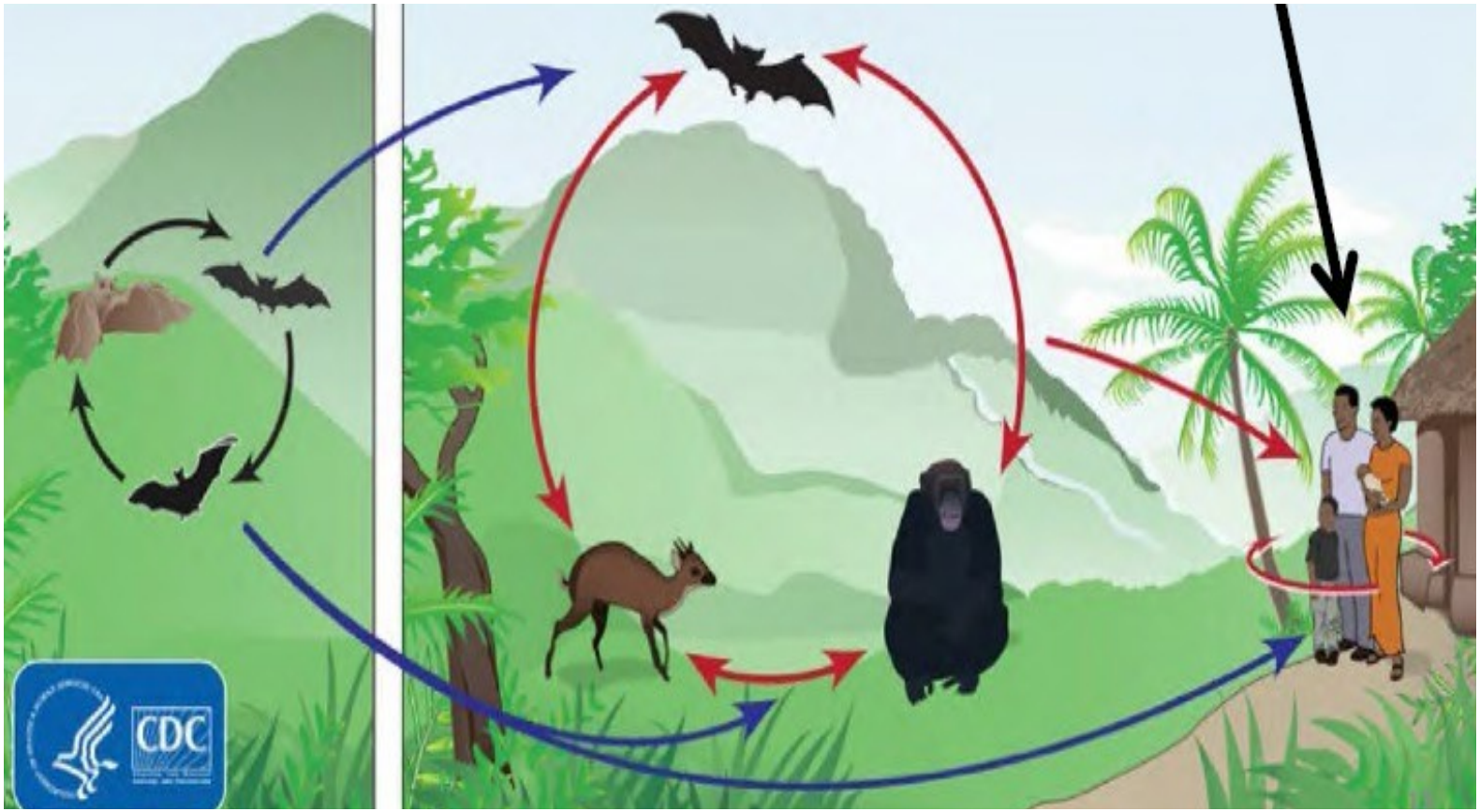
Overview of Ebola epidemiology

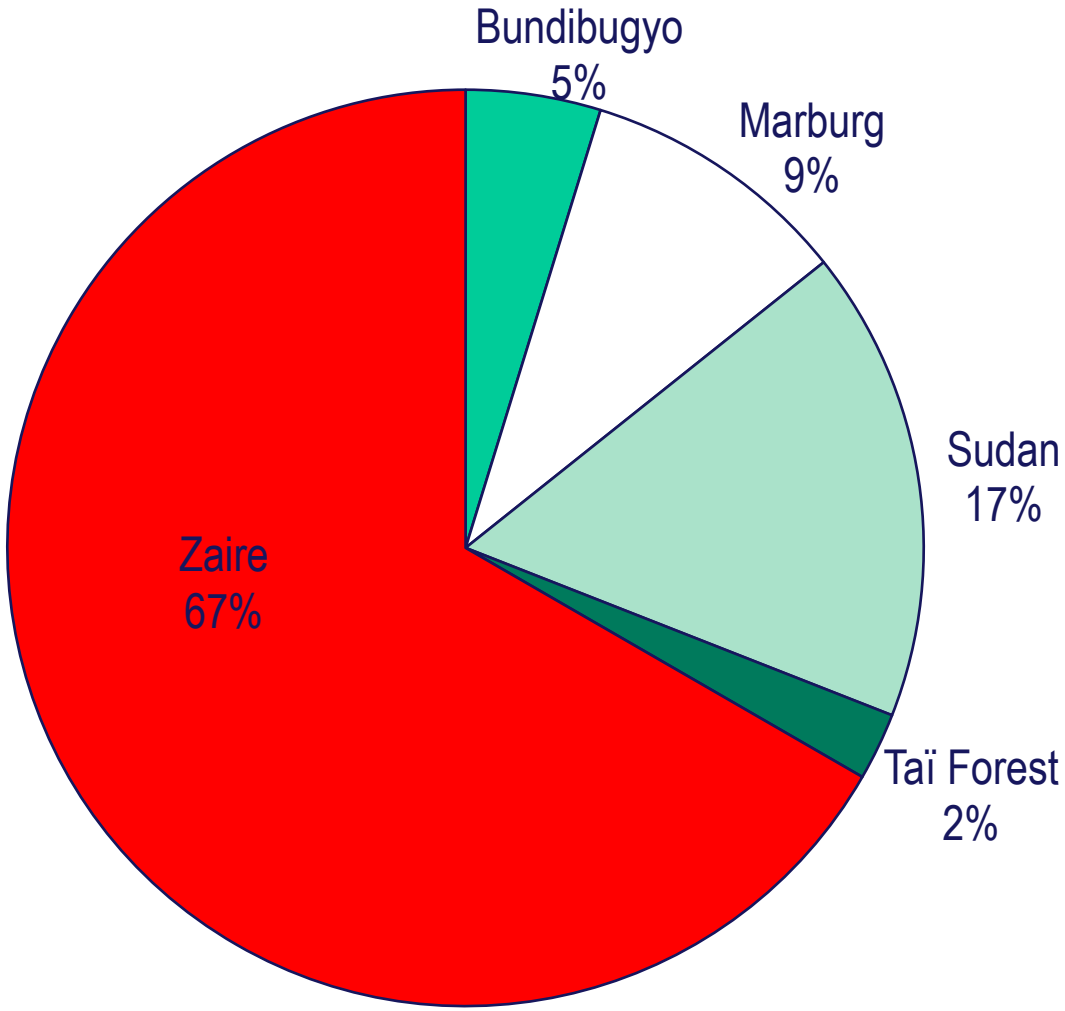
October 2018

Yambuku Mission Hospital, DRC (Zaire), 1976

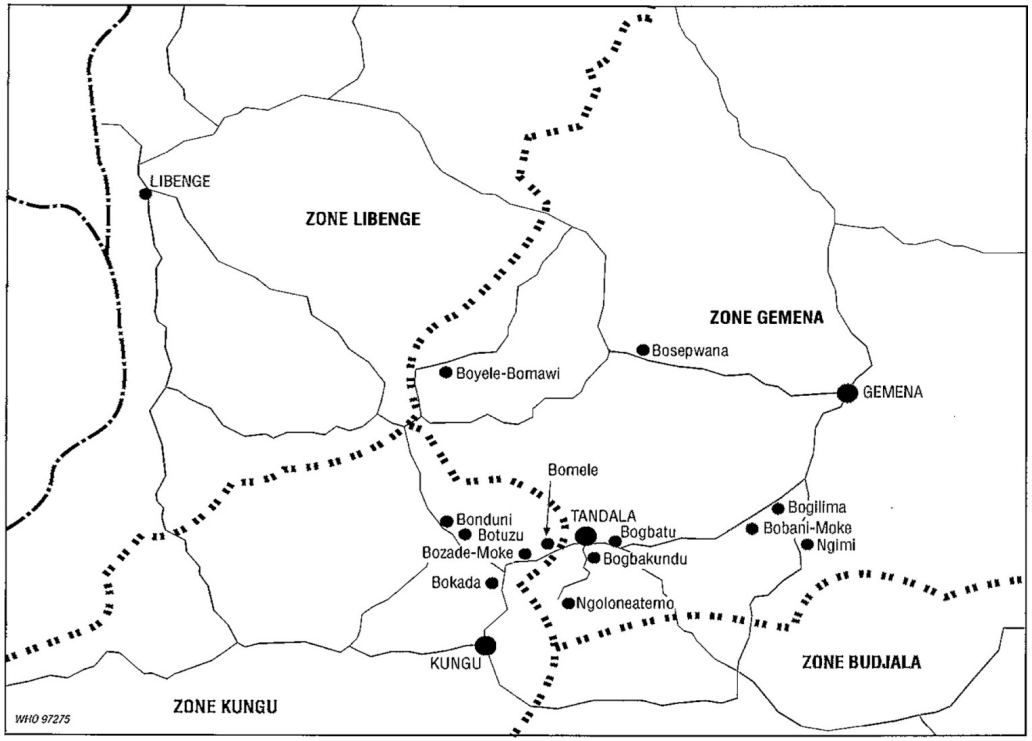
Ebola emergence: current hypotheses



Filovirus strains, Africa



Ebola haemorrhagic fever surveillance, Zaire, 1981–1985: IFA positive possible, probable and clinical cases

