EBOla vaccine Deployment, Acceptance and Compliance

A guidebook on Community Engagement, Communications, and Technology for Clinical Trials in Outbreak Settings

AUTHORS

London School of Hygiene & Tropical Medicine:
BETH SMOUT, WILL SCHULZ, HEIDI LARSON

Johnson & Johnson Global Public Health:
ANNIK WILLEMS, PAULA MC KENNA

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Zoetic Science (an Ashfield company, Macclesfield, UK): **Morgan McKenzie, Patrick Hoggard**

Participants in the EBODAC Symposium, Dakar, 2017

Illustrations by **Sam Bradd**

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1. Introduction

The 2014-2016 Ebola outbreak devastated communities across Guinea, Liberia and Sierra Leone, claiming more than 11,000 lives[1]. No specific vaccine or drug was available to either treat or prevent Ebola Virus Disease (EVD), leading multiple international research groups to rapidly mobilise and work to establish clinical trials of candidate Ebola vaccines and treatments in the midst of the epidemic. The ethical, scientific and logistical challenges of setting up rapid and robust clinical trials in such a context were significant, creating the risk that the sensitivities, anxieties and realities of potential trial participants and communities could be neglected rather than placed at the heart of the research itself[2]. From establishing basic lines of communication in the midst of chaos, to meeting the ideals of ethical standards in highly compromising environments, every aspect of clinical research becomes more difficult when the deadly illness that a trial intervention is meant to prevent or treat is actively circulating in the trial area, creating fear and anxiety and consuming already-scarce resources. Yet if the 2014-16 West African Ebola outbreak is any indication, then we can expect this to be the working model for some of the most crucial medical research in years to come. In this document, we have used this outbreak as a working model to prepare for these future challenges. It is necessary, therefore, to carefully examine the challenges trialists have faced in the Ebola out-break, and identify ways to mitigate them, so as to ensure research can continue being conducted in outbreak contexts at a high level of scientific rigor, cultural acceptability, and ethical propriety.

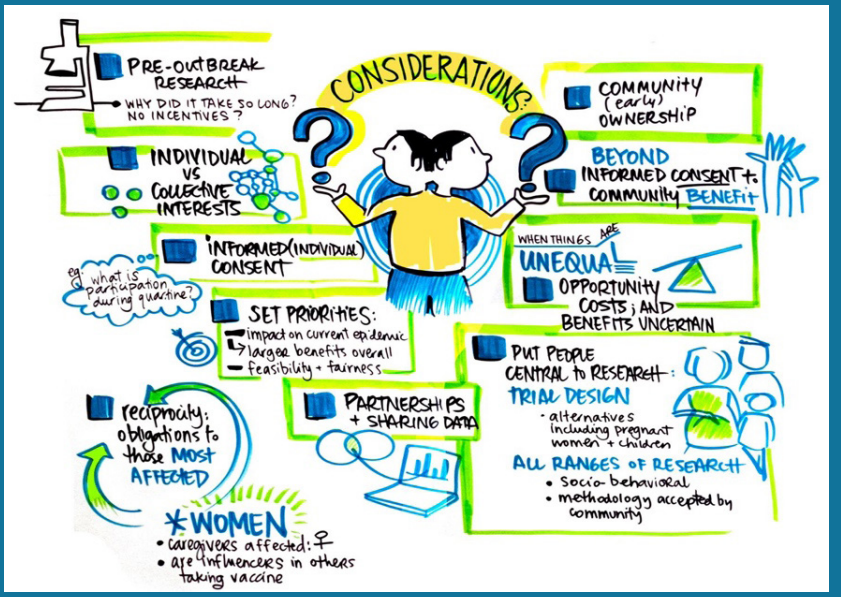
The international community's initial slow and uncoordinated reaction to the emerging crisis has received considerable criticism from multiple expert panels established to evaluate the global emergency response to Ebola[3][4][5][6][7][8]. Included among their findings was a generalised failure to understand or consider the socio-cultural and political context within which the response was occurring until a late stage, and often only when facing resistance.

Paul Farmer writes that the outbreak raised questions regarding the relationship between "contagion, lethality, stigma and long neglect"[9]. After decades of structural violence across the region,[10] a lack of trust between communities and international and national actors posed challenges for community engagement efforts. This served as the backdrop to both overt and covert resistance towards the response and public health interventions[11][12][13], compounded by negative messages which focused on the disease having no available cure and a high mortality rate[14]. In general, community engagement throughout the crisis has been criticised for its one-sided, top-down approach, focusing on the delivery of information to elicit behaviour change and to "correct" misperceptions rather than engaging in dialogue to understand people's perceptions, concerns and fears.

Despite numerous reflections and recommendations related to community engagement in the Ebola response, only one expert panel has identified any findings or recommendations around engaging communities specifically for clinical trials taking place during an outbreak.[15] This document has therefore been prepared as a repository for the knowledge gained during the Ebola outbreak. It draws upon the experiences of the EBODAC (EBOla Vaccine Deployment, Acceptance and Compliance) Consortium, who have been supporting communications, community engagement, and several enabling technologies for the EBOVAC-Salone Ebola vaccine trial, investigating the safety and immunogenicity of a candidate prime-boost Ebola vaccine in Kambia district, northern Sierra Leone, in consultation with other individuals and groups involved in both Ebola and non-Ebola clinical trials.

2. Ethical Challenges

Numerous ethical challenges face clinical trials taking place in outbreak situations. This document focuses on issues that can serve as potential challenges for communications and community engagement teams working on clinical trials, taking an example-based approach which is intended to be illustrative, though not exhaustive.



PRIORITISATION OF RESEARCH

As was seen during the 2014-2016 Ebola outbreak, epidemic situations can lead to an influx of research groups into the affected region, with the need to discover an effective treatment or vaccine regarded as being more urgent than ever, if neither already exist. However, this creates a situation where there are a limited number of willing patients or volunteers available for a multitude of different research studies, each aiming to recruit individuals at the same time to test a wide array of experimental vaccines and therapeutics. Critical – and often difficult – questions need to be asked about priority-setting for research during epidemics, to provide the greatest possible benefit for participants under imminent threat of the disease, to provide optimal care to patients already suffering the disease, and to ensure that research activities do not distract from the primary emergency response effort.

Some ethicists believe that given the urgency of an outbreak response, priority should be given to research which has the potential to usefully thwart the current epidemic, rather than that which could only benefit future outbreaks, particularly as the outcome (especially if positive) would be likely to also have great value for the response to any future epidemic. Not only is this fairer to the individuals involved in clinical trials, who would be more likely to themselves benefit from their participation, but it also increases the chances of clinical trials being accepted by communities, if immediate and direct benefits from the research are likely. However, there are circumstances in which this prioritisation of research would not apply: if the probability of benefits from the research were uncertain (i.e. the protective or curative effects of the intervention are unknown); if the potential costs of the research outweigh its benefits (for example by diverting resources from the general outbreak response); or if the outbreak may subside before the intervention is actually tested – as was the case with most trials of vaccines during the Ebola epidemic in Guinea, Liberia and Sierra Leone.

PRIORITISATION OF PARTICIPANTS

Managing demand for a candidate intervention can be a particular challenge for clinical trials operating against the backdrop of an epidemic. While individuals may have significant concerns about participating in medical research, particularly when that research is led by foreign institutions and personnel, experimental treatments and vaccines may also seem like a potential lifeline to panicked communities when there are no licensed interventions available for the disease. The consequences of this for informed consent are discussed below, but on an operational level there are usually very limited supplies of such vaccines and treatments available, because clinical trial protocols typically

have caps on the number of participants they can recruit. There has been significant debate about the acceptability of denying demand in these circumstances, with some arguing that denying somebody the right to an intervention which might be effective is wrong, especially when the case fatality rate from the disease in question is high. These are discussions which research groups should prioritise with both licensing authorities and local regulatory bodies when planning trials in an epidemic, with their input being absolutely critical to answering these questions.

