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1 Does the public know when a scientific controversy is over? Public perceptions of

2 hydroxychloroquine in France between April 2020 and June 2021

3 Short title: Public perceptions of hydroxychloroquine in France

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16 **Abstract**

17 Objectives:

18 In the early stages of the COVID-19 pandemic, chloroquine and its derivatives such as

19 hydroxychloroquine (HC) were widely commented upon both within the scientific community and in

20 the media. This paper explores the different factors that influenced public perceptions in France of

21 the efficacy of HC as well as their evolution between April 2020 and June 2021.

22 Methods

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

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

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

26   sociodemographic variables and attitudes toward politics and science.

27   Results

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

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

30   ineffective rose gradually from 6% to 21%.

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

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

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

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

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

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

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

38   associated with belief of HC proven inefficacy.

39   Across the whole period, a majority of respondents were uncertain. Even in 2021, 41.5% stated that

40   the data were insufficient to decide whether or not HC is effective and 25.2% stating that they did

41   not know.

42   Conclusion

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

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

45   consequences on attitudes towards science and medicine.

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

47 **Introduction**

48 Of all the treatments that have raised and dashed hopes of curing COVID-19, chloroquine and its

49 derivatives, especially hydroxychloroquine (hereafter HC) occupies a special place because of the

50 intensity of the debates surrounding it. In the early stages of the pandemic, HC, were widely

51 commented upon both within the scientific community and in the media. This public debate had

52 several consequences. First, they sent research on unfruitful avenues, as evidenced by the

53 multiplication of clinical trials on HC—often of poor quality (1,2)—that yielded negative results

54 (3,4) and by the difficulties in recruiting patients for trials that tested other molecules (5). Second,

55 several people who took HC to treat COVID-19 infection, either through self-medication or

56 prescription, suffered adverse effects (6–8), and patients affected by diseases commonly treated with

57 HC (such as malaria or lupus) faced stock-outs due to an explosion of demand for the drug (9). Third,

58 the debates on hydroxychloroquine had a temporary impact on health policy in some countries,

59 where exceptional authorizations of use were enacted, and a durable one in others (10,11), such as

60 in Brazil where a "hydroxychloroquine alliance" was formed between intellectuals, physicians, and

61 politicians (12). Fourth and lastly, the confrontational nature of the debate led to insults and attacks

62 against doctors and scientists on the Internet (13,14) as well as legal actions against scientific

63 advisers to governments, such as in France, accused of mass killing for asking to respect the rules of

64 clinical research.

65 In this article, we analyze the evolution of the French public's perceptions of the efficacy of HC across

66 a period of more than a year (April 2020-June 2021). Although media coverage of HC is now over, the

67 efficacy of HC is still put forward in conspiracy theories, even as these develop in new directions, such

68 as resistance to vaccination or the promotion of treatments like ivermectin. The unfolding of public

69 debates in France is interesting in that it raises the question of the reception of therapeutic promises

70 in the public sphere, both in terms of public perceptions of promising treatments and of their

71 perceptions after a scientific consensus has been established. The recall of episodes from the

72 HIV/AIDS epidemic during the COVID-19 pandemic shows that controversies surrounding some

73 treatments or medical technologies more generally can have durable effects on social

74 representations (15). This phenomenon can cause problems for health authorities. A case in point is

75 that of vaccine hesitancy, which is fueled by the now discredited belief that vaccines cause autism or

76 multiple sclerosis (16). The public reception of "new" treatments has so far received little attention.

