

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

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- 2 hydroxychloroquine in France between April 2020 and June 2021
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- 15 Abstract

16 Objectives:

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

22 This article draws on 5 surveys conducted among representative samples of the French population

23 (projects COCONEL and TRACTRUST ; quota method, N=1006 ; 1004 ; 2006 ; 1014 and 1005). We

24 asked questions on the effectiveness of chloroquine against COVID-19. We also collected

25 sociodemographic variables and attitudes toward politics and science.

26 <u>Results</u>

27 Between April and June 2021, the proportion of respondents who believed in the efficacy of HC

28 decreased rapidly from 35% to 14%. The proportion of respondents who believed that HC is

29 ineffective rose gradually from 6% to 21%.

30 After adjusting for the temporal effect, the logistic regression showed a very strong association

31 between political orientation and the belief in the efficacy of HC. Respondents who felt closest to the

32 more radical parties (far right and far left) were more likely to believe in the efficacy of HC than those

33 who felt closest to the political center (O.R. 2.48 [1.95-3.15] and 1.87 [1.44-2.43]).

34 The role of trust in the government and in science and of the degree of political engagement were

35 investigated in the two waves conducted after the scientific consensus was established during the

36 summer of 2020. High levels of trust in the government and in science and of politicization are

37 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

40 not know.

41 <u>Conclusion</u>

42 Because media coverage of scientific controversies is higher in times of uncertainty than after these

43 controversies have died down, the publicization of therapeutic promises can have lasting

44 consequences on attitudes towards science and medicine.

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

46 Introduction

47 Of all the treatments that have raised and dashed hopes of curing COVID-19, chloroquine and its 48 derivatives, especially hydroxychloroquine (hereafter HC) occupies a special place because of the 49 intensity of the debates surrounding it. In the early stages of the pandemic, HC, were widely 50 commented upon both within the scientific community and in the media. This public debate had 51 several consequences. First, they sent research on unfruitful avenues, as evidenced by the 52 multiplication of clinical trials on HC-often of poor quality (1,2)-that yielded negative results 53 (3,4) and by the difficulties in recruiting patients for trials that tested other molecules (5). Second, 54 several people who took HC to treat COVID-19 infection, either through self-medication or 55 prescription, suffered adverse effects (6-8), and patients affected by diseases commonly treated with 56 HC (such as malaria or lupus) faced stock-outs due to an explosion of demand for the drug (9). Third, 57 the debates on hydroxychloroquine had a temporary impact on health policy in some countries, 58 where exceptional authorizations of use were enacted, and a durable one in others (10,11), such as 59 in Brazil where a "hydroxychloroquine alliance" was formed between intellectuals, physicians, and 60 politicians (12). Fourth and lastly, the confrontational nature of the debate led to insults and attacks 61 against doctors and scientists on the Internet (13,14) as well as legal actions against scientific 62 advisers to governments, such as in France, accused of mass killing for asking to respect the rules of 63 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 71 HIV/AIDS epidemic during the COVID-19 pandemic shows that controversies surrounding some

72 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.

76 Indeed, in a context where disease management is performed under a medical monopoly,

77 therapeutic promises are generally seen as concerning mainly doctors and patients. The first studies 78 on attitudes towards HC have focused mainly on doctors (17). Few studies, in France or abroad, have 79 explored the factors involved in the formation of public opinion on the efficacy of HC. Although the 80 French polling institute IFOP did include a question on perceptions of the efficacy of HC in its April 81 2020 survey showing a very high of respondents believing in the efficacy of HC (59%), this has not led 82 to in-depth studies of the factors influencing these perceptions (18). Outside of France, available 83 studies on the topic were conducted on samples that were not representative of the entire 84 population (19-21). In this paper, we are particularly attentive to the effects of political orientation 85 and attitudes towards science on public perceptions of the efficacy of HC. Indeed, research on public 86 controversies surrounding science suggests that political orientation plays a role in the acceptance or 87 refusal of certain medical technologies (22,23). More generally, political orientation appears to 88 influence public perceptions of the scientific consensus (24,25). This was likely to be the case during 89 the COVID-19 pandemic in France given that many political representatives, on both sides of the 90 political spectrum, became personally involved in advocating for HC or defending Professor Didier 91 Raoult and that the debate around this treatment was a major topic in the political news (26). 92 Available studies also suggest that attitudes towards science are an important factor in the perceived 93 efficacy of certain treatments (27). Thus, numerous studies have shown that adherence to false 94 beliefs on topics ranging from the danger of vaccines to creationism is correlated with interest and 95 trust in science in general (28,29).

