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#### REVIEW ARTICLE

### How can health systems be strengthened to control and prevent an Ebola outbreak? A narrative review

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The emergence and re-emergence of infectious diseases are now more than ever considered threats to public health systems. There have been over 20 outbreaks of Ebola in the past 40 years. Only recently, the World Health Organization has declared a public health emergency of international concern (PHEIC) in West Africa, with a projected estimate of 1.2 million deaths expected in the next 6 months. Ebola virus is a highly virulent pathogen, often fatal in humans and non-human primates. Ebola is now a great priority for global health security and often becomes fatal if left untreated. This study employed a narrative review. Three major databases – MEDLINE, EMBASE, and Global Health – were searched using both 'text-words' and 'thesaurus terms'. Evidence shows that low- and middle-income countries (LMICs) are not coping well with the current challenges of Ebola, not only because they have poor and fragile systems but also because there are poor infectious disease surveillance and response systems in place. The identification of potential cases is problematic, particularly in the aspects of contact tracing, infection control, and prevention, prior to the diagnosis of the case. This review therefore aims to examine whether LMICs' health systems would be able to control and manage Ebola in future and identifies two key elements of health systems strengthening that are needed to ensure the robustness of the health system to respond effectively.

Keywords: Ebola virus; outbreak; prevention; control; health system; low- and middle-income countries

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The emergence and re-emergence of infectious, zoonotic, high-risk diseases are now more than ever considered threats to public health systems (1–3). The most profound consequences of the recent outbreak of Ebola virus disease (EVD) were felt in Western Africa due to the failure of today's health governance (4). Rid and Emanuel (5) argue that global response mechanisms were relatively poor as a consequence of poor infrastructure, fragmented health systems, and inadequate experimental treatments. This paper addresses an overarching research question: What have been the weaknesses of primary healthcare systems in low- and middle-income countries (LMICs), and how might they be strengthened to ensure better control and prevention of Ebola outbreaks in future?

#### Methods

This study utilised a narrative review of the papers focusing on EVD and health systems in relation to control and prevention in the primary healthcare context. Petticrew and Roberts (6, p. 39) argued that narrative review refers to 'a systematic review that synthesises the individual studies narratively' (rather than by means of a metaanalysis). This involves systematically extracting, checking, and narratively summarising information on their methods and results relating to a specific research question to provide 'informative and evidence-based' answers. The Institute of Medicine (7, p. 82), however, alerts the narrative reviewer to the danger of incorrect conclusions, and ultimately wrong decisions or recommendations if they 'fail to acknowledge or address the risk of reporting biases, neglect to appraise the quality of individual studies included in the review, and (they) are subject to errors during the data extraction and analysis'.

Three major electronic databases (MEDLINE, EM-BASE, and Global Health) were searched using both 'textwords' and 'thesaurus terms', focusing on Ebola and

Infection Ecology and Epidemiology 2015. © 2015 Krishna Regmi et al. This is an Open Access article distributed under the terms of the Creative Commons Attribution-NonCommercial 4.0 International License (http://creativecommons.org/licenses/by-nc/4.0/), permitting all non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited. Citation: Infection Ecology and Epidemiology 2015. **5**: 28877 - http://dx.doi.org/10.3402/iee.v5.28877 health systems in LMICs. These databases were considered the best known, having international coverage of over 80 countries and about 15,000 journals indexed, alongside their vast resources capturing the fields of medicine, international health, and related disciplines.

#### The disease

Ebola virus is a highly virulent pathogen. It is an RNA virus and member of the filovirus family, one of four families of viruses which can cause viral haemorrhagic fever, a severe multisystem syndrome which is often fatal in humans and non-human primates. The incubation period varies between 1 and 21 days; however, patients are not considered infectious until they develop symptoms (8). During outbreaks, the risk of person-to-person transmission through contact with body fluids from infected patients is very high, particularly during the late stage of the disease (9) and touching cadavers has been shown to be a significant risk factor associated with developing EVD (10–12). Indeed, in Guinea, during the 2014 EVD outbreak, 60% of cases were found to be linked to traditional burials (13).

Despite the severity of the symptoms, a 56% survival rate may be seen in the present outbreak, but considerably higher rates have been seen in previous outbreaks; for example, in Uganda, the case fatality rate for Bundibugyo strain infections was only 25% and in Europe it was only 22%, mainly due to proper intensive care with appropriate supportive therapy (14–16).

