

## EBOLA VIRUS DISEASE OUTBREAKS IN AFRICA AND THE 2014 EPIDEMIC

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### Background

Ebola virus disease (EVD) has transgressed from a curious tropical disease of Africa to an international health emergency threat worldwide in 2014. The first occurrence of EVD was reported in 1976 in the Democratic Republic of Congo (then Zaire) during a highly fatal outbreak of haemorrhagic fever.<sup>1</sup> Since 1976 and before 2014, a total of 23 outbreaks of EVD has been reported in Africa (figure 1). During these outbreaks, 2,345 laboratory confirmed cases cumulatively were reported of which 1,541 were fatal.

The history of EVD has been characterized by unpredictable outbreaks in mostly secluded and very rural settings of equatorial Africa. The first outbreaks in 1976-1979 were followed by a period of apparent quiescence up to and including 1993 (figure 2). Since 1994, outbreaks of EVD have been recorded regularly in east and central Africa, but the 2014 EVD epidemic in West Africa is the first on record in this region and the largest in the history of outbreaks of this disease. At time of writing, the EVD situation in Guinea, Liberia and Sierra Leone continues to deteriorate with widespread and persistent transmission.

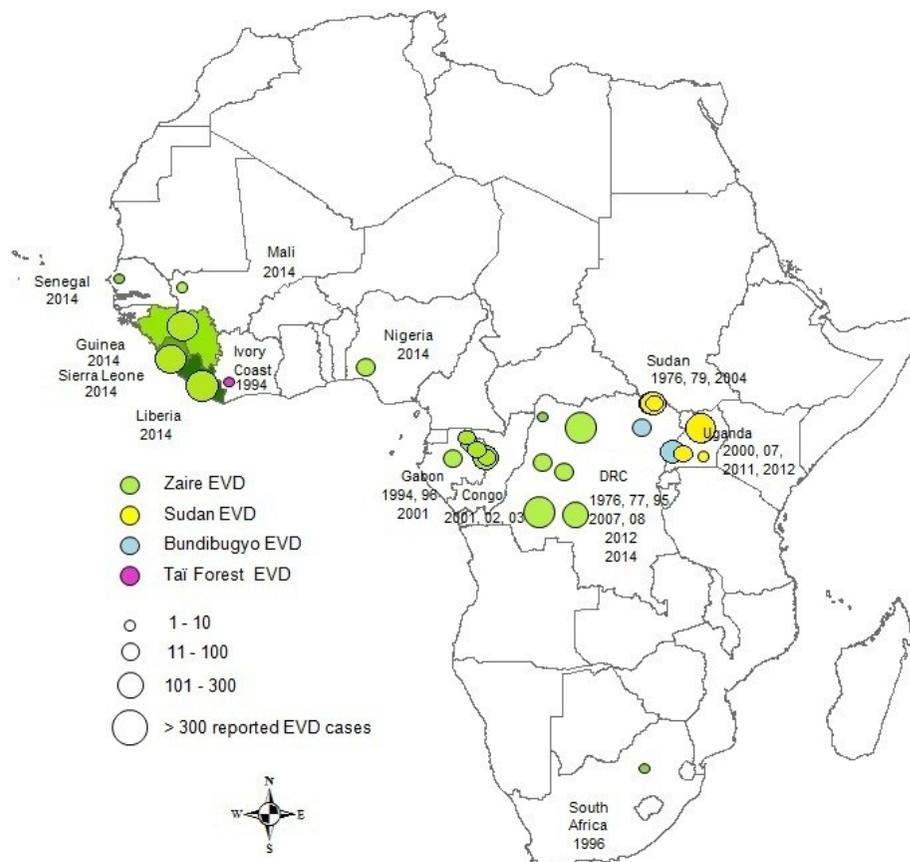
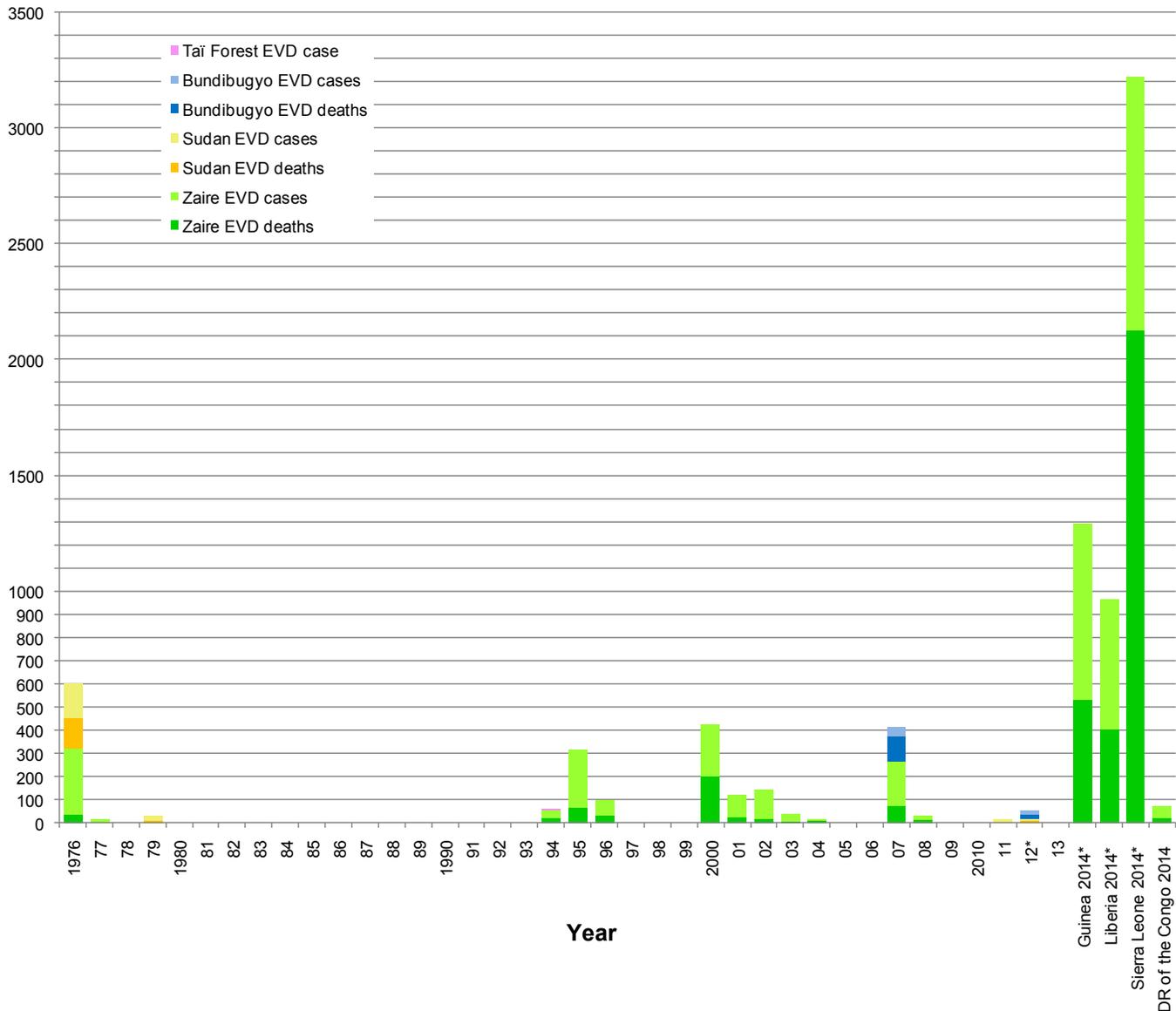