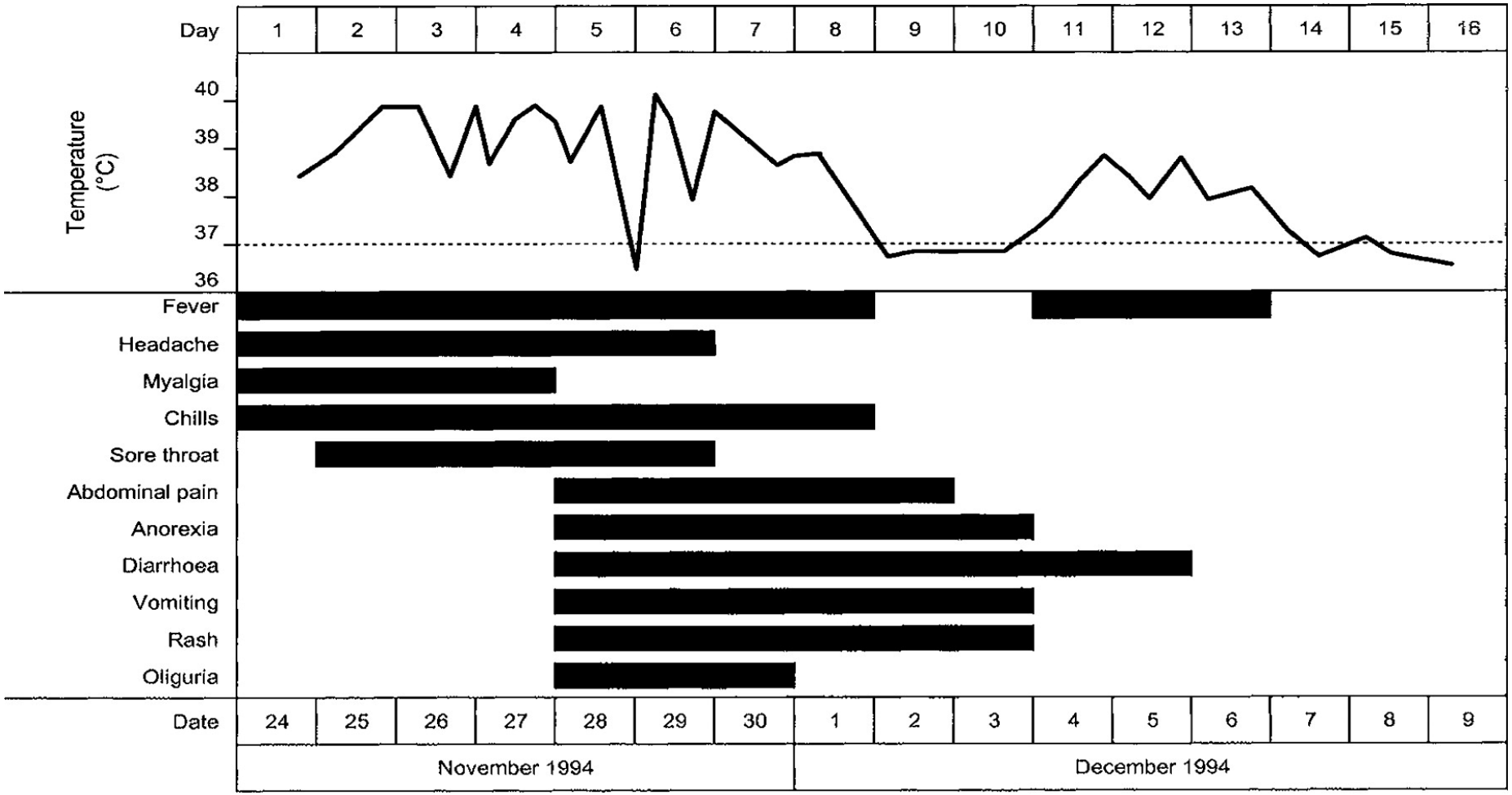


Case definition	1981 (n = 0)	1982 (n = 4)	1983 (n = 36)	1984 (n = 27)	1985 (n = 31)	1981–1985 (n = 98)
Possible	0	0	0	1	2	3
Clinical	0	1	4	2	4	11
Probable	0	2	5	0	0	7
Total	0	3	9	3	6	21

NOTE. n = no. of surveillance reports investigated.