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

78 therapeutic promises are generally seen as concerning mainly doctors and patients. The first studies

79 on attitudes towards HC have focused mainly on doctors (17). Few studies, in France or abroad, have

80 explored the factors involved in the formation of public opinion on the efficacy of HC. Although the

81 French polling institute IFOP did include a question on perceptions of the efficacy of HC in its April

82 2020 survey showing a very high of respondents believing in the efficacy of HC (59%), this has not led

83 to in-depth studies of the factors influencing these perceptions (18). Outside of France, available

84 studies on the topic were conducted on samples that were not representative of the entire

85 population (19–21). In this paper, we are particularly attentive to the effects of political orientation

86 and attitudes towards science on public perceptions of the efficacy of HC. Indeed, research on public

87 controversies surrounding science suggests that political orientation plays a role in the acceptance or

88 refusal of certain medical technologies (22,23). More generally, political orientation appears to

89 influence public perceptions of the scientific consensus (24,25). This was likely to be the case during

90 the COVID-19 pandemic in France given that many political representatives, on both sides of the

91 political spectrum, became personally involved in advocating for HC or defending Professor Didier

92 Raoult and that the debate around this treatment was a major topic in the political news (26).

93 Available studies also suggest that attitudes towards science are an important factor in the perceived

94 efficacy of certain treatments (27). Thus, numerous studies have shown that adherence to false

95 beliefs on topics ranging from the danger of vaccines to creationism is correlated with interest and

96 trust in science in general (28,29).

97 In addition to the issues raised by a pandemic that has been exceptional in its scope and impact, the

98 controversy over HC brought to the fore the issues for health democracy that can arise with the

99 unregulated media coverage of scientific issues in a context where patient autonomy and public

100 engagement in health are encouraged. In France, after a period of intense coverage, the mainstream

101 media reported the scientific consensus on the inefficacy of HC. Yet, some doctors—especially

102 Professor Didier Raoult—continued to defend the efficacy of HC on social networks and, in some

103 cases, to prescribe the drug to COVID-19 patients. Several studies have shown that the correction of

104 false information has less effect than its initial communication (30). Misinformation can even be

105 amplified by contentious groups. We can therefore expect that people who trust science, the

106 mainstream media and feel closest to the governing party have followed the scientific consensus on

107 the inefficacy of HC, and conversely, that those who do not continue to hold views that go against

108 this consensus.

109 After reviewing the evolution of public debates on HC in France, this paper explores the different

110 factors that influenced perceptions of the efficacy of HC between April 2020 and June 2021 based on

111 5 surveys conducted on representative samples of the French population. We show that public

112 perceptions of the drug were less polarized than suggested by the media at the time: not only did a

113 large proportion of respondents declare that they were uncertain about the efficacy of HC, but levels

114 of uncertainty remained high throughout the study period. We also show that political orientation

115 and trust in science or the government were continuously associated with the belief in the efficacy of

116 HC.

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

118 While collective mobilizations around potential treatments have occurred in other epidemic contexts

119 —such as AZT for HIV (Epstein, 1996)—the temporality and scope of the COVID-19 pandemic gave

120 exceptional and international public visibility to the therapeutic promise of HC (31). The debates

121 surrounding HC are now considered exemplary of the issues involved in the representation of science

122 in the public sphere (32). In France, these debates were particularly intense from March to June

123 2020. They touched upon a variety of issues ranging from the merits of clinical trials, the ethical

124 dilemmas facing doctors in a context of uncertainty, the risk of putting unfounded hopes into new (or

125 old)treatments and the relationship between science, pharmaceutical companies and politicians

126 (15,26). The debates over HC were also linked to France's colonial history. In the 17the century, a

127 scientific and political controversy emerged around the use of quinquina (33). More recently, HC has

128 been used massively in the fight against malaria in former French colonies including northern African

129 countries. Professor Raoult, a major advocate of HC use against COVID largely drew on this colonial

130 and postcolonial history to call into question the necessity and quality of contemporary scientific

131 norms (34).

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

133 The mainstream media began to take an interest in this potential treatment after the regional press

134 broadcast the 25 February statement posted by Professor Raoult on the social media accounts of the

135 University Hospital Institute Méditerranée Infection (IHU) (26). With the gradual recognition of the

136 severity of the COVID-19 pandemic, President Emmanuel Macron announced the lockdown of the

137 country on 16 March, effective the day after. That same day, Professor Raoult posted a video that

138 went viral in which he presented the results of a clinical study by the IHU supporting the efficacy of

139 HC. In this context of urgency and uncertainty, the various media widely echoed the ensuing debates,

140 giving voice to a diversity of stakeholders (35). Internationally, Elon Musk and Donald Trump

141 repeated Professors Raoult's claims, thereby increasing media coverage of HC (9).

