

# The Forgotten Plague: Psychiatric Manifestations of Ebola, Zika, and Emerging Infectious Diseases

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## Abstract

The media and public health generally focus on the biological and physical ramifications of epidemics. Mental health issues that coincide with emerging diseases and epidemics are rarely examined and sometimes, even eschewed due to cultural considerations. Psychiatric manifestations of various infectious diseases, especially with a focus on Ebola Virus disease (EVD) and Zika Virus, are discussed in this commentary to illustrate the continued need of care after the resolution of the actual illness. Various infectious diseases have associations with mental illness, such as an increased risk of obsessive-compulsive disorders and Tourette syndrome in children with Group B streptococcal infection. Current EVD literature does not demonstrate a strong association of mental illness symptoms or diseases but there is a necessity of care that extends beyond the illness. Patients and their families experience depression, anxiety, trauma, suicidal ideation, panic and other manifestations. Zika virus has been associated neuronal injury, genetic alteration that affects fetal development and detrimental maternal mental health symptoms are being documented. While funding calls from the international community are present, there are no specific epidemiological data or fiscal estimates solely for mental health during or after infectious diseases epidemics or disasters that support health care providers and strengthen policies and procedures for responding to such situations. Therefore, those on the frontlines of epidemics including emergency physicians, primary care providers and infectious disease specialists should serve communicate this need and advocate for sustained and increased funding for mental health programs to heighten public awareness regarding acute psychiatric events during infectious diseases outbreaks and offer treatment and support when necessary.

**Keywords:** Ebola, emerging disease, psychiatry, Zika

## INTRODUCTION

“We can look forward with confidence to a considerable degree of freedom from infectious diseases at a time not too far in the future. Indeed ... it seems reasonable to anticipate that within some measurable time ... all the major infections will have disappeared.” - The Evolution and Eradication of Infectious Diseases.<sup>[1]</sup>

From the HIV/AIDS epidemic that captivated world attention in the 1980s and 1990s to the severe acute respiratory syndrome in 2002 and 2003 to the H1N1 influenza pandemic of 2009 to the Ebola virus outbreak in 2013 and the Zika virus outbreak in 2016,<sup>[2]</sup> few assertions in medicine have been so thoroughly disproven by only the passage of time. By the nature of their training and focus, scientists and the media tend to focus exclusively on the biological effects of such infectious diseases

and rarely stop to examine the psychic havoc these epidemics leave in their wake. We will present an overview of the status of mental health in the context of epidemics and discuss the primary and secondary psychiatric conditions of emerging epidemics, including fiscal perspectives of the minimal resources for mental health issues in epidemics. Both of these points illustrate the hidden plight of mental health crises during epidemics and highlight crucial components of the need for comprehensive medical and mental health evaluations by physicians in an emergency setting.

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From 2013 to 2016, the West African Ebola virus disease (EVD) epidemic galvanized physical, human, and financial resources to sequester mortality and morbidity, but long-term morbidity, especially the mental health of afflicted families, individuals, and social networks, persists. Although the immediate biological threat of EVD may be currently mitigated, increases in acute sequelae (e.g., increases in family or survivor mental health disparities and reductions in mental health services) cause long-term impacts that are potentially outside traditional biological and fiscal paradigms of epidemic response.

## GENERAL OVERVIEW OF NEUROPSYCHIATRIC MANIFESTATIONS OF INFECTIOUS DISEASES

Sporadic infectious diseases have associations with various neuropsychiatric disorders. For instance, Borna virus, found globally among several warm-blooded hosts, has some human associations with neuropsychiatric disease.<sup>[3,4]</sup> In fact, certain bacterial agents have been shown to increase the risk of mental illness as well. Risk of obsessive-compulsive disorders and Tourette syndrome may be elevated in children with Group B streptococcal infection.<sup>[5]</sup> This is known as pediatric autoimmune neuropsychiatric disorders associated with streptococcal infections. Pediatric psychiatric illnesses show an increased predominance with human B-cell antigen D8/17, the marker for elevated risk of poststreptococcal rheumatic heart disease.<sup>[4,5]</sup> Lyme disease, by *Borrelia* species through ticks, can be associated with verbal and memory loss and confusion.<sup>[4,6]</sup> Depression, dementia, and psychosis, and other postinfection psychiatric symptoms are reported in most parasitic infections, including leptospirosis.<sup>[4,7]</sup> And finally, neurocysticercosis can be linked with seizures and epilepsy.<sup>[4]</sup> These psychiatric manifestations of well-known infections demonstrate the importance of evaluating beyond the medical component. However, even without direct damage to neurons or cerebral tissue by bacteria, viruses, rickettsiae, or prions themselves, infectious diseases can have profound impact on the human psyche. This impact extends not only to the afflicted but also to health-care workers and family members who have taken care of them.