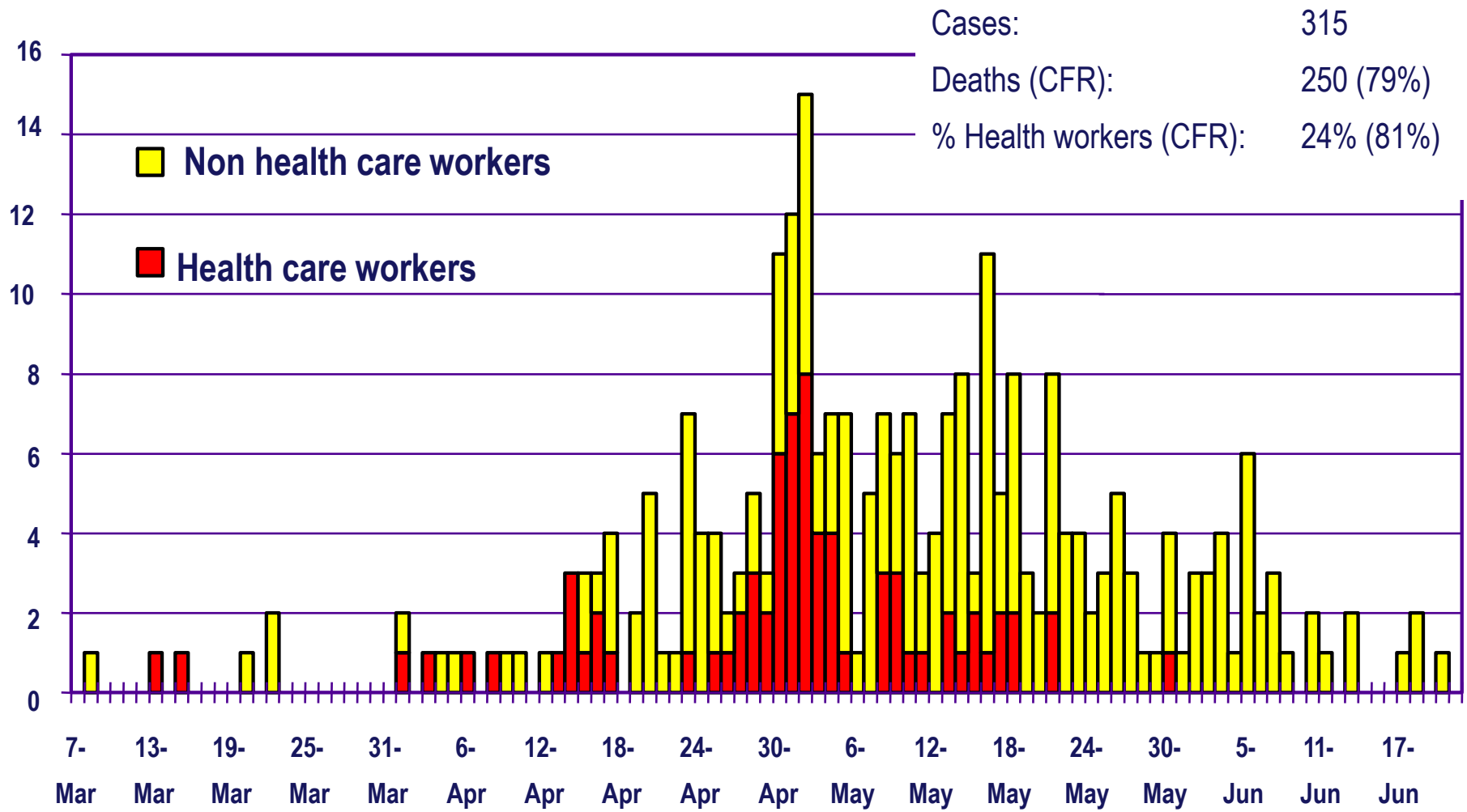
Source: Jezek Z, et al, JID 1999

Clinical course, Ebola virus infection, patient presumably