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A review of strategies used to retain participants in clinical research during an infectious disease outbreak: The PREVAIL I Ebola vaccine trial experience

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ABSTRACT

Introduction: This article describes a retrospective review of participant follow-up and retention strategies in the Partnership for Research on the Ebola Virus in Liberia (PREVAIL) I Vaccine Trial. It illustrates and analyzes strategies used to retain participants in an emergency clinical research response vaccine trial conducted during the 2014 Ebola outbreak in Liberia.

Methods: An anecdotal review of participant retention strategies developed and employed during the PREVAIL I vaccine trial.

Results: Though other factors likely contributed to the high retention rate of trial participants, the unique PREVAIL I follow-up process described resulted in an exceptionally high participant retention rate (97.8%) through 12 months of follow-up, increased the ability to obtain meaningful trial results, and provided a platform through which to respond to social issues in an emergency clinical research response setting.

Conclusion: Successful strategies were developed and employed in the PREVAIL I vaccine trial that resulted in extraordinarily high participant retention and follow-up rates during an infectious disease outbreak. This review illustrates that employing host country social mobilization concepts within a modified clinical research management framework is highly correlated to elevated rates of retention and minimal loss to follow-up. These strategies also contributed to increased data quality and enhanced adherence to protocol requirements. The increased ability to respond to social issues such as stigma, job retention and relationship conflicts was an additional and significant benefit of this follow-up methodology.

1. Background

In August 2014, eight months after the initial Ebola cases were identified in Guinea, the World Health Organization (WHO) declared the Ebola outbreak in West Africa a public health emergency of international concern [1]. A robust multilateral response followed from governments, non-governmental organizations, private industry and others as it became clear that the pandemic would grow to an unprecedented scale.

The Liberian Minister of Health (MoH) requested assistance from the United States (US) government in developing an accelerated clinical research program on promising Ebola vaccines and therapeutics. The US Department of Health and Human Services accepted the request, and in November 2015, The Liberia-US Joint Clinical Research Program, known as Partnership for Clinical Research on Ebola Virus in Liberia (PREVAIL), was formed. A team organized by the Division of Clinical Research, National Institute of Allergy and Infectious Diseases, National Institutes of Health, U.S. Department of Health and Human Services worked collaboratively with the Liberian Ministry of Health and Liberian clinical research staff to establish the capacity, protocols, ethical approvals, national and international consensus, and other research components enabling the initiation of a trial of two leading Ebola vaccine candidates 4 months later.

2. Introduction

Infectious disease outbreaks are increasing in our progressively interconnected global environment. During an infectious disease outbreak, the primary focus is, understandably, on treating those who are sick and preventing transmission of infection to their contacts.

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However, by simultaneously conducting well-designed clinical trials, clinical researchers can provide the global public health community clear evidence on the safety and efficacy of candidate treatments, vaccines, and other preventive measures and ultimately offer the best opportunity to lessen the severity of disease outbreaks and save lives both during the outbreak and afterwards.

Clinical research is a relatively new pursuit in the context of outbreak settings. Traditionally, during an outbreak, available resources and human capital have been largely concentrated on epidemiology, contact tracing, and clinical management of affected individuals. However, it has become increasingly evident that rigorous clinical research to characterize novel emerging infectious diseases, such as Ebola, influenza H1N1 pdm09, and Zika, is a critical element to informing effective response efforts and developing medical countermeasures to end outbreaks and prevent future ones.

It was of critical importance to employ local Liberians as integral partners in a clinical research response in this setting. Knowledge regarding social mobilization concepts, particularly in a country still reeling from civil disruption and curtailment of civil liberties, was paramount. The Liberian team gave counsel on many facets of the clinical research management process to include engaging community leaders in problem-solving and using continuous bidirectional dialogue with clinical research volunteers by Social Mobilization Committee staff with various community stakeholders.

This paper outlines trial participant retention strategies employed in an Ebola vaccine trial conducted during an infectious disease outbreak in a resource-poor, population-dense setting in urban Liberia.

3. The trial

The trial, titled “A Phase II/III Trial to Evaluate the Safety and Efficacy of the ChAd3 and the rVSVΔG-ZEBOV Investigational Ebola Vaccines in Liberia,” was designed to test two vaccine candidates and a placebo for safety and the prevention of EVD over a one-year period. A Phase 2 sub study was embedded to evaluate safety and immunogenicity of the vaccine candidates. The trial was launched on February 2, 2015. As Ebola cases declined in Liberia in the ensuing months, the Phase 3 component was deemed not feasible. Original plans for the expanded trial were to recruit 28,000 participants from several sites, starting at Redemption Hospital in Monrovia, Liberia. When the Phase 3 component was eliminated, recruitment was restricted to enrollment of a smaller number of participants only at the Redemption site.

