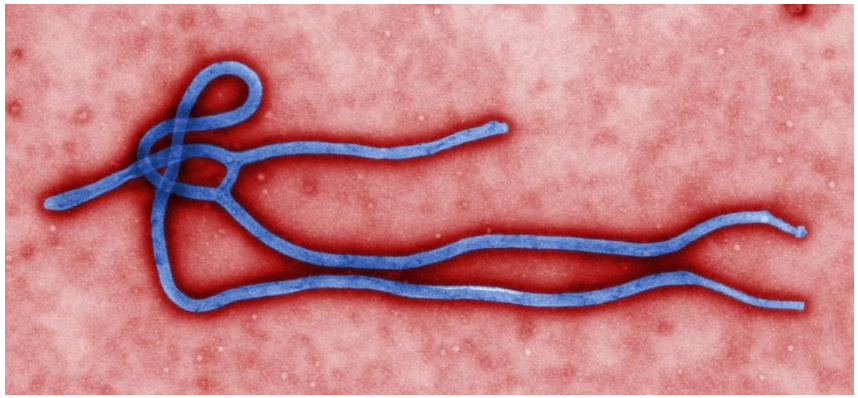
Ebola Outbreak 2014

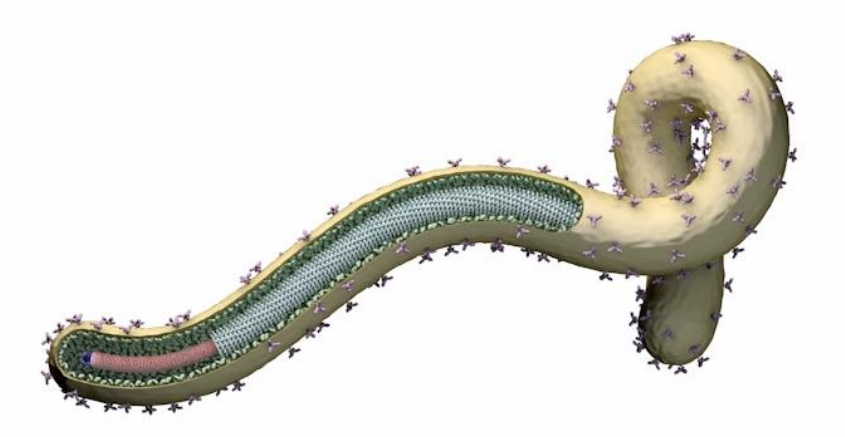
2014.11.19

채윤태

Ebola virus (EBOV)

- Group : Group V ((-)ssRNA)
- Order : *Mononegavirales*
- Family : *Filoviridae*
- Genus : *Ebolavirus*
- Species
  - ***Zaire Ebolavirus*** **(EBOV)**
  - *Sudan Ebolavirus*
  - *Tai Forest Ebolavirus*
  - *Bundibugyo Ebolavirus*
  - *Reston Ebolavirus*





"Ebola virus virion" by CDC/Cynthia Goldsmith
INTERACTIVE PERSPECTIVE, NEJM

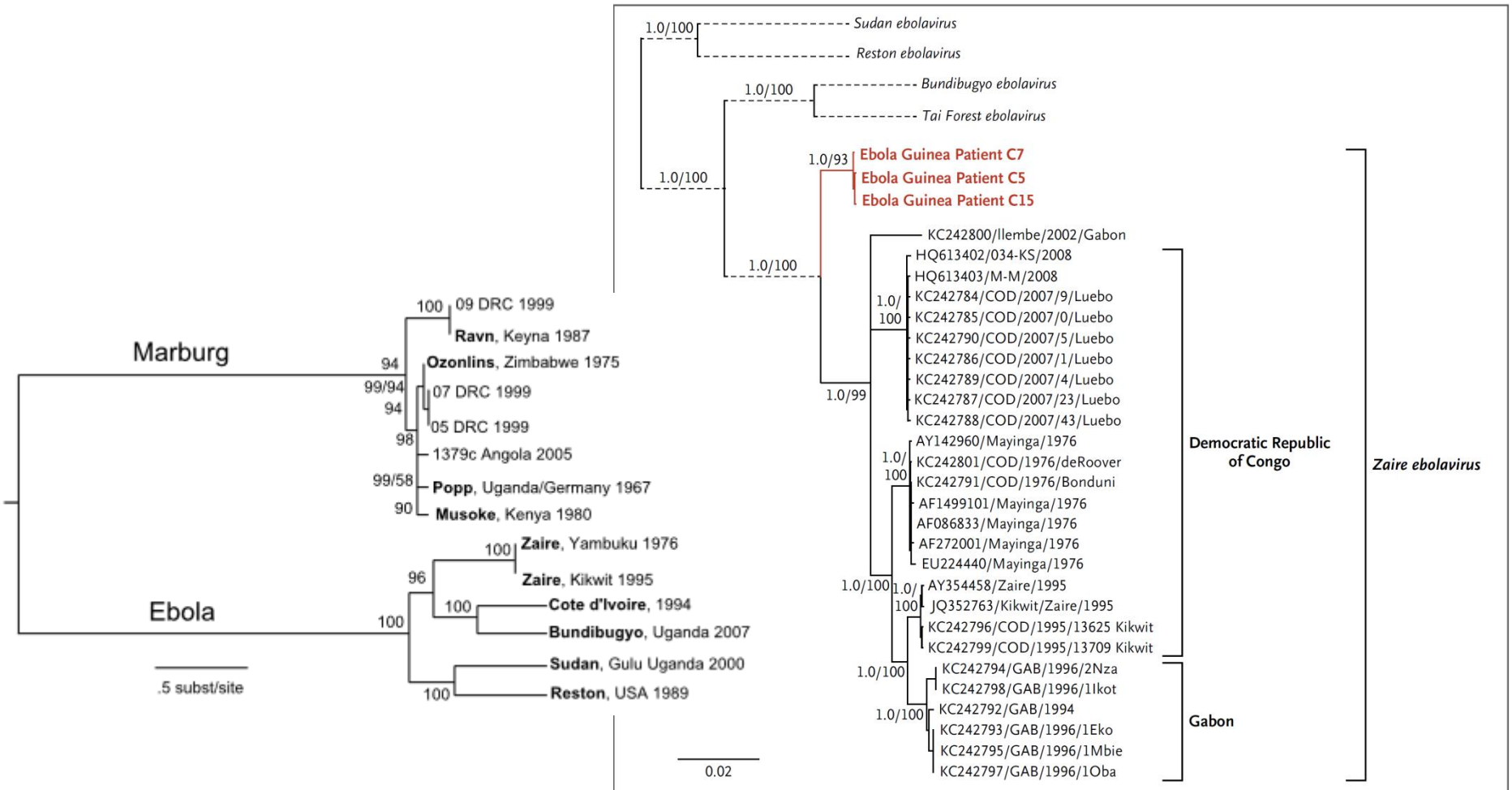


Figure 3. Phylogenetic Analysis of the Ebolavirus Genus, Including the EBOV Strains from Guinea.

The phylogenetic tree was inferred with the use of the Bayesian Markov Chain Monte Carlo method. A second tree that was inferred for the same set of sequences with a maximum-likelihood method confirmed the Bayesian tree (data not shown). Bayesian posterior probabilities and bootstrap percentages (1000 replicates of the maximum-likelihood tree) are shown on the branches. For clarity of presentation, the branches for the non-EBOV species were shortened and condensed (dashed branches). The GenBank accession number, strain designation, country of origin, and year of isolation are indicated on the EBOV branches. The EBOV Guinea strain is available from the European Virus Archive (www.european-virus-archive.com).

"Filovirus phylogenetic tree" by ChyranandChloe - Towner JS, et al.

N Engl J Med 2014;371:1418-25.

Pathogenesis

- enters the patient through mucous membranes, breaks in the skin, or parenterally and **infects** many cell types, including **monocytes, macrophages, dendritic cells, endothelial cells, fibroblasts, hepatocytes, adrenal cortical cells and epithelial cells**

- **incubation period** may be related to the **infection route** (e.g., 6 days for injection versus 10 days for contact)

- migrates from the initial infection site to **regional lymph nodes** and subsequently to the **liver, spleen** and **adrenal gland**

- **lymphocytes** undergo **apoptosis** resulting in decreased lymphocyte counts

http://www.cdc.gov/vhf/ebola/hcp/clinician-information-us-healthcare-settings.html

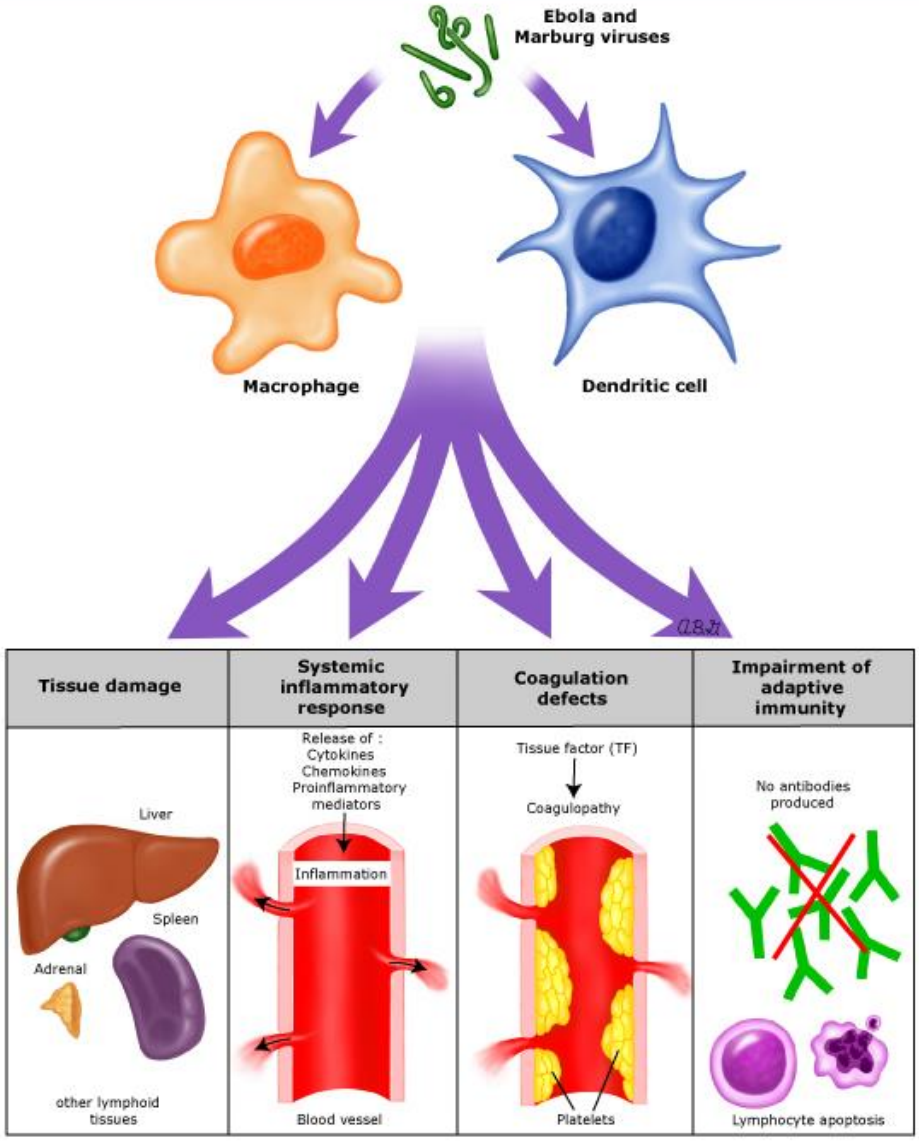
- **Hepatocellular necrosis** occurs and is associated with dysregulation of clotting factors and subsequent **coagulopathy**

- **Adrenocortical necrosis** also can be found and is associated with **hypotension** and **impaired steroid synthesis**

- trigger a **release of pro-inflammatory cytokines** with subsequent **vascular leak** and impairment of clotting ultimately resulting in **multi-organ failure and shock**

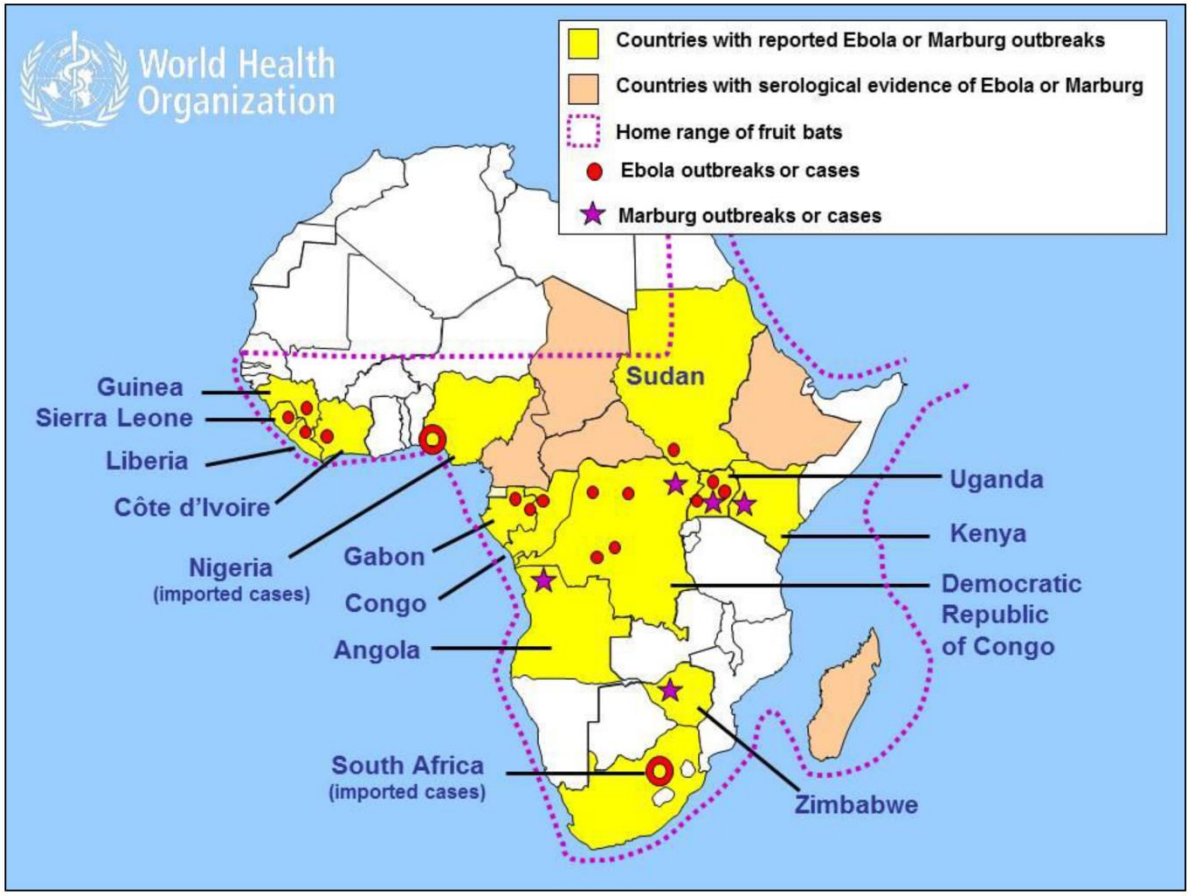
http://www.cdc.gov/vhf/ebola/hcp/clinician-information-us-healthcare-settings.html

Pathogenesis of Ebola and Marburg hemorrhagic fevers

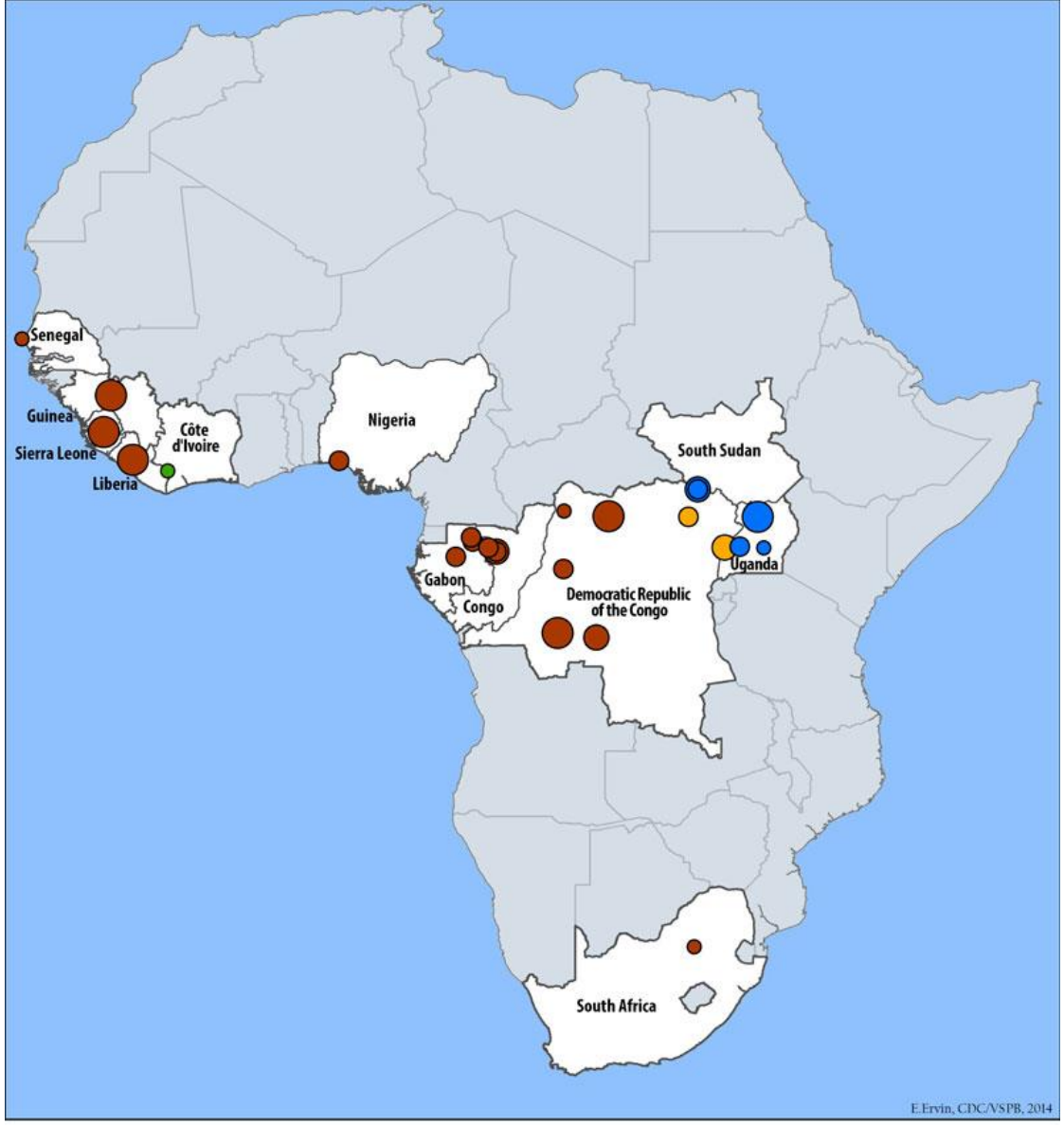


Epidemiology

Figure 1. Geographical distribution of Ebola and Marburg outbreaks in Africa (1967-2014)



