Chapter 1

Managing Ebola in Low-resource Settings: Experiences from Uganda

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Additional information is available at the end of the chapter

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Abstract

Five outbreaks of Ebola virus disease of the Sudan Ebola virus and the Bundibugyo Ebola virus occurred in Uganda from 2000 to 2012. The attack rates and the case fatality rates were much higher for the former than the later. Fever and bleeding manifestations associated with the clustering of cases were typical clinical features. Close contact with infected person was probably the major route of spread. Apparent asymptomatic and atypical Ebola infection was demonstrated in some close contacts, suggesting past unrecognised exposure or cross-reacting antibodies. A zoonotic connection was apparent in monkeys and asymptomatic villagers. The Ministry of Health together with its partners contained the outbreaks, sometimes with delays, but at least once promptly. Early detection and communication yielded the best ideal outcomes. A community-based response ensured timely case search and contact tracing for the isolation and management of patients. The syndrome-based EVD case definition and the laboratory screening tests for Ebola were used to detect cases. However, their unknown specificity and sensitivity and their low positive predictive values were a major weakness in the screening process. Validation of the criteria and the tests at the local level was essential. There were gaps in isolation procedures as 64% of the health care workers were infected after the isolation units were established. Palliative treatment was an important part of management as it improved survival and public confidence. Therefore, survival and not just quarantine must be emphasized and be a critical component of EVD management. Substantial investment in human resource for health is needed to attract, reward, retain and compensate health workers. Collaboration and partnerships at national and international level is vital in building health systems for early surveillance and management of emerging infections. The Uganda experience provides opportunities for further research on some of these strategies that could improve the management and control of Ebola in low resource countries.

Keywords: Ebola, outbreaks, detection, management, resources

1. Introduction

1.1. Ebola Virus Disease (EVD)

Five outbreaks of EVD occurred in Uganda between 2000 and 2012 [1–4]. In this paper, we describe our experience, challenges and opportunities that existed during the Ebola outbreaks in Uganda. The Gulu outbreak in 2000 was the largest and most complex occurrence in the midst of an insurgency and severely deteriorated social services [5]. The first reported outbreak of EVD was identified in 1976, in the DR Congo, on the border of Sudan [6]. Since then, there have been 26 outbreaks in Equatorial Africa occurring in DR Congo, Gabon, Sudan and Uganda. The majority of these outbreaks were minor. The most serious outbreak occurred in West Africa in 2014 causing some 23,000 cases and 11,000 deaths in Liberia, Guinea and Sierra Leone [7]. Of the five known species (EBOV, SUDV, RESTV, TAFV, BDBV) only three are associated with disease. The *Zaire ebolavirus* has the highest case fatality (90%) while the *Sudan ebolavirus* is medium at 50–55% [8]. The *case fatality for the Bundibugyo ebolavirus* is low at 34%. There is no known cure yet for the disease. Ebola symptoms mimic several common diseases in the tropics including malaria.

Lymphoid tissue such as the liver, spleen, and thymus are critical targets which are often severely damaged leading to liver necrosis, bleeding manifestations and shock. Organ damage leads to a series of metabolic dysfunctions which maintain blood pressure homeostasis [9, 10]. Fruit bats are potential reservoirs of the *Zaire ebolavirus* through direct contact with freshly killed bats or when ingested as food [11]. Asymptomatic infection of between 4– 15% among the pygmies in Gabon and DR Congo [12] has been demonstrated suggesting some previous exposure to Ebola or cross-reacting strains Ebola has been isolated from seminal fluids 61 days after onset of illness [13]. This may be a potential source of infection in large outbreaks in low resource settings. Direct contact with body fluids of an infected person (dead or alive) via broken skin or mucosal surfaces is probably the most important route of infection [14]. The intramuscular route is perceived to be more effective [14]. In poor healthcare settings, contaminated needles and syringes are likely sources of infection. Re-use of needles, for instance, played a key role in escalating the epidemics in Sudan and DR Congo in 1976 [15].

1.2. Ebola outbreaks in Uganda 2000–2012

In 2000, some 425 cases and 224 deaths occurred in Gulu district and 31 health care workers were infected. The affected village was Rwot Obillo, 14 km north of Gulu towards the border with South Sudan. The local community was inaccessible because of on-going military operations against insurgency in the area. On the 8th of October, 2000, three student nurses died in Lacor hospital [1]. On the 12th of October the Sudan Ebola virus was confirmed among the blood samples taken. Nearly 2 million people most of whom lived in camps were at risk in the region [16]. Rural residents commuted to Gulu town for fear of Ebola and abduction from LRA rebels. Two patients in Gulu escaped to Masindi and Mbarara districts, but were followed, isolated and contained. The outbreak lasted 6 months.