How participants are recruited into studies depends upon both the situational context within which the research is taking place, as well as the nature of the intervention being tested. During the Ebola epidemic, it was clear that the most efficient pathway for enrolling participants into therapeutic trials was through Ebola Treatment Units (ETUs), where those who were infected with the virus (and therefore symptomatic) were already quarantined. Vaccine trials, by contrast, needed to conduct recruitment in healthy populations, to evaluate whether the candidate vaccines would prevent infection with Ebola. While some trials enrolled participants on a first-come, first-served basis or specifically targeted high risk populations such as healthcare workers, the EBOVAC-Salone trial of the Ad26.ZEBOV/MVA-BN-Filo prime-boost vaccine regimen in Kambia, northern Sierra Leone, used a household lottery system to determine the order in which households were visited and their members invited to individually consent to participate in the study if they wished to do so.[16] This strategy was decided upon following social science research within the trial community identifying concerns around fairness and representation, with a widely held belief among the community being that access to resources strongly depends upon connections with individuals in positions of power. It was therefore considered vital that the EBOVAC-Salone trial should select participants for the study based on a random and transparent process.

Debates regarding demand go hand-in-hand with those over the prioritisation of individuals or groups for participation in clinical research. During the Ebola epidemic, substantial criticism was levelled at the “blatant injustice” of expatriate healthcare workers being the first to be offered experimental treatments such as Zmapp when they contracted the disease, while the thousands of local staff and ordinary community members who became sick were not afforded the same opportunity.[17] In the words of the Los Angeles Times, “the decision to offer them the experimental treatment — while dozens of African doctors and nurses have perished — has provoked outrage, feeding into African perceptions of Western insensitivity and arrogance, with a deep sense of mistrust and betrayal still lingering over the exploitation and abuses of the colonial era.”[18]

Similarly, the inclusion of children and pregnant women in clinical trials is a topic of much debate. On the one hand, these two groups are seen as particularly vulnerable, and therefore should not be placed on the "front line" of research that may have unanticipated side-effects. Yet on the other hand this same vulnerability can be construed, in an outbreak context, to mean that children and pregnant women ought to receive every possible protection from the disease, including interventions that have yet to be fully tested. Moreover, excluding them from participating in research studies may also prevent these groups from being able to access the intervention being studied if any license or recommendations warn against its use, for lack of an evidence base. These conflicting ethical obligations are reflected in CIOMS guidelines, which state that fairness requires that these groups "not be excluded from research nor should they bear a disproportionate share of the burdens of research participation".[19] In an attempt to balance these responsibilities during the Ebola outbreak, both children and pregnant women were included in various clinical trials of therapeutics and vaccines, and an age de-escalation approach (starting with older children and adolescents and progressing to younger children as investigators gained greater confidence in the intervention's safety) was used by some vaccine trial teams at the request of the national regulator.

BOX 1: MITIGATING EXCESS DEMAND

When faced with an abundance of would-be participants in a trial with a limited number of doses to administer, trialists may take one of several approaches to determine who can participate in the trial.

1. First-come first-served: The simplest method, but privileges those with early knowledge of the trial, and may exclude the most vulnerable.
2. Lottery: Seeks to ensure that participation in the trial is truly random, and can select participants at various different levels (community, household, individual, etc.). However, the voluntary nature of participation still needs to be assured – a lottery should reflect an invitation to participate rather than lead somebody to believe that they have been selected by the trial team and are unable to decline.
3. Risk prioritisation: Seeks to protect those who are most vulnerable to the epidemic disease before any others. On the other hand, it may not be appropriate to administer a candidate vaccine or treatment to such individuals, as they may be more susceptible to possible side-effects.

COMMUNITY INVOLVEMENT

Recognising the social context of clinical trials is vitally important for effective community involvement. During the Ebola epidemic, there was a tendency to prioritise the biomedical aspects of research over the social context, with the neglected social aspects of these trials then creating problems for researchers further down the line. Not only can including the local community in planning trial protocols ensure that they are engaged in the process and their views taken into consideration, but it may also improve the community's understanding of the trial and thus facilitate the informed consent process. Similarly, the roles of local researchers, academics and ethical and regulatory authorities are critical; even those with limited previous experience of reviewing clinical trial protocols can have valuable insights to contribute to the design of clinical trials. Individuals, rather than researchers, are central to medical research; their needs, ideas and opinions must be listened to and accorded the same degree of importance as those of clinical trial experts, academic ethicists and regulatory officials. Indeed, the involvement of members of the community within which the trial is taking place in the design and implementation of the study is considered a requirement for making "moral progress in international health research."[20]

INFORMED CONSENT

By their very nature, clinical trials deal in uncertainties; those conducted during epidemics are occurring at a time when communities are likely to be searching for solutions. This can be advantageous for participant recruitment, but poses ethical challenges around the nature of informed consent in situations where perceptions of risks versus benefits may be altered by fear. At the same time, the fear-laden environment of a public health emergency can make it difficult to build trust with a community, and can create any number of negative impressions that can make people uncomfortable with the idea of participating in a clinical trial. As a result of these conflicting pressures, trialists must walk a fine line, promoting the trial to the community and emphasising the efforts they have made to maximise participants' safety, and at the same time being clear about the uncertainties associated with the trial, and the risks that participants must understand to give informed consent. This is a difficult combination of messages to send, and this may itself create confusion or mistrust if the community is not familiar with clinical research and perceives the mixed messages as duplicitous.

However, these challenges are themselves based on the assumption that an individual is able to consent for themselves. In the case of therapeutics, individuals may be too sick to be able to consent to receiving an experimental treatment; recommendations from the World Health Organisation (WHO) allow for surrogate consent in such circumstances.[21] Even if a hospitalised patient is able to consent for themselves, the informed consent process may require contextual adaptation, and such adaptations can create further challenges. For example, the team running the JIKI trial of favipiravir in an ETU in Gueckedou, Guinea, faced challenges obtaining informed consent in the high-risk zone of the ETU, noting that the mandatory personal protective equipment (PPE) "clearly hampered communication and the perception of free choice for the patient" by distancing health workers from the patient and making the patient's dire predicament highly salient during the process.[22] Prospective participants may struggle to evaluate the risks specific to a clinical trial, which may be distorted against the backdrop of risks associated with the epidemic itself.

Given these circumstances, and in an environment of clinical trial illiteracy, in regions where local languages may be entirely oral (i.e. with no written script), alternative means of obtaining informed consent must be considered. One systematic review found that an average of 47% of participants enrolled in clinical trials across Africa understand basic research concepts such as randomisation, although none of these trials were recruiting participants during an epidemic.[23] Multiple trials recruiting during the Ebola outbreak used visual aids, such as flipcharts designed to break informed consent forms down into a more manageable 'storyboard' form, to facilitate the process.[24 25 26] Previous work in The Gambia indicates that using a multimedia form of informed consent – combining video animations with audio information in a choice of languages – can lead to significantly improved understanding of clinical trial information, as compared to a standard informed consent process consisting of the provision of verbal information, followed by signing or thumb-printing a paper form.[27] The WHO recommend considering an audio or video consenting strategy if the context demands it,[28] and so it is highly important that research teams understand the environment within which they are working and consult with local community members (as well as the national regulatory and ethical authorities) so as to adapt the process appropriately to ensure that the consent provided by participants when enrolling into clinical trials is truly informed.

3. Social, Cultural, and Political Context

> Outbreaks and associated clinical trials often bring communities face-to-face with responders from other parts of their country, and indeed other parts of the world, who begin with little mutual understanding of each other's agendas, expectations, procedures, and priorities. Developing this mutual understanding is crucial to establish whether a trial can be conducted in a certain community, both because the trialists must understand the community in order to comport themselves appropriately, and also because the community must understand the trialists in order to give informed consent. Hence one of the first tasks that researchers encounter is that of establishing lines of communication with the community, which in turn entails identifying community leaders.