Figure 1: Geographical distribution of Ebola virus disease (EVD) outbreaks in Africa to date. Imported cases of EVD have been reported in South Africa in 1996 and in Senegal, Nigeria and Mali in 2014. (Adapted from data available on <http://www.cdc.gov/vhf/ebola/outbreaks/history/distribution-map.html>).



\*lab-confirmed cases only

Figure 2: Time-line indicating outbreaks by region/country of Ebola virus disease by year to date (19 October 2014 for West Africa and 23 October 2014 for DRC). Numbers of cases and numbers of deaths are indicated for each outbreak. (From data available on <http://www.cdc.gov/vhf/ebola/outbreaks/history/distribution-map.html>)

### Aetiology and ecology

Ebola virus disease is caused by infection with ebola virus species which are members of the *Filoviridae* family. This family includes three genera: *Cuevavirus*, *Ebolavirus* and *Marburgvirus*. These filoviruses are named for their filamentous, pleomorphic shape (figure 3). A total of five species of *Ebolavirus* are recognized to date: *Zaire ebolavirus*, *Sudan ebolavirus*, *Bundibugyo*

*ebolavirus*, *Tai Forest ebolavirus* and *Reston ebolavirus*.<sup>2</sup> *Zaire ebolavirus* and *Sudan ebolavirus* have been associated with the most sizeable and fatal outbreaks in humans. The virus causing the current outbreak in West Africa has been identified as *Zaire ebolavirus* although the genomes of the circulating isolates are only 97% homologous to isolates from previous outbreaks.<sup>3</sup> Genetic characterization and

molecular clocking analysis has estimated the introduction of this virus into West Africa in 2004. It has been evolving in its ecological niche there ever since

and apparently spilled over into the human population for the first time in 2013.<sup>4</sup>

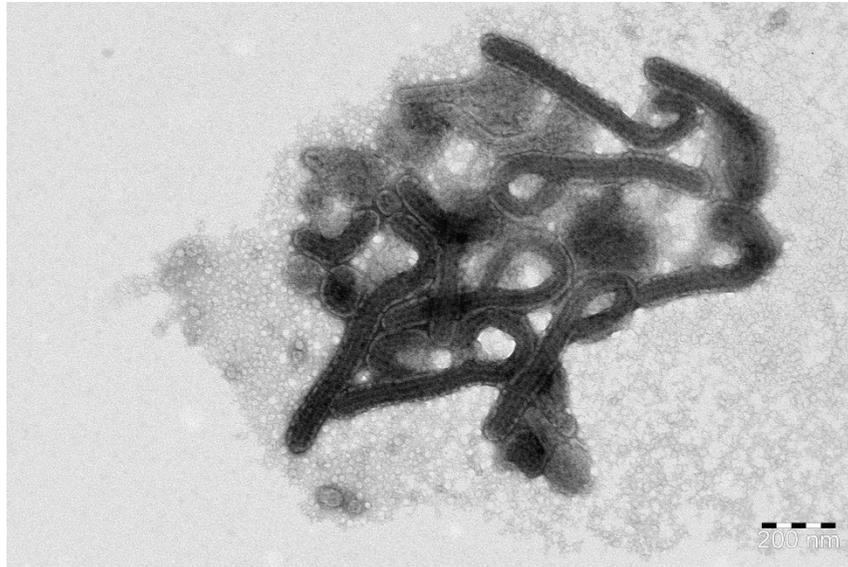


Figure 3: Electron micrograph of a cluster of Ebola virus virions  
(Courtesy: Dr Monica Birkhead, NICD)

Current knowledge suggests that certain species of arboreal fruit bats are the natural reservoir for filoviruses.<sup>5</sup> The bats implicated as hosts are seemingly unaffected by infection with the ebola viruses but the exact mechanism of transmission within bat populations, and also from bats to other forest dwelling animals and humans, is not clear. Virus transmission through contact with infected blood and tissues of these bats, as well as other infected animals, is considered a major risk factor for spill over to the human population. Human-to-human transmission in turn occurs through direct contact with the blood and bodily fluids of a person infected with EVD - hence the propensity of outbreaks to perpetuate amongst families and in the healthcare setting. The World Health Organization estimates that up to 60% of cases reported during the 2014 West Africa outbreak are directly linked to exposures incurred through performing burial rites and ceremonies which include very intimate contact with the bodies of patients that died of EVD.<sup>6</sup>

#### **Summary of the Ebola virus disease outbreak in West Africa to date**

Case investigations have traced back the index case of the outbreak to a two year old child from the Guéckédou Prefecture in Guinea. The child died on the 6<sup>th</sup> December 2013.<sup>3</sup> The World Health Organization formally announced the outbreak in March 2014. This outbreak of EVD is unprecedented in many ways. Firstly, it is the first outbreak of EVD in this region of West Africa (figure 1). Secondly, it is the largest outbreak of EVD recorded to date with recorded cases (as of 19 October 2014) four times (at time of writing) the total number for all outbreaks prior to 2014 (figure 4). There are many socio-economic and public health related drivers that are fuelling the outbreak and thwarting conventional efforts to contain it.<sup>7-9</sup> The affected West African countries are some of the most impoverished in Africa with highly dysfunctional health care systems. In the aftermath of the civil conflicts that have characterized the recent histories of these

countries, the health and other infrastructure remains dilapidated. Hospitals are ill equipped and, in Liberia, one medical doctor is available per 100,000 of the population.<sup>10</sup> The poor health system correlates with a poor disease surveillance capacity and inability to recognize disease outbreaks and trends. In addition, the literacy rates of these countries are amongst the worst in Africa which in turn complicates effective communication to communities and social mobilization, which are integral parts of outbreak control and prevention measures. Mobility between communities in the region is common with people travelling for social and economic reasons in-country as well as across borders. These factors, including the late recognition of the outbreak, contribute to the wide and increasing distribution of EVD cases in affected countries.

