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Intention to participate in a COVID-19 vaccine clinical trial and to get vaccinated against COVID-19 in France during the pandemic

Maëlle Detoc, Sébastien Bruel, Paul Frappe, Bernard Tardy, Elisabeth Botelho-Nevers, Amandine Gagneux-Brunon

Centre d’investigation clinique-INSERM 1408, University Hospital of Saint-Etienne, France
Department of General Practice, Faculté de Médecine Jacques Lisfranc, Université Jean Monnet, Université de Lyon, Saint-Etienne, France
Groupe Immunité des Muqueuses et Agents Pathogènes, Université Jean Monnet, Université de Lyon, Saint-Etienne, France
PRESAGE Institute, Université de Lyon, Saint-Etienne, France

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Abstract
Introduction: The world is facing the COVID-19 pandemic. The development of a vaccine is challenging. We aimed to determine the proportion of people who intend to get vaccinated against COVID-19 in France or to participate in a vaccine clinical trial.

Methods: We conducted an anonymous on-line survey from the 26th of March to the 20th of April 2020. Primary endpoints were the intention to get vaccinated against COVID-19 if a vaccine was available or participate in a vaccine clinical trial.

Results: Three thousand two hundred and fifty nine individuals answered the survey; women accounted for 67.4% of the respondents. According to their statements, 2.512 participants (77.6%, 95% CI 76.2–79%) will certainly or probably agree to get vaccinated against COVID-19. Older age, male gender, fear about COVID-19, being a healthcare worker and individual perceived risk were associated with COVID-19 vaccine acceptance. Vaccine hesitancy was associated with a decrease in COVID-19 vaccine acceptance. One thousand and five hundred respondents (47.6% 95% CI 45.9–49.3%) will certainly or probably agree to participate in a COVID-19 vaccine clinical trial. Older age, male gender, being a healthcare worker and individual perceived risk were associated with potential acceptance to participate in a COVID-19 vaccine clinical trial. Vaccine hesitancy was associated with refusal for participation in a COVID-19 vaccine clinical trial.

Conclusions: Nearly 75% and 48% of the survey respondents were respectively likely to accept vaccination or participation in a clinical trial against COVID-19. Vaccine hesitancy will be the major barrier to COVID-19 vaccine uptake.

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1. Introduction

In December 2019, China reported the first cases of Coronavirus Disease (COVID-19) due to a new Coronavirus: the Severe Acute Respiratory Syndrome-Coronavirus 2 (SARS-CoV 2). The world is now facing a pandemic, more than 27 millions of people have become infected worldwide, cases are described in more than 200 hundred countries, and more than 800,000 people died [1].

In 2019, the World Health Organization identified ten threats to global health [2]. Among these threats, vaccine hesitancy, the risk of a global influenza pandemic, and the risk of emergence of high-threat pathogens such as Middle-East Respiratory Syndrome and/or Severe Acute Respiratory Syndrome were identified. Since this statement, COVID-19 had emerged. Developing COVID-19 vaccines is a crucial challenge, and several candidates are currently under basic development [3]. Some of them will be tested in Phase I trials in the weeks to come [4]. The time it takes to develop a vaccine is estimated to be 1 or 1.5 years as different steps are necessary during the clinical development of a vaccine [5]. Recruitment of volunteers in a vaccine clinical trial is a real challenge [6], and some trials are stopped due to difficulties in recruitment. Vaccine hesitancy may also have an impact on recruitment in COVID-19 vaccine clinical trial [7]. After its clinical development, a COVID-19 vaccine will also face the challenge of acceptance by the general population in a post-crisis context.
The impact of the current pandemic on the intention to participate in a COVID-19 vaccine clinical trial and on the intention to get vaccinated against COVID-19 vaccine is not obvious. This is a particular concern in France, which has been shown to be the leader-country of vaccine hesitancy [8]. The aim of this study was to evaluate the intention to get vaccinated against COVID-19 among the general population and healthcare personnel, in the context of the current pandemic.