IDENTIFYING LEADERSHIP & POWER MAPPING

It is often not difficult to identify a community's formal political leadership, however it is important to consider that traditional or religious figures may play variously competing or complementary roles as well. These roles may not be obvious to trialists, either because they are unfamiliar with the community's culture, or because political leaders choose not to highlight them, thinking that their involvement is unnecessary, or that it would undermine their own authority. It is valuable, however, to seek out any individual (e.g. elders, healers) with respect or influence in the community, solicit their advice, and endeavour to enlist their support, even if it does not seem strictly necessary. Doing so can bring further insights about a community, and even if such an individual does not turn out to be a very active ally, engaging with them early on shows respect, while ignoring them may cause insult and provoke them to reactively oppose the research project.

Given the great urgency of an outbreak scenario, and the desire to conduct research as quickly as possible, trialists are often prone to categorise a community (as well as its inhabitants and leaders) as either "resistant" or "compliant". It is vital that groups involved in both the emergency response to the epidemic and clinical trials move beyond the concept of "the community" being a homogenous entity that is either resistant or compliant, and instead recognise the diversity of views, dynamics and networks that exist within communities. Mapping the formal and informal power structures of each community may be particularly useful when planning engagement activities.

Similarly, it is important not to assume communities are fearful of clinical research; there can be a tendency for both researchers and organisations involved in the broader response to presume communities have few proactive reasons to accept clinical trials. However, positive reasons for trial participation have been frequently reported by participants in Ebola clinical trials. Some participants described a sense of altruistic duty to help protect their communities, whereas others said they were motivated by curiosity about the novel experience of participating in a clinical trial, and a hope that something good would come out of it.[29]

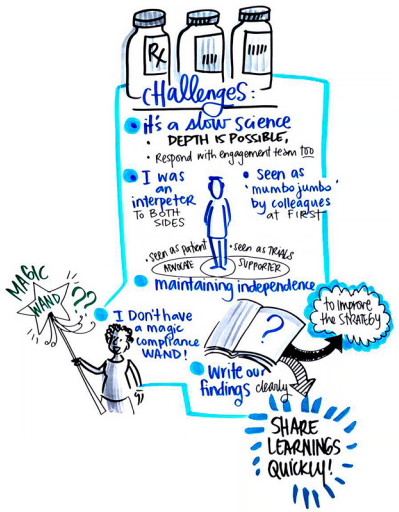
BOX 2: WHO IS "THE COMMUNITY"?

A key question to be asked by both researchers and community engagement teams during any intervention is: What (or who) constitutes ***"the community"***? As discussed, communities are all-too-often regarded as single, homogenous entities, where power dynamics and influence follow official hierarchies and remain stable over time, regardless of the external environment. In line with recognising the complex dynamics that exist within communities, it is also important that research teams ask themselves who they are consulting with, and who they are ignoring, when planning research and engagement activities, and whether the inputs and views that those individuals are expressing are truly representative of the community. While hierarchies need to be respected, those with less agency should also have their voices heard, particularly as their opinions and perspectives may not always align with those of key stakeholders or local authority figures.

THE ROLE OF SOCIAL SCIENTISTS

Social scientists – most notably anthropologists – have come to play an increasingly significant role in the outbreak response and associated clinical trials, following the growing recognition that success or failure has much to do with the trialists' ability to relate to and understand the ways of the community experiencing the outbreak and participating in the trials. Using methods such as surveys, interviews, and participant observation, social scientists can elucidate the community's hopes and fears, understand their habits and expectations, and identify what aspects of the planned research may need to be revised to be acceptable to the people involved. Social scientists use specialised methods to collect crucial information that may not even occur to the biological scientists who traditionally lead decision-making in clinical trials.

Despite the widespread acknowledgement that social scientists bring great value to clinical trials, however, their roles and methods are often poorly understood by decision makers on the ground, making their status within trial teams a particular challenge. This is not surprising, but it sometimes leads to underuse or misuse of social scientists' skills. There are many accounts of social scientists being swept into ad-hoc roles such as managing patients, physical labour, or clerical work, which are inconsistent with their skill sets, but which they may feel obliged to carry out due to the urgent atmosphere of an outbreak response. Sometimes this can be seen to derive from a lack of understanding or respect for the value of social scientists, many of whom report being referred to as "social workers" by their clinical colleagues, with a key question being whether social scientists belong to the trial or the community.



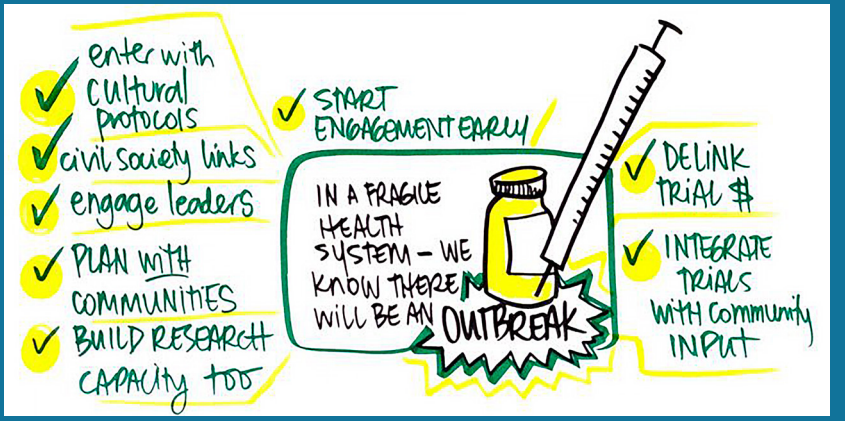
Differentiating between the roles of social scientists and community engagement teams can be especially problematic. While anthropologists are employed by the trial, they must establish trust with the community, giving the impression that community members can rely on them to act as their advocate, with regard to any issues or disputes with the trialists. At the same time, the trialists tend to view anthropologists as their advocates in the community, a role which is more appropriate to community engagement teams. On the one hand, social scientists' relationships in the community, built through research encounters, can be used to help solve problems and encourage compliance. On the other hand, this could compromise their independence and potentially abuse the trust built with the communities they work within. This puts anthropologists and other social scientists, who typically place high value on the community's autonomy, in a difficult position.

Clinical trial researchers and management staff should be encouraged to strengthen their understanding of the role of social scientists, and vice versa, ensuring that they receive inductions regarding the focus, priorities and constraints that they each face. In particular, clinical trialists need to understand what social scientists are and are not, and ensure that social scientists are fully integrated into clinical trial teams rather than seen simply as accessories to clinical science. In addition, social scientists can do more to enhance their own relevance to clinical research teams. Social scientists working in an outbreak setting should be operational, practical and present their work in a way which can be accessible to inform and influence the conduct of clinical and outbreak response interventions.

Traditionally, social science has often been regarded as a "slow science", with its relevance in emergencies challenged by some. Despite the importance of in-depth, detailed anthropological research conducted over a generous period of time, social science research demonstrated during the Ebola epidemic that it can also be a "fast science", providing real-time information and feedback which was crucial in understanding communities and guiding both the emergency response and clinical trial activities.

4. Community Engagement in Practice

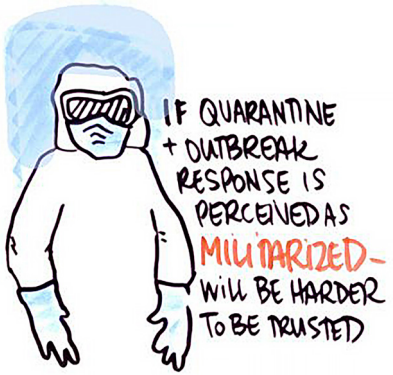
In addition to being a crucial aspect of ethical trial design and associated social research activities, community engagement is also a practical process which demands creative problem solving. The guiding principles of community engagement are ethical and intellectual ideals, and it is important that researchers continue to strive to meet them. However, those working in an outbreak context often find their task to be one of making the best of a bad situation, in which these ideals may seem so distant that it is difficult to navigate towards them, let alone reach them. In emergencies there will always be forceful arguments for expediency over idealism, and so those who seek to defend community engagement's core values should be prepared for the ways they will be tested and challenged.



