Does the public know when a scientific controversy is over? Public perceptions of hydroxychloroquine in France between April 2020 and June 2021

Short title: Public perceptions of hydroxychloroquine in France

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Abstract

Objectives:

In the early stages of the COVID-19 pandemic, chloroquine and its derivatives such as hydroxychloroquine (HC) were widely commented upon both within the scientific community and in the media. This paper explores the different factors that influenced public perceptions in France of the efficacy of HC as well as their evolution between April 2020 and June 2021.

Methods

This article draws on 5 surveys conducted among representative samples of the French population (projects COCONEL and TRACTRUST ; quota method, N=1006 ; 1004 ; 2006 ; 1014 and 1005). We asked questions on the effectiveness of chloroquine against COVID-19. We also collected sociodemographic variables and attitudes toward politics and science.

Results

Between April and June 2021, the proportion of respondents who believed in the efficacy of HC decreased rapidly from 35% to 14%. The proportion of respondents who believed that HC is ineffective rose gradually from 6% to 21%.

After adjusting for the temporal effect, the logistic regression showed a very strong association between political orientation and the belief in the efficacy of HC. Respondents who felt closest to the more radical parties (far right and far left) were more likely to believe in the efficacy of HC than those who felt closest to the political center (O.R. 2.48 [1.95-3.15] and 1.87 [1.44-2.43]).

The role of trust in the government and in science and of the degree of political engagement were investigated in the two waves conducted after the scientific consensus was established during the summer of 2020. High levels of trust in the government and in science and of politicization are associated with belief of HC proven inefficacy.

Across the whole period, a majority of respondents were uncertain. Even in 2021, 41.5% stated that the data were insufficient to decide whether or not HC is effective and 25.2% stating that they did not know.

Conclusion

Because media coverage of scientific controversies is higher in times of uncertainty than after these controversies have died down, the publicization of therapeutic promises can have lasting consequences on attitudes towards science and medicine.

Keywords: COVID-19 ; chloroquine ; surveys ; public attitude ; sociology

Introduction

Of all the treatments that have raised and dashed hopes of curing COVID-19, chloroquine and its derivatives, especially hydroxychloroquine (hereafter HC) occupies a special place because of the intensity of the debates surrounding it. In the early stages of the pandemic, HC, were widely commented upon both within the scientific community and in the media. This public debate had several consequences. First, they sent research on unfruitful avenues, as evidenced by the multiplication of clinical trials on HC—often of poor quality (1,2)—that yielded negative results (3,4) and by the difficulties in recruiting patients for trials that tested other molecules (5). Second, several people who took HC to treat COVID-19 infection, either through self-medication or prescription, suffered adverse effects (6–8), and patients affected by diseases commonly treated with HC (such as malaria or lupus) faced stock-outs due to an explosion of demand for the drug (9). Third, the debates on hydroxychloroquine had a temporary impact on health policy in some countries, where exceptional authorizations of use were enacted, and a durable one in others (10,11), such as in Brazil where a “hydroxychloroquine alliance” was formed between intellectuals, physicians, and politicians (12). Fourth and lastly, the confrontational nature of the debate led to insults and attacks against doctors and scientists on the Internet (13,14) as well as legal actions against scientific advisers to governments, such as in France, accused of mass killing for asking to respect the rules of clinical research.

In this article, we analyze the evolution of the French public’s perceptions of the efficacy of HC across a period of more than a year (April 2020-June 2021). Although media coverage of HC is now over, the efficacy of HC is still put forward in conspiracy theories, even as these develop in new directions, such as resistance to vaccination or the promotion of treatments like ivermectin. The unfolding of public debates in France is interesting in that it raises the question of the reception of therapeutic promises in the public sphere, both in terms of public perceptions of promising treatments and of their perceptions after a scientific consensus has been established. The recall of episodes from the

