



## Barriers and motivations for participation in preventive vaccine clinical trials: Experience of 5 clinical research sites



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### ARTICLE INFO

#### Article history:

Received 7 May 2019

Received in revised form 10 September 2019

Accepted 11 September 2019

Available online 19 September 2019

#### Keywords:

Vaccine

Vaccine clinical trial

Motivations

Barriers

Participation

Recruitment

### ABSTRACT

Recruitment in preventive vaccine trials (PVT) is challenging due to common barriers to clinical research and lack of vaccine confidence. Identifying determinants of participation can help to improve recruitment. A prospective survey was conducted in 5 French clinical investigational sites. People asked to participate in a PVT were given a questionnaire whether they decided to participate or not in the trial. A total of 341 people answered the survey: 210 accepting and 131 declining to participate in a PVT. Acceptors were significantly younger (38.5 vs 54.9 years old), more likely to be involved in early phase trials, had a higher level of education ( $p < 0.005$ ) and a significantly better general opinion concerning vaccines (92.3% versus 72.3%,  $p < 0.005$ ) compared with those who declined. Factors associated with acceptance or refusal were evaluated in 224 people in the 4 sites where both groups were included. In a multivariate analysis, three factors: older age, having heard about PVT through multiple sources and financial incentives were significantly associated with refusal to participate in the PVT. A generally favourable opinion of vaccines was associated with acceptance. The main motivation for participation was altruism (93.2%) whereas fear of side effects was at the forefront of the barriers (36.6%). Information given by the physician was a key point for decision-making in 70.2% of those who accepted. In brief, vaccine hesitancy may decrease recruitment in PVTs; reinforcing altruism and quality of information given are key points in acceptance of participation in PVT.

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### 1. Introduction

Vaccination is one of the greatest successes in modern medicine, resulting in more than 2–3 million fewer deaths per year [1]. Development of new vaccines remains crucial in the context of outbreaks due to emerging pathogens [2] and is part of promising strategies to fight antimicrobial resistance and healthcare-associated infections [3]. Despite an increase in vaccine development [4] with more than 7300 vaccine trials registered in clinical trial.gov [5], vaccine clinical development remains time- and cost-consuming [6]. Despite lack of data on preventive vaccine

trials (PVTs), recruitment failure is the primary reason for discontinuation in clinical drug trials, occurring in one out of five trials [7]. Due to the cost associated with the clinical development of a vaccine and the public health benefits expected, reaching optimal recruitment in PVTs is crucial.

In a web survey conducted in the US, likelihood of participating in a vaccine trial was found to be lower compared to a trial for new medication or a medical device among diagnosed volunteers [8], suggesting that participation in a PVT and therefore recruitment for these trials may be associated with specific factors that need to be studied more closely. In fact, vaccine hesitancy and doubts about vaccine safety in the general population [9] might have a negative impact on recruitment of volunteers in PVTs. Therefore, investigative teams working in PVTs may face common challenges

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to clinical trials in general such as mistrust of research, difficulties in recruitment, enrollment, and retention of study participants [10–12]. These teams may also be confronted with specific concerns about vaccines that have not yet been studied in depth. To date, barriers to participation in a vaccine trial, together with motivators, have been poorly evaluated and published studies mainly deal with HIV, HCV and HPV vaccines [13].

Identifying motivators and barriers may help investigators to address potential participants' concerns and to improve recruitment in these trials. In the present study, our aim is to identify factors associated with the acceptance or refusal to participate in PVTs (phases 1 to 4) among healthy and diagnosed volunteers seen in five clinical vaccine investigational sites in France.

## 2. Material and methods

The study took place from September 2016 to March 2018 at 5 investigational sites among which 4 are part of I-Reivac "Innovative Clinical Research Network In Vaccinology" [14]. Consecutive potential participants who received a proposal to participate in a PVT in these centers, whatever their decision regarding participation in the trial, were asked to answer a survey. Eligible trials were PVTs of all study phases with (i) Institutional Review Board approval, (ii) ongoing recruitment, and (iii) whatever the infectious disease targeted by the vaccine studied. Early-phase studies were defined as phases 1 and 2a trials and later-phase studies as phases 2b and 3 (see Table 1). Early-phase PVTs were offered to healthy people and late-phase PVTs were offered to patients. Only PVTs conducted in adults were considered in this study.