"TOP-DOWN" VERSUS "BOTTOM-UP"

In outbreak response, and in public health interventions generally, it is commonplace to see expressions of distaste for so-called "top-down" approaches, in favour of "bottom-up" approaches. Yet, while this notion has become a truism of global health, contemporary projects and interventions continue to suffer criticism for being excessively "top-down," a phrase which in practice connotes authoritarianism, and the kind of elite manipulation that was so often the governing technique of colonial rulers. Part of the reason for this continued shortcoming may be the broad, all-encompassing assumption that top-down decision making is always bad: in practice, there are many decisions that must be made by an executive authority (particularly in the context of emergencies), and so those tasked with working under these difficult conditions may come to view the prejudice against top-down approaches as less of a "guiding principle," and more of a "nice idea," apt to be discarded whenever it is inconvenient.

It may be better, therefore, to develop a more nuanced model that considers "top-down" and "bottom-up" not as mutually exclusive philosophies of intervention, but rather as complementary working dynamics that can coexist well or poorly. As was seen during the response to the 2014-2016 West African Ebola outbreak, epidemics tend to trigger an influx of research organisations into affected countries, and for many of them this is the first time they have worked in such contexts. On a very practical level, it is often impossible (not to mention arrogant, disrespectful, and usually illegal) to conduct research in an unfamiliar country without first seeking the approval of national authorities. These national authorities include not only the formal ethical and regulatory bodies, whose approval to conduct a clinical trial is mandatory before participant recruitment can begin, but also other relevant political leaders – particularly those working within the Ministry of Health – and outbreak response institutions. Government support is not just beneficial, but essential, as it provides not only legal permission to conduct research, but also social legitimacy, which is vital to the success of subsequent engagement and communication with the community. Critically, it is not simply the case that the agreement of key figures in national leadership is a positive thing; a lack of such support can create serious obstacles to a clinical trial's running, or even actively block a study from taking place altogether.



However, it should be acknowledged that a "top-down" approach is not generally appropriate as a means of engaging the community within which a clinical trial is to run. While traditional authority figures and other senior stakeholders are often the first point of contact for researchers hoping to establish a trial within a particular community, the opinions and inputs of community members living and working within the area served by any prospective trial site should come to the fore when planning both clinical research activities and their associated community engagement strategies.

National-level authorities should remain involved in this process, and may need to be consulted as to the practicalities of certain suggestions arising from the local community, but it is important to ensure that the opinions of national-level stakeholders are not given undue weight over those of individuals belonging to the trial community itself. It should, however, be noted that this refers to the provision of practical advice and guidance, rather than formal regulatory and ethical approvals which are provided at national level, and without which no clinical trial can proceed.

In particular, researchers should refrain from approaching communities with a pre-determined clinical trial protocol in hand, developed without the input of community members or consultation with the relevant country representatives. This paternalistic approach to conducting research can result in imposing protocols which are not acceptable to the communities (and governments) they are meant to serve, which, apart from being disrespectful, will ultimately damage the recruitment of participants. Even in an outbreak, when time is limited, this kind of consultation should be considered an absolute necessity, and not something that can be discarded in the interests of expediency. Indeed, this form of prior discussion may be even more critical in such a context, when ethical debates around issues such as trial design can be especially contentious. In particular, local attitudes towards the use of placebos and the acceptability of randomisation are particularly important considerations for researchers working to design clinical trial protocols in an epidemic, and should be accorded the same importance as debates around the scientific validity of alternative trial designs, together with the extent of any ongoing outbreak and the preferences and expectations of national government and the ethical and regulatory authorities.

BOX 3: HOW TRIALS DIFFER FROM PROVEN INTERVENTIONS

The nature of messaging around clinical trials is very different from that for proven, routine health interventions. This difference can be particularly striking during an epidemic, where communities are already oversaturated with health information from a multitude of sources - and particularly focused towards instructions on what they should or should not do in order to protect themselves from disease. In a situation where people are focused on finding solutions, it is particularly vital that community engagement teams working on clinical trials emphasise that while they are coordinated and aligned with the emergency response, the clinical trial is not a part of the response effort specifically and that the intervention being tested in the trial is experimental. As has been emphasised above when discussing informed consent, it is critically important for community members to understand that the nature of the clinical trial is to test something the efficacy of which is still unknown, and therefore they must continue to protect themselves, following national guidelines, against the disease itself.

Community Advisory Boards (CABs) have become a fairly common approach to ensuring that communities are appropriately consulted in both the planning and implementation of clinical trials. Their composition depends upon the context of the research itself, but they provide a mechanism for researchers, stakeholders, community members and trial participants to meet for updates on research progress, receive feedback on any issues of particular concern or rumours circulating within the community, and ensure that local beliefs and norms are discussed and factored into research activities. Different consultation mechanisms may be more appropriate, depending on the environment, but it is critical for clinical trial teams to have mechanisms in place to receive regular feedback from community members and trial participants, and to ensure that they and other stakeholders are considered equal members of the research planning and implementation process.

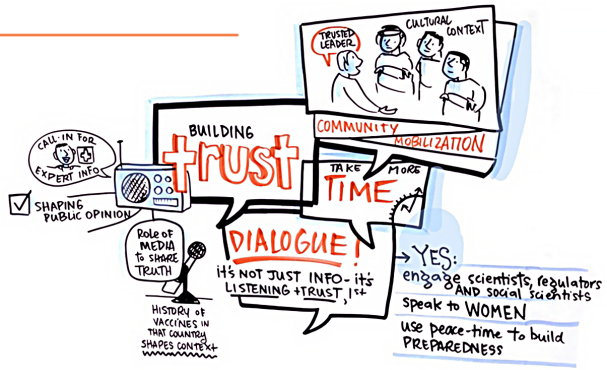
Teams conducting community engagement for clinical trials within an outbreak situation are faced with numerous challenges, with the context of the epidemic itself being perhaps the most significant of these. So much of any emergency response is focused on working as rapidly as possible in order to end the outbreak, but clinical trials focused on developing preventative vaccines or treatments for the disease in question are working against the clock to recruit sufficient numbers of participants before an outbreak ends, in order that critical research questions might be answered. However, community engagement is not simply a "tickbox exercise" which can be completed overnight. Engaging with communities, particularly those who are unfamiliar to the research team, or who themselves are unfamiliar with clinical trials, is a continual, iterative process.

Trust between communities and researchers is fundamental for the success of clinical research, but requires dedicated time, energy and understanding. Even during an epidemic, when time is of the essence, time still needs to be devoted to engaging with communities before a clinical trial begins. Such an investment from the very outset of the study will ultimately make the research a great deal easier to conduct later on.

WORKING WITH THOSE NEW TO CLINICAL RESEARCH

In order to protect the rights of participants, clinical trials are bound by several layers of rules, regulations and guidelines which can be difficult to comprehend to individuals, communities and organisations with no history of interaction with medical research. This is particularly important to acknowledge when planning clinical trials in the context of an epidemic, where affected communities may have never been exposed to such research. In contrast, many communities in low income countries are likely to have extensive experience with development projects, with the expectations fostered by these interactions and the relative flexibility of such projects compared to clinical trials creating potential challenges for researchers working to establish trials in the area. Asked how clinical trials differed from development projects, during a panel discussion, Paramount Chief Bai Farama Tass bubu N'Gbak IV (of Magbema Chiefdom, Kambia, Sierra Leone) joked, "There is a lot of paperwork." Humour aside, this comment accurately conveys the greater complexity and detail-oriented challenges of conducting clinical trials, compared to usual development projects.

First, development projects often have a broad focus, with the scope of their work allowing for activities which often contribute to the broader social and economic development of the community within which they are operating. Clinical trials, on the other hand, tend to focus exclusively on healthcare. Their ability to offer more widespread development to the community beyond this may be limited by funding restrictions and, critically, by what is considered ethically appropriate. Individual reimbursement of expenses for travel and lost earnings, together with capacity-building activities which ensure access to appropriate medical care, are generally regarded as integral to the running of ethical research studies. However, offers of money, improvements to infrastructure or material goods which could be considered a routine aspect of a development project may be interpreted as an inappropriate inducement to participate in a clinical trial.[30] Meanwhile, community members who hope to gain employment from the clinical trial may be disappointed if certain highly-qualified positions cannot be recruited locally. Such boundaries and the rationale behind them should be clearly explained to local leaders in order to minimise the risk of communities feeling as though they are being exploited by research teams.