HIV/AIDS epidemic during the COVID-19 pandemic shows that controversies surrounding some treatments or medical technologies more generally can have durable effects on social representations (15). This phenomenon can cause problems for health authorities. A case in point is that of vaccine hesitancy, which is fueled by the now discredited belief that vaccines cause autism or multiple sclerosis (16). The public reception of “new” treatments has so far received little attention. Indeed, in a context where disease management is performed under a medical monopoly, therapeutic promises are generally seen as concerning mainly doctors and patients. The first studies on attitudes towards HC have focused mainly on doctors (17). Few studies, in France or abroad, have explored the factors involved in the formation of public opinion on the efficacy of HC. Although the French polling institute IFOP did include a question on perceptions of the efficacy of HC in its April 2020 survey showing a very high of respondents believing in the efficacy of HC (59%), this has not led to in-depth studies of the factors influencing these perceptions (18). Outside of France, available studies on the topic were conducted on samples that were not representative of the entire population (19–21). In this paper, we are particularly attentive to the effects of political orientation and attitudes towards science on public perceptions of the efficacy of HC. Indeed, research on public controversies surrounding science suggests that political orientation plays a role in the acceptance or refusal of certain medical technologies (22,23). More generally, political orientation appears to influence public perceptions of the scientific consensus (24,25). This was likely to be the case during the COVID-19 pandemic in France given that many political representatives, on both sides of the political spectrum, became personally involved in advocating for HC or defending Professor Didier Raoult and that the debate around this treatment was a major topic in the political news (26). Available studies also suggest that attitudes towards science are an important factor in the perceived efficacy of certain treatments (27). Thus, numerous studies have shown that adherence to false beliefs on topics ranging from the danger of vaccines to creationism is correlated with interest and trust in science in general (28,29).

In addition to the issues raised by a pandemic that has been exceptional in its scope and impact, the controversy over HC brought to the fore the issues for health democracy that can arise with the unregulated media coverage of scientific issues in a context where patient autonomy and public engagement in health are encouraged. In France, after a period of intense coverage, the mainstream media reported the scientific consensus on the inefficacy of HC. Yet, some doctors—especially Professor Didier Raoult—continued to defend the efficacy of HC on social networks and, in some cases, to prescribe the drug to COVID-19 patients. Several studies have shown that the correction of false information has less effect than its initial communication (30). Misinformation can even be amplified by contentious groups. We can therefore expect that people who trust science, the mainstream media and feel closest to the governing party have followed the scientific consensus on the inefficacy of HC, and conversely, that those who do not continue to hold views that go against this consensus.

After reviewing the evolution of public debates on HC in France, this paper explores the different factors that influenced perceptions of the efficacy of HC between April 2020 and June 2021 based on 5 surveys conducted on representative samples of the French population. We show that public perceptions of the drug were less polarized than suggested by the media at the time: not only did a large proportion of respondents declare that they were uncertain about the efficacy of HC, but levels of uncertainty remained high throughout the study period. We also show that political orientation and trust in science or the government were continuously associated with the belief in the efficacy of HC.

Evolution of public debates on HC in France between April 2020 and June 2021

While collective mobilizations around potential treatments have occurred in other epidemic contexts —such as AZT for HIV (Epstein, 1996)—the temporality and scope of the COVID-19 pandemic gave exceptional and international public visibility to the therapeutic promise of HC (31). The debates surrounding HC are now considered exemplary of the issues involved in the representation of science

in the public sphere (32). In France, these debates were particularly intense from March to June 2020. They touched upon a variety of issues ranging from the merits of clinical trials, the ethical dilemmas facing doctors in a context of uncertainty, the risk of putting unfounded hopes into new (or old)treatments and the relationship between science, pharmaceutical companies and politicians (15,26). The debates over HC were also linked to France's colonial history. In the 17the century, a scientific and political controversy emerged around the use of quinquina (33). More recently, HC has been used massively in the fight against malaria in former French colonies including northern African countries. Professor Raoult, a major advocate of HC use against COVID largely drew on this colonial and postcolonial history to call into question the necessity and quality of contemporary scientific norms (34).

Figure 1. Evolution of attitudes toward HC in France and media coverage

The mainstream media began to take an interest in this potential treatment after the regional press broadcast the 25 February statement posted by Professor Raoult on the social media accounts of the University Hospital Institute Méditerranée Infection (IHU) (26). With the gradual recognition of the severity of the COVID-19 pandemic, President Emmanuel Macron announced the lockdown of the country on 16 March, effective the day after. That same day, Professor Raoult posted a video that went viral in which he presented the results of a clinical study by the IHU supporting the efficacy of HC. In this context of urgency and uncertainty, the various media widely echoed the ensuing debates, giving voice to a diversity of stakeholders (35). Internationally, Elon Musk and Donald Trump repeated Professors Raoult's claims, thereby increasing media coverage of HC (9).

