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► To cite this version:

Romain Lutaud, Jeremy K Ward, Paul Dévigne, Dimitri Scronias, Stephanie Gentile, et al.. Navigating through uncertainty and controversy: lessons from the COVID-19 crisis. A crosssectional survey among French general practitioners, at the epicenter of a global scientific controversy in Marseilles (part II). 2023. hal-04045608

HAL Id: hal-04045608

<https://hal.science/hal-04045608>

Preprint submitted on 24 Mar 2023

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Navigating through uncertainty and controversy: lessons from the COVID-19 crisis. A cross-sectional survey among French general practitioners, at the epicenter of a global scientific controversy in Marseilles (part II).

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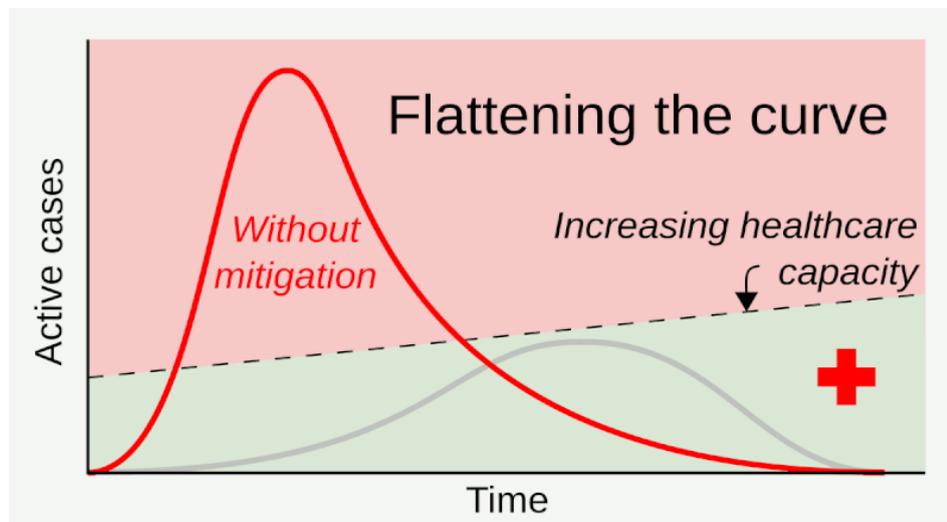
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INTRODUCTION

At the very beginning of the year 2020 the SARS-CoV-2 epidemic became worldwide, introducing a major health crisis as well as a knowledge crisis. The inevitable rush for a treatment was the origin of a unique controversy in France, over the use of hydroxychloroquine (HCQ) and azithromycin (AZ), promoted by the research center IHU Mediterranee Infection in Marseille (IHU), directed at the time by Professor Didier Raoult.

In France, the first official cases of COVID-19 were announced on 24 January 2020 and the first lockdown started on 17 March 2020 and lasted until 11 May 2020. During this 55 days period, the main public health actors as the General Direction for Health (DGS) or the High Council for Public Health (HCSP) issued guidelines for primary care physicians whose main goals were clear (2) (3) (4): taking care of patients while containing the spread of the virus (flattening the curve) and its morbi-mortality, avoiding overcrowding French hospitals (and especially intensive care units) and preventing the depletion of various medical resources such as surgical or FFP2 masks hydro-alcoholic solutions or PCR diagnosis tests.



In the absence of effective treatment and the general uncertainty, official guidelines were the following (5) (6) (7) : the severe forms of COVID-19 required hospital care - the common forms required outpatient care with only symptomatic treatments and self-monitoring with a period of strict isolation at home and social distancing for 14 days. Because of limited resources, the biological diagnosis, which at the time was only possible by carrying out a PCR test, was restricted to patients with clinical severity criteria, hospitalized patients with respiratory symptoms,

symptomatic patients with severity risk factors, symptomatic health professionals and organ donors. The mass screening strategy with PCR tests for any symptomatic patient or contact cases was only introduced in the official guidelines from 13 May 2020, two days after the end of the first lockdown.

