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Emergency response in a global health crisis: epidemiology, ethics, and Ebola application

Jennifer Salerno PhD [a,*], WayWay M. Hlaing PhD [b], Thomas Weiser MD, MPH [c], Catherine Striley PhD [d], Lisa Schwartz PhD [e], Frederick J. Angulo DVM, PhD [f], Verla S. Neslund JD [g]

[a] Department of Oncology, Faculty of Health Sciences, McMaster University, Hamilton, Canada
[b] Division of Epidemiology and Population Sciences, Department of Public Health Sciences, University of Miami, Miami, FL
[c] Portland Area Indian Health Service, Portland, OR
[d] Department of Epidemiology, College of Public Health and Health Professions and College of Medicine, University of Florida, Gainesville
[e] Department of Clinical Epidemiology and Biostatistics, Faculty of Health Sciences, McMaster University, Hamilton, Canada
[f] Division of Global Health Protection, Center for Global Health, Centers for Disease Control and Prevention, Atlanta, GA
[g] CDC Foundation, Atlanta, GA

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ABSTRACT

Purpose: The link between ethics and epidemiology can go unnoticed in contemporary gatherings of professional epidemiologists or trainees at conferences and workshops, as well as in teaching. Our goal is to provide readers with information about the activities of the College and to provide a broad perspective on a recent major issue in epidemiology.
Methods: The Ethics Committee of the American College of Epidemiology (ACE) presented a plenary session at the 2015 Annual Meeting in Atlanta, GA, on the complexities of ethics and epidemiology in the context of the 2014–2015 Ebola virus disease outbreak and response in West Africa. This article presents a summary and further discussion of that plenary session.
Results: Three main topic areas were presented: clinical trials and ethics in public health emergencies, public health practice, and collaborative work. A number of key ethical concepts were highlighted and discussed in relation to Ebola and the ACE Ethics Guidelines.
Conclusions: The Ebola virus disease outbreak is an example of a public health humanitarian crisis from which we hope to better understand the role of professional epidemiologists in public health practice and research and recognize ethical challenges epidemiologists faced.

Introduction

The 2014–2015 Ebola Virus Disease (EVD) outbreak in West Africa is the largest Ebola outbreak with >28,000 reported confirmed, probable, and suspected cases and >11,000 deaths [1]. The disease impact on local communities was escalated compared with prior outbreaks due to a number of interacting biological and social complexities including increased mobility, poverty and a lack of health care infrastructure, disease transmission, and burial culture and customs [2].

The Ethics Committee (Chair [J.S.], Past-Chair [T.W.] and Committee Members [W.M.H., C.S.]) sponsored a plenary session at the American College of Epidemiology (ACE) Annual Meeting held in Atlanta, GA, September 27–29, 2015, to discuss the EVD outbreak and highlight the balance between scientific and ethical aspects of an emergency response in a global health crisis such as the EVD outbreak. This article presents a summary and further discussion of that plenary session. The plenary session dealt with three subtopics: (1) clinical trials and ethics in the EVD public health emergency (L.S.); (2) public health practice: the emergency response to the EVD epidemic by the Centers for Disease Control and Prevention (CDC; F.A.); and (3) collaborative work: the CDC Foundation (V.N.). The purpose of this publication is also to provide readers with information about the activities of the College and to give readers of the *Annals of Epidemiology* a broad perspective on a recent major issue in infectious disease epidemiology.

* Corresponding author. Program in Evidence-Based Care, McMaster University, Juravinski Hospital, G Wing, Rm 220, 1280 Main Street West, Hamilton, ON L8S 4L8. Tel.: +1 (905) 527-4322x42879; fax: +1 (905) 526-6775.
E-mail address: salernoj@mcmaster.ca (J. Salerno).

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Clinical trials and ethics in public health emergencies

Randomized controlled clinical trials (RCTs) are considered the top-tier level of evidence when it comes to establishing the effectiveness of a treatment, device, or other intervention and the causality. In the case of the EVD outbreak in 2014, there was a paucity of evidence-based treatment or prevention methods for EVD. Therefore, the question was not "Which type of clinical trial to perform among the options of a superiority, equivalence or noninferiority RCT?" but rather "How can we immediately provide those affected with a safe and effective intervention at all?" Arguably, "it is unethical to withhold any intervention from victims of disasters" and it is incumbent on researchers and health care professionals to consider "what is the minimal ethical intervention" (Concerted European Action for Coping with Disaster Minutes of the Euro-ActDis Meeting, Paris, 19; 20 April 1990). Despite initial controversy over whether the conduct of clinical trials in epidemic situations should adhere to the highest scientific standards and advance through the usual phased development approach or be allowed to be conducted in a more expedited fashion, agreement was reached that the pace of clinical trial design in the situation of the EVD outbreak must be accelerated, "the recipients of experimental interventions, locations of studies, and study design should be based on the aim to learn as much as we can as fast as we can without compromising patient care or health worker safety, with active participation of local scientists, and proper consultation with communities." ("Statement on the WHO Consultation on Potential Ebola Therapies and Vaccines": http://www.who.int/mediacentre/news/statements/2014/ebola-therapies-consultation/en/).

