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

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1 **Barriers and motivations for participation in preventive vaccine**

2 **clinical trials: experience of 5 clinical research sites**

3

4 **Abstract**

5 Recruitment in preventive vaccine trials (PVT) is challenging due to common barriers to
6 clinical research and lack of vaccine confidence. Identifying determinants of participation can
7 help to improve recruitment. A prospective survey was conducted in 5 French clinical
8 investigational sites. People asked to participate in a PVT were given a questionnaire whether
9 they decided to participate or not in the trial. A total of 341 people answered the survey: 210
10 accepting and 131 declining to participate in a PVT. Acceptors were significantly younger
11 (38.5 vs 54.9 years old), more likely to be involved in early phase trials, had a higher level of
12 education ($p < 0.005$) and a significantly better general opinion concerning vaccines (92.3 %
13 versus 72.3 %, $p < 0.005$) compared with those who declined. Factors associated with
14 acceptance or refusal were evaluated in 224 people in the 4 sites where both groups were
15 included. In a multivariate analysis, three factors: older age, having heard about PVT through
16 multiple sources and financial incentives were significantly associated with refusal to
17 participate in the PVT. A generally favourable opinion of vaccines was associated with
18 acceptance. The main motivation for participation was altruism (93.2%) whereas fear of side
19 effects was at the forefront of the barriers (36.6%). Information given by the physician was a
20 key point for decision-making in 70.2% of those who accepted. In brief, vaccine hesitancy
21 may decrease recruitment in PVTs; reinforcing altruism and quality of information given are
22 key points in acceptance of participation in PVT.

23

24 **Keywords:** vaccine, vaccine clinical trial, motivations, barriers, participation, recruitment

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28 **Introduction**

29 Vaccination is one of the greatest successes in modern medicine, resulting in more
30 than 2 to 3 million fewer deaths per year [1]. Development of new vaccines remains crucial in
31 the context of outbreaks due to emerging pathogens [2] and is part of promising strategies to
32 fight antimicrobial resistance and healthcare-associated infections [3]. Despite an increase in
33 vaccine development [4] with more than 7 300 vaccine trials registered in clinical trial.gov
34 [5], vaccine clinical development remains time -and cost- consuming [6]. Despite lack of data
35 on preventive vaccine trials (PVTs), recruitment failure is the primary reason for
36 discontinuation in clinical drug trials, occurring in one out of five trials [7]. Due to the cost
37 associated with the clinical development of a vaccine and the public health benefits expected,
38 reaching optimal recruitment in PVTs is crucial.

39 In a web survey conducted in the US, likelihood of participating in a vaccine
40 trial was found to be lower compared to a trial for new medication or a medical device among
41 diagnosed volunteers [8], suggesting that participation in a PVT and therefore recruitment for
42 these trials may be associated with specific factors that need to be studied more closely. In
43 fact, vaccine hesitancy and doubts about vaccine safety in the general population [9] might
44 have a negative impact on recruitment of volunteers in PVTs. Therefore, investigative teams
45 working in PVTs may face common challenges to clinical trials in general such as mistrust of
46 research, difficulties in recruitment, enrollment, and retention of study participants [10–12].
47 These teams may also be confronted with specific concerns about vaccines that have not yet
48 been studied in depth. To date, barriers to participation in a vaccine trial, together with
49 motivators, have been poorly evaluated and published studies mainly deal with HIV, HCV
50 and HPV vaccines [13].

51 Identifying motivators and barriers may help investigators to address potential
52 participants' concerns and to improve recruitment in these trials. In the present study, our aim
53 is to identify factors associated with the acceptance or refusal to participate in PVTs (phases 1

54 to 4) among healthy and diagnosed volunteers seen in five clinical vaccine investigational
55 sites in France.

56

57 **Material and methods**

58 The study took place from September 2016 to March 2018 at 5 investigational sites among
59 which 4 are part of I-Reivac “Innovative Clinical Research Network In Vaccinology” [14].

60 Consecutive potential participants who received a proposal to participate in a PVT in these
61 centers, whatever their decision regarding participation in the trial, were asked to answer a
62 survey. Eligible trials were PVTs of all study phases with (i) Institutional Review Board
63 approval, (ii) ongoing recruitment, and (iii) whatever the infectious disease targeted by the
64 vaccine studied. Early-phase studies were defined as phases 1 and 2a trials and later-phase
65 studies as phases 2b and 3 (See Table 1). Early-phase PVTs were offered to healthy people
66 and late-phase PVTs were offered to patients. Only PVTs conducted in adults were
67 considered in this study.

