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Stillbirths and neonatal deaths surveillance during the 2014–2015 Ebola virus disease outbreak in Sierra Leone

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Abstract

Objective: To determine the rate of stillbirth and neonatal death reporting and testing for Ebola virus during the 2014–2015 Ebola virus disease (EVD) outbreak in Sierra Leone.

Methods: A cross-sectional study was performed using information from the Sierra Leone National Ebola Laboratory database to identify stillbirths and neonatal deaths that had been tested for Ebola virus from July 2, 2014, to October 18, 2015. Outcomes included the percentage of all tested deaths attributable to stillbirths and neonatal deaths, the proportion of stillbirths and neonatal deaths attributable to Ebola virus, and the annualized rate of stillbirths and neonatal deaths.

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AUTHOR CONTRIBUTIONS

TO contributed to study conception, study design, data analysis, data interpretation, drafting the manuscript, and revising the manuscript. SDB contributed to study conception, data interpretation, drafting the manuscript, and revising the manuscript. ASN contributed to obtaining local approval for the study, data interpretation, and revising the manuscript. DJJ, SE, and JTR contributed to study conception, study design, data interpretation, and revising the manuscript. KS contributed to data analysis, data interpretation, and revising the manuscript. DMD contributed to data interpretation and revising the manuscript.

CONFLICTS OF INTEREST

The authors have no conflicts of interest.

Results: In total, 1726 stillbirths and 4708 neonatal deaths were tested for Ebola virus, representing 2.6% and 7.2% of the total deaths tested (n=65 585), respectively. Of these, 25 stillbirths and neonatal deaths tested positive, accounting for 0.3% of EVD cases. In 2015, the annualized total number of reported stillbirths was higher than expected (3079 vs 1634), whereas reported neonatal deaths were lower (6351 vs 7770).

Conclusions: Stillbirth and neonatal death reporting and testing improved over time. Systematic recording of these indicators might be used alongside retrospective surveillance to respond to the adverse effects of EVD on maternal and child health and guide response efforts for subsequent outbreaks.

Keywords

Ebola virus disease; Maternal and child health; Mortality; Neonatal death; Sierra Leone; Stillbirth; West Africa

1 | INTRODUCTION

The 2014–2015 Ebola virus disease (EVD) outbreak was the first to occur in West Africa and the largest recorded to date. A total of 14 124 people were affected by EVD in Sierra Leone, with a fatality rate of 28%.[1]

Despite the size and scope of the EVD outbreak, little is known about its effect on the delivery of maternal and child health (MCH) services and other health outcomes in Sierra Leone. There were reports that pregnant women avoided healthcare facilities during the outbreak owing to distrust and fear of contracting EVD.[2] Similar to Sierra Leone, available data also indicated a decline in the use of MCH services, including prenatal care visits, treatment of pregnant women for malaria, deliveries in a healthcare facility, and outpatient pediatric visits, during the EVD outbreak in Guinea and Liberia.[3–6] Reduced facility hours, facility closures, and service suspensions were regional and could be facility-specific, suggesting that the impact was not uniformly distributed across the region.[3,5–7]

Two reports from previous outbreaks indicate that pregnant women with EVD are at increased risk of severe illness and death, and that fetal and neonatal outcomes are very poor, with no previously documented neonatal survivors beyond 19 days of life.[8,9] Five case reports and four small descriptive cohort studies identified 13 pregnant women with EVD during the outbreak in West Africa, of whom eight survived, four died, and one had an unknown outcome.[10–17] Among the pregnancies reported, all except one ended in spontaneous abortion, fetal loss, or neonatal loss.[10–18] However, one neonate that had been exposed in utero was declared EVD-free after treatment with two experimental drugs and at 12-months of age, she showed age-appropriate neurodeveolpment with absent pathology.[18]

Before the EVD outbreak, Sierra Leone had made substantial progress regarding several MCH indicators.[19] Nonetheless, this country still had one of the highest mortality rates worldwide for mothers, infants, and children aged younger than 5 years.[19–21] According to the 2013 Sierra Leone Demographic and Health Survey,[19] the stillbirth ratio and neonatal death rate were 8.2 and 39.0 per 1000 live births, respectively. Furthermore, Sierra Leone

did not meet the 2015 United Nations Millennium Development Goals that aimed to reduce the mortality rate for children aged younger than 5 years by two-thirds, reduce the maternal mortality ratio by three-quarters, and achieve universal access to reproductive health.[20]

Although the effect of the EVD outbreak on MCH service delivery and outcomes in Sierra Leone is unclear, data collected through national surveillance for deaths during the outbreak can provide some insight into the number of stillbirths and neonatal deaths that occurred during that period. In October 2014, the Government of Sierra Leone required, through the Safe and Dignified Burial Mandate, that all deaths nationwide be reported and investigated, and all the deceased be tested for Ebola virus and safely buried.[22,23] The data collected under this system provide a unique opportunity to assess stillbirths and neonatal mortality that occurred during the EVD outbreak.