Apart from communities themselves, research teams may find themselves collaborating with organisational partners with little knowledge of clinical trials. Aid and development institutions may be non-traditional partners for research, but can offer on-the-ground experience that is particularly valuable in an epidemic. While it is critical to ensure that these teams receive the necessary training around the essentials of clinical trials and Good Clinical Practice (GCP), their contextual familiarity together with their network of contacts mean that these organisations can play a pivotal role in the planning and implementation of research activities during an epidemic. In addition, their involvement and subsequent training and knowledge accrual can vitally contribute to local capacity building for future clinical research.

IDENTIFYING STICKING POINTS: THE EXAMPLE OF BLOOD THEFT

Communications and engagement with communities around any health intervention has challenges, and these are even greater during a disease outbreak where senses of fear and uncertainty are understandably heightened. Conducting clinical trials of experimental vaccines and treatments in such an environment further compounds these challenges, as clinical trials often involve protocol-mandated requirements and procedures which may be unfamiliar (and hence concerning) to communities who are unfamiliar with them. Nevertheless, anthropologists have highlighted the importance of recognising the legitimacy of communities' interpretations of research practices, which must not automatically be dismissed as misunderstandings caused by ignorance about these procedures.[31]

Blood testing, for example, is often a routine component of clinical trial protocols, in order to determine the safety, efficacy and immunogenicity of experimental therapeutics or vaccines against Ebola. While blood tests may be regarded as standard practice to researchers, these can often create anxieties among clinical trial participants - particularly those for whom routine blood testing may be unfamiliar. Previous experiences with giving blood may be limited to blood donation to family members or friends who are unwell, and this can create an exaggerated expectation of the volume of blood to be sampled for the purposes of a clinical trial. Moreover, the monetary value ascribed to donated blood, in environments where individuals are routinely able to buy blood in exchange for cash, may contribute to perceptions of a clandestine trade in the blood given by trial participants for safety and immunogenicity testing within a clinical trial.[32]

These concerns are only exacerbated by the uncertainties that often surround the rationale for sampling blood within a clinical trial, and what happens to that blood sample once it has been taken. Various trials have experienced rumours around blood stealing[33 34], although the specific motivations perceived to be behind blood theft vary. Research has identified that an adult's decision regarding whether or not they (or their child) should join a clinical trial often involve weighing up concerns around blood testing against benefits which the trial may provide – particularly as this often includes the provision of free, reliable healthcare to study participants. To quote a mother in the Gambia whose child joined a Medical Research Council (MRC) study of a pneumococcal vaccine, *"I heard MRC steals blood. I believe it. I saw them take blood from patients. I feared for my child to join but I had to hence she gets treatment there."*[35]

BOX 4: *KOLA* AND DIFFERING CONCEPTS OF RESPECT

The encounter between global research ethics and local cultures is not always easy or instinctive. Traditional practices such as the giving of kola as a 'greeting gift' in Sierra Leone are considered very important and a sign of respect for both local customs and authority figures.[36] However, this action could also be seen as a bribe or inducement for allowing research teams to conduct clinical trials in a particular community. There are rarely easy answers to such situations, and those working on clinical trials will often need to decide for themselves what is the right course of action. There is no universally applicable approach to community engagement. Those leading clinical trials must be prepared to engage in difficult judgement calls, and to do so effectively they require experience and training, and cannot simply follow a checklist of engagement activities to fulfil this role.

On a practical level, clinical trials often do not provide feedback to participants regarding the results of their blood tests. Since participants may be most familiar with diagnostic blood tests, wherein sharing the results of the test is a routine expectation, this may enhance suspicions as to the real motives behind the procedure. While providing immunogenicity data to these individuals throughout their participation may be impossible, researchers should consider providing regular feedback on safety parameters in order to break down the mysteries surrounding these tests and facilitate an understanding among participants and communities of what blood sampling can tell us and why it is important for research teams to conduct.

It's not only blood sampling which can prove a controversial protocol requirement for clinical trials; many studies advise or mandate the use of contraception to prevent pregnancy among female participants or the female partners of male participants given the lack of available data on the impact of

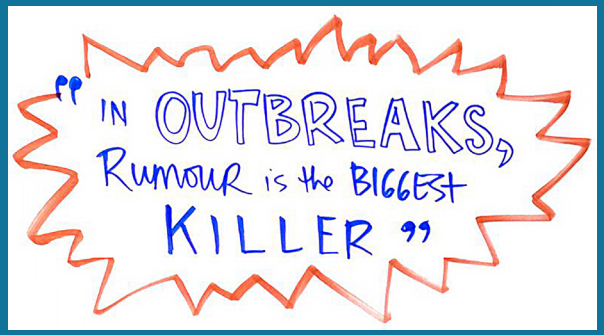
receiving the experimental intervention on a pregnant woman or her unborn foetus. Depending on the context within which the trial is operating, this can be problematic. Both vaccine trials and routine immunisation campaigns for licensed vaccines, such as those against polio, have faced recurrent fears that the vaccine may cause infertility[37 38 39 40]; it is therefore not surprising that requiring contraception use as an eligibility criterion for a clinical trial can add to fears about population control.

GUIDELINES FOR COMMUNITY ENGAGEMENT

Questions have been asked as to whether it is even possible to develop generalisable guidelines for community engagement for clinical trials in epidemic situations, given the importance of context in determining how a clinical trial should be conducted and the non-generalisability of experiences and perspectives. Good Participatory Practice (GPP) guidelines are available for biomedical HIV prevention trials, with the aim of providing systematic guidance to those conducting clinical trials on how to engage with stakeholders and community members when designing and implementing HIV trials. The guiding principles of the GPP guidelines are respect, mutual understanding, integrity, transparency, accountability and community stakeholder autonomy.[41] These guidelines are seen to have both legitimised the role of community engagement in clinical trials, emphasising the importance of placing communities and individuals at the heart of medical research. However, guidelines do not necessarily apply perfectly to every context, nor are science or communities static entities. It is therefore important to ensure any guidelines that are developed are flexible enough to ensure that they allow consideration of the individual context within which any given trial is recruiting participants, and to remain relevant despite changes in the landscape, being updated and revised whenever necessary. AVAC (formerly the AIDS Vaccine Advocacy Coalition) recommend that GPP and any other guidelines which outline the management of community engagement with emerging pathogens are used as a global reference point or framework, intended to legitimise the involvement of community engagement in clinical trials and to understand its importance and impact.[42]

5. Rumours

Rumours are generally defined as unverified information, circulated informally. In the context of disease outbreaks, which evoke much public fear and anxiety, people are more prone to spreading rumours, since any information – about the disease, where it is spreading, what kinds of protection are available, and, particularly, news of supposed cures – is highly desirable. When the actual scientific answers to these questions are absent or uncertain, it is natural to resort to rumour to decide what to do. Unfortunately, rumours often carry harmful inaccuracies, and so it is important for those conducting clinical trials in outbreak contexts to maintain constant awareness of rumours pertaining to their research.



The news media often receive particular blame for spreading misconceptions and fomenting fear. While journalists have great power to cement a rumour in the public mind, and their incentives do not always align with those of researchers, it should be acknowledged that the media rarely cause problems by spreading deliberate lies. Rather, news reporting primarily reflects journalists' own level of knowledge, and the quality of sources they have access to, so if a person approaches a reporter with a story about scientists doing improper research on innocent civilians, and the reporter does not have any information to contradict that story, they will understandably feel responsible for alerting the nation to an issue of public welfare. Journalists do not have a responsibility to promote clinical trials. While they do have a responsibility to check their facts, this can be exceedingly difficult in the area of scientific research, which involves highly specialised knowledge and in which seemingly fine distinctions can make a world of difference. Hence trialists must actively work to circulate high-quality information to journalists and respond quickly to any requests for information. Failing to do so can lead to a situation that quickly spirals out of control.