In the beginning of the first wave of COVID-19, the city of Marseille became the epicenter of a national then international (8) (9) scientific controversy over a potential treatment when the IHU promoted the use of HCQ (later combined with AZ: HCQ/AZ). Debate over the use of HCQ rapidly took a central place in the media, reaching its peak during the first weeks of the lockdown and strongly divided the scientific community as well as the public opinion on the matter (10) (11) (12). Through social networks and extensive media coverage, the IHU director Professor Didier Raoult became an unavoidable public figure on the subject (13), by publicly promoting the use of hydroxychloroquine and taking unconventional positions about the pandemic impact or management (14) (15) (16).

In this controversial context, filled with uncertainty and evolving guidelines, the medical community was shaken (16). While the scientific authorities remained sceptical towards the use of HCQ/AZ (17) (18) (19), a growing number of practitioners started to be in favour of this potential treatment raising interrogations about the necessity and the ethics of strict scientific methodology in emergency situations (20) (21). Thus started a fracture inside the medical world that rapidly spread in the public debates, involving practitioners and patients as well especially in Marseille (22)

Our study's greatest strength probably lies within the rare opportunity that we had to get data in the very heart of the first wave of COVID-19 in France, and to provide an unique glimpse at medical behaviors among GPs at a time and place where both uncertainty and controversy had reached their climax : in spring 2020 during the first lockdown, we conducted a mixed-method study consisting of a qualitative study (66 interviews) and a cross-sectional survey which is the subject of this present article.

Understanding the main factors involved in medical practises and behaviors in time of crisis is a major but complex goal : it is multi-factorial and involved sociological factors (23). We aimed to describe the links between overall medical practice and the personal opinions of physicians. As we will see, the judgement on hydroxychloroquine was very much related to factors such as risk perception or position on scientific methodology in case of crisis, or adherence to recommendations in general. We also wanted to understand the possible influence of the IHU centre and the overall impact of the controversy in Marseille, (7) (16).

METHODS

Participants

The following study is a cross-sectional survey that was conducted among GPs in the city of Marseille, France, between t April the 20th 2020 and May the 18th 2020. Over a total of 949 GPs working in Marseille and registered on the URPS-ML PACA, we were able to reach email contact with 417 of them (45%),. Over the 417 interrogated GPs, 25 (6%) could not be contacted and 134 (12%) were not eligible [GPs practicing exclusively in hospitals or long-term care facilities, GPs practicing exclusively alternative medicine (such as homeopathy or acupuncture)]. Our final sample was finally composed of 258 GPs.

Questionnaire design

The questionnaire, composed of a total of 35 questions, was pilot-tested for clarity, length and face validity with 5 GPs, It explored the impact of the pandemic on the medical activity of the GPs, their practices and compliance to official guidelines, the referral of potential COVID-19 patients to the IHU center, their opinions about mass screening policy, use of HCQ/AZ, scientific methodology and their feelings concerning the impact of the pandemic or the controversy on their practise. The questionnaire also collected data on the individual and professional characteristics of the respondents: gender, age, solo or group practice and training practice.

Statistical analysis

In order to correct potential bias in participants, a computing method to weight the sample was used to obtain a representative database of the Marseille GP population regarding age, gender, location of practice and volume of activity, and density of health care supply in the practice district. These data are publicly available on SIRSéPACA (gender, GP density) and CartoSanté (age). All presented percentages are weighted results.

Data were analysed using SAS 9.2 (SAS institute, Cary, NC, USA) and R version 2.13.0 (<http://www.r-project.org/>). All reported *P* values were two-tailed, and a *P* value < 0.05 was considered to be significant.

Regulatory and ethical aspects

The survey was approved by an ethical committee of IHU Méditerranée N°2020-017

RESULTS

Study participants

Over the 258 GPs, 142 participated in the cross-sectional survey {response rate 55%} (**figure 1 flow charts**) which represents 15% of GPS practicing in Marseille.