WHO, Ebola and Marburg virus disease epidemics: preparedness, alert, control, and evaluation



EBOLAVIRUS OUTBREAKS BY SPECIES AND SIZE, 1976 - 2014

Species

- Zaire ebolavirus
- Sudan ebolavirus
- Tai Forest ebolavirus
- Bundibugyo ebolavirus

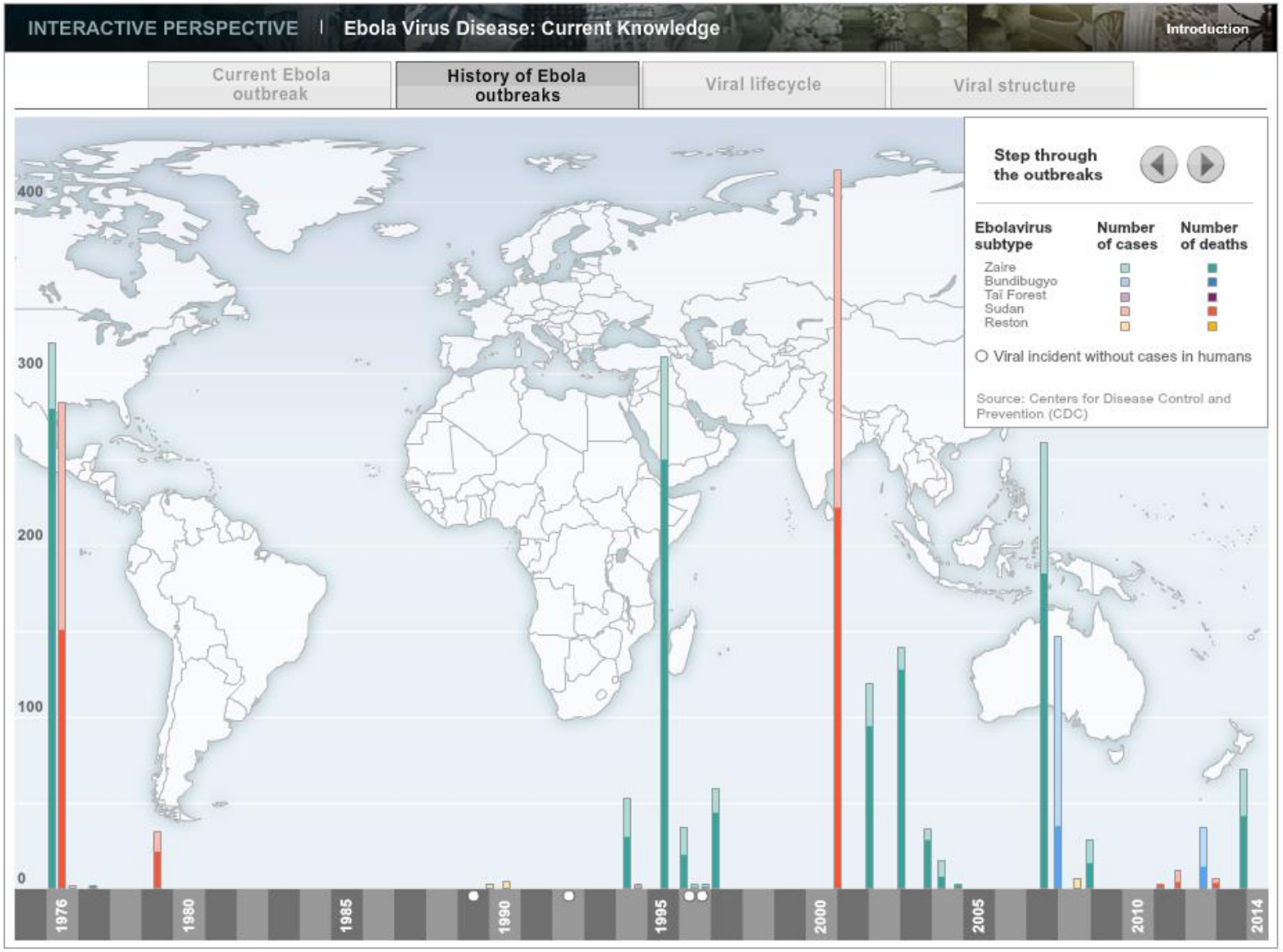
Number of Cases

- 1 - 10
- 11 - 100
- 101 - 300
- Greater than 300 reported cases

N W E S

0 245 490 980 Miles

http://www.cdc.gov/vhf/ebola/outbreaks/history/distribution-map.html



INTERACTIVE PERSPECTIVE, NEJM

Table: Chronology of previous Ebola virus disease outbreaks

Year	Country	Ebolavirus species	Cases	Deaths	Case fatality
2012	Democratic Republic of Congo	Bundibugyo	57	29	51%
2012	Uganda	Sudan	7	4	57%
2012	Uganda	Sudan	24	17	71%
2011	Uganda	Sudan	1	1	100%
2008	Democratic Republic of Congo	Zaire	32	14	44%
2007	Uganda	Bundibugyo	149	37	25%
2007	Democratic Republic of Congo	Zaire	264	187	71%
2005	Congo	Zaire	12	10	83%
2004	Sudan	Sudan	17	7	41%
2003 (Nov-Dec)	Congo	Zaire	35	29	83%
2003 (Jan-Apr)	Congo	Zaire	143	128	90%
2001-2002	Congo	Zaire	59	44	75%
2001-2002	Gabon	Zaire	65	53	82%
2000	Uganda	Sudan	425	224	53%

http://www.who.int/mediacentre/factsheets/fs103/en/

1996	South Africa (ex-Gabon)	Zaire	1	1	100%
1996 (Jul-Dec)	Gabon	Zaire	60	45	75%
1996 (Jan-Apr)	Gabon	Zaire	31	21	68%
1995	Democratic Republic of Congo	Zaire	315	254	81%
1994	Cote d'Ivoire	Taï Forest	1	0	0%
1994	Gabon	Zaire	52	31	60%
1979	Sudan	Sudan	34	22	65%
1977	Democratic Republic of Congo	Zaire	1	1	100%
1976	Sudan	Sudan	284	151	53%
1976	Democratic Republic of Congo	Zaire	318	280	88%

http://www.who.int/mediacentre/factsheets/fs103/en/

The NEW ENGLAND JOURNAL of MEDICINE

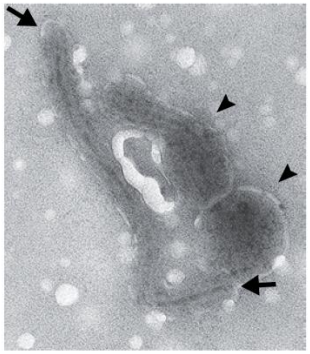
BRIEF REPORT

Emergence of Zaire Ebola Virus Disease in Guinea

Sylvain Baize, Ph.D., Delphine Pannetier, Ph.D., Pharm.D., Lisa Oestereich, M.Sc., Toni Rieger, Ph.D., Lamine Koivogui, Ph.D., N'Faly Magassouba, Ph.D., Barrè Soropogui, M.Sc., Mamadou Saliou Sow, M.D., Sakoba Keïta, M.D., Hilde De Clerck, M.D., Amanda Tiffany, M.P.H., Gemma Dominguez, B.Sc., Mathieu Loua, M.D., Alexis Traoré, M.D., Moussa Kolié, M.D., Emmanuel Roland Malano, M.D., Emmanuel Heleze, M.D., Anne Bocquin, M.Sc., Stephane Mély, M.Sc., Hervé Raoul, Ph.D., Valérie Caro, Ph.D., Dániel Cadar, D.V.M., Ph.D., Martin Gabriel, M.D., Meike Pahlmann, Ph.D., Dennis Tappe, M.D., Jonas Schmidt-Chanasit, M.D., Benido Impouma, M.D., Abdoul Karim Diallo, M.D., Pierre Formenty, D.V.M., M.P.H., Michel Van Herp, M.D., M.P.H., and Stephan Günther, M.D.

Figure 1. Map of Guinea Showing Initial Locations of the Outbreak of Ebola Virus Disease.

The area of the outbreak is highlighted in red. The main road between the outbreak area and Conakry, the capital of Guinea, is also shown. The map was modified from a United Nations map.



Meliandou Village, Guéckédou
9 Deaths from Dec. 2, 2013, to Feb. 8, 2014
2 Deaths on March 26, 2014
First recorded cases of the outbreak

(S1) Child, 2 yr of age
Fever, black stool, vomiting
Onset Dec. 2, 2013; died Dec. 6, 2013

(S2) Sister of S1, 3 yr of age
Fever, black diarrhea, vomiting
Onset Dec. 25, 2013; died Dec. 29, 2013
(S3) Mother of S1 and S2
Bleeding
Died Dec. 13, 2013
(S4) Grandmother of S1 and S2
Fever, diarrhea, vomiting
Died Jan. 1, 2014
(S5) Nurse
Fever, diarrhea, vomiting
Onset Jan. 29, 2014; died Feb. 2, 2014
(S6) Village midwife
Fever
Hospitalized in **Guéckédou** Jan. 25, 2014; died Feb. 2, 2014

Dandou Pombo Village, Guéckédou
6 Deaths from Feb. 11 to March 31, 2014

(S13) Family member of S6, took care of S6
Fever, hemorrhage
Onset Feb. 4, 2014; died Feb. 11, 2014

Dawa Village, Guéckédou
8 Deaths from Jan. 26 to March 27, 2014

(S7) Sister of S4, attended funeral of S4
Fever, diarrhea, vomiting, hemorrhage
Onset Jan. 20, 2014; died Jan. 26, 2014
(S8) Attended funeral of S4
Fever, bleeding
Onset Jan. 25, 2014; died Jan. 30, 2014

(S9–S12)
Onset Feb. 2–16, 2014; died Feb. 11–March 5, 2014

Gbandou Village, Guéckédou
3 Deaths from March 9 to March 12, 2014

Guéckédou

Guéckédou Baladou District
First onset Feb. 23, 2014
14 Deaths from March 1 to March 31, 2014
C1 C2 C5

Guéckédou Farako District
First onset Feb. 24, 2014
4 Deaths from Feb. 28 to March 25, 2014
C6 C7 Mother-in-law of S14
Died March 22, 2014

Family members of S14

S14 Health care worker at **Guéckédou** hospital
Fever, diarrhea, vomiting
Onset Feb. 5, 2014
Went to **Macenta** hospital; died Feb. 10, 2014

Macenta
15 Deaths from Feb. 10 to March 29, 2014

(S15) Doctor at Macenta hospital; took care of S14
Vomiting, bleeding, hiccups
Onset Feb. 19, 2014; died Feb. 24, 2014
Funeral in **Kissidougou**

C13 Contact with S15 and affected family members of S15
Onset March 3, 2014; died March 12, 2014
2 Further deaths in family
C8 C9 C10 C11

C12 Family member of S15 and contact of S14
Died Feb. 28, 2014, in **Nzérékoré**

C14 Contact with C12 in Macenta
Hospitalized in Macenta March 6, 2014
Died March 16, 2014, in **Nzérékoré**

Kissidougou
5 Deaths from March 7 to March 26, 2014

(S16) Brother of S15
Fever, vomiting
Onset Feb. 24, 2014; died March 7, 2014
(S17) Brother of S15
Fever, vomiting, hiccups
Onset Feb. 24, 2014; transferred from **Guéckédou** hospital to Kissidougou; died March 8, 2014

C15

The NEW ENGLAND JOURNAL of MEDICINE

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Ebola Virus Disease in West Africa — The First 9 Months of the Epidemic and Forward Projections

WHO Ebola Response Team*

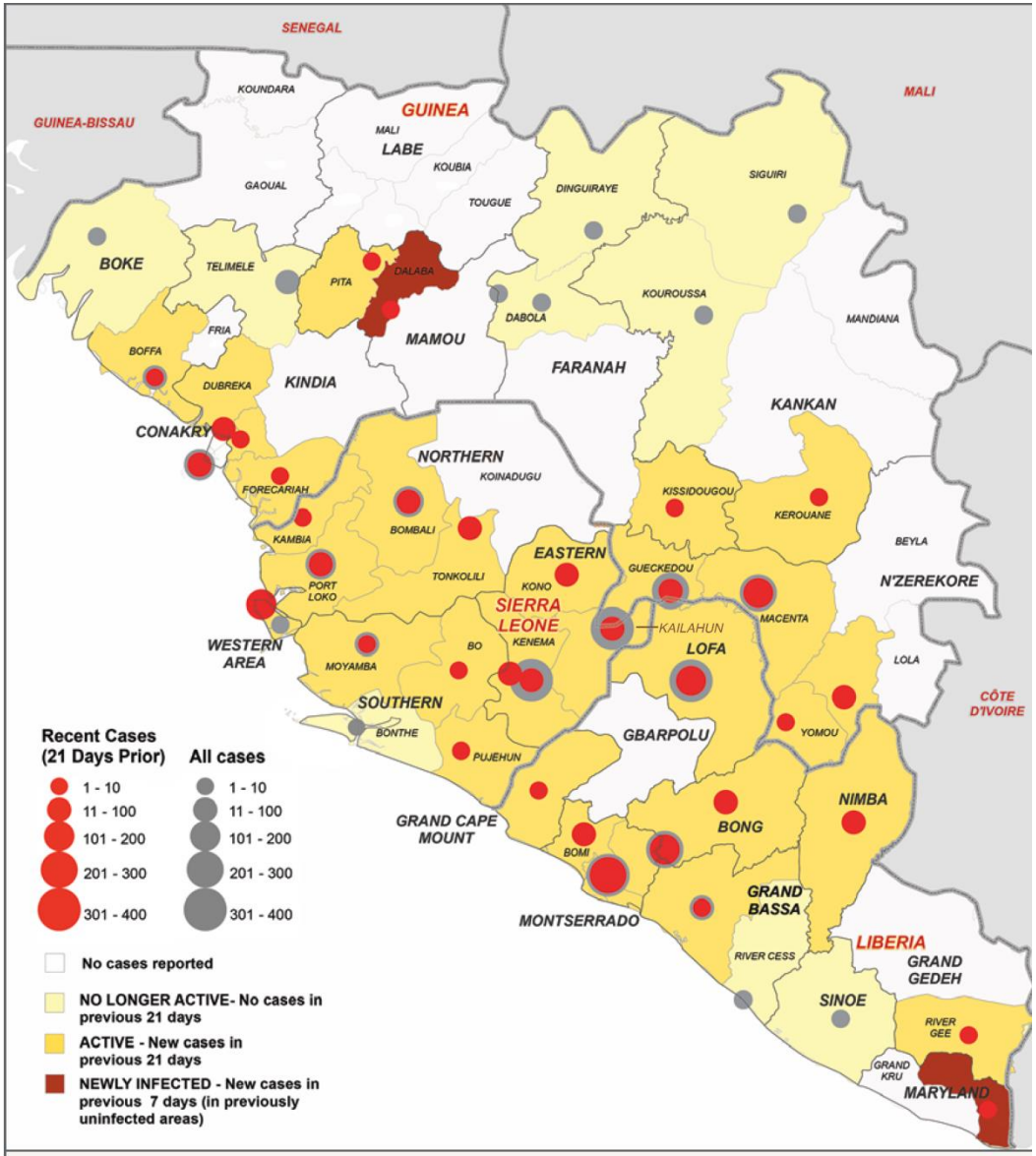


Figure 1. Districts Affected by Ebola Virus Disease in Three Countries in Africa.

The map shows the districts that have been affected by Ebola virus disease in Guinea, Liberia, and Sierra Leone. Gray circles indicate the total numbers of confirmed and probable Ebola cases reported in each affected district, and red circles the number reported during the 21 days leading up to September 14, 2014.

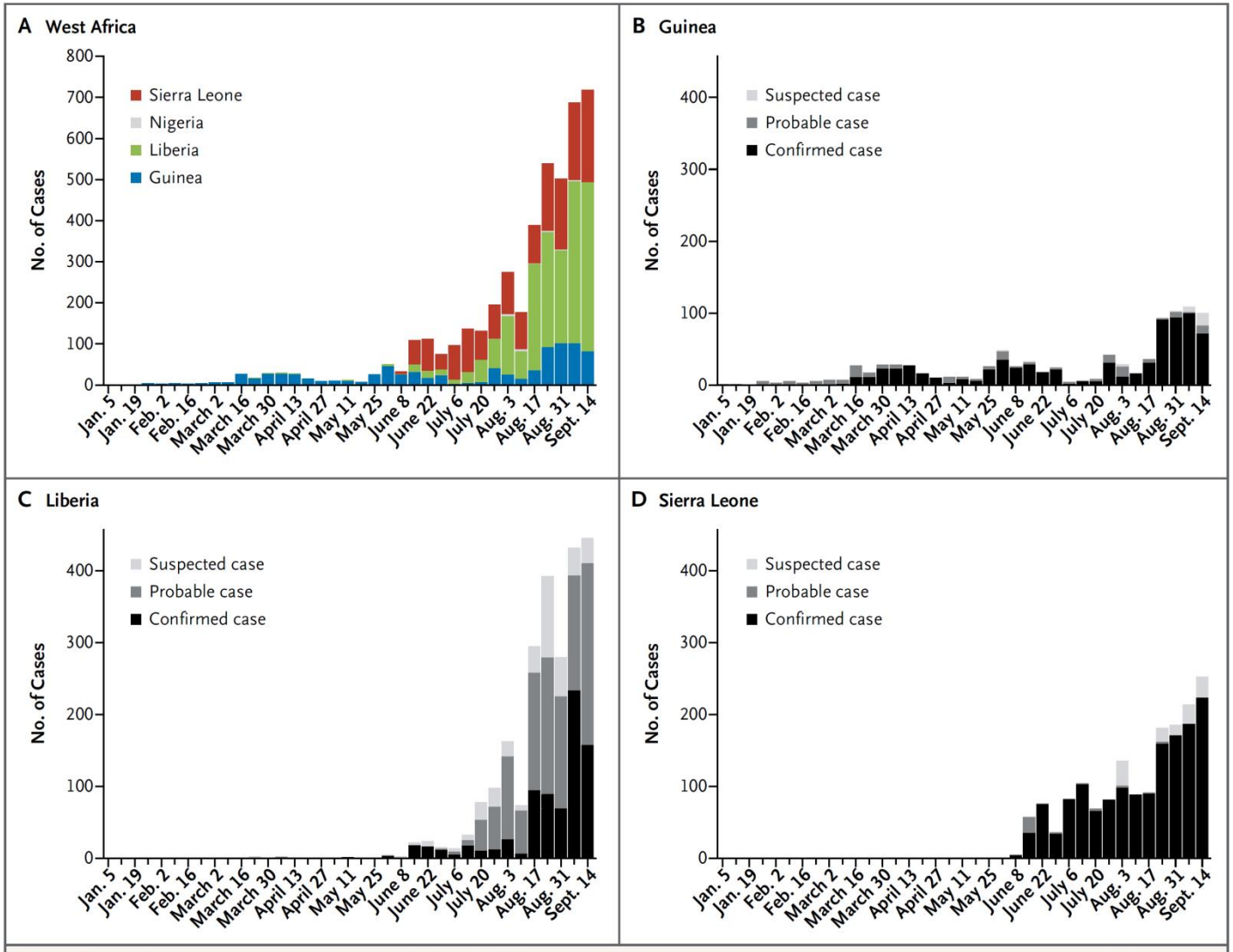


Figure 2. Weekly Incidence of Confirmed, Probable, and Suspected Ebola Virus Disease Cases.