There have been over 20 outbreaks of EVD in the past 40 years in Africa, including Zaire in 1976, Sudan in 1976, Congo (DRC) in 1995, Uganda in 2000-2001, and Congo (ROC) in 2003. These have shown the importance of preparedness to deal with the situation (17, 18) in order to minimise human loss. In 2014, the outbreak of EVD in West Africa was declared as a public health emergency of international concern (PHEIC) by the World Health Organization (WHO), with a projected estimate of 1.2 million deaths (19, 20). As of 13 September 2015, there have been 28,220 reported confirmed, probable, and suspected cases of EVD (21). EVD, by nature, mostly affects economically deprived/poor countries where there is limited capacity to respond to the incidences of disease. This in turn impacts negatively on national infrastructure and disease management (22). Though there is some evidence of controlling and managing infectious disease using appropriate means, the controlling of diseases or infection using health systems intelligence is patchy.

#### Problem analysis

Zoonoses are defined as infectious diseases that are naturally transmitted between wild or domesticated vertebrate animals and humans (23, 24). More than 60% of human infections arise from zoonotic pathogens; they are responsible for billions of cases of human disease and millions of deaths annually and are considered to represent an increasing threat to global health (24). Although many zoonotic infections are stably established (enzootic) in animal populations and transmit from animals to people with little or no subsequent person-to-person transmission, some such as Ebola virus can spread efficiently within the human population leading to localised outbreaks (24). Statistics reveal that children and mothers who are poor and marginalised are particularly vulnerable to this disease (25), especially in developing nations where health and environment systems are fragile, fragmented, and non-responsive in meeting people's healthcare needs. It has been argued that the lack of strong public healthcare delivery systems has been a key factor in the failure to halt the development of the disease (26). Community ignorance due to poor education and knowledge, and ineffective primary care systems at the local levels, are likely to lead to the development of myths, stigma, and anxiety associated with EVD and its mode of transmission, constraining adoption of methods of protection and personal hygiene practices (27). Osungbade and Oni (28) claim that the control measures for EVD were undermined by several factors: lack of a clinically proven vaccine and virus-specific treatment, weak health systems including poor environment, and traditional socio-cultural beliefs and practices. Furthermore, healthcare professionals are not appropriately trained in how to manage cases during an outbreak situation, and the resources needed to prevent the spread of disease are unavailable (2). Demographic changes, changing human behaviour, political violence in civil war and ethnic conflicts, ignorance, and poor health infrastructure are considered as key determinants for exacerbating these problems (3, 29). These attributes would certainly create some challenges in disease identification, notification, and characterisation, as well as undermining collaborative endeavours for the access to and provision of disease surveillance and treatment (30).

Ebola is now a great priority for global health security (26, 31). The multiple challenges identified would require a range of interventions to halt an epidemic. LMICs are not coping with the current challenges of Ebola, not only because they have poor and fragile systems, but also because there are poor infectious surveillance and response systems in place. That has had an impact due to the poor epidemiological responses to emerging disease outbreaks, therefore community initiatives would be important for disease prevention, surveillance, and community-based treatment and support (32). Evidence shows that large-scale and coordinated efforts, both at national and international levels, contribute to supporting both affected and at-risk nations through developing response systems and strengthening health capacities (26, 33).

Identification of potential cases is always problematic in several LMICs, particularly with respect to contact tracing and infection control, as well as prevention prior to diagnosis. Several studies demonstrate that better disease surveillance, improved education, improved knowledgeassociated socio-ecological factors, and improved financial capacities would improve the local and national health system in terms of control measures (28, 34). Borchert et al. (35) claim that three important systems at the public health levels – laboratory systems, information systems, and networking and coordination systems – would be able to detect and then respond to health threats. In addition, developing some tools and approaches related to diagnostics and novel therapies, including vaccines, and implementing an early warning reporting system (EWARS), would certainly contribute to health system improvement (27).

Thus, poor health systems have significant impacts in terms of their ability to strengthen disease surveillance, patients' care (and isolation), infection control, developing incident management systems, and disease test/screening. It is, therefore, important to improve EVD care and support at both the individual and the systemic levels (31). In addition, WHO's capacity is important in playing a role in the development of new essential vaccines (4).

The exact impact of EVD is still unknown, but it has clearly left a great burden on health systems as well as threatening the sustainability of health programmes, besides which insecurity, civil strife, and political instability might lead to displacement of populations (36, 37). Since 2014, Guinea has recorded a significant decline (over 31%) in outpatient visits to hospitals due to the combination of EVD with other diseases (38). Child health services were affected the most, as the evidence reveals that cases of diarrhoea and acute respiratory infection among under-5 children decreased significantly by about 60%, mainly due to adverse effects [reduced hours, service closures, loss of health workers (10% of the deaths) and service suspensions] on service access and utilisation. Iyengar et al. (39) argue that the outbreak has developed a profound risk of escalating the mortality and morbidity of maternal and newborn patients; for example, in Liberia, a 9-14% reduction in antenatal visits, and the proportion of deliveries utilising the healthcare facilities has dropped by 9-33%, so it is important to prioritise maternal and newborn survival issues in such humanitarian crises.