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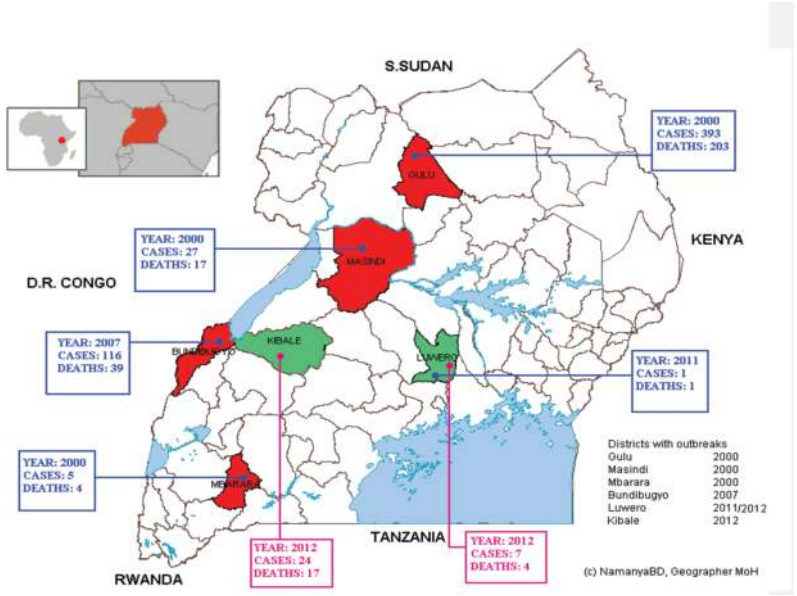

Figure 1. Outbreaks of Ebola in Uganda by district, 2000–2012. Source: Adapted from Ebola outbreak reports 2000-2012; WHO Health Mapper Mapping software, version 4.2

Four more Ebola outbreaks caused by Sudan Ebola virus occurred with increasing frequency in 2011 and 2012 [3, 4]. The primary cases were from rural areas. In 2007, the Bundibugyo Ebola virus caused the second outbreak [17]. Major transmission of the early cases was associated with patient care and burial rituals [2]. The diagnosis was delayed but once detected it took just 3 weeks to contain the outbreak [18]. Serious action was launched and isolation established. Community mobilisation and action contained the outbreak. Some 116 cases and 39 deaths were confirmed, and 14 health care workers were among the victims. Unlike in the Gulu outbreak, the health care workers contracted infection before the isolation units were established.

1.2.1. Luwero outbreaks: 2011, 2012

More outbreaks occurred in Luwero in 2011 and 2012. Early detection was key in limiting the Luwero 2011 outbreak to a single case [3]. On the 5th of May, a 13-year-old girl was admitted to Bombo hospital with a history of fever, diarrhea and vomiting. She was isolated and her blood was investigated. She developed vaginal bleeding and deteriorated and died the following day. The Sudan Ebola subtype was detected and confirmed. The results were communicated quickly to the community on the media and by house to house messages by word of mouth. Contacts were followed up by the community. No new case was discovered or reported. This is the ideal desirable scenario for Ebola containment. In December 2012, hardly six months after the Kibaale outbreak, a second Ebola outbreak resurfaced in Luwero

district [4]. The outbreak was confirmed within days and contained in 6 weeks leaving 7 cases with 4 deaths.

1.2.2. Kibaale outbreak, 2012

Earlier in July 2012, an Ebola outbreak occurred in the district of Kibaale [4]. The index case was a 16-year-old female from a remote rural community. She fell sick while preparing forest land with her husband for planting season. On admission, she complained of fever, diarrhea and vomiting. She developed a nose bleed just before she died. Nine relatives who participated at the funeral died including a mother, and several sisters who contracted the infection died. A priest who led the burial ceremony also died. One health care worker who attended to her also died. Community action followed up 408 contacts during which some 24 cases and 17 deaths were confirmed. The outbreak was contained in six weeks.