Table 1. Demographic Characteristics and Signs and Symptoms in Confirmed and Probable Ebola Case Patients with a Definitive Clinical Outcome in Guinea, Liberia, Nigeria, and Sierra Leone.*

Variable	All Patients	Patients Who Died	Patients Who Recovered	Odds Ratio (95% CI)†
		no./total no. (%)		
Demographic characteristics				
Male sex	685/1415 (48.4)	515/1056 (48.8)	170/359 (47.4)	0.93 (0.73–1.19)
Age group				
<15 yr	190/1378 (13.8)	145/1021 (14.2)	45/357 (12.6)	1.18 (0.83–1.71)
15–44 yr	838/1378 (60.8)	577/1021 (56.5)	261/357 (73.1)	0.48 (0.36–0.62)
≥45 yr	350/1378 (25.4)	299/1021 (29.3)	51/357 (14.3)	2.47 (1.79–3.46)
Health care worker	158/1429 (11.1)	112/1067 (10.5)	46/362 (12.7)	0.86 (0.60–1.27)
Signs and symptoms				
General symptoms				
Fever‡	1002/1151 (87.1)	746/846 (88.2)	256/305 (83.9)	1.34 (0.92–1.95)
Fatigue	866/1133 (76.4)	633/829 (76.4)	233/304 (76.6)	0.94 (0.68–1.28)
Loss of appetite	681/1055 (64.5)	498/778 (64.0)	183/277 (66.1)	0.92 (0.69–1.23)
Vomiting	753/1114 (67.6)	566/816 (69.4)	187/298 (62.8)	1.19 (0.89–1.59)
Diarrhea	721/1099 (65.6)	555/813 (68.3)	166/286 (58.0)	1.42 (1.06–1.89)
Headache	553/1035 (53.4)	407/757 (53.8)	146/278 (52.5)	1.03 (0.78–1.36)
Abdominal pain	439/992 (44.3)	311/715 (43.5)	128/277 (46.2)	0.85 (0.64–1.13)
Muscle pain	385/990 (38.9)	293/728 (40.2)	92/262 (35.1)	1.24 (0.92–1.67)
Joint pain	374/950 (39.4)	283/695 (40.7)	91/255 (35.7)	1.32 (0.98–1.80)
Chest pain	254/686 (37.0)	196/488 (40.2)	58/198 (29.3)	1.53 (1.07–2.20)
Cough	194/655 (29.6)	150/462 (32.5)	44/193 (22.8)	1.74 (1.18–2.61)
Difficulty breathing	155/665 (23.3)	123/472 (26.1)	32/193 (16.6)	1.68 (1.10–2.63)
Difficulty swallowing	169/514 (32.9)	138/375 (36.8)	31/139 (22.3)	2.22 (1.41–3.59)
Conjunctivitis	137/658 (20.8)	109/465 (23.4)	28/193 (14.5)	2.03 (1.29–3.29)
Sore throat	102/467 (21.8)	82/339 (24.2)	20/128 (15.6)	1.94 (1.13–3.46)
Confusion	84/631 (13.3)	68/446 (15.2)	16/185 (8.6)	2.00 (1.14–3.71)
Hiccups	108/947 (11.4)	91/699 (13.0)	17/248 (6.9)	2.15 (1.27–3.82)
Jaundice	65/627 (10.4)	52/443 (11.7)	13/184 (7.1)	1.83 (0.99–3.63)
Eye pain	48/622 (7.7)	39/438 (8.9)	9/184 (4.9)	1.95 (0.95–4.40)
Rash	37/642 (5.8)	30/453 (6.6)	7/189 (3.7)	1.90 (0.86–4.83)
Coma or unconsciousness	37/627 (5.9)	34/445 (7.6)	3/182 (1.6)	4.59 (1.61–19.34)

Table 1. (Continued.)

Variable	All Patients	Patients Who Died	Patients Who Recovered	Odds Ratio (95% CI)†
		no./total no. (%)		
Unexplained bleeding	168/932 (18.0)	140/693 (20.2)	28/239 (11.7)	1.83 (1.20–2.90)
Hematemesis	26/670 (3.9)	20/503 (4.0)	6/167 (3.6)	1.07 (0.44–3.01)
Blood in stool	48/843 (5.7)	35/614 (5.7)	13/229 (5.7)	0.98 (0.52–1.96)
Bleeding gums	19/837 (2.3)	18/608 (3.0)	1/229 (0.4)	6.69 (1.35–121.32)
Bloody nose	16/836 (1.9)	15/610 (2.5)	1/226 (0.4)	8.02 (1.54–148.62)
Bloody cough	20/831 (2.4)	16/605 (2.6)	4/226 (1.8)	1.63 (0.58–5.82)
Other bleeding	8/657 (1.2)	5/493 (1.0)	3/164 (1.8)	0.45 (0.11–2.23)
Bleeding at injection site	20/833 (2.4)	19/605 (3.1)	1/228 (0.4)	6.51 (1.32–118.04)
Blood from vagina§	14/431 (3.2)	13/290 (4.5)	1/126 (0.8)	6.0 (1.11–112.4)
Blood in urine	10/827 (1.2)	9/601 (1.5)	1/226 (0.4)	5.14 (0.90–98.73)
Bleeding under skin	5/827 (0.6)	5/604 (0.8)	0/223	NA

Table 2. Estimates of Epidemiologic Variables for Confirmed and Probable Ebola Cases, According to Country, as of September 14, 2014.*

Variable	All Countries		Guinea		Liberia		Nigeria		Sierra Leone	
	no. of days	no. of patients with data	no. of days	no. of patients with data	no. of days	no. of patients with data	no. of days	no. of patients with data	no. of days	no. of patients with data
Incubation period										
Single-day exposures										
Observed†	9.4±7.4	500	10.7±8.7	35	9.5±6.6	259	NC	<10	9.0±8.1	201
Fitted‡	9.1±7.3	500	9.9±9.8	35	9.4±6.7	259	NC	<10	8.5±7.6	201
Multi-day exposures										
Observed†	11.4±NA	155	10.9±NA	20	11.7±NA	79	NC	<10	10.8±NA	48
Fitted‡	9.7±5.5	155	8.3±4.5	20	9.9±5.7	79	NC	<10	9.9±5.6	48
Serial interval§										
Observed	15.3±9.1	92	19.0±11.0	40	13.1±6.6	26	NC	<10	11.6±5.6	25
Fitted¶	15.3±9.3	92	19.0±11.2	40	13.1±7.8	26	NC	<10	11.6±6.3	25
R_0‖										
Mean (95% CI)	—		*1.71 (1.44–2.01)*		*1.83 (1.72–1.94)*		*1.2 (0.67–1.96)*		*2.02 (1.79–2.26)*	
Doubling time — days (95% CI)	—		*17.53 (13.18–26.64)*		*15.78 (14.4–17.37)*		*59.75 (13.27–∞)*		*12.84 (10.92–15.66)*	
R**										
Mean (95% CI)	—		*1.81 (1.60–2.03)*		*1.51 (1.41–1.60)*				*1.38 (1.27–1.51)*	
Doubling time — days (95% CI)	—		*15.7 (12.9–20.3)*		*23.6 (20.2–28.2)*		*NC*		*30.2 (23.6–42.3)*	
Interval from symptom onset										
To hospitalization	5.0±4.7	1135	5.3±4.3	484	4.9±5.1	245	4.1±1.4	11	4.6±5.1	395
To hospital discharge	16.4±6.5	267	16.3±6.1	152	15.4±8.2	41	NC	<10	17.2±6.2	70
To death	7.5±6.8	594	6.4±5.3	248	7.9±8.0	212	NC	<10	8.6±6.9	128
To WHO notification	6.1±8.5	2185	7.5±10.4	743	6.0±8.7	797	3.9±2.3	11	4.5±5.0	634
Interval from WHO notification										
To hospital discharge	11.8±7.2	312	11.1±5.8	164	11±8.0	41	NC	<10	12.7±8.4	102
To death	−3.0±13.8	584	−4.4±14.4	300	−1.8±13.6	221	NC	<10	−1.6±9.2	58
Interval from hospitalization										
To hospital discharge	11.8±6.1	290	11±5.4	159	12.8±8.1	40	NC	<10	12.4±5.8	86
To death	4.2±6.4	121	2.5±3.4	36	4.5±6.0	63	NC	<10	4.4±6.0	17
Duration of hospital stay — days††	6.42		4.99		6.72		NC		6.88	

	rate (95% CI)	no. of patients with data	rate (95% CI)	no. of patients with data	rate (95% CI)	no. of patients with data	rate (95% CI)	no. of patients with data	rate (95% CI)	no. of patients with data
Case fatality rate										
All cases, based on current status	37.7 (36.1–39.2)	3747	57.5 (53.7–61.1)	677	34.7 (32.4–37.1)	1616	40.0 (19.8–64.3)	15	31.6 (29.3–34.1)	1439
All cases, based on definitive outcome	70.8 (68.6–72.8)	1737	70.7 (66.7–74.3)	542	72.3 (68.9–75.4)	739	45.5 (21.3–72.0)	11	69.0 (64.5–73.1)	445
Before August 18	71.3 (68.7–73.7)	1244	68.7 (64.3–72.8)	454	79.8 (75.7–83.4)	416	50.0 (23.7–76.3)	10	65.4 (60.4–70.1)	364
August 18–September 14	59.9 (54.7–64.9)	354	80.7 (71.2–87.6)	88	41.1 (34.3–48.2)	190	NC	<10	84.0 (74.1–90.6)	75
All hospitalized cases, based on definitive outcome	64.3 (61.5–67.0)	1153	64.7 (60.1–68.9)	450	67.0 (62.0–71.7)	361	40.0 (16.8–68.7)	10	61.4 (56.1–66.5)	332
According to sex										
Male	72.2 (69.1–75.1)	874	68.5 (62.6–73.9)	254	74.9 (70.4–79.0)	395	NC	<10	71.9 (65.7–77.5)	221
Female	69.9 (66.7–73.0)	818	72.7 (67.3–77.6)	286	71.6 (66.4–76.3)	317	NC	<10	64.4 (57.7–70.6)	208
According to age group										
<15 yr	73.4 (67.2–78.8)	218	78.1 (67.3–86.0)	73	70.7 (60.1–79.5)	82	NC	<10	71.4 (59.3–81.1)	63
15–44 yr	66.1 (63.1–69.0)	1012	64.9 (59.5–69.9)	319	70.6 (66.1–74.8)	422	NC	<10	61.4 (55.4–67.0)	264
≥45 yr	80.4 (76.2–84.0)	398	78.6 (71.1–84.6)	140	81.1 (74.4–86.4)	164	NC	<10	82.2 (73.1–88.8)	90
According to occupation										
Health care worker	69.4 (62.1–75.8)	170	56.1 (41.0–70.1)	41	80.0 (68.7–87.9)	65	NC	<10	68.4 (55.5–79.0)	57
Non–health care worker	70.9 (68.6–73.1)	1567	71.9 (67.8–75.6)	501	71.5 (68.0–74.8)	674	NC	<10	69.1 (64.3–73.5)	388

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Clinical Illness and Outcomes in Patients with Ebola in Sierra Leone

J.S. Schieffelin, J.G. Shaffer, A. Goba, M. Gbakie, S.K. Gire, A. Colubri, R.S.G. Sealfon, L. Kanneh, A. Moigboi,* M. Momoh, M. Fullah,* L.M. Moses, B.L. Brown, K.G. Andersen, S. Winnicki, S.F. Schaffner, D.J. Park, N.L. Yozwiak, P.-P. Jiang, D. Kargbo, S. Jalloh, M. Fonnie,* V. Sinnah,* I. French, A. Kovoma,* F.K. Kamara, V. Tucker, E. Konuwa, J. Sellu, I. Mustapha, M. Foday, M. Yillah, F. Kanneh, S. Saffa,* J.L.B. Massally, M.L. Boisen, L.M. Branco, M.A. Vandi, D.S. Grant, C. Happi, S.M. Gevao, T.E. Fletcher, R.A. Fowler, D.G. Bausch, P.C. Sabeti, S.H. Khan,* and R.F. Garry, for the KGH Lassa Fever Program, the Viral Hemorrhagic Fever Consortium, and the WHO Clinical Response Team†

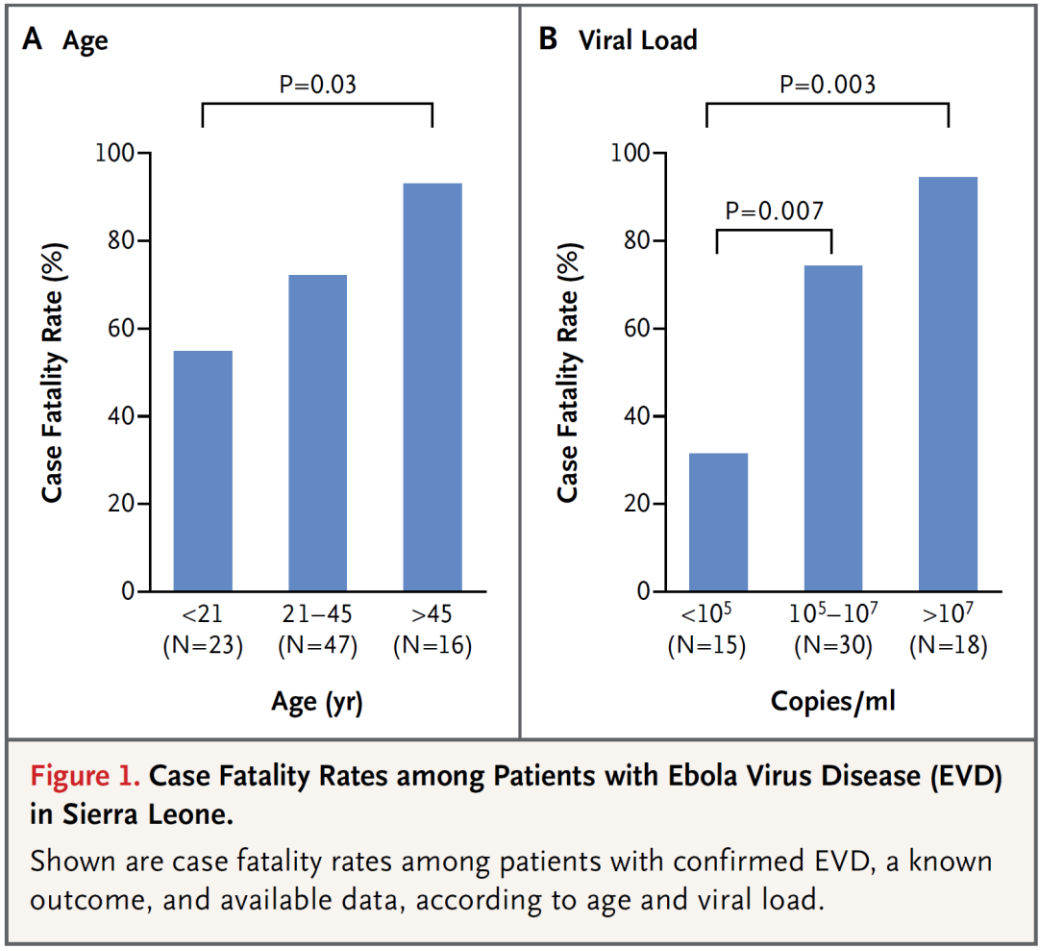


Figure 1. Case Fatality Rates among Patients with Ebola Virus Disease (EVD) in Sierra Leone.

Shown are case fatality rates among patients with confirmed EVD, a known outcome, and available data, according to age and viral load.

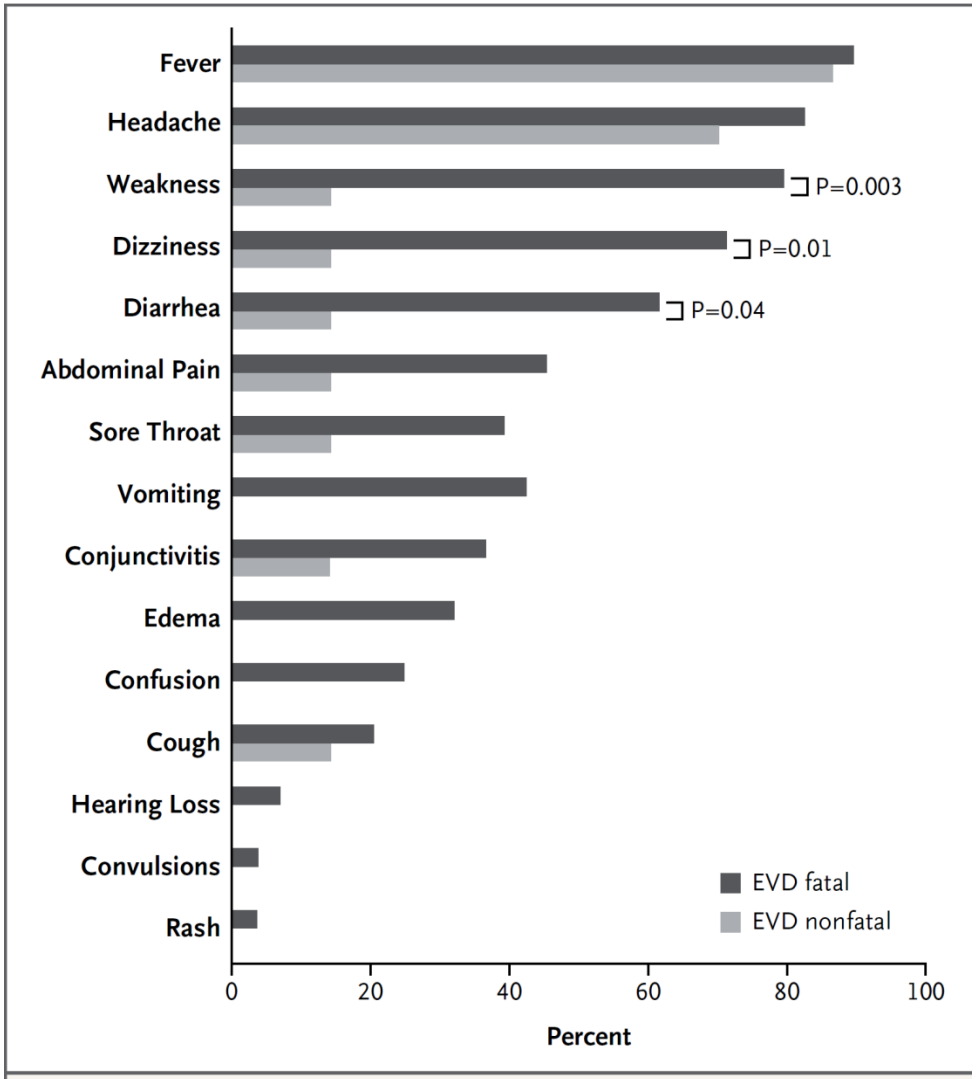


Figure 2. Signs and Symptoms in Patients with Fatal and Nonfatal EVD.