Potential participants in a PVT who accepted to answer this survey received a self-administered questionnaire with six demographical questions and sixteen questions that would differ slightly according to their decision regarding participation in the PVT. Demographical data and motivations or barriers to participation in the proposed PVT were requested. Willingness to participate in a hypothetical experimental preventive vaccine against HIV, HBV or influenza virus was also assessed. These 3 diseases were selected because HBV vaccine has been controversial in France, vaccine coverage against seasonal influenza remains low, and HIV is a frightening disease as far as the general public is concerned. All 3 diseases can be contracted anywhere. All questions were previously validated and tested by volunteers and infectious diseases specialists involved in the study.

### 2.1. Ethics

The local ethics committee of the University Hospital of Saint-Etienne approved these anonymous surveys in February 2016 (number IRBN732015/CHUSTE). A declaration to the French National Commission for Data Protection (Commission Nationale Informatique et Libertés) was made.

### 2.2. Statistics

To compare characteristics of acceptors and decliners, differences between proportions were analyzed by chi-squared test or Fisher's exact test. To identify factors associated with acceptance or refusal to participate, we did not use the data of people from site number 2, as the latter could only collect questionnaires from acceptors. A p-value below 0.05 was considered to be statistically significant. To adjust for confounding factors, we conducted a multivariate analysis to test association between the explanatory variables and the decision to accept participation in a PVT with a p-value below 0.2 significance level in the univariate analysis.

The software used for collecting recorded data was Microsoft Excel and SPSS software (NYC 24.0) was used for statistical analysis.

## 3. Results

Table 1 summarizes the population distribution between each clinical research site and features of the proposed PVTs. Nine different PVTs were active at the time of the survey in the 5 sites (see Table 1). During the study period, approximately five hundred individuals were asked to participate in a PVT at the 5 sites.

### 3.1. Respondents to the survey and their characteristics

Table 2 summarizes the main characteristics of survey respondents. A total of 341 potential participants in a PVT answered the survey: 210 accepted the proposal to enroll in a PVT (acceptors) and 131 declined the proposal (decliners). For site 2, only acceptors replied to the questionnaire. The majority were female (68.9%, 235 out of 341) and the mean age was 45.1 years  $\pm$  18.2. Distribution of acceptors was balanced between early and late phases. Two hundred and twenty-four respondents (66.9%) were acquainted with clinical research and 69 (20.4%) had previously participated in a clinical trial. Fifty-nine respondents (17.4%) asked their general practitioner (GP)'s for advice regarding their participation in the PVT and 67.8% (40/59) followed it. Decliners were significantly older, had a lower level of education and in general had more children than acceptors (see Table 2).

### 3.2. Factors associated with agreement to enroll in a PVT

Only participants on sites 1, 3, 4 and 5 were included in this analysis (n = 224). People included in this analysis were invited to participate mainly in late-phase trials. In the univariate analysis presented in Table 3, Older age (OR = 0.97 (95% IC: 0.95–0.98- for one year increase in age (p < 0.005)), having heard about PVT through multiple sources (OR = 0.09 (95% IC = 0.01–0.75), p = 0.006) and proposal for a financially compensated study (0.48 (95% IC = 0.28–0.80)) p < 0.005) were negatively associated with accepting participation to the PVT. In the multivariate analysis (after adjustment for age, clinical research awareness, advice from GPs, having children, having heard about PVT through multiple sources, and financially compensated studies), these confounding factors were also associated with refusal to participate. In the univariate and multivariate analyses, having a favorable opinion about vaccines was the only factor associated with agreement to participate in the PVT (p < 0.005, OR: 4.98 (95% CI = 1.88–13.2)).