Although the outbreak has remained largely confined to Guinea, Liberia and Sierra Leone, a total of four cases have been exported outside of these borders since July 2014. The first case involved a Liberian national travelling to Lagos, Nigeria. The patient was identified and isolated but set off a nosocomial outbreak resulting in a total of 20 cases. The outbreak has since been contained.<sup>11</sup> A case of EVD was confirmed in Dakar, Senegal, involving a Guinea national who travelled via bus to the city, with no secondary cases. In September 2014, a person travelling from Liberia to the USA was diagnosed and hospitalised for EVD. To date, two additional cases of EVD have been noted in nurses who tended to this patient. Likewise, there has been a secondary infection involving a nurse who cared for a patient evacuated for treatment of EVD in Spain. In October 2014, a young child whose mother died of EVB in Guinea was brought back to Mali. This child consequently developed and died of EBV.

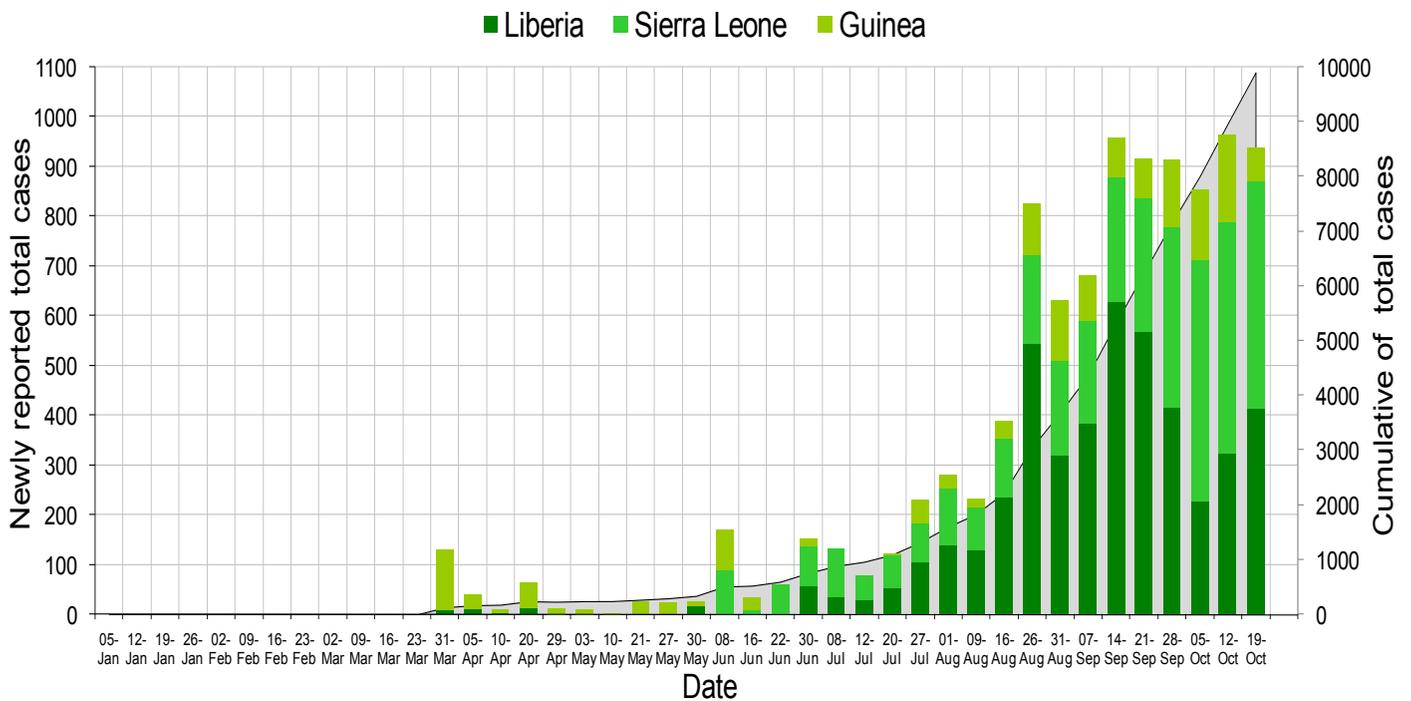


Figure 4: Epidemic curve for the current Ebola virus disease outbreak in Guinea, Liberia and Sierra Leone by date from the initial announcement of the outbreak in March 2014 (adapted from total case data reported by the Centers for Disease Control and Prevention and World Health Organization as of 19 October 2014).