In France, media discussions of emerging clinical data on HC were accompanied by a political debate. On 3 April, a former Minister of Health, Philippe Douste-Blazy, launched a petition to allow doctors to prescribe the drug. This demand was taken up by different political figures, especially by prominent members of the main conservative party « Les Républicains ». Despite the lack of evidence, the acting Minister of Health Olivier Veran issued a decree on 25 March authorizing the prescription of

HC for serious cases in the hospital setting (2020-314). On 27 March, Professor Raoult posted the results of another IHU study on social networks, and his team continued to promote HC for the early management of COVID-19. This high-profile promotion prompted several intellectuals and media personalities to come to the IHU to be treated and to make the case for the drug. Professor Raoult and the IHU gradually entered "pop culture," both in the form of cultural expressions (tags, paintings, tattoos) and via a very active Facebook group (created on 20 March) that led to intense exchanges on social networks (36). A mobilization for the generalization of the use of HC took place, despite the French government's reluctance and the COVID-19 Scientific Council's reminder to respect the rules of clinical research (37). An IFOP survey reported that at the beginning of April 2020, 98% of French people knew what HC was and 59% believed that it was effective against COVID-19 (18). As more and more clinical data became available, the efficacy of HC was increasingly contested by the scientific community. The trajectory of public debates was nevertheless disrupted by what came to be known as the "Lancet gate" scandal. Indeed, a study reporting the high toxicity of HC in the Lancet on 22 May was retracted on June 4 for fraudulent data, casting doubt on the growing scientific consensus. While this study had led to the suspension of the WHO trials and to the publication on 27 May of a French decree prohibiting the prescription of HC for the treatment of COVID-19, its retraction reinforced the positions of HC promoters, who loudly denounced the quality of international research. Around the same time, meta-analyses were published that pointed to the inefficacy of HC against COVID-19. The intermediate results of the Recovery trial published on 5 June showed an absence of effect of HC, and the WHO Solidarity trial published on 15 October confirmed this finding (5). In view of these data, the WHO officially declared HC to be ineffective against COVID-19. These events, however, were insufficient to stop some doctors from promoting HC in the media, and Professor Raoult continued to defend HC on the social media accounts of the IHU and in scientific articles. Nevertheless, the promoters of HC became increasingly marginalized, and media coverage of the drug began to decrease (see Figure 1). A recent report by the CNRS ethics committee criticized the behavior of HC promoters, explicitly describing it as a form of scientific populism (38).

Methods

Data collection

This study draws on data from five surveys conducted between 7 April 2020 and 9 June 2021 as part of two research projects: COCONEL (dir. Patrick Peretti-Wattel) and TRACTRUST (dir. Laetitia Atlani-Duault). The COCONEL survey was approved by the ethics committee of the IHU (#2020-018) and the TRACTRUST survey by the IRB of the Biomedical Research Institute INSERM CEEI (#20-722). The surveys consisted of self-administered online questionnaires and were conducted on representative samples of the French population. Quota sampling was used to match the French general population with regards to gender, age and population density in the region of residence (as per official census data). The characteristics of the five surveys are presented in Table 1.

Because public debates on HC evolved quite rapidly, we reformulated the main questions and included new variables in the surveys throughout the study. While this limited the comparability of the data, our study nevertheless offers a unique look at the evolution of public perceptions of the efficacy of HC in France over more than a year.

In the first two surveys in April, a filter question asked respondents whether or not they knew the chloroquine-based protocol, and a second question asked those who knew this protocol: “In your opinion, is this chloroquine protocol an effective or ineffective treatment against Coronavirus?” Responses options were: “Yes,” “No,” and “I don’t know.” In the last three surveys (June 2020, November 2020 and June 2021), the filter question was no longer asked because the overwhelming majority of French people had heard about HC by June 2020. In view of the fact that public debates increasingly focused on the developing scientific consensus, the second question was changed to: “In your opinion, is the current state of knowledge sufficient to settle the scientific debate on the efficacy of chloroquine and its derivatives against the coronavirus?” Response options were: “Yes, and I think chloroquine and its derivatives are a good treatment against coronavirus,” “Yes, and I

think chloroquine and its derivatives are not a good treatment against coronavirus," "No, I think data are still insufficient" and "I don't know."