The objective of the present study was to determine the number of stillbirths and neonatal deaths that underwent Ebola virus testing during the outbreak in Sierra Leone, as well as the proportion of such deaths that could be attributed to EVD.

2 | MATERIALS AND METHODS

A cross-sectional study was performed using information from the Sierra Leone National Ebola Laboratory database to identify all still-births and neonatal deaths that had been tested for Ebola virus from July 2, 2014, to October 18, 2015. The current investigation did not meet the definition of research involving human subjects, as determined from ethical review by the Centers for Disease Control and Prevention (CDC), Atlanta, USA.

The Sierra Leone National Ebola Laboratory database was developed during the EVD outbreak to capture all the results of reverse transcription polymerase chain reaction (RT-PCR) testing for Ebola virus that had been performed at any of the country's laboratories. The database includes results of tests performed on live and deceased individuals since July 2, 2014, that were reported to the Sierra Leone Ministry of Health and Sanitation. Test results included sociodemographic information (name, age, sex, and district of death); a unique identifier; laboratory identification number; date of symptom onset; specimen type; date on which specimen was collected, received, and tested; results of Ebola virus RT-PCR testing; and a comment field where pertinent observations could be added.

No single variable in the Sierra Leone National Ebola Laboratory database identifies a stillbirth or a neonatal death. Therefore, an exploratory analysis of the data was performed to develop a comprehensive list of terms used in the free text comment field to identify such events. A confirmed stillbirth was then defined as any laboratory record that contained the word "stillbirth" or "stillborn" and had either a stated age of zero or no information given on age. A probable stillbirth was defined as either any record that gave an age of zero but did not contain the words "stillbirth" or "stillborn" in the free text comment field or any record that contained the word "stillbirth" or "stillborn" and listed the age as older than zero but younger than 1 month. A neonatal death was defined as any record that listed the age as 1 month or younger (but higher than zero), did not contain the words "stillbirth" or "stillborn,"

and had a specimen type listed that was consistent with postmortem testing (tissue sample, oral swab, or cardiac puncture).

As the Sierra Leone National Ebola Laboratory database contains records of all tests performed, an individual who was tested multiple times for EVD could have multiple records. Therefore, the database was manipulated to create a dataset with one record per individual: any records marked “repeat,” “retest,” or “follow-up” were removed. In all, 11 384 duplicate records (10.9% of all laboratory records) were identified and removed.

The numbers of stillbirths and neonatal deaths tested, and the percentage of all deaths that they accounted for, were plotted by week and then compared with the number of confirmed EVD cases reported in Sierra Leone. The expected numbers of stillbirths and neonatal deaths were estimated by multiplying the reported 2013 stillbirth ratio (8.2 per 1000 live births) and the neonatal death rate (39.0 per 1000 live births) by the total number of live births reported by the Sierra Leone Office of Birth and Deaths in 2013. National data were used to estimate the expected numbers of stillbirths and neonatal deaths for each district because district-specific ratios and/or rates are not published.

Reporting of deaths and subsequent laboratory testing for Ebola virus was not routinely performed for most deaths until after the Safe and Dignified Burial Mandate was declared in October 2014. The total number of deaths tested for Ebola virus increased until the last week of April 2015 and stabilized thereafter. The annualized numbers of stillbirths and neonatal deaths were estimated using deaths tested for Ebola virus after April 27, 2015 (week 18), dividing this number by the number of weeks in which the data were collected (n=25), and then multiplying the result by the number of weeks in a year (n=52).

The Sierra Leone National Ebola Laboratory database was downloaded on October 18, 2015. All analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC, USA).

3 | RESULTS

A total of 104 662 samples were tested for Ebola virus during the present study period. Of these, 65 585 (62.7%) tests were performed postmortem.

Figure 1 shows the time course of RT-PCR testing during the EVD outbreak. Following implementation of the Safe and Dignified Burial Mandate, the total number of laboratory tests performed weekly and the number of tests performed postmortem increased during week 1 of 2015 and leveled out after week 18 of 2015.