Participation à l'étude

Utilisation du répertoire de l'Union Régionale des Professionnels de Santé – Médecine Libérale de la région PACA

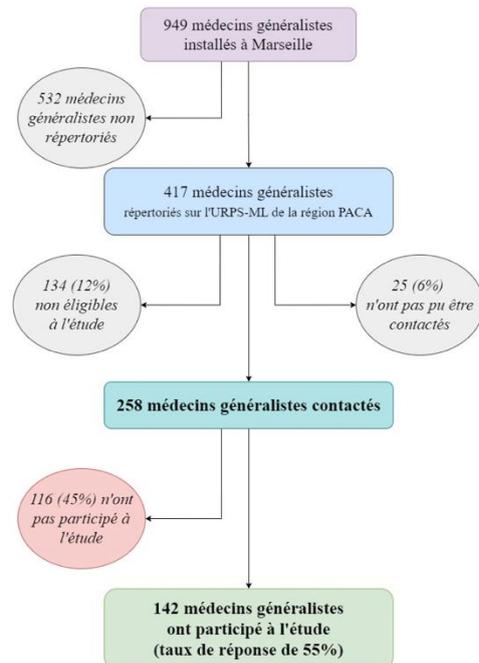


Sur les 12% non éligibles :

- pratique exclusive en milieu hospitalier
- pratique exclusive en soins de longue durée
- pratique exclusive de médecine alternative



Nombre total de participant N = 142
 Environ 15% des généralistes marseillais
 Taux de réponse important : 55%



Their various characteristics such as gender, age or type of practice are summarized in **table 1**.

	N (total 142)	%
Gender		
Male	94	65.9
Female	48	34.1
Age		
< 50	45	31.5
50 - 60	41	29.0
> 60	56	39.3

Type of practice		
solo practice	60	42.4
group practice	74	52.2
health center	8	5.4
Location of doctorate		
Aix-Marseille Université	123	83.3
other	19	13.7
Time of practice in Marseille		
< 5 years	14	10,1
5 - 15 years	26	18,4
> 15 years	101	71,4
Experience in IHU'S infectious diseases ward during studies or practice		
yes	62	43,7
no	80	56,3
Other professionnall activity		
university supervisor	26	18.5
union activity	9	6.24
public halth activity	10	7.08
other	83	59.9

Table 1: socio-demographic characteristics of the interrogated GPs

referral of potential COVID-19 patients towards the IHU center

A majority of 60.6% (n = 86) GPs referred potential COVID-19 patients to the IHU center. Among these 86 GPs, 70.4% of them did it in order to get their patient an HCQ prescription and 63.9% did it in order to have a PCR diagnosis even though they had no medical indication to do so, according to official guidelines at the time.

Among the 29.4% of GPs that didn't refer patients to the IHU center; 8.20% didn't know about the IHU center, 17.2% were geographically too distant to the IHU center and 38.6% disagreed with the mass screening policy of the IHU center. Specific situations associated with IHU center referral or not are detailed in **figure 1** and **figure 2**.

Approval of IHU center protocols and low compliance with official guidelines

About the mass screening policy ; a majority of 70.9% strongly agreed and 20.65% somewhat agreed to consider it as a chance for patients, giving a total of 91.5% GPs having a positive opinion on this practice.

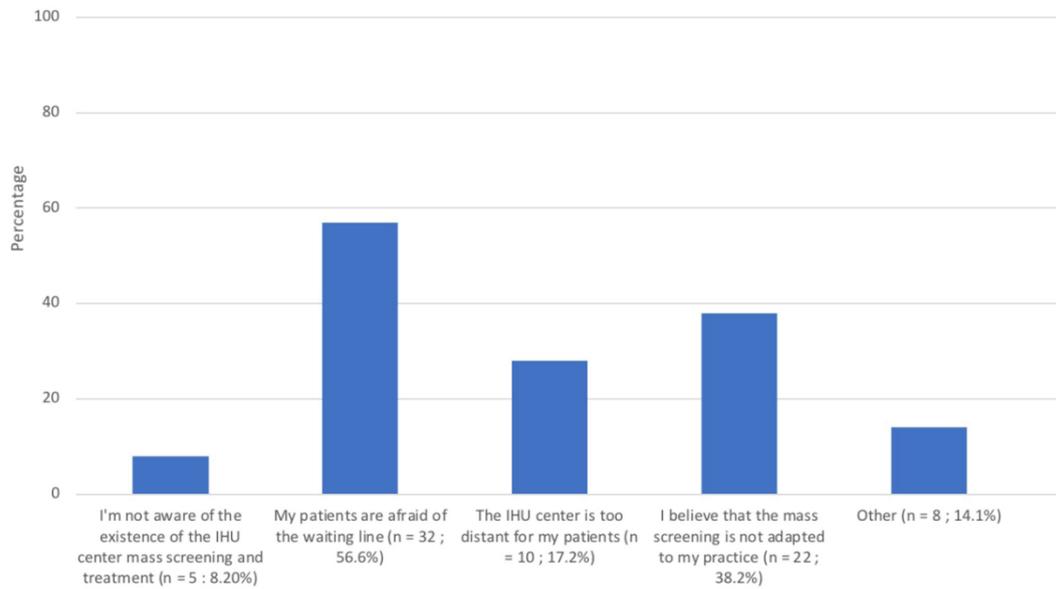
On the HCQ/AZ use as treatment for confirmed COVID-19 patients ; 36.31% strongly agreed and 37.98% somewhat agreed to consider it as a chance for patients, giving a total of 74.6% GPs having a positive opinion on the use of those drugs. Also, when asked about having doubts on the efficacy and safety of this treatment; 21.88% strongly disagreed and 39.34% somewhat disagreed to having doubts, giving a total of 59.85% GPs having full confidence in the efficacy and safety of those drugs.