infected during necropsy of infected chimpanzee



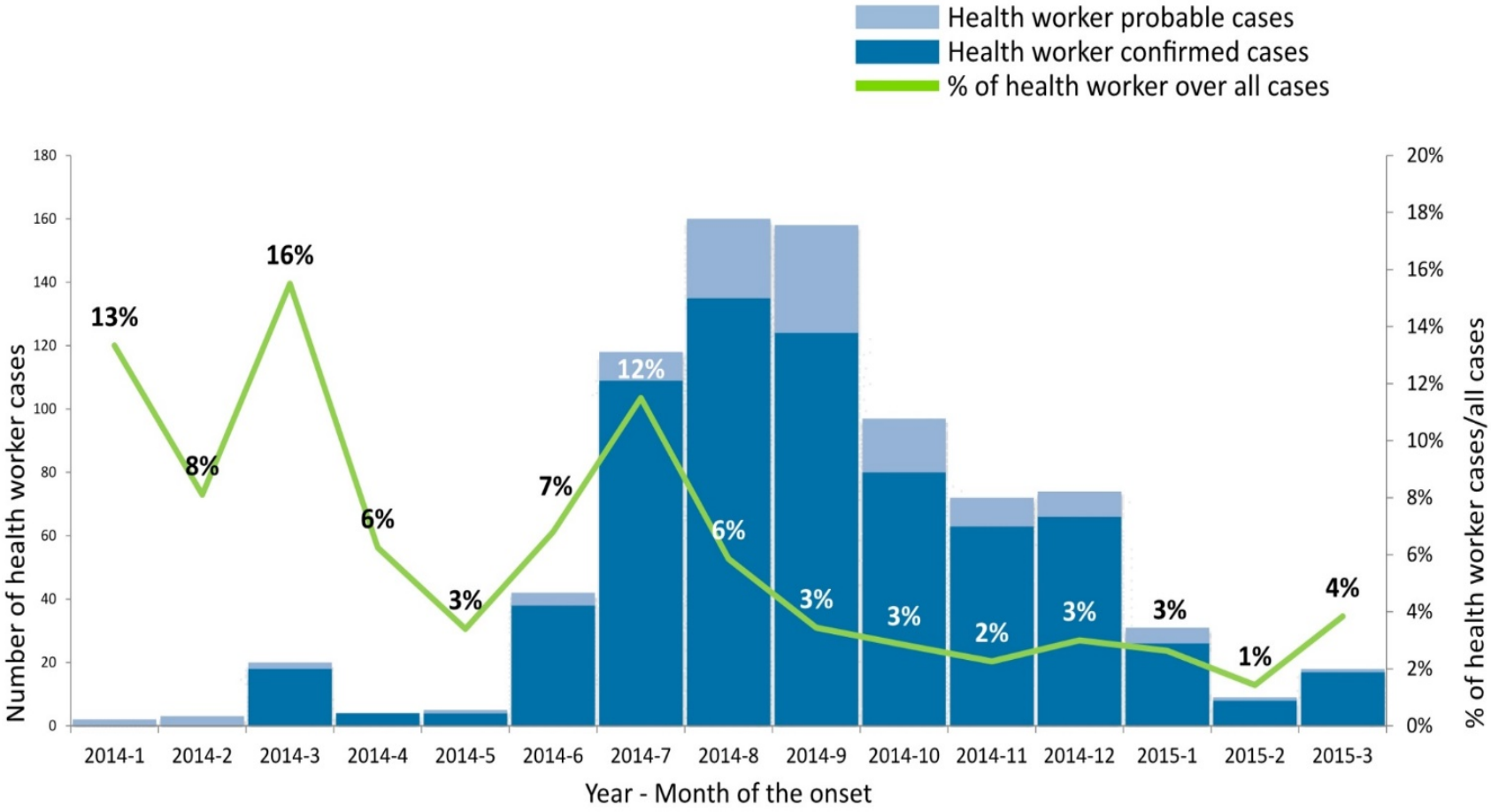
Formenty P et al. J Infect Dis. 1999;179:S48-S53

