

PLOS Science Wednesday: Hi Reddit, I'm Sara Carazo and my recent PLOS NTDS article discusses the challenges of implementing a clinical trial during the Ebola emergency in Guinea – Ask Me Anything!

PLOSScienceWednesday¹ and r/Science AMAs¹

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Abstract

Hi Reddit, I am Sara Carazo, a medical doctor working for a long time with MSF (Médecins Sans Frontières). In 2005 I participated to the MSF response to a Marburg epidemic in Angola and in December 2014-January 2015 I was the MSF medical referent person for the Ebola clinical trial testing favipiravir in Gueckédou, Guinea. Since 2014 I am doing a PhD in Epidemiology at Laval University, Québec. My current research topic is on measles vaccination. My colleagues and I recently published in PLOS NTDS the article: Challenges in preparing and implementing a clinical trial at field level in an Ebola emergency: A case study in Guinea, West Africa. It is a viewpoint where we critically review all the challenges that we encountered to implement a clinical trial in the context of an uncontrolled Ebola virus epidemic and a vulnerable resource-poor setting of rural Guinea. I will be answering you questions at 1pm ET – Ask Me Anything!

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Since the drug is a viral RNA polymerase inhibitor, does it have the potential to work on other filoviruses or even retroviruses or is it just specific to Ebola? How does the classification of a virus affect its treatment method?

[kasmith362](#)

Sara: First, the efficacy of favipiravir has not been yet demonstrated. There are encouraging conclusions on tolerance and it merits further study in patients with medium to high viremia. But, if an antiviral is working on Ebola virus disease it will clearly have the potential on other filoviruses. I can't go further on virology, as it is not at all my domain.

How many different ethic committees needed to give their approval for the trial? If there were investigators from multiple institutions, did all the different institutions have to give approval?

[randogirl007](#)

Sara: Indeed, the participation of multiple institutions needed different ethics committees approvals. Three ethics committees approved the protocol: the institutional review board of the Institut National de la Santé et de la Recherche Médicale (Inserm, France), the Médecins Sans Frontières International Ethics Committee and the Guinean Comité National d'Éthique pour la Recherche en Santé.

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What were common beliefs among the community regarding Ebola that were not found in science?

[conservio](#)

Sara: It is important to understand that Ebola disease had never happened before in Western Africa. Besides, communities in forest guinea have a complete different interpretation of disease and traditional healers are key persons in the community. Lot of anthropological work has been done, but I don't have in-deep knowledge of it. I recommend to check: www.ebola-anthropology.net

Thank you for doing this AMA.

How did your medical team address the ostracization of Ebola patients from their communities, even after being cleared of the virus? How did your medical team's cultural approach change concerning explaining medical information pre vs post outbreak?

Did you find any connections regarding the social handling of Ebola in Guinea to the aversion of measles vaccinations in first world countries?

[Traveling_wonder](#)

Sara: Ostracization was a real problem for Ebola survivors. The way we tried to improve it was with a team of social workers that accompanied discharged patients and tried to help explaining relatives and neighbours that there was not risk for them. In urban context, like Conakry, associations of Ebola survivors were crucial for the process of re-integration. About measles vaccination and ebola, I don't really see many parallelisms. Social handing of Ebola is based on fear for a disease that is killing more than 50% of infected persons, often entire families as it is usually clustered. I perfectly understand the fear and the reactions to Ebola disease, mainly when not clear information is given. Even if we can consider measles vaccination refusal in first world countries also based on misinformation, I would say that it is the lack of perception of a risk for measles (and the pretended risk of vaccination) what is driven the refusal for vaccination.

The section on administering favipiravir to pregnant women was interesting. Did the ethics approval ever come through? What revisions to the process do you think should be made so that particularly vulnerable groups can get specific ethical clearance on a timeline that allows administration of a potentially life saving treatment?

[p1percub](#)

Sara Carazo: The ethics approval for the compassionate use of favipiravir in pregnant women arrived two weeks after trial initiation. I consider necessary to have a formal protocol approved by ethics committees for this kind of compassionate use, because it is the way for protecting vulnerable groups. Probably the process could have been started a bit earlier, but it is important to understand that all the pre-field preparation was done in 7 weeks and the field preparation in 6 weeks. A record time to start a clinical trial, moreover if we consider the circumstances of the setting.

First, thank you for doing this AMA!

As I'm sure you've seen today, France recently ruled that 8 currently recommended vaccines (including the measles vaccine) will become mandatory in 2018. Given that one major area of your research is the measles vaccine, what is your opinion on mandatory vaccines? Do you believe that a decent portion of the world can overcome the fear/distrust of vaccines?

[cottonholloa](#)

Sara: I think that a decent portion of the world have overcome the fear/mistrust of vaccines, as vaccination coverages are high in most of the countries. Personally I do not believe in mandatory vaccination, but in better understanding and handling the origin of vaccine hesitancy and refusal.

Technical (IT) challenges in resource-poor settings are well-known. Specifically what IT tools did you use or attempt to use to collect data and securely share with the international community of epidemiologists, stakeholders and decision makers?