142 In France, media discussions of emerging clinical data on HC were accompanied by a political debate.

143 On 3 April, a former Minister of Health, Philippe Douste-Blazy, launched a petition to allow doctors to

144 prescribe the drug. This demand was taken up by different political figures, especially by prominent

145 members of the main conservative party « Les Républicains ». Despite the lack of evidence, the

146 acting Minister of Health Olivier Veran issued a decree on 25 March authorizing the prescription of

147   HC for serious cases in the hospital setting (2020-314). On 27 March, Professor Raoult posted the

148   results of another IHU study on social networks, and his team continued to promote HC for the early

149   management of COVID-19. This high-profile promotion prompted several intellectuals and media

150   personalities to come to the IHU to be treated and to make the case for the drug. Professor Raoult

151   and the IHU gradually entered "pop culture," both in the form of cultural expressions (tags, paintings,

152   tattoos) and via a very active Facebook group (created on 20 March) that led to intense exchanges on

153   social networks (36). A mobilization for the generalization of the use of HC took place, despite the

154   French government's reluctance and the COVID-19 Scientific Council's reminder to respect the rules

155   of clinical research (37). An IFOP survey reported that at the beginning of April 2020, 98% of French

156   people knew what HC was and 59% believed that it was effective against COVID-19 (18). As more and

157   more clinical data became available, the efficacy of HC was increasingly contested by the scientific

158   community. The trajectory of public debates was nevertheless disrupted by what came to be known

159   as the "Lancet gate" scandal. Indeed, a study reporting the high toxicity of HC in the Lancet on 22

160   May was retracted on June 4 for fraudulent data, casting doubt on the growing scientific consensus.

161   While this study had led to the suspension of the WHO trials and to the publication on 27 May of a

162   French decree prohibiting the prescription of HC for the treatment of COVID-19, its retraction

163   reinforced the positions of HC promoters, who loudly denounced the quality of international

164   research. Around the same time, meta-analyses were published that pointed to the inefficacy of HC

165   against COVID-19. The intermediate results of the Recovery trial published on 5 June showed an

166   absence of effect of HC, and the WHO Solidarity trial published on 15 October confirmed this finding

167   (5). In view of these data, the WHO officially declared HC to be ineffective against COVID-19. These

168   events, however, were insufficient to stop some doctors from promoting HC in the media, and

169   Professor Raoult continued to defend HC on the social media accounts of the IHU and in scientific

170   articles. Nevertheless, the promoters of HC became increasingly marginalized, and media coverage of

171   the drug began to decrease (see Figure 1). A recent report by the CNRS ethics committee criticized

172   the behavior of HC promoters, explicitly describing it as a form of scientific populism (38).

173 **Methods**

174 <u>Data collection</u>

175 This study draws on data from five surveys conducted between 7 April 2020 and 9 June 2021 as part

176 of two research projects: COCONEL (dir. Patrick Peretti-Wattel) and TRACTRUST (dir. Laetitia Atlani-

177 Duault). The COCONEL survey was approved by the ethics committee of the IHU (#2020-018) and the

178 TRACTRUST survey by the IRB of the Biomedical Research Institute INSERM CEEI (#20-722). The

179 surveys consisted of self-administered online questionnaires and were conducted on representative

180 samples of the French population. Quota sampling was used to match the French general population

181 with regards to gender, age and population density in the region of residence (as per official census

182 data). The characteristics of the five surveys are presented in Table 1.

183 Because public debates on HC evolved quite rapidly, we reformulated the main questions and

184 included new variables in the surveys throughout the study. While this limited the comparability of

185 the data, our study nevertheless offers a unique look at the evolution of public perceptions of the

186 efficacy of HC in France over more than a year.

187 In the first two surveys in April, a filter question asked respondents whether or not they knew the

188 chloroquine-based protocol, and a second question asked those who knew this protocol: "In your

189 opinion, is this chloroquine protocol an effective or ineffective treatment against Coronavirus?"

