious Diseases* published the results of a small randomized clinical trial, described as well-designed but underpowered, that failed to uncover positive effects of remdesivir on severe COVID-19 (Norrie 2020; Wang et al. 2020). The same day, Antony Fauci announced positive results of NIAID-sponsored trial of this drug (Kolata et al. 2020). Although these results were far from spectacular—remdesivir reduced the duration the disease, though not the mortality from COVID-19—Fauci insisted on the drugs' promise. He justified his decision to prematurely disclose the results of NIAID's remdesivir trial by citing ethical concerns: the fear that confused patients would abandon a promising clinical experiment (Reuters 2020b). Fauci did not mention that the original aim of the NIAID clinical trial, to display better survival of COVID-19 patients, was changed later (Rowland 2020). President Trump who, from mid-April 2020 on, muted his praise of hydroxychloroquine, presented the results of NIAID's remdesivir trial as an important success of the U.S. drug industry. The White House's economic adviser Larry Kudlow declared: "These are confidence-inspiring things that will help open the economy and get folks back to work." As a result, stock markets have risen on hopes that the new drug could help countries emerge from lockdowns (BBC 2020; Reuters 2020a).

TAG and PrEP4All Collaboration activists had a somewhat different reaction to the proclamation of remdesivir's efficacy. Earlier, TAG activist James Krellenstein had already drawn attention to the risks associated with the chaotic conduct of ongoing clinical trials of COVID-19 therapies (Gonsalves 2020). In a joint declaration of April 30, 2020, TAG and PrEP4All spokespersons explained that they welcomed the results from a randomized controlled trial of therapies for COVID-19, but were troubled by the way these results were made public by Fauci:

> [S]eriously concerned about claims that data from a National Institutes of Allergy and Infectious Diseases (NIAID) study of the Gilead drug remdesivir—briefly described yesterday in a press release—justify an instantaneous change to "a new standard of care" for all studies of treatment for COVID-19 disease. (…) Our concerns regarding whether this is sufficient cause for remdesivir to become standard of care in all COVID-19 treatment trials are based on the extremely limited amount of data that was disclosed, which precludes clinicians, scientists, and community members from independently assessing the basis for Dr. Fauci's remarks. (…) It is essential that there is careful review of the full results before making decisions about the standard of care for new and on-going trials for treating COVID-19 disease. Furthermore, studies should not be described by press release with only limited subsets of crucial data included. (TAG and PrEP4All 2020)

In 1995, shortly after the development of the tritherapy for AIDS, Antony Fauci declared that "the scientific community quickly learned the importance of including AIDS activists in the administrative policy-making process (…) AIDS activists became an invaluable resource in the design of clinical trials" (Fauci 1995). A quarter

of a century later, Anthony Fauci is still NIAID's director, TAG campaigners are still proposing a critical view of the management of randomized clinical trials, doing it (again) mainly as outsiders, and drugs are still at the center of commercial and political struggles. The results of the clinical trial of remdesivir, published on May 20, 2020, in the *New England Journal of Medicine*, confirmed its—relatively modest—efficacy (Beigel et al. 2020). Since this drug is viewed as one of the two pharmaceuticals proven to work against COVID-19 (the second is dexamathazone), in late June the United States bought virtually all the stocks of remdisivir for the next three months, leaving none for the rest of the world (Boseley 2020).

Conclusion: Activism, Social Media and a Miracle Drug

The argument that all concerned citizens, and not only a handful of experts, should be allowed to participate in debates on scientific topics, especially on issues that involve them directly, from air pollution and the use of nuclear energy to access to promising new therapies, is a seductive one. The problem, in our view, lies in the all-too pervasive notion of lay participants, whose abstractness conceals the plurality of motives that effectively prompt individuals and collectives to engage in a scientific discussion, as well as the precise nature of their contribution to scientific debate. "Biocommunicable cartographies" (Briggs and Hallin 2016) have become even more intricate since Charles Briggs and Daniel Hallin started to lay out the concept of "biocommunicability," 10 or 12 years ago (Briggs and Hallin 2007). The growing role of social media in the communicability of biomedical knowledge clearly plays a crucial part in this complexification, although it should not be reduced to a case of mere technological determinism. The expansion of "communicable cartographies" (Briggs 2011), induced by the rise of social media, created "cultural models for the production, circulation, and reception of health knowledge" (Briggs and Hallin 2016: 7). If only because the apparently open and reciprocal horizontality of social media created opportunities for alternative strategies of self-presentation, including the rather paradoxical, still highly successful, self-portrait as an outsider favored by some powerful insiders all around the world (government officials, heads of states, established scientists and physicians, etc.) who regularly indulge in anti-institutional tweets and posts.

Since the beginning of the COVID-19 pandemic, signing an on-line petition, looking at a video posted on YouTube, liking a Facebook site, or re-tweeting a message on health-related issues posted on a celebrity's account have been equated by some commentators with new forms of patient/citizen activism. At the same time, politicians who publicized the use of hydroxychloroquine, such as Bolsonaro and Trump, depicted themselves as courageous defenders of the interests of "the people" against the stifling views of experts—a strategy they had already adopted previously to justify their rejection of the scientific consensus on climate change (Guilherme 2020; Oreskes and Conwey 2015). However, far from being the expression of a movement for the democratic re-appropriation of science by lay people, enthusiasm for untested and potentially toxic therapies promoted by conservative social media and populist politicians have had just the opposite effect: silencing debates over the social and political underpinnings of science. Activism focused on environmental or health-related issues works very differently. Above all, it influences policy

by showing that there is no such thing as value-free expertise grounded in neutral, exclusively technical considerations. To paraphrase Briggs, it takes a lot of work of "linguistification" to make "evidence" look like "facts that speak for themselves" (Briggs 2011: 462).

What remains to be understood is the exact role played by the "COVID-19 moment" in the ongoing transformation of science communication. Does it merely provide us with the metaphorical magnifying glass through which preexisting tendencies become more easily noticeable? Has it accelerated some of the foregoing changes in the circulation of scientific, including biomedical, knowledge, and if so, to what extent and how did that happen? Or has the crisis induced by the pandemic both in scientific and political arenas created an opportunity for some actors to explore new, disruptive strategies? One can easily find examples that seem to validate one or the other of these hypotheses, depending on where one looks. However, without a large-scale, empirical, collective, multidisciplinary, and comparative investigation, we will never be able to fully comprehend the manifold processes that made the "hydroxychloroquine saga" possible, together with other disturbing episodes in science and health communication over the past months.

Not all scientists engage with societal issues as wilfully and spontaneously as some do. Astrophysicists who observe black holes do not influence people's lives in the same way that nuclear physicists do. Nevertheless, very few scientific activities have no effect whatsoever on society. As Steven Shapin puts it, science is "never pure" (Shapin 2010). Activists' serious, sustained engagement with scientific issues—be it through collaboration, counter-expertise, or well-grounded protests—highlight the political and socioeconomic underpinnings of science and technology, therefore opening spaces for discussion, critique, and change. The COVID-19 epidemic is a planetary event, and efforts to control the disease have immense social, economic, and political ramifications. The indispensable public debates on these ramifications should not, however, be confused with celebrities' endorsements and the viral propagation of carefully crafted statements on social media. Just as context matters, forms of intervention matter, too.

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