### 3.3. Acceptors' motivations

Two hundred and six acceptors (98%) from the five research sites answered the specific questionnaire about their reasons for participating in a PVT, 131 (63.6%) people in early-phase trials (healthy people), 75 (36.4%) in late-phase trials (patients). Details are shown in Table 4. Altruism was the main reason that encouraged 192 of them (93.2%) to consent to participation in a PVT with no difference between healthy and patient participants. Financial incentives encouraged 118 of them (57.3%) to accept the proposal; this was a motivation for 110 healthy participants (84%) and 8 (10.7%) patients (p < 0.005). The direct potential benefit of being protected by the vaccine was a reason for agreeing to participate for 80 respondents (39.3%) – 38 (50.7%) patients vs 42 (32.1%) healthy participants (p = 0.008). The fact that they felt at risk for the targeted disease in the study was declared by 81 of them (38.8%) – 36 (48.0%) patients vs 45 (34.4%) healthy participants (p = 0.054). Points that helped them to accept enrollment were the quality of

**Table 1**  
Design of proposed vaccine trials (PVT).

Microorganism targeted	Phase	Healthy volunteers accepted	Sexe eligible for study	Age	Site visit number	Vaccine Injection number	Financial compensation	Status of study vaccine	Sites of investigation	Number of accepting people (n = 210)	Number of declining people (n = 131)
<i>Clostridium difficile</i> **	3	No	All	50 years and older	4 or 11 depends arm and phone contact every two weeks	3	Yes	Experimental	1, 3	n = 8 (3.8%)	n = 36 (27.5%)
<i>Streptococcus pneumoniae</i>	2b	No	All	18 years and older	9	2 or 3 (depends arm)	No	Marketed	3	n = 21 (10%)	n = 5 (3.8%)
<i>Staphylococcus aureus</i>	2b	No	All	18 years to 85 years	5 and 1 contact phone	1	No*	Experimental	4, 5	n = 48 (22.9%)	n = 30 (22.9%)
Respiratory Syncytial Virus	2	Yes	Female	18 years to 45 years	5	1	Yes	Experimental	1, 2	n = 90 (42.9%)	n = 37 (28.2%)
Ebola virus**	2	Yes	All	18 years to 65 years	11 or 12 depends arm	2	Yes	Experimental	4	n = 2 (1%)	n = 0
Pneumococcal	2b	No	All	18 years to 75 years	10	2	No	Marketed	3	n = 1 (0.5%)	n = 0
Malaria	1	Yes	Female	18 years to 35 years	9 and 6 contact phone	3	Yes	Experimental	2	n = 15 (7.1%)	n = 0
<i>Shigella sonnei</i>	1	Yes	All	22 years to 50 years	5	1	Yes	Experimental	2	n = 25 (14.9%)	n = 0
<i>Clostridium difficile</i>	3	No	All	50 years and older	6	3	No*	Experimental	3	n = 0	n = 23 (17.6%)

\* Reimbursement of travel costs.

\*\* Study was suspended during 1 year due to investigation on potential adverse events.

the information provided by the physician for 145 respondents (70.4%) without differences between healthy and patient participants, the subject of the trial for 124 (60.2%) –48% of patients vs 67.2% of healthy participants ( $p = 0.007$ ), the medical follow-up for 120 (58.2%) of them with no difference between healthy participants and patients. Financial incentive was a key point for 98 (47.6%) –88 (67.2%) healthy participants vs 10 (13.3%) patients ( $p < 0.005$ ). Their GP's opinion was a key point for 63 out of the 206 respondents (30.6%), particularly in patients, 34 (45.3%) compared to healthy participants ( $n = 29$ , 22.1%), ( $p < 0.005$ ).

#### 3.4. Barriers for decliners

The reasons for declining the opportunity to participate in a PVT given by the 131 decliners –94 (71.8%) potential patient participants and 37 potential healthy participants (28.2%) - are shown in Table 4. Key barriers to uptake were firstly the fear of side effects for 48 participants (36.6%) with no difference between potential healthy and patient participants (respectively 38 (40.4%) patients and 10 (27%) healthy participants ( $p = 0.15$ )). Difficulties in attending protocol appointments were reported as a barrier by 38 of them (29%) (respectively 20 (21.3%) and 18 (48.6%) potential patient and healthy participants). Twenty-six (19.8%) were afraid of vaccine components, with a significant difference between healthy people ( $n = 14$ , 37.8%) and patients declining participation ( $n = 12$ , 12.8%),  $p < 0.005$ .

