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ORIGINAL RESEARCH ARTICLE

Opinions, beliefs and knowledge of people with multiple sclerosis on COVID-19 pandemic and vaccine



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ARTICLE INFO

KEYWORDS:

multiple sclerosis
COVID-19 pandemic
vaccines
opinions
questionnaire

ABSTRACT

BACKGROUND: Considering the potential COVID-19 impact on pwMS health and the importance of vaccination for this population, we decided to assess: (a) pwMS' beliefs and knowledge on COVID-19 pandemic; (b) their acceptance towards COVID-19 vaccination and (c) pwMS' opinions on general vaccination.

METHODS: Observational study, based on a cross-sectional (10-20th September 2020) online survey, conducted in a cohort of pwMS' followed at two Portuguese hospitals. The survey included measures to characterize the sample and a questionnaire designed to assess the topics defined for this study.

RESULTS: 270 respondents completed the full survey (response rate 58.2%). pwMS greatest concern during the pandemic was an aggravation of MS, especially by patients older than 50 years old. Almost 40% of the patients older than 50 felt that the pandemic negatively affected their MS related medical assistance. Most patients believed they would recover from COVID-19 infection. More than half of the responders feared a MS aggravation if they got COVID-19; this was more pronounced in patients with progressive MS. About 12% of the participants did not want to be vaccinated and almost 40% was unsure. Regarding vaccines in general, almost a third of the participants feared their side effects or MS related complications.

CONCLUSION: Having knowledge of pwMS' opinions on COVID-19 pandemic impact and vaccination is useful to better address these issues. Fears and expectations towards vaccination must be discussed with pwMS.

1. INTRODUCTION

The Coronavirus disease of 2019 (COVID-19) is the disease caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection and it was first identified as a pandemic on 11th March 2020 (Möhn et al., 2020). pwMS may be affected by this pandemic in several aspects, not only by the risk of infection, but also due to profound healthcare system institutional restructuring which could affect their consultations and treatments. Current literature evidence appears to point towards a protective effect provided by vaccination on pwMS by decreasing their infectious risk. Despite previously claimed deleterious effect of vaccination in pwMS, vaccines do not appear to be associated

with an increased risk of developing MS, having a first clinical demyelinating event or to be related to a higher risk of relapse. However, there is still some reluctance among patients and doctors when it comes to vaccination in MS (Farez et al., 2019; Lebrun and Vukusic, 2019).

Considering the potential COVID-19 impact on pwMS health and the importance of a vaccine for this population, we decided to assess pwMS' beliefs and knowledge on COVID-19 pandemic and to evaluate their acceptance towards vaccination in this context. We hypothesize that the majority of MS patients are willing to be vaccinated against COVID-19. However, misinformation and some fears regarding vaccination in MS might still influence patients' perspectives, as well as other factors (as age, gender, education, employment, or MS phenotype or perceived

Abbreviations: MS, multiple sclerosis; CNS, central nervous system; PwMS, people with multiple sclerosis; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; COVID-19, coronavirus disease of 2019; DMT, disease modifying therapy; CIS, clinically isolated syndrome; RRMS, relapse-remitting MS; PPMS, primary progressive MS; SPMS, secondary progressive MS; OD, odds ratio; CI, confidence interval.

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<https://doi.org/10.1016/j.msard.2021.103113>

Received 21 April 2021; Received in revised form 5 June 2021; Accepted 22 June 2021

Available online 26 June 2021

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risk of being infected with COVID-19) that influence general population beliefs (Ehde et al., 2021; Neumann-Böhme et al., 2020). We proposed to understand the current pwMS' knowledge and beliefs on general vaccination to contextualize opinions on COVID-19 vaccine.

2. MATERIALS AND METHODS

We performed a cross-sectional observational study in two Portuguese hospitals from Amadora-Sintra and Loures counties, two large populational areas of the metropolitan area of Lisbon severely affected by the COVID-19 pandemic. The study included MS or CIS patients (in the latter, under DMT) diagnosed before March 2020 and was based on an online survey. The patients were invited to participate in the study by a telephone interview and, to those who consented, the survey was sent by email. Answering the survey was voluntary and anonymity was assured. All patients that could not fully understand the concept of the study, its questions (dementia or language barrier, for instance), or did not have a valid e-mail, were excluded. Ethics committee approval was obtained.

