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From HIV to Ebola: Ethical Reflections on Health Research in the Global South and Recommendations from INSERM and IRD

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Preface

The French National Institute for Health and Medical Research (Institut national de la santé et de la recherche médicale; Inserm) and the Research Institute for Development (Institut de Recherche pour le Développement; IRD) have different histories and research interests. Inserm researchers focus on fundamental and applied biomedical research and epidemiology, while those at IRD target applied research on development issues outside of Europe, to further cooperation and reduce inequalities.

Political, scientific, and economic conditions have gradually aligned the two research institution's concerns.

Pandemics are not new: throughout the 19th century, outbursts of plague and cholera resulted in cooperation among major Western powers to protect against scourges. Since 1947, the World Health Organization (WHO) has been treating public health problems on a larger scale.

However, the HIV epidemic has played a decisive role in accelerating the convergence between the institutions. The complementarity between fundamental and clinical research in virology and field research, as well as the importance of the humanities and social sciences, were vital to best understand the individual and collective experiences of the contagions. The creation in November 1988 of the French National Agency for Research on AIDS (ANRS), an independently funded agency housed by Inserm since 2012, led to unprecedented interactions between researchers from the two institutions. It also encouraged the emergence of joint projects where researchers got to know each other and learned to work together, particularly within the ANRS Coordinated Action for "Developing Countries," which facilitated the development of research "platforms" (the first was created in Dakar in 1990) in several African and Asian countries affected by HIV and hepatitis C (1999) and B (2005).

Since 1999, the Office of Scientific and Technical Research Overseas (ORSTOM), renamed IRD, has approached other research institutions to set up joint units and encourage joint projects outside Europe. These experiences were accompanied by an awareness of the issues and ethical problems surrounding research in limited-resource countries, an area where IRD has vast experience that it was able to share within the joint units and used in 2002 when IRD developed a *Code of Ethics for Research in Developing Countries*, revised in 2008.

Inserm also has a long history of dealing with the practical ethical issues of research, which in fact formed the basis for the creation of the National Consultative Ethics Committee in 1983. Since the 2000s, Inserm has included the global South when considering ethics. The institute participates in debates on the ethics of biomedical research in Southern countries, through training in clinical research and international research programs, while it has contributed in the field for several years through the clinical trial platforms created in Africa.

Numerous research-related ethical issues arise in and with Southern countries, such as the ownership of biological substances and, more generally, collected data. Other issues concern how field studies are conducted (with the temptation to collect samples quickly and send them to the best-equipped laboratories), and how new treatments are tested (with the proliferation of clinical trials, in a context of patient dependence and asymmetries in power and knowledge). Ethical reflection also concerns "health governance," involving representatives from civil society (associations), in a context where the State's role in healthcare is diminishing, the circulation of counterfeit pharmaceuticals or medicines that do not meet health regulations developed in the North is increasing, and the health care marketplace is becoming more open (offering the richest an alternative to the "inhospitable" hospitals).

In addition to its past work in the affected countries, IRD has benefited from a multidisciplinary orientation, which proved of great strategic importance for the HIV epidemic. Anthropologists,

sociologists, demographers, historians, and geographers have contributed to understanding the health landscape, refining treatment programs and developing protocols in accordance with existing international ethical regulations that were revised as knowledge and societies evolved. IRD intends to contribute to the discussion on the tensions between universal research ethics and how to incorporate the richness and diversity of cultures as well as the pitfalls of communication, with its own issues and problems that are often minimized under the euphemism "raising public awareness."^{1 2}

Inserm and IRD quickly mobilized to tackle the current Ebola epidemic. The first identification of the culpable viral strain in March 2014 at the P4 Jean Mérieux Laboratory, run by Inserm, made it possible to quickly define the clinical and epidemiological therapeutic priorities, which Inserm and IRD are still contributing to today. IRD teams already working in the countries affected by the epidemic were able to facilitate this research with their knowledge of the socio-anthropological dimensions they had studied for many years.

If AIDS could be called a "reformer" of societies, including how they conduct research, the 2014–2015 Ebola outbreak, marked by a regional spread of the virus that had never been seen before and raising concerns—even panic due to the speed and increase in international movements—illustrated the importance of rapid coordination among research institutions and the joint implementation of their expertise. The immediate mobilization of the social sciences has been remarkable and attests to the lessons learned during the HIV epidemic.

This paper, intended to spur debates in the scientific communities, presents ethical discussions between the institutions when facing the epidemiological challenges of HIV and Ebola.

Introduction

The human immunodeficiency virus (HIV) and Ebola virus are both responsible for highly lethal infections in humans that are incurable, but with radically different rates of disease progression and routes of transmission. Although these two viruses

¹ - After the 2008 WHO study on the social determinants of public health, the journal *The Lancet* published a report in 2014, entitled "Culture and Health," stating that neglect of local cultures is the greatest barrier to the advancement of health care. [http://www.thelancet.com/pdfs/journals/lancet/PIIS0140-6736\(14\)61603-2.pdf](http://www.thelancet.com/pdfs/journals/lancet/PIIS0140-6736(14)61603-2.pdf)

² - IRD Advisory Committee on Deontology and Ethics (Comité consultatif de déontologie et d'éthique; CCDE), 2013. *Ethique de l'information scientifique dans les pays du Sud* (Ethics of Scientific Information in Southern Countries). CCDE Opinion Piece, 24 May 2013, IRD, Marseilles, 14p.

³ - A consultation of bibliographic databases confirms that 1996 was a pivotal year: on average, there are fifteen times more

were identified in roughly the same period (Ebola virus in 1976 and HIV in 1983), the epidemics have evolved quite differently: to date, about 40 million people have died of HIV infection worldwide and close to 13,000 people have died of Ebola virus disease (EVD) since 1976.

The ethical tensions caused by HIV infection have transformed practices in health care and health research. The exceptional character of the current Ebola outbreak in West Africa also contributes, in its own way, to pushing the boundaries of ethical reflection on health research.

Using lessons learned from both epidemics, this Inserm-IRD joint paper encourages researchers and their institutions to take ethical thinking beyond the scope of research per se and to look more closely at this "South" (or more precisely, these "Souths") where research is and will be conducted.

Ethical understanding gained from HIV

The HIV epidemic has deeply influenced research ethics in health throughout the world, and especially in countries in the global South. Numerous gains in ethics research have been made in connection with the HIV epidemic. The year 1996 was pivotal in the development of the ethics of health research in most Southern countries³ and in the formal application of ethics regulations, in accordance with international laws.