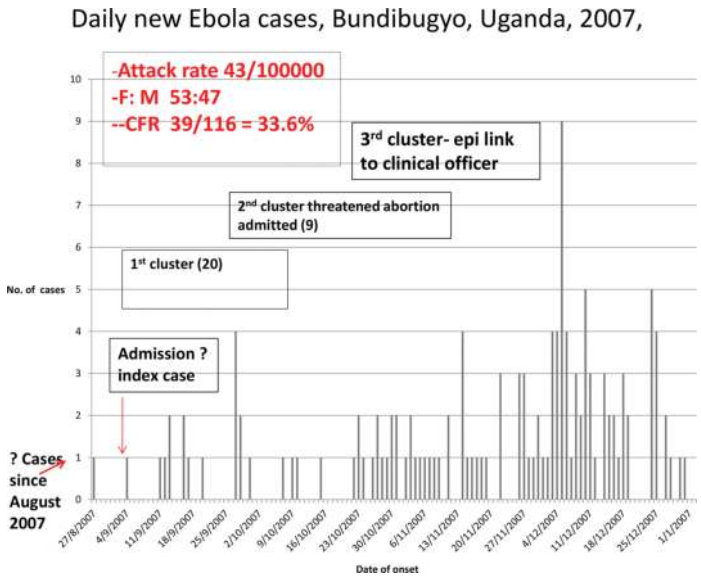

Figure 2. Clustering of Ebola cases by week, Bundibugyo, 2007–2008.

1.3. Clinical manifestations of cases

Cases were identified using an adapted WHO syndrome based criteria for "suspect", "probable" and "confirmed" cases. Clustering of cases (**Figure 2**) associated with sudden onset of fever particularly among health care givers is highly suspicious. The most common symptoms were fever, headache, anorexia and diarrhea. However, in a few cases (15%) no fever was observed in patients on admission. This observation and unsuspected source of infection poses [5] a potential danger to health care givers. Bleeding tendencies occurred in about 50% of the cases of SUDV, but less than 30% in the BDBGV outbreaks. The diagnosis was often compli-

cated by the several locally endemic febrile conditions which mimicked Ebola such as malaria which accounts for up to 50% of cases at the outpatient clinics Uganda.

1.4. Risk factors

Some significant observations were made on risk factors. The outbreaks occurred between June and December coinciding with the rainy season, during which fields are prepared for planting. It was also a fruit season. Known primary cases occurred in the rural areas. Access to fruits partially eaten by non-human primates was common during the season and may have been a potential source of infection.

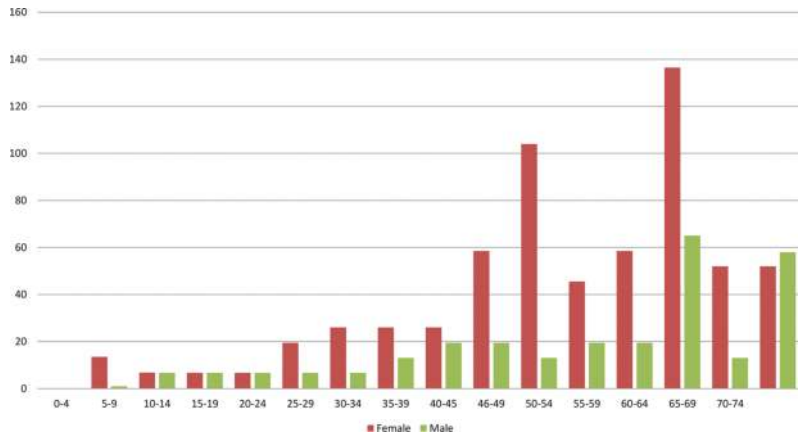

Figure 3. Attack rates per 10,000 inhabitants by gender and age, Gulu district, Uganda, 2000.

Age and gender were associated with infection in Gulu district. There was a 16-fold risk increase with increasing age between children and the elderly and was highest at 60–64 years age group. The attack rates among children between 5–14 years were the lowest (**Figure 3**). In Gulu district, the high risk in elderly women is associated with their role in cleansing and preparing the dead before burial [19]. In Bundibugyo too, participation in some ritual ceremonies was associated with a 7-fold increase in risk [2]. Contact with a known case carried between four to sevenfold increases in risk. Visiting a hospital or a hospitalized patient was associated with a ninefold increase in risk. The possibility of a zoonotic connection or cross reacting local strains was observed as some SUDV Ig G antibodies were confirmed in the monkey carcasses and a few asymptomatic local residents [1].