190 Responses options were: "Yes," "No," and "I don't know." In the last three surveys (June 2020,

191 November 2020 and June 2021), the filter question was no longer asked because the overwhelming

192 majority of French people had heard about HC by June 2020. In view of the fact that public debates

193 increasingly focused on the developing scientific consensus, the second question was changed to: "In

194 your opinion, is the current state of knowledge sufficient to settle the scientific debate on the

195 efficacy of chloroquine and its derivatives against the coronavirus?" Response options were: "Yes,

196 and I think chloroquine and its derivatives are a good treatment against coronavirus," "Yes, and I

197 think chloroquine and its derivatives are not a good treatment against coronavirus," "No, I think data

198 are still insufficient" and "I don't know."

199 In accordance with the above questions, public perceptions of the efficacy of HC were recoded in the

200 first two surveys into the following three modalities: "belief that HC is effective," "belief that HC is

201 ineffective," and "uncertainty." In the last three surveys, these perceptions were recoded into the

202 following four modalities: "belief that HC is effective," "belief that HC is ineffective," "uncertainty due

203 to insufficient data," and "uncertainty due to not knowing."

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

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

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

207 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

208

209 *Table 1 – Characteristics of the five surveys*

210 Statistical analysis.

211 Several variables were recoded to ensure comparability and interpretability: "Educational level" was

212 recoded into three groups and "age" was recoded into four groups.

213 The association between variables was measured using Pearson's correlation coefficient for numeric

214 variables and the chi-square test for categorical variables. Estimated proportions were interpreted

215 based on the margins of error provided by pooling institutes, which ranged from 1.4 to 3.1 points.

216 The factors associated with perceptions of the efficacy of HC were explored using binomial logistic

217 regression analyses. A theory-driven variable selection was performed. Statistical analyses were

218 conducted using Python (Pandas–Scipy–Statsmodel).

219 **Results**

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

221 Following peak media exposure in March 2020 (Figure 1), almost all respondents had heard about

222 hydroxychloroquine, with only 7% declaring that they had never heard about it in early April. The

223 majority of respondents were uncertain about the efficacy of HC, either due to insufficient data or

224 due to not knowing. Moreover, 35% of respondents believed that HC is effective against COVID-19,

225 and 6% believed that it is ineffective (Table 1).

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

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

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

229 they believed HC to be effective. The proportion of respondents who believed that HC is ineffective

230 rose gradually from 6% in April 2020 to 21% in June 2021. These findings contrast with the large

231 proportion of respondents who were uncertain about the efficacy of HC (either due to insufficient

232 data or due to not knowing), a figure that increased slightly from 60% in April 2020 to 64% in June

233 2021.

234 <u>Factors associated with the belief in the efficacy of hydroxychloroquine and their evolution</u>

235 To account for the main factors associated with the belief in the efficacy of HC, we performed a

236 logistic regression on the entire dataset. The dates of each survey were included in the model as

237 covariates (Table 2).

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

239   The model showed a strong effect of time on public perceptions of the efficacy of HC. After adjusting

240   for this effect, we observed a very strong association between political orientation and the belief in

241   the efficacy of HC. All other things being equal, respondents who were close to the more radical

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

243   close to the political center (2.48 [1.95-3.15] and 1.87 [1.44-2.43]). Likewise, respondents who were

244   close to the right were more likely to hold this belief than those who were close to the political

245   center (1.43 [1.10-1.85]). Respondents who were not close to any political party were less likely to

246   believe in the efficacy of HC compared to those who were close to the political center (0.38 [0.29-

247   0.49]).

248   Older respondents (above 70 years) were more likely to believe in the efficacy of HC than younger

249   ones (below 35 years) (1.36 [1.10-1.69]). Respondents with a high level of education were more likely

250   to believe that HC is ineffective than those with a low level of education (1.47 [1.20-1.79]).