4. The timeline

Inclusion criteria for this trial included testing positive for EVD. Therefore, a rapid response was required to optimize trial results. As depicted in Fig. 1, Liberia and the United States agreed to a clinical research partnership in October of 2014. PREVAIL commenced recruitment at Redemption Hospital in February of 2015.

5. The setting

The vaccine trial was conducted at Redemption Hospital in New Kru Town (NKT), a densely populated community of Monrovia, Liberia and one of the hardest hit by Ebola. According to the Chairperson, District 6, New Kru Town [2], New Kru Town has a population of 82,696 with 10,200 dwelling structures. Redemption Hospital is a no-cost, government-subsidized medical facility and was chosen because of its large population base, a willingness to partner in clinical research, and its high-performing clinical staff. When the PREVAIL I trial began, Redemption was closed to the community because of the general fear of Ebola and the deaths of healthcare workers in the facility resulting from Ebola infection. Redemption Hospital clinical staff had no previous experience with clinical research.

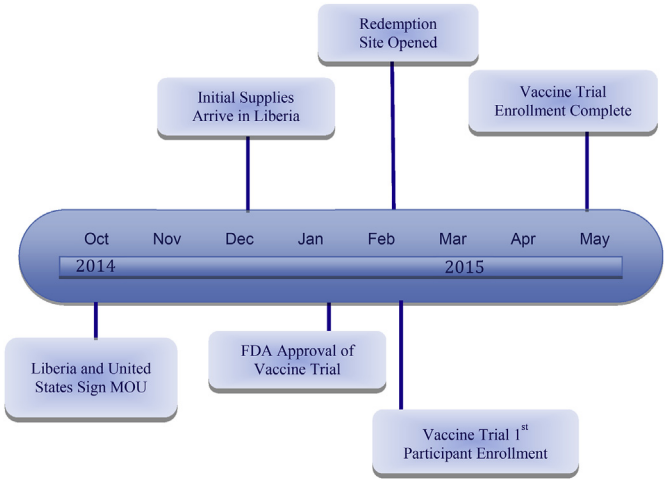

Fig. 1. Evolution of Ebola response, PREVAIL.

Adding to these complexities, the NKT community is characterized by:

- No official street names and home addresses
- High rates of poverty
- Dense population
- High mobility
- Inherent distrust of the Liberian government, medical science, and clinical research trials

6. The myths and the challenges

There were several community myths surrounding Ebola, including those listed in Table 1, which was generated by the PREVAIL SMC team. Reinforcing the validity of one of these myths articulated below, Idoko, et al. noted “… in certain parts of West Africa blood is considered sacred and children are thought to be made ill by blood sampling.” [3].

The trial team recognized that conducting a vaccine trial under these circumstances would be extremely challenging and require a great deal of support and input from social mobilization experts in Liberia. Educational backgrounds of PREVAIL SMC experts include sociology, biology, and epidemiology. Professional experiences include mobilizing communities, providing health promotion education, case investigation, and contact tracing. The U.S. members of this team added clinical research education and experience to the team skillset. An extremely robust and culturally confident team was engaged in PREVAIL to address social fears and stigma. Building trust would be critical, as noted in Hurd et al., “Trust is the cornerstone of clinical trial recruitment and retention.’ [4].

The logistical setting in which PREVAIL I was conducted posed a significant challenge. Davis et al. touted a comprehensive database as an effective method of retention and noted, “In addition to participants' mailing address and phone contact numbers, the names, addresses and phone numbers of family members, neighbors, friends, information on the participant's birth date, occupation, and social security and driver's license numbers, should be noted.” [5]. In New Kru Town, there are no street addresses, limited numbers of cell phone users, no home phones, and minimal birth information or identification of any sort. The PREVAIL I trial team needed to be creative and work intimately with their PREVAIL social mobilization counterparts to surmount these issues.

7. Methods

This is an anecdotal review of participant retention strategies developed and employed during the PREVAIL I vaccine trial. Due to the urgent nature of initiating this vaccine clinical trial during the