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

78 **Ethics.** The local ethics committee of the University Hospital of Saint-Etienne approved these
79 anonymous surveys in February 2016 (number IRBN732015/CHUSTE). A declaration to the

80 French National Commission for Data Protection (**Commission Nationale Informatique et**
81 **Libertés**) was made.

82 **Statistics.** To compare characteristics of acceptors and decliners, differences between
83 proportions were analyzed by chi-squared test or Fisher's exact test. To identify factors
84 associated with acceptance or refusal to participate, we did not use the data of people from
85 site number 2, as the latter could only collect questionnaires from acceptors. A p-value below
86 0.05 was considered to be statistically significant. To adjust for confounding factors, we
87 conducted a multivariate analysis to test association between the explanatory variables and the
88 decision to accept participation in a PVT with a p-value below 0.2 significance level in the
89 univariate analysis. The software used for collecting recorded data was Microsoft Excel and
90 SPSS software (NYC 24.0) was used for statistical analysis.

91

92 **Results**

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

97 *Respondents to the survey and their characteristics*

98 Table 2 summarizes the main characteristics of survey respondents. A total of 341 potential
99 participants in a PVT answered the survey: 210 accepted the proposal to enroll in a PVT
100 (acceptors) and 131 declined the proposal (decliners). For site 2, only acceptors replied to the
101 questionnaire. The majority were female (68.9%, 235 out of 341) and the mean age was 45.1
102 years \pm 18.2. Distribution of acceptors was balanced between early and late phases. Two
103 hundred and twenty-four respondents (66.9%) were acquainted with clinical research and 69
104 (20.4%) had previously participated in a clinical trial. Fifty-nine respondents (17.4%) asked
105 their general practitioner (GP)'s for advice regarding their participation in the PVT and 67.8
106 % (40/59) followed it. Decliners were significantly older, had a lower level of education and
107 in general had more children than acceptors (See Table 2).

108 *Factors associated with agreement to enroll in a PVT*

109 Only participants on sites 1, 3, 4 and 5 were included in this analysis (n=224). People
110 included in this analysis were invited to participate mainly in late-phase trials. In the
111 univariate analysis presented in Table 3, Older age (OR= 0.97 (95% IC: 0.95-0.98- for one
112 year increase in age ($p < 0.005$)), having heard about PVT through multiple sources (OR=0.09
113 (95% IC=0.01-0.75), $p = 0.006$) and proposal for a financially compensated study (0.48 (95%
114 IC=0.28-0.80)) $p < 0.005$) were negatively associated with accepting participation to the PVT.
115 In the multivariate analysis (after adjustment for age, clinical research awareness, advice from
116 GPs, having children, having heard about PVT through multiple sources, and financially
117 compensated studies), these confounding factors were also associated with refusal to

118 participate. In the univariate and multivariate analyses, having a favorable opinion about
119 vaccines was the only factor associated with agreement to participate in the PVT ($p < 0.005$,
120 OR: 4.98 (95% CI=1.88-13.2)).

121 *Acceptors ' motivations*

122 Two hundred and six acceptors (98%) from the five research sites answered the specific
123 questionnaire about their reasons for participating in a PVT, 131(63.6%) people in early-
124 phase trials (healthy people), 75 (36.4%) in late-phase trials (patients). Details are shown in
125 Table 4. Altruism was the main reason that encouraged 192 of them (93.2%) to consent to
126 participation in a PVT with no difference between healthy and patient participants. Financial
127 incentives encouraged 118 of them (57.3%) to accept the proposal; this was a motivation for
128 110 healthy participants (84%) and 8 (10.7%) patients ($p < 0.005$). The direct potential benefit
129 of being protected by the vaccine was a reason for agreeing to participate for 80 respondents
130 (39.3%) -38 (50.7 %) patients vs 42 (32.1%) healthy participants ($p = 0.008$). The fact that they
131 felt at risk for the targeted disease in the study was declared by 81 of them (38.8%) -36
132 (48.0%) patients vs 45 (34.4%) healthy participants ($p = 0.054$). Points that helped them to
133 accept enrollment were the quality of the information provided by the physician for 145
134 respondents (70.4%) without differences between healthy and patient participants, the subject
135 of the trial for 124 (60.2%) -48 % of patients vs 67.2 % of healthy participants ($p = 0.007$), the
136 medical follow-up for 120 (58.2%) of them with no difference between healthy participants
137 and patients. Financial incentive was a key point for 98 (47.6%) -88 (67.2%) healthy
138 participants vs 10 (13.3 %) patients ($p < 0.005$). Their GP's opinion was a key point for 63 out
139 of the 206 respondents (30.6%), particularly in patients, 34 (45.3%) compared to healthy
140 participants ($n = 29$, 22.1%), ($p < 0.005$).