251   The models per survey (Supplementary A and B) show that respondents with a high level of

252   education were more likely than those with a low level to believe that HC is effective at the beginning

253   of the study period (1.77 [1.27-2.49] for April 2020 survey), but more likely to believe that it is

254   ineffective at the end of this period (1.64 [1.12-2.40] for the June 2021 survey). The effect of political

255   orientation on the belief in the efficacy of HC was very strong. Thus, respondents who feel close to

256   far right parties were more likely than those close to the political center to believe that HC is

257   effective at the beginning of the study period (3.33 [1.93-5.73] for the April 2020 survey) and all the

258   way until the end (2.89 [1.43-5.84] for the June 2021 survey). Respondents close to far left parties

259   were also more likely than those close to the political center to hold this belief from June 2020

260   onwards (2.44 [1.10-5.37] for the June 2020 survey).

261   <u>Factors associated with the belief in the efficacy of hydroxychloroquine after the scientific consensus</u>

262   <u>was reached</u>

263 *Table 4. Binomial logistic regressions of the answers regarding HC (over the survey of November 2020*

264 *and June 2021)*

265 In June 2020, a scientific consensus on the inefficacy of HC began to form (see section on the

266 evolution of public debates). In view of this, specific questions on politicization, interest and trust in

267 science, and trust in the government were included in the November 2020 and June 2021 surveys.

268 The data collected in these two surveys were combined in the binomial logistic model (Table 3).

269 After the consensus was established, women were less likely than men to believe that HC is

270 ineffective (0.63 [0.49-0.82]). Respondents with a high level of education were more likely to believe

271 that HC is ineffective (1.62 [1.19-2.21] compared to respondents with a low level of education), as

272 were high-income earners (2.16 [1.13-4.14] compared to low-income earners).

273 After adjusting for level of politicization, the effect of political orientation disappeared, except for

274 respondents close to the far right, who were less likely than those close to the political center to

275 believe that HC is ineffective (0.38 [0.22-0.66]). By contrast, trust in the government had a strong

276 effect on the belief in the efficacy of HC. Thus, respondents with a low level of trust in the

277 government were twice as likely to believe that HC is effective (2.02 [1.46-2.79]) and twice less likely

278 to believe that it is ineffective (0.51 [0.39-0.67]) than those with a high level of trust. The level of

279 politicization also had an effect on the belief in the efficacy of HC, as respondents with a high level of

280 politicization were twice as likely to believe in the efficacy of HC than those with a low level of

281 politicization (1.85 [1.32-2.59]).

282 Trust in science also appeared to have an effect, as those with a low level of trust were twice as likely

283 to believe that HC is effective than those with a high level of trust (2.20 [1.61-3.02]). Respondents

284 who had no interest in science were twice less likely to accept the scientific consensus that HC is

285 ineffective than those who did (0.62 [0.47-0.81]).

286 The importance of uncertainty

287 By the end of 2020 and during 2021, the majority of respondents were uncertain about the efficacy

288 of HC, with 41.5% stating that the data were insufficient to decide whether or not HC is effective and

289 25.2% stating that they did not know. While political orientation, level of politicization, trust in

290 science, and trust in the government determined the ratio between the belief that HC is effective and

291 the belief that it is ineffective, uncertainty consistently remained the majority option (Figure 2).

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

293 *government.*

294 The factors associated with uncertainty due to insufficient data were not the same as those

295 associated with uncertainty due to not knowing (Table 3). Indeed, the factors that distinguished

296 respondents who stated that they were uncertain due to insufficient data were a high level of trust in

297 science (0.68 [0.52-0.90] compared to respondents with a low level of trust in science) and a high

298 income (1.75 [1.20-2.55] compared to low-income earners). By contrast, several factors were

299 associated with uncertainty due to not knowing: being a woman (1.45 [1.14-1.83] compared to men),

300 having a low level of education (0.61 [0.45-0.81] compared to respondents with a low level of

301 education), feeling close to no party (1.87 [1.18-2.96] compared to respondents close to the political

302 center), and having a low level of politicization (0.61 [0.46-0.82] compared to respondents with a

303 high level of politicization). Having no interest in science (1.96 [1.08-3.57] compared to respondents

304 with an interest in science) and answering "don't know" to the question on trust in the government

305 (1.96 [1.08-3.57]) or trust in science (5.51 [3.20-9.50]) were also associated with uncertainty due to

306 not knowing.