#### Strategic options

Hewlett et al. (40) argue that there must be an adequate understanding of local people's socio-political and economic situations, as well as psychological insight into how health service users, health practitioners, and the local people may respond to a biological crisis to ensure that response efforts bring appropriate strategies to minimise such suffering (41). Similarly, appropriate measures to protect healthcare professionals physically and emotionally, and to train them to provide appropriate, safe clinical care, are essential. In addition, providing education and training support to healthcare professionals on disease control and surveillance, and generating awareness of veterinary public health (2) are necessary to reduce the risk of contracting disease, as the vast majority of transmissions of Ebola during an outbreak such as the current one are person-to-person (25). Recent experiences have thrown up a substantial research agenda. This would focus on building up an Ebola isolation unit, strengthening disease surveillance, and identifying and examining the source of the outbreak, so as to introduce prevention and control measures (42).

The WHO (43) representation of health systems encompasses both organisations and people, together with their actions, directed towards meeting people's healthcare needs through design and delivery of responsive and financially fair systems. These thereby offer the best or most efficient care using available human and material resources. Ebola cannot be eradicated, but it can be managed. Robust health systems – enhancing and strengthening capacity to develop constant surveillance and outbreak verification within the public health infrastructure – are an essential step to the control and management of current and future Ebola virus outbreaks (44).

As we have seen in relation to HIV/AIDS and cholera, outbreaks place particular stress on those public health systems that are least able to cope with them. Senior managerial capacity is diminished as front-line staff are infected. Additionally, the ability to undertake efficient and effective supervision of district-level management and front-line staff is compromised. These staff will themselves be already facing extraordinary demands on their capacity and capability to deal directly with the outbreak at the local level. If management systems are already weak in general, in the event of an Ebola outbreak they will be stretched beyond their breaking point. While external support will understandably be directed towards providing additional resource for the immediate management of the outbreak, it is important that longer term support is also provided to ensure that local health systems are strengthened and better prepared for a future outbreak or threat of an outbreak. In Antoun and Reich's (45) view, health systems should be reformed in such a way that they seek to 'improve performance, advance equity, and resolve challenges'. In addition, bringing the system into focus through a systems-thinking lens, that is, designing/ evaluating system-level interventions with system-wide effects, assessing the main effects within the contextual paradigms and involving multi-disciplinary and multiple stakeholders, would help to understand the situations better in terms of knowing not only what works, but what works for whom under what circumstances (46).

Better systems thinking would make health systemsstrengthening investments and interventions effective, as it would bring an opportunity for interaction between the actors and components of the systems. Similarly, other prevention measures are

- 1. restriction of the movement of persons and goods from epidemic-affected areas and coordination for the effective combating of epidemic outbreaks in the future (47);
- 2. engaging with key community members decreasing stigma, fear, and demoralising perceptions (48);
- 3. adopting a multi-disciplinary approach, including case identification and management, infection control, and social mobilisation, as well as understanding of local contexts to develop and adapt prevention messages and control measures (49); and
- 4. establishing intersectoral as well as trans-disciplinary surveillance response systems through EWARS, adequate collaboration, funding, participation from wider stakeholders, research innovation for vaccine development and pursuing global health initiatives to establish surveillance systems with EWARS, including research-action interventions (27).

At the broader level, an holistic approach is clearly needed, 'understanding [...] the nature of public health systems and the shifts from a medical paradigm to a more holistic paradigm' (50), encompassing human ecology, socioeconomic, political, environmental and policy agendas, with appropriate division of responsibilities locally, nationally, and globally through interdisciplinary collaboration (2, 51). Kim-Farley (52) argues that 'only through worldwide concerted action will the effort to control infectious disease be effective'. Additionally, trained/qualified healthcare professionals with adequate supplies of personal protective equipment, and the development of standard operating procedures, are needed (33). It is equally important to set up permanent testing/disease surveillance facilities in under-served areas - the sort of places that would be able to run a qRT-PCR block, ELISAs, and rapid diagnostic tests at point of care (53), as well as basic immunohistochemistry with enough generators and technology to be able to store supplies. Third, communitybased strategies emphasising prevention, treatment, response, and recovery are paramount. Building up health infrastructure is the sensible long-term solution for managing Ebola, and is a necessary response to the combination of rapid population growth and a decaying health system in several African countries. In addition, positive thinking towards Ebola patients/survivors, and exploring appropriate community supports (education, counselling and psycho-social supports) are critical to minimise potential anxiety, myths, and stigma (32).