Impact of the controversy on the professional activity and COVID-19 severity perception

A majority of 53.52% totally agreed or somewhat agreed that the controversy over HCQ/AZ was a source of difficulties when confronted to confirmed COVID-19 patients asking for treatments. Over the 86 (60.2%) GPs that referred patients to the IHU center, 47.6% answered that they did it because patients generally asked them to.

About the COVID-19 severity perception among the GPs ; 33.17% considered the disease as low risk (score from 0 to 4), 34.79% as moderate risk (score from 5 to 6) and 32.04% considered it high risk (score from 7 to 10).

Situations associated with the absence of IHU center referral (N = 56)



Situations associated with IHU center referral (N = 86)

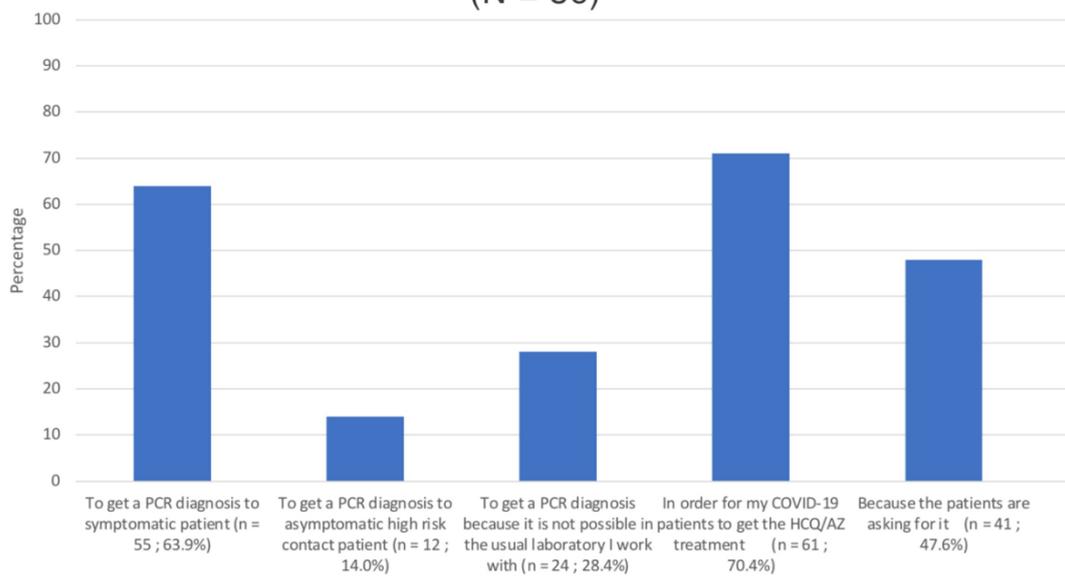


Figure 1 and 2: Specific situations associated with IHU referral or not of COVID-19 patients.

Opinions concerning the importance of scientific methodology in emergency situations

Regarding the evidence-based medicine methods ; only 41.3% were in favor of conducting a randomized controlled trial, 28.5% were not favorable and 30.0% had no opinion on the matter. Another question was about the idea that a doctor in an emergency situation (such as the COVID-19 crisis) has the responsibility to circumvent the methodological standards of clinical trials in order to treat patients ; when asked about their approval of this statement, 27.38% strongly agreed and 37.09% somewhat agreed giving a total of 64.78% of GPs being positive to it.