#### 3.5. Attitudes according to the different scenarios offered

Decliners were asked if their answer would have been different if the targeted disease affected them: this was the case in 27.3%

(35/128) of respondents who might have agreed to participate in the PVT. The same proportion would have agreed to enroll in the clinical trial if the drug tested had not been a vaccine. Among acceptors, 29% (59/195), 44.5% (90/202), 42.4% (86/203) would have declined to participate if the evaluated vaccine had been respectively against influenza, HIV and HBV. Among the decliners 9.2% (12/130), 16% (21/130), 26.4% (34/129) would have agreed to participate if the evaluated vaccine had been respectively against HIV, HBV, influenza.

## 4. Discussion

Our survey identified motivations and barriers to participation in a PVT among adults asked to participate in trials studying real vaccines in development. These factors have been rarely studied in PVTs in general. A recent study explored barriers to enrollment in PVTs from the point of view of investigators with experience in PVTs [15], not among people approached for participation in PVTs. Previous studies that evaluated these factors among potential participants usually focused on a unique vaccine trial in young adults, or were conducted considering hypothetical vaccine trials [13]. The people interviewed in our study, were potential participants in an actual PVT carried out at 5 French clinical research sites. Nine PVTs with different targeted diseases and different phases of development were proposed.

Factors and motivators associated with participation in a PVT have been identified in this wide-ranging survey. Our study showed that having a favorable opinion about vaccines was the only independent factor associated with agreement to enroll in a PVT, emphasizing the impact of opinions about vaccines on recruitment in a PVT. Vaccine hesitancy was in fact listed as

**Table 2**  
Demographical characteristics of the panel population.

n (%)	Panel population (n = 341)	Accepting people (n = 210)	Declining people (n = 131)	p
<b>Site</b>				<0.005
1	73 (21.4)	34 (16.2)	39 (29.8)	
2	96 (28.2)	96 (45.7)	0 (0.0)	
3	92 (27)	30 (14.3)	62 (47.3)	
4	58 (17)	35 (16.7)	23 (17.6)	
5	22 (6.5)	15 (7.1)	7 (5.3)	
<b>Age</b>	45.1 ± 18.2 (n = 320)	38.5 ± 14.5 (n = 192)	54.9 ± 18.9 (n = 128)	<0.005
<b>Gender</b>				NS
Female	235 (68.9)	150 (71.4)	85 (64.9)	
Male	106 (31.1)	60 (28.6)	46 (35.1)	
<b>Level of education</b>				<0.005
High level	176 (51.6)	128 (61)	48 (36.6)	
<b>To have children</b>	217 (63.6)	113 (53.8)	104 (79.4)	<0.005
<b>Distance between clinical trial center and home (n = 207)</b>				NS
<10 km	133 (39.3)	89 (43)	44 (33.6)	
Between 10 and 30 km	83 (24.6)	51 (24.6)	32 (24.4)	
Between 30 and 50 km	29 (8.6)	15 (7.2)	14 (10.7)	
>50 km	93 (27.5)	52 (25.1)	41 (31.3)	
<b>Clinical research awareness</b>				NS
Yes	224 (66.9)	135 (65.9)	89 (68.5)	
<b>Prior participation to a clinical trial</b>	69 (20.4)	48 (23.2)	21 (16)	NS
<b>Study awareness by...</b>				
Physician of the clinical center team	135 (39.9)	65 (31.4)	70 (53.4)	<0.005
Other physician	60 (17.8)	34 (16.4)	26 (19.8)	NS
Poster	8 (2.4)	6 (2.9)	2 (1.5)	NS
Media	10 (3)	10 (4.8)	0 (0)	0.011
Word of mouth	29 (8.6)	24 (11.6)	5 (3.8)	0.013
Internet	23 (6.8)	17 (8.2)	6 (4.6)	NS
Postal letter	37 (10.9)	30 (14.5)	7 (5.3)	0.009
More than one source of information (physician and other)	17 (5)	6 (2.9)	11 (8.4)	0.022
<b>Study compensated</b>	213 (62.5)	140 (66.7)	73 (55.7)	0.042
<b>Study phase</b>				<0.005
Phases 1 and 2a (early)	169 (49.6)	132 (62.9)	37 (28.2)	
Phases 2b, 3 (late)	172 (50.4)	78 (37.1)	94 (71.8)	
<b>Vaccination opinion</b>				<0.005
Positive opinion	286 (84.6)	192 (92.3)	94 (72.3)	
<b>Treating physician opinion requested</b>	59 (17.4)	37 (17.8)	22 (16.8)	NS
Opinion followed	40 (67.9)	28 (75.7)	12 (54.4)	
<b>Opinion of those around you requested</b>	140 (41)	82 (39.2)	60 (46.5)	