96 In addition to the issues raised by a pandemic that has been exceptional in its scope and impact, the 97 controversy over HC brought to the fore the issues for health democracy that can arise with the 98 unregulated media coverage of scientific issues in a context where patient autonomy and public 99 engagement in health are encouraged. In France, after a period of intense coverage, the mainstream 100 media reported the scientific consensus on the inefficacy of HC. Yet, some doctors—especially 101 Professor Didier Raoult—continued to defend the efficacy of HC on social networks and, in some 102 cases, to prescribe the drug to COVID-19 patients. Several studies have shown that the correction of 103 false information has less effect than its initial communication (30). Misinformation can even be 104 amplified by contentious groups. We can therefore expect that people who trust science, the 105 mainstream media and feel closest to the governing party have followed the scientific consensus on 106 the inefficacy of HC, and conversely, that those who do not continue to hold views that go against 107 this consensus.

108 After reviewing the evolution of public debates on HC in France, this paper explores the different 109 factors that influenced perceptions of the efficacy of HC between April 2020 and June 2021 based on 110 5 surveys conducted on representative samples of the French population. We show that public 111 perceptions of the drug were less polarized than suggested by the media at the time: not only did a 112 large proportion of respondents declare that they were uncertain about the efficacy of HC, but levels 113 of uncertainty remained high throughout the study period. We also show that political orientation 114 and trust in science or the government were continuously associated with the belief in the efficacy of 115 HC.

116 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

121 in the public sphere (32). In France, these debates were particularly intense from March to June 122 2020. They touched upon a variety of issues ranging from the merits of clinical trials, the ethical 123 dilemmas facing doctors in a context of uncertainty, the risk of putting unfounded hopes into new (or 124 old)treatments and the relationship between science, pharmaceutical companies and politicians 125 (15,26). The debates over HC were also linked to France's colonial history. In the 17the century, a 126 scientific and political controversy emerged around the use of quinquina (33). More recently, HC has 127 been used massively in the fight against malaria in former French colonies including northern African 128 countries. Professor Raoult, a major advocate of HC use against COVID largely drew on this colonial 129 and postcolonial history to call into question the necessity and quality of contemporary scientific 130 norms (34).

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

132 The mainstream media began to take an interest in this potential treatment after the regional press 133 broadcast the 25 February statement posted by Professor Raoult on the social media accounts of the 134 University Hospital Institute Méditerranée Infection (IHU) (26). With the gradual recognition of the 135 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 136 137 went viral in which he presented the results of a clinical study by the IHU supporting the efficacy of 138 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 139 140 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