Stillbirths and neonatal deaths documented during the EVD outbreak are outlined in Figure 2. A total of 1726 stillbirths (371 confirmed and 1355 probable) and 4708 neonatal deaths were tested for Ebola virus. Stillbirths and neonatal deaths accounted for 2.6% and 7.2% of the total deaths tested (n=65 585), respectively. The absolute numbers of both stillbirths and neonatal deaths tested increased until week 18 of 2015 and remained stable thereafter. However, as shown in Figure 2A, stillbirths and neonatal deaths as a proportion of all deaths tested increased over the entire period of observation, even after week 18 of 2015. The median age of the neonatal deaths was 1 day (interquartile range 1–5 days).

Among the 6434 stillbirths and neonatal deaths tested, 25 (0.4%) cases—comprising three stillbirths and 22 neonatal deaths— had positive RT-PCR test results for Ebola virus, confirming death had occurred in the presence of Ebola virus infection. Stillbirths and neonatal deaths accounted for 0.3% of all confirmed EVD cases reported. Confirmed EVD-related stillbirths and neonatal deaths occurred from week 42 of 2014 through to week 22 of 2015 (Fig. 2B). The number of confirmed EVD-related stillbirths and neonatal deaths peaked during week 52 of 2014, which was after the peak for total confirmed EVD cases.

As shown in Table 1, the numbers of stillbirths and neonatal deaths tested for Ebola virus varied over time and by district of residence. The Western Area district had the highest number of stillbirths (n=450) and neonatal deaths tested (n=945). The percentage of all deaths tested that were stillbirths ranged from 0.3% in the Kailahun district to 10.4% in the Kono district. The percentage of all deaths tested that were neonatal deaths ranged from 2.2% in the Kailahun district to 11.9% in the Western Area district. The annualized number of stillbirths was higher than expected among nine of the 13 districts (69.2%), whereas the annualized number of neonatal deaths was higher than expected among five (38.5%) of the 13 districts.

4 | DISCUSSION

Following implementation of the Sierra Leone Safe and Dignified Burial Mandate, the study found that the total numbers of stillbirths and neonatal deaths tested increased initiallly and then over time stabilized. Twice as many stillbirths were estimated to have occurred than were expected on the basis of previously available data. The number of neonatal deaths decreased slightly when compared with the expected numbers.

The reasons for these findings are unclear. Possible explanations include increased reporting of stillbirths as a result of the national burial mandate; increased pregnancy loss as a result of the usual causes of fetal loss (e.g. malaria) in a setting of reduced access to prenatal care and facility-based deliveries; and increased pregnancy loss as a result of Ebola virus infection. Although, reporting of deaths and subsequent postmortem testing in Sierra Leone occurred after the peak of the EVD outbreak, few stillbirths or neonatal deaths tested positive for Ebola virus. Thus, it is more likely that the rise in stillbirths observed in the present study reflects increased reporting and reduced access to prenatal services and facility-based delivery during the EVD outbreak.

The observed variability in the numbers of stillbirths and neonatal deaths reported and tested by district could reflect inconsistent implementation of the national burial mandate. Alternatively, error might have been introduced into the estimates of the expected numbers of stillbirths and neonatal deaths when the national stillbirth ratio and neonatal death rates were applied to district populations. Finally, stillbirth and neonatal death rates might naturally vary across districts because care-seeking behaviors and access to maternal services also display between-district variance. During the 2014–2015 Ebola outbreak in Guinea, investigators found that health facility hours, closures, and service suspensions were both regional and facility-specific.[3] Consequently, comparisons of numbers across districts should be made with caution.

In the present study, three stillbirths tested positive for Ebola virus, with additional information available for two of these deaths. Investigation of positive Ebola virus test results from swabs collected from these two stillbirths was the first indication that their mothers had been infected and provided evidence of transplacental transmission of Ebola virus from surviving mothers to unborn fetuses; one of these cases has been previously published.[13] These cases raise concerns that pregnancies conceived during the EVD epidemic could act as reservoirs of Ebola virus and result in exposure and subsequent infection among birth attendants. They also highlight that documentation and testing of stillbirths for Ebola virus can identify previously unknown chains of transmission in the community, warranting investigation for additional cases and contacts.