Year	District	Cases detected	Deaths	CFR
2000	Gulu	393	203	51.7%
	Mbarara	5	4	80.0%
	Masindi	27	17	63.0%

Year	District	Cases detected	Deaths	CFR
Total[a]		**425**[b]	**224**	**52.7%**
2007	Bundibugyo	116[c]	39	34 %
2011	Luwero	1	1	100%
2012, Jun-Aug	Kibaale	24[d]	17	70%
2012, Nov-Dec	Luwero	7	4	57%

Source: Ebola situation analysis reports 2000-2012

Table 1. Ebola cases by year and district, Uganda, 2000–2012

2. The national response

The national response was multisectoral and led by the President who directed all sectors to get mobilised and participate. The Ebola national task force in the Ministry of Health led the implementation of the strategic work plans. The task force reported to the Office of the Prime Minister, the leader of government business. Working groups were set up in the following areas: planning and coordination, surveillance and laboratory service, public education, case management, and logistics management (**Figure 4**).

Figure 4. Organization of the national response.

One national joint plan was developed to which the various collaborators subscribed both at national and international level. International support including expertise was integrated into the national plan endorsed by national and international stakeholders including bilateral development partners.

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A syndrome-based case definition was adapted from the WHO[1] guidelines and used for community-based active case search. A flow chart (**Figure 5**) integrated and harmonized the participation of the various actors. Community mobilization focused on public education and active case search by the community optimized through media. Full participation of church leaders, school principals and local political leadership and mobile teams was the cornerstone of community effort. Isolation and triage units were set up in district hospitals. Health care workers were recruited and paid risk allowances to boost motivation and dedication. Workers with previous experience and institutional memory were preferred and redeployed. Daily report updates and press briefings were openly communicated to the public at all levels. Similar arrangements were set up at the district, county, sub county, parish and village levels (**Figure 4**).

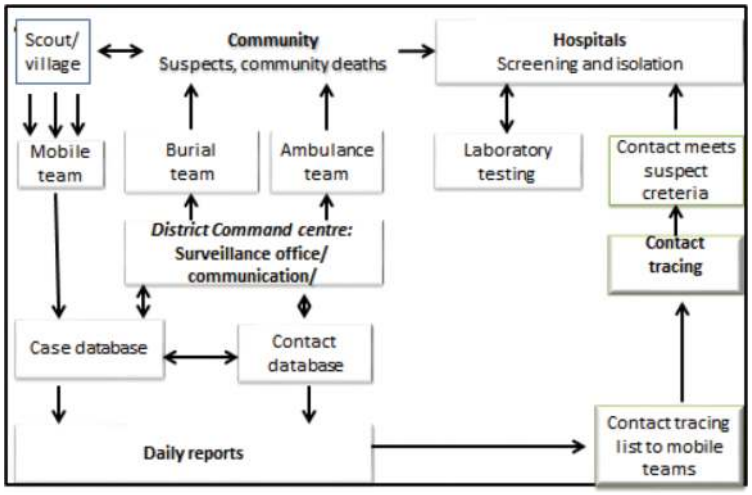

Figure 5. Flow chart for community based surveillance.

A cascade of training starting with training of trainers countrywide was carried out within days. Each village appointed a village health team led by a chairman and secretary (scout) to coordinate the implementation. At district level, a district task force coordinated the response. Incentives were paid to them for each Ebola case reported and revalidated. Burial and safe disposal of the dead was coordinated by a district burial coordinator who liaised with the hospital coordinator and the village health teams. Trained burial teams with past experience were recruited, retrained and liaised with the village scout to ensure safe and timely burials. On discharge, the patients went through a series of stringent protocols and check lists conducted by trained counsellors. Post Ebola clinics and clubs were set up for follow up of health and social outcomes.

1 Adapted from the WHO (2003)

3. Examples of best practice

3.1 Successful community action

There were some examples when timely community action effectively stopped the spread of these Ebola outbreaks. The best examples were demonstrated in Masindi district (2000) and the Luwero district (2011). A known case escaped from Gulu hospital to her ancestral home in Masindi district because her nurse died. The patient belonged to an extended family of 73 members residing in the district. The local community imposed quarantine on the members of the extended family. Transmission was prevented beyond the extended family - of the 27 new cases in the district 25 were from the extended family and only one case came from the general population (**Figure 6**). Thus, transmission beyond the extended family of the index case was effectively prevented by early detection and action and quarantine imposed by the community [20].