Factors associated with low compliance towards the official guidelines

Age seemed to be the most important factor associated with low compliance towards official guidelines and global approval of HCQ/AZ treatment, low perception of the severity of COVID-19 or judging unnecessary or unethical to wait for well-designed double blind controlled trials. Indeed, GPs over 50 years-old referred more patients to the IHU center ($p = 0.039$) and tended to refer patients in order to get them HCQ/AZ treatment ($p = 0.011$). Also, there was a correlation between approving the statement that a doctor has the responsibility to circumvent the methodological standards of clinical trials in order to treat patients in emergency situations and referring patients to the IHU center for them to get HCQ/AZ treatment.

There was a significative correlation between age and approval of the HCQ/AZ treatment ($p < 0.001$) and between referring patients to the IHU center and approving the HCQ/AZ treatment ($p < 0.001$). However, there was no clear link between factors such as gender, type and structure of practice. More specific factors are detailed in **table 2** and **table 3**.

	N	%	p-value
<i>GPs referring patients to the IHU center (N = 86)</i>			
Age			
< 50	21	47.69	0.039
50 – 60	32	76.28	
> 60	33	59.47	
Gender			
Male	29	59.00	0.780
Female	58	61.49	
The HCQ/AZ treatment is a chance for patients			
yes	73	68.86	0.001
no	13	36.91	

Having doubts about the use of HCQ/AZ because there is a lack of scientific data			
agreed	25	45.51	0.006
not agreed	61	70.24	

	n	%	p-value
GPs referring patients to the IHU center in order to get them the HCQ/AZ treatment (N = 61)			
Age			0.011
< 50	11	22.53	
50 – 60	22	54.45	
> 60	28	59.41	
Gender			0.290
Male	18	36.58	
Female	43	45.88	
Referring patients to the IHU center to get them a PCR diagnosis			0.018
yes	48	78.55	
no	13	51.19	
Referring patients to the IHU center because they generally ask for it			0.270
yes	26	64.49	
no	34	75.84	
Being in favor of randomized controlled trials for the evaluation of HCQ/AZ			0.760
agreed	24	41.06	
not agreed	37	43.88	
The HCQ/AZ treatment is a chance for patients			< 0.001
yes	57	53.66	
no	4	11.02	
Having doubts about the use of HCQ/AZ because there is a lack of scientific data			0.002
agreed	14	25.19	
not agreed	47	53.82	
In emergency situations, doctors must circumvent the methodological standards of clinical trials in order to treat patients			< 0.001
agreed	50	55.13	
not agreed	10	20.19	

Tableau 2 and 3 : tirs croisés

Discussion

A strong approval of IHU center positions among GPs in Marseille

The most striking result of our study is the strong endorsement of the IHU centre's positions among

general practitioners in Marseille during the first weeks of the pandemic. Not only a significant majority of GPs referred their potential COVID-19 patients to the IHU center, but they mostly did it because they wanted to get their patients the HCQ/AZ treatment.

We also found correlations between these medical practices and key positions regarding controversy: low risk perception of COVID-19 severity, approval of mass screening policy, questioning the relevance of strict scientific methodology in emergency situations and obviously having a positive opinion about using HCQ/AZ. These results suggest that the IHU center not only appeared as a local figure of authority but had an influence on medical practices as well : GPs perceived IHU as an effective place of care for their patients.

Generation gap: restrictive logic vs restorative logic

Our results raise the issue of the lack of adherence to recommendations the interrogated GPs, especially among the oldest. This suggest a a deeper cause such as the existence of a certain vision of medicine, pre-existing in the medical community: differences in principles in the way they form their judgements and their medical desision and the way of conceiving pharmacological treatment.

Older GPs could prefer the idea of treating their patients, despite the lack of strict scientific evidence, This way of conceiving pharmacological treatment corresponds to Rosman's (2010) logic of 'instant repair' through drugs, relatively widespread in France compared to other European countries such as the Netherlands(Rosman, 2010). Indeed, a number of constraints beyond knowledge and uncertainty bear on the doctor-patient interaction: the need to establish and maintain the relationship with the patient; the need for legitimacy; and the management of the consultation in a context where patients expect a quick improvement of their situation. In this context, providing patients with a prescription often constitutes a solution to a complicated problem. International comparisons of prescription practices suggest that using drugs as a tool to respond to the patient's complaint seems to be particularly popular among French GPs (Rosman, 2010).