THE EXAMPLE OF GHANA

One example of rumours derailing clinical trials comes from Ghana, where planned clinical trials of candidate Ebola vaccines fell prey to false claims, which provoked public outcry and led to the trials being delayed for so long that their backers ultimately gave up, and used data from sites in other countries. Prominent among these rumours were claims that researchers were exploiting Ghanaians and putting their lives at risk in what newspapers described as a "secret" experiment.

The reports that the trials in Ghana were being done "in secret" appeared to come as an unintended consequence of non-disclosure agreements, and regulations that prohibited researchers from conducting any public sensitisation prior to receiving national approval to proceed with the trial. In the days before approval was expected to be given to a trial site in Hohoe, journalists at the Ghanaian radio station Starr FM got wind of it and began interviewing people around Hohoe, including researchers who insisted they could not give any information about the trial (in accordance with their non-disclosure agreements), and local students who claimed to have been approached about possible participation in the trial. Researchers later denied conducting recruitment at that time, but Starr FM generated a firestorm of controversy when it published the story on its website, beginning with the sentence, "Fear has gripped students … following a decision to use them as 'Guinea Pigs' for an upcoming Ebola vaccine trial in Ghana."

What followed next was a heated condemnation penned by Tawiah Evans of the self-styled "Coalition for Ghana's Independence Now," which intimated that the supposedly secret trials were aimed at spreading Ebola in the Ghanaian public. Soon after, another condemnation was issued in the form of a press release by the regional office of a major political party, whose local MPs had reportedly been deluged with complaints from citizens furious about the improper trials. This set off a chain reaction of Ghanaian politicians seeking to distance themselves from the unpopular trials, and calling for their suspension. Although this decision was not technically within the Parliament's remit, the Ghana Ministry of Health and FDA had little choice but to halt the trials in the face of public and political outcry.

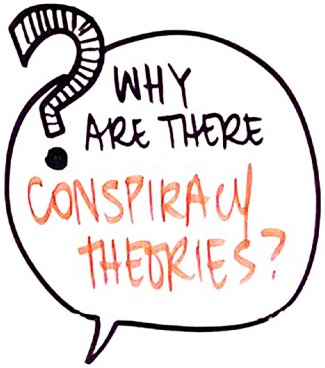
The situation was further complicated by the fact that the Minister of Health was traveling abroad at the time, and was therefore unable to address Parliament until several weeks after the start of the controversy. It then evolved that the Ghana Academy of Arts and Sciences (GAAS), an honorary academic society based in Accra, had been nursing reservations about the proposed vaccine trials for many months. The GAAS scientists, perceiving themselves to be sidelined in the process, chose to make their doubts public at the height of the controversy, in the form of a paid advertisement in a local newspaper. This added further fuel to the fire, creating the impression that bona fide scientists doubted the trials' safety, and giving MPs greater confidence that they were right to block the research from proceeding.

In the end, neither trial took place in Ghana, even though Parliament finally approved them to proceed five months after the initial suspension, since by the time this approval was granted, trial sites in other countries had made sufficient progress to render the Ghanaian trials redundant. Nonetheless, the trials' suspension represents a significant setback to the control of Ebola Virus Disease, a disappointment to those who hoped to see Ghana's scientific research sector rise to this challenge and flourish in the long run, and a cautionary tale for those conducting clinical trials in the context of an emergency response. It illustrates the importance of monitoring rumours and responding effectively, to prevent such unnecessary derailments in future.

BOX 5: THE CAUSES OF CONSPIRACY THEORIES

Conspiracy theories are often difficult to understand, since allegations of sinister secretive behaviour on the part of scientists and government may seem absurd to those who work in public health, identify with its beneficent motives, and know of the many mechanisms in place designed to prevent improper research. However, these fears often draw upon histories of colonial exploitation, which in many cases did include unethical experimentation on African people. In any country, moreover, the presence of a disease outbreak can create general panic, as well as an information vacuum, which together can foster the development of extreme rumours and conspiracy theories very rapidly.

HOW TO MANGE RUMOURS



Trialists can keep track of rumours in several ways. First, strong lines of communication between front-line community workers and the central management of the trial is essential. Although there exist highly sophisticated systems for monitoring rumours in the media (see below), the most damaging rumours are likely to arise near to the trial site, and those working directly with the community are likely to be the first to hear of them. This means that the best way to detect harmful rumours quickly is to establish clear guidelines for rumour reporting amongst all staff, and include rumour monitoring as a regular fixture of staff meetings, soliciting rumour reports every few days as well as encouraging staff to report any worrying misinformation spontaneously, as soon as they encounter it. Furthermore, all staff must receive training in appropriate responses when confronted by journalists or members of the public making complaints or asking questions that suggest a rumour is circulating. As the Ghana case exemplifies, even the simple response, "I am not able to talk about the trial," can be portrayed in a very negative light. Instead of giving, "No comment," or making a similar response, staff should know who on their trial's communications team is prepared to give a response that can quell concerns quickly, rather than merely dismiss them. In this way, having a staff that is well-prepared for handling rumours can prevent small misunderstandings from getting out of hand.

Digital media monitoring can be used to complement human information networks and detect misinformation arising directly from the news media, or from other parts of the country or the world. A variety of media monitoring services can be purchased for tracking the news media, as well as social media, which is a significant benefit in an era when services like Twitter have become outlets for citizens' concerns about the behaviour of their governments. If the trial budget does not allow for the purchase of one of these professional media monitoring services, free alternatives are available that perform reasonably well in searching the online news media, although social media monitoring is often not an option in free services. In either case, the method of using these systems is simple: the user assembles a set of keywords that reliably detect any story referring to their trial, and uses them to define a search that is executed at least once a day to collect potentially relevant stories and review them for any rumours or misinformation. In setting up these keywords, it is wise to remember that laypersons are unlikely to know or care about the official name of a trial or its institutional branding. Moreover, those who are most apt to spread misinformation about a trial are those who know the least factual information about it. So, the most valuable keywords to employ are those relating to the disease (and various common misspellings), the location in which the trial is to take place, and a variety of synonyms for "trial" such as, "research," "experiment," and "test," accepting the possibility that the staff tasked with reviewing the search results may need to sort through more irrelevant articles in order to be sure they are aware of any article that truly does refer to the trial in question.

It is also valuable to conduct brainstorming sessions early on in the trial review process, to identify the most likely points of confusion for journalists and the general public. Varying levels of research literacy can create uncertainty around concepts like randomisation, placebos, and blinding. The scientific value of giving a placebo in a clinical trial is not obvious to people unfamiliar with clinical research, and without proper explanation can easily seem strange, suspicious, or even malicious, especially in the context of a disease outbreak. One particularly common concern associated with vaccination is the fear that the vaccine might carry a risk of imparting the disease it is meant to protect against. Communications experts should develop clear, simple responses to these anticipated concerns, and prepare summary "cheat sheets" for all staff who are likely to encounter these sorts of questions.

Finally, it is important to consider the possibility of “positive rumours” - for example false claims that the vaccine being tested is 100% safe or effective, when this is not yet known, that it cures the disease in question, has other positive effects on health that are not true (such as increasing vigour), or that participants will receive greater compensation than is actually the case. Although these rumours do not cause problems in the same way that negative rumours do, and would be expected to act in such a way as to increase enrolment in the trial, it is ethically impermissible to allow participants to enrol based on false expectations of the trial, since this violates the principle of informed consent. Therefore trialists must take every effort to quell false rumours of all kinds, not just those which are critical of the trial.

6. Enabling Technologies

Increasingly, technologies are being used to facilitate both clinical trials and wider public health campaigns. It has become clear that the use of enabling technologies is vitally important in improving health services, patient care, and the management of future Ebola outbreaks in resource-limited settings. The positive impact of information and communication technologies (ICTs) on healthcare delivery systems in low-resource locations, such as in parts of Africa, has been demonstrated by numerous projects.