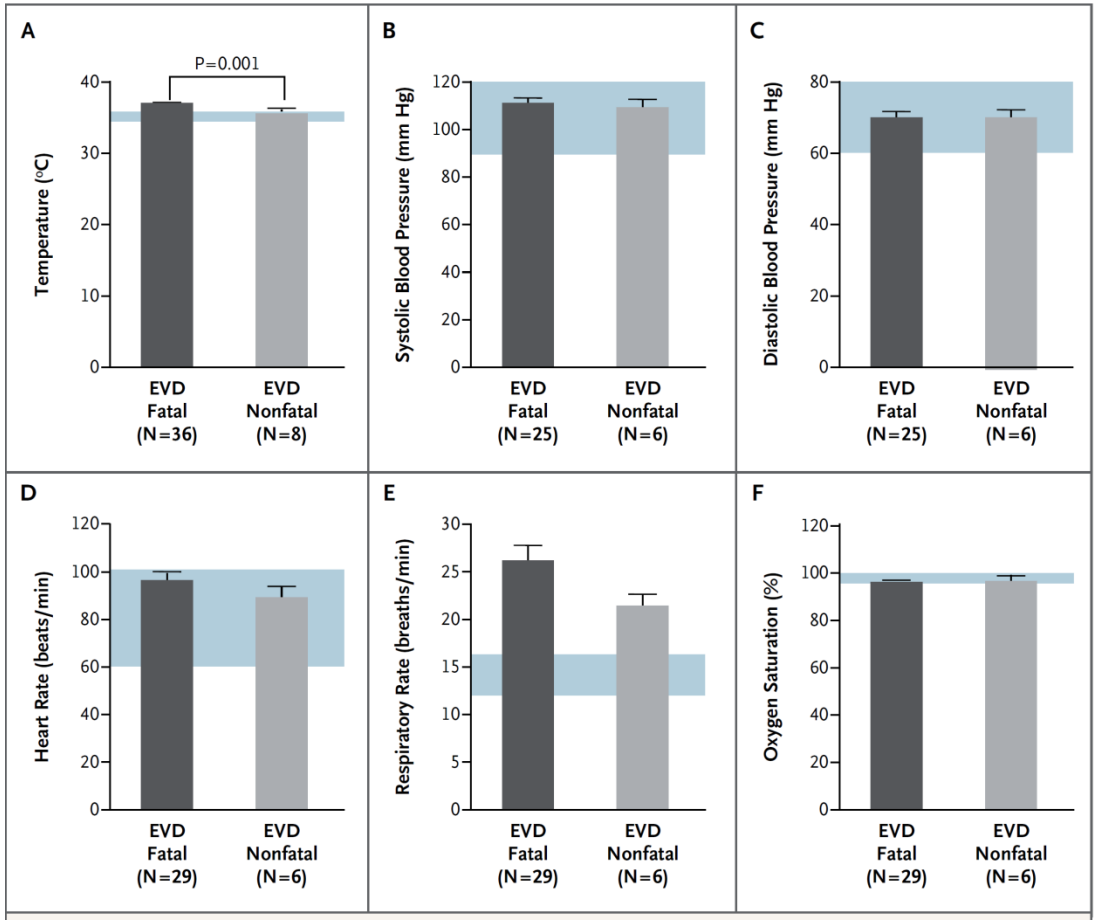


Figure 3. Vital Signs in Patients with Fatal and Nonfatal EVD.

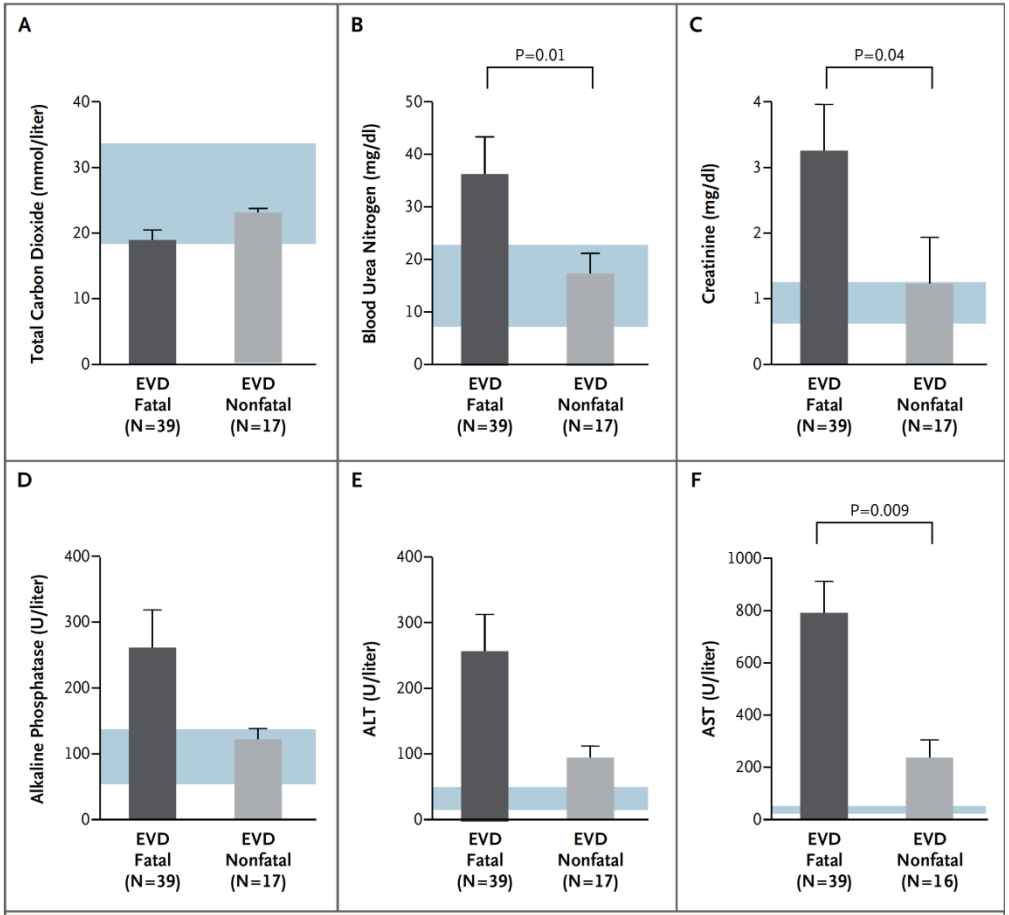


Figure 4. Comparison of Metabolic Measures in Patients with Fatal and Nonfatal EVD.

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Clinical Presentation of Patients with Ebola Virus Disease in Conakry, Guinea

Elhadj Ibrahima Bah, M.D., Marie-Claire Lamah, M.D., Tom Fletcher, M.R.C.P., Shevin T. Jacob, M.D., M.P.H., David M. Brett-Major, M.D., M.P.H., Amadou Alpha Sall, Ph.D., Nahoko Shindo, M.D., Ph.D., William A. Fischer II, M.D., Francois Lamontagne, M.D., Sow Mamadou Saliou, M.D., Daniel G. Bausch, M.D., M.P.H.&T.M., Barry Moumié, M.D., Tim Jagatic, M.D., Armand Sprecher, M.D., James V. Lawler, M.D., M.P.H., Thierry Mayet, M.D., Frederique A. Jacquerioz, M.D., María F. Méndez Baggi, M.D., Constanza Vallenas, M.D., Christophe Clement, M.D., Simon Mardel, M.D., Ousmane Faye, Ph.D., Oumar Faye, Ph.D., Baré Soropogui, Pharm.D., Nfaly Magassouba, D.V.M., Ph.D., Lamine Koivogui, Pharm.D., Ph.D., Ruxandra Pinto, Ph.D., and Robert A. Fowler, M.D.C.M.

Table 3. Clinical Complications and Outcomes for 37 Patients with EVD.

Variable	Value
Hospital mortality — no. (%)	16 (43)
Median length of stay in hospital (IQR) — days	8 (6–11)
Known complications in hospital — no. (%)	
Hemorrhage	
Any	19 (51)
Gastrointestinal	9 (24)
Subconjunctival	4 (11)
Intravenous catheter site	4 (11)
Nasorespiratory tract	2 (5)
Renal failure*	2 (5)
Seizure	2 (5)
Oral candidiasis	1 (3)
Hypoxemia	1 (3)

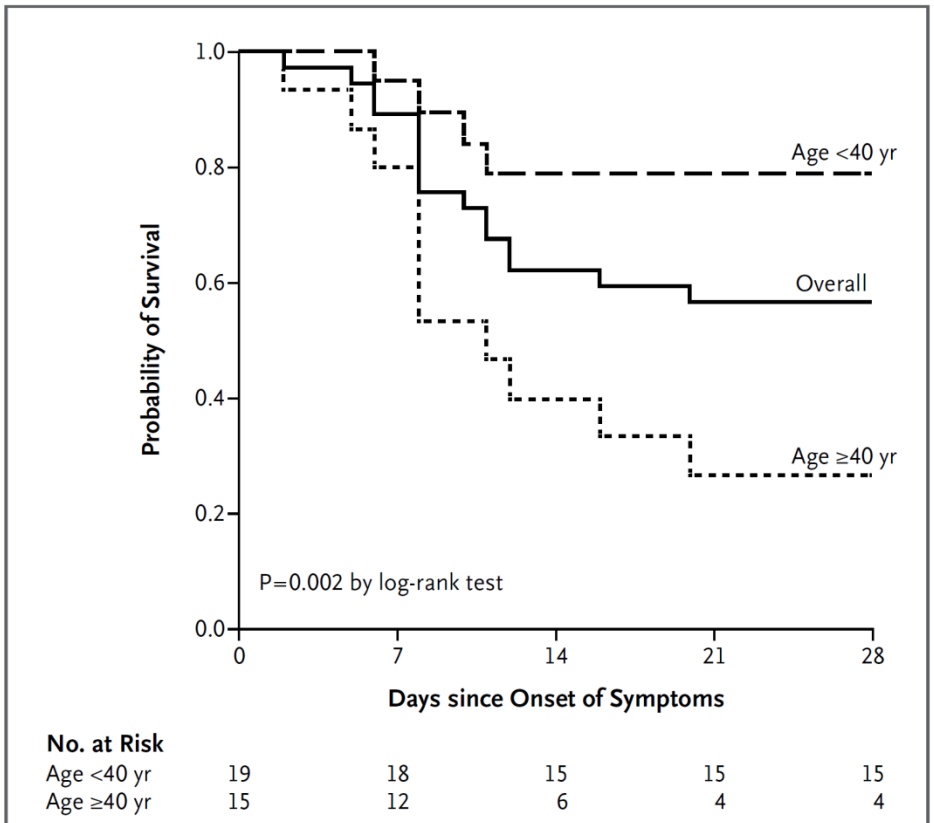


Figure 1. Kaplan–Meier Estimate of the Probability of Survival among Patients with Ebola Virus Disease, According to Age.

World Health Organization

EBOLA RESPONSE ROADMAP SITUATION REPORT UPDATE

14 NOVEMBER 2014

HIGHLIGHTS

- There have been 14 413 reported Ebola cases in eight countries since the outbreak began, with 5177 reported deaths.
- Case incidence continues to increase in Sierra Leone, and transmission also remains intense in Guinea and Liberia.
- A total of 4 cases, including 3 deaths, have been reported in Mali.

CASES / DEATHS

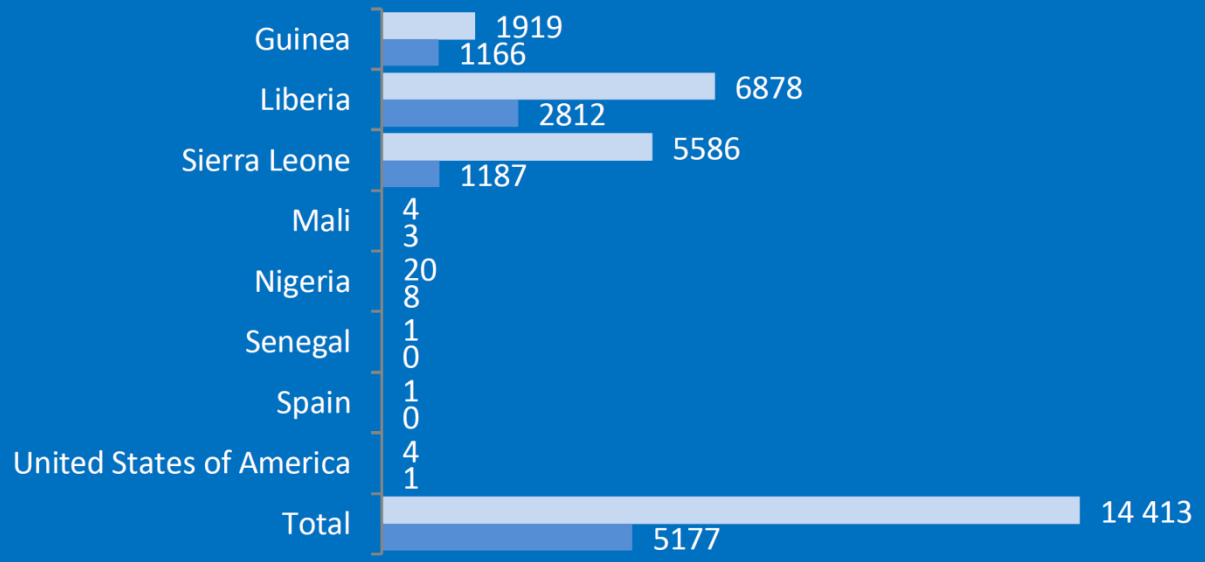


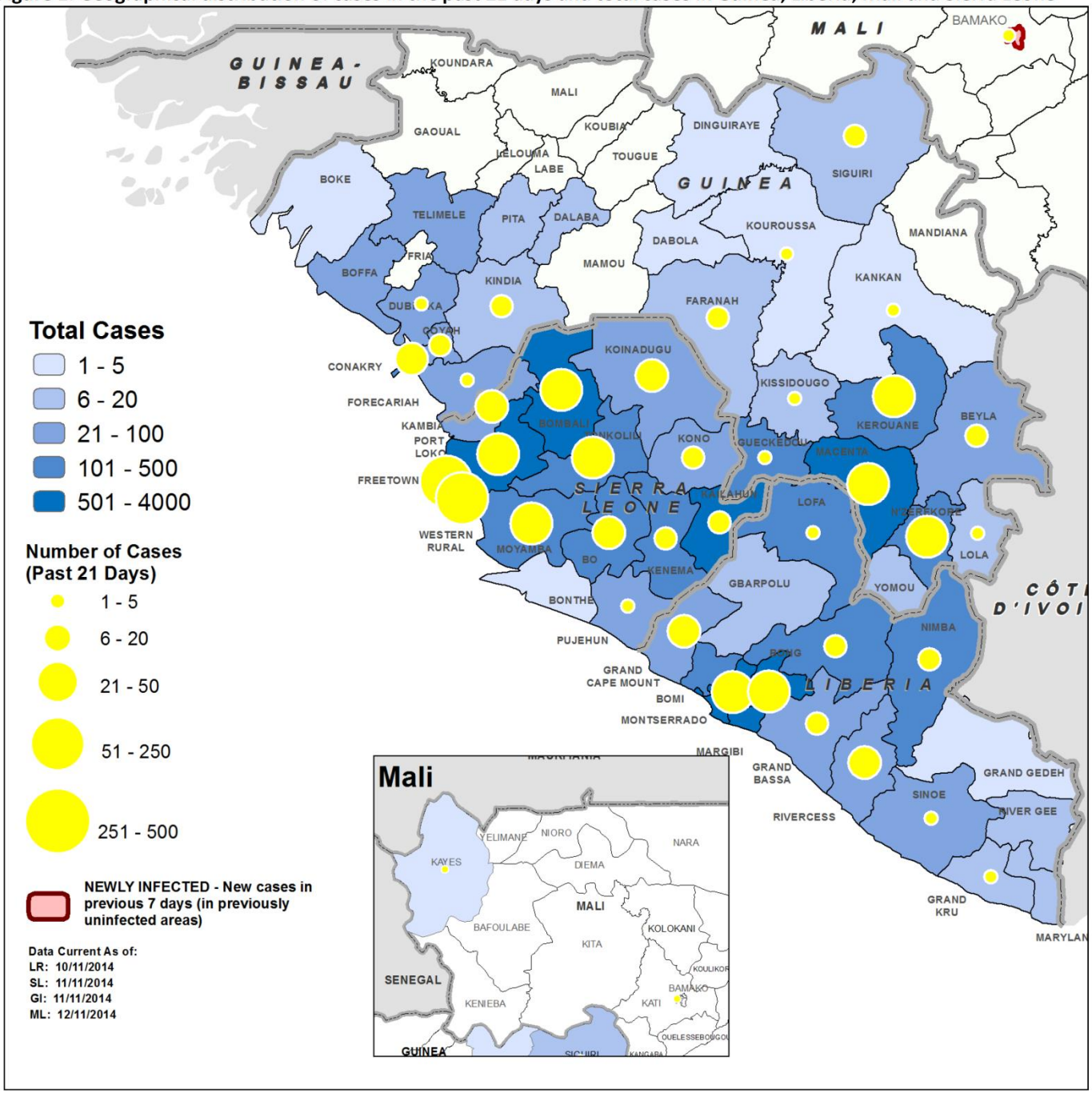
Table 1: Confirmed, probable, and suspected cases in Guinea, Liberia, and Sierra Leone