The HIV epidemic was a catalyst for all these processes. The announcement in 1996 of the efficacy of Highly active antiretroviral therapies (HAART) for HIV immediately resulted in strong reactions, initially by militant movements in the North, then in the South ("treatment activists"), demonstrating against the lack of North/South equity in access to AIDS treatments, and, more generally, addressing the ethics of HIV treatment research in countries in the global South. At the same time, a convergence of international initiatives, also arising from the HIV epidemic (see the "Ethique, droit et VIH (Ethics, Law and HIV)

publications on the ethics of health research in Africa, referenced in the PubMed database, in the ten years after 1996 than in the ten previous years. Starting in 2000, there are no longer any medical reviews that have not addressed the topic, whether directly in the form of investigations or recommendations, or indirectly by requiring that authors ensure that their research complied with ethics before publishing it. The year 1996 marks the end of discussions on the ethics of health research that were solely confined to countries in the global South and entry into an era where the ethics of research became a major issue in all countries.

network", created in 1993)^{4,5} and national initiatives led by local researchers resulted in the gradual implementation, starting in 1998, of ethics committees for health research in most African countries.⁶ Increased attention on gender inequalities in international programs led to including women in these committees, which now include gender issues when tackling health research projects. However, their numbers on these committees remain low.

The history of health research on the HIV epidemic in the global South has shaped the current landscape of research ethics in at least four major areas: (1) consideration of contextual vulnerabilities and their transformation into "capabilities," (2) involving communities in the research process, (3) developing research partnerships, and (4) recognizing the political aspects of health research.

1) Consideration of contextual vulnerabilities and their transformation into "capabilities"

Social science research (especially in anthropology) on HIV infection first resulted in exposing and deconstructing the culturalism that was in vogue when explaining the epidemic in Africa in the 1990s, namely: (i) describing local culture as the main cause of the epidemic's magnitude, and more precisely the culture of sexuality, alluded to through a notion of "African sexuality," described (fantasized) as very different from European sexuality; and (ii) culture as also being the primary cause for the limited impact of prevention campaigns.

The concept of "risk group," imported from epidemiology when AIDS was discovered (the days of the 4-Hs: hemophiliacs, homosexuals, heroin addicts, and Haitians), has been called into question because: (i) it does not take into account the spread of the disease outside the groups, nor of the variability of risk within a group; and (ii) it promotes stigmatization of people or social groups, and even discrimination or exclusion. Based on this criticism, situations were addressed in terms of "risk behaviors" rather than belonging to a group, then "risk situations" to stop placing responsibility on individuals for their exposure to a risk that mainly depends on structural determinants, which led to

⁴ - Initiatives supported by various institutional actors such as the EU, for example public projects like NEBRA [Networking For Ethics On Biomedical Research In Africa], a project coordinated by Inserm, and EDCTP [European and Developing Countries Clinical Trial Partnership], or private ones (for example, Informed Consent/Sidaction)

⁵ - Creation of the Pan-African Bioethics Initiative (PABIN), in 2001 in Lusaka (Zambia), and organization of the Third Conference on Good Health Research Practices in Africa, in 2003, in Addis Ababa (Ethiopia)

⁶ - In 1998 in Mali, 2001 in Senegal, 2002 in Burkina Faso, etc.

⁷ - Paicheler G. Modèles pour l'analyse de la gestion des risques liés au VIH : liens entre connaissances et actions, *Sciences Sociales et Santé*, 1997, Vol. 15, no. 4, pp. 39-70.

reflecting on the social construction and perception of risk.⁷

The concept of "vulnerability" was then introduced with three identified levels: (i) the vulnerability of individuals (education, resources, social environment); (ii) vulnerability related to health programs (the capacity of these programs to meet needs); and (iii) social vulnerability (political, economic, and socio-cultural).⁸ This led to talking about exposure to risk and the capacity to limit this risk and taking into account all the social factors that increase risk for some individuals and social groups or categories. The notion of social vulnerability helped show that failure to uphold individual rights contributes to the health risk, and Jonathan Mann, head of WHO's Global Programme on AIDS,⁹ included human rights in public health, which renewed the ethical approach to research.

Amartya Sen and Martha Nussbaum, meanwhile, developed the notion of "capability," by including the subjective dimension of quality of life. This concept of "capability" changed the idealistic and largely impractical conception of the universality of human rights, by including micro-economic and social data.¹⁰ Researchers were sensitized to power relations related to economic dependence and the risk of bias in defining or applying the fundamental rules of medical ethics. Following Amartya Sen,¹¹ they are increasingly aware that participants' freedoms are an integral part of the ethics of research and development. Therefore, "abstract freedoms" should be transformed into concrete capacities to act as and to become—to the extent possible—an agent of their health. The human development approach through "capabilities" has the power to question research institutions about their responsibilities, given the vulnerability of participants in the Southern context. It also challenges the power asymmetry between researchers and participants in the ethics of development, by requiring that guaranteed access to the minimal "capabilities" for access to health care is a condition for legitimizing research.

The bio-ethics and ethics of research, when practiced in politically and economically vulnerable areas, require a precise description of the issues for

⁸ - Tarantola D. Effets des conflits sur le risque et la vulnérabilité vis-à-vis du VIH-Sida en Afrique. Ebauche d'une méthode analytique, in Desclaux A., Raynaut C., *Urgence, précarité et lutte contre le VIH-Sida en Afrique*, L'Harmattan, 1997, pp. 19-34.

⁹ - Fee E, Parry M, Jonathan Mann, HIV/AIDS, and human rights. J Public Health Policy. 2008 Apr;29(1):54-71. doi: 10.1057/palgrave.jphp.3200160.

¹⁰ - Amartya Sen, *The Quality of Life*, Clarendon Press, Oxford, 1990.

¹¹ - Amartya Sen, *Development as Freedom*, Oxford University Press, Oxford, 1999.

all participants. The competencies of local researchers and community representatives along with a commitment to anthropological studies on the representations of the disease and local societal differences and inequalities are required in order to take into account and transform contingent vulnerabilities. Considering the rules of research in context turn vulnerabilities into "capabilities" for genuinely participatory research,¹² in which the various parties share their subjective and cultural knowledge and representations of the disease, for example.

2) Involving communities in the research process

Recognition of this involvement first emerged in countries in the North in the form of demands made by social groups that were initially marginalized (primarily gay men), modeled on advocacy groups (Act-Up, AIDES, TRT-5, etc.).¹³ This model for associations was developed and transformed in Southern countries, resulting in original forms that enabled the groups to be recognized and make demands in ways that worked with local social configurations.¹⁴ Associations for people living with HIV (PLHIV) gradually emerged as interlocutors in the regulatory process for research, often intervening as intermediaries between health officials and the research teams.¹⁵ Networks were also set up, bringing together associations from several countries that have gained concrete expertise in the ethics of health research.¹⁶ They set out to assert participants' right to no longer simply be "subjects," but rather to be increasingly seen as research actors.¹⁷ These people, sometimes referred to as "community representatives" or "association members," gained real power to ensure their opinions on research methods and goals were adopted, as well as their conditions for implementation, and legitimized the "Community Advisory Boards" (CABs), which had failed to fully represent study participants and communities involved in the first studies.¹⁸ By 2015, these actors

had become indispensable in the implementation of health research. Through a dual approach of critical and operational analysis, social science research has contributed to these changes, particularly by analyzing the conditions for informing trial participants in an intercultural context and by proposing participatory ethics systems. These include involving community "ethics mediators" in trials, by studying their impact and producing an analysis of the ethics of social relationships between researchers and communities in clinical trials in Africa that is historically and anthropologically situated.^{19 20}

3) The development of partnerships in research

The development of collaborative research has gradually established itself in circumstances combining several elements:

- The globalization of the HIV epidemic, which, despite the different epidemiological situations and resource gaps between countries, has led to a type of globalized health research, unprecedented in human history. A global medical culture surrounding HIV is developed, fueled, and paced by the biannual global conferences.²¹
- The existence of scientific communities in Southern countries, made up of skilled researchers trained in the international context and able to compete with researchers from the North.
- Recognition of the value in, and even the need for, conducting multi-centric studies across several countries.
- International funding systems for health research.
- An explanation of the North-South ethical issues for research, especially those submitted through social sciences analyses

¹² - M. Botbol-Baum, *Bioéthique pour les pays du Sud*, L'Harmattan, Paris, 2005.