In resource-limited settings, it is very common for patients to not be followed up correctly due to the lack of a robust patient identification system. Often, patients do not have a known address, and so it is difficult to keep a record of patient details and history. In clinical trials and public health campaigns, ICTs can help to ensure that participants and patients are followed up correctly by their healthcare facilities in order to receive timely care and vaccinations, which is especially important for vaccines administered as a prime-boost regimen. In this section we discuss several technologies used to keep track of participant identity (biometrics including fingerprint and iris scanning) and maintain communication and follow-up with participants (MOTECH communication platform).

ICTS IN SUPPORT OF CLINICAL TRIALS

ICTs have played a crucial role in clinical trial programmes. The EBODAC project is supporting the EBOVAC clinical trials programme by helping to ensure that the Ebola study vaccines (which are administered as a prime-boost regimen) are accepted and received successfully in resource-limited settings. Additionally, EBODAC has contributed to preparing communities for future Ebola outbreaks and vaccination strategies. In order to continue vaccinating patients effectively, EBODAC implemented various ICTs in areas of Western Africa to effectively identify individual patients and record their information accurately.
EBODAC facilitated the introduction and installation of patient identification tools to ensure that the correct participant received both prime and boost vaccines at the right time. As the EBOVAC clinical trials programme took place at a time when Ebola was still widespread, there was a possibility that participants would try to "share" their study vaccinations out of a motivation to protect friends or family members.

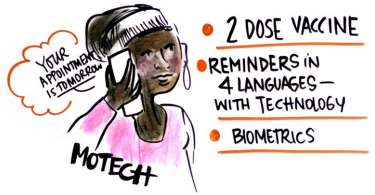
First generation biometric tools, including iris scanners and fingerprinting, were utilised to uniquely identify study participants and to recognize them at subsequent clinic visits. The biometric traits measured are unique to every individual, and so it allowed clinical teams to correctly identify each participant throughout the duration of the follow-up phase of the study. These biometric kits included an iris scanning camera, digital fingerprinting device, a laptop to capture patient demographics, a printer to enable the printing of a vaccination card, printer cartridges, and a reserve battery pack. Over time, the technology of the iris scanners was upgraded to be a handheld mobile tablet-based device. In EBODAC, the biometric tools were integrated with an electronic data capture system and mobile phone technology to maintain contact with participants, and to remind them of necessary clinic visits. These were well accepted by participants.

The MOTECH system (which had previously been successfully implemented in other public health campaigns, including maternal health programmes in India and Ghana) was introduced. The premise of MOTECH, in terms of the EBODAC project, was that trial participants would be able to use their own mobile phones to receive pre-recorded voice messages in their own language reminding them of necessary clinic visits as part of the trial. A number of metrics were used to assess the success of the MOTECH system, including:

- the number of participants consenting to receiving voice message
- how often participants answered the phone
- how long participants listened to the messages
- the correlation between participants listening to voice messages and attending follow-up appointments

Quantitative data on the impact of the MOTECH system is currently being gathered, however, initial feedback has shown that it has been very well received by both clinical staff and study participants.

Using the various technologies introduced during the EBOVAC clinical trials programme, it was possible for recruitment listings to be downloaded in order to inform trial sites how many patients were expected on each day. This capacity planning tool was developed to allow the team to optimally manage the numbers of study participants they could see on any given day by planning individual appointments based on the clinical team's capacity. Integration of the technologies used in EBODAC was possible by using a unique identification number for each participant, which was generated by the biometric system.



BOX 6: ICTS IN SUPPORT OF WIDER PUBLIC HEALTH CAMPAIGNS

Another example of the use of ICTs outside the clinical trial setting comes from the Uganda-based ICT4MPOWER project, in which child health cards were created so that healthcare workers could quickly identify and treat children. These health cards simplified the clinical staff's paperwork to one form, allowing instant retrieval of patient information. Old records were digitised using battery-powered scanners. The local teams were eager to participate and embraced the new technologies with unexpected enthusiasm, having endured years of hand-writing and calculating data manually, which ultimately left too much room for human error.
The increase in administrative efficiency ultimately led to quicker clinical decision-making and improved patient care. Test results were received more quickly and the supply of pharmaceuticals corresponded more accurately to the needs of each health centre at any given time (in contrast to the prior situation, in which drugs were delivered based on past orders which often did not reflect current needs).
This technology facilitated tracking patient vaccinations to ensure people were followed up correctly for their second dose, and to record the reasons why people were not followed up (such as there being no nurse present or no vaccine available, or that the patient was unaware of the follow-up appointment). In one district, it was possible to greatly reduce the number of vaccine dropouts, thus ensuring that every patient received the correct dosage. This system has now been implemented in approximately 400 health centres, which would undoubtedly bolster preparedness for clinical trials or in the event of a disease outbreak.

OVERCOMING BARRIERS

In order to achieve the benefits of ICTs, there are some challenges to overcome. In remote locations in Sub-Saharan Africa, lack of electricity and connectivity is a common obstacle. This has a great impact on the types of ICTs that can be used in resource-limited settings, as electrical power and data transfer are fundamental to their usability.

Prior to the implementation of EBODAC, there were concerns that locals would be reluctant, or refuse to take part in the programme, due to lack of awareness of the project, or wariness of external intervention. As the trial took place at the time of the 2014–2016 outbreak of Ebola virus, many people were sensitive about the collection of personal data and associated it with the disease. Additionally, there were concerns that locals would not take part in a project that would lead to stigmatization. For example, it was not possible to put photographs on the participant identification cards as it may have led to the participant being "associated" with Ebola, and expose them to the stigma of such an association. Furthermore, the Ministries of Health in countries with Ebola virus were initially hesitant about the mechanisms for hosting the data. Their main concern lay with the storage and confidentiality of the data gathered by the project.

An additional barrier in some countries is the strong cultural beliefs of the communities, which may prevent the use of biometric technologies such as fingerprint and iris scanners. For example, during the early implementation of a health card system, it was believed that such a system would not be feasible in Uganda, due to the lack of local knowledge around ICTs and strong cultural principles. The following subsections discuss ways of overcoming these individual barriers.

Research

When planning ICT projects in clinical trials, it is important to begin by carrying out formative research in some of the most resource-limited areas to determine the exact materials required, and whether the technology solutions would be accepted. In general, the first step in implementing any ICT should be to perform a landscape assessment to see what is currently in place, and then to build on the existing infrastructure. In some communities, the use of mobile phones was more common than initially estimated, and so it was possible to obtain better tools to work with. This also highlighted the need for technical support and improved community knowledge on how to put the systems into practice. In low-resource settings, sustainability and simplicity is key to the uptake and maintenance of new technologies.

Robust training

High quality staff training is paramount for projects such as EBODAC to run smoothly. In EBODAC, healthcare staff training was delivered in the form of a "Train-the-Trainer" system. It is important to have a strong understanding of the local communication style in order to deliver the most effective training. From an educational perspective, a mobile training support tool (MOTS) has been developed. Interactive training modules in line with the national curriculum were developed to provide community health workers with refresher training on vaccines and emergency response practices. These training materials were delivered to the mobile phones of remote workers as audio files in local languages, in order to make the training as effective as possible and accessible even to those with limited literacy.

Community engagement and outreach strategies

In terms of improving the knowledge of ICTs in resource-limited settings, employing community engagement and sensitisation strategies prior to implementation is extremely important. Such strategies also contribute to managing any initial reticence against external intervention. Despite the initial concerns, almost all people consented to receive mobile phone messages and also agreed to have their biometric data captured. Indeed, local communities were eager to get involved upon gaining a clear understanding of the goals of the project. This was largely attributable to the time spent building a relationship with the communities prior to implementation.

Support from local leaders was shown to contribute to the overall awareness and adoption of the programme. Meetings with local chiefs and religious leaders can be organised to solidify the relationship between the project and the community, and alleviate any fear of the technologies (such as the iris scanners). Close collaboration with governments, in particular the Ministries of Health, to provide information on ICTs and the goals of the project is imperative

for successful adoption. Members of the EBODAC consortium visited the Ministry of Health in Sierra Leone in order to ease their concerns regarding the storage of the participant data. Explaining the built-in security systems of the ICTs helped to reassure them that the system was safe and secure, and the necessary contracts were then put in place.