The survey included basic demographic and MS questions (age by classes, sex, educational level, employment, MS phenotype, duration of the disease and DMT) and questions regarding COVID-19 pandemic and its impact on MS, patients' beliefs on vaccination and their willingness to be vaccinated against SARS-CoV-2. Previously published questionnaires on the pandemics' impact on pwMS' lives and their willingness to be vaccinated (Rezaeimanesh et al., 2020; Sahraian et al., 2020) were consulted and considered during our questionnaire's design. By the time the questionnaire was created, there was no prediction on when vaccination would start, as COVID-19 vaccines were under development. The questionnaire was validated by four neurologists with experience in treating pwMS and by both hospitals' ethical committees. It was then presented as a Google Form® and its link was sent by email to patients. The questionnaire was available online during 10-20th September 2020 and data collection was made during the same month. For each question, it was only possible to choose one answer. Data was analyzed with IBM SPSS Statistics 26®, with calculation of the Qui-square and p-value (statistically significant if < 0.05) for each hypothesis. Non-parametric statistics were used because of the size of our population. Regarding the variable "age", several cutoffs were tested and we chose the one that yielded statistical significance. We analyzed each answer provided with other variables from different questions, as part of exploratory data analysis. For question 3, a logistic regression was applied, after separating the possible answers in two groups (COVID-19 will not influence MS vs fearing a symptomatic recrudescence), to determine which was the independent factor influencing the answers (age vs progressive phenotype).

3. RESULTS

Demographic Data

A total of 270 patients from both hospitals completed the form (463 emails sent, response rate 58.2%). The main demographic characteristics of this population are presented in table 1.

Progressive phenotypes were more often reported in older ages (22.2% vs 5.3%, p < 0.001). 22.7% of patients aged 40-59 were unemployed and 55.9% of the same age range were precociously retired.

3.1. Results on pwMS opinions, beliefs, and knowledge on COVID-19 pandemic

Regarding patients' concern towards COVID-19 pandemic, the most frequently reported concern was fearing a MS worsening because of COVID-19 (33.7%). The next reported concern was the high prevalence of cases and deaths by COVID-19 in the general population (22.2%), followed by the pandemics' economic impact (19.6%). 10.4% of the

Table 1
Study population's demographic characteristics (N = 270)

Characteristics	No. (%)
Sex	
Female	205 (76.3%)
Age Groups	
18-29 years	39 (14.1%)
30-39 years	65 (24.1%)
40-49 years	85 (31.9%)
50-59 years	60 (22.2%)
60-69 years	19 (7.0%)
70-79 years	2 (0.7%)
Phenotype Distribution	
Clinically Isolated Syndrome (CIS)	4 (1.5%)
Relapse-Remitting MS (RRMS)	168 (62.2%)
Primary Progressive MS (PPMS)	18 (7.0%)
Secondary Progressive MS (SPMS)	10 (3.7%)
Patient unaware of his/phenotype	70 (25.6%)
Median disease duration since diagnosis	7 years [Interquartile range (IQR) = 9]
DMT efficacy	
Moderate efficacy ¹	121 (48.1%)
High efficacy ²	98 (32.6%)
None of these	51 (19.3%)
Employment	
Employed	175 (64.8%)
Unemployed	25 (9.3%)
Retired	54 (20.0%)
Student	16 (5.9%)
Literary Degree	
Primary School	4 (1.5%)
Basic School	14 (5.2%)
High School	103 (37.8%)
Superior Degree	125 (46.7%)
Professional Degree	24 (8.9%)

¹ Beta interferon, dimethyl fumarate, glatiramer acetate and teriflunomide.