## EBOLA VIRUS DISEASE AND MENTAL HEALTH

EVD has been the focus of a large volume of research and its various manifestations have been documented. EVD is a *Filoviridae* that causes a deadly hemorrhagic fever; the most recent outbreak had a case fatality rate of 70%.<sup>[8]</sup> Zoonotic transmission begins when a human comes in contact with the bodily fluids of an infected animal. Human transmission starts when a new host comes in contact with body fluids of a patient with active symptoms or who has died from EVD.<sup>[8]</sup> Symptoms include the following: abrupt onset of fever, chills, low-grade fever, malaise, diffuse erythematous, nonpruritic maculopapular rash developing 5–7 days postinfection, gastrointestinal, hemorrhagic, neurological, ocular, and other nonspecific symptoms.<sup>[8]</sup> As of June 2016, the last

transmission of EVD from 2013 to 2016 West Africa epidemic occurred 42 days prior, which is equal to two cycles of the viral incubation period.<sup>[9]</sup> Over the course of the epidemic, health professionals reported that mental health services were overwhelmed due to loss of life, grief, and extreme anxiety experienced by patients, family members, and health-care professionals.<sup>[10]</sup>

According to the available literature, there are no diagnostic psychological features of EVD. However, there are reports of sequelae during and in the postinfectious period that are critical for patient management. A study of survivors during the 1995 Ebola epidemic in Kikwit, Democratic Republic of Congo, reported initial feelings of fear, denial, and shame.<sup>[11]</sup> Their most traumatic experiences were watching others die in isolation wards and reluctance of medical providers to provide care.<sup>[11]</sup> A 2014 study regarding the evaluation of psychological distress and social support of Nigerian patients infected by EVD found that survivors experienced inability to concentrate, lack of sleep, unhappiness, or depression.<sup>[12]</sup> Furthermore, the study stated that “...development of psychological distress could be predicted by loss of family member...”<sup>[12]</sup> News reports state that patients blame themselves and cannot move out of bed.<sup>[10]</sup>

Epidemic outbreaks, such as EVD, create multiple, seemingly insurmountable challenges in restoring health between the onset of an infection and recovery. The long-term internal anguish suffered by members of families of those who succumbed to the disease demonstrate a mental “iceberg effect.” According to the WHO, there are 28,610 confirmed, probable, and suspected cases of EVD.<sup>[13]</sup> EVD can cause vulnerabilities, social stigma, distress, and isolation at an individual level. Individuals can experience fear, anxiousness, numbness, and detachment.<sup>[14]</sup> While on a macro level, whole communities may experience fear, isolation, and suffering during or after an infectious disease epidemic.<sup>[14]</sup> This was seen during the 2009–2010 H1N1 influenza pandemic where individuals in the US experienced confusion, anxiety, and increased risky behaviors (e.g., smoking, drinking, drug misuse, recklessness, and unsafe work practices) as a result of the uncertainties. Communities and businesses were concerned about the availability of medications, workforce shortages, and mitigation strategies.<sup>[15]</sup> Responders and public health professionals, such as the patients they care for and their families, experience some of these same mental health issues as well.

In fact, health-care workers are just as equally affected by the mental health repercussions of the epidemic as they care for patients with EVD; a significant percentage will experience posttraumatic stress disorder.<sup>[16]</sup> Psychosocial implications include confusion, anger, and serious stigma from communities against patients and health-care workers returning home.<sup>[17]</sup> Contention exists between communities and health officials over policies that try to reduce transmission by alternating long-standing cultural burial practices.<sup>[10]</sup>

The WHO and other emergency relief partners have joined together to address mental health during this EVD epidemic and in other humanitarian assistance events. These partners have developed operational guidance publications for humanitarian actors by the WHO, employment programs in nongovernmental organization (e.g., debriefing sessions), and Mental Health Sphere Handbook Standards (assuring a minimum health standard) as well as other humanitarian standards.<sup>[14]</sup> To provide psychological care for patients and their families, proactive guidelines should be implemented. While specific recommendations are beyond the scope of this piece, components suggested by the Inter-Agency Standing Committee (IASC) guidelines on mental health are worth noting and consist of a four-tiered intervention pyramid approach:<sup>[18]</sup>

1. Restoring the affected population's basic services and security
2. Strengthening family and community networks
3. Providing psychosocial support to distressed individuals (e.g., during the acute stage of the illness, during laboratory testing periods, and before discharge)
4. Providing specialized mental health intervention for severely affected survivors (based on the clinical training and mental health guidelines in emergency response efforts).