NS: Not significant.

**Table 3**  
Univariate and multivariate analysis of factors associated with acceptance Only participants on sites 1, 3, 4 and 5 were included in this analysis (n = 224). Site 2 only included accepting people and was then not included in this analysis.

Explanatory variables	Univariate analysis OR (95% CI)	p	Multivariate analysis aOR (95%CI)	p
Age OR for one year increase in age	0.97 (0.95–0.98)	<0.005	0.94 (0.91–0.96)	<0.005
Male gender	1.25 (0.74–2.09)	NS	–	–
Having Children	0.66 (0.37–1.20)	NS	1.89 (0.77–4.69)	NS
Prior participation in a PVT	0.92 (0.46–1.85)	NS	–	–
Clinical research awareness	0.64 (0.38–1.10)	NS	0.71 (0.38–1.38)	NS
Asking treating physician's opinion	1.60 (0.85–3.00)	NS	1.24 (0.53–2.88)	NS
Favorable opinion about vaccines	3.04 (1.49–6.23)	0.002	4.98 (1.88–13.2)	<0.005
Multiples source of information	0.09 (0.01–0.75)	0.006	0.09 (0.01–0.77)	0.028
Higher level of education	1.18 (0.7–1.99)	NS	–	–
Information by the physician of the clinical research team	0.72 (0.43–1.20)	NS	–	–
Early Phase	1.10 (0.63–1.92)	NS	–	–
Financial incentives	0.48 (0.28–0.80)	<0.005	0.16 (0.07–0.37)	<0.005

NS: Not significant.

one top barrier with “some effect” on PVT recruitment by researchers in Belgium [15]. In addition, Rikin *et al.* observed in 191 elderly Hispanic people, that being vaccinated against seasonal flu the year before increased by 2.6 times the acceptance of participation in a PVT [16]. In the same way, we also observed that a third of the decliners declared they would participate in a trial if the drug tested was not a vaccine. This difference in willingness to participate in a trial according to the type of product tested was previously reported in a US study [8]. Therefore gaining a better understanding of their opinion on vaccines by people

asked to participate in a PVT may help to target favorable people and increase recruitment.

Altruistic motivation has been shown to play an important role in vaccination decisions [17]. In clinical research –whether in non-vaccine trials [18] or in PVTs [13]– altruism has been shown to be a major motivation for participation in trials, a fact we also observed here. To target people with altruistic motivation may improve recruitment. Promoting altruistic participation in PVTs could prove an effective strategy in the promotion of clinical research vaccination as observed in blood donations [19].

