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Short Communication

Recrudescence of Ebola virus disease outbreak in West Africa, 2014–2016

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ABSTRACT

Objectives: There have been errors in determining the end of the Ebola virus disease (EVD) epidemic when adhering to the criteria of the World Health Organization. The present study aimed to review and learn from all known recrudescence events in West Africa occurring in 2014–2016.
Methods: Background mechanisms of five erroneous declarations in Guinea, Liberia, and Sierra Leone during 2014–2016 were reviewed.
Results: Three cases of recrudescence were suspected to have been caused by sexual contact with survivors, one to be due to international migration, and one was linked to a potentially immunocompromised mother. The three sexual transmission events involving survivors—the first two in Liberia and one in Sierra Leone—required 164 days, >150 days, and approximately 180 days, respectively, from discharge of the survivors to confirmation of the recrudescent case.
Conclusions: The events of recrudescence were associated with relatively uncommon routes of transmission other than close contact during burial or care-giving, including sexual transmission, possible immunocompromise, and migration. Recognition of the sexual transmission risk among survivors could potentially involve discrimination, which may lead to under-ascertainment.
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Introduction

The end of an outbreak must be determined objectively (Nishiura et al., 2016). For the Ebola virus disease (EVD) outbreak in West Africa from 2014 to 2016, the World Health Organization (WHO) recommended securing 42 days (World Health Organization, 2015), or twice the observed maximum incubation period, from the time at which the last case was found negative for the virus at second testing. Subsequently, the country without EVD cases would enter a period of heightened surveillance lasting 90 days to monitor for any other occurrence of infection.

As there have been errors in determining the end of an outbreak when adhering to the criteria mentioned above, it would be valuable to learn from the events of EVD recrudescence occurring in Liberia, Guinea, and Sierra Leone. This will inform wiser decision-making in the future. The present study aimed to review all known recrudescence events in West Africa occurring during the period 2014–2016.

Materials and methods

A recrudescence event was defined as the reappearance of at least one confirmed case of EVD in a country where the end of EVD had been declared in advance. The term 'recrudescence' is used, because the reappearance of EVD in West Africa has been associated with persistent activity of infection arising from already infected humans. WHO reports and other sources were reviewed in an analysis of all known recrudescence events occurring from 2014 to 2016 (World Health Organization, 2016; Sheri, 2015; Farge and Giahyue, 2015; Dahl et al., 2016; Dakaractu, 2016; Center for Infectious Disease Research and Policy, 2016).

In the statistical analysis, the background mechanisms of erroneous declarations of the end of an EVD outbreak in West Africa during 2014–2016 were investigated. A survey of the demographic variables of recrudescent cases was performed (i.e., age and sex), and the most likely source of infection and the dates of illness onset and confirmation were also obtained. By examining the date of confirmation of the purported last case (i.e., the case before the recrudescent case) and the date on which the outbreak

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was declared to have ended, the following were calculated: (1) the time interval between successive confirmations, (2) the number of days from burial or the second negative testing result of the last case, and (3) the number of days in heightened surveillance.

Results

A total of five cases of recrudescence were identified (Figure 1): three occurred in Liberia and one each in Guinea and Sierra Leone (World Health Organization, 2016; Sheri, 2015; Farge and Giahyue, 2015; Dahl et al., 2016; Dakaractu, 2016; Center for Infectious Disease Research and Policy, 2016). Two were male and three were female (Table 1). One of the three cases in Liberia was caused by inter-country migration, and therefore may be better stated as recurrence rather than recrudescence (World Health Organization, 2016; Dakaractu, 2016). That case was associated with viral exposure at a funeral in Guinea (Dakaractu, 2016). Sexual transmission involving survivors was suspected for three cases (World Health Organization, 2016; Sheri, 2015; Center for Infectious Disease Research and Policy, 2016). Of these, one in Liberia was documented as linked to a survivor who had recovered 164 days before confirmation of the recrudescent case (Dahl et al., 2016). Similarly, the recrudescent female case in Sierra Leone is believed to have been due to sexual transmission (World Health Organization, 2016; Center for Infectious Disease Research and Policy, 2016). In Guinea, three probable unconfirmed deaths considered as consistent with EVD were observed in advance of the confirmed recrudescence on March 17, 2016 (World Health Organization, 2016; Dahl et al., 2016; Dakaractu, 2016). Virologically, the causative virus of the recrudescence event was demonstrated to be closely related to the virus isolated previously in the same country (Dahl et al., 2016; Dakaractu, 2016). The route of transmission in a 15-year-old male in Liberia remains unknown, but intra-household transmission during the mother's pregnancy from the immunocompromised mother to the 15-year-old boy was suspected (World Health Organization, 2016; Farge and Giahyue, 2015).

The time interval from laboratory confirmation of the perceived last case to confirmation of the recrudescent case ranged from 101 to 140 days (Table 1). All observed intervals were longer than the mean serial interval; i.e., the time from illness onset in the primary case to that in the secondary case, estimated at 15.3 days (WHO Ebola Response Team, 2016). From the latest date of either burial or second negative test result, it took 92–122 days to confirm the cases of recrudescence – all more than double the 42-day waiting period. Recrudescence events occurred 51–79 days after the declaration of the end of the outbreak. The time lags from declaration to recrudescence were all within the 90-day period of heightened surveillance. The three sexual transmission events involving survivors—the first two in Liberia and one in Sierra Leone—required 164 days, >150 days, and approximately 180 days, respectively, from discharge of survivors to confirmation of the recrudescent case.