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146 HC for serious cases in the hospital setting (2020-314). On 27 March, Professor Raoult posted the 147 results of another IHU study on social networks, and his team continued to promote HC for the early 148 management of COVID-19. This high-profile promotion prompted several intellectuals and media 149 personalities to come to the IHU to be treated and to make the case for the drug. Professor Raoult 150 and the IHU gradually entered "pop culture," both in the form of cultural expressions (tags, paintings, 151 tattoos) and via a very active Facebook group (created on 20 March) that led to intense exchanges on 152 social networks (36). A mobilization for the generalization of the use of HC took place, despite the 153 French government's reluctance and the COVID-19 Scientific Council's reminder to respect the rules 154 of clinical research (37). An IFOP survey reported that at the beginning of April 2020, 98% of French 155 people knew what HC was and 59% believed that it was effective against COVID-19 (18). As more and 156 more clinical data became available, the efficacy of HC was increasingly contested by the scientific 157 community. The trajectory of public debates was nevertheless disrupted by what came to be known 158 as the "Lancet gate" scandal. Indeed, a study reporting the high toxicity of HC in the Lancet on 22 159 May was retracted on June 4 for fraudulent data, casting doubt on the growing scientific consensus. 160 While this study had led to the suspension of the WHO trials and to the publication on 27 May of a 161 French decree prohibiting the prescription of HC for the treatment of COVID-19, its retraction 162 reinforced the positions of HC promoters, who loudly denounced the quality of international 163 research. Around the same time, meta-analyses were published that pointed to the inefficacy of HC 164 against COVID-19. The intermediate results of the Recovery trial published on 5 June showed an 165 absence of effect of HC, and the WHO Solidarity trial published on 15 October confirmed this finding 166 (5). In view of these data, the WHO officially declared HC to be ineffective against COVID-19. These 167 events, however, were insufficient to stop some doctors from promoting HC in the media, and 168 Professor Raoult continued to defend HC on the social media accounts of the IHU and in scientific 169 articles. Nevertheless, the promoters of HC became increasingly marginalized, and media coverage of 170 the drug began to decrease (see Figure 1). A recent report by the CNRS ethics committee criticized 171 the behavior of HC promoters, explicitly describing it as a form of scientific populism (38).

13

172 Methods

173 Data collection

174 This study draws on data from five surveys conducted between 7 April 2020 and 9 June 2021 as part 175 of two research projects: COCONEL (dir. Patrick Peretti-Wattel) and TRACTRUST (dir. Laetitia Atlani-176 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 177 178 surveys consisted of self-administered online questionnaires and were conducted on representative 179 samples of the French population. Quota sampling was used to match the French general population 180 with regards to gender, age and population density in the region of residence (as per official census 181 data). The characteristics of the five surveys are presented in Table 1. 182 Because public debates on HC evolved quite rapidly, we reformulated the main questions and 183 included new variables in the surveys throughout the study. While this limited the comparability of 184 the data, our study nevertheless offers a unique look at the evolution of public perceptions of the 185 efficacy of HC in France over more than a year. 186 In the first two surveys in April, a filter question asked respondents whether or not they knew the 187 chloroquine-based protocol, and a second question asked those who knew this protocol: "In your 188 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, 189 190 November 2020 and June 2021), the filter question was no longer asked because the overwhelming 191 majority of French people had heard about HC by June 2020. In view of the fact that public debates 192 increasingly focused on the developing scientific consensus, the second question was changed to: "In 193 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, 194

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."

203 The following variables were collected in all five surveys: gender, age, education level, income and

204 political orientation. Given the increasing focus on the developing scientific consensus in public

205 debates, the following variables were collected in the last three surveys: level of politicization,

206 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

207

208 Table 1 - Characteristics of the five surveys

209 <u>Statistical analysis.</u>

- 210 Several variables were recoded to ensure comparability and interpretability: "Educational level" was
- 211 recoded into three groups and "age" was recoded into four groups.
- 212 The association between variables was measured using Pearson's correlation coefficient for numeric
- 213 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.

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

218 Results

219 <u>A declining belief in the efficacy of hydroxychloroquine with high levels of uncertainty</u>

- 220 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
- 222 majority of respondents were uncertain about the efficacy of HC, either due to insufficient data or
- 223 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).

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

226 The proportion of respondents who believed in the efficacy of HC decreased rapidly from 35% to 20%

227 between April and June 2020. It remained low until June 2021, when 14% of respondents stated that

228 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

- 230 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.

233 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).