Prevention of stillbirths and neonatal deaths was likely challenging in the setting of worsening MCH services during the EVD outbreak. Similar to Liberia and Guinea, Sierra Leone probably experienced a reduced availability of health facility services.[2–5] Poor outcomes might also be linked to weak pre-outbreak healthcare infrastructure, as well as the physical and mental health effects of the outbreak on pregnant women. Indeed, such effects could last for many years.[24] The longevity of poor MCH outcomes as a result of the 2014–2015 Ebola outbreak in West Africa is unknown.

The present analysis had several limitations. First, the numbers of stillbirths and neonatal deaths per 1000 live births could not be calculated because an estimate of the number of live births that occurred during the study period was lacking. This limitation made it difficult to compare this study findings in Sierra Leone to other countries. Regardless, the numbers of stillbirths and neonatal deaths were high, and remained high even weeks after the last confirmed EVD case. This finding suggested that the stillbirths and neonatal deaths reported in the present study resulted from causes other than Ebola virus infection (e.g. malaria), although the EVD outbreak might also have affected services necessary to prevent the occurrence of still-births and neonatal deaths.

Second, it is possible that the present study underestimated the numbers of stillbirths and neonatal deaths that occurred throughout the EVD outbreak, particularly at its peak. A delay occurred in implementing the national burial mandate, and reporting of deaths did not stabilize until February 2015. Even after this point, unpublished CDC estimates suggest that, at most, 80% of expected deaths were reported nationwide. Additionally, neonatal deaths could have been underestimated because the current analysis focused on postmortem testing and excluded neonates that might have been tested while they were alive, but who subsequently died, irrespective of the test results.

Finally, the effect of EVD on stillbirths and neonatal deaths might have been underestimated. The use of observational laboratory surveillance data was limited and could not provide insights regarding the causes of stillbirths and neonatal deaths, other than coincident infection with Ebola virus at the time of death. Surveillance data on deaths among pregnant women were not available and, even if mothers were tested, the present study could not link stillbirths and neonates to their mothers from the available information. Nonetheless, the weakening of the healthcare infrastructure and care-seeking delays among pregnant women because of fear during the EVD outbreak are well-documented and could

have led to increased stillbirths and neonatal deaths from causes known before the outbreak.[6,25]

In conclusion, the findings of the present study indicated that it is both possible and important to collect data on MCH indicators during catastrophic infectious disease outbreaks that might result in disruption of the routine healthcare infrastructure. Although the overall occurrence of EVD among stillbirths and neonatal deaths was low in the present study, an alarming number of such events continued to be reported toward the end of the outbreak. During future EVD outbreak responses, consideration should be given to ensuring that routine MCH services continue. In addition, programs focused on preventing the usual causes of stillbirths and neonatal deaths should be prioritized in the post-outbreak period.

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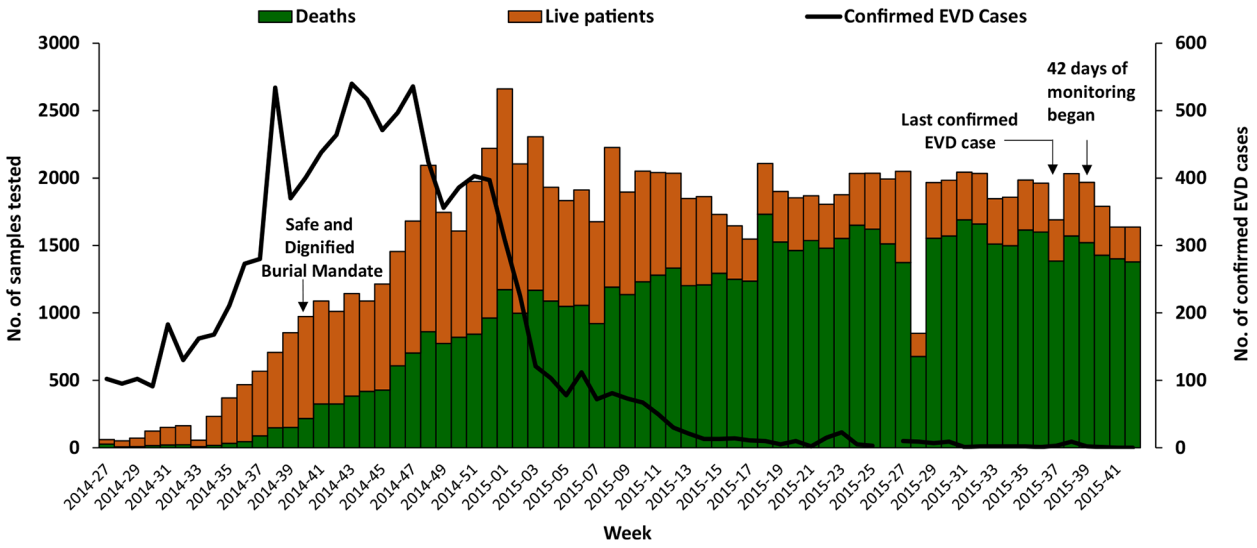

FIGURE 1.