¹³ - Dodier, N. 2003. *Leçons Politiques de L'épidémie de Sida*. Paris: Edition de l'Ecole des Hautes Etudes en Sciences Sociales. 349p. Broqua, C. 2006. *Agir pour ne pas mourir !* Paris, Presses de Sciences Po. 406p.

¹⁴ - Billaud, A. 2011. "Le pouvoir fonctionne.' Les experts profanes face au VIH/SIDA à Dakar (Sénégal)." Doctoral dissertation in sociology. Paris: EHESS.

¹⁵ - Couderc, M. 2011. "Enjeux et pratiques de la recherche médicale transnationale en Afrique. Analyse anthropologique d'un centre de recherche clinique sur le VIH à Dakar (Sénégal)." Doctoral dissertation in anthropology. University Aix-Marseille III, 507p.

¹⁶ - cf. The Coalition RESPECT, which connects several community-based associations for ethical research and care in Africa (Nigeria, Senegal, Burkina Faso, Cameroon, and Côte d'Ivoire)

¹⁷ - For example, the Ethics, Rights and Health Network (Réseau Ethique, Droits et Santé; REDS) in Cameroon, an association created in 1998 that aims to promote education,

legal, and ethics analysis, and the development of policies related to AIDS. <http://www.plateforme-elsa.org/structure/reds/> (consulted 5 May 2015)

¹⁸ - Couderc, M., & Desclaux Sall, C. (2014). "De l'information des patients à l'engagement associatif des personnes vivant avec le VIH participant à une recherche médicale au Sénégal — cohorte ANRS 1215." *Bulletin de la Société de Pathologie Exotique* 107 (4): 286–91

¹⁹ - Geissler, P. W., & Molyneux, S. (2011). *Evidence, Ethos and Experiment: The Anthropology and History of Medical Research in Africa*. Berghahn Books

²⁰ - Desclaux, A., Desclaux Sall, C., Sow, K. (2015). "Un seul modèle pour tous ? De la diversité des modes d'engagement communautaire dans la recherche à Dakar, Sénégal." In: Otis J., Bernier M., Levy J. J. (eds), *La recherche communautaire VIH/sida. Des savoirs engagés*. Montreal, Presses de l'Université du Québec, pp. 212–220

²¹ - Between 15,000 and 20,000 people attend these conferences, depending on the year; the 20th conference took place in 2014 in Melbourne.

that have elevated research ethics to a study object.

The process of the internationalization of health research, underway since the early 20th century,²² has accelerated, and the regulations for scientific cooperation between States have been modified and improved.

In France, the ANRS funding mechanism has helped create a model for collaborative decision-making partnerships, beginning with its involvement in HIV research in Southern countries (1993) and organization of this research through "ANRS sites" in Africa and Asia (since 1995).²³ This model comes closer to the definition proposed by the IRD Advisory Committee on Deontology and Ethics (CCDE), where it specifies that "the partnership can be defined as a gathering of actors who work together by maintaining equitable relationships in the research steps (...). In this collaboration model, all actors must be seen as equal and complementary."²⁴

Even if the asymmetry of economic resources often characterizes the relationships between scientific institutions in the North and those in the South, research programs are defined through a process of co-construction, which ensures that mutual interests underlie how research is conducted, that decisions are made collaboratively, and that research costs are shared equitably. These dimensions are among the project evaluation criteria, outlined in the ANRS Code of Ethics for Research in Developing Countries, created in 2002 and revised in 2008, in order to take into account growing demands concerning ethics, partnership, and community participation.²⁵

4) Recognizing the policy aspects of health research

Health research on HIV in countries in the global South was aligned with and implicated into defining international health policies very early on.

This was especially the case for clinical research on antiretroviral drugs (ARVs). The period 1997–2003 marked a time when the international community

recognized the need to treat AIDS patients in countries in the global South,²⁶ but international consensus still did not promote the use of antiretroviral drugs in these countries. Consequently, research activities not only sought to study the therapeutic efficacy of treatments or to identify the best treatment combinations but actively sought to promote access and use in countries in the global South,²⁷ using an evaluative analysis process and aspiring to ethical coherence.

This commitment continued after 2003 following the WHO declaration in favor of universal access to ARVs in countries in the global South, though access remained limited due to the high price of drugs. Clinical studies helped provide the arguments to allow for the use of generic ARV drugs, based on their efficacy.²⁸ Meanwhile, health economics research on drug pricing spelled out price-setting mechanisms (in terms of intellectual property rights, global trade agreements, and production environments), in order to advocate for lower prices to make these treatments affordable for countries in the South.²⁹ The concept of intellectual property regarding drugs was substantially modified, even if the failure of the Doha Round during World Trade Organization negotiations forced us to be vigilant, particularly on the issue of access to generic treatments.

In the early 2000s it was once again HIV research that revived the debate on the impact of user fees for health care and emphasized the need to promote access to care by providing drugs and health services for free to patients at service delivery points, by including these issues into the broader framework of national (social protection schemes) and international (such as the Global Fund to Fight AIDS, Tuberculosis and Malaria) solidarity mechanisms.

Illustrating the assertion that health research should be conducted with the goal of guiding public health decisions, HIV research helped to highlight its political dimensions, with a view to strengthening the health care system in countries in the global

²² - Lowy, I. 2001. *Virus, Moustiques et Modernité. La fièvre jaune au Brésil, Entre science et politique*. Paris, Editions des archives contemporaines, 363p.

²³ - Taverne, B., Ndoye, I., Delaporte, E. 2014. "L'espace et le temps pour travailler ensemble : construction d'un centre de recherche sur le VIH au Sénégal." In *Expériences du partenariat au Sud : le regard des sciences sociales*. Vidal, L. (ed). Symposiums and Seminars. IRD Center in Bondy, Marseilles: IRD, pp. 201–212.

²⁴ - CCDE, 2012. "Ethique du partenariat dans la recherche scientifique à l'IRD," IRD, Marseilles, 11p.

²⁵ - Code of Ethics for Research in Developing Countries (Charte d'éthique de la recherche dans les pays en développement), Paris, ANRS 2002, 2008, 12p.

²⁶ - cf United Nations, Resolution adopted by the General Assembly, August 2001, A/RES/S-26/2, 18 p.

²⁷ - Msellati, P., L. Vidal, L., Moatti J.-P. 2001. *L'accès aux traitements du VIH/sida en Côte d'Ivoire*. Paris: ANRS.; Desclaux, A., Lanièce, L., Ndoye, I., Taverne, B. 2004. *The Senegalese Antiretroviral Drug Access Initiative. An Economic, Social, Behavioural and Biomedical Analysis*. Paris: ANRS, UNAIDS, WHO; 230 p.