In accordance with the above questions, public perceptions of the efficacy of HC were recoded in the first two surveys into the following three modalities: "belief that HC is effective," "belief that HC is ineffective," and "uncertainty." In the last three surveys, these perceptions were recoded into the following four modalities: "belief that HC is effective," "belief that HC is ineffective," "uncertainty due to insufficient data," and "uncertainty due to not knowing."

The following variables were collected in all five surveys: gender, age, education level, income and political orientation. Given the increasing focus on the developing scientific consensus in public debates, the following variables were collected in the last three surveys: level of politicization, interest and trust in science, and trust in the government.

Name of the survey	Date of administration	Number of respondents
COCONEL1	7-9 April 2020	1,006
COCONEL2	23-27 April 2020	1,004
COCONEL3	19-24 June 2020	2,006
TRACTRUST1	13-16 November 2020	1,014
TRACTRUST2	8-9 June 2021	1,005

Table 1 – Characteristics of the five surveys

Statistical analysis.

Several variables were recoded to ensure comparability and interpretability: "Educational level" was recoded into three groups and "age" was recoded into four groups.

The association between variables was measured using Pearson's correlation coefficient for numeric variables and the chi-square test for categorical variables. Estimated proportions were interpreted based on the margins of error provided by pooling institutes, which ranged from 1.4 to 3.1 points.

The factors associated with perceptions of the efficacy of HC were explored using binomial logistic regression analyses. A theory-driven variable selection was performed. Statistical analyses were conducted using Python (Pandas–Scipy–Statsmodel).

Results

A declining belief in the efficacy of hydroxychloroquine with high levels of uncertainty

Following peak media exposure in March 2020 (Figure 1), almost all respondents had heard about hydroxychloroquine, with only 7% declaring that they had never heard about it in early April. The majority of respondents were uncertain about the efficacy of HC, either due to insufficient data or due to not knowing. Moreover, 35% of respondents believed that HC is effective against COVID-19, and 6% believed that it is ineffective (Table 1).

Table 2. Distribution of attitudes toward HC socio-demographic characteristics and political affiliation

The proportion of respondents who believed in the efficacy of HC decreased rapidly from 35% to 20% between April and June 2020. It remained low until June 2021, when 14% of respondents stated that they believed HC to be effective. The proportion of respondents who believed that HC is ineffective rose gradually from 6% in April 2020 to 21% in June 2021. These findings contrast with the large proportion of respondents who were uncertain about the efficacy of HC (either due to insufficient data or due to not knowing), a figure that increased slightly from 60% in April 2020 to 64% in June 2021.

Factors associated with the belief in the efficacy of hydroxychloroquine and their evolution

To account for the main factors associated with the belief in the efficacy of HC, we performed a logistic regression on the entire dataset. The dates of each survey were included in the model as covariates (Table 2).

Table 3. Binomial logistic regressions of the answers regarding HC (over the 5 surveys)

The model showed a strong effect of time on public perceptions of the efficacy of HC. After adjusting for this effect, we observed a very strong association between political orientation and the belief in the efficacy of HC. All other things being equal, respondents who were close to the more radical parties (far right and far left) were more likely to believe in the efficacy of HC than those who were close to the political center (2.48 [1.95-3.15] and 1.87 [1.44-2.43]). Likewise, respondents who were close to the right were more likely to hold this belief than those who were close to the political center (1.43 [1.10-1.85]). Respondents who were not close to any political party were less likely to believe in the efficacy of HC compared to those who were close to the political center (0.38 [0.29-0.49]).

Older respondents (above 70 years) were more likely to believe in the efficacy of HC than younger ones (below 35 years) (1.36 [1.10-1.69]). Respondents with a high level of education were more likely to believe that HC is ineffective than those with a low level of education (1.47 [1.20-1.79]).