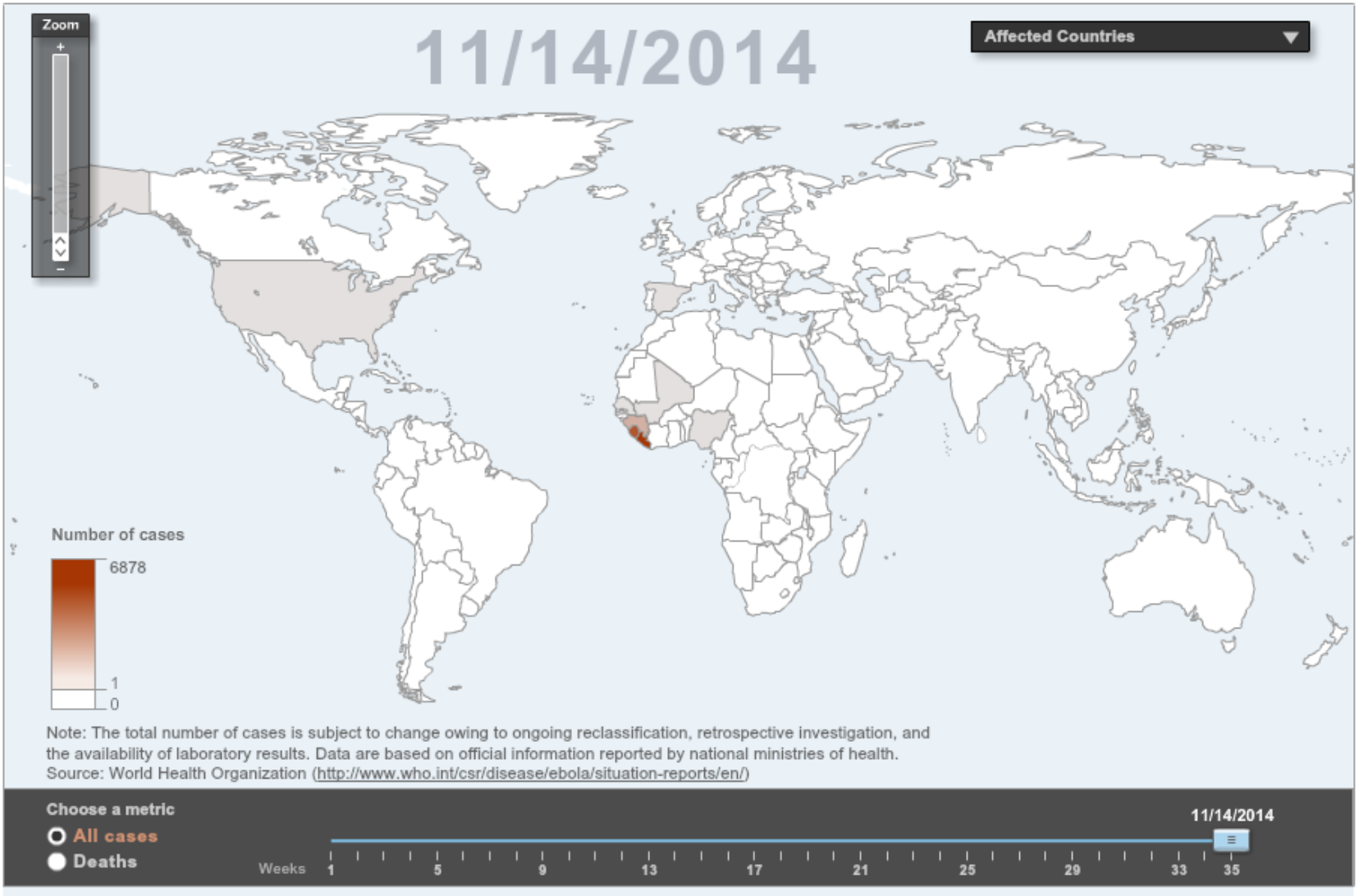
Country	Case definition	Cumulative Cases	Cumulative Deaths
Guinea	Confirmed	1647	958
	Probable	208	208
	Suspected	64	0
	All	**1919**	**1166**
Liberia	Confirmed	2562	*
	Probable	1716	*
	Suspected	2600	*
	All	**6878**	**2812****
Sierra Leone	Confirmed	4683	978
	Probable	79	174
	Suspected	824	35
	All	**5586**	**1187**
Total		**14 383**	**5165**

Table 2: Ebola virus disease cases and deaths in Mali, Spain, and the United States of America

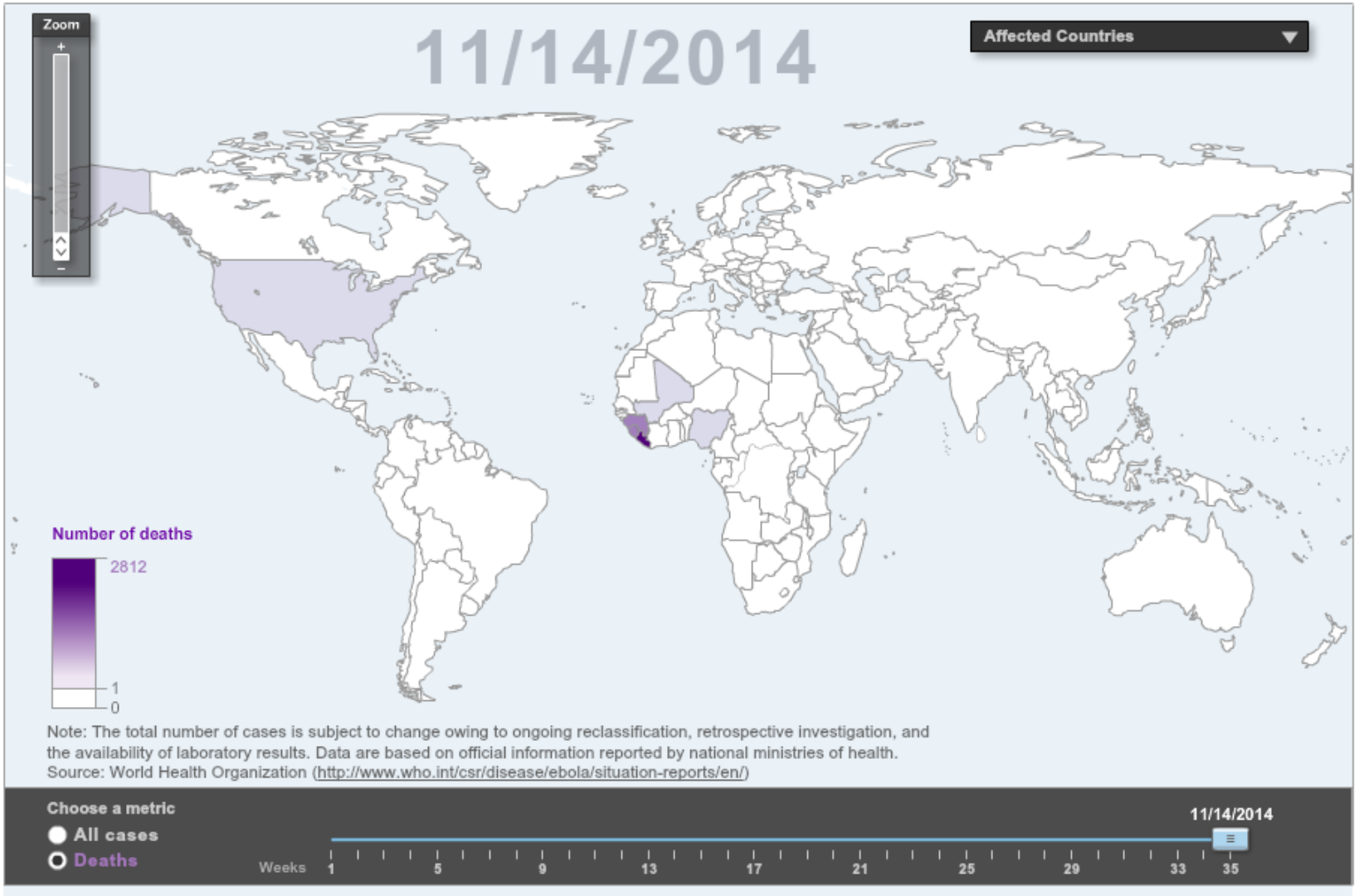
Country	Cumulative cases					Contact tracing
	Confirmed	Probable	Suspect	Deaths	Health-care workers	Listed contacts to be followed
Mali	3	1	0	3	50%	268
Spain	1	0	0	0	100%	0
United States of America*	4	0	0	1	75%	0

Figure 1: Geographical distribution of cases in the past 21 days and total cases in Guinea, Liberia, Mali and Sierra Leone





Current Ebola outbreak | History of Ebola outbreaks | Viral lifecycle | Viral structure



Note: The total number of cases is subject to change owing to ongoing reclassification, retrospective investigation, and the availability of laboratory results. Data are based on official information reported by national ministries of health.
Source: World Health Organization (http://www.who.int/csr/disease/ebola/situation-reports/en/)

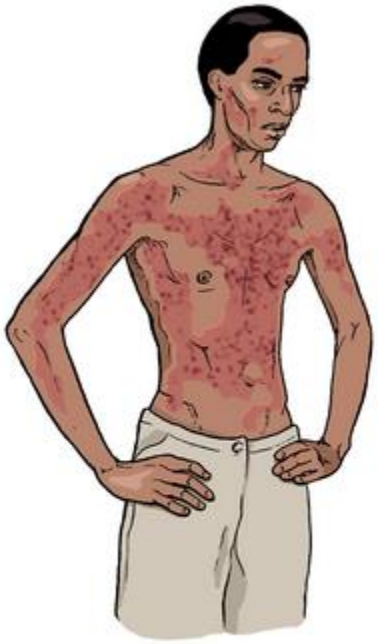
Clinical Manifestations

- Incubation period
  - 2~21 days (average 8~10 days)

- Symptoms and signs
  - Initial: Fever, chills, myalgias, malaise, anorexia
  - After 5 days: GI symptoms, such as nausea, vomiting, watery diarrhea, abdominal pain
  - Other: Headache, conjunctivitis, hiccups, rash, chest pain, shortness of breath, confusion, seizures
  - Hemorrhagic symptoms in 18% of cases

- Other possible infectious causes of symptoms
  - Malaria, typhoid fever, meningococcemia, Lassa fever, other bacterial infections (e.g., pneumonia)

- **Lab**
  - Leukopenia
    - with lymphopenia followed later by elevated neutrophils and a left shift
  - Thrombocytopenia (50,000~100,000)
  - Elevated Amylase ; pancreatic involve
  - Transaminitis (>1000 IU/L) ; AST>ALT
  - Coagulation
  - Renal abnormalities



Skin rash

Stomach pain

Vomiting

http://www.cdc.gov/vhf/ebola/resources/infographics.html

Transmission

- Virus present in high quantity in blood, body fluids, and excreta of *symptomatic* EVD-infected patients

- Opportunities for **human-to-human** transmission
  - **Direct contact** (through broken skin or unprotected mucous membranes) with an EVD-infected **patient's blood or body fluids**
  - **Sharps injury** (with EVD-contaminated needle or other sharp)
  - **Direct contact** with the **corpse** of a person who **died of EVD**
  - **Indirect contact** with an EVD-infected patient's blood or body fluids via a **contaminated object** (soiled **linens** or used **utensils**)

- Ebola can also be transmitted via contact with blood, fluids, or meat of an infected animal
  - Limited evidence that dogs become infected with Ebola virus
  - No reports of dogs or cats becoming sick with or transmitting Ebola

- Human-to-Human **Transmission**
  - Infected persons are **not contagious until onset of symptoms**
  - **Infectiousness** of body fluids (e.g., viral load) **increases as patient becomes more ill**
    - Remains from **deceased** infected persons are **highly infectious**
  - Human-to-human transmission of Ebola virus via inhalation (aerosols) has not been demonstrated

Ebola virus is thought to persist in reservoir species in areas where it is endemic. Humans, apes, and other mammalian species develop severe disease and are therefore considered end hosts rather than reservoir species.[11] Viral antibodies and RNA have been identified in three species of fruit bats from the Pteropodidae family (*Hypsignathus monstrosus, Epomops franqueti,* and *Myonycteris torquata*). Rodents are also potential reservoirs.[15] Reston ebolavirus has been identified in domestic pigs in the Phillipines.[18] Other species may serve as viral reservoirs. Once humans are infected, person-to-person transmission occurs after direct contact with infected bodily fluids or tissues.

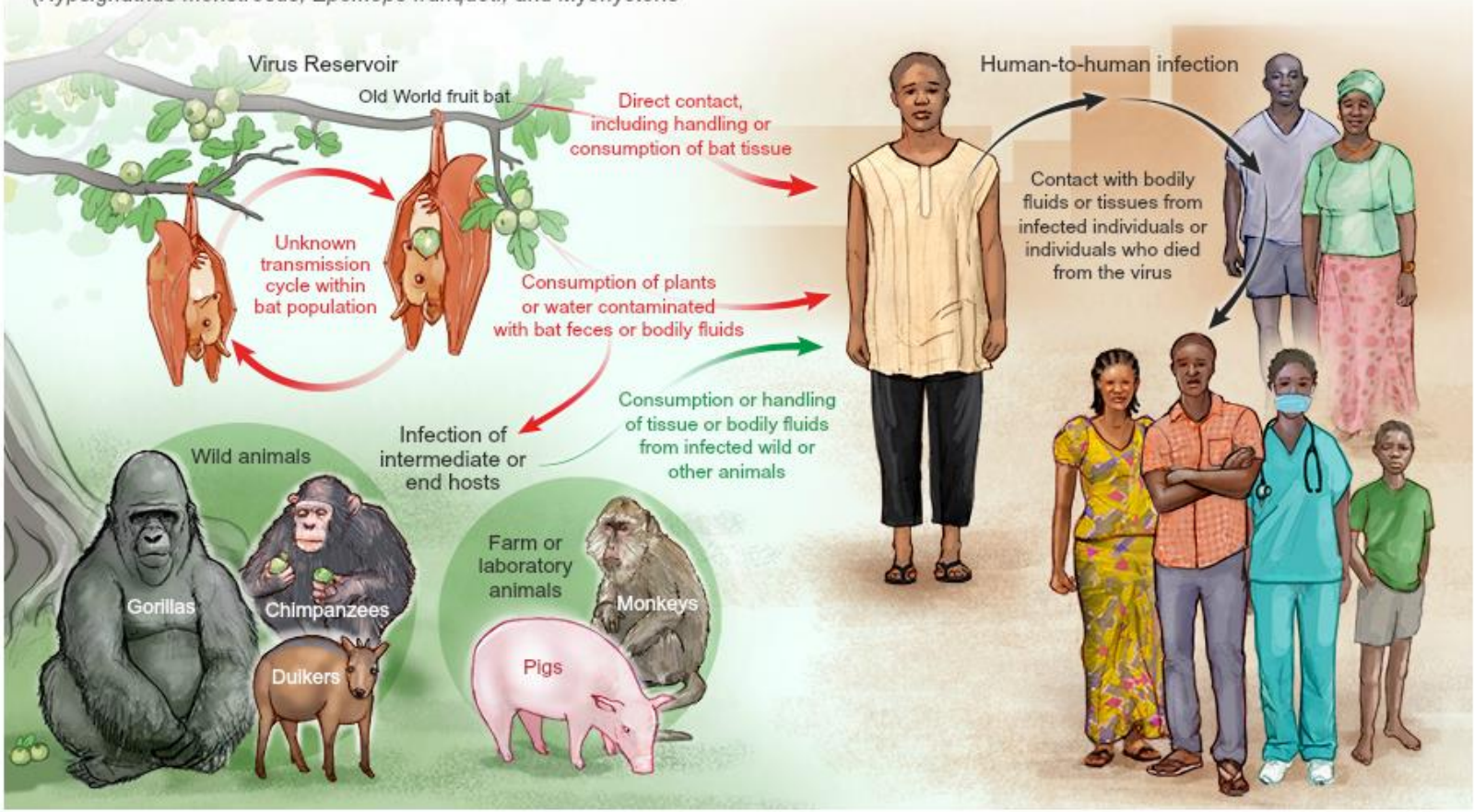
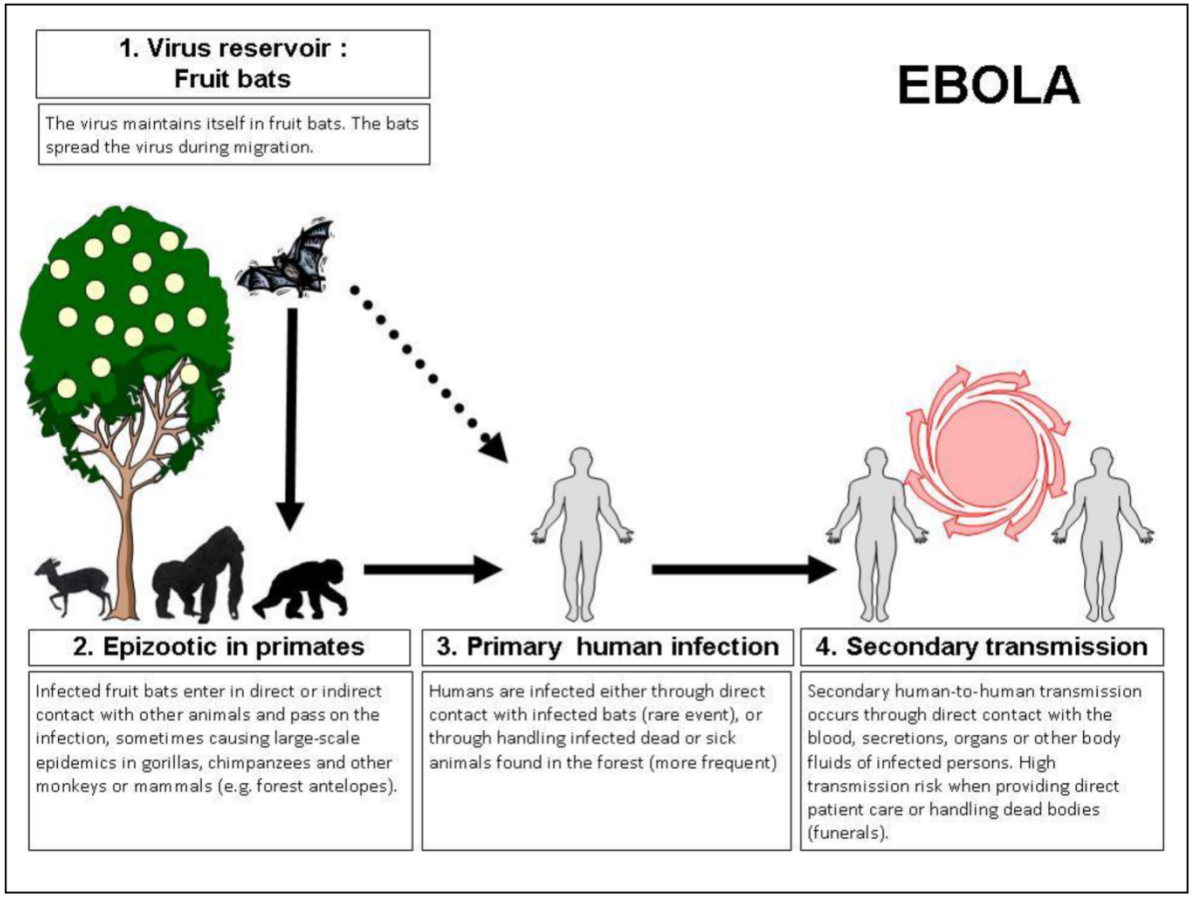
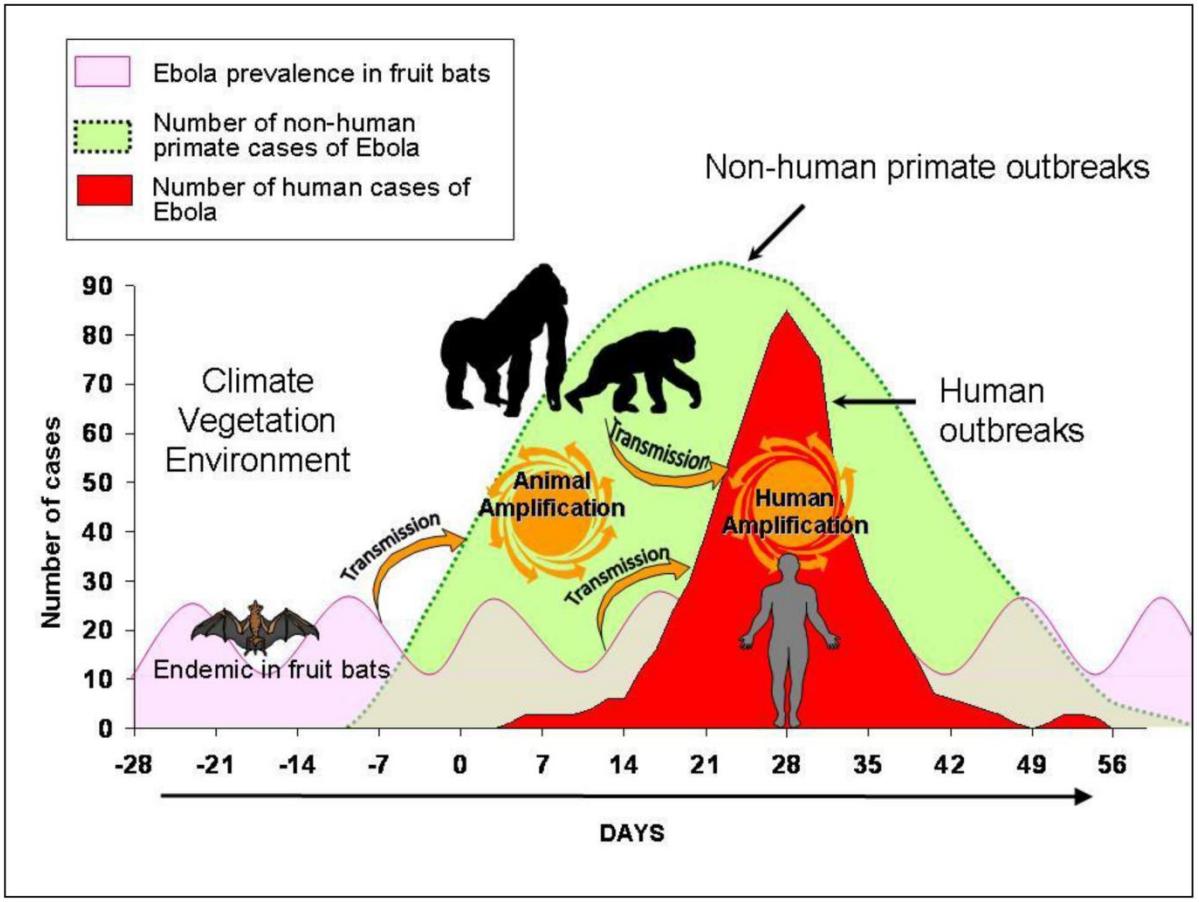