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

238 The model showed a strong effect of time on public perceptions of the efficacy of HC. After adjusting 239 for this effect, we observed a very strong association between political orientation and the belief in 240 the efficacy of HC. All other things being equal, respondents who were close to the more radical 241 parties (far right and far left) were more likely to believe in the efficacy of HC than those who were 242 close to the political center (2.48 [1.95-3.15] and 1.87 [1.44-2.43]). Likewise, respondents who were 243 close to the right were more likely to hold this belief than those who were close to the political 244 center (1.43 [1.10-1.85]). Respondents who were not close to any political party were less likely to 245 believe in the efficacy of HC compared to those who were close to the political center (0.38 [0.29-246 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]).

250 The models per survey (Supplementary A and B) show that respondents with a high level of 251 education were more likely than those with a low level to believe that HC is effective at the beginning 252 of the study period (1.77 [1.27-2.49] for April 2020 survey), but more likely to believe that it is 253 ineffective at the end of this period (1.64 [1.12-2.40] for the June 2021 survey). The effect of political 254 orientation on the belief in the efficacy of HC was very strong. Thus, respondents who feel close to 255 far right parties were more likely than those close to the political center to believe that HC is 256 effective at the beginning of the study period (3.33 [1.93-5.73] for the April 2020 survey) and all the 257 way until the end (2.89 [1.43-5.84] for the June 2021 survey). Respondents close to far left parties 258 were also more likely than those close to the political center to hold this belief from June 2020 259 onwards (2.44 [1.10-5.37] for the June 2020 survey).

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

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

264 In June 2020, a scientific consensus on the inefficacy of HC began to form (see section on the 265 evolution of public debates). In view of this, specific questions on politicization, interest and trust in 266 science, and trust in the government were included in the November 2020 and June 2021 surveys. 267 The data collected in these two surveys were combined in the binomial logistic model (Table 3). 268 After the consensus was established, women were less likely than men to believe that HC is 269 ineffective (0.63 [0.49-0.82]). Respondents with a high level of education were more likely to believe 270 that HC is ineffective (1.62 [1.19-2.21] compared to respondents with a low level of education), as 271 were high-income earners (2.16 [1.13-4.14] compared to low-income earners). 272 After adjusting for level of politicization, the effect of political orientation disappeared, except for 273 respondents close to the far right, who were less likely than those close to the political center to 274 believe that HC is ineffective (0.38 [0.22-0.66]). By contrast, trust in the government had a strong 275 effect on the belief in the efficacy of HC. Thus, respondents with a low level of trust in the 276 government were twice as likely to believe that HC is effective (2.02 [1.46-2.79]) and twice less likely 277 to believe that it is ineffective (0.51 [0.39-0.67]) than those with a high level of trust. The level of 278 politicization also had an effect on the belief in the efficacy of HC, as respondents with a high level of 279 politicization were twice as likely to believe in the efficacy of HC than those with a low level of 280 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]).

285 <u>The importance of uncertainty</u>

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.

293 The factors associated with uncertainty due to insufficient data were not the same as those 294 associated with uncertainty due to not knowing (Table 3). Indeed, the factors that distinguished 295 respondents who stated that they were uncertain due to insufficient data were a high level of trust in 296 science (0.68 [0.52-0.90] compared to respondents with a low level of trust in science) and a high 297 income (1.75 [1.20-2.55] compared to low-income earners). By contrast, several factors were 298 associated with uncertainty due to not knowing: being a woman (1.45 [1.14-1.83] compared to men), 299 having a low level of education (0.61 [0.45-0.81] compared to respondents with a low level of 300 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 301 302 high level of politicization). Having no interest in science (1.96 [1.08-3.57] compared to respondents 303 with an interest in science) and answering "don't know" to the question on trust in the government 304 (1.96 [1.08-3.57]) or trust in science (5.51 [3.20-9.50]) were also associated with uncertainty due to 305 not knowing.