The models per survey (Supplementary A and B) show that respondents with a high level of education were more likely than those with a low level to believe that HC is effective at the beginning of the study period (1.77 [1.27-2.49] for April 2020 survey), but more likely to believe that it is ineffective at the end of this period (1.64 [1.12-2.40] for the June 2021 survey). The effect of political orientation on the belief in the efficacy of HC was very strong. Thus, respondents who feel close to far right parties were more likely than those close to the political center to believe that HC is effective at the beginning of the study period (3.33 [1.93-5.73] for the April 2020 survey) and all the way until the end (2.89 [1.43-5.84] for the June 2021 survey). Respondents close to far left parties were also more likely than those close to the political center to hold this belief from June 2020 onwards (2.44 [1.10-5.37] for the June 2020 survey).

Factors associated with the belief in the efficacy of hydroxychloroquine after the scientific consensus was reached

Table 4. Binomial logistic regressions of the answers regarding HC (over the survey of November 2020 and June 2021)

In June 2020, a scientific consensus on the inefficacy of HC began to form (see section on the evolution of public debates). In view of this, specific questions on politicization, interest and trust in science, and trust in the government were included in the November 2020 and June 2021 surveys. The data collected in these two surveys were combined in the binomial logistic model (Table 3).

After the consensus was established, women were less likely than men to believe that HC is ineffective (0.63 [0.49-0.82]). Respondents with a high level of education were more likely to believe that HC is ineffective (1.62 [1.19-2.21] compared to respondents with a low level of education), as were high-income earners (2.16 [1.13-4.14] compared to low-income earners).

After adjusting for level of politicization, the effect of political orientation disappeared, except for respondents close to the far right, who were less likely than those close to the political center to believe that HC is ineffective (0.38 [0.22-0.66]). By contrast, trust in the government had a strong effect on the belief in the efficacy of HC. Thus, respondents with a low level of trust in the government were twice as likely to believe that HC is effective (2.02 [1.46-2.79]) and twice less likely to believe that it is ineffective (0.51 [0.39-0.67]) than those with a high level of trust. The level of politicization also had an effect on the belief in the efficacy of HC, as respondents with a high level of politicization were twice as likely to believe in the efficacy of HC than those with a low level of politicization (1.85 [1.32-2.59]).

Trust in science also appeared to have an effect, as those with a low level of trust were twice as likely to believe that HC is effective than those with a high level of trust (2.20 [1.61-3.02]). Respondents who had no interest in science were twice less likely to accept the scientific consensus that HC is ineffective than those who did (0.62 [0.47-0.81]).

The importance of uncertainty

By the end of 2020 and during 2021, the majority of respondents were uncertain about the efficacy of HC, with 41.5% stating that the data were insufficient to decide whether or not HC is effective and 25.2% stating that they did not know. While political orientation, level of politicization, trust in science, and trust in the government determined the ratio between the belief that HC is effective and the belief that it is ineffective, uncertainty consistently remained the majority option (Figure 2).

Figure 2. Distribution of attitude toward HC regarding political identification and trust in science and government.

The factors associated with uncertainty due to insufficient data were not the same as those associated with uncertainty due to not knowing (Table 3). Indeed, the factors that distinguished respondents who stated that they were uncertain due to insufficient data were a high level of trust in science (0.68 [0.52-0.90] compared to respondents with a low level of trust in science) and a high income (1.75 [1.20-2.55] compared to low-income earners). By contrast, several factors were associated with uncertainty due to not knowing: being a woman (1.45 [1.14-1.83] compared to men), having a low level of education (0.61 [0.45-0.81] compared to respondents with a low level of education), feeling close to no party (1.87 [1.18-2.96] compared to respondents close to the political center), and having a low level of politicization (0.61 [0.46-0.82] compared to respondents with a high level of politicization). Having no interest in science (1.96 [1.08-3.57] compared to respondents with an interest in science) and answering “don’t know” to the question on trust in the government (1.96 [1.08-3.57]) or trust in science (5.51 [3.20-9.50]) were also associated with uncertainty due to not knowing.