Figure 2. Hypothesis of Ebola virus transmission at the human-animal interface



WHO, Ebola and Marburg virus disease epidemics: preparedness, alert, control, and evaluation

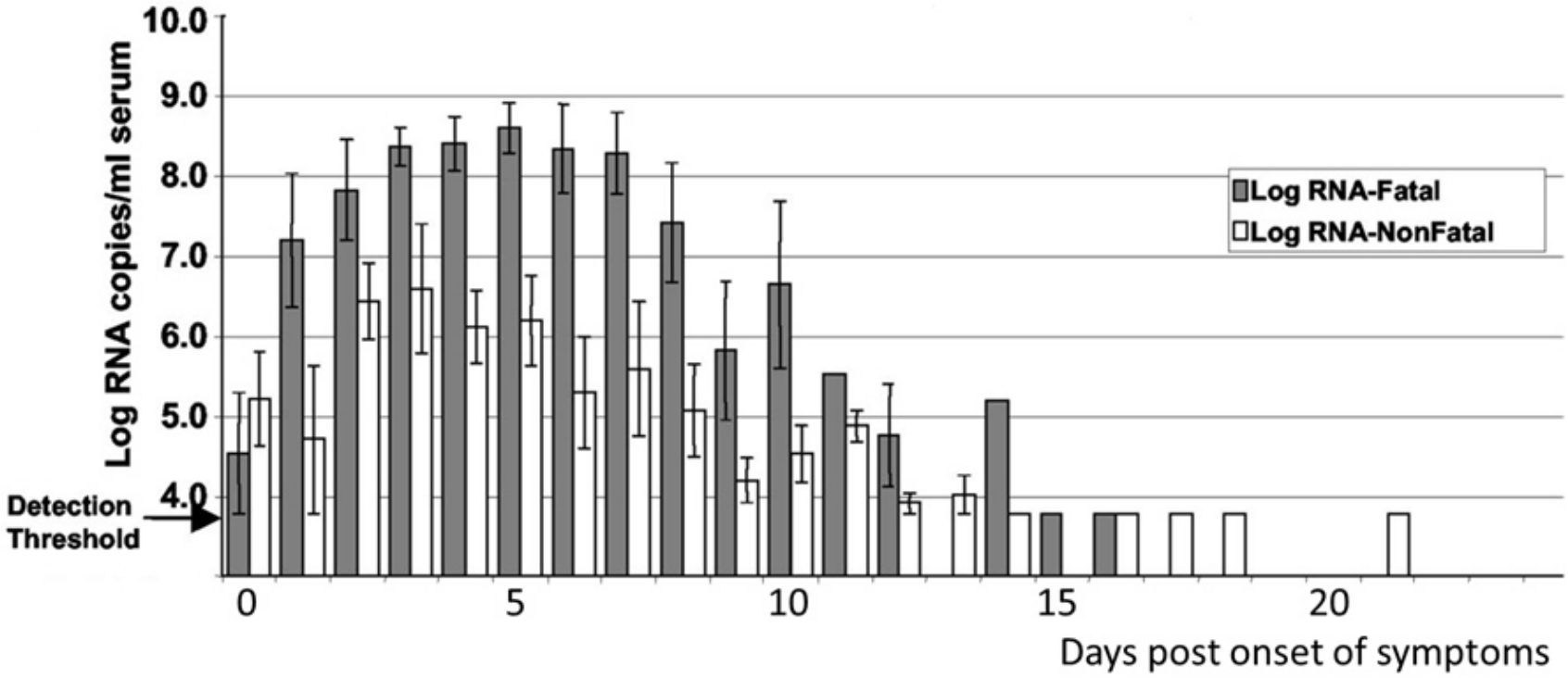
Figure 4. Ebola: Epidemic curves in humans and animals at the human-animal interface



WHO, Ebola and Marburg virus disease epidemics: preparedness, alert, control, and evaluation

http://upload.wikimedia.org/wikipedia/commons/e/e4/Bushmeat_-_Buschfleisch_Ghana.JPG

Figure 1. Ebola virus RNA copy levels in sera over time from 45 Ebola Virus Disease (EVD) patients (27 fatal, 18 non-fatal)[14]



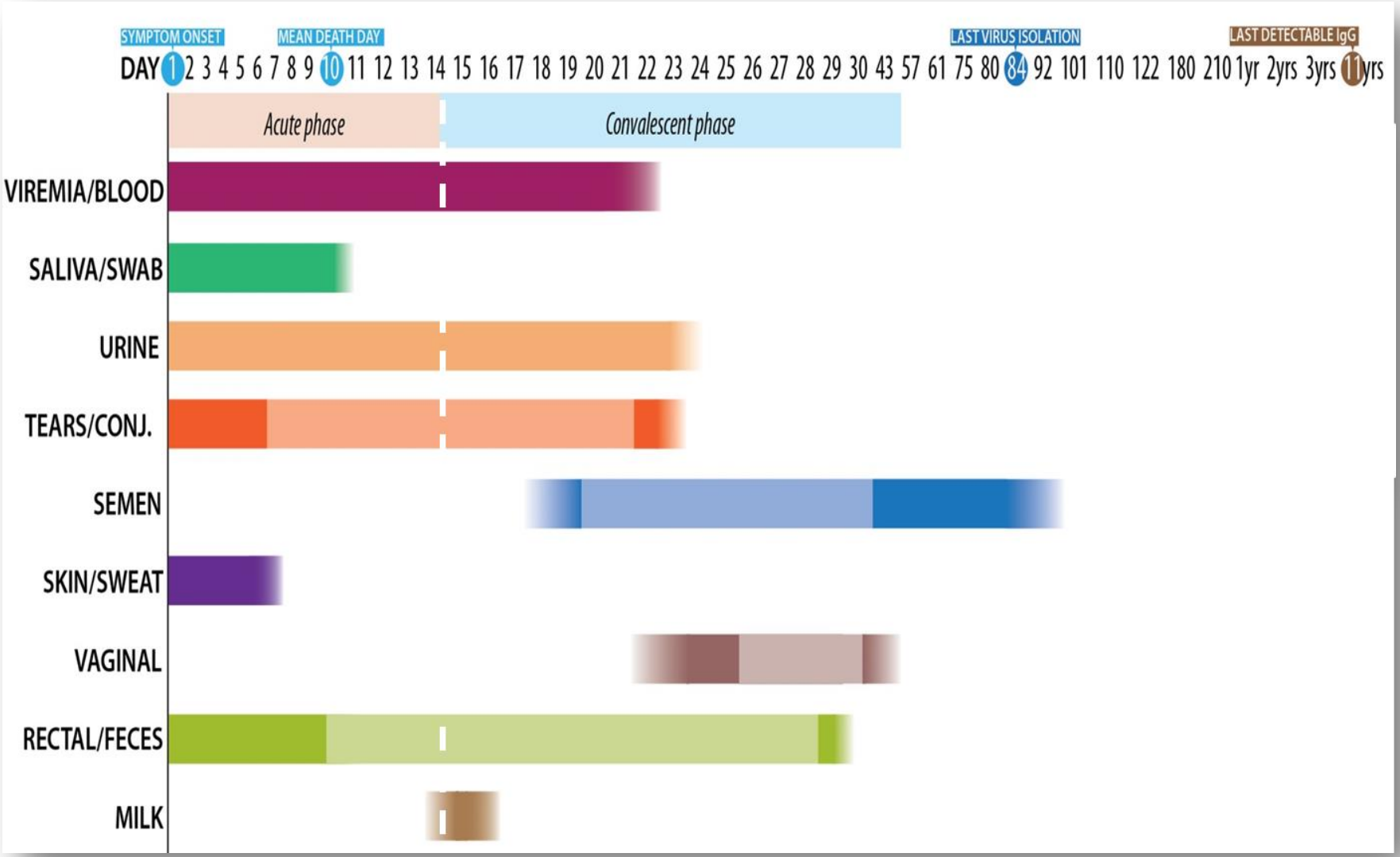
Towner JS et al. J. Virol. 2004, 78(8):4330.

Table 1. Ebola virus detection by reverse-transcription polymerase chain reaction (RT-PCR) in body fluids collected from EVD patients during an outbreak in Gulu, Uganda14 and the maximum described persistence after symptom onset described in the literature[16,18-20]

Body Fluid	Acute phase of illness number detected/number tested (percent)	Convalescent phase of illness number detected/number tested (percent)	Last day detected after symptom onset described in the literature	Comments
Skin	1/8 (13%)	0/4 (0%)	6	
Saliva	8/12 (67%)	0/4 (0%)	8	
Urine	0/7 (0%)	0/4 (0%)	23	Ebola virus antigen has been detected in the urine in other studies[20]
Stool / Feces	2/4 (50%)	n/d	29	
Breast milk	1/1 (100%)	1/1 (100%)	15	Ebola infects circulating macrophages which are present in breast milk[16]
Semen	n/d	1/2 (50%)	101	Sexual transmission of Marburg virus (but not Ebola virus) has been described[36]
Vaginal fluid	n/d	n/d	33	

http://www.cdc.gov/vhf/ebola/transmission/human-transmission.html

Detection of Ebola Virus in Different Human Body Fluids over Time



Ebola 101 for Healthcare Professionals, CDC

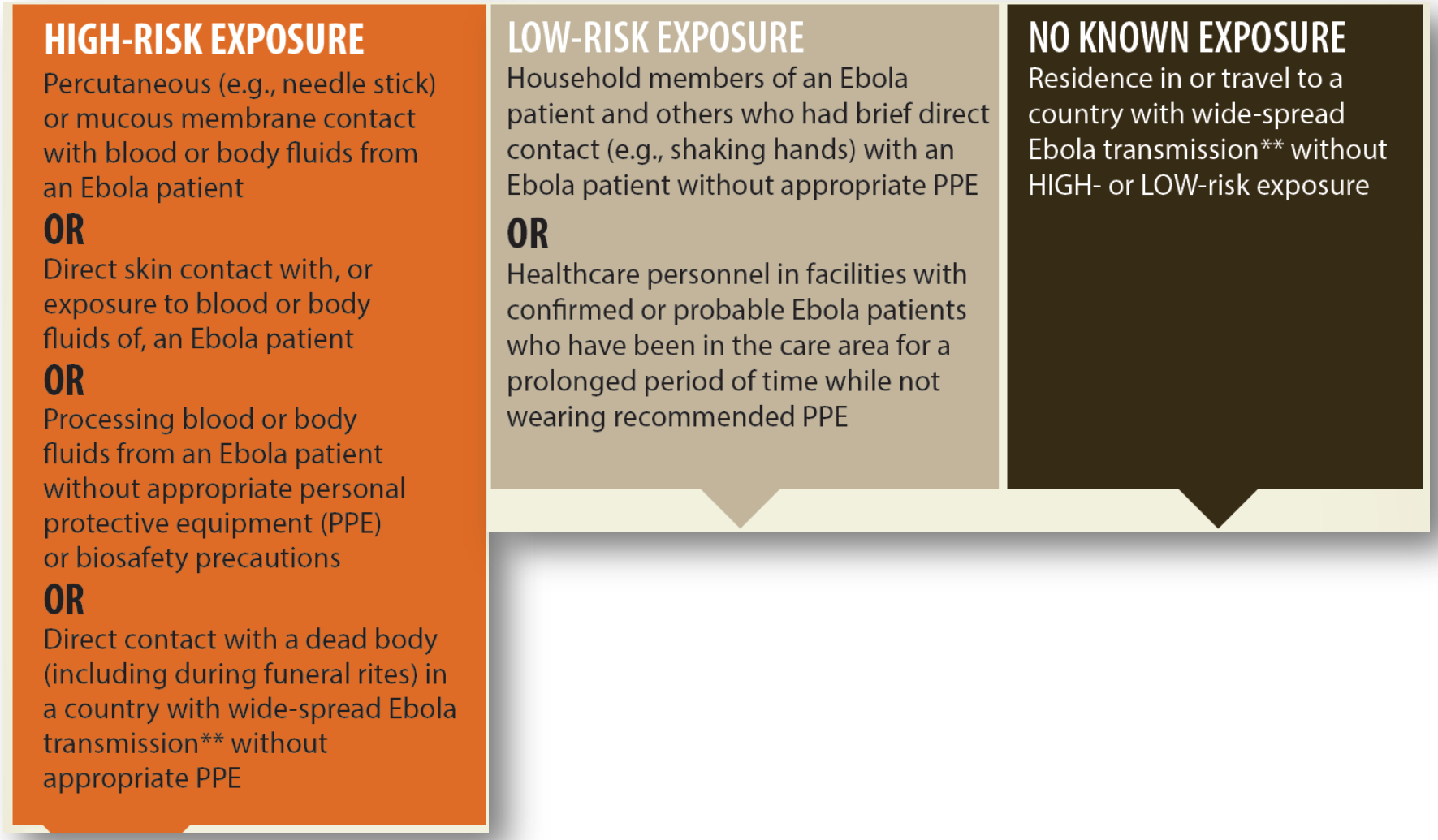
When is someone able to spread the disease to others?

Ebola only spreads when people are sick.

A patient must have symptoms to spread the disease to others.

U.S. Department of Health and Human Services
Centers for Disease Control and Prevention

EVD Risk Assessment



**CDC Website to check current affected areas: www.cdc.gov/vhf/ebola

Ebola 101 for Healthcare Professionals, CDC

CDC, Interim U.S. **Guidance for** Monitoring and Movement of Persons with Potential **Ebola Virus Exposure** 2014.10.27

Exposure Category	Clinical Criteria	Public Health Actions

High risk includes any of the following:
• Percutaneous (e.g., needle stick) or mucous membrane exposure to blood or body fluids of a person with Ebola while the person was symptomatic
• Exposure to the blood or body fluids (including but not limited to feces, saliva, sweat, urine, vomit, and semen) of a person with Ebola while the person was symptomatic without appropriate personal protective equipment (PPE)
• Processing blood or body fluids of a person with Ebola while the person was symptomatic without appropriate PPE or standard biosafety precautions
• Direct contact with a dead body without appropriate PPE in a country with widespread Ebola virus transmission
• Having lived in the immediate household and provided direct care to a person with Ebola while the person was symptomatic
	Fever (subjective fever or measured temperature ≥100.4°F/38°C) OR any of the following:*
	• severe headache
	• muscle pain
	• vomiting
	• diarrhea
	• stomach pain
	• unexplained bruising or bleeding
		• Implement rapid isolation with immediate contact of public health authorities to arrange for safe transport to an appropriate healthcare facility for Ebola evaluation
		• Medical evaluation is required.
		  ○ Isolation orders may be used to ensure compliance
		  ○ Air travel is permitted only by air medical transport
		• If medically evaluated and discharged with a diagnosis other than Ebola, conditions as outlined for asymptomatic individuals in this exposure category will apply

	Asymptomatic (no fever or other symptoms consistent with Ebola)	• Direct active monitoring
		• Public health authority will ensure, through orders as necessary, the following minimum restrictions:
		  ○ Controlled movement: exclusion from all long-distance and local public conveyances (aircraft, ship, train, bus, and subway)
		  ○ Exclusion from public places (e.g., shopping centers, movie theaters), and congregate gatherings
		  ○ Exclusion from workplaces for the duration of the public health order, unless approved by the state or local health department (telework is permitted)
		• Non-congregate public activities while maintaining a 3-foot distance from others may be permitted (e.g., jogging in a park)
		• Federal public health travel restrictions (Do Not Board) will be implemented to enforce controlled movement
		• If travel is allowed, individuals are subject to controlled movement
		  ○ Travel by noncommercial conveyances only
		  ○ Coordinated with public health authorities at both origin and destination
		  ○ Uninterrupted direct active monitoring

Exposure Category	Clinical Criteria	Public Health Actions

Some risk includes any of the following:
• In countries with widespread Ebola virus transmission: direct contact while using appropriate PPE with a person with Ebola while the person was symptomatic
• Close contact in households, healthcare facilities, or community settings with a person with Ebola while the person was symptomatic
  ○ Close contact is defined as being for a prolonged period of time while not wearing appropriate PPE within approximately 3 feet (1 meter) of a person with Ebola while the person was symptomatic
	Fever (subjective fever or measured temperature ≥100.4°F/38°C) OR any of the following:*
	• severe headache
	• muscle pain
	• vomiting
	• diarrhea
	• stomach pain
	• unexplained bruising or bleeding
		• Implement rapid isolation with immediate contact of public health authorities to arrange for safe transport to an appropriate healthcare facility for Ebola evaluation
		• Medical evaluation is required
		  ○ Isolation orders may be used to ensure compliance
		  ○ Air travel is permitted only by air medical transport
		• If medically evaluated and discharged with a diagnosis other than Ebola, conditions as outlined for asymptomatic individuals in this exposure category will apply