Ebola virus testing during the outbreak in Sierra Leone. The graph outlines the number of samples tested for Ebola virus using the reverse transcription polymerase chain reaction and the number of confirmed EVD cases by week. The total number of tests performed was 104 662. The Safe and Dignified Burial Mandate required all deaths nationwide be reported and investigated, and all the deceased be tested for Ebola virus and safely buried. An EVD outbreak can be declared over after 42 days since the last confirmed case has tested negative twice for the virus on blood samples. The data were obtained from the Sierra Leone National Ebola Laboratory database for the period July 2, 2014, to October 18, 2015. Abbreviation: EVD, Ebola virus disease.

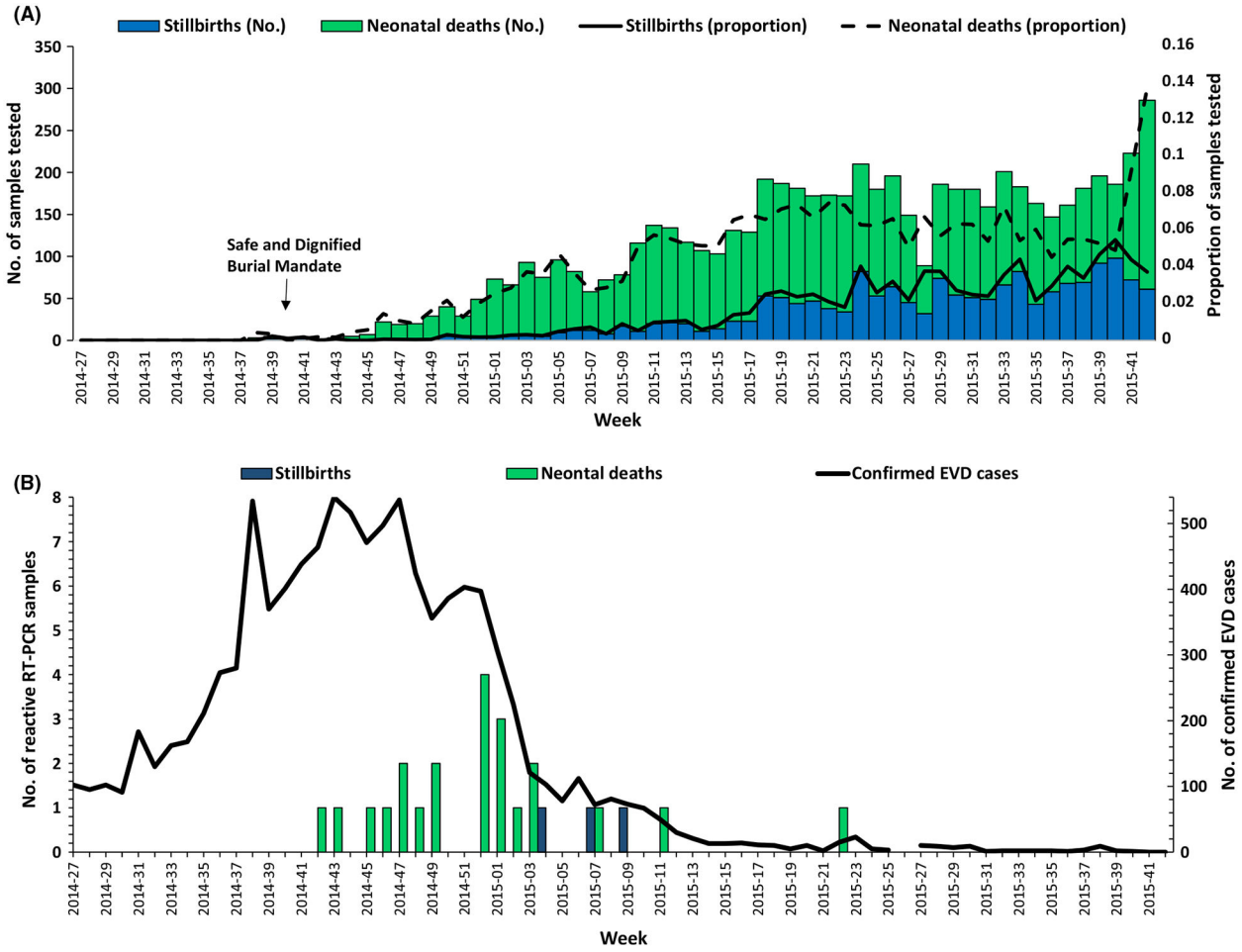

FIGURE 2.