Discussion

The controversy over HC will long remain a cautionary tale for researchers (31), as it brought to the fore the limits of pre-publications, the dangers of publicizing certain studies, and the importance of conducting high-quality clinical trials. The treatment of the scientific controversy by journalists, intellectuals, scientists, and political representatives is also a case study on how to publicly discuss

medical treatments, and more generally scientific research, in a context of uncertainty (26). Within the scientific community, the handling of the controversy reignited a number of debates on questions of publication and citation and more generally on public perceptions of medical research (32). While it is necessary to draw lessons from this episode for the conduct of research, whose temporality does not correspond to that of the media (39), the scope and intensity of the debates on HC also highlight the importance of better understanding their public reception. It would be a mistake to consider this episode as belonging entirely to the past. Beyond the fact that certain actors, in particular doctors, have continued to advocate HC for the treatment of COVID-19, this controversy could have long-term consequences felt in the years to come in the areas of medicine, science, and politics. The continued centrality of HC in conspiracy theories promoted by far-right organizations is a case in point (36).

Have the urgency of the COVID-19 pandemic and the desire to believe in a cure resulted in a polarization between promoters and opponents of HC? The IFOP survey published on April 6, 2020, found that 59% of French people believed in the efficacy of HC, which suggested that the enthusiasm for this treatment was strong in the early stages of the pandemic (with 21% that answered “don’t know”) (18). The survey that we conducted one week later showed that only one third of respondents (35%) considered HC effective against COVID-19, reflecting a rapid decline in this enthusiasm. Yet, peaks in demand for HC and in internet searches do not mean that everyone was carried away by hope, even though many may have initially been seduced by this therapeutic promise. Indeed, while our April 2020 survey found a low proportion of respondents who believed that HC is ineffective, it also found a high proportion of respondents who were uncertain about the efficacy of the drug. Moreover, perceptions of HC evolved rapidly over the study period. The proportion of respondents who believed HC to be effective decreased gradually, and conversely the proportion of those who believed it to be ineffective rose over time. However, the total number of respondents who believed HC to be effective or ineffective remained small compared to that of

respondents who were uncertain. These findings indicate that public perceptions of HC were less polarized than suggested by the media.

Perceptions of the efficacy of HC were socially distributed. From the beginning of the study period, there was a very strong association between political orientation and the belief that HC is effective. Respondents close to the far right, and later those close to the right or the far left, were more likely to hold this belief than those close to the political center. This could be an effect of the political opposition to the governmental policies, especially for respondents from the far left who criticized the lockdown strategy for its effects on social inequalities. This finding may also be explained by the fact that political figures of the right and far right defended HC (26) as part of their criticism of the government's handling of the crisis and its refusal to authorize this promising treatment. Another possible explanation is that HC was largely promoted on social media accounts associated with the right and the far right (36). Conversely, respondents close to the political center, who tend to adhere to the recommendations of health agencies, were more likely to believe that HC is ineffective. The politicization of HC is also reflected in the fact that respondents with no political orientation were more likely to state that they were unsure about its efficacy.

The results of the November 2020 and June 2021 surveys (Table 3) shed light on the effects of politicization and attitudes towards science. The association between level of politicization and the belief that HC is effective suggests that perceptions of the drug were largely rooted in a political reading of the government's handling of the crisis. Trust in science diminished the likelihood of believing that HC is effective and, conversely, increased the likelihood of believing that it is ineffective. This is consistent with the existing literature, particularly on vaccination, which shows that attitudes towards science, and more generally towards institutions, has an effect on the perception of new medical technologies (16,40). Yet, while the effect of trust in science was strong in our study (at a factor of nearly 2), it does not fully explain perceptions of HC among the French public.