² Cladribine, fingolimod, natalizumab, ocrelizumab, and rituximab.

participants were concerned about their disease's progression because of the postponing of medical appointments and/or hospital treatments or rehabilitation. Patients older than 50 years old, when comparing to patients younger than 50 years old, reported more frequently that their major concern was fearing MS aggravation due to the postponing of medical care (22.2% vs 5.3%, Chi-square = 17.487, df = 1, p-value < 0.001)

When asked about the impact of COVID-19 in one's health, in case of infection, more than a half of the participants (51.9%) thought they would be able to be cured, but recovery would take longer, and any possible complication would be more severe because of their MS or their MS treatment. On the other hand, 8.5% believed that COVID-19 could be fatal because of their MS or their DMT. The belief in a fatal outcome was most common on pwMS using high-efficacy DMT (15.3% of the participants under high-efficacy DMT vs. 4.7% of the participants under moderate-efficacy, Qui-square = 9.095, df = 1, p = 0.003).

When asked about the impact of COVID-19 on patients' MS, in case of infection, 40.4% feared an aggravation of MS symptoms and sequelae if they were infected and 17.8% feared a new MS relapse, caused by COVID-19. Fearing a symptomatic recrudescence (aggravation of MS symptoms or a new relapse) if they were infected with COVID-19 was more often reported by pwMS with progressive phenotypes (64.3% vs. 27.8%, Qui-square = 7.156, df = 2, p = 0.028) and by patients older than 50 years old (50.6% vs. 36%, Qui-square = 5.047, df = 1, p = 0.025). Progressive phenotype was an independent predictor of fearing a symptomatic recrudescence related to COVID-19 (logistic regression, OR = 0.394, 95%CI = 0.170 - 0.913, p = 0.027).

When selecting the sentence that best characterized COVID-19 pandemic impact on MS control, 22.2% of the participants felt less supported in medical terms because of consultations, exams, or treatments postponing. Those who were older than 50 years felt less supported in medical terms (37% older than 50 vs. 15.9% younger than 50,

Qui-square = 14.694, df = 1, p < 0.001), which was also reported by those whose DMT did not require a hospital admission (25.7% vs. 7.7%, Qui-square = 7.867, df = 1, p = 0.005).

We did not find any relation between sex, employment, education, duration of disease or phenotype and the answers given to the previous questions. The frequency of each answer regarding the questions about COVID-19 pandemic is presented on [table 2](#).

3.2. Results on pwMS opinions, beliefs, and knowledge on COVID-19 vaccine

When asked about patient’s willingness in being vaccinated, 48.9% of the participants would accept the vaccine. 39.2% of the participants were unsure and 11.9% did not wish to be vaccinated. pwMS with progressive phenotypes answered more frequently that they do not want to be vaccinated than those with other forms (31% vs. 11.6%, Qui-square = 7.570, df = 1, p = 0.006). Most of those patients who were unsure had a RRMS or CIS phenotype (92.2% vs. 7.8%, Qui-square = 4.451, df = 1, p = 0.035).

On the other hand, when asked about patient’s opinion on COVID-19 vaccine, 71.5% of the responders believed that a COVID-19 vaccine will be very useful to achieve pandemic control. 14.6% believed that the vaccine’s efficacy can be diminished by their DMTs, but they did not wish to change medication because their MS was controlled. This option was most often selected by patients under high efficacy DMT (58.8% vs. 41.2%, Qui-square = 5.700, df = 1, p = 0.017). pwMS with progressive phenotypes feared more frequently that an eventual vaccine against SARS-CoV-2 might aggravate MS than those with RRMS or CIS (20.7% vs 7%, Qui-square = 5.723, df = 1, p = 0.017).

We did not find any relation between age, sex, employment, education, duration of disease and the answer to the previous questions. The frequency of each answer regarding the questions about the opinion on COVID-19 vaccination is presented on [table 3](#).

3.3. Results on pwMS opinions, beliefs, and knowledge on vaccines

Regarding vaccines in general, 41.5% of the participants did not think that vaccines might influence their MS. By contrast, 16.7% feared their side effects and 12.6% were concerned about a possible MS aggravation or a relapse related to vaccination.

Patients with a superior education degree feared less often a MS exacerbation potentially caused by vaccines or their side effects (35.4% vs. 64.6%, Qui-square = 5.652, df = 1, p = 0.017). Patients fearing vaccines (including those who fear vaccines side effects and those who fear vaccines might aggravate their MS) had a mean disease duration since diagnosis superior than those who did not fear vaccines (Kruskal-Wallis H test, p = 0.009). Furthermore, pwMS that did not want to be vaccinated against SARS-CoV-2 or that were unsure appeared to fear more frequently vaccines’ side effects or an MS aggravation potentially caused by them (69.9% vs. 43.5%; Qui-square = 15.311, df = 1, p < 0.001).