In the aftermath of the EVD outbreak, researchers have left us with a legacy of innovative and nontraditional trial methods. In the early days of the outbreak, researchers worked with aid agencies to refine the "adaptive randomized trial," whereby multiple investigational interventions can be simultaneously evaluated and compared with a shared control group receiving supportive care. If the intervention displays effectiveness, it would then be provided to all who are affected in the trial [3]. An adaptive design is different from the traditional RCT as it uses data collection in the context of a trial to inform the longitudinal nature of that same trial or a new trial. It allows for a pragmatic response to changes in context while considering statistical properties [4]. Although these nontraditional or adaptive trials (e.g., Bayesian, Cluster RCTs, Step Wedge designs) are not necessarily new methods, few Institutional Review Boards (IRBs) are familiar with these methods so they lack experience and criteria for adequate review. This could create a delay in using these pragmatic trials in a health crisis such as the EVD outbreak in West Africa.

Another proposed solution is the concept of the "monitored emergency use of unregistered and experimental interventions" [5] as an alternative to the compassionate use of drugs, which is in use with success in Canada. The proposed solution aims to address current US legislation in which drug access for use in emergency responses is impeded by drug evaluation in ongoing clinical trials, as such: "the US Secretary determines that provision of the investigational drug or investigational device will not interfere with the initiation, conduct, or completion of clinical investigations to support marketing approval" (21 US. Code § 360bbb Expanded access to unapproved therapies and diagnostics). In hindsight, in the face of a humanitarian crisis such as the EVD outbreak, first and foremost, the overriding principle should have been the urgent provision of relevant and potentially impactful (yet unapproved) treatment(s) to as many affected individuals as possible. The ACE Ethics Committee will continue to find opportunities for further discourse on how these principles can be prioritized.

The ACE Ethics Guidelines, and other institutions and authorities, state that informed consent for research studies should be obtained from all research participants and should include disclosure of the purposes of the study, the scientific methods and procedures, any anticipated risks and benefits, and the right to refuse participation or to withdraw from the research at any time without repercussions [6,7]. In the EVD situation, whether an affected individual has the capacity to make an informed consent decision has been scrutinized, with the role of therapeutic misconception raised as a key ethical issue. That is, are individuals ambiguous in their thinking as to whether enrollment in a clinical study will lead to medical benefit versus participation in research that will solely contribute to general scientific knowledge? The ethical principle remains that research participants must voluntarily consent to the research without coercion, manipulation, or undue incentives for participation. In an EVD stricken environment, one could argue that any treatment prospect could be potentially coercive such that affected individuals would likely take any treatment over none. Does this constitute an informed decision in which the only other choice is supportive care? On the other hand, one could argue that an EVD patient who weighs the options of the receipt of any treatment versus standard, that is, supportive care, does so, while adhering to the ethical practice of an informed and voluntary decision-making process, though from a limited number of choices. The ACE Ethics Guidelines, which are currently under revision, suggest that informed consent procedures may be waived in instances of disease outbreak investigations, but these do not extend to participating in clinical trials of experimental treatments, in general, or specifically in the face of a rapidly escalating public health crisis [6]. The brevity in the current guidelines are noted, with revisions to elaborate on the need to assess and enhance participant comprehension, especially in vulnerable populations [8].

Public health practice: CDC's emergency response to the EVD epidemic

The CDC was at the forefront of the EVD emergency response. CDC activities during the EVD emergency response focused on controlling the outbreak. The collection of data from patients during a disease control effort is usually considered "public health practice" and therefore is usually judged to not involve human subjects research. Nonetheless, all data collection proposals by CDC during the response to the EVD epidemic were reviewed by representatives of CDC's Human Subjects Research Office for a determination of whether the activities involved human subjects research. All projects judged to involve human subjects research were then submitted to IRBs in-country and at the CDC.

From the CDC's perspective, the control activities surrounding the EVD epidemic can be described in four phases: (1) explosive growth; (2) initial control; (3) getting to zero; and (4) maintaining vigilance. During the first phase, CDC activities included: seeking resources, establishing incident management, expanding laboratory and treatment capacity, establishing safe burial teams, initiating infection-control training, disseminating risk-reduction messages, and ensuring medical care for responders. During this first phase, there were 16 projects involving data collection from humans that underwent Human Subjects Research Office review; all were determined to not involve human subjects research because their primary intent was emergent disease. During the second phase, CDC efforts expanded to increase assistance with controlling remote outbreaks. In the second phase, there were 28 project submissions for Human Subjects Research Office review; all were determined to not involve human subjects. During phase 3 of the outbreak, CDC remained involved in all the activities from the