Percentage of healthcare workers, confirmed as EVD cases,Kikwit Zaire, 1995



Source: WHO, CDC, Benowitz et al. 2014

Percentage of healthcare workers, confirmed as EVD cases in West Africa, 2014-2015



**All cases include health worker and non-health worker confirmed and probable cases.*

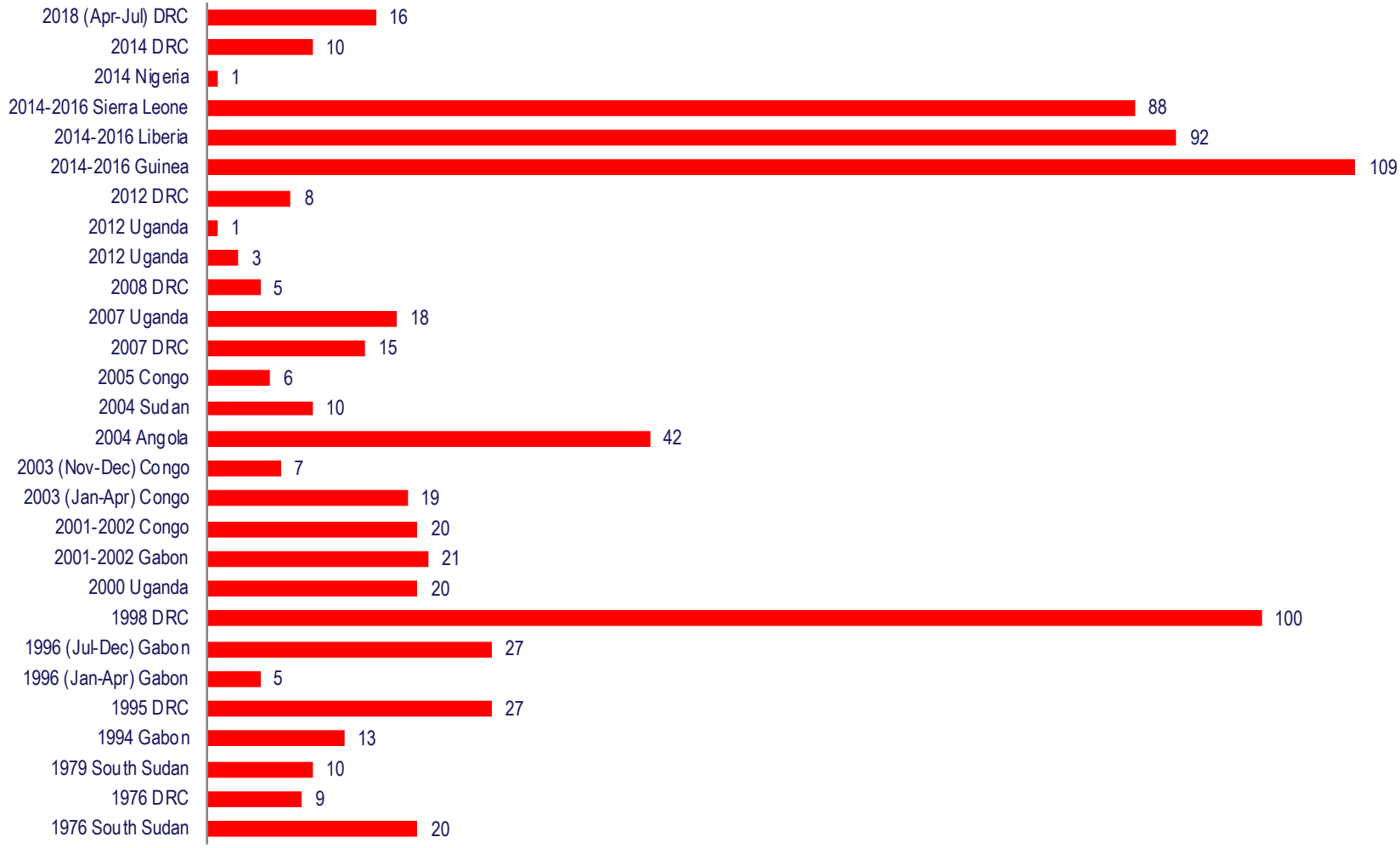
Source: WHO

