



Factors influencing participation in an Ebola vaccine trial among front-line workers in Guinea



Kyra H. Grantz^{a,b}, Pauline Claudot^c, Micky Kambala^d, Mariama Kouyaté^e, Aboubacar Soumah^e, Yap Boum^e, Aitana Juan-Giner^e, Jean-Paul Jemmy^d, Derek A.T. Cummings^{a,b}, Rebecca F. Grais^{e,*}

^a Emerging Pathogens Institute, University of Florida, Gainesville, FL 32611, USA

^b Department of Biology, University of Florida, Gainesville, FL 32611, USA

^c Ecole Normale Supérieure-Lyon, France

^d Médecins Sans Frontières-Operational Center, Belgium

^e Epicentre, 8 rue Saint Sabin, 75011 Paris, France

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ABSTRACT

Background: Alongside the clinical aspects of the immunogenicity and safety trial of an Ebola vaccine deployed among front-line workers, a qualitative study was conducted to describe motivations behind individuals' decisions to participate – or not to participate – in the study.

Methods: In July and August 2015, focus group discussions and semi-structured individual interviews were conducted in Conakry, Guinea. Individuals were eligible for the qualitative study if they met the inclusion criteria of the immunogenicity and safety study irrespective of their participation. Surveys were also conducted among several institution and department heads of staff included in the study as well as vaccine trial staff members. Discussion and interview transcripts were analyzed using content thematic analysis.

Results: Interviews and focus groups were conducted among 110 persons, of whom about two-thirds (67%) participated in the vaccine trial. There was at least one group interview conducted at each participating trial site, along with numerous formal and informal interviews and conversations through the enrollment period. Participants were often motivated by a desire to save and protect themselves and others, contribute to scientific progress, or lead by example. Non-participants expressed concerns regarding the risk and costs of participation, particularly the fear of unknown side effects following vaccination, and distrust or fear of stigmatization.

Conclusions: Despite the unique nature of the 2014–2015 Ebola outbreak, front-line workers employed much of the same logic when choosing to participate as in other clinical trials in similar settings. Special consideration should be given to addressing perceived inequity, misunderstanding, and mistrust among the target populations in future trials.

Clinical trial registry number: This trial is registered with the Pan African Clinical Trials Registry, number PACTR201503001057193.

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1. Introduction

The 2014–2015 Ebola epidemic in West Africa was unprecedented in its size and scope. West Africa was officially declared Ebola-free in January 2016, though several isolated flare-ups have been reported since [1]. There were 28,646 confirmed, probable, and suspected cases of Ebola virus disease (Ebola) and 11,323

reported deaths as of April 2016, though many suspect the true burden was much higher [2].

A Phase III trial in Guinea and Sierra Leone [3] to assess the efficacy of an Ebola vaccine (the 'Ebola ça suffit' trial) began in March 2015. The trial used a novel cluster-randomized ring vaccination design to assess the efficacy of the recombinant, replication-competent vesicular stomatitis virus (rVSV) vaccine (Merck) [3,4]. Interim results published in August 2015 indicated that the rVSV vaccine had high efficacy, after which immediate vaccination was offered to all identified rings [5]. Subsequent analysis of this trial has confirmed a protective effect of the rVSV

* Corresponding author at: 8 rue Saint Sabin, 75011 Paris, France.

E-mail address: Rebecca.Grais@epicentre.msf.org (R.F. Grais).

Table 1
Front-line workers (FLWs) invited to participate in the Frontline Workers Study.

Category	Examples
Healthcare workers in Ebola treatment center	Doctors, nurses, nursing aides, laboratory technicians, housekeepers, support and administrative personnel
Healthcare workers in other healthcare setting	Doctors, nurses, nursing aides, laboratory technicians, housekeepers, support and administrative personnel
Ebola response workers	Security teams, burials teams, ambulance teams

vaccine [6]. The rVSV vaccine has now been given to nearly 200,000 individuals in an ongoing outbreak in the Democratic Republic of Congo [7,8].