## ZIKA VIRUS AND MENTAL HEALTH

The latest emerging plague, Zika, has less research that explores its natural clinical progression. Investigations to delineate this are underway, including new diagnostic tools and therapeutics.<sup>[19]</sup> The novel nature of this virus causes "... neurologic complications; these include congenital microcephaly (in addition to other developmental problems among babies born to women infected during pregnancy), Guillain-Barré syndrome, myelitis, and meningoencephalitis...."<sup>[20]</sup>

Major signs and symptoms for a suspected case include the following: "...acute onset of low-grade fever (37.8°C–38.5°C), maculopapular pruritic rash, arthralgia (notably the small joints of hands and feet), and conjunctivitis (nonpurulent)...."<sup>[20]</sup> This arbovirus (a type of flavivirus) is incredibly important for emergency department (ED) health-care teams to diagnose and manage. In 2016, the US Food and Drug Administration had requested that all blood establishments in Miami-Dade County cease blood collection immediately.<sup>[21,22]</sup> Probable cases include positive immunoglobulin M (IgM) titers and an epidemiological link for transmission. Confirmation is performed through RNA, serum antigen, or IgM antibody tests.<sup>[23]</sup> However, there are currently no psychological signs or symptom that can be used for screening purposes. Psychological issues are usually secondary to the disease, similar to EVD.

Evidence is pointing to how the virus infects neuronal cells, causing the neurological complications. Researchers

point to the need for longitudinal cohorts of newborns in epidemic areas that evaluate neurodevelopment milestones. This allows for the assessment of the virus's impact on "... neuronal migration, organization, and myelination.(that could lead to)... major (e.g., lissencephaly and schizencephaly) and minor (e.g., focal dysplasias) brain malformations, and "functional" neuropsychiatric syndromes including intellectual impairment and autism...."<sup>[24,25]</sup> Autism spectrum conditions can lead to secondary psychological sequela, such as depression and anxiety.<sup>[26]</sup> Various viral and immunology researchers have commented on how pathogens, such as Zika, could play a contributory role in the development of a variety of psychiatric diseases. This is in the event of milder central nervous system infections causing psychiatric issues, such as autism, bipolar disorder, schizophrenia, attention deficit and hyperactivity disorder, and epilepsy.<sup>[27]</sup> These effects may be dependent on the features of the virus and the trimester the infection occurred.<sup>[27]</sup> It is unlikely that we will understand the true extent of the neuropsychiatric manifestations of Zika for quite some time.

In addition to the potential neuropsychiatric effects of Zika on the fetus, there is also the stress and guilt that the mothers may carry, especially those that live in nonendemic regions who were infected while traveling to endemic areas and who passed the infection on to their fetus. Even in endemic areas, mothers with microcephalic children in Brazil have reported instances of people staring, receiving unsolicited health advice, seeing other parents pull their children away due to fear of infection, and even being refused entry to public transportation due to their "demon babies." In addition, women are being abandoned by the fathers of affected children.<sup>[28]</sup> In 2016, pregnant women in both Brazil and Puerto Rico showed high levels of stress, anxiety, and depression in both those infected with Zika and those who had not been.<sup>[29,30]</sup>

## FISCAL PERSPECTIVES

The WHO, along with other international organizations, has articulated the great need to sustain mental health services and funding, supported by general epidemiological data and fiscal need estimates. There are no specific epidemiological data or fiscal estimates solely for mental health during or after infectious diseases epidemics or disasters at the time of this report.<sup>[31]</sup> General mortality rates are available, and general comparisons serve as the best illustration. The effects of mental health issues are far more pervasive when compared to traditional epidemic infectious disease epidemiology, such as EVD and Zika. Over 800,000 people die from suicide per year globally, which is over 66,000 people/month, according to the latest data from the WHO regarding suicide prevention.<sup>[32]</sup> This figure is almost three times greater than the overall EVD epidemic mortality.

Available data estimating mental health burden during an outbreak as a cause of epidemics have been reported in several studies. First, suicides related to EVD are most likely

underreported, potentially due to societal factors or stigmas and medical record data reporting system weaknesses in countries plagued by EVD. Studies may be limited due to epidemiological and pathology factors of EVD (e.g., high mortality rate, disease onset, incidence rate, etc.). One notable study is from 1995, where 60 survivors from an EVD outbreak in Kikwit were interviewed and risk factors for social isolation were illustrated as a result, which increased the risk of suicide and other mental health conditions.<sup>[11]</sup> During convalescence, approximately one-third of participants reported feeling rejected by their social support networks (family, friends, and neighbors); approximately one-half had no income; and two out of five participants felt grief for family members who did not survive the disease. All participants reported strengthened relationships with religion due to surviving EVD. Interestingly, according to the CDC, risk factors for suicide include local epidemics of suicide, isolation, loss, physical illness, and barriers to accessing mental health treatment; protective factors include family and community support and religious beliefs that discourage suicide.<sup>[33]</sup> These emergency mental health needs call for the fiscal support for the use of social workers, community leaders, community health workers, and religious partners (e.g., hospital pastoral care professionals) as culturally appropriate case management resources to combat the tide of mental illness for a convalescing country through building in-country community resilience.