	Asymptomatic (no fever or other symptoms consistent with Ebola)	• Direct active monitoring
		• The public health authority, based on a specific assessment of the individual's situation, will determine whether additional restrictions are appropriate, including:
		  ○ Controlled movement: exclusion from long-distance commercial conveyances (aircraft, ship, train, bus) or local public conveyances (e.g., bus, subway)
		  ○ Exclusion from public places (e.g., shopping centers, movie theaters), and congregate gatherings
		  ○ Exclusion from workplaces for the duration of a public health order, unless approved by the state or local health department (telework is permitted)
		• Non-congregate public activities while maintaining a 3-foot distance from others may be permitted (e.g., jogging in a park)
		• Other activities should be assessed as needs and circumstances change to determine whether these activities may be undertaken
		• Any travel will be coordinated with public health authorities to ensure uninterrupted direct active monitoring
		• Federal public health travel restrictions (Do Not Board) may be implemented based on an assessment of the particular circumstance
		  ○ For travelers arriving in the United States, implementation of federal public health travel restrictions would occur after the traveler reaches the final destination of the itinerary

Exposure Category	Clinical Criteria	Public Health Actions

Low (but not zero) risk includes any of the following:
• Having been in a country with widespread Ebola virus transmission within the past 21 days and having had no known exposures
• Having brief direct contact (e.g., shaking hands), while not wearing appropriate PPE, with a person with Ebola while the person was in the early stage of disease
• Brief proximity, such as being in the same room for a brief period of time, with a person with Ebola while the person was symptomatic
• In countries without widespread virus Ebola transmission: direct contact while using appropriate PPE with a person with Ebola while the person was symptomatic
• Traveled on an aircraft with a person with Ebola while the person was symptomatic
	Fever (subjective fever or measured temperature ≥100.4°F/38°C) OR any of the following:*
	• vomiting
	• diarrhea
	• unexplained bruising or bleeding
		• Implement rapid isolation with immediate contact of public health authorities to arrange for safe transport to an appropriate healthcare facility for Ebola evaluation
		• Medical evaluation is required.
		  ○ Isolation orders may be used to ensure compliance
		  ○ Air travel is permitted only by air medical transport
		• If medically evaluated and discharged with a diagnosis other than Ebola, conditions as outlined for asymptomatic individuals in this exposure category will apply

	Asymptomatic (no fever, vomiting, diarrhea, or unexplained bruising or bleeding)	• No restrictions on travel, work, public conveyances, or congregate gatherings
		• Direct active monitoring for:
		  ○ U.S.-based healthcare workers caring for symptomatic Ebola patients while wearing appropriate PPE
		  ○ Travelers on an aircraft with, and sitting within 3 feet of, a person with Ebola
		• Active monitoring for all others in this category

No identifiable risk includes: • Contact with an asymptomatic person who had contact with person with Ebola • Contact with a person with Ebola before the person developed symptoms • Having been more than 21 days previously in a country with widespread Ebola virus transmission • Having been in a country without widespread Ebola virus transmission and not having any other exposures as defined above	Symptomatic (any)	• Routine medical evaluation and management of ill persons, as needed
	Asymptomatic	• No actions needed

Ebola case-classification criteria, WHO

Classification	Criteria
Suspected	Any person, alive or dead, who has (or had) sudden onset of high fever and had contact with a suspected, probable or confirmed Ebola case, or a dead or sick animal OR any person with sudden onset of high fever and at least three of the following symptoms: headache, vomiting, anorexia/ loss of appetite, diarrhoea, lethargy, stomach pain, aching muscles or joints, difficulty swallowing, breathing difficulties, or hiccup; or any person with unexplained bleeding OR any sudden, unexplained death.
Probable	Any suspected case evaluated by a clinician OR any person who died from 'suspected' Ebola and had an epidemiological link to a confirmed case but was not tested and did not have laboratory confirmation of the disease.
Confirmed	A probable or suspected case is classified as confirmed when a sample from that person tests positive for Ebola virus in the laboratory.

Case Definitions, CDC

- **Person Under Investigation** (**PUI**):
  - A person who has both consistent signs or symptoms and risk factors as follows:
    - Elevated body temperature or subjective fever or symptoms, including severe headache, fatigue, muscle pain, vomiting, diarrhea, abdominal pain, or unexplained hemorrhage

    AND

    - An epidemiologic risk factor within the 21 days before the onset of symptoms

- **Confirmed Case**:
  - A PUI with laboratory-confirmed diagnostic evidence of Ebola virus infection

Identify, Isolate, Inform: Emergency Department Evaluation and Management of Patients with Possible Ebola Virus Disease

1 Identify exposure history:
Has patient lived in or traveled to a country with widespread Ebola transmission or had contact with an individual with confirmed Ebola Virus Disease within the previous 21 days?

NO → Continue with usual triage and assessment

YES

2 Identify signs and symptoms:
Fever (subjective or ≥100.4°F or 38.0°C) or Ebola-compatible symptoms: headache, weakness, muscle pain, vomiting, diarrhea, abdominal pain, or hemorrhage

NO →
- **A.** Continue with usual triage and assessment
- **B.** Notify relevant health department
- **C.** Monitor for fever and symptoms for 21 days after last exposure in consultation with the relevant health department

YES

3 Isolate and determine personal protective equipment (PPE) needed
Place patient in private room or separate enclosed area with private bathroom or covered, bedside commode. Only essential personnel with designated roles should evaluate patient and provide care to minimize transmission risk. The use of PPE should be determined based on the patient's clinical status:
- Is the patient exhibiting obvious bleeding, vomiting , copious diarrhea or a clinical condition that warrants invasive or aerosol-generating procedures (e.g., intubation, suctioning, active resuscitation)?

YES

4 Inform
- **A.** IMMEDIATELY notify the hospital infection control program and other appropriate staff
- **B.** IMMEDIATELY report to the health department

NO →
For clinically stable patients, healthcare worker should at a minimum wear:
- **A.** Face shield & surgical face mask
- **B.** Impermeable gown
- **C.** 2 pairs of gloves

If patient's condition changes, reevaluate PPE

YES →
- **A.** Use PPE designated for the care of hospitalized patients **http://www.cdc.gov/vhf/ebola/hcp/procedures-for-ppe.html**
- **B.** If the patient requires active resuscitation, this should be done in a pre-designated area using pre-designated equipment.

5 Further evaluation and management
- **A.** Complete history and physical examination; decision to test for Ebola should be made in consultation with relevant health department
- **B.** Perform routine interventions (e.g. placement of peripheral IV, phlebotomy for diagnosis) as indicated by clinical status
- **C.** Evaluate patient with dedicated equipment (e.g. stethoscope)

U.S. Department of Health and Human Services
Centers for Disease Control and Prevention

November, 5 2014 CS_252427

Diagnosis

Timeline of Infection	Diagnostic tests available
Within a few days after symptoms begin	• Antigen-capture enzyme-linked immunosorbent assay (ELISA) testing • IgM ELISA • Polymerase chain reaction (PCR) • Virus isolation
Later in disease course or after recovery	• IgM and IgG antibodies
Retrospectively in deceased patients	• Immunohistochemistry testing • PCR • Virus isolation

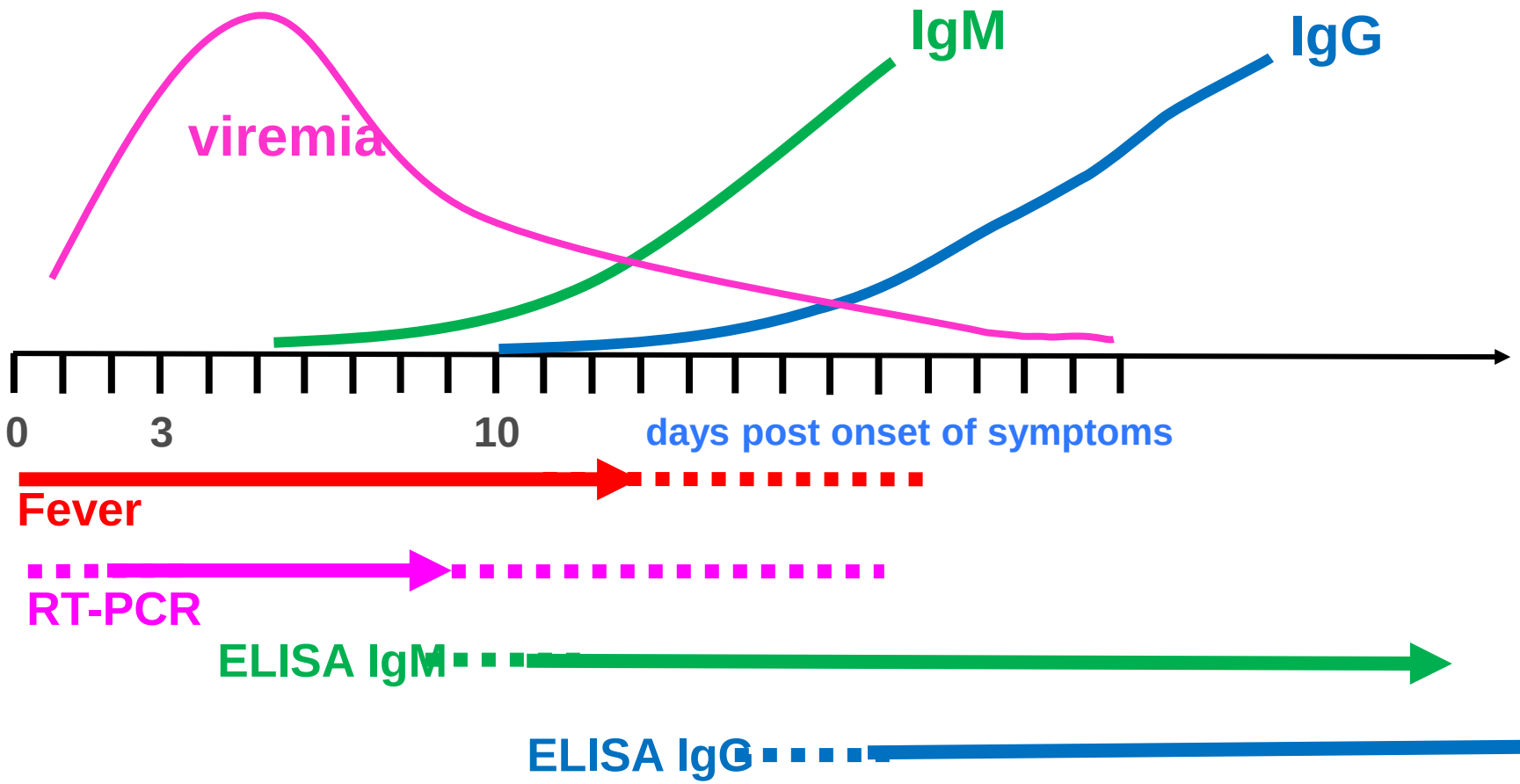
http://www.cdc.gov/vhf/ebola/diagnosis/index.html

- The **timing** of specimen collection
  - Specimens for molecular detection should ideally be taken when a patient exhibits symptoms that meet the case definition of EVD
  - If specimens are collected **less than 3 days after onset of symptoms**, **additional specimens** will be needed if the test result on the **first specimen is negative**
  - The **second specimen** should be collected **at least 48 hours after the first specimen**
  - Whole blood for serological testing can be collected after 8 days of onset of symptoms

Laboratory Guidance for the Diagnosis of Ebola Virus Disease Interim Recommendations, WHO

EVD: Expected diagnostic test results over time

Critical information: Date of onset of fever/symptoms



IgM: up to 3 – 6 months IgG: 3 – 5 years or more (life-long persistance?)

Ebola 101 for Healthcare Professionals, CDC

- For **early detection** of Ebola virus in suspect or probable cases
  - **viral RNA** or viral **antigen**

- Laboratory-confirmed cases must test positive for the presence of the Ebola virus
  - virus **RNA** by **RT-PCR**
  - Ebola **antigen** by a specific Antigen detection test
  - **IgM antibodies** directed against Ebola

- **Two negative RT PCR** test results, at least 48 hours apart, are required for a clinically **asymptomatic patient to be discharged** from hospital

Laboratory Guidance for the Diagnosis of Ebola Virus Disease
Interim Recommendations, WHO

INTERIM GUIDANCE FOR

Specimen Collection, Transport, Testing, and Submission for Patients with Suspected Infection with Ebola Virus Disease

NOTIFICATION & CONSULTATION

Hospitals should follow their state and/or local health department procedures for notification and consultation for Ebola testing requests before contacting CDC.

CDC cannot accept any specimens without prior consultation.

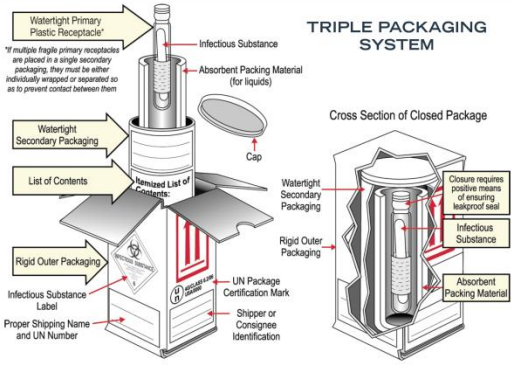
FOR CONSULTATION, CALL THE CDC EMERGENCY OPERATIONS CENTER AT

770-488-7100

TRANSPORTING SPECIMENS WITHIN THE HOSPITAL / INSTITUTION

In compliance with 29 CFR 1910.1030, specimens should be placed in a durable, leak-proof secondary container for transport within a facility. To reduce the risk of breakage or leaks, do not use any pneumatic tube system for transporting suspected Ebola virus disease specimens.

PACKAGING & SHIPPING CLINICAL SPECIMENS TO CDC



Specimens collected for Ebola virus disease testing should be packaged and shipped without attempting to open collection tubes or aliquot specimens.

Specimens for shipment should be packaged following the basic triple packaging system which consists of a primary container (a sealable specimen bag) wrapped with absorbent material, secondary container (watertight, leak-proof), and an outer shipping package.

THE SUBMISSION PROCESS

Contact your state and/or local health department and CDC (770-488-7100) to determine the proper category for shipment based on clinical history and risk assessment by CDC and to obtain detailed shipping guidance and required CDC submission documents. State guidelines may differ and state or local health departments should be consulted before shipping.

INFORMATION ON SHIPPING & TRACKING IS AVAILABLE AT

www.cdc.gov/ebola

a CLIA-accredited laboratory. Virus isolation may also be attempted. Serologic testing for IgM and IgG antibodies will be completed for certain specimens and to monitor the immune response in confirmed Ebola virus disease patients (#CDC-10310 Ebola Serology).

Lassa fever is also endemic in certain areas of West Africa and may show symptoms similar to early Ebola virus disease. Diagnostic tests available at CDC include but are not limited to RT-PCR, antigen detection, and IgM serology, all of which may be utilized to rule out Lassa fever in patients who test negative for Ebola virus disease.

- **PHYSICAL INACTIVATION**
  - moderately thermolabile
  - can be inactivated by heating for 30 minutes to 60 minutes at 60°C, boiling for 5 minutes
  - gamma irradiation (1.2 x106 rads to 1.27 x106 rads) combined with 1% glutaraldehyde
  - moderately sensitive to UVC radiation

http://www.phac-aspc.gc.ca/lab-bio/res/psds-ftss/ebola-eng.php

- **Biosafety recommendations** for laboratories conducting diagnostic testing for EVD with appropriate biosafety level 4 (BSL4)/BSL3 facilities

  - **Virus isolation** should be done only in a maximum containment **BSL4 laboratory**
  - The **inactivation** of specimens, depending on the detection protocol used, should be performed under **BSL3** conditions
  - For **non-inactivated** samples, **RT PCR** and **enzyme-linked immunosorbent assay (ELISA)** testing can be performed at a **BSL3** laboratory
  - If samples have been **inactivated** (i.e. cell lysis) **RT PCR** and **ELISA** testing can be performed at a **BSL2** laboratory

Laboratory Guidance for the Diagnosis of Ebola Virus Disease Interim Recommendations, WHO

Class III Biological safety Cabinet

- Biosa… c
  testi…
  - S… e
    a… a
    s…
  - F… x
    a…
  - U…
    tl…
    N…
    P…
    d…

Table 2. Summary of Recommended Biosafety Levels for Infectious Agents

BSL	Agents	Practices	Primary Barriers and Safety Equipment	Facilities (Secondary Barriers)
1	Not known to consistently cause diseases in healthy adults	Standard microbiological practices	■ No primary barriers required. ■ PPE: laboratory coats and gloves; eye, face protection, as needed	Laboratory bench and sink required
2	■ Agents associated with human disease ■ Routes of transmission include percutaneous injury, ingestion, mucous membrane exposure	BSL-1 practice plus: ■ Limited access ■ Biohazard warning signs ■ "Sharps" precautions ■ Biosafety manual defining any needed waste decontamination or medical surveillance policies	Primary barriers: ■ BSCs or other physical containment devices used for all manipulations of agents that cause splashes or aerosols of infectious materials ■ PPE: Laboratory coats, gloves, face and eye protection, as needed	BSL-1 plus: ■ Autoclave available
3	Indigenous or exotic agents that may cause serious or potentially lethal disease through the inhalation route of exposure	BSL-2 practice plus: ■ Controlled access ■ Decontamination of all waste ■ Decontamination of laboratory clothing before laundering	Primary barriers: ■ BSCs or other physical containment devices used for all open manipulations of agents ■ PPE: Protective laboratory clothing, gloves, face, eye and respiratory protection, as needed	BSL-2 plus: ■ Physical separation from access corridors ■ Self-closing, double-door access ■ Exhausted air not recirculated ■ Negative airflow into laboratory ■ Entry through airlock or anteroom ■ Hand washing sink near laboratory exit
4	■ Dangerous/exotic agents which post high individual risk of aerosol-transmitted laboratory infections that are frequently fatal, for which there are no vaccines or treatments ■ Agents with a close or identical antigenic relationship to an agent requiring BSL-4 until data are available to redesignate the level ■ Related agents with unknown risk of transmission	BSL-3 practices plus: ■ Clothing change before entering ■ Shower on exit ■ All material decontaminated on exit from facility	Primary barriers: ■ All procedures conducted in Class III BSCs or Class I or II BSCs in combination with full-body, air-supplied, positive pressure suit	BSL-3 plus: ■ Separate building or isolated zone ■ Dedicated supply and exhaust, vacuum, and decontamination systems ■ Other requirements outlined in the text

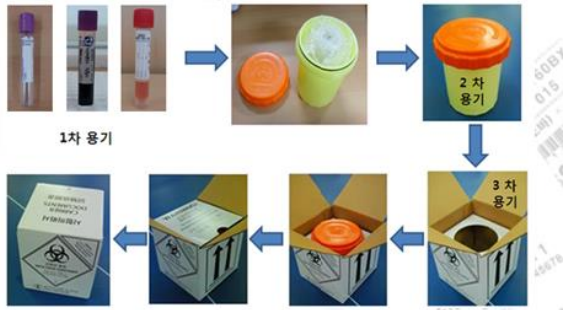
http://www.cdc.gov/biosafety/publications/bmbl5/bmbl5_sect_iv.pdf