2. Methods

We conducted an anonymous online survey (Lime Survey®) from the 26th of March to the 20th of April 2020 among adult general population and adult patients. The survey was proposed to individuals via social networks (Facebook, Twitter), shared by email, on the website of the University Hospital of Saint-Etienne (France), and in centers for COVID-19 diagnosis and in medical centers. We developed a standardized questionnaire based on a literature review.

The questionnaire addressed: (1) demographic characteristics (age, chronic medical conditions), (2) fears about COVID-19, (3) history of vaccination against pandemic H1N1 influenza and seasonal influenza, (4) intention to get vaccinated if a COVID-19 vaccine was available, (5) vaccine hesitancy. According to the WHO Strategic Advisory Group of Experts on Immunization, vaccine hesitancy refers to delay in acceptance or refusal of vaccines despite availability of vaccination services. Vaccine hesitancy is complex and context specific, varying across time, place and vaccines. It is influenced by factors such as complacency, convenience and confidence [9]. We evaluated participants’ self-reported vaccine hesitancy according to the WHO definition using three previously adapted questions: “Have you ever refused a vaccine for yourself or a child because you considered it as useless or dangerous?” “Have you ever postponed a vaccine recommended by a physician because of doubts about it?” “Have you ever had a vaccine for a child or yourself despite doubts about its efficacy” [10]. If a participant answered yes to one of these proposals, he or she was considered to be “vaccine hesitant”.

The questionnaire included items to be answered on a 5-level Likert scale including a “don’t know” option to evaluate intention to participate in a clinical trial and to get vaccinated if a vaccine was available. We combined survey responses into two categories (strongly agree/agree, don’t know/disagree/strongly disagree) and ran ordinal regression models to examine demographic and attitudinal factors predictive of respondents’ willingness to get vaccinated against COVID-19. To identify suitable candidate variables for regression models, we first conducted univariate analysis using a chi-squared test. Candidates that were significant at p < 0.1 in univariate analyses were then included in a multivariable regression model. Data were analyzed using SPSS version 24.0.

The protocol complied with the data privacy laws of the National Commission for Informatics and Civil Liberties and was approved by the institutional review board with the number IRBn422020/CHUSTE. Full dataset (complete answers to the survey) and codebook are available on: https://osf.io/jjp6cx/?view_only=41a48461846448c4843d08567d881a2e.

3. Results

During the study period, 3656 people opened the web links for the online survey, 3259 (89.1%) people answered the online questionnaire. Demographic characteristics are displayed in Table 1. Women accounted for 67.4% of the respondents. Seven hundred and eighty-seven (24.1%) respondents reported a chronic medical condition. Vaccine hesitancy was observed in 1150 respondents (35.3% 95% CI 33.6–36.9%). Two thousand four hundred-thirty four (74.7% 95% CI 73.2–76.2%) respondents had fears about COVID-19; 2124 (65.2% 95% CI 63.6–66.8%) respondents considered themselves at risk for COVID-19.

3.1. Willingness to get vaccinated against COVID-19

According to their statements, 2512 participants (77.6%, 95% CI 76.2–79.0%) will certainly or probably be willing to get vaccinated against COVID-19. Among the 1063 men, 883 (83.1% 95% CI 80.8–85.3%) are COVID-19 vaccine acceptors, 1629 women among the 2196 respondents (74.2% 95% CI 72.3–76.0%) are COVID-19 vaccine acceptors (p < 0.005). The proportion of vaccine hesitant respondents who would probably be willing to get vaccinated against COVID-19 vaccine was 61.9% (95% CI 59.1–64.7%) during the current pandemics. The proportion of healthcare workers willing to get vaccinated was 81.5%, and this proportion was 73.7% in non-healthcare workers (p < 0.005). Factors associated with COVID-19 vaccine acceptance are displayed in Table 2. In multivariable analysis, older age, male gender, fear about COVID-19, be healthcare workers and individual perceived risk remained associated with COVID-19 vaccine acceptance. Vaccine hesitancy was associated with lower acceptance of a COVID-19 vaccine.