There is a continued need to expand health-care spending in the US and globally, not only on future infectious disease epidemics but also on the overlooked epidemic of mental health illness arising from these epidemics. In many cases, these two categories of disease and diseases within these categories are competing against each other for fiscal funding. The WHO places mental health in its noncommunicable disease category, and spending diverted to infectious diseases by the WHO weakens its already underfunded mental health programs.<sup>[34,35]</sup> While there are additional health system strengthening and development avenues to improve mental health in areas after an epidemic, funding is insufficient. Collecting data is critical to making evidence-based funding and programmatic decision-making. Epidemiological data should be obtained to describe mental health issues that arise concomitantly with any epidemic and monitor the impact of mental health programs. New global health-care workforce with the training to address mental health issues during or after an epidemic has no new resources.<sup>[35]</sup> Thus, vital mental health services cannot be conducted without major sustainable resources committed by the global community in addition to its integration in epidemic response protocols.

## DISCUSSION

Correctly diagnosing, treating, and managing these patients with emerging infectious diseases are critical for the ED teams. Emergency psychiatric events can be a key indication for hospital admission, leading to a potential categorical DSM-V diagnosis of a mental illness due to another medical

condition.<sup>[36]</sup> Therefore, if there are any psychiatric signs or symptoms in the medical history and physical that can begin to suggest an emerging infectious disease, this could increase the suspicion of a practitioner's overall diagnosis and lead to better treatment outcomes of the whole patient. For instance, a person presenting to the ED with signs and symptoms of Zika or Ebola virus should be asked about social support, family ties, any recent deaths, especially due the virus, and the patient's recent mood. These questions would help screen for psychiatric emergencies such as suicidal ideation with intent and plan, which would be another strong indication for admission. Further neuropsychiatric and clinical research, psychiatric screening could be used alongside other modalities (e.g., laboratory tests and imaging) as a screening tool in ED's. In addition, physicians can mitigate detrimental impact upon families and networks of the patient.

Physicians and health-care teams are not waiting for the research to guide policy in response to these diseases. Given that there is a dearth of academic literature directly regarding mental health and epidemics, mental health issue during epidemics is a practical subtopic within disaster psychiatry and is a critical component of disaster management plans and operations. This is seen in event debriefing and psychological first aid publications from the WHO, such as the Ebola Psychological First Aid for health professionals (physicians) and community health members.<sup>[14]</sup> According to the WHO, an epidemic or pandemic is a public health emergency. It is not a function of risk of mortality or morbidity but actual crude mortality rate when it reaches 1 per 10,000 per day or when the under-five mortality rate reaches 2 per 10,000 per day.<sup>[37]</sup> Thus, short-term relief and emergency humanitarian assistance are undertaken to alleviate these calamities, such as the EVD epidemic.<sup>[37]</sup> Recently, the WHO and other key stakeholders have generated general clinical guidelines and programmatic guidelines for mental health operations in humanitarian situations. This is reflected in the mhGAP Humanitarian Intervention Guide and consists of the following: "...brief modules (regarding) the assessment and management of acute stress, grief, moderate-severe depressive disorder, posttraumatic stress disorder, psychosis, epilepsy/seizures, intellectual disability, harmful use of alcohol and drugs, suicide, and other significant mental health complaints..."<sup>[38]</sup> Programmatic guidance and other critical documentation is also available and has been noted in other sections.<sup>[39]</sup>

Physicians, particularly those in emergency medicine and emergency psychiatry, have an opportunity to continue to serve as vocal public advocates for patients' health-care needs, in addition to being international first responders. Physicians should play a long-term central role in implementing recently published recommendations, including the IASC guidelines on mental health.<sup>[18]</sup> Mr. Thomas Kurmann, Director of Development for the United States branch of Doctors without Borders/Médecins Sans Frontières, stated that "The real spike (in funding) came in September... (2014 when) ... there was a lot of media coverage and that translates into

additional donations.<sup>29[40]</sup> Physicians can continue to advocate for funding to research these viruses and increase access and responsiveness to detect and treat these diseases, as seen with the recent funding released by the CDC to local, state, and territorial health departments.<sup>[41]</sup> Being on the frontlines, emergency physicians can serve in important communication and advocacy roles that facilitate sustained and increased funding for mental health programs and heighten public awareness regarding acute psychiatric events during infectious diseases outbreaks.<sup>[42]</sup> These emerging infectious diseases outbreaks need to address the mental health emergencies of patients through increased funding, awareness, and research as their psychic toll will likely always outweigh their somatic ones.

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