❖ 진단방법

- 유전자 검사 (Real-time RT-PCR 등)
- 항체 검출검사 (IgM ELISA, IgG ELISA 등)
- 항원 검출 검사 (Antigen-capture ELISA 등)
- 바이러스 분리 검사

BL3+ 실험실

검체 이송 도구(3차 수송용기



질병관리본부

에볼라대응 의료기관교육자료(응급센터용), 질병관리본부

Treatment

- **Supportive care**
  - preventing intravascular volume depletion, correcting profound electrolyte abnormalities, and avoiding the complications of shock
    - careful hemodynamic monitoring, and **intravenous fluid** repletion requirements may be high (eg, 5 to 10 liters per day)
    - reduced effective arterial blood volume despite extracellular fluid volume overload (ie, "third spacing")
    - nutrition support
    - Intensive nursing
  - Symptomatic management of fever and gastrointestinal symptoms
    - Avoid NSAIDS
  - Multisystem organ failure can develop and may require
    - Oxygenation and mechanical ventilation
    - Correction of severe coagulopathy
    - Renal replacement therapy

- evaluated and treated for concomitant malaria

- Empiric antimicrobial treatment
  - vomiting, diarrhea, and/or other signs of severe gastrointestinal dysfunction and/or signs of sepsis

- **Experimental therapies**
  - A "cocktail" of three monoclonal antibodies directed against the Ebola viral glycoprotein ("**ZMapp**")
  - **whole blood or serum** from **convalescent** Ebola virus disease **survivors**
    - World Health Organization has issued interim guidance
  - Other treatment approaches
    - Brincidofovir
    - RNA interference agent (TKM-Ebola) : Tekmira
    - Ribavirin has no in-vitro or in-vivo effect on Ebola virus

Prevention

- **Quickly identifying and isolating patients with known or suspected Ebola**
  - Screening patients when they first enter the healthcare system
  - Laying out facilities to make it easier to screen and diagnose suspected cases
  - Implementing strict policies for visitation
  - Closely monitoring healthcare workers for fever or other symptoms
  - Implementing effective healthcare worker sickness notification and leave policies

- **Protecting patients and healthcare workers**
  - Good hand hygiene practices
  - Use of appropriate personal protective equipment (PPE)
  - Following safe injection practices and drawing blood safely

- **Cleaning up safely**
  - Performing environmental cleaning and disinfection
  - Managing waste safely and appropriately

- **Managing patients safely and compassionately**
  - Establishing and following protocols for notifying authorities about suspected Ebola patients
  - Safe initial management of suspected Ebola cases while awaiting patient transport to another setting
  - Communicating with patients to effectively and compassionately educate them about their suspected illness and what to expect during their treatment process

Guidance on Personal Protective Equipment To Be Used by Healthcare Workers During Management of Patients with Ebola Virus Disease in U.S. Hospitals, Including Procedures for Putting On (Donning) and Removing (Doffing), CDC 2014.10.20

- key principles
  - Prior to working with Ebola patients, all healthcare workers involved in the care of Ebola patients must have received **repeated training** and have demonstrated **competency in performing all Ebola-related infection control practices and procedures**, and specifically in **donning/doffing proper PPE**
  - While working in PPE, healthcare workers caring for Ebola patients should have **no skin exposed**
  - The overall safe care of Ebola patients in a facility must be overseen by an **onsite manager** at all times, and each step of every PPE donning/doffing procedure must be supervised by a **trained observer** to ensure proper completion of established PPE protocols

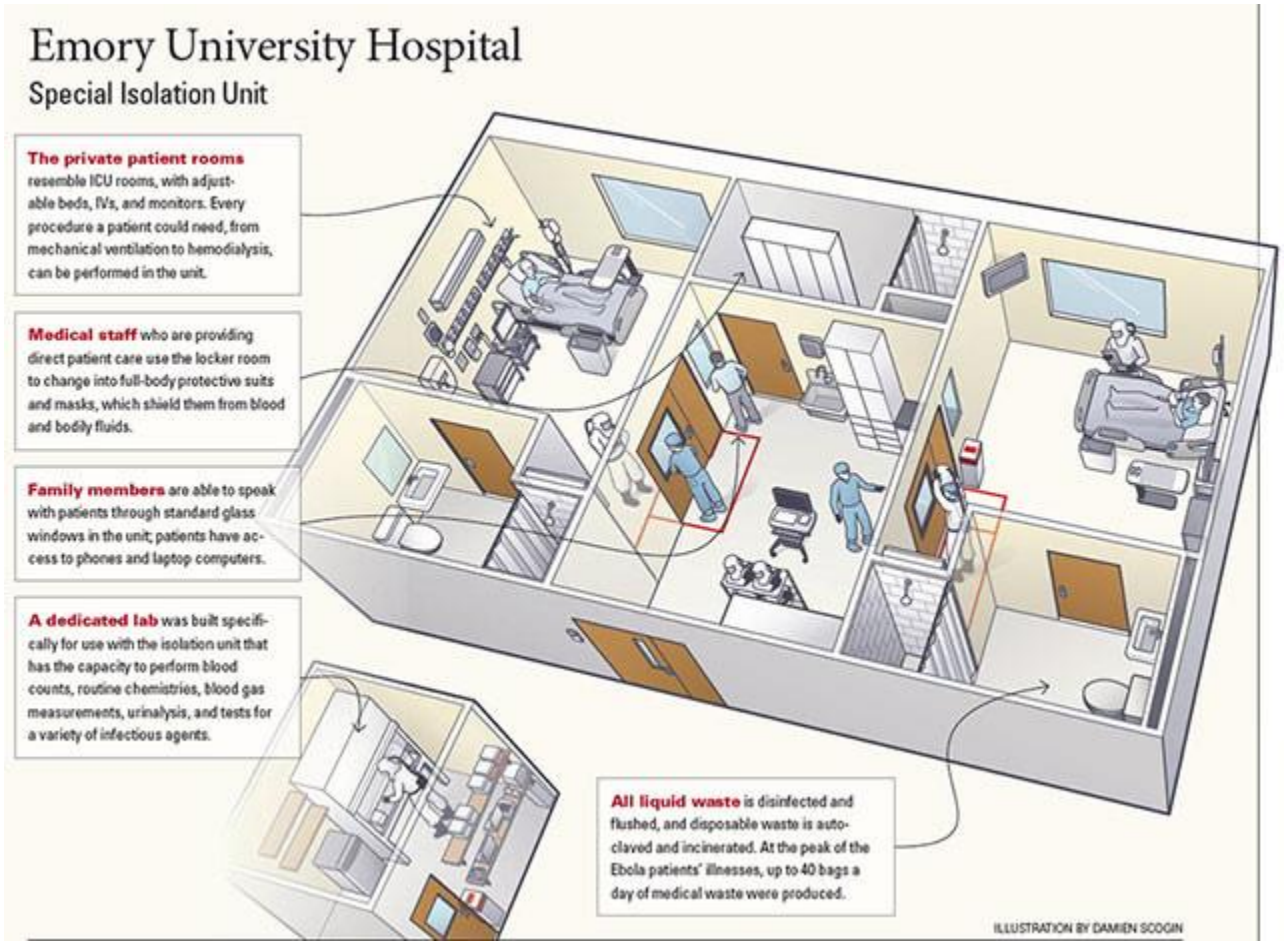
Patient Recovery

- Case-fatality rate 71% in the 2014 Ebola outbreak
  - Case-fatality rate is likely much lower with access to intensive care

- Patients who survive often have **signs of clinical improvement** by the **second week** of illness
  - Associated with the development of virus-specific antibodies
  - Antibody with neutralizing activity against Ebola persists greater than 12 years after infection

- Prolonged convalescence
  - Includes arthralgia, myalgia, abdominal pain, extreme fatigue, and anorexia; many symptoms resolve by 21 months
  - Significant arthralgia and myalgia may persist for >21 months
  - Skin sloughing and hair loss has also been reported

해외 격리시설


Emory University Hospital
Special Isolation Unit
The private patient rooms resemble ICU rooms, with adjustable beds, IVs, and monitors. Every procedure a patient could need, from mechanical ventilation to hemodialysis, can be performed in the unit.
Medical staff who are providing direct patient care use the locker room to change into full-body protective suits and masks, which shield them from blood and bodily fluids.
Family members are able to speak with patients through standard glass windows in the unit; patients have access to phones and laptop computers.
A dedicated lab was built specifically for use with the isolation unit that has the capacity to perform blood counts, routine chemistries, blood gas measurements, urinalysis, and tests for a variety of infectious agents.
All liquid waste is disinfected and flushed, and disposable waste is autoclaved and incinerated. At the peak of the Ebola patients' illnesses, up to 40 bags a day of medical waste were produced.
ILLUSTRATION BY DAMIEN SCOGIN


© picture alliance/dpa


BRITAIN
1 Half-suits and gloves
Doctors step into these for contact with patients
2 Isolator tent
Completely surrounds hospital bed
3 Air pressure unit
Controls air pressure within tent
4 Isolator trolley
To pass food, drink and medicine safely to patient
5 Air waistcoat
Pumps air around doctor's body to stay cool within half-suit
RISK: Britain can treat just two ebola patients securely at any
© George Jaworskyj

국내 상황

EBOLA VIRUS DISEASE (EVD)

1. 의료기관에서 에볼라바이러스병 대응에 대한 개요

1-1. 해야 할 일

- ○ 에볼라바이러스병에 대한 병원의 대응 계획을 실행
- ○ 전용 욕실을 갖추었거나 별도의 공간으로 분리된 장소에 환자 격리
- ○ 개인보호장비(PPE) 표준 프로토콜을 준비하고 환자 치료 영역에 비치
- ○ 환자 면접조사
  - – 응급실 오기 전 처음 증상 발병의 날짜와 증상 발현의 순서
  - – 상세하고 정확한 여행 기록 (예를 들어, 날짜, 시간, 위치)
  - – 증상 발병의 초기이후부터 환자가 접촉한 사람들의 이름 및 연락처
- ○ 환자의 증상 및 노출력 등을 고려하여 유행국가 여행력이 없는 경우에는 반드시 감별진단 등을 고려할 것 (예 : 말라리아, 장티푸스 등)

1-2. 하지 말아야 할 일

- ○ 적절한 개인보호장비 없이 환자와 신체적 접촉을 하지 말 것
- ○ 환자에게 필요한 의료서비스를 간과하지 말 것
- ○ 불필요한 검사 또는 의료행위를 수행하지 말 것

의료기관용 에볼라 대응 관리지침 10.27 , 질병관리본부

1-3. 단계별 대응방법

STEP 1 스크리닝

- 38℃ 이상의 발열
- 심한 두통, 근육통, 허약감, 설사, 구토, 설명되지 않은 출혈
- 지난 21일간 에볼라 유행지역을 방문했거나 에볼라 환자와 노출되었는지 여부

STEP 2 에볼라바이러스병이 의심된다면

- 다른 의료진과 환자 상태 평가
- 병원내 감염관리실로 발생상황을 알림
  보건당국(관할 보건소 및 질병관리본부)에 즉시 보고

  (에볼라대응핫라인 : 043-719-7777)

STEP 3 의심환자에게 설명

- 격리한 이유와 국가지정입원치료병원이송이 필요함을 설명
- 의심환자에게 마스크 착용(대화, 재채기 등에 의한 분비물 수를 줄이기 위해)

STEP 4 환자 격리

- 의심환자는 독립된 공간에 격리
- 전담인력은 반드시 개인보호장비*를 착용하고 이외 인력은 접촉제한

  *** 환자의 상태(발열 또는 기타 분비물이 많은 경우)에 따라 부록 1을 참고하여 장비 착용**

STEP 5 보고 및 이송

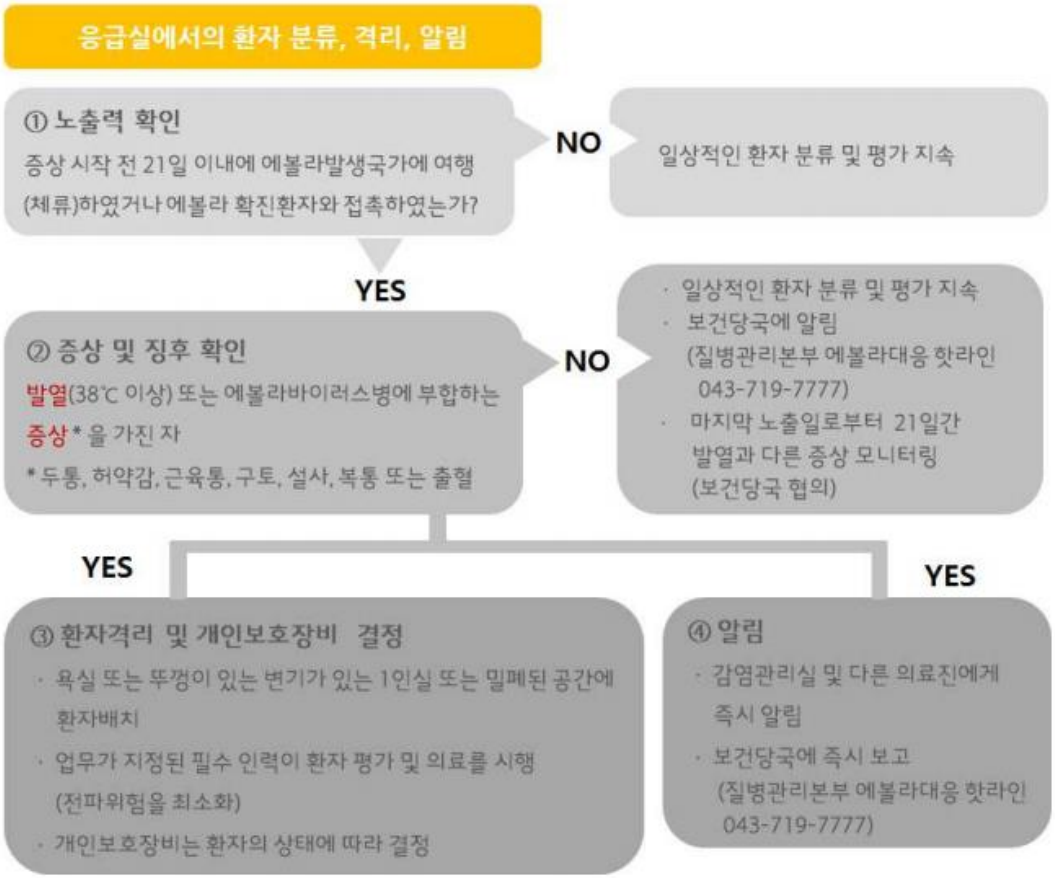
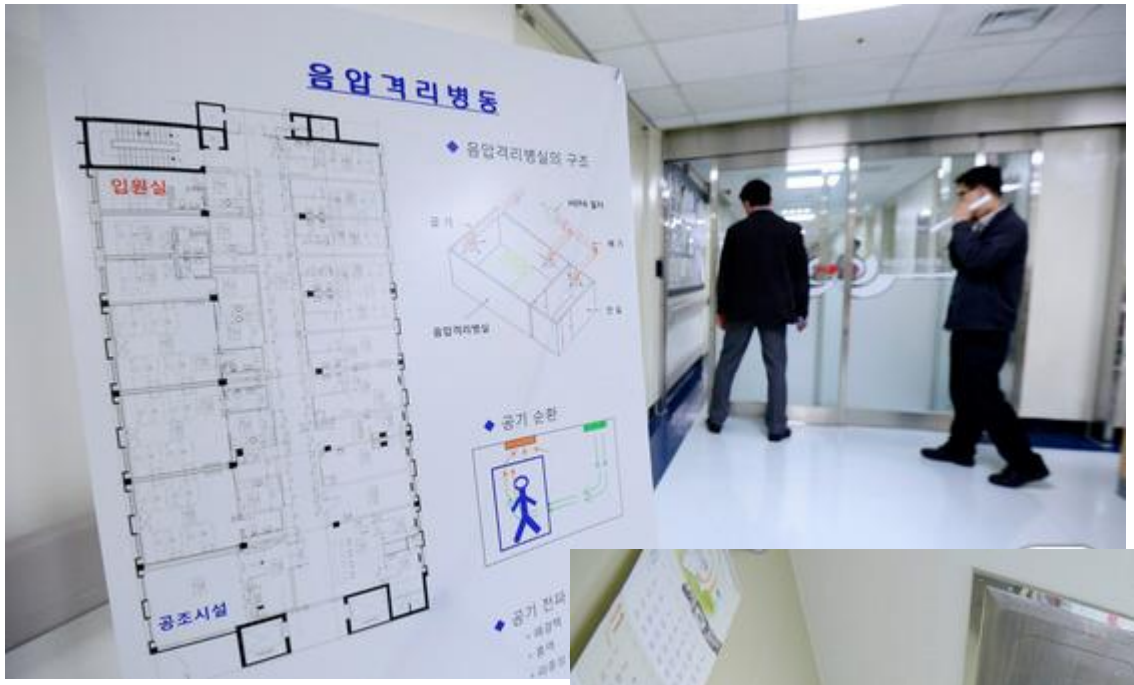


그림 3. 응급실에서의 환자 분류, 격리, 알림

의료기관용 에볼라 대응 관리지침 10.27 , 질병관리본부


음압격리병동
입원실
◆ 음압격리병실의 구조
◆ 공기 순환
공조시설


news 1

문제점과 앞으로의 과제

- 의료진 파견 결정시까지 민주적 의사결정 절차 부재
  - 대다수 감염내과 의사들 조차도 대통령의 독단으로 생각
- 국내의 부적합한 격리시설
- 파견 의료진 또는 내/외국인 환자가 발생할 경우 격리와 진단, 치료에 이르는 과정이 제대로 이루어질지 심히 우려
  - 국가지정격리병원에서 자신의 지정유무조차 모름
  - 질병관리본부는 환자문의에 무책임한 태도로 일관
  - 국가지정격리병원에서 의심환자를 진료할 때 적절한 개인보호장구가 지급되지 않음

- 보건복지부, 질병관리본부에서 10월 27일자로 발표한 [의료기관용 에볼라 대응 관리지침] – 국가지정격리병원 외 의료기관용 – 에도 원칙적인 이야기를 나열하고 있을 뿐 개별 의료기관이 개인보호장구를 어떻게 확보할 수 있을지에 대해서는 나와있지 않으며, 환자이송시에도 관할보건소의 지시에 따라 국가지정격리병원으로 이송하라고만 되어있어, 국가지정격리병원 외 의료기관에 환자가 내원했을시 큰 혼란이 우려

- 의료진 파견과는 별개로 의심 또는 추정 환자의 식별 및 격리, 진단 및 치료에 대한 준비를 철저히 해야 하겠고, 이송절차에 있어서도 실행가능한 구체적인 지침이 마련되어야 하겠다. 특이 지정격리병원 외의 의료기관에 환자가 내원하였을 경우에 대비한 추가적인 보완책이 있어야 할 것으로 보임

경청해 주셔서 감사합니다!