Synthesising the strategic options outlined above would suggest four broad domains within which specific problems are encountered. The first is the wider social and economic context within which outbreaks of Ebola have occurred. The second is the lack of vaccines and virusspecific treatments. The third is the nexus of systemic weaknesses in the healthcare delivery system. The fourth is the absence of meaningful community engagement. Of these four domains, the first may be the most important for achieving long-term sustainable impact, but is the domain least amenable to intervention during the course of a particular episode. The second domain will be considered briefly below. However, it is the third and fourth domains, which we see as being inextricably linked, which offer the best prospects for medium-term intervention, thereby strengthening the capability of the health system to respond more effectively to any future outbreak.

#### Vaccines and therapies

Prior to the EVD outbreak in West Africa, progress in developing effective vaccines and therapies had been slow, in part due to the low numbers of cases associated with EVD outbreaks. Since the recent outbreak, progress has been accelerated and a number of therapies have been tested in clinical trials; however, none to date have successfully demonstrated a significant therapeutic effect (27). Additionally, as noted by Tully et al. (54), current treatments are expensive, production can be difficult to scale up, none are suitable for use prophylactically, and all require supervision from already overstretched front-line workers in overstretched Ebola treatment centres.

Perhaps more usefully, development of an effective vaccine should offer long-term, preferably lifelong, protection for an individual as well as protection for unvaccinated individuals in the community through herd immunity. To expedite the development of a suitable vaccine, international consortia have been formed to accelerate collaborative multisite trials of two candidate Ebola virus vaccines: cAd3-EBOZ and rVSV-EBOV, while a third vaccine, a combination prime-boost vaccination regimen of Ad26- and MVA-EBOV entered a Phase I trial (54). Crucially, ethical and regulatory approvals for these trials were prioritised to reduce the time taken to initiate clinical trials. Henao-Restrepo et al. (55) report on the interim analysis of a trial of rVSV-ZEBOV in Guinea, West Africa. The VSV-EBOV vaccine consists of a vesicular stomatitis virus genetically engineered to express Ebola glycoproteins; and the vaccine variant known as rVSV-ZEBOV specifically expresses glycoproteins of the Zaire Ebola virus or ZEBOV. The trial, involving 7651 people, indicated that rVSV-ZEBOV might be highly efficacious and safe in preventing EVD, and is most likely effective at the population level when delivered during an EVD outbreak via a ring vaccination strategy - a similar strategy to that used in the final stages of the smallpox eradication campaign (56). However, a number of adverse events were reported during the study and safety assessment is ongoing. It is also unclear at this stage how a wide-scale immunisation programme would be funded or implemented within LMICs in the future.

#### Health system strengthening

The literature identifies a number of discrete areas of systemic weakness: training of healthcare professionals; poor infection surveillance and response systems; infection control; contact tracing; laboratory systems; information systems; networking and coordination systems; and community ignorance and absence of community engagement. A strategy of health systems strengthening would address these through two closely connected strategic developments. The first would be the decentralisation of systemic planning and management, and the second would be an enhanced agenda of community engagement.

Decentralisation allows for more responsive decisionmaking (57). This is particularly critical when a system is in crisis mode. The most effective deployment of local resources is a matter best determined closest to the point of impact. Reassignment, or the co-option of *ad hoc* local resources, should not be contingent on higher level authorisation. Appropriate training programmes, designed in accord with national and regional guidelines but tailored to the local circumstance, will ensure that valuable knowledge (both of disease-specific issues and of the operation of general management and disease response systems) is most effectively disseminated.

Decentralisation can strengthen the functioning of routine systems. Even when these are developed in keeping with quite stringent central requirements, decentralisation encourages better feedback and generates a deeper understanding of their underlying purpose. Decentralisation also frees the local healthcare system from log-jams that may occur at higher levels of the system. The experience of HIV/AIDS has taught us that one of the most debilitating impacts of an outbreak is the absence of senior officers at the higher levels of the system, which can lead to systemic paralysis throughout the system.

Decentralisation and enhanced community engagement go hand in hand. Recent experiences confirmed by the available literature inform us that trust is a critical factor in ensuring an effective community-level response. This is itself predicated on a genuine two-way dialogue which generates understanding – practitioner understanding of community knowledge, beliefs and views, and community understanding of the rationale for measures being implemented (50). In the context within which there is a strong motivation for family members to hide incidences, community knowledge is vital. This will be provided when community members feel that they can trust the response that disclosure will initiate. Full community engagement is also critical to the identification of *ad hoc* resources that may be co-optable at the local level.

#### Conclusion

Health systems strengthening does not offer a panacea. And health systems strengthening is most effective when it is implemented as part of a longer term strategy of health systems development. As countries move stutteringly into remission, it is paramount that the recent experience, particularly the aspect of disease surveillance and monitoring with community engagement, is thoroughly evaluated, that longer term lessons are learnt, and that measures are implemented that can lessen the impact of any future outbreaks and (we would argue) can make the local healthcare system more effective in its more normal day-to-day operation.

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