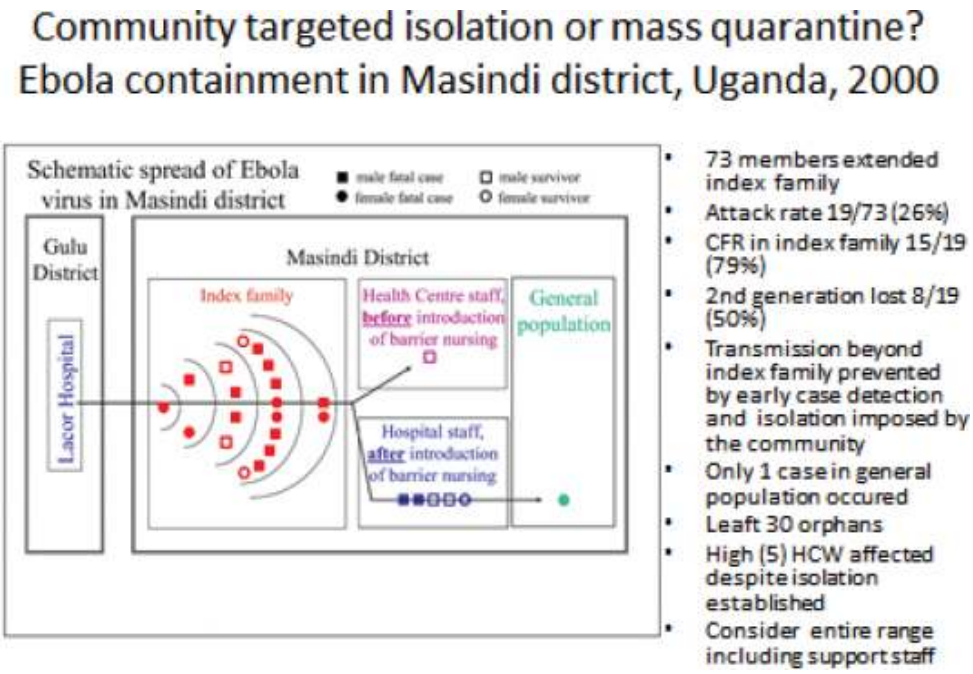

Figure 6. Community based Ebola containment of Ebola in Masindi district, Uganda, 2000.

3.2 Early detection and action

The Luwero outbreak of 2011 demonstrated the critical role of early detection and action in containing the outbreaks [3]. The single case outbreak was contained within one week. This

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excellent outcome occurred when a case was promptly diagnosed and confirmed to have Ebola. She was immediately isolated and the community was mobilized to start the public response including education, active contact tracing and isolation. This is the most desirable outcome as demonstrated by the critical timelines in **Figure 7**. The need for early diagnosis and action cannot be overemphasized.

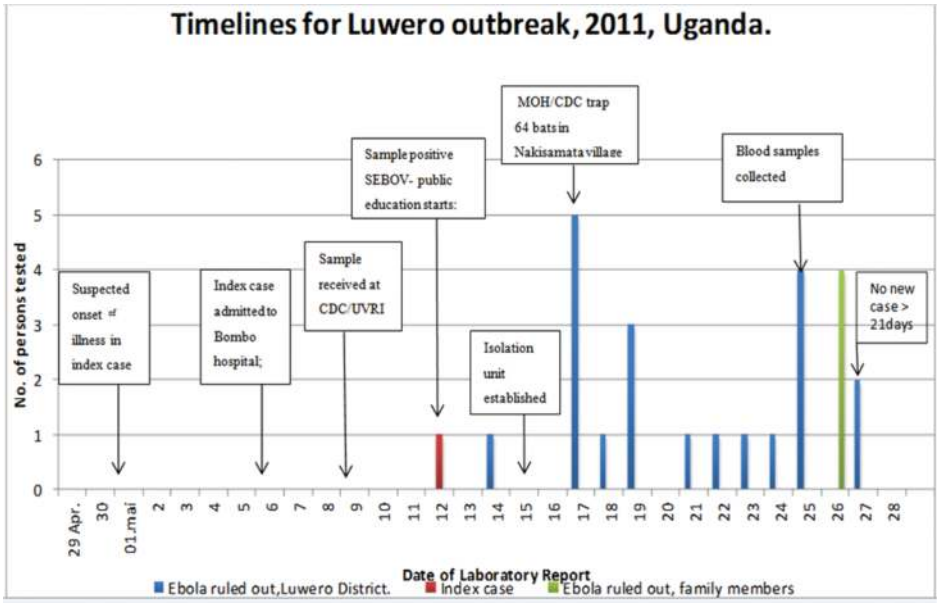

Figure 7. Early Ebola detection and containment, Luwero district, Uganda, 2011.