While the youngest regarding the drug prescribing, tend to be more restrictive and concerned with the risk-benefit balance (27). Drug prescribing becomes a practice practiced with reserve or parsimony' and in line with recommendations for good practice (Rosman, 2010: 23).

It is interesting to note that compliance with official recommendations was often developed locally in

coordination with other general practitioners (often through local professional networks) rather than being a direct result of consulting official documents,

Such a segregation between a passive and cautious attitude (restrictive logic) against an active and curative attitude (restorative logic) could explain the massive responsiveness of older GPs to the IHU center positions. Professor Didier Raoult not only established himself as a reassuring figure but also as the one who gave healing power back to primary care practitioners when official guidelines could have been perceived as an obstacle to the restorative logic of care. The late introduction of EBM methodology concepts in the medical studies (25) (26), could also explain this « generation gap ».

The importance of Marseille: geographical and socio-cultural factors

Looking through socio-cultural glasses could explain our main results ; Marseille is a very independent city in France (28) that still has a strong cultural identity that often emerges as a dissenting or as opposition to the centralized Parisian authority (29). The majority of GPs were trained in Marseille, and a sense of loyalty to the university that trained them clearly played a role, combined with resentment against public health authorities located in Paris.

Another way of understanding this lower adherence to national protocols: in Marseilles, doctors take care of a population that accumulates social vulnerabilities (the poorest district in Europe) and are often confronted with a disconnect between the official recommendations and the reality in the field, where it is often necessary to "tinker".

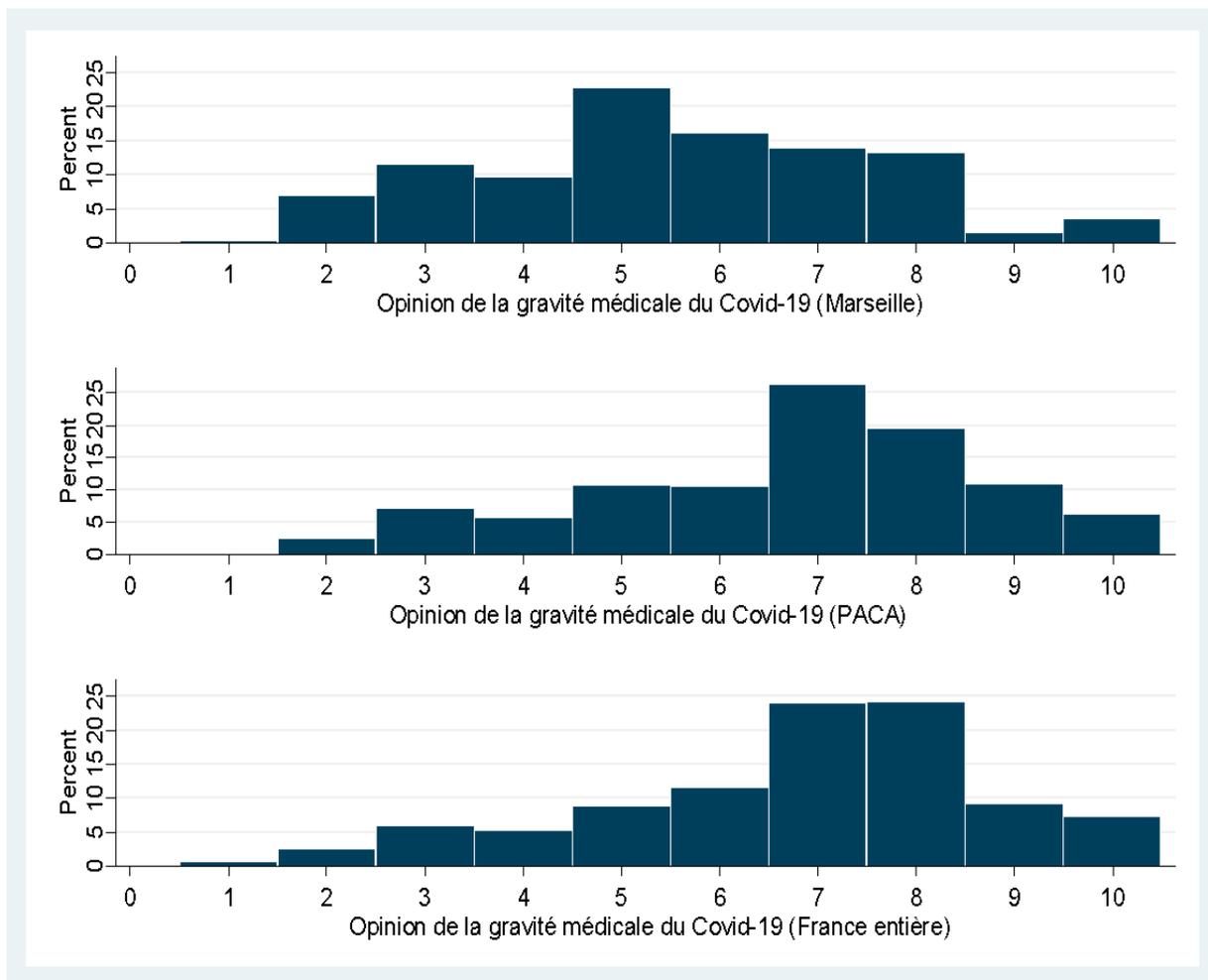
GPs are indubitably influenced by their environment and are part of the population they are treating, and adopted attitudes comparable to those of the general population. Olympique de Marseille (OM) football club supporters hanging supportive banners at the entrance of the IHU facility (30), can easily be seen as a socio-cultural determinant in the controversy, the rejection of Parisian authority being a key element of the football club but more broadly of the local culture.