Stillbirths and neonatal deaths surveillance during the Ebola virus outbreak in Sierra Leone. The data were obtained from the National Ebola Laboratory database for the period July 2, 2014, to October 18, 2015. (A) The graph outlines the number of stillbirths (n=1726) and neonatal deaths (n=4708) tested for Ebola virus using the reverse transcription polymerase chain reaction (RT-PCR) and the percentage of stillbirths and neonatal deaths relative to the total number of postmortem tests by week. The safe and dignified burial mandate required all deaths nationwide be reported and investigated, and all the deceased be tested for Ebola virus and safely buried. (B) The graph depicts the number of confirmed EVD cases and the number of stillbirths and neonatal deaths with positive RT-PCR test results by week. Abbreviation: EVD, Ebola virus disease.

TABLE 1

Observed, annualized, and expected stillbirths and neonatal deaths tested for Ebola virus, by district.[a]

District	Total population[c]	No. of deaths tested for Ebola virus[d]	Stillbirths[b]				Neonatal deaths[b]			
			No. tested (observed)[e]	No. tested (annualized)	No. expected[f]	Percentage of (annualized/ expected) stillbirths	No. tested (observed)[e]	No. tested (annualized)	No. expected[f]	Percentage of (annualized/ expected) neonatal deaths
Bo	575 478	6405	210 (5.4)	437	127	344.1	407 (10.5)	847	602	140.7
Bombali	606 544	4964	11(0.4)	23	108	21.3	290(10.6)	603	512	117.8
Bonthe	200 781	2095	46(3.5)	96	28	342.9	121(9.1)	252	134	188.1
Kailahun	526 379	1184	2 (0.3)	4	323	1.2	15 (2.2)	31	1538	2.0
Kambia	345 474	2949	145 (7.2)	302	57	529.8	118 (5.9)	245	272	90.1
Kenema	609 891	4424	65 (2.8)	135	159	84.9	120 (5.2)	250	758	33.0
Koinadugu	409 372	1862	8 (0.6)	17	91	18.7	146(11.7)	304	433	70.2
Kono	506 100	3146	206 (10.4)	428	170	251.8	153 (7.8)	318	807	39.4
Moyamba	318 588	4106	50(1.9)	104	25	416.0	203 (7.7)	422	118	357.6
Port Loko	615 376	6082	140 (3.5)	291	222	131.1	280 (7.1)	582	1056	55.1
Pujehun	346 461	1969	75 (5.7)	156	104	150.0	84 (6.4)	175	494	35.4
Tonkolili	531435	3923	72 (3.0)	150	115	130.4	171(7.1)	356	546	65.2
Western Area[g]	1 500 234	14 851	450 (5.7)	936	105	891.4	945(11.9)	1966	500	393.2
Total	7 092 113	57 960	1480 (4.3)	3079	1634	188.4	3053 (8.9)	6351	7770	81.7

Abbreviation: EVD, Ebola virus disease No., Number.

[a] Data obtained from the Sierra Leone National Ebola Laboratory database. Values are given as number (percentage) number, unless indicated otherwise.

[b] Data were restricted to the period with stable numbers of stillbirths and neonatal deaths reported and tested for Ebola virus using the reverse transcription polymerase chain reaction (April 27 to October 18, 2015).

[c] Data obtained from the final results of the 2015 Sierra Leone Population and Housing Census.[26]

[d] Excludes data with missing information on the district of death.

[e] Denominator for the percentage of observed tests that were stillbirths and neonatal deaths was the district-specific number of deaths tested.

[f] Expected numbers of tests for stillbirths and neonatal deaths per year for each district were calculated by multiplying the national stillbirth ratio of 8.2 per 1000 live births and the neonatal death rate of 39.0 per 1000 live births by the total number of live births reported in 2013.[19]

[g] Includes the Western Rural and Western Urban districts.