306 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

311 medical treatments, and more generally scientific research, in a context of uncertainty (26). Within 312 the scientific community, the handling of the controversy reignited a number of debates on 313 questions of publication and citation and more generally on public perceptions of medical research 314 (32). While it is necessary to draw lessons from this episode for the conduct of research, whose 315 temporality does not correspond to that of the media (39), the scope and intensity of the debates on 316 HC also highlight the importance of better understanding their public reception. It would be a 317 mistake to consider this episode as belonging entirely to the past. Beyond the fact that certain actors, 318 in particular doctors, have continued to advocate HC for the treatment of COVID-19, this controversy 319 could have long-term consequences felt in the years to come in the areas of medicine, science, and 320 politics. The continued centrality of HC in conspiracy theories promoted by far-right organizations is a 321 case in point (36).

322 Have the urgency of the COVID-19 pandemic and the desire to believe in a cure resulted in a 323 polarization between promoters and opponents of HC? The IFOP survey published on April 6, 2020, 324 found that 59% of French people believed in the efficacy of HC, which suggested that the enthusiasm 325 for this treatment was strong in the early stages of the pandemic (with 21% that answered "don't 326 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 327 328 enthusiasm. Yet, peaks in demand for HC and in internet searches do not mean that everyone was 329 carried away by hope, even though many may have initially been seduced by this therapeutic 330 promise. Indeed, while our April 2020 survey found a low proportion of respondents who believed 331 that HC is ineffective, it also found a high proportion of respondents who were uncertain about the 332 efficacy of the drug. Moreover, perceptions of HC evolved rapidly over the study period. The 333 proportion of respondents who believed HC to be effective decreased gradually, and conversely the 334 proportion of those who believed it to be ineffective rose over time. However, the total number of 335 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 lesspolarized than suggested by the media.

338 Perceptions of the efficacy of HC were socially distributed. From the beginning of the study period, 339 there was a very strong association between political orientation and the belief that HC is effective. 340 Respondents close to the far right, and later those close to the right or the far left, were more likely 341 to hold this belief than those close to the political center. This could be an effect of the political 342 opposition to the governmental policies, especially for respondents from the far left who criticized 343 the lockdown strategy for its effects on social inequalities. This finding may also be explained by the 344 fact that political figures of the right and far right defended HC (26) as part of their criticism of the 345 government's handling of the crisis and its refusal to authorize this promising treatment. Another 346 possible explanation is that HC was largely promoted on social media accounts associated with the 347 right and the far right (36). Conversely, respondents close to the political center, who tend to adhere 348 to the recommendations of health agencies, were more likely to believe that HC is ineffective. The 349 politicization of HC is also reflected in the fact that respondents with no political orientation were 350 more likely to state that they were unsure about its efficacy.

351

352 The results of the November 2020 and June 2021 surveys (Table 3) shed light on the effects of 353 politicization and attitudes towards science. The association between level of politicization and the 354 belief that HC is effective suggests that perceptions of the drug were largely rooted in a political 355 reading of the government's handling of the crisis. Trust in science diminished the likelihood of 356 believing that HC is effective and, conversely, increased the likelihood of believing that it is 357 ineffective. This is consistent with the existing literature, particularly on vaccination, which shows 358 that attitudes towards science, and more generally towards institutions, has an effect on the 359 perception of new medical technologies (16,40). Yet, while the effect of trust in science was strong in 360 our study (at a factor of nearly 2), it does not fully explain perceptions of HC among the French 361 public.