### Summary on Ebola virus disease outbreak in the Democratic Republic of Congo to date (19 October 2014)

A total of six EVD outbreaks were recorded in the Democratic Republic of Congo (DRC) from 1976 to 2012. Three of these outbreaks have occurred since 2007. It is noteworthy that more than 40% of all EVD cases reported before 2014 occurred in the DRC during these outbreaks. In August 2014 the World Health Organization was notified of an EVD outbreak in the Equateur Province of the DRC. The index patient was a pregnant female who was involved in the slaughtering and handling of bush meat prior to her death. A total of 68 cases of which 49 had a fatal outcome have been reported to date. Molecular sequencing analysis has shown that the ongoing outbreaks in the DRC and West Africa are unrelated.<sup>17</sup>

### South African laboratory capacity for responding to the Ebola virus disease outbreak

The National Institute for Communicable Diseases (NICD) has a long-standing history of conducting laboratory investigations of potential haemorrhagic fever cases in South Africa and the southern African region. After the first reports of Lassa, Ebola and Marburg fevers in the 1960s and 1970s, a decision was made to

establish a Biosafety Level 4 (BSL4) facility in South Africa. This laboratory was commissioned in 1980 as a strategic national and regional facility for responses to African haemorrhagic fevers. It is currently managed by the Centre for Emerging and Zoonotic Diseases (CEZD) of the NICD and is the only maximum security facility operating in Africa (figure 5). CEZD is recognized as a World Health Organization Collaborating Center for Reference and Research of Viral Haemorrhagic Fevers and Arboviruses. It is also a member of the WHO Emerging and Dangerous Pathogens Laboratory Network to perform diagnosis and investigation of outbreaks caused by highly dangerous pathogens. Apart from the laboratory capacity to diagnose such cases, the NICD is also providing support to the National Department of Health in terms of contributions to the development of relevant guidelines, testing of potential cases, identification of risk cases and outbreak response measures. CEZD has confirmed nearly 200 cases of CCHF in South Africa since 1981<sup>10</sup>, and has also been involved in the investigation and confirmation of imported haemorrhagic fever cases over several decades (table 1).<sup>12-15</sup> Since April 2014, a total of 18 suspected cases of haemorrhagic fever were tested for EVD in South Africa. At time of writing no cases of EVD have been confirmed in South Africa.



Figure 5: Scientists working in the Biosafety Level 4 facility at the National Institute for Communicable Diseases (NICD), Sandringham, Johannesburg.

Table 1: Summary of sporadic imported cases of viral haemorrhagic fever in South Africa, 1975 to date (October 2014).

Year	Brief outbreak history	Number of secondary cases identified	Viral haemorrhagic fever diagnosed	Reference #
1975	Australian backpacker travelled from Zimbabwe to South Africa. Possible exposure to bats during trip. Patient died	Two cases (nurse and travel companion), resulting in one fatality	Marburg virus disease	13
1996	Gabonese healthcare worker travelled to South Africa and presented to a Johannesburg hospital. Patient recovered	One case (nurse), resulting in one fatality	Ebola virus disease	14
2007	Nigerian healthcare worker treated in South African hospital for presumptive diagnosis of typhoid fever. Patient died	No secondary cases	Lassa fever	Unpublished
2008	Index case from Zambia evacuated to South Africa for medical treatment with presumptive diagnosis of tick bite fever. Patient died	Three secondary cases (paramedic, nurse and hospital cleaner, all fatal) and one tertiary case (nurse, not fatal)	Lujo fever	15

### Field laboratory support in Sierra Leone

Laboratory diagnosis of suspected EVD cases plays an integral part in the effort to combat the ongoing EVD outbreak in West Africa. Rapid confirmation of Ebola virus infectious status of individuals is critical for patient management and isolation, but also for contact tracing and identification of probable new transmission chains. Owing to a lack of capacity and expertise in EVD diagnosis within the health care systems of the affected countries, mitigation of this problem can be achieved by deployment of mobile laboratories from institutions and agencies that do have the necessary experience. The National Institute for Communicable Disease Mobile Laboratory Unit (NICD MLU) was deployed through the mechanism of the Global Outbreak Alert and Response Network (GOARN) of the World Health Organization (WHO) on the 17<sup>th</sup> of August, 2014, in order to set up

Ebola diagnostic capacity in Freetown, Sierra Leone. As of the 23<sup>rd</sup> of October, 2014, the NICD MLU had tested a total of 2,497 submissions from suspected EVD cases, amounting to an average of 42 samples tested daily during 9 weeks of operation (figure 6).