4. Challenges

4.1 Delayed action

Delays in early detection prolonged the spread of infection and late action. The respective districts experienced the following delays: in the districts of Gulu district (6 weeks delay); Bundibugyo (6 months); Kibaale (6 weeks). Most (75%) of the delays were at community level. Once the diagnosis was made, it took between 5 and 17 days to contain the outbreaks in Luwero and Kibaale respectively: only 5 days in Luwero; some 17 days in Kibaale. The corresponding figure for the Gulu epidemic was longer (91 days). It also took 41 days to contain the Bundibugyo outbreak. Thus late detection facilitated the extensive spread of the infection in both instances.

District	Gulu, 2007		Bundibugyo, 2007		Kibaale, 2012		Luwero, 2012	
Time	Date	Days since onset	Date	Days since onset	Date	Days since onset	Date	Days since onset
Onset of strange disease in community	19/09/2000	0	07/08/2007	0	12/6/2012	0	13/10/12	0
Report to Ministry Health	9/10/2000	20	27/09//2007	51	12/07/2012	30	7/11/2012	24
Investigation: Blood sampled	12/10/2000	23	29/09/2007	53	13/07/2012	31	8/11/2012	25
Blood confirmation Ebola	14/10/2000	25	28/11/2007	60	27/07/2012	45	12/11/2012	29
Declaration national action	15/10/2000	26	29/11/2007	61	28/07/2012	46	13/11/2012	30
Last case	14/01/2001	91	08/01/2008	71	14/08/2012	63	17/11/2012	34
Total days epidemic lasted		**117**		**101**		**63**		**34**
From laboratory confirmation to last case		91		41		17		5

Source: Ebola situation analysis reports 2000-2012

Table 2. Timelines from onset of illness to containment by district, Uganda, 2000–2012.

District	Identified by mobile teams	Revalidated by supervisors as cases	Regarded by supervisors as non-cases	Positive predictive value (%)
Gulu	1069	536	533	50.1
Bundibugyo	192	116	76	60.4
Kibaale	115	24	91	20.8
Luwero	36	7	29	19.4

*. Reclassified later to 425 cases only.

Table 3. Positive predictive value by case definition by district, Uganda.

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4.2 Validity of case definition

There were weaknesses in the application of the clinical syndrome case definition. The sensitivity and specificity of the definition were not known. The positive predictive value of the criteria used was low (Table 3). Some atypical Ebola cases presented without fever or bleeding. Fever was absent in 15% of cases while bleeding tendencies were observed only in 30-53% of admissions in Gulu. The validity of the case definition too was not known at local level. The positive predictive value of the case definition was low. Reassessment by supervisors validated less than half as true cases. Table 3 shows the low positive predictive values in the districts of Luwero (19.4%), Kibaale (20.8%), Bundibugyo (60.4%) and Gulu (50.1%).

4.3 Laboratory -challenges in reliability

Laboratory tests helped in the management of admissions and their discharge. Simple tests were used to detect and confirm Ebola: PCR, antigen detection, and immunoglobulin 1g M, and very rarely virus isolation. Surprisingly, less than 50% of the "suspected" and "probable" cases yielded positive laboratory results. Only half of the suspected and probable cases yielded positive laboratory results (Table 4). This low positive predictive value for the laboratory tests is a major weakness and delayed early diagnosis and action. The sensitivity and specificity and positive predictive values of the tests were also not known. The local validation of these tests is therefore essential. It is therefore critical to build laboratory capacity and skills at the national level to support outbreak management as well as conduct serosurveys in the population.

Laboratory status	Number	Proportion %
Gulu district		
Laboratory positive	195	45.8
Bundibugyo district		
Laboratory positive	42	21.9
Laboratory negative	74	38.5
Laboratory negative but probable	76	39.6
Total tested	**192**	**100**
Total lab positive and probable combined (42+76)/192	116	60.4

Table 4. Proportion of positive laboratory results of suspected Ebola cases by district, 2000–2012.