307 **Discussion**

308 The controversy over HC will long remain a cautionary tale for researchers (31), as it brought to the

309 fore the limits of pre-publications, the dangers of publicizing certain studies, and the importance of

310 conducting high-quality clinical trials. The treatment of the scientific controversy by journalists,

311 intellectuals, scientists, and political representatives is also a case study on how to publicly discuss

312   medical treatments, and more generally scientific research, in a context of uncertainty (26). Within

313   the scientific community, the handling of the controversy reignited a number of debates on

314   questions of publication and citation and more generally on public perceptions of medical research

315   (32). While it is necessary to draw lessons from this episode for the conduct of research, whose

316   temporality does not correspond to that of the media (39), the scope and intensity of the debates on

317   HC also highlight the importance of better understanding their public reception. It would be a

318   mistake to consider this episode as belonging entirely to the past. Beyond the fact that certain actors,

319   in particular doctors, have continued to advocate HC for the treatment of COVID-19, this controversy

320   could have long-term consequences felt in the years to come in the areas of medicine, science, and

321   politics. The continued centrality of HC in conspiracy theories promoted by far-right organizations is a

322   case in point (36).

323   Have the urgency of the COVID-19 pandemic and the desire to believe in a cure resulted in a

324   polarization between promoters and opponents of HC? The IFOP survey published on April 6, 2020,

325   found that 59% of French people believed in the efficacy of HC, which suggested that the enthusiasm

326   for this treatment was strong in the early stages of the pandemic (with 21% that answered "don't

327   know") (18). The survey that we conducted one week later showed that only one third of

328   respondents (35%) considered HC effective against COVID-19, reflecting a rapid decline in this

329   enthusiasm. Yet, peaks in demand for HC and in internet searches do not mean that everyone was

330   carried away by hope, even though many may have initially been seduced by this therapeutic

331   promise. Indeed, while our April 2020 survey found a low proportion of respondents who believed

332   that HC is ineffective, it also found a high proportion of respondents who were uncertain about the

333   efficacy of the drug. Moreover, perceptions of HC evolved rapidly over the study period. The

334   proportion of respondents who believed HC to be effective decreased gradually, and conversely the

335   proportion of those who believed it to be ineffective rose over time. However, the total number of

336   respondents who believed HC to be effective or ineffective remained small compared to that of

337　respondents who were uncertain. These findings indicate that public perceptions of HC were less

338　polarized than suggested by the media.

339　Perceptions of the efficacy of HC were socially distributed. From the beginning of the study period,

340　there was a very strong association between political orientation and the belief that HC is effective.

341　Respondents close to the far right, and later those close to the right or the far left, were more likely

342　to hold this belief than those close to the political center. This could be an effect of the political

343　opposition to the governmental policies, especially for respondents from the far left who criticized

344　the lockdown strategy for its effects on social inequalities. This finding may also be explained by the

345　fact that political figures of the right and far right defended HC (26) as part of their criticism of the

346　government's handling of the crisis and its refusal to authorize this promising treatment. Another

347　possible explanation is that HC was largely promoted on social media accounts associated with the

348　right and the far right (36). Conversely, respondents close to the political center, who tend to adhere

349　to the recommendations of health agencies, were more likely to believe that HC is ineffective. The

350　politicization of HC is also reflected in the fact that respondents with no political orientation were

351　more likely to state that they were unsure about its efficacy.

352

353　The results of the November 2020 and June 2021 surveys (Table 3) shed light on the effects of

354　politicization and attitudes towards science. The association between level of politicization and the

355　belief that HC is effective suggests that perceptions of the drug were largely rooted in a political

356　reading of the government's handling of the crisis. Trust in science diminished the likelihood of

357　believing that HC is effective and, conversely, increased the likelihood of believing that it is

358　ineffective. This is consistent with the existing literature, particularly on vaccination, which shows

359　that attitudes towards science, and more generally towards institutions, has an effect on the

360　perception of new medical technologies (16,40). Yet, while the effect of trust in science was strong in

361　our study (at a factor of nearly 2), it does not fully explain perceptions of HC among the French

362　public.