141 *Barriers for decliners*

142 The reasons for declining the opportunity to participate in a PVT given by the 131 decliners -
143 94 (71.8%) potential patient participants and 37 potential healthy participants (28.2%) - are

144 shown in Table 3. Key barriers to uptake were firstly the fear of side effects for 48
145 participants (36.6%) with no difference between potential healthy and patient participants
146 (respectively 38 (40.4%) patients and 10 (27%) healthy participants ($p=0.15$)). Difficulties in
147 attending protocol appointments were reported as a barrier by 38 of them (29%) (respectively
148 20 (21.3%) and 18 (48.6%) potential patient and healthy participants). Twenty-six (19.8%)
149 were afraid of vaccine components, with a significant difference between healthy people
150 ($n=14$, 37.8%) and patients declining participation ($n=12$, 12.8%), $p<0.005$).

151

152 *Attitudes according to the different scenarios offered*

153 Decliners were asked if their answer would have been different if the targeted disease affected
154 them: this was the case in 27.3% (35/128) of respondents who might have agreed to
155 participate in the PVT. The same proportion would have agreed to enroll in the clinical trial if
156 the drug tested had not been a vaccine. Among acceptors, 29% (59/195), 44.5% (90/202),
157 42.4% (86/ 203) would have declined to participate if the evaluated vaccine had been
158 respectively against influenza, HIV and HBV. Among the decliners 9.2 % (12/130), 16%
159 (21/130), 26.4% (34/129) would have agreed to participate if the evaluated vaccine had been
160 respectively against HIV, HBV, influenza.

161

162

163

164 **Discussion**

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

175 Factors and motivators associated with participation in a PVT have been identified in
176 this wide-ranging survey. Our study showed that having a favorable opinion about vaccines
177 was the only independent factor associated with agreement to enroll in a PVT, emphasizing
178 the impact of opinions about vaccines on recruitment in a PVT. Vaccine hesitancy was in fact
179 listed as one top barrier with “some effect” on PVT recruitment by researchers in Belgium
180 [15]. In addition, Rikin *et al.* observed in 191 elderly Hispanic people, that being vaccinated
181 against seasonal flu the year before increased by 2.6 times the acceptance of participation in a
182 PVT [16]. In the same way, we also observed that a third of the decliners declared they would
183 participate in a trial if the drug tested was not a vaccine. This difference in willingness to
184 participate in a trial according to the type of product tested was previously reported in a US
185 study [8]. Therefore gaining a better understanding of their opinion on vaccines by people
186 asked to participate in a PVT may help to target favorable people and increase recruitment.
187 Altruistic motivation has been shown to play an important role in vaccination decisions [17].
188 In clinical research -whether in non-vaccine trials [18] or in PVTs [13]- altruism has been
189 shown to be a major motivation for participation in trials, a fact we also observed here. To

190 target people with altruistic motivation may improve recruitment. Promoting altruistic
191 participation in PVTs could prove an effective strategy in the promotion of clinical research
192 vaccination as observed in blood donations [19].

193 We also identified factors and barriers associated with refusal to participate in PVTs,
194 older age being the major independent factor associated with refusal. Recruiting the elderly in
195 PVTs may thus be challenging, as has also been reported by researchers in the vaccine field
196 [15]. Therefore this point seems crucial since among all 9 trials conducted during our study
197 period, 4 included elderly participants. Some vaccine-preventable diseases affect older people
198 in particular and many vaccines in development target the elderly [3]. Older people who
199 considered they were in good health were more likely to participate in a PVT than those who
200 considered their health as poor [20]. Regardless of age, the way older people see their health
201 may influence their participation in PVT and this should be taken into account before
202 enrollment in a PVT.

203 Financial incentives for participating in a PVT were negatively associated with acceptance in
204 our survey, notably in late-phase trials, as frequently and previously reported [13]. This
205 observation may be due to the inclusion of participants > 40 years-old in our analysis whereas
206 financial incentives are a stronger motivation for young people [21]. Indeed, in a study with
207 elderly Hispanic people where different scenarios were proposed to potential participants in a
208 PVT against seasonal influenza [16], when an \$80 financial incentive was proposed, the
209 proportion of people that agreed to participate decreased by 12.2% compared to no incentive.
210 However, when we included acceptors, enrolled mainly in early-phase studies, in the analysis,
211 financial incentives helped 49% of them to make a decision. This is probably linked to the
212 fact that only early-phase studies received financial incentives [22] and in these phases
213 participants are frequently healthy volunteers.

214 Having heard about the PVT through multiple sources was found as the third independent
215 factor for refusal here. It may be due to the fact that the people interviewed were approached

216 for participation mainly in late phase trials and were not coming spontaneously to the center.
217 By contrast in other settings, the use of multiple recruitment sources simultaneously was
218 found to be beneficial to recruitment [23].