5 Case management: challenges and opportunities

5.1 Infection control and barrier nursing

Despite availability of personal protective materials, gaps remained in the practice of barrier nursing. These gaps were more pronounced among support staff especially drivers, cleaners

and attendants. In Gulu, nosocomial infection persisted as 64% of the 31 health care workers got infected after the measures were put in place. Of the 6 health care workers infected in Masindi, five got infected after barrier nursing was instituted. In contrast, the infections among staff occurred before isolation units were established in Bundibugyo. Overcrowding and inadequate staff and supplies was a common feature in the isolation wards. Proper and timely use of protective materials was sometimes not followed especially when the patients were relatives. Procedures for washing and cleansing of ambulances were often taken lightly as gadgets such as cell phones were sometimes used indiscriminately. There was complacency in the general wards. A false sense of security could have been created by establishment of isolation units hence the need to train all workers in infection control. The surgical and maternity wards in particular were a major source of new inadvertent infections. Regular drills and training are essential within healthcare settings. It must also be extended to all other support staff including administrators, drivers and relatives providing bed side nursing.

5.2 Human resource and financing challenges

Caring for Ebola is a labor intensive and costly undertaking. For instance, the estimated direct costs of treating an Ebola case in the most affected countries in West Africa (Guinea, Sierra Leone and Liberia) ranged from USD 500 to 900 for those surviving and much more for the non survivors [21]. In the USA the costs of caring for one such patient was about USD 350,000 per week [22]. In Uganda, the government budget allocation for the health sector is USD 28 per capita. Therefore external support was mobilized and funds had to be diverted from the primary health care programmes in order to mount the national response. Human resources for health too are a major constraint in health delivery in Africa. Unlike developed countries, Uganda has a doctor: population ratio of 1:25,000 and the corresponding figure for nurses is 1:4000. Low salaries and lack of motivation continue to undermine performance. Poor motivation and low salaries did not attract health care workers into the isolation units leave alone the health facility. Risk allowances were introduced and this incentive provided the much needed motivation and improved performance in the isolation units. The availability of personal protective materials maintained staff confidence and commitment in the isolation wards. This demonstrated that the workers if adequately compensated can improve performance. Thus workers when well-paid and motivated can perform beyond expectations. Compensation was provided for the health care workers who died in the line of duty, but not for the other non-medical victims. A social health insurance scheme should be considered for future outbreaks.

5.3 Improving Survivalsurvival

Differences in severity and survival were demonstrated between the two Ebola subtypes. Unlike in the Gulu outbreak, the later did not spread to other districts. The attack rates and the case fatality rates were higher in Sudan subtype (Table 5). The *c*ase fatality rate was higher (53.1%), in the Gulu outbreak compared with that in Bundibugyo (34%). The attack rates were also lower for the Bundibugyo virus than that in Gulu, p=0.001. However, the observed outcomes in severity and survival may also have been associated to differences on condition

on admission, bleeding manifestation, and possible antigenic differences. It was also observed that death was more associated with bleeding tendencies and vomiting, p= < 0.001. The long term effects on survivors showed increased risk of chronic health outcomes after recovery. Of the 70 survivors followed for 2 years in Bundibugyo, 14% had blurred vision, 28% had retro-orbital pain, and 23% had hearing loss. Difficulty in swallowing, muscle pain and memory loss was also reported [23]. Also, the Gulu Ebola survivors were unable to resume work one year post recovery [24].

Parameter	Ebola cases by case definition		
	Gulu, n= 324	Bundibugyo, n=116	
	p=value		
% Male cases (95% CI)	37 (32.0–42.4)	53 (43.5–61.7)	0.005
% Women cases (95% CI)	63 (57.7–68.2)	47 (38.3–56.5)	0.005
Attack rates/100,000 population (95% CI)	97(79–118)	43 (31–58)	
	0.001		
Case fatality rate % (95% CI)	53.1 (47.7–58.5)	34 (25.0–42.2)	0.005

Table 5. Attack rates and case fatality by district, 2000–2007.