363

364 Public debates on the efficacy of HC are at the crossroads of different temporalities: that of the

365 pandemic, marked among other things by the implementation of governmental measures like the

366 lockdown, that of the media, which put certain issues on the agenda but not others, that of scientific

367 research, in particular the conduct of clinical trials, and then that of exchanges between individuals,

368 whether in the family circle or in digital spaces. The statements of public authorities were cautious at

369 first, but eventually made it clear that HC is ineffective against COVID-19. The media initially reported

370 on the promises of this treatment, then on the lack of evidence for its efficacy, and finally on the

371 negative results of clinical trials. Learned societies such as the French Society of Pharmacology and

372 Therapeutics issued statements mentioning that HC is ineffective. Our five surveys reflect these

373 temporalities. They show a gradual decline in the number of respondents who believed in the

374 efficacy of HC and an increase in the number of respondents who believed in its inefficacy. Those

375 who continued to defend this treatment even after the scientific consensus was reached had the

376 lowest levels of trust in institutions and the government, and were unsurprisingly largely associated

377 with the political parties most opposed to the government. Thus, in June 2021, 45% of respondents

378 who were close to the political center believed that HC is ineffective, while only 11% of those who

379 were close to the far right held this belief. This difference may be explained by differentiated uses of

380 information sources, with alternative media and social networks pursuing the campaign in support of

381 HC and Professor Raoult. Another possible explanation is the persistence of the memory of the

382 controversy among respondents with the lowest levels of trust in institutions and the government.

383 Importantly, the proportion of respondents who believed in the efficacy or the inefficacy of HC (i.e.

384 respondents who had an opinion on the drug) and that of respondents who were uncertain about its

385 efficacy remained stable throughout the study period. Indeed, levels of uncertainty remained high

386 even after the scientific consensus was reached. It should be noted, however, that respondents who

387 were uncertain due to not knowing were not the same as those who were uncertain due to

388 insufficient data. Uncertainty due to not knowing was in fact associated with not having an opinion

389   on other aspects of the pandemic. These findings indicate that perceptions of the drug were not

390   overly polarized, and therefore highlight the importance of measuring uncertainty to avoid artificially

391   polarizing analyses. Research in the field of agnotology, which has developed over the last decade as

392   part of the history and sociology of science, can help to make sense of these findings. This research

393   examines how certain actors work to maintain false beliefs or keep controversies alive even after a

394   scientific consensus has been reached (41). Some of the most notable examples are the tobacco

395   industry's creation of uncertainty about the effects of smoking, the oil industry's efforts to cast doubt

396   on the human origins of global warming, and the sugar industry's attempts to orient research

397   towards the hypothesis that fat rather than sugar is the cause of obesity. This research has shown

398   that public controversies allow for the instrumentalization of scientific knowledge (42,43) and that

399   moments of intense public debate have lasting effects since doubts about their actual outcome can

400   be remobilized later to defend certain positions—as illustrated by the case of vaccine hesitancy (16).

401   Insofar as the debates on HC gave visibility to different conceptions of science and to the problems of

402   knowledge production in biomedical research—as evidenced by the "Lancet gate" scandal, which

403   seems to have been a turning point, and by the multiplication of working papers of varying quality—

404   the high levels of uncertainty observed in our study can easily be instrumentalized towards a critique

405   of institutions. More generally, uncertainty can encourage distrust in the efficacy (or inefficacy) of

406   certain treatments and can push part of the public towards the most radical forms of complementary

407   and alternative medicine. This is a major concern given that alternative treatments can also

408   contribute to the propagation of conspiracy theories (21).

409   Lastly, our analysis of public perceptions of HC call into question the idea that belief in fallacious

410   ideas is the product of low levels of education. While having a high level of education was associated

411   in our study with having an opinion on HC (as opposed to being uncertain), this opinion was not

412   necessarily in line with the developing scientific consensus, especially in the early stages of the

413   pandemic. Conversely, a low level of education was associated not so much with the belief in the

414   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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