We did not find any relation between pwMS opinions on vaccination in general and sex, age, employment, disease phenotype or DMTs. The frequency of each answer regarding the questions about the opinion on vaccination is presented on [table 3](#).

4. DISCUSSION

COVID-19 is currently the most concerning health issue worldwide, and it is important to assess its real impact on pwMS health. There is no evidence that pwMS have a higher probability of having a more severe infection; however, it seems that pwMS with higher disability or other risk factors that play out in the general population detain a higher risk of unfavorable prognosis if infected ([Louapre et al., 2020](#); [Willis and Robertson, 2020](#)). Possibly with the exception of the anti-CD20, it also seems that DMT does not increase the risk of having severe COVID-19

Table 2
Answers distribution to the questions about COVID-19 pandemic (N = 270)

Question	Possible answers	No. (%)	Commentary	
“What is your main concern regarding the COVID-19 pandemic?”	Fearing an MS aggravation if I am infected with COVID-19.	90(33.3%)		
	The high prevalence of cases and deaths by COVID-19 in general population.	60 (22.2%)		
	The economic impact of the pandemic in my life or in general society.	54 (20.0%)		
	Fear of dying because of COVID-19.	28 (10.4%)		
	Fearing an MS aggravation because of the postponing of consultations and/or treatments at hospitals or other health institutions (for example, physiotherapy).	28 (10.4%)	More frequently reported by pwMS older than 50 years-old (p < 0.001).	
	The quarantine psychological effects.	10 (3.7%)		
	“Supposing you were infected by COVID-19, how do you think this would impact your general health?”	I will be able to cure the infection, but it will take longer, and I might get more serious complications because of my MS or because of my MS treatment.	139 (51.5%)	
		The infection will take a course similar to that of the general population and, most likely, I will be able to cure myself.	74 (27.4%)	
		The infection will probably be fatal because of my MS or because of my MS treatment.	23 (8.5%)	More frequently reported by pwMS under high-efficacy DMT (p = 0.003).
		Since I have other conditions (for example, arterial hypertension, cardiac disease, diabetes, respiratory diseases, etc.), I am more vulnerable to COVID-19.	21 (7.8%)	
Because of my MS treatment, I will be more protected from COVID-19.		13 (4.8%)		
“Supposing you were infected by COVID-19, how do you think this would impact your MS?”	COVID-19 will probably not have any influence on my MS.	113 (41.9%)		
	Aggravation of symptoms and sequelae from MS due to COVID-19 infection.	109 (40.4%)	More frequently reported by pwMS with progressive phenotypes (p = 0.027).	
	A new MS relapse caused by COVID-19.	48 (17.8%)		
“Which of the following sentences best describe COVID-19 pandemic impact on your MS?”	This pandemic did not affect me in any aspect, namely in my MS control.	79 (29.3%)		
	This pandemic affected me social and professionally, but not in what concerns my MS.	73 (27.0%)		

(continued on next page)

Table 2 (continued)

Question	Possible answers	No. (%)	Commentary
	I felt less supported in medical terms, because my consultations, exams or treatments were cancelled.	60 (22.2%)	More frequently selected by pwMS older than 50 years-old ($p < 0.001$) and by those who did not require a hospital admission for their DMT ($p = 0.005$).
	I felt more isolated and vulnerable while facing COVID-19 pandemic because I have MS.	43 (15.9%)	
	My symptoms got worse during the pandemic.	15 (5.6%)	

infection (Giovannoni et al., 2021). It is known that viral infections may trigger relapses and temporary worsening of MS symptoms. However, a higher risk of MS relapse or a disease aggravation in well controlled patients has not been linked to SARS-CoV-2 infection (Giovannoni et al., 2020).

Recent publications based in surveys that studied the knowledge and beliefs of pwMS on COVID-19 pandemic have shown a clear concern with COVID-19's effects on MS and a key belief that this new infection might negatively affect MS natural history (Rezaeimanesh et al., 2020; Sahraian et al., 2020). This is in line with our study in which a possible MS deterioration caused by COVID-19 was the major concern related to the pandemic more frequently reported (33.7% of the participants). In one of these studies, more than 60% of patients believed that COVID-19 could induce an MS attack or worsen their disease process (Rezaeimanesh et al., 2020). Our study also showed that this fear was more pronounced in patients with progressive phenotypes, while the former found out that the most frequent concern of PPMS patients was indeed MS worsening.