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Tailoring technologies to maximise participant engagement

In EBODAC, the MOTECH mobile phone technology was used to maintain contact with trial participants. Prior to setting up the MOTECH system, it was anticipated that many people in the local communities shared mobile phones, and so the pre-recorded phone calls were scheduled for around 7am in order to increase the probability of contacting the correct participant. Furthermore, to avoid any stigmatization of participants, no names or personal information were included in the voice messages. As the MOTECH system had been previously used in other projects, it was customized for use in a clinical trial, including allowing participants the ability to choose their preferred language in which to receive their message.

Voice messages were reviewed by a committee made up of locals, government members and students from nearby universities to ensure they were appropriate for the purpose. The option of using a voice recording to communicate with participants was elected because it was found to be the most effective in these communities and helped to overcome any literacy issues. A voice message would be sent three times, followed by an SMS message if it had not been possible to contact the participant. Working with local network providers to ensure that the calls were delivered to participants from a unique telephone number (as opposed to different unfamiliar numbers) also increased the likelihood of participants answering the call. These measures undoubtedly contributed to the success of the MOTECH technology during EBODAC.

Overcoming the barriers of electrical power and mobile connectivity

One of the most challenging aspects of working in resource-limited areas is the lack of connectivity. To overcome this issue during clinical trials various options are available, including the use of batteries, solar chargers or petrol-powered generators to provide a suitable power source. For example, the biometric kit used in the EBODAC project had a battery life of eight hours, which was critical in communities that had either an intermittent or non-existent electricity supply. As another example, the child health cards that were developed in Uganda were designed so that they could be read by battery-powered scanners in areas with no electricity. The information could then be passed up the healthcare chain to update the patient record.

Although mobile phone coverage in urban areas in Africa is often good, in more remote areas in resource poor settings, mobile phone signals are more haphazard, and it may be necessary to use satellite technology or work with telephone providers to improve this in clinical trial sites.

Collaboration with local and international partners

Partnerships with local and international technology companies were important in facilitating the smooth installation of ICTs in the EBODAC project. As many ICTs require constant access to the internet, teams are currently investigating their capacity to function offline, so that they can be used in cases of unreliable internet access. In general, technologies (such as mobile apps) tend to be designed for use in more developed countries. Designing an app or technology in developed countries for use in resource-limited settings is not always logical. It cannot be assumed that technologies designed in Western countries will function and be well-received in locations that are profoundly different in both material and cultural ways. Therefore, it is important to first visit the area in which the technology will be used, in order to grasp the challenges and gauge the local situation. Technologies can then be designed accordingly, and will be better tailored for use in the target settings. For example, the biometric system in EBODAC was developed to be used offline given the connectivity issues in the target community.

RECOMMENDATIONS FOR USING ENABLING TECHNOLOGIES IN CLINICAL TRIALS

Use previous learnings and experiences

In terms of future scope for enabling technologies in resource-limited settings, EBODAC and similar public health projects have demonstrated a lot of promise for continuing to employ and strengthen the use of ICTs in clinical trials and beyond. There are plans to further roll out the MOTS training support programme for healthcare workers to the broader Kambia district in Sierra Leone in 2019. If the pilot programme is well received, the Ministry of Health can decide to take ownership of the programme so that they can continue to use the platform to train community health workers beyond the EBOVAC clinical trial programme.

Need for flexibility

Systems that work in one country or region may not necessarily be transferable to another region, and so it is important to be flexible in terms of strategy. For example, the MOTECH system has been implemented in India with the aim of improving maternal healthcare,[45] but this may not be feasible in locations with poor mobile network coverage. However, biometric systems have broadened the range of technologies that can be used in areas that do not have reliable internet connectivity. As mentioned above, in regards to network and telecom providers, it is highly recommended to check the availability of cellular networks, and to work in collaboration with local providers.

Need for harmonisation

To continue moving forward with ICT projects and strengthening the healthcare efforts in response to Ebola virus disease, the way technology is employed in resource-limited settings needs to be harmonised. This requires synchronisation not only within the organisations involved, but also with the government. Having all the necessary regulations in place and providing leadership will make a significant difference to the implementation of these projects. One report has detailed the importance of the Ministries of Health in providing government leadership to deploy e-health strategies in resource-limited settings. There should be firmer policies in place with regard to implementing technologies, so as to avoid delays in deployment and to gain approvals more quickly.

The use of ICTs in projects such as EBODAC, or as part of a wider public health campaign, has impacted the quality and efficiency of health service delivery in resource-limited settings. Perhaps most importantly, the ability to track patients in order to make sure timely care and prime-boost vaccinations are provided has allowed high quality data generation, which has been instrumental to the EBOVAC-Salone trial. Continuing to develop these technologies and ensuring that they can be effectively scaled-up in the event of a future Ebola outbreak requires flexible strategy based on previous learnings, strong leadership from the organisations involved and the government, and transparent partnership with the communities affected. Through these means, it is possible for ICTs to meaningfully impact the management and control of future Ebola outbreaks.

Additionally, the epidemic brought about a wider understanding and awareness of Ebola disease across Western Africa (and Africa as a whole), including how the virus is transmitted. The use of ICTs for surveillance, reporting signs and symptoms, and using GPS to plot the spread of disease can facilitate the rapid assembly of response teams. The increased awareness and understanding of Ebola virus has been invaluable to public health efforts and provides a silver lining to the tragedy of the outbreak. As a result, the response to and containment of future outbreaks would undoubtedly be quicker.

Experiences from EBODAC give us a plausible model of piloting technologies in the context of clinical studies, refining them, and bringing them to scale, in partnership with ministries having built local capacity to support the platforms along the way. The position that we are in now is better than in 2015, however we are still not there yet. To improve preparedness is to strengthen public health systems in the most vulnerable countries to function not just during epidemics, but all the time. More effective engagement with communities, non-government organisations and the private sector will ultimately lead to a wider support network for implementing technologies in these settings.

CONCLUSION

The 2014-2016 West African Ebola epidemic presented both significant challenges and opportunities for conducting clinical trials in an outbreak setting. Given the circulating fears, rumours and misconceptions surrounding the emergency response to the disease, coupled with the lack of familiarity that many affected countries and communities had with clinical trials, trial-focused community engagement was crucial. However, these trials also demonstrated that despite this context and the enormous challenges faced by research groups trying to establish robust clinical trials in the most difficult of situations, it was possible to structure community engagement activities in such a way that participants remained at the heart of research.

Collaborations between clinical research teams, community engagement experts and social scientists allowed the development of rapid feedback loops between participants, community members and the trial itself, enabling participants' input into trial processes and procedures. Valuable lessons were learned, too, about the subtle context-dependency of ethics for trials being done in a challenging setting, in which the imperative to protect the public from infection must be balanced against the need to avoid undue pressure on potential participants. This experience also furnished useful insights into various approaches to address rumours and conspiracy theories, which flourish in the absence of official information, but can be mitigated by advance sensitization and clear lines of communication. The uses of enabling technologies were also highlighted, with crucial adjustments made to operate in a challenging setting, for example using battery packs where electricity is unreliable, and utilizing local-language voice messages to accommodate those with limited literacy.

Moving forward, the lessons from this crisis need to be used to improve the planning and implementation of clinical trials in the future, both in routine settings and crises. As the Ebola epidemic demonstrated, the community's involvement in any crisis situation is absolutely critical to its success. A lack of time should not be regarded as an excuse for not developing an understanding of the context within which a clinical trial is set to work, or for failing to engage properly with individuals at both national and local level from the moment of a study's inception; embedding both social scientists and community engagement experts into clinical trial teams should be standard practice as it provides essential contextual knowledge for planning and implementation. Even so, more must be done to ensure that community members are regarded as equal partners in research rather than the passive recipients of research studies. After all, these are the individuals who will ultimately determine whether or not any trial is implemented successfully.

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