²⁸ - Laurent, C., C. Kouanfack, S. Koulla Shiro, et al. 2004. "Effectiveness and Safety of a Generic Fixed-Dose Combination of Nevirapine, Stavudine, and Lamivudine in HIV-1-Infected Adults in Cameroon: Open-Label Multicentre Trial." *The Lancet* 364(9428): 29–34.

²⁹ - Orsi, F., M.P. Carrieri, B. Coriat, et al. 2010. "Call for Action to Secure Universal Access to Antiretroviral Therapy in Developing Countries." *The Lancet* 375(9727): 1693–4.

South and eliminating North/South inequalities in the health and social welfare sectors.

Ethical challenges posed by Ebola

The Ebola virus was first identified in 1976 during an outbreak of hemorrhagic fever simultaneously affecting the Democratic Republic of the Congo and Sudan. Responsible up until 2014 for about twenty epidemics located in Central and East Africa,³⁰ this virus did not generate the same large-scale investment in research as in HIV. The pharmaceutical industry as a whole took little interest in an infection that was confined to a few outbreaks limited in place and time,³¹ and at that point Ebola studies had mainly been conducted because of the underlying concern about bioterrorism.³² Then when the West Africa outbreak, the longest and most deadly to date, was declared in March 2014, no vaccine or treatment was ready for immediate use.^{33 34}

In July 2014, the United States, and then Europe, used an experimental treatment—ZMapp—that had not been tested in humans yet, on a compassionate basis (that is, for treatment and not research), on humanitarian health care workers repatriated from Africa. This launched a discussion on curative treatments, highlighting a two-sided ethical debate: do we have the right to use a drug that has not successfully gone through the various stages of clinical approval for its safety and efficacy? And most importantly, what should be done for the care givers and thousands of people infected in West Africa?^{35 36}

On 11 August, a panel of international experts was convened by WHO to investigate and evaluate the ethical implications of decisions for the potential use of non-approved clinical interventions. It stated: "In the particular circumstances of this outbreak, and provided certain conditions are met, the panel reached consensus that it is ethical to offer unproven interventions with as yet unknown efficacy and adverse effects, as potential treatment or prevention. Ethical criteria must guide the provision of such interventions. These include transparency about all aspects of care, informed consent,

freedom of choice, confidentiality, respect for the person, preservation of dignity and involvement of the community." The experts unanimously agreed that "there is a moral duty to also evaluate these interventions (for treatment or prevention) in the best possible clinical trials under the circumstances in order to definitively prove their safety and efficacy or provide evidence to stop their utilization."

Unsatisfied by simply offering this advice, the expert panel identified areas that require more detailed analysis and review, including:

- "Ethical ways to gather data while striving to provide optimal care under the prevailing circumstances;
- Ethical criteria to prioritize the use of unregistered experimental therapies and vaccines;
- Ethical criteria for achieving fair distribution in communities and among countries, in the face of a growing number of possible new interventions, none of which is likely to meet demand in the short term."³⁷

Therefore, the issues concerning research and access to the best available interventions that arose for HIV also remain for Ebola. In early September 2014, the International Bioethics Committee and the Intergovernmental Bioethics Committee of UNESCO issued a joint statement in support of WHO for emergency and ethical implementation of necessary measures. The major achievements gained through the North-South solidarity in the fight against HIV provide a roadmap; however, in the context of the West African Ebola epidemic, research must start anew in tackling considerable challenges. The main ones are: (1) the urgent context within which the research must occur, (2) weak health services and people's vulnerability, (3) problems surrounding communication with communities, and (4) sharing research costs and benefits.

1) Conducting research in an emergency context

In taking stock of their actions against Ebola in 2014, international institutions and non-governmental organizations (NGOs) such as

³⁰ - WHO, Ebola virus disease, No. 103, updated April 2015 <http://www.who.int/mediacentre/factsheets/fs103/en/>

³¹ - Interview with Eric Leroy. 27 March 2014 SciDev.Net Afrique Sub-Saharienne, "Ebola: Où en est la recherche?" <http://www.scidev.net/afrique-sub-saharienne/sante/actualites/ebola-o-en-est-la-recherche.html#>

³² - Sophie Arie. 6 August 2014. Ebola: an opportunity for a clinical trial? *BMJ* 2014;349:g4997. www.bmjjournals.org/content/349/bmj.g4997.

³³ - Mullard A. 2014. "Experimental Ebola drugs enter the limelight," *The Lancet* Vol 384 23 August 2014, [http://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(14\)61371-4/fulltext](http://www.thelancet.com/journals/lancet/article/PIIS0140-6736(14)61371-4/fulltext)

³⁵ - H. Chneiweiss, C. Longuet. 14 August 2014 "Use of unapproved treatments against Ebola: what are the ethical issues?" Inserm Press Room <http://presse.inserm.fr/en/use-of-unapproved-treatments-against-ebola-what-are-the-ethical-issues/14575/>

³⁶ - A S. Fauci. 2014. "Ebola, Underscoring the Global Disparities in Health Care Resources," *N Engl J Med* 371;12 nejm.org, 18 September 2014.

³⁷ - WHO. Ethical considerations for use of unregistered interventions for Ebola virus disease (EVD). Summary of the panel discussion. WHO statement. 12 August 2014 <http://www.who.int/mediacentre/news/statements/2014/ebola-ethical-review-summary/en/>

Médecins Sans Frontières (MSF) unanimously lamented “the inefficiency and delays of health care systems and humanitarian aid in their response to emergencies.”³⁸ On 8 August, WHO announced that the epidemic was “a public health emergency of international concern.” At the same time, the compassionate use of experimental treatments in the North, with no equivalent in the South, was covered in the media. At that point WHO convened research institutions, drug companies with vaccines and treatments that showed promising results in animal models, NGOs, donors and representatives from the affected countries, who decided to implement a variety of research projects through public-private partnerships (based on models used in studies of HIV treatments).

Beginning in the summer of 2014, the emergency was twofold: besides the imperative to stop the epidemic, advances also had to be made in vaccine and treatment research, which has virtually stood still for nearly 40 years. The challenge was to conduct a clinical study in a few months that would normally take several years. WHO, AVAREF (African Vaccine Regulatory Forum) and national regulatory agencies set up flexible decision-making procedures based on rapid data review, to expedite the roll-out of the various phases of clinical research without sacrificing the scientific and ethical criteria that protect research participants.

Three vaccine candidates showing positive results in preclinical phases were quickly proposed for phase I trials in healthy volunteers in various European, American, and African countries. Phases II and III were launched concurrently in the epidemic area in early 2015, in accordance with a consensus between regulators and governments in order to produce scientific information as quickly as possible. The three countries affected by the epidemic opted for innovative study plans: “ring vaccination” around cases of the disease and vaccinations for frontline workers in Guinea; staged vaccinations of frontline workers in Sierra Leone; and a conventional randomized trial design in Liberia (the end of the epidemic in Liberia required that this study be relocated to Guinea).