3.2. Willingness to participate in a COVID-19 vaccine clinical trial

One thousand and five hundred and fifty two respondents (47.6% 95% CI 45.9–49.3%) will certainly or probably be willing to participate in a COVID-19 vaccine clinical trial. Among the 1063 men, 634 (59.6% 95% CI 56.7–62.5%) will probably accept to participate in a COVID-19 vaccine clinical trial, this proportion is significantly greater than women (41.8% 95% CI 39.7–43.9%, p < 0.005). The percentage of potential participants in a COVID-19 vaccine clinical trial was 56.8% (53.4–60.2%) in the 50–64 years age group, and 58.7% (95% CI 52.8–64.6%) in the 65–80 years age group. Healthcare workers are more prone to participate in a vaccine clinical trial than non-healthcare workers (50.5% vs 45.4%, p < 0.005). Factors associated with COVID-19 vaccine clinical trial acceptance are displayed in Table 3.

4. Discussion

In this online survey, we observed that nearly three quarters of the respondents would accept a vaccine against COVID-19 although 35% of the respondents were qualified as “vaccine hesitant”. Moreover, around a half of the respondents would accept to participate in a clinical trial for a COVID-19 vaccine. Concerning the intention to get vaccinated, our results are similar to the results of the longitudinal Coconel study conducted by the Observatoire Régional de Santé Provence Alpes Côte d’Azur [11] and to results of investigations conducted in the USA [12,13]. Similar to coconel, we observed that men were more prone to get vaccinated than women. Women accounted for the vast majority of our study respondents, suggesting that in real-life settings, COVID-19 vaccine acceptance could be greater. In addition, older individuals are more prone to get vaccinated in both studies, this is probably due to a greater perceived risk of getting infected and developing a severe disease in older people. We analyzed factors associated with perceived risk of SARS-CoV-2 infections, and with fear about COVID-19. Male gender and older age were not associated with perceived individual risk but were associated with fear about COVID-19 (data not shown). In the same vein, healthcare workers were more prone to get vaccinated or to participate in a vaccine clinical trial than the others. We hypothesized that healthcare workers perceived a greater risk to get infected. Healthcare workers are particularly
vulnerable and accounted for 10% of the infected people in Italy, and in Greece [14,15]. On the contrary, expecting a low infection risk is associated with a lower willingness to get vaccinated [16]. Seventy-eight percent of healthcare workers considered themselves at-risk to get infected, however after adjustment on age, gender, and comorbidities, being a healthcare worker was not associated with perceived risk to get infected, but with fear about COVID-19 (data not shown).

Around the half of the respondents will accept to participate in a COVID-19 vaccine clinical trial. In the context of a clinical trial, men were also more prone to participate. Fears about COVID-19 were not associated with willingness to participate in a clinical trial, but with perceived risk to get infected, but with fear about COVID-19 (data not shown).

The proportion of French People favorable to a COVID-19 vaccine can appear low, but we have to put this in perspective with the fact that the vaccine would be a new vaccine, and that vaccine coverage against 2009 H1N1 pandemic influenza was only 11.1% in France [18]. However, a greater proportion of respondents to our survey declared they had been vaccinated against 2009 H1N1 pandemic influenza, so this observation may suggest that the respondents are more pro-vaccine than the general pop-