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

224 The purpose of the PVT was also found to be a key factor in decision-making (See
225 Table 3), as highlighted by the fact that acceptors or decliners would change their minds if the
226 proposed trial was related to HIV, HBV or influenza trials. These data are concordant with
227 previous results summarized by our team [13]. These findings underline the role of
228 knowledge about disease and the perceived risk for the acceptance of a vaccine [26]. Indeed,
229 the acceptance of a possible vaccine is associated with the knowledge of the usefulness of
230 vaccines [27]. So it would be important during study presentation to potential participant to
231 insist on available safety data and to explain in detail the targeted diseases.

232 Most of the acceptors obtained information from the medical staff at the research site, and the
233 quality of information helped 70% of the acceptors to make their decision. The research clinic
234 staff are the major source of information for potential participants, particularly in the elderly
235 as previously shown [20]. In our panel, 20% of respondents asked for their GP's opinion on
236 their participation in a PVT and followed it in more than 50% of cases. In the US, 55% of the
237 participants aged over 60 years in an influenza PVT, considered that their physician needs to
238 be comfortable with their participation [20]. In parallel to this study, we conducted a study in
239 primary care physicians and treating specialists and around 60% of them wanted to be
240 involved in the decision-making by their patients about participation in PVT [28]. However,
241 physicians considered they were undertrained about clinical research, and would like more

242 information about the PVT to participate in the decision-making process [28]. It would be
243 important to inform the patient's GP of the proposal made to his or her patient. Explaining the
244 protocol to them could allow a more constructive exchange in the decision-making process.

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

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

266
267 ***Conflict of interest***

268 The authors declare that they have no conflict of interest.

269 *Author's contributions*

270 MD, EBN conceived the study and the questionnaire. MD, AGB and EBN carried out data
271 analysis. All authors critically reviewed this manuscript. All authors read and approved of the
272 final manuscript.

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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

Table 2: Demographical characteristics of the panel population

n (%)	Panel population (n=341)	Accepting people (n=210)	Declining people (n=131)	P
Site				<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)	
Age	45.1 ± 18.2 (n=320)	38.5 ± 14.5 (n=192)	54.9 ± 18.9 (n=128)	<0.005
Gender				0.204
Female	235 (68.9)	150 (71.4)	85 (64.9)	
Male	106 (31.1)	60 (28.6)	46 (35.1)	
Level of education				<0.005
High level	176 (51.6)	128 (61)	48 (36.6)	
To have children	217 (63.6)	113 (53.8)	104 (79.4)	<0.005
Distance between clinical trial center and home (n=207)				0.259
<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)	
Clinical research awareness				0.621
Yes	224 (66.9)	135 (65.9)	89 (68.5)	
Prior participation to a clinical trial	69 (20.4)	48 (23.2)	21 (16)	0.112
Study awareness by...				
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)	0.422
Poster	8 (2.4)	6 (2.9)	2 (1.5)	0.419
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)	0.196
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
Study compensated	213 (62.5)	140 (66.7)	73 (55.7)	0.042
Study phase				<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)	
Vaccination opinion				
Positive opinion	286 (84.6)	192 (92.3)	94 (72.3)	<0.005
Treating physician opinion requested	59 (17.4)	37 (17.8)	22 (16.8)	0.814
Opinion followed	40 (67.9)	28 (75.7)	12 (54.4)	
Opinion of those around you requested	140 (41)	82 (39.2)	60 (46.5)	

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)	0.399	-	-
Having Children	0.66 (0.37 – 1.20)	0.173	1.89 (0.77-4.69)	0.165
Prior participation in a PVT	0.92 (0.46 – 1.85)	0.818	-	-
Clinical research awareness	0.64 (0.38-1.10)	0.111	0.71 (0.38-1.38)	0.317
Asking treating physician's opinion	1.60 (0.85 – 3.00)	0.137	1.24 (0.53-2.88)	0.619
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)	0.535	-	-
Information by the physician of the clinical research team	0.72 (0.43-1.20)	0.206	-	-
Early Phase	1.10 (0.63-1.92)	0.726	-	-
Financial incentives	0.48 (0.28 – 0.80)	<0.005	0.16 (0.07-0.37)	<0.005

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)	0.603
...To help neighbors/to protect others	135 (65.5)	91 (69.5)	44 (58.7)	0.12
...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)	0.319
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)	0.927
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)	0.309
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)	0.635
Barriers for declining people	All Respondents (n=131, %)	Early-phase trials proposal (Healthy people (n= 37, %))	Late-phase trials proposal (Patients (n= 94, %))	p
<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)	0.15
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)	0.401
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)	0.676
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)	0.83
I don't want to be injected with the product	13 (9.92)	2 (5.4)	11 (11.7)	0.278
My treating physician advised me not to participate	5 (3.82)	0 (0)	5 (5.3)	0.153
I'm afraid of needles	3 (2.29)	2 (5.4)	1 (1.1)	0.137
I feel that my interest comes after that of the realization of the study	3 (2.29)	0 (0)	3 (3.2)	0.272
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