The search for new treatments was conducted with the same urgency. Clinical trials with the most advanced treatments had to be quickly constructed. ZMapp was not among the earliest clinical trials because its slow production did not allow for quick

availability of the quantities of treatment needed for a trial (trials were not started until spring 2015). Treatments that already had bio-safety data in humans were selected for the first treatment trials: brincidofovir, favipiravir, TKM-Ebola, and convalescent sera. Inserm sponsored the JIKI trial in Guinea to evaluate favipiravir, marketed in Japan for the treatment of influenza (in lower doses than in the JIKI trial).

A strategy debate with ethical implications ensued on selecting the studies: large randomized phase III studies, with a placebo control group (subjects only receiving supportive care)—these studies theoretically ensure the highest scientific quality of results—or small trials that could more quickly but only summarily evaluate the tolerance and efficacy of the experimental treatments, which would be given to everyone without a control group (phase IIb trials)?^{39 40 41} The debate was decided in the field: the ministers of health and MSF, which managed most of the Ebola treatment centers (ETCs), wanted all patients to have equal access to new interventions and ruled out randomization. The first clinical trials were begun in December 2014.

However, the treatment and vaccine trials began after the epidemic peaked in autumn 2014, and most will probably not reach the number of inclusions needed to fully determine the efficacy of the interventions studied.⁴² Preliminary results from the JIKI multi-centric favipiravir trial in Guinea have been available since February 2015.⁴³ Encouraging for patients in early stages, these results led to the treatment’s immediate availability in ETCs in Guinea. Research on new EVD diagnostic tests that are faster and easier to administer have also begun to bear fruit, with three new tests approved by WHO, which should enable more efficient monitoring and management of new outbreaks.

To better anticipate the next epidemic, two initiatives have been developed in the field of research on emerging infectious diseases: (1) REACTing (“REsearch and ACTion targeting emerging infectious diseases”), piloted by AVIESAN (the French Life Sciences and Healthcare Alliance), which includes Inserm and IRD, with the goal of being ready before an epidemic outbreak and quickly implementing the necessary interventions at the operational and research levels; and (2) GLOPID-R (Global Research Collaboration for Infectious Disease Preparedness), an

³⁸ - MSF, Pushed to the Limit and Beyond: A year into the largest ever Ebola outbreak, Report on 2014.

³⁹ - Decan Butler, Ebola drug trials set to begin amid crisis, 4 September 2014, Vol 513, *Nature*, 13

⁴⁰ - Steven Joffe, Evaluating Novel Therapies During the Ebola Epidemic, *JAMA* 1 October 2014 Vol 312, Number 13

⁴¹ - Erika Check Hayden, Ethical dilemma for Ebola trials, *Nature* 515, 177 (13 November 2014)

<http://www.nature.com/news/ethical-dilemma-for-ebola-drug-trials-1.16317>

⁴² - Erika Check Hayden, Ebola teaches tough lessons about rapid research, *Nature* 521, 405–406 (28 May 2015)

http://www.nature.com/news/ebola-teaches-tough-lessons-about-rapid-research-1.17623?WT.ec_id=NATURE-20150528

⁴³ - <http://www.inserm.fr/espace-journalistes/ebola-resultats-preliminaires-de-l-essai-jiki-pour-tester-l-efficacite-du-favipiravir> (site consulted 16 May 2015)

international network supported by the European Union, which brings together organizations that fund research in ten countries, including France, on the five continents. This initiative aims to facilitate a rapid and coordinated global response, through "preparedness," upstream of the outbreak of infectious disease epidemics.

On 11 May 2015, Dr Margaret Chan, Director-General of WHO, stated that: "The Ebola R&D effort has mobilized people, institutions and resources in ways never seen before. (...) We are likely very close to having a vaccine that can protect against Ebola. We have four rapid diagnostics to detect infection, and two of these are point-of-care. We have much more information about which therapeutic interventions may or may not work. (...) What we see emerging, over a very short time, is a new model for the accelerated development, testing, and approval of new medical products during emergencies caused by any emerging or re-emerging infectious disease."⁴⁴

2) Weak health services and vulnerability of populations

According to the latest United Nations Development Programme report, the three countries affected by Ebola are among the fifteen poorest countries on the planet. The adult literacy rates are 25% in Guinea, 43% in Sierra Leone, and 43% in Liberia.⁴⁵ State structures are fragile, and the healthcare system is precarious and virtually paralyzed by the Ebola epidemic. Health care and research materials, including infrastructure and equipment for ETCs and high-security laboratories, had to be imported. In this context, and given the lack of local experience in health research, research projects were primarily designed in the North and led in the field by experienced teams from the North who collaborated with improvised, inexperienced local teams created on site.

One specific aspect to highlight is the vulnerability of local health care workers when coping with the disease in a context of minimal health facilities. Over 5% of Ebola victims are caregivers, often women with precarious status (volunteers and trainees). Deficient equipment and poor protection practices in health structures, at least initially, were responsible for the spread of the epidemic among professionals,⁴⁶ which further weakened health services.⁴⁷ Medical care for local healthcare staff affected by EVD especially raises questions about

the circumstances for applying ethical regulations.⁴⁸

⁴⁹ Expats from Northern countries are repatriated into specialized facilities where they receive experimental treatments under compassionate use and the best care. They have about an 80% probability of survival. In the ETCs, symptomatic treatment for patients results in a 40% to 50% probability of survival. Realizing the problem, the United States, the United Kingdom and France opened treatment centers for affected health care workers in Liberia, Sierra Leone, and Guinea, respectively, where the probability of survival was increased.

People with EVD are extremely fragile. When they are admitted into the ETC, they are generally already very sick and exhausted. They suffer major psychological stress: they are shunned by their communities, have often already lost at least one family member, and are forced to enter into a center that holds all the Ebola patients, and where they are received and treated by anonymous workers wearing full protective equipment. Women are particularly vulnerable to the disease's psychosocial effects; their stigmatization is exacerbated by their pre-existing low social status that will not ensure any social recognition, especially if the death of a husband has left them as widows who must care for their children. Moreover, maintaining the mother-child relationship is difficult in the ETCs, if children are hospitalized or separated from their mothers. Terrifying rumors circulate in these centers, characterizing them as places to die, or even places where the sick are eliminated. In these circumstances, some patients refuse, at least initially, infusions and medicines, and sometimes even food. However, proper communication with local caregivers, families, and other patients generally leads to resuming the treatment plan.