An additional duty of the NICD MLU is to strengthen Sierra Leone's capacity to deal with the current and future outbreaks of EVD. Training and integration of Sierra Leonean laboratory personnel in operation of the MLU is ongoing. The continued operation of the NICD MLU is highly appreciated by Sierra Leonean authorities and organizations involved in controlling the outbreak, particularly the World Health Organization, and it is expected to play an important role in the coming months to support containment efforts.



Figure 6: Professor Janusz Paweska and Dr. Petrus Jansen van Vuren performing inactivation of blood specimens submitted from suspected EVD patients in Freetown, Sierra Leone.

### Conclusion

The intervention strategies designed to contain the outbreak of EVD in West Africa have still to bear fruit. The World Health Organization stipulates in its roadmap the goal of containing the outbreak in the next six to nine months.<sup>16</sup> The NICD is providing an expert laboratory diagnostic service for EVD nationally as well as regionally for the SADC community. The NICD is also supporting international efforts to contain the EVD outbreak in West Africa by providing much needed laboratory diagnosis of EVD in Sierra Leone.

### Acknowledgments

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### References

1. World Health Organization. Ebola haemorrhagic fever in Zaire, 1976. *Bull World Health Org* 1978; 56: 271-93.
2. Carrol SA, Towner JS, Sealy TK et al. Molecular evolution of viruses of the Family Filoviridae based on 97 whole-genome sequences. *J Virol* 2013; 87(5): 2608-2616.
3. Baize S, Pannetier D, Oestereich L et al. Emergence of Zaire Ebola virus disease in Guinea – preliminary report. *NEJM* 2014; DOI:10.1056/NEJMoa1404505.
4. Gire SK, Goba A, Andersen KG et al. Genomic surveillance elucidates Ebola virus origin and transmission during the 2014 outbreak. *Science* 2014; DOI: 10.1126/science.1259657.
5. Groseth A, Feldmann H, Strong, JE. The ecology of Ebola virus. *Trends Microbiol* 2007; 15(9): 408-416.
6. World Health Organization. Sierra Leone: A traditional healer and a funeral. <http://www.who.int/csr/disease/ebola/ebola-6-months/sierra-leone/en/> (Accessed: 24 October 2014).
7. Weyer J, Blumberg LH, Paweska JT. Ebola virus disease in West Africa – an unprecedented outbreak. *SAMJ* 2014; 104 (8): 555-556.

8. Fauci AS. Ebola – underscoring the global disparities in health care resources. *NEJM* 2014; 371(12): 1084-1086.
9. Chan M. Ebola virus disease in West Africa – no early end to the outbreak. *NEJM* 2014; 371: 1183-1185.
10. World Health Organization. Ebola situation in Liberia – non-conventional interventions needed. <http://www.who.int/mediacentre/news/ebola/8-september-2014/en/> (accessed 24 October 2014).
11. World Health Organization. WHO declares end of Ebola outbreak in Nigeria. <http://www.who.int/mediacentre/news/statements/2014/nigeria-ends-ebola/en/> (accessed 24 October 2014).
12. Kemp A, Msimang V, Weyer J, Paweska JT. Crimean-Congo haemorrhagic fever and tick bite fever in South Africa, 2012-2014. *Communicable Diseases Surveillance Bulletin* 2014; 12(3):59-62.
13. Gear JSS, Cassel GA, Gear AJ, et al. Outbreak of Marburg virus disease in Johannesburg. *BMJ* 1975; 4:489-493.
14. Richards GA, Murphy SRN, Jobson R. Unexpected Ebola virus in tertiary setting: Clinical and epidemiological aspects. *Crit Care Med* 2000; 28(1):240-244.
15. Paweska JT, Sewlall NH, Kziasek TJ, et al. Nosocomial outbreak of novel arenavirus infection, southern Africa. *Emerg Infect Dis* 2009; 15(10):1598-1602.
16. World Health Organization. Ebola response roadmap. <https://extranet.who.int/ebola/#> (accessed 24 October 2014).
17. World Health Organization. Virological analysis: no link between Ebola outbreaks in West Africa and Democratic Republic of Congo. <http://www.who.int/mediacentre/news/ebola/2-september-2014/en/> (accessed on 27 October 2014).