A sub-study of the ‘Ebola ça suffit’ trial addressed vaccine performance among front-line workers (FLWs), defined as those actively working to respond to the Ebola epidemic and who, through their daily work, were considered high-risk for Ebola exposure (Table 1). By some measures, healthcare workers, a key population of front-line workers, were more than 30 times more likely to be infected with Ebola than the general population [9,10]. This study was intended to complement the ‘Ebola ça suffit’ trial by offering more information on immunogenicity endpoints and focusing on a high-risk population likely to be targeted in future prevention and response efforts.

The FLWs immunogenicity study began in March 2015 with participants from six healthcare institutions in Conakry, Guinea. Participants were expected to visit a vaccination site for inclusion screening, blood sampling and clinical follow-up for a minimum of 4 scheduled visits over 3 months and 6 months for a sub-set of participants. Participants were also asked to maintain a symptom diary and take their temperature regularly. Participation was voluntary and medical care for side effects of the vaccine, as well as health problems not linked to the trial during follow-up, was provided free of charge. Participants were also offered a travel allowance of 30,000 Guinean francs (approximately \$4USD), and juice and cookies at each visit. The vaccine trial team was Guinean, with the exception of 4 staff members without direct contact with participants.

Alongside the clinical aspects of the vaccine trial, a qualitative study was conducted to describe motivations behind individuals’ decisions to participate – or not to participate – in the study, with the associated goals of improving engagement as the trial progressed and informing future trials or use of the vaccine. Here, we present the results of our qualitative study. We found six prevailing themes in the reasoning behind most FLWs’ decisions: seeking protection; balancing risks and rewards; setting an example; distrust of international organizations; fear of stigmatization; and contributing to scientific progress. We discuss the social, political, and ethological factors highlighted by participants and lessons learned for future trials.

2. Methods

2.1. Study participants and setting

Each of the six primary sites participating in the vaccine trial were targeted sites for enrollment in the qualitative study. These included 3 hospitals, 2 community medical centers, and one health center that provided community-based response services (including clinical care, surveillance, and burial services, among others) and had admitted likely or confirmed Ebola cases.

Enrollment began with an introductory visit and semi-structured interview with the director of the six medical institu-

tions and, when possible, the director of each participating department. The director or institute head would then present the study to their staff and the qualitative study staff could begin discussing possible recruitment of participants. The only criteria for enrollment in the qualitative study were willingness and availability to participate and meeting the immunogenicity study’s inclusion criteria (Table 1). Recruitment was targeted broadly towards all types of eligible FLWs. Care was taken to include individuals from various jobs, services, and age classes, and to include responses from both men and women. Recruitment was based primarily on FLWs’ availability in each institution and there was no pre-imposed limit on the number of participants. Members of the vaccine trial team, such as health promoters, referring doctors, and investigators, were also interviewed. Due to time constraints of their duties, no medical personnel directly in charge of vaccination were formally interviewed, though they did offer some insight during informal conversation with study staff.

2.2. Interviews

The study staff prepared interview guides to structure their inquiries. These guides were modified to match the profile of the interview subjects. Interviews with directors and FLWs targeted for enrolment focused on four topics: (1) their knowledge of Ebola virus disease (EVD) and the ongoing outbreak; (2) their understanding of clinical trials in general and the context and protocol for this specific vaccine trial; (3) their considerations when deciding whether to participate; and (4) relevant individual characteristics or beliefs, such as profession, educational background, and religious or political beliefs. Directors were interviewed individually, while FLWs were either interviewed individually or in a discussion group of other FLWs. Interviews were organized primarily based on availability of the FLWs and were often brief, typically no more than 45 min, so that interviewees could remain focused on their professional duties.

Three topics were emphasized in interviews with the vaccine trial team: (1) their knowledge of and perception of the outbreak and vaccine trial; (2) the theoretical, ideal, and practical duties of their position; and (3) their individual profiles and background in clinical research and outbreak response. Interviews with vaccine trial staff tended to be longer (up to two and a half hours, in one case). Two focus groups of health promoters were held in addition to individual and group interviews of investigators, doctors, and other key staff members.