**Table 4**  
Motivations and barriers to participate in a PVT.

Motivations for accepting people	All Respondents (n = 206, %)	Early-phase trials proposal (Healthy people (n = 131, %))	Late-phase trials proposal (Patients (n = 75, %))	p
<i>Reasons that would encourage you to consent to participate in a preventive vaccine trial were...</i>				
...To help research/to do advance science	192 (93.2)	123 (93.9)	69 (92)	NS
...To help neighbors/to protect others	135 (65.5)	91 (69.5)	44 (58.7)	NS
...Because the study is compensated	118 (57.3)	110 (84)	8 (10.7)	<0.005
...Because I feel at-risk for the disease/the topic	81 (39.3)	45 (34.4)	36 (48)	0.054
...To protect myself from the disease prevented by the vaccine	80 (38.8)	42 (32.1)	38 (50.7)	0.008
<i>Points that helped me make my decision to participate in a PVT were...</i>				
Quality of information provided by the physician	145 (70.4)	89 (67.9)	56 (74.7)	NS
Theme of the clinical trial	124 (60.2)	88 (67.2)	36 (48)	0.007
Medical follow-up planned for this study	120 (58.2)	76 (58)	44 (58.7)	NS
Financial incentives if such were the case	98 (47.6)	88 (67.2)	10 (13.3)	<0.005
Possibility to withdraw at any time	92 (44.6)	62 (47.3)	30 (40)	NS
Opinion of my general practitioner or referent physician	63 (30.6)	29 (22.1)	34 (45.3)	<0.005
Opinion of my entourage/relatives	59 (28.6)	39 (29.8)	20 (26.7)	NS
<b>Barriers for declining people</b>	<b>All Respondents (n = 131, %)</b>	<b>Early-phase trials proposal (Healthy people(n = 37, %))</b>	<b>Late-phase trials proposal (Patients (n = 94, %))</b>	<b>p</b>
<i>Reasons that would discourage you to consent to participate in a PVT were...</i>				
I'm afraid about side effects	48 (36.6)	10 (27)	38 (40.4)	NS
I don't have time to come to appointments	38 (29.0)	18 (48.6)	20 (21.3)	0.002
I live too far away	30 (22.9)	1 (2.7)	29 (30.9)	0.001
I'm afraid about components of the vaccine	26 (19.85)	14 (37.8)	12 (12.8)	0.001
I'm not sure how effective the vaccine is	19 (14.50)	10 (27)	9 (9.6)	0.011
My entourage advised me against it	15 (11.45)	3 (8.1)	12 (12.8)	NS
I don't trust studies promoted by pharmaceutical companies	15 (11.45)	0 (0)	15 (16)	0.010
I've been scared since trial drug in Rennes (France)	13 (9.92)	0 (0)	13 (13.8)	0.017
I'm not a guinea pig	9 (6.87)	0 (0)	9 (9.6)	0.051
I have a bad experience in the past	5 (3.82)	1 (2.7)	4 (4.3)	NS
I do not want to participate in a research project	12 (9.16)	0 (0)	12 (12.8)	0.023
I'm against vaccination	13 (9.92)	4 (10.8)	9 (9.6)	NS
I don't want to be injected with the product	13 (9.92)	2 (5.4)	11 (11.7)	NS
My treating physician advised me not to participate	5 (3.82)	0 (0)	5 (5.3)	NS
I'm afraid of needles	3 (2.29)	2 (5.4)	1 (1.1)	NS
I feel that my interest comes after that of the realization of the study	3 (2.29)	0 (0)	3 (3.2)	NS
I don't think I'm at risk of getting the disease affected by this vaccine	0 (0.00)	–	–	–
The study is not adequately compensated	0 (0.00)	–	–	–
Beliefs/Religion/Culture	0 (0.00)	–	–	–
Others	24 (18.32)	1 (2.7)	23 (24.7)	0.003

NS: Not significant.

We also identified factors and barriers associated with refusal to participate in PVTs, older age being the major independent factor associated with refusal. Recruiting the elderly in PVTs may thus be challenging, as has also been reported by researchers in the vaccine field [15]. Therefore this point seems crucial since among all 9 trials conducted during our study period, 4 included elderly participants. Some vaccine-preventable diseases affect older people in particular and many vaccines in development target the elderly [3]. Older people who considered they were in good health were more likely to participate in a PVT than those who considered their health as poor [20]. Regardless of age, the way older people see their health may influence their participation in PVT and this should be taken into account before enrollment in a PVT.

Financial incentives for participating in a PVT were negatively associated with acceptance in our survey, notably in late-phase trials, as frequently and previously reported [13]. This observation may be due to the inclusion of participants > 40 years-old in our analysis whereas financial incentives are a stronger motivation for young people [21]. Indeed, in a study with elderly Hispanic people where different scenarios were proposed to potential participants in a PVT against seasonal influenza [16], when an \$80

financial incentive was proposed, the proportion of people that agreed to participate decreased by 12.2% compared to no incentive. However, when we included acceptors, enrolled mainly in early-phase studies, in the analysis, financial incentives helped 49% of them to make a decision. This is probably linked to the fact that only early-phase studies received financial incentives [22] and in these phases participants are frequently healthy volunteers.