In the case of participating in a treatment trial, conditions are not optimal for free and informed consent, even if the protocol is explained in the patient's language and the consent form has been signed in accordance with international ethical standards. In a context of an oral tradition, the document will be signed, sometimes with an "X", then photographed through various secure means depending on the center, and then destroyed according to strict bio-security rules in high-risk areas. In fact, as is true everywhere, the dialogue with and the confidence in the caregiver are the most important determining factors in a patient's

⁴⁴ - WHO, <http://www.who.int/dg/speeches/2015/ebola-research-remark/en/>

⁴⁵ - UNDP, Human Development Report 2014, <http://hdr.undp.org/en/data>

⁴⁶ - Delamou A, Beavogui AH, Kondé MK, van Griensven J, De Brouwere V. "Ebola: better protection needed for Guinean health-care workers." *The Lancet* 2015; 385: 503–04

⁴⁷ - Jacques D A Ndawinz, "Prevention of HIV spread during the Ebola outbreak in Guinea," *The Lancet* 2015; 385:1393

⁴⁸ - Miriam Shuchman, Sierra Leone doctors call for better Ebola care for colleagues. *The Lancet* , Vol 384 , Issue 9961, e67 [http://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(14\)62388-6/fulltext?rss=yes](http://www.thelancet.com/journals/lancet/article/PIIS0140-6736(14)62388-6/fulltext?rss=yes)

⁴⁹ - Yakubu A., The Ebola outbreak in Western Africa: ethical obligations for care, *J Med Ethics* 2014;0:1–2. doi:10.1136/medethics-2014-102434

decisions. This confidence is not easy to establish in a socio-political context where authoritarian public health interventions have reinforced the ubiquitous feeling among people in “fragile” States that health services have a greater interest in making a profit than maintaining public health.

The inclusion of groups that are universally considered to be vulnerable—pregnant women, children, and people unable to provide informed consent—is a sensitive issue. In most treatment trials, they would be excluded in principle on ethical grounds. The issue deserves in-depth discussion, given the extreme EVD case fatality rate. In order to not exclude potentially life-saving interventions, children are generally accepted in treatment trials. For similar reasons, people who are unable to give informed consent may also be included in the protocols, provided someone who may lawfully do so signs the informed consent for them (which is not always easy in practice). Opinion is divided for pregnant women (who have an EVD case fatality rate close to 100%!). In the end, either they were excluded from the main treatment trial, but could benefit from experimental treatments under compassionate use, or they were included in the protocol contingent on the results from an intermediary analysis of drug toxicity of those first enrolled. It will be necessary to re-assess these practices once the emergency context has subsided to determine if they are relevant in the case of EVD (or another disease with high lethality).

National health officials, MSF, and national caregivers were generally the spokespersons for patients and clinical trial participants. For example, they refused to conduct randomized trials with a control group without experimental treatment.⁵⁰ They also reaffirmed the need to prioritize care in the research imperatives.

Ebola survivors play an important role. Many have become indispensable in prevention and care, despite the trauma they have experienced and continue to endure. Their words are important, both to reassure patients that they know what they are going through and to inform health care professionals who can improve their practices. Their physical and mental health are the subject of observational cohorts (such as the Inserm-IRD cohort in Guinea),⁵¹ designed to better understand the sequelae left by the infection (more and more frequently reported), to better prevent and treat

them. Associations of Ebola survivors are forming in the different countries to provide a meeting space to share experiences and promote “self-support”; to ensure that the needs of those who are infected, convalescing or cured are recognized; and to contribute, individually or collectively, to the response to the epidemic, particularly through social mobilization. These associations could follow the example set by associations of people living with HIV and play a greater role in selecting future research projects, especially since doctors and other health professionals, who themselves are EVD convalescents or survivors, are among their active members.

3) Problems surrounding communication with communities

“Experiences from the AIDS response have shown us that, even in the early days of the emergency public health response, the individual must be at the centre. The dignity and rights of individuals, families and communities are non-negotiable. Extraordinary measures will be required to stop the Ebola outbreak and community engagement is critical to addressing the cultural misunderstandings that clash with bio-medical efforts to treat people and prevent further infections.”⁵² This statement was made by UNAIDS, which contributes to the United Nations efforts to fight Ebola (via UNMEER—UN, Mission for Ebola Emergency Response), on 8 December 2014. However, despite experience gained during the HIV pandemic and earlier Ebola outbreaks that encourages “working with the community and not against it,”⁵³ communication with people affected by Ebola has been difficult since the start of the epidemic, and one year later, lack of trust persists, especially in remote or hard-to-reach areas.

Mistakes were made, such as the authoritarian quarantine of families, groups or even entire neighborhoods. Abrupt messages were delivered like “bush meat is unfit for consumption,” while in rural settings it has always been an important protein source. Many rumors were circulating (and still circulate in some places), such as the collusion between caregivers and governing parties to eliminate patients.

Actions were also taken to strengthen relationships with communities (based on models drawn from the fight against AIDS): in addition to massive campaigns through posters and television and radio

⁵⁰ - WHO, Ethical issues related to study design for trials on therapeutics for Ebola Virus Disease
http://apps.who.int/iris/bitstream/10665/137509/1/WHO_HIS_KER_GHE_14_2_eng.pdf

⁵¹ - POSTEBOGUI, (Re)Vivre après Ebola : Evaluation et accompagnement des patients déclarés guéris d'une infection par le virus Ebola en Guinée, INSERM

⁵² - UNAIDS, HIV and Ebola: Securing Health for the Future, 8 December 2014.

http://www.unaids.org/sites/default/files/media_asset/20141208_Ebola_CRP4_35PCB.pdf

⁵³ - CORDS/SACIDS, Enseignements tirés des derniers épisodes épidémiques d’Ebola pour guider la gestion des risques actuels, Summary of the meeting on 1–2 September 2014. www.cordsnetwork.org/files/report...in.../report-ebola-meeting_french/

spots (involving community radio stations), the work with faith-based organizations stands out, having enabled the widespread practice of safe and dignified burials, carried out by the National Red Cross and Red Crescent Societies. Survivors also play an important role among their peers. Communities' fears of the ETCs prompted health professionals to stand before them with ETC "open-door days" (before they were put into operation). Areas were set up in these areas so that families could communicate with patients.

The impact of these actions on the creation of social trust must still be assessed, in relation to the social interpretations of risk and interpretations of scientific knowledge, which may subsequently be updated, such as the risk of virus transmission through sperm. An active sociological and anthropological study is underway to clarify all the social, economic, political, and cultural dimensions of the epidemic and response. In September 2014, anthropologists working in West Africa created the Ebola SSH Network (West African Social Sciences and Humanities Network on Ebola), which brings together members working in ten countries, under the coordination of IRD, with support from ANRS and IMMI (Institut de Microbiologie et de Maladies Infectieuses).⁵⁴ The Ebola SSH Network organized the first social sciences conference on the Ebola epidemic in West Africa (EBODAKAR 2015, Dakar, 19–21 May 2015)⁵⁵ to share analyses in anthropology and the social sciences on the epidemic over the last year. A group of anthropologists also published recommendations on vaccination and treatment research on an Internet platform, the Ebola Response Anthropology Platform, aimed at government and humanitarian actors in the local response to Ebola.⁵⁶

WHO convened a meeting, including representatives from several governments and the pharmaceutical industry, on 23 October 2014 to examine the many issues concerning ultimate access to the experimental vaccines for Ebola virus disease. Participants concluded that community participation and social mobilization were necessary to prepare people to understand and accept the clinical trials and vaccination campaigns.⁵⁷ Health professionals were the first to be enrolled in the vaccination trials, begun in early 2015.