Isolation isolated cases, provided quality care, improved survival and increased public trust. Patient survival differed from outbreak to outbreak but improved as management of palliative care was established. In Gulu, survival improved over time (**Figure 8**). Mortality declined from 100% at the onset, to just around 10% towards the end of the outbreak. Timely community detection promoted care and survival. Motivation of care givers was critical to this improved performance of health care workers. It was demonstrated that quality palliative care positively influenced survival [1]. Future interventions therefore should integrate health staff motivation in their budgets.

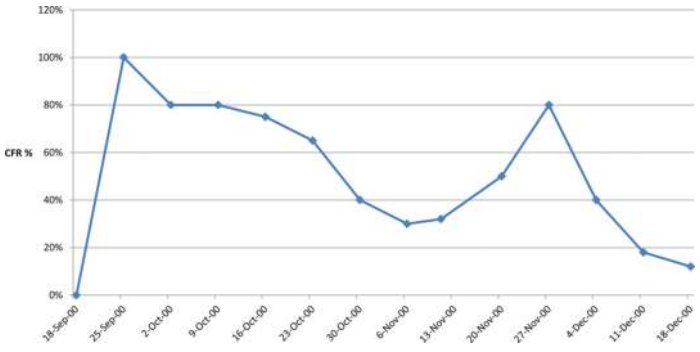

Figure 8. Case fatality rate of Ebola cases by week, Gulu district, Uganda, 2000.

6. Conclusion

Early detection and action resulted in the best outcomes for the outbreak containment. Community leadership and mobilization, including the media for action was vital in managing these Ebola outbreaks. The need to strengthen laboratory capacity for early detection of the infection cannot be overemphasized. Supportive treatment improved lives, reduced case fatality, isolated cases and indeed increased public confidence and health seeking behavior. Care and survival and not just quarantine should therefore be emphasized as a critical component of the interventions. There were serious gaps in barrier nursing as nosocomial infections continued despite institution of isolation units. Infection control strategies should be institutionalized to protect both the health workers and the support staff in the units and the general wards. There is a need to develop and implement a human resource strategy and plan that attracts rewards and retains health workers. Such plans should strengthen health care systems in order to respond effectively to future epidemics. There is a need for the international partnerships and collaboration to be strengthened so as to augment the national efforts. Such partnerships should build capacity for health systems for surveillance and care.

Surveillance of emerging infections should be strengthened by establishing networks and centers of excellence for sharing of information and monitoring emerging infections. Inventories and rapid response teams at national and international level should be shared so as to provide timely emergency stocks, expertise and technical support. The large outbreaks especially in West Africa impacted badly on social services and the economy. Early detection and action based on community effort remains the best option for low resource settings, which capacity should be integrated into primary health care and village health teams to mitigate post Ebola health outcomes.

Appendices

APPENDIX 1
Adapted WHO *Case definition of Ebola virus disease for Uganda*

Suspected cases	• Sudden onset of *fever and at least 4 of the following* symptoms in a resident of or visitor to the affected areas in the district: *vomiting, diarrhea, abdominal pain, conjunctivitis, skin rash, unexplained bleeding from any body part, muscle pain, intense fatigue, difficulty swallowing, difficulty breathing, hiccups, or headache* since suspected onset, • OR sudden *onset of fever* in any person who had *contact* with a person with *suspected, probable, or confirmed* EHF • OR *sudden death* in a person in the community without any other explanation.
Probable case	• *Suspected* EHF in any person (dead or alive) with *at least* 3 of the following symptoms: *vomiting, diarrhoea, or unexplained bleeding from any site, conjunctivitis, or skin rash*; AND

	• Either an epidemiologic *link* to a person with probable or confirmed EHF, OR
	• Either no specimen collected for laboratory testing or a negative laboratory result in a specimen collected 0-3 days after onset of symptoms in a person with suspected EHF.
Confirmed case	• Laboratory confirmation of infection by isolation of virus from any body fluid or tissue, OR
	• Detection *of viral antigen* in any body fluid or tissue by antigen-detection ELISA, reverse transcription-PCR, or immuno-histochemistry, OR
	• Demonstration of serum Ebola virus-specific IgG antibodies by ELISA, with or without IgM, in any person with suspected or probable EHF.
Contact	A person who had slept in the same household and/or had direct physical contact with a person (dead or alive) with suspected, probable, or confirmed EHF, and/or had been exposed to an infected person or to an infected person's secretions, excretions, tissues, or linen within 3 weeks after that person's onset of illness.

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