Marseille where there is a fairly poor population, so the disconnection between the official recommendations and the reality in the field, where it is often necessary to "tinker", is at the origin of a delegitimation of the official guidelines

The local responsiveness of Marseille to the controversy is also strongly suggested by the PANELCOVID study. This national cross-sectional survey was conducted in a national panel of 3300 liberal general practitioners randomly selected from the French National Register in April 2020.

The results of this survey were used to compare the responses to our questionnaire between Marseille, the Provence-Alpes-Côte-d'Azur (PACA) region and France. In Marseille the severity of COVID-19 was perceived as lower. We found that physicians in southern France reported that the hydroxychloroquine debate had made it difficult for them to deal with patients' treatment requests. Their adherence to official recommendations was also lower (ref papier EJPH)



limits and precautions?

In our sample, there was a selection bias due to the over-representation of general practitioners as tutors in our study (18.5% compared to a national average of about 10% (31)). But the potential effect of this bias is unclear and could probably have further reduced the low adherence to the recommendations given that general practitioners are expected to have EBM-based practices.

While our focus was on the factors that enabled hydroxychloroquine to be prescribed, we do not want to suggest that all French GPs were in favour of it or that the factors we put forward played in exactly the same way in the practices of every GP. Sociologists have shown that there are a variety of

ways of responding to uncertainty among French GPs, characterised by varying degrees of distance towards best practice recommendations (Bloy, 2008). There are various ways of incarnating the ‘professional prudentialism’ in medicine and differences in how much GPs rely on their practical wisdom rather than on official guidelines (Champy, 2018).

Implications for research and practice:

Our results are valuable I considering the sequence of events it captures: one of the biggest historical scientific controversies of the last decades that put epistemological questioning on the table and is therefore useful for understanding attitudes and behaviours that deviate from scientific standards in general.

The IHU center, led by the massive media coverage of Professor Didier Raoult, seemed to have a significant impact on the overall perception of the crisis of the GPs in Marseille and a noticeable influence on their practice. It appears that a generation gap fractured the medical world. Political and socio-cultural aspects have obviously played a role in the french everlasting climate of political mistrust, exacerbated by pandemic issues, where the IHU center could have appeared as a political contestation figure rather than just a local reference in infectious diseases. This could explain why, even among the medical community, the debates took a political and subjective turns, when they should have been more objective and more rational than ever.

Finally, our study raises the question of the role that GPs should play in emergency situations such as the COVID-19 crisis. In order to harmonize the application of public health guidelines, maybe we have to re-think the place of GPs in decision-making strategies or plural professional network in liberal medicine.

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