The qualitative study was structured recursively; that is, investigators continued to refine the interview guides as the study progressed in order to pursue certain recurring themes within the topics above that proved important during earlier interviews. At times with the assistance of an interpreter, the investigative team would record the interview and focus group conversations and then re-transcribe these recordings for content analysis based on the interview themes developed for each group.

Thematic content analysis was applied as a method to systematically code the text data and to identify themes and patterns [11,12]. Both deductive and inductive approaches to data analysis were utilized [13,14]. General categories were outlined based on prior research on participation in vaccine studies and discussions with the study staff. Additional codes and categories were directly derived from the data included beliefs, opinions, social pressures and social norms.

Two researchers read the transcripts line-by-line and labeled concepts. Major themes and sub-themes were identified within and across categories and the broad themes identified. Throughout the process, the researchers triangulated the qualitative data with the existing literature and ongoing events in the field concerning the epidemic. Constant comparative technique was applied, but

the iterative process of concurrent data collection and analysis was not conducted due to study logistics and translation of interview transcripts. The most illustrative of opinions, perceptions and behaviors most frequently expressed are reported, as well as examples of isolated and unique behavior [15].

Investigators also took careful notes on their observations of interpersonal interactions, the general atmosphere of each location, and the configuration of the interview or focus group in a field notebook, which were then transcribed in Microsoft Word.

2.3. Ethical considerations

The qualitative study was included in the vaccine trial protocol approved by the ethical committees of Médecins Sans Frontières, the World Health Organization, and Guinea. All data is confidential and was anonymized during transcriptions. Staff at the University of Florida did not interact with participants nor access personally identifiable data and thus did not engage in human subjects research.

Inclusion in the study was voluntary and was not contingent upon participation in the parent vaccine trial. All participants were asked to orally consent to the study following a presentation describing the study goals and procedures given by the qualitative study staff or the institute or department head.

3. Results

Between July and August 2015, testimony was collected from 110 FLWs, of whom about two-thirds participated in the vaccine trial (Table 2), as well as several institution and department heads and vaccine trial staff members. There was at least one group interview at each participating trial site, along with numerous formal and informal interviews and conversations through the enrollment period.

Themes of participation and non-participation

3.1. Theme 1: protection in a high-risk setting

Protecting oneself and one's family was the most commonly provided argument in favor of participating, particularly among young women with children and older women: "because, if I am protected, I won't infect my family", said one FLW. Interviewees explained that protecting themselves also limited their other patients' exposure to EVD and would allow them to continue providing urgently-needed medical care. Participation became a way to contribute to general safety. Participants were "doing what has to be done" and "risking everything for everyone". Participants frequently invoked their "sacrifice" and "service" to their families, to their country, even to "Africa" and "the world".

Table 2
Participant characteristics for the FLW vaccine trial and qualitative study.

	FLW study (n = 2016)	Qualitative study (n = 110)
Mean Age (years)	33.4	34.6
Vaccinated, n (%)	2016 (100)	75 (67.0)
Male, n (%)	1512 (75.0)	45 (40.0)
Workplace, n (%)		
Ebola Treatment Center	408 (20.2)	11 (10.0)
Ebola outreach services	621 (30.8)	22 (20.0)
Hospital	484 (24.0)	19 (17.3)
Health center	314 (15.6)	45 (40.1)
Clinic	37 (1.8)	3 (2.0)
Other	152 (7.5)	10 (9.0)

While the majority of FLWs seemed to recognize their elevated risk of EVD exposure, several referenced the risk of infection from routine activities outside of work – taking the bus, or going to an overcrowded market – rather than from sick patients. Medical workers, though, frequently referenced the unknown risks and dangers they faced: "We don't know who we're dealing with in our job", said one, and "anybody and everybody comes to the hospital" said another. There was a general feeling that "the natural order of things" had been upset, with patients now a threat to daily life. "I want to be healthy", said one interviewee. A majority of FLWs expressing these views saw the vaccine as a way to "get out of this" difficult situation and "to return to normal life".