On the other hand, most of the participants of our study believed that they would be able to get cured from COVID-19. It is however important to state that, during the time our survey was available (September), the number of active cases had significantly decreased since the first pandemic wave. In our study the belief in a fatal outcome was more frequent in pwMS under high-efficacy DMT, while the DMT effect was not considered in other previous studies.

10.4% of the participants identified fearing an MS progression due to postponing of medical appointments, exams or treatments as their major concern related to the pandemic and, regarding its impact on MS management, 22.2% felt less supported in medical terms. We highlight that both aspects were reported more frequently by patients aged more than 50 years old. pwMS who did not require a hospital admission for their DMT to be administrated also reported to be less medically supported. The COVID-19 pandemic has had a profound impact on healthcare systems functioning and organization (Neumann-Böhme et al., 2020). The growing number of COVID-19 patients led to several institutional reorganizations that implied a severe shortage of medical consultations, exams and elective treatments and had a deleterious impact on people with chronic diseases (Tonna et al., 2020; Varanda et al., 2020). The confinement measures applied in order to reduce community contamination had also a severe impact on social services resources (Mariani et al., 2020; Varanda et al., 2020). Telemedicine emerged as a solution to maintain follow-up of MS patients and of patients with other chronic diseases but clear and systematic recommendations addressing the content and periodicity of the teleconsultations were lacking in the beginning of the pandemic. The two hospitals that performed this study had MS teleconsultations; yet, standardized protocols were missing in that time and this fact might explain these results. Patients treated with intravenous administered DMT felt more accompanied; this aspect also

Table 3

Answers distribution to the questions about vaccination (N = 270)

Question	Possible answers	No. (%)	Commentary
“Considering the possibility of an effective and free of charge COVID-19 vaccine being available in the next months, would you accept to be vaccinated?”	Yes	132 (48.9%)	
	Unsure	106 (39.3%)	
	No	32 (11.9%)	This answer was selected more frequently by pwMS with progressive phenotypes ($p = 0.006$)
“Considering the possibility of an effective and free of charge COVID-19 vaccine being available in the next months, what is your opinion about it?”	The vaccine will be very useful to control the pandemic.	193 (71.5%)	
	I believe that the vaccine efficacy might be decreased by my MS treatment, but I do not intend to change medication because my MS is controlled.	40 (14.8%)	This answer was selected more frequently by patients doing high-efficacy DMT's ($p = 0.017$).
	I believe that the vaccine might aggravate my MS or cause a relapse.	23 (8.5%)	This answer was selected more frequently by patients with progressive phenotypes ($p = 0.017$).
	The vaccine will not be useful to control the pandemic.	14 (5.2%)	
“What is your opinion about vaccines in general?”	I do not think vaccines might influence MS.	112 (41.5%)	
	I think vaccines might protect me from various diseases that might aggravate my MS.	79 (29.3%)	
	I fear vaccines' side effects.	45 (16.7%)	Patients with a superior education degree fear less often a MS exacerbation caused by vaccination or its side effects ($p = 0.017$), but those who fear them had their MS diagnosis earlier ($p = 0.023$). pwMS who did not wish to be vaccinated for COVID-19 or that were unsure fear more frequently vaccine's side effects or a consequent MS aggravation ($p = 0.001$).
	I fear vaccines might aggravate my MS or cause a relapse.	34 (12.6%)	

supports the idea that telemedicine was not perceived as routine care by patients. Furthermore, elderly patients might not be able to utilize certain types of technology, alongside with the higher probability of having more comorbidities, which might aggravate the isolation notion. We believe that the feeling of isolation occurred in many other healthcare settings as many patients lost regular access to their primary care centers and others ceased their activities in physiotherapy programs.