| Table 1 | Demographic characteristics of the responders to the on-line survey, data are expressed by n and (%). |
|---------|-----------------------------------------------------------------------------------------------------|
| N = 3259 (%) |
| Gender | Male 1063 (32.6) | Female 2196 (67.4) |
| Age | Under 30 years old 670 (20.6) | 30–49 years old 1502 (46.1) | 50–64 years old 803 (24.6) | 65–80 years old 271 (8.3) | Over 80 years old 13 (0.4) |
| Health care workers | Yes 1421 (43.6) | No 1838 (56.4) |
| Chronic medical conditions | Hypertension 627 (19.2) | Diabetes 260 (8.0) |
| Chronic lung disease | 68 (2.1) | Chronic cardiac failure 139 (4.3) |
| Chronic renal insufficiency | 92 (2.8) | Immunosuppressive medication 63 (1.9) |
| Are you afraid of the new coronavirus? | Yes, a lot 766 (23.5) | Yes, a little 1668 (51.2) |
| I don't know | 176 (5.4) | Not really 549 (16.8) |
| No | 100 (3.1) |
| Do you feel at risk of getting infected by the new coronavirus | Yes, a lot 644 (19.8) | Yes, a little 1480 (45.4) |
| I don't know | 426 (13.1) | Not really 615 (18.9) |
| No | 94 (2.9) |
| Vaccine hesitancy | Have you ever refused a vaccine for yourself or a child because you considered it as useless or dangerous? 395 (12.1) |
| Have you ever postponed a vaccine recommended by a physician? 341 (10.5) | Have you ever had a vaccine for a child or yourself despite doubts about its efficacy? 570 (17.5) |
| Global vaccine hesitancy 1150 (35.3) |
| If a preventive vaccine clinical trial against the new coronavirus existed, would you agree to participate? | Yes certainly 923 (28.3) |
| Yes possibly | 629 (19.3) | I don't know 767 (23.5) |
| Not really | 604 (18.5) | No, possibly 336 (10.3) |
| Definitely no | 128 (3.9) |
| If a vaccine against the new coronavirus was available for next season, would you get vaccinated? | Yes certainly 776 (23.8) |
| Yes possibly | 1754 (53.8) | I don't know 394 (12.1) |
| Not really | 207 (6.4) | Definitely no 128 (3.9) |
ulation in France, and more often healthcare workers. We observed a similar prevalence of vaccine hesitancy than in a recent study in France, which identified a prevalence of 40% [10]. One limitation of our work may be the use of social media to recruit study participants. Social media users who use platforms, such as Facebook and Twitter, as health information sources are more prone to get vaccinated against seasonal influenza in the United States of America [19]. Furthermore, a great number of healthcare workers answered the survey and we observed that healthcare workers were more prone to get vaccinated or to participate in a vaccine clinical trial independently of the perceived risk to get contaminated. However, vaccine hesitancy also affects healthcare workers [20–22]. In our study sample, vaccine hesitancy affects around 30% of the healthcare workers and 40% of the non-healthcare workers.

Our work suffers from limitations. First, our sample is not completely representative of the French general population, and the great amount of HCWs may overestimate the proportion of individuals with intentions to get vaccinated. In a recent report, in 7 European countries, the proportion of individuals with intention to get vaccinated against COVID-19 was 73.9%, but in France, it was only 62% [23]. This survey was also conducted on line but a priori in a representative panel of 1,000 individuals per country. Secondly, we did not precise in our survey, the type of clinical trials, and intention to participate may change between early and later phases clinical trials [7].

| Table 2 | Factors associated with COVID-19 vaccine acceptance expressed with odds ratio (ref: reference), in multivariable analysis, only variables with a p-value < 0.1 in univariate analysis were integrated in the model. |
|---------|----------------------------------------------------------------------------------------------------|
|         | Univariate analysis | p                | Mutivariable analysis | p                |
| Gender  | Female              | Ref              | <0.001              | Ref              | <0.001              |
|         | Male                | 1.707 (1.417–2.058) | <0.001              | 1.878 (1.529–2.306) | <0.001              |
| Age     | Under 30 years old | Ref              | <0.001              | Ref              | <0.001              |
|         | 30–49 years old    | 1.506 (1.231–1.842) | <0.001              | 1.532 (1.230–1.909) | <0.001              |
|         | 50–64 years old    | 2.246 (1.758–2.870) | <0.001              | 1.445 (1.259–1.658) | <0.001              |
|         | 65–80 years old    | 2.692 (1.854–3.908) | <0.001              | 1.395 (1.198–1.624) | <0.001              |
|         | Over 80 years old  | 5.593 (0.723–43.293) | 1.412 (0.827–2.412) | <0.001              |
| Healthcare workers | No | Ref              | <0.001              | Ref              | <0.001              |
|         | Yes                | 1.574 (1.329–1.864) | 1.533 (1.269–1.851) | <0.001              |
| Chronic medical conditions | No | Ref              | 0.1                | 0.891 (0.713–1.113) | 0.22                |
|         | Yes                | 2.095 (1.757–2.499) | 2.445 (1.998–2.991) | <0.001              |
| Fear about COVID-19 | No | Ref              | <0.001              | Ref              | <0.001              |
|         | Yes                | 1.831 (1.549–2.163) | <0.001              | 1.510 (1.269–1.851) | <0.001              |
| Perceived individual risk | No | Ref              | <0.001              | Ref              | <0.001              |
|         | Yes                | 1.574 (1.329–1.864) | 1.533 (1.269–1.851) | <0.001              |
| Vaccine hesitancy | No | Ref              | <0.001              | Ref              | <0.001              |
|         | Yes                | 0.279 (0.236–0.331) | 0.275 (0.230–0.329) | <0.001              |