Discussion

The recrudescence events were not associated with the common routes of EVD transmission, such as close contact during burials or care-giving, but rather with other routes or reasons, including sexual transmission, possible immunocompromise, and migration. While use of a 42-day waiting period posed practical difficulties from 2014 to 2016, the present exercise was not intended to criticize that fixed, transparent criterion. Even with the use of a more objective approach, including serial interval distribution (e.g., as applied for Middle East respiratory syndrome in South Korea (Nishiura et al., 2016)), this may not have sufficiently captured the involvement of sexual transmission and other reasons for recrudescence.

The need to consider the prevention of sexual transmission via survivors when declaring the end of an epidemic poses a dilemma. This is because the recognition of such a risk among survivors could potentially involve discrimination, and fear of stigma may lead to under-ascertainment.

The results of this study suggest that the supposed end of an EVD epidemic could be divided objectively into several different types. For instance, the restriction of movement for cases and exposed individuals—i.e., socially 'costly' interventions—could be ceased through use of a 42-day waiting period. This may not necessarily ensure a long enough waiting time for an uncommon route of infection. Meanwhile, heightened surveillance and the avoidance of risky sexual intercourse should be set at >180 days, i.e. the observed maximum in this study, echoing a study on the transmission network (Mate et al., 2015); ideally this duration should be set at 9 months considering the persistence of the virus in semen (Deen et al., 2015). These are essential to monitor and prevent recrudescence through uncommon routes of transmission. It is intended to investigate the objective determination of the outbreak in a more explicit manner using mathematical modeling techniques.

Ethical approval

Not applicable.

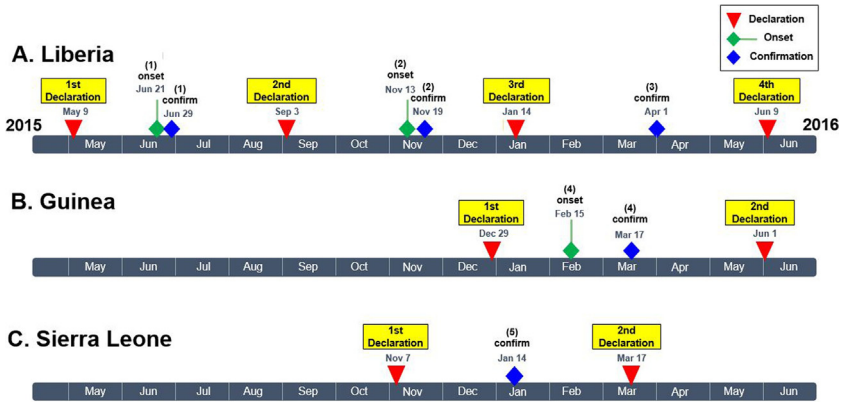


Figure 1. Time-line of events: declaration of Ebola-free status and of recrudescence in Liberia, Guinea, and Sierra Leone. The time at confirmation of recrudescent cases is indicated with blue diamonds; the time of illness onset is also indicated with a green diamond, if available.

Table 1
Recrudescence of Ebola virus disease in West Africa, 2014–2016.

Country	Source of infection	Age, years	Sex	Interval between successive confirmations (days)[a]	Days from burial or second negative testing result of last case[b]	Days in heightened surveillance	Ref.
Liberia	Suspected sexual intercourse	17	Male	101 (Mar 20 to Jun 29, 2015)	93	51	World Health Organization (2016), Sheri (2015), Farge and Giahyue (2015), Dahl et al. (2016)
Liberia	Unknown, suspected bodily fluids (of pregnant mother)	15	Male	130 (Jul 12 to Nov 19, 2015)	119	77	World Health Organization (2016), Sheri (2015), Farge and Giahyue (2015), Dahl et al. (2016)
Liberia	Migration, bodily fluids (funeral)	30	Female	133 (Nov 20, 2015 to Apr 1, 2016)	120	78	World Health Organization (2016), Sheri (2015), Farge and Giahyue (2015), Dahl et al. (2016), Dakaractu (2016)
Guinea	Suspected sexual intercourse and under-ascertainment	37	Female	140 (Oct 29, 2015 to Mar 17, 2016)	121	79	World Health Organization (2016), Dakaractu (2016)
Sierra Leone	Suspected sexual intercourse	22	Female	123 (Sep 13, 2015 to Jan 14, 2016)	111[c]	68	World Health Organization (2016), Center for Infectious Disease Research and Policy (2016)

[a] Duration from confirmation of the last case to confirmation of the re-emerging case.
[b] Duration from burial or the second negative testing result of the last case to confirmation of the re-emerging case.
[c] A declaration was made on the day following the negative laboratory test and, thus, the specified date minus 42 does not equal 68 days, as in the next column to the right.

Conflict of interest

The authors declare no conflicts of interest.

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