[hiroo-onoda](#)

Sara: I would say that the main IT challenge was the transmission of information from high to low-risk area. We installed a scanner in high risk area to be able to scan every document that was filled inside the high risk area (drug follow-up, clinical symptoms check list, etc). These documents were later printed and all information collected in appropriate electronic formats. I would say it was laborious but precise to ensure correct data collection. Other electronic devices allowing decontamination were later developed to collect electronic data directly from the high-risk zone, but I don't think they were finally implemented (at least sure not in Guéckedou).

Ever since I was in middle school and wanted to be a virologist or a pathologist and I was wondering where/ how did you go about getting your job as a researcher and not just another doctor?

[1JiveTurkey](#)

Sara: Well, I would say that you have to get a training on that (I am doing epidemiology) and to find the right environment to do research.

What would you want the younger people to know about this?

[NlkaTheGreat](#)

Sara: I would say that what we all should learn is that there is need to prioritize research for all neglected diseases, which are mainly the ones happening in developing countries.

Since you obviously couldn't implement a randomized control trial, how do you plan to evaluate the efficacy of this treatment?

Also, is PCR the typical method for evaluating disease progression in clinical trials like this, or are there other methods that wouldn't have worked for this particular situation?

Thanks for doing this AMA! I'm a college student interested in studying epidemiology and I find this stuff fascinating.

[RolledDoll33](#)

Sara: For efficacy evaluation, the trial design planned a comparison with historical data on mortality in the same Ebola treatment center. There was then a pretrial target of mortality to consider that further evaluation of favipiravir was pertinent. The idea was to test different treatments in different sites and to later perform randomized trials comparing the treatments that had shown promising results. PCR is the standard method to evaluate presence of Ebola virus.

Did the participants agree easily to the follow-up? I've never done a humanitarian trip, but my colleagues have, and they told me their patients usually don't come back. Salutations de MTL :)

[Miss-Messy-In-Ayland](#)

Sara: We wondered the same when we planned the 30-day follow-up visit. At discharge, we explained that there will be a medical consultation and a blood sample taken with the objectives of helping and treating them if there was any problem, but also we talked about getting more knowledge to help future patients. We also gave a telephone number to communicate with a doctor and we paid in advance the travel costs. To our surprise, all patients came back for their follow-up visit

Thank you for doing this. So if there is a severe outbreak in a country as large as Nigeria what will be the preferred strategy for vaccination. Will it still be ring vaccination (of probable and confirmed cases)? Or will vaccination prioritise vulnerable populations (healthcare workers, border control etc.)?

[Laolu Laolu](#)

Sara: Ring vaccination is mostly vaccination of contacts (cases will not benefit from vaccination). In my opinion, in case of rural epidemic the best strategy would target all members of a community where any case is diagnosed. Besides all healthcare workers of a broader region should receive the vaccine. But it is clear that the strategy has to be context-specific and needs to be preceded of a lot of communication with communities.

Will there ever be a way to 'cure' ebola once it has been contracted?

[Pr_Revoving](#)

Sara: There are encouraging advances. Probably, as with other serious infectious diseases, we will find a way of reducing mortality with antivirals and other treatments, which does not mean that we will be able to save all the patients. What we learned it is that a high viral load, often related to age and to the type of transmission, is associated to an early and extremely severe affectation of renal function, making its treatment really complicated.

When Ebola pandemic arises, it may spread so quickly, but clinical trials often require much time. Then which will you have priority speed or precision?

[gongmong](#)

Sara: One of the lessons learnt was that there is a need for anticipation in ebola and other emerging diseases: - have potential treatment and dosage available - build strong links with NGOs and local researchers in southern countries - have designs and teams ready to conduct trials.

Why are you doing this as a clinical trial instead of just humanitarian use exemption? What is your control group.

[jabanobotha](#)

Sara: Because we want to build knowledge and to carefully control the administration of an experimental drug. Giving drugs in a context of humanitarian use exemption is neither helping to

develop future guidelines, nor giving strong arguments to make treatments available or to develop new ones if the existing are not working. About control group, there is a long justification of our choice for a trial without control group in the publication of JIKI trial results (Sissoko et al). It was the only ethical and feasible trial to perform according to us and the objectives of demonstrating feasibility and obtaining preliminary evidence of efficacy can be attained.

Is the position of coordinator there a common job? How much of a role are the investigative staff on site to answer questions about the consent? Do you tend to follow European ich in those scenarios or American gcp?

[applebottomdude](#)

Sara: I worked as a research coordinator for MSF, which was a completely new position because we didn't have these kind of collaborations before. We (MSF and INSERM research personnel) were completely involved in the development of the informed consent and in the training of the local staff (also research staff) responsible to give the information in the local language. We were present in the site every day for any question.

Did you have the opportunity to work with any of the original Ebola researchers?

[Koraxtheghou!](#)

Sara: Who are the original Ebola researchers?

I wanted to know how does a disease like this break out in the first place? A lot of indigenous tribes often have healing herbs or medicines that we will look into and often deconstruct and replicate in the lab. Was there any such local solution in this instance?

[musical_throat_punch](#)

Sara: To my knowledge, no any local "solution" has been found in any Ebola outbreak in the story.