| Table 3 | Factors associated with potential participation in a COVID-19 vaccine trial expressed with odds ratio, in multivariable analysis, only variables with a p-value < 0.1 in univariate analysis were integrated in the model. (Ref: reference). |
|---------|----------------------------------------------------------------------------------------------------|
|         | Univariate analysis | p                | Mutivariable analysis | p                |
| Gender  | Male                | 2.057 (1.773–2.388) | <0.001              | 1.881 (1.532–2.309) | <0.001              |
|         | Female              | Ref              | <0.001              | Ref              | <0.001              |
| Age     | Under 30 years old | Ref              | <0.001              | Ref              | <0.001              |
|         | 30–49 years old    | 1.043 (0.868–1.254) | 1.518 (1.220–1.888) | 1.481 (1.297–1.690) | 1.408 (1.229–1.612) | 1.494 (0.881–2.531) |
|         | 50–64 years old    | 1.797 (1.461–2.211) | 1.481 (1.297–1.690) | 1.408 (1.229–1.612) | 1.494 (0.881–2.531) |
|         | 65–80 years old    | 1.941 (1.458–2.585) | 1.408 (1.229–1.612) | 1.494 (0.881–2.531) | 1.408 (1.229–1.612) | 1.494 (0.881–2.531) |
|         | Over 80 years old  | 0.608 (0.185–1.993) | 0.608 (0.185–1.993) | 0.608 (0.185–1.993) | 0.608 (0.185–1.993) |
| Healthcare workers | No | Ref              | 0.004              | Ref              | 0.007              |
|         | Yes                | 1.223 (1.065–1.405) | 1.540 (1.275–1.860) | 1.540 (1.275–1.860) | 1.540 (1.275–1.860) |
| Chronic medical conditions | No | Ref              | 0.32               | Ref              | 0.32               |
|         | Yes                | 1.085 (0.924–1.274) | 1.085 (0.924–1.274) | 1.085 (0.924–1.274) | 1.085 (0.924–1.274) |
| Fear about COVID-19 | No | Ref              | 0.17               | Ref              | 0.17               |
|         | Yes                | 0.895 (0.764–1.048) | 0.928 (0.784–1.099) | 0.928 (0.784–1.099) | 0.928 (0.784–1.099) |
| Perceived individual risk | No | Ref              | 0.006              | Ref              | 0.006              |
|         | Yes                | 1.226 (1.061–1.417) | 1.235 (1.061–1.439) | 1.235 (1.061–1.439) | 1.235 (1.061–1.439) |
| Vaccine hesitancy | No | Ref              | <0.001              | Ref              | <0.001              |
|         | Yes                | 0.502 (0.433–0.582) | 0.512 (0.4411–0.595) | 0.512 (0.4411–0.595) | 0.512 (0.4411–0.595) |
In conclusion, during the pandemics, around 75% of the French people would agree to get vaccinated. Due to the burden of the disease, and the potential natural immunity, it may well be possible that this proportion would be enough to obtain a herd effect [24]. Antecedents of vaccine hesitancy may affect vaccine acceptance even in a context of a pandemic due to an emerging pathogens. Around fifty percent will agree to participate in a COVID-19 vaccine clinical trial; we can hope that vaccine trials would not be stopped because of recruitment difficulties.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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