The anthropological aspects of some treatment research, such as the JIKI favipiravir study, were

also discussed among multi-disciplinary research teams. Community officials were approached to discuss the project before its implementation. But rumors and conspiracy theories about the treatment centers also affect the treatment trials. They are difficult to analyze and refute, given that the uncertainty of the efficacy of the interventions (inherent to research) cannot be explained away, and that the relationship to the treatment plan is not always clearly understood.

4) Sharing research costs and benefits

Given the Ebola virus' epidemic characteristics, there was little investment in research to fight EVD before 2014. After declaring the Ebola epidemic in West Africa a public health emergency of international concern in August 2014, WHO held several meetings on vaccines and experimental treatments. During a meeting on 23 October 2014 bringing together ministers from many countries, NGOs, major donors, academic researchers and the health industry, it was concluded that the affected countries and the manufacturers could not cover the needs alone. A proposal was made to establish a "club" of donors.⁵⁸ Hence, research costs were shared: the manufacturers provided their available experimental vaccines and treatments, and the implementation of clinical research protocols would be funded by public and private institutions, such as Inserm, the National Health Service (NHS), the National Institutes of Health (NIH/NIAID), the Wellcome Trust, the Bill and Melinda Gates Foundation, and the European Commission.

Making research results available to people will require a considerable international commitment, presumably using proven mechanisms implemented by the Global Fund to Fight AIDS, Tuberculosis, and Malaria, but also by Gavi, the Vaccine Alliance that is financed by many governments and private organizations. On 11 December 2014, Gavi announced that its board of directors approved the purchase of vaccines that would be administered to at-risk populations in the affected countries and would allocate aid to rebuild the health and immunization systems, once a safe and effective vaccine is recommended by WHO.⁵⁹ This mechanism for advanced commitment on the markets should create a favorable environment for the creation and sustainable production of sufficient buffer stock of vaccines that can be mobilized quickly.

⁵⁴ - Réseau Ouest-africain de Sciences Humaines et Sociales sur Ebola, <http://shsebola.hypotheses.org/>

⁵⁵ - EBODAKAR 2015, <http://ebodakar2015.sciencesconf.org/>

⁵⁶ - http://www.ebola-anthropology.net/key_messages/emergency-ebola-anthropology-network-advisory-brief-culture-and-clinical-trials/

⁵⁷ - WHO, WHO High-level meeting on Ebola vaccines access and financing <http://www.who.int/mediacentre/news/ebola/23-october-2014/en/>

⁵⁸ - Ibid.

⁵⁹ - Gavi, <http://www.gavi.org/Library/News/Press-releases/2014/Gavi-commits-to-purchasing-Ebola-vaccine-for-affected-countries/>

In terms of treatment, following the announcement of the interim results of the (relative) efficacy of favipiravir for patients in an early stage of EVD in February 2015, the President of the Republic of Guinea wanted to see it provided for free to all patients in Guinea, as with any other care in an Ebola treatment center. In all likelihood, this will be true for all Ebola therapies, even if we do not know in advance how efforts will be divided between manufacturers and international public (and even private) institutions.

During a forum entitled, "Forum on the African voice and leadership to accelerate the evaluation of potential Ebola therapies and vaccines in West Africa," held in Dakar in January 2015 and attended by the ministers of health from the five Ebola affected countries in West Africa, it was recommended to develop the infrastructure and human resources for research and local production of therapies, such as immunoglobulins obtained through the fractionation of plasma.⁶⁰ In the future "post-Ebola" context, many international partners believe that beyond the provision of specific interventions for Ebola, the health systems in the affected countries must be strengthened.

Recommendations

These recommendations are for researchers, research institutions, and research donors in the global South. International ethics principles and best practices in force for clinical research provide the foundation for designing research projects, in compliance with the laws of the countries where research activities will take place. For more detailed recommendations, it is worthwhile to refer to the following documents from ANRS and IRD, which have extensive experience in health research in the global South: the ANRS "Code of Ethics for Research in Developing Countries" and the "Guide for Best Practices in Research for Development" and "Partnership ethics in scientific research at IRD" from the IRD Consultative Committee for Deontology and Ethics (CCDE).

This joint paper from the Inserm Ethics Committee and the IRD CCDE on health research in the global South includes recommendations that go beyond reaffirming the principles ensuring people are protected and respected and highlight the ethical need to co-design research projects and share their benefits with research actors and communities in the global South. Ethics also include advocating for greater international solidarity towards the disadvantaged populations in the North and the South who have links to the research. Without being

specific to research on Ebola virus disease, these recommendations have clearly been inspired by the experience of the EVD outbreak, characterized by: (1) a context where public trust had not been obtained and had to be created, by focusing all attention on what is acceptable (or not) for patients, (2) interventions in an emergency context that may always favor relegating ethics to the background, and (3) failing health systems, especially since being affected by EVD.

Our recommendations are to:

1) Encourage research projects on priority issues specific to the global South

Considerable attention, justifiably so, has been focused on research on HIV, tuberculosis, and malaria. But the current Ebola outbreak reminds us that other diseases affect people in the poorest countries and that knowledge gaps about diseases with pandemic potential must be filled. WHO coordinates a Special Program for Research and Training (WHO TDR Program) on diseases of poverty. Drugs for Neglected Diseases initiative (DNDi) is a collaborative, non-profit organization that is developing treatments for neglected diseases. Foundation for Innovative New Diagnostics (FIND) works to develop better diagnostic tests for poverty-related diseases. However, more must be done. Research institutions and donors should encourage research projects on the issues faced by people in the South, such as neglected tropical infections and mounting public health problems in Southern countries for which the specific characteristics are poorly understood, such as chronic non-infectious diseases. Zoonotic diseases with epidemic potential can have a major impact on global public health (including the Ebola virus and other viruses that cause hemorrhagic fevers; coronaviruses such as SARS-CoV and MERS-CoV; and new influenza viruses such as H5N1 virus). These diseases should be prioritized in training programs and by research evaluation bodies (priority funding mechanisms for these projects and career-level recognition and support for researchers involved in these topics). In the event of a public health emergency, faster approval mechanisms for funding should allow for rapid implementation of research platforms, across all disciplines (biomedical sciences, social sciences, and humanities).

⁶⁰ - Forum sur la voix et le leadership africains pour accélérer l'évaluation des traitements et des vaccins potentiels du virus

Ebola en Afrique de l'Ouest - Déclaration et engagements des partenaires, 3 p.

2) Encourage the multi-disciplinary approach for research projects in the South

The HIV pandemic and Ebola epidemics have shown the complexity of interventions and research in diverse cultural, economic, social, and political environments whose reference points are sometimes far from those of transnational medical research. It is now recognized that cultural values and systems have far-reaching effects on people's health. Therefore, understanding the structural and cultural determinants of behaviors influencing health is crucial⁶¹. Without this understanding, the success of the research and biomedical interventions remains uncertain. Thus, multidisciplinarity and the interactions between biomedical research and the social sciences and humanities must be promoted and put to greater use, starting with the design-stage of a clinical trial. Moreover, a social sciences and public health component should be systematically added to clinical trials and studies and covered in the budget. Research in public health, health policy and health economics is also important for understanding the capacities for transforming health systems in the South and facilitating their evolution toward efficacy and equity.