Public debates on the efficacy of HC are at the crossroads of different temporalities: that of the pandemic, marked among other things by the implementation of governmental measures like the lockdown, that of the media, which put certain issues on the agenda but not others, that of scientific research, in particular the conduct of clinical trials, and then that of exchanges between individuals, whether in the family circle or in digital spaces. The statements of public authorities were cautious at first, but eventually made it clear that HC is ineffective against COVID-19. The media initially reported on the promises of this treatment, then on the lack of evidence for its efficacy, and finally on the negative results of clinical trials. Learned societies such as the French Society of Pharmacology and Therapeutics issued statements mentioning that HC is ineffective. Our five surveys reflect these temporalities. They show a gradual decline in the number of respondents who believed in the efficacy of HC and an increase in the number of respondents who believed in its inefficacy. Those who continued to defend this treatment even after the scientific consensus was reached had the lowest levels of trust in institutions and the government, and were unsurprisingly largely associated with the political parties most opposed to the government. Thus, in June 2021, 45% of respondents who were close to the political center believed that HC is ineffective, while only 11% of those who were close to the far right held this belief. This difference may be explained by differentiated uses of information sources, with alternative media and social networks pursuing the campaign in support of HC and Professor Raoult. Another possible explanation is the persistence of the memory of the controversy among respondents with the lowest levels of trust in institutions and the government. Importantly, the proportion of respondents who believed in the efficacy or the inefficacy of HC (i.e. respondents who had an opinion on the drug) and that of respondents who were uncertain about its efficacy remained stable throughout the study period. Indeed, levels of uncertainty remained high even after the scientific consensus was reached. It should be noted, however, that respondents who were uncertain due to not knowing were not the same as those who were uncertain due to insufficient data. Uncertainty due to not knowing was in fact associated with not having an opinion

on other aspects of the pandemic. These findings indicate that perceptions of the drug were not overly polarized, and therefore highlight the importance of measuring uncertainty to avoid artificially polarizing analyses. Research in the field of agnotology, which has developed over the last decade as part of the history and sociology of science, can help to make sense of these findings. This research examines how certain actors work to maintain false beliefs or keep controversies alive even after a scientific consensus has been reached (41). Some of the most notable examples are the tobacco industry's creation of uncertainty about the effects of smoking, the oil industry's efforts to cast doubt on the human origins of global warming, and the sugar industry's attempts to orient research towards the hypothesis that fat rather than sugar is the cause of obesity. This research has shown that public controversies allow for the instrumentalization of scientific knowledge (42,43) and that moments of intense public debate have lasting effects since doubts about their actual outcome can be remobilized later to defend certain positions—as illustrated by the case of vaccine hesitancy (16). Insofar as the debates on HC gave visibility to different conceptions of science and to the problems of knowledge production in biomedical research—as evidenced by the "Lancet gate" scandal, which seems to have been a turning point, and by the multiplication of working papers of varying quality—the high levels of uncertainty observed in our study can easily be instrumentalized towards a critique of institutions. More generally, uncertainty can encourage distrust in the efficacy (or inefficacy) of certain treatments and can push part of the public towards the most radical forms of complementary and alternative medicine. This is a major concern given that alternative treatments can also contribute to the propagation of conspiracy theories (21).

Lastly, our analysis of public perceptions of HC call into question the idea that belief in fallacious ideas is the product of low levels of education. While having a high level of education was associated in our study with having an opinion on HC (as opposed to being uncertain), this opinion was not necessarily in line with the developing scientific consensus, especially in the early stages of the pandemic. Conversely, a low level of education was associated not so much with the belief in the efficacy of HC, but with not knowing whether or not HC is effective. When studying public

perceptions of controversies, it is important to take into consideration the fact that different social groups have very different levels of engagement with media debates. As studies on ordinary relations to politics have shown (44), one of the main social divides in France is that between, on the one hand, people whose cultural practices connect them to the public sphere and who have positive attitudes towards institutions, and, on the other hand, people who are not connected to the public sphere and who display much lower levels of trust in the state and its actors (45).

Conclusion

While the controversy over HC is not the first nor the last to emerge surrounding a new but ultimately disappointing treatment (46,47), it received enormous media coverage in the early stages of the COVID-19 pandemic in France. After the scientific consensus on the inefficacy of HC was reached, public health authorities issued statements that were clear and readily available, but that received little attention in public debates. Because media coverage of scientific controversies is typically higher in times of uncertainty than after these controversies have died down, the publicization of therapeutic promises can have lasting consequences on attitudes towards science and medicine (48), and this despite the existence of fact-checking activity. Researchers should take into consideration this asymmetry when publicly discussing medical treatments or vaccines (49), and more generally scientific research, in a context of uncertainty.

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