3.2. Theme 2: costs and benefits of participation

For many, the decision to participate came down to a calculus between the perceived risks of the study and the offered compensations. Most non-participants referenced the experimental nature and perceived "risk" of the vaccine when explaining their refusal to participate. By February 2015, the epidemic had slowed, and individuals felt they could control their exposure through prescribed preventative measures until the epidemic ended. "It's enough just to be careful", said one hospital employee. Others embraced a more fatalistic outlook, questioning how prevention efforts could be useful when there was still no cure for Ebola: "A vaccine, to do what?". Vaccination, on the other hand, carried with it uncertain success and potential short-term side effects (like headaches or nausea) and long-term health issues. One department head claimed the 3-month observation window was "not enough to study the side effects; they could happen three, five, ten years later".

Many decided the time and effort required was not outweighed by the direct and indirect benefits of participation. Simply put by several interviewees, "time is money". Several participants (medical doctors or other senior personnel in particular) were offended at being offered what they deemed insignificant compensation ("only" 30,000GNF, "a miserable soda can"), and thus refused to participate. Several questioned why they weren't given a cash payment, "the way they do for whites in the west".

The blood draw was referenced frequently by non-participants. In fact, many seemed to ignore the risks of vaccination itself but heavily considered the blood draw when deciding whether to participate. Several interviewees balked at the amount of blood collected ("so much blood") and felt inadequately compensated for "all they took out".

By far the greatest perceived benefit to participation, as discussed above, was the opportunity for participants to "protect themselves" from EVD. Several interviewees referenced a statement in the informed consent documents that the vaccine was "not guaranteed" to be effective and therefore decided that participation had insufficient benefits. For some, the benefits of compensation besides vaccination encouraged participation. Some felt being able to participate was "amazing luck" or even a privilege "owe[d]" to them that would be silly not capitalize on. Non-medical personnel, such as triage workers, orderlies, and janitors, especially were motivated by the medical care offered during the trial "because, if you get sick or whatever, [the medical staff] are here to explain it to us".

3.3. Theme 3: setting an example

Several healthcare workers indicated that their participation was driven by a desire to be consistent with their own advice to patients and to lead by example. As health professionals, they said, they must "follow our own advice" and be "ready to do whatever needs to be done". "It's part of the job", said one doctor, to act as

torchbearers. Doctors at community medical and health centers seemed especially swayed by these arguments.

Individuals in supervisory roles also expressed the idea that their participation in the trial might influence their employees to participate. One group of nurses and doctors said of their supervisor, “he’s actually the one who gave us the courage [to participate]”. Interestingly, though, there was a level of distrust between some FLWs and their supervisors or directors. One nurse complained that employees had no way of knowing whether their supervisor, who was encouraging eligible persons to be vaccinated, had herself been vaccinated: “She can say whatever she wants, but anyway we haven’t seen [it]”. Such sentiments were most commonly expressed when there was already a level of dissension or mistrust between FLWs and their supervisors. Other supervisors were wary to unduly influence their employees’ informed consent and chose not to actively encourage participation, regardless of their own participation status.

3.4. Theme 4: distrust and contempt towards international organizations

The otherworldly nature of the epidemic gave rise to many conspiracy theories, including that Ebola had been introduced by whites in order to eradicate the population, or that the epidemic was a ploy by the pharmaceutical companies that hoped to profit by forcing expedited (and perhaps less ethically stringent) vaccine trials and production. FLWs often referred to “Ebola industry” and “the whites” who were bound to benefit from the outbreak, vaccine trial and eventual licensure and production of the vaccine. They expressed dismay at being asked to “become lab rats” and “sacrifice themselves” when they “were already suffering enough”. Some were even suspicious that blood was not collected to determine vaccine performance, but instead was being used for other purposes, like screening Ebola patients for quarantine.

Suspicion of the vaccine trial organizers was heightened by the fact that staff members did not participate in the trial. One doctor wondered why the study staff had themselves not been vaccinated when they faced many of the same exposure risks as many FLWs. Non-participants invoked metaphors of poisoning: “It’s as if someone was offering you a glass of water without drinking themselves”, or “Imagine if you were invited to dinner and they brought in a dish that your host would not even touch”.