3) Collaborating with complete reciprocity between North and South researchers

North-South collaboration is a necessity because researchers from the South are better at understanding the local issues and cultural, social, economic, and political contexts in which the research is conducted and because the purpose of the research is their health and that of their community. Therefore, researchers from the North and the South, co-principal investigators, or co-investigators on joint teams can each contribute their expertise and learn from each other in partnerships based on mutual interest. Researchers from the North have the ethical duty to strengthen the capacities of young researchers from the global South through training (if possible, by facilitating access to degree programs) and the capacities of teams by updating local research infrastructure. Also, no efforts should be made to routinely seek to provide stability or to attract elites trained in the South to the North, but rather, to help them return to

their countries to settle in so they may launch studies locally through the support mechanisms of scientific partnerships, such as those proposed by IRD to support young research teams.

Conversely, researchers from the South must help train researchers from the North who invest themselves in research in the global South, particularly on socio-cultural dimensions, for more functional and equitable collaborations. Sharing research outcomes equitably between partners, whether it is a database, publications, or other possible outputs, is particularly important. The principle of co-ownership—or joint ownership—of data between the various investigators should be promoted and made explicit in research agreements.

In health research, it is also imperative to set up partnerships with other actors and decision makers from the South, such as health officials, community leaders, and patient associations and ethics organizations, to improve the acceptability, design, and implementation of research.

4) Pay greater attention to gender issues in research in the South

Gender inequalities that structure societies both in the South and the North have multiple implications on research on several levels. Even though EVD infection rates do not appear higher in women than in men, unlike HIV infection, more detailed epidemiological analysis is needed to understand the exposure differences and factors related to gender. Therapeutic trials, as with other studies, should produce data disaggregated by sex to understand these differences, and any research conducted in the South should include a component that specifically considers gender. Moreover, it is not ethically acceptable to simply exclude pregnant women from clinical trials. Specific studies should investigate the extremely high lethality of Ebola virus disease for pregnant women and should also strive to propose treatments for them. Ensuring men and women have equal access to research careers must also be promoted, both in the South and the North. Although the principle of parity in ethics committees has been recognized by all, in practice, the participation of female researchers and women in general, especially from local communities, in the decisions of these committees, needs to be increased in many countries.

⁶¹ - Moulin A.-M. (ed) 2015. Autour du virus Ebola.
Anthropologie & Santé, n°11,
<http://anthropologiesante.revues.org/1884>

5) Broaden reflection on the benefits for the participants and communities who are co-producers of the knowledge

Research cannot always provide direct benefits to its participants. Nevertheless, it is desirable to unite medical ethics with research ethics by considering participants' medical needs that still need to be covered and, if possible, to propose responses to these needs (such as access to a health intervention outside of the research), as recommended in the Declaration of Helsinki, especially when health systems are unable to provide these responses. In the event when such care would disrupt the research methodology or results, a system should be set up so that a care package complements provisions in the research. It does not seem ethical to leave participants of therapeutic trials without care because of shortcomings in the national health system; research ethics do not contradict medical ethics, which dictate an obligation to provide care, by defining standards for this purpose. Equity in participants' access to research and care, including exposure to research-related risks, is also an important aspect that must be routinely made explicit in the draft protocol, as well as researchers' plans to promote such equity. For clinical research, it is also necessary to specify what provisions will ensure the continuity of care for participants after the research stage (the end of the study or when the individual leaves the study), especially when the research identifies new diagnoses or more effective treatments (see lessons learned during research on antiretroviral therapies). Solutions must be anticipated and effectively implemented in collaboration with local health services and government health officials.

For several decades, it has been acknowledged that research in the global South should benefit people in the South, and, therefore, research projects must specify the short-, medium-, and long-term benefits for the study population, while complying with the general interest and health strategy of the relevant countries that the research proposals must explicitly take into account. These aspects can be defined or adjusted with representatives of participants from the populations involved, through an approach that carefully considers local demands within the partnership framework. This simultaneously enables defining fairer interventions and instilling or building trust, an important aspect when it is not straightforward, as seen in the context of the Ebola outbreak. Study participants devote their time and entrust research teams with personal knowledge and information. Thus, they must be seen as co-producers of the research findings. Careful attention

must be given to fair reimbursement of any costs incurred through participation in a research project, including the "loss of earnings" from time devoted to the project, which can be high for poor and precarious populations. We must also anticipate the possible consequences for participants when information is shared, beyond the need to maintain confidentiality and protect personal data in compliance with international standards and national regulations.

Mechanisms for sharing results and, when necessary, promoting new practices in relationships with partners, including community-based organizations and health officials, must be set up so that the research fully assumes its role in driving the development of health. In addition to research, donors should discuss strengthening local health structures so they can apply research outcomes.

6) Maintain a high level of ethical standards, even in emergency and limited-resource situations

The randomized, placebo-controlled study has been accepted as having the highest scientific level in clinical research, but it may pose an ethical problem in the case of a disease with high and rapid lethality like Ebola virus disease. Even if the efficacy and toxicity of an experimental treatment is unknown, the best (or the presumed best) treatment must be provided to all participants. For example, a randomized clinical trial comparing two promising experimental treatments is preferred, or even a non-randomized study in which the intervention is provided to all and compared to the expected results based on a cohort established before the intervention study began (even with the existence of bias). On another topic, at a time when effective therapies are available, observational research on hepatitis B and C without direct benefits for people participating in the research seems not anymore ethically acceptable to us, even—and especially—in the case of North-South asymmetry in accessing good medical care for these types of hepatitis. Approving health interventions that have already been approved in the North is also problematic. An emergency situation such as the Ebola epidemic, where standards for care can be applied differently in the field, depending on the actors and situations that are "under duress" (attendance peaks and wide variations in equipment at treatment sites), should not justify lowering requirements for research ethics. Local adaptation of research ethics in terms of practical standards must take into account participants' perceptions of what is and is not acceptable. Protocols must consider systems

whereby participants or their representatives can evaluate the ethics of research projects, with a constructive and collaborative objective.

Simultaneous submission to an ethics committee in the North, where the study promoter is based, and to one in the South, where the study will take place, can guarantee the project's ethical quality, in principle. This is recommended in the Declaration of Helsinki, although the only mandatory step is the submission to the ethics committee of the country where the study will be conducted. Preliminary evaluation procedures in protocols should, in an emergency context, allow for obtaining an ethical opinion quickly. We should examine the ways that field application is assessed, ethics provisions are defined in the protocols, and how these provisions are adapted to local situations. Methodological proposals still need to be consolidated for these evaluations, which should garner suggestions from research subjects using a participatory model.

7) Implement mechanisms for rapid sharing of scientific information during public health emergencies

Research results in biomedical sciences, social sciences, and the humanities must be shared as quickly as possible when they may yield interventions that positively influence the handling of a public health emergency. This ethical issue requires setting up mechanisms that ensure sharing does not impede researchers who must publish in scientific journals. Therefore, new mutual ethical and editorial standards, including the lowering or exemption of fees for "fast track" publications, should be discussed and adopted by the scientific editors, on a global scale, so that advances in research can benefit people as quickly as possible.

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