Having heard about the PVT through multiple sources was found as the third independent factor for refusal here. It may be due to the fact that the people interviewed were approached for participation mainly in late phase trials and were not coming spontaneously to the center. By contrast in other settings, the use of multiple recruitment sources simultaneously was found to be beneficial to recruitment [23].

Fear of side effects was at the forefront of the barriers to participation in a PVT as we have previously reviewed [13] and this was pointed out by more than 30% of decliners. Safety concerns about vaccines were also reported for over 40% of French participants in the vaccine confidence project [9]. It seems thus to be very important for investigators to be transparent and clearly describe available safety results to participants [24,25].

The purpose of the PVT was also found to be a key factor in decision-making, as highlighted by the fact that acceptors or decliners would change their minds if the proposed trial was related to HIV, HBV or influenza trials. These data are concordant with previous results summarized by our team [13]. These findings underline the role of knowledge about disease and the perceived risk for the acceptance of a vaccine [26]. Indeed, the acceptance of a possible vaccine is associated with the knowledge of the usefulness of vaccines [27]. So it would be important during study presentation to potential participant to insist on available safety data and to explain in detail the targeted diseases.

Most of the acceptors obtained information from the medical staff at the research site, and the quality of information helped 70% of the acceptors to make their decision. The research clinic staff are the major source of information for potential participants, particularly in the elderly as previously shown [20]. In our panel, 20% of respondents asked for their GP's opinion on their participation in a PVT and followed it in more than 50% of cases. In the US, 55% of the participants aged over 60 years in an influenza PVT, considered that their physician needs to be comfortable with their participation [20]. In parallel to this study, we conducted a study in primary care physicians and treating specialists and around 60% of them wanted to be involved in the decision-making by their patients about participation in PVT [28]. However, physicians considered they were undertrained about clinical research, and would like more information about the PVT to participate in the decision-making process [28]. It would be important to inform the patient's GP of the proposal made to his or her patient. Explaining the protocol to them could allow a more constructive exchange in the decision-making process.

Our study has several limitations. Due to the study design, the population of participants was quite heterogeneous. We chose to include potential participants for different types of PVT (Phases 1 to Phases 3) as well as healthy and diagnosed volunteers to bring insights into motivations and barriers to participation in PVTs in general. In fact previous data had only focused on a specific vaccine. Moreover our study was performed in the real-life setting of investigational sites and reflected the challenges that investigators involved in vaccinology have to face. One of the sites did not have access to participants who refused because their proposed trials mainly involved healthy volunteers who presented themselves spontaneously. To reduce this potential bias we did not integrate their observations in the analysis of factors associated with acceptance. Although we did not have full details on people who refused to answer this survey, it is likely that the response rate was lower among people who declined participation in PVTs. This can suggest that barriers to participation in PVTs have not yet been fully explored since decliners seem difficult to reach for interview.

In conclusion, in this study that interviewed potential participants in real PVTs, we observed that the way vaccines are seen by the public has an impact on recruitment. Fostering vaccine-confident participants may improve recruitment in PVTs. Financial incentives and multiplication of information sources are not suitable for all types of potential participants, particularly in trials including the elderly. The quality of the information given by the medical staff in the clinical research center is a crucial issue, and the possibility for shared decisions with primary care physicians reinforces the need for specific training of all physicians regarding clinical research.

## 5. Author's contributions

MD, EBN conceived the study and the questionnaire. MD, AGB and EBN carried out data analysis. All authors critically reviewed

this manuscript. All authors read and approved of the final manuscript.

## 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.

## Acknowledgements

The authors wish to thank i-Reivac sites for their participation and their help in sending the survey, particularly clinical research associates of the sites: Ms S. Bouillau, Ms S. Bendele, Ms N. Nedjaï, Ms S. Saleh-Mghir, Ms G. Badre and Mr S. Bourret. The authors also wish to thank Mr Philippe Michelucci and Ms Glynn Thoiron for providing English editing of the manuscript.

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