3.5. Theme 5: stigmatization of trial participants

During the Ebola epidemic, there was great social stigma against those caring for and interacting with the sick [16,17]. Interviewees expressed fear of being exiled should there be undesirable effects of vaccination, especially if the side effects resemble EVD symptoms. Several FLWs were hesitant to subject themselves to taunts of “I told you so” and “It’s all your own fault, you only had to say no”, they said. Participants could be chastised for colluding with foreigners and other suspicious entities, for endangering their colleagues and family if they are forced to stop working, and for selling or degrading their body by accepting compensation to be vaccinated and have blood drawn.

Some participants wanted to hide their participation from family and friends, in order to avoid reproach should the trial be unsuccessful or cause side effects. The time demands and travel required by participation made such secrecy difficult and stressful, and likely discouraged potential participants. Several non-participants who had at first seemed enthusiastic to participate admitted to being dissuaded by family members when they mentioned the trial.

While there was certainly risk of stigmatization – participants were “unaware” and “idiots”, according to one administrator

who chose not to participate – others recognized the sacrifice participants were making. “They are brave,” said the same administrator following the release of the preliminary results of the ring vaccination trial. “I didn’t have that kind of courage. If we get a vaccine soon, it will be thanks to them, not thanks to me.”

3.6. Theme 6: motivation to aid in development of a vaccine

Some participants dismissed concerns of criticism or marginalization in favor of greater aspirations for scientific progress. One participant said “I don’t care about critics; they can laugh all they want, but I will still participate. It’s the only way we can have progress”, and another claimed “If we don’t let foreigners help us, we’ll never get anywhere.” Nurses, doctors and department heads were mostly likely to frame their choice to participate as a matter of scientific progress. They would compare the Ebola vaccine trial to other clinical trials, understanding that clinical trials were “just how it works” and other drugs and remedies, like the Ebola vaccine, “had to be tested before they could be used”.

4. Discussion

Our investigation showed that the motives for participating in the vaccine trial among front-line workers were numerous and multifaceted. Idealism, manifested as a desire to save others, contribute to scientific progress, or lead by example, combined with a healthy sense of pragmatism (protecting oneself, one’s family, one’s patients) were the primary motives for participation. Fear was likely a strong motivator during the Ebola outbreak; participants in this study and in another survey of healthcare workers in Nigeria reported anxiety about their high levels of exposure and the many uncertainties surrounding the outbreak [18], though clinical trial participants outside of emergency settings also frequently refer to a desire to protect themselves [19–22]. Access to medical care throughout the clinical trial was a motivating factor for several participants, an occurrence that seems common in areas with a limited-capacity healthcare system [22–24].

Many studies of clinical research report high levels of therapeutic misconception, in which participants conflate medical research with medical care, or confusion regarding study aims and procedures [21–23,25–31]. The Ebola outbreak response especially was plagued by rumors and confusion regarding the disease’s provenance, manifestation, and treatment options, even among healthcare workers [18,32,33]. Misinformation has huge implications on recruitment and informed consent procedures. In one study in Burkina Faso, 70% of participants, who displayed high levels of therapeutic misconception, had decided to participate before meeting with staff at the trial site, on the basis of information spread through the community [22]. In this study, staff reported that up to one-quarter of those interviewed misunderstood or were indifferent to the goals and procedures of the vaccine trial, including a few who confused “vaccine trial” with “vaccine”. Every effort should be made to present disclosure and consent materials in an understandable, transparent manner. The staff of this vaccine trial found tailoring their rhetoric to address the diverse backgrounds and experiences of FLWs improved both understanding and participation. The information-giving process should be flexible to allow study teams to adjust their approaches to address heterogeneity in the target population and respond to individual misconceptions, concerns, and interests [26,27,34].