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363 Public debates on the efficacy of HC are at the crossroads of different temporalities: that of the 364 pandemic, marked among other things by the implementation of governmental measures like the 365 lockdown, that of the media, which put certain issues on the agenda but not others, that of scientific 366 research, in particular the conduct of clinical trials, and then that of exchanges between individuals, 367 whether in the family circle or in digital spaces. The statements of public authorities were cautious at 368 first, but eventually made it clear that HC is ineffective against COVID-19. The media initially reported 369 on the promises of this treatment, then on the lack of evidence for its efficacy, and finally on the 370 negative results of clinical trials. Learned societies such as the French Society of Pharmacology and 371 Therapeutics issued statements mentioning that HC is ineffective. Our five surveys reflect these 372 temporalities. They show a gradual decline in the number of respondents who believed in the 373 efficacy of HC and an increase in the number of respondents who believed in its inefficacy. Those 374 who continued to defend this treatment even after the scientific consensus was reached had the 375 lowest levels of trust in institutions and the government, and were unsurprisingly largely associated 376 with the political parties most opposed to the government. Thus, in June 2021, 45% of respondents 377 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 378 379 information sources, with alternative media and social networks pursuing the campaign in support of 380 HC and Professor Raoult. Another possible explanation is the persistence of the memory of the 381 controversy among respondents with the lowest levels of trust in institutions and the government. 382 Importantly, the proportion of respondents who believed in the efficacy or the inefficacy of HC (i.e. 383 respondents who had an opinion on the drug) and that of respondents who were uncertain about its 384 efficacy remained stable throughout the study period. Indeed, levels of uncertainty remained high 385 even after the scientific consensus was reached. It should be noted, however, that respondents who 386 were uncertain due to not knowing were not the same as those who were uncertain due to 387 insufficient data. Uncertainty due to not knowing was in fact associated with not having an opinion

388 on other aspects of the pandemic. These findings indicate that perceptions of the drug were not 389 overly polarized, and therefore highlight the importance of measuring uncertainty to avoid artificially 390 polarizing analyses. Research in the field of agnotology, which has developed over the last decade as 391 part of the history and sociology of science, can help to make sense of these findings. This research 392 examines how certain actors work to maintain false beliefs or keep controversies alive even after a 393 scientific consensus has been reached (41). Some of the most notable examples are the tobacco 394 industry's creation of uncertainty about the effects of smoking, the oil industry's efforts to cast doubt 395 on the human origins of global warming, and the sugar industry's attempts to orient research 396 towards the hypothesis that fat rather than sugar is the cause of obesity. This research has shown 397 that public controversies allow for the instrumentalization of scientific knowledge (42,43) and that 398 moments of intense public debate have lasting effects since doubts about their actual outcome can 399 be remobilized later to defend certain positions—as illustrated by the case of vaccine hesitancy (16). 400 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 401 402 seems to have been a turning point, and by the multiplication of working papers of varying quality— 403 the high levels of uncertainty observed in our study can easily be instrumentalized towards a critique 404 of institutions. More generally, uncertainty can encourage distrust in the efficacy (or inefficacy) of 405 certain treatments and can push part of the public towards the most radical forms of complementary 406 and alternative medicine. This is a major concern given that alternative treatments can also contribute to the propagation of conspiracy theories (21). 407

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

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414 perceptions of controversies, it is important to take into consideration the fact that different social 415 groups have very different levels of engagement with media debates. As studies on ordinary relations 416 to politics have shown (44), one of the main social divides in France is that between, on the one 417 hand, people whose cultural practices connect them to the public sphere and who have positive 418 attitudes towards institutions, and, on the other hand, people who are not connected to the public 419 sphere and who display much lower levels of trust in the state and its actors (45).

420 Conclusion

421 While the controversy over HC is not the first nor the last to emerge surrounding a new but

422 ultimately disappointing treatment (46,47), it received enormous media coverage in the early stages

423 of the COVID-19 pandemic in France. After the scientific consensus on the inefficacy of HC was

424 reached, public health authorities issued statements that were clear and readily available, but that

425 received little attention in public debates. Because media coverage of scientific controversies is

426 typically higher in times of uncertainty than after these controversies have died down, the

427 publicization of therapeutic promises can have lasting consequences on attitudes towards science

428 and medicine (48), and this despite the existence of fact-checking activity. Researchers should take

429 into consideration this asymmetry when publicly discussing medical treatments or vaccines (49), and

430 more generally scientific research, in a context of uncertainty.

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