Vaccination is still a highly debated topic and misinformation towards it remains, both in medical personnel and patients (Harrison and Wu, 2020). The importance of vaccination should be discussed with the

patients early, to ensure every pwMS has his/her vaccination program updated, whether he/she initiate a DMT or not. Several investigation groups worldwide have analyzed the opinions and beliefs of the general population regarding a COVID-19 vaccine, and their results showed that they depended on the population's trust in its government and its political preferences (Kreps et al., 2020; Lazarus et al., 2020), the accessibility to the vaccine (Reiter et al., 2020), the baseline effectiveness of the vaccine and its attributes (Harapan et al., 2020; Kreps et al., 2020), and demographic and geographic factors (Malik et al., 2020; Neumann-Böhme et al., 2020). An European study showed that about 71-75% of Portuguese residents would like to be vaccinated (Neumann-Böhme et al., 2020). More importantly, it also showed that, globally, the most significant reason for hesitating to get vaccinated against COVID-19 is the concern about the vaccine potential side effects (55%), followed by the belief that this vaccine might not be safe (15%) (Neumann-Böhme et al., 2020). In our study, 11.9% of the participants did not want to be vaccinated and 39.3% were still unsure. The most frequently selected opinions that may explain this result were fearing vaccines' side effects (16.7%) and a MS aggravation caused by vaccination (12.6%). Furthermore, 14.8% believed that the vaccine efficacy might be decreased by their MS treatment, which might also have contributed to this response. pwMS presenting progressive phenotypes answered more frequently that they do not want to be vaccinated and it was also this group that feared most often a deleterious effect on their MS because of the vaccine. The majority of those patients who are unsure about the vaccine have a RRMS or CIS phenotype, and no relation with age was found.

Patients with a superior education fear less often a MS exacerbation caused by vaccines or their side effects which highlights the notion that access to correct information has significant impact on the perspective patients have on vaccination. On the other hand, pwMS who most often fear vaccines have had their diagnosis for a relatively longer time than those who do not share this fear. This illustrates the need to clarify old-fashioned notions patients might have on these matters. These aspects stress the need to better inform patients on this subject, particularly on COVID-19 vaccine, as only 50% of the participants wish to be vaccinated. However, in the period this questionnaire was available, the AstraZeneca® vaccine trial had been suspended because of a serious neurological adverse reaction. This fact may have influenced the participants' answers.

Our study showed a lesser will to be vaccinated (48.9% vs 66% and 80.9%) when comparing to two other studies that evaluated this issue (Ehde et al., 2021; Serrazina et al., 2021). One possible explanation is that by the time our questionnaire was sent to our cohort, COVID-19 vaccines were still being developed and there was no prediction on when vaccination would start.

Having knowledge of pwMS' opinions on COVID-19 pandemic impact is useful to optimize communication and to organize healthcare systems to minimize the isolation sensation reported by patients during the pandemic. Considering the potential severity of COVID-19, fears and expectations towards COVID-19 vaccination must be discussed with pwMS.

Our study has several limitations. First, our results were taken from a convenience sample and were solely based on participants answers. As such, we had no means of verifying if the selected options were correct (for example, regarding phenotype or DMT in use). Furthermore, it would be interesting to include psychological factors in our questions, as well as trying to identify in which sources of information our patients rely on. Other drawback of our study was the fact that this questionnaire was presented in an online format, which excluded, in first instance, patients who did not have an email account. It might also have excluded patients who did not have an easy access to the internet.

CRedit authorship contribution statement

Joana Moniz Dionísio: Methodology, Investigation, Formal

analysis, Writing – original draft, Writing – review & editing, Visualization, Supervision. **Mariana Santos:** Conceptualization, Methodology, Validation, Formal analysis, Writing – review & editing, Visualization, Supervision. **Ana Martins Rodrigues:** Investigation. **André Rêgo:** Investigation. **Joana Vítor:** Investigation. **Sofia Delgado:** Investigation. **Rita Pinheiro:** Investigation. **Pedro Neves:** Investigation. **Carlos Figueiredo:** Investigation. **José Bandeira Costa:** Investigation. **José Vale:** Validation, Writing – review & editing. **Vasco Salgado:** Validation. **Ángela Timóteo:** Conceptualization, Methodology, Validation, Writing – review & editing, Visualization, Supervision.

Declaration of Competing Interest

The authors declare that they have no competing interest.

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