Though non-participation often appeared to be a choice of inertia more than an active decision to not participate, there are still many factors that discouraged enrollment. Concerns regarding the risk and costs of participation, particularly the fear of unknown side effects following vaccination, was a commonly avowed reason

for non-participation. Such concerns are regularly found in participants of many backgrounds and can be difficult to divorce from the experimental nature of clinical research [20,21,27,30,35–38]. And while fear may have encouraged some to seek vaccination as a protective measure, it also kept many from seeking clinical care, promoted stigmatization of Ebola responders, and likely lead some FLWs to avoid the vaccine trial [17,18,39].

A similar qualitative study of an Ebola vaccine trial in Sierra Leone found that the perceived fairness or unfairness of the vaccine trial was critical to the success of their engagement efforts [40]. We observed several manifestations of this desire for equity in the complaints of inadequate compensations, in the anger that only FLWs (not the trial staff and not family) were asked to participate, and in the common refrain among participants that it would have been “unfair” to miss their chance at vaccination. (Participants in our trial were not the only Ebola responders to request increased compensation for their effort; some healthcare workers in Nigeria requested money and life insurance to participate in Ebola response teams [18]). Perhaps the most extreme extension of this perceived inequity is the deep-seated mistrust of international organizations, government agencies, and medical professionals that hampered response efforts and indubitably impacted recruitment in this vaccine trial. Distrust or skepticism of the medical community and Western organizations is not unique to West Africa, though it is certainly amplified in countries like Guinea with a history of conflict, racism, oppression, and colonial research [28,35,40–43].

Concerns about blood collection represent the intersection of mistrust and misperception. Fears of blood theft, misuse of blood, or over-collection are widespread in sub-Saharan Africa and must be seriously considered during trial planning and implementation [40,44,45]. The Sierra Leone team had success in allaying such fears by addressing specific concerns in one-on-one conversations and targeted community outreach [40]. This points to a broader strategy of addressing misperceptions, mistrust, and fears in the target population. Researchers must identify and understand the provenance of such misunderstandings, including historical and social factors, and work to address these in a clear and directed fashion. Providing consistent and clear information throughout recruitment and the informed consent process is critical to improving participation and community engagement as well as ensuring consent is fully informed.

Study staff also stressed the importance of developing respectful and productive relationships with department heads and other authorities in target institutions. However, it is critical to know the audience’s relationship to authority when attempting to recruit participants, and doubly important to recognize that authority does not always derive from workplace hierarchies. In fact, community and family leaders, friends, and even colleagues may be just as, if not more, important authorities and advisers [34,40,46]. The majority of participants stated they consulted with others before choosing whether to participate. The staff of this study found that collaborative meetings, in which there was equitable discussion among and between potential participants, were more effective in recruiting subjects in healthcare settings than meetings structured as a classroom presentation, without discussion between FLWs. If instituted in the community as well, these roundtable discussions may help establish a sense of communitarianism and general goodwill towards the trial and in turn eliminate the spread of misinformation and risk of stigmatization.

An improved understanding of how potential participants weighed their decision to participate in an Ebola vaccine trial can provide researchers with valuable information in their own trial design and enrollment efforts. One study conducted during the ongoing 2018–2019 outbreak in the Democratic Republic of Congo reports high acceptance of the rVSV vaccine among community

members, though considerable challenges to vaccination and outbreak response remain [47,48]. In this study, we found that, in spite of the unique nature of the 2014–2015 Ebola outbreak and the targeted population of front-line workers, many of the same considerations informed the decision whether to participate in an Ebola vaccine trial as in other clinical trials in geographically and sociologically similar areas. Perhaps the most unique features of this population were the increased sentiment of participation as a public service, a fitting attitude among those in medicine and public health, and the stigmatization of the target population for their association with Ebola. The spread of misinformation and hysteria, driven largely by sensationalist and inaccurate media reports and hearsay, may have negatively influenced people’s understanding and opinion of the outbreak and vaccine trials, and are an important factor to consider in future outbreaks of this scope.

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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Authors’ Contributions

Initial analysis and interpretation of the data was done by KHG, PC, AJG, DATC and RFG. The manuscript was drafted by KHG. All authors were involved in the revision of the manuscript for intellectual content and approved the final version.

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