Ebola outbreak, Ikanamongo, DRC, 2014

- Cases: 66
- Deaths: 49 (74%)
- Health workers: 8
- Duration: August-October

Duration of Ebola outbreak (weeks), 1976-2018

(outbreaks with > 10 cases)

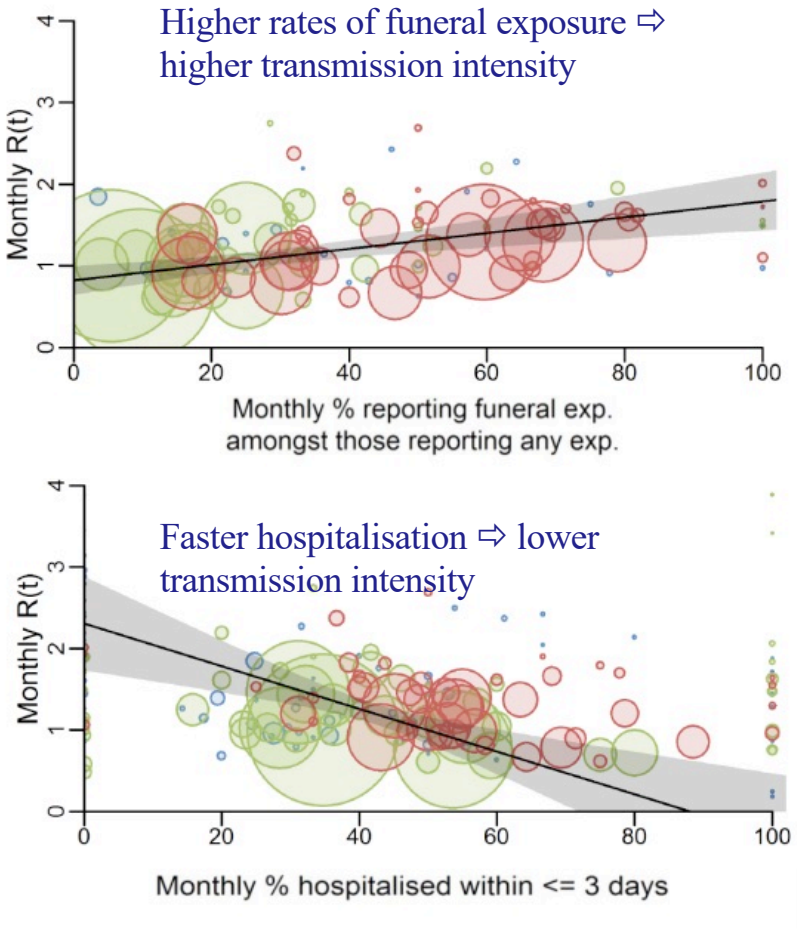


Source: WHO

Ebola, weeks to first epidemic peak 1976-2018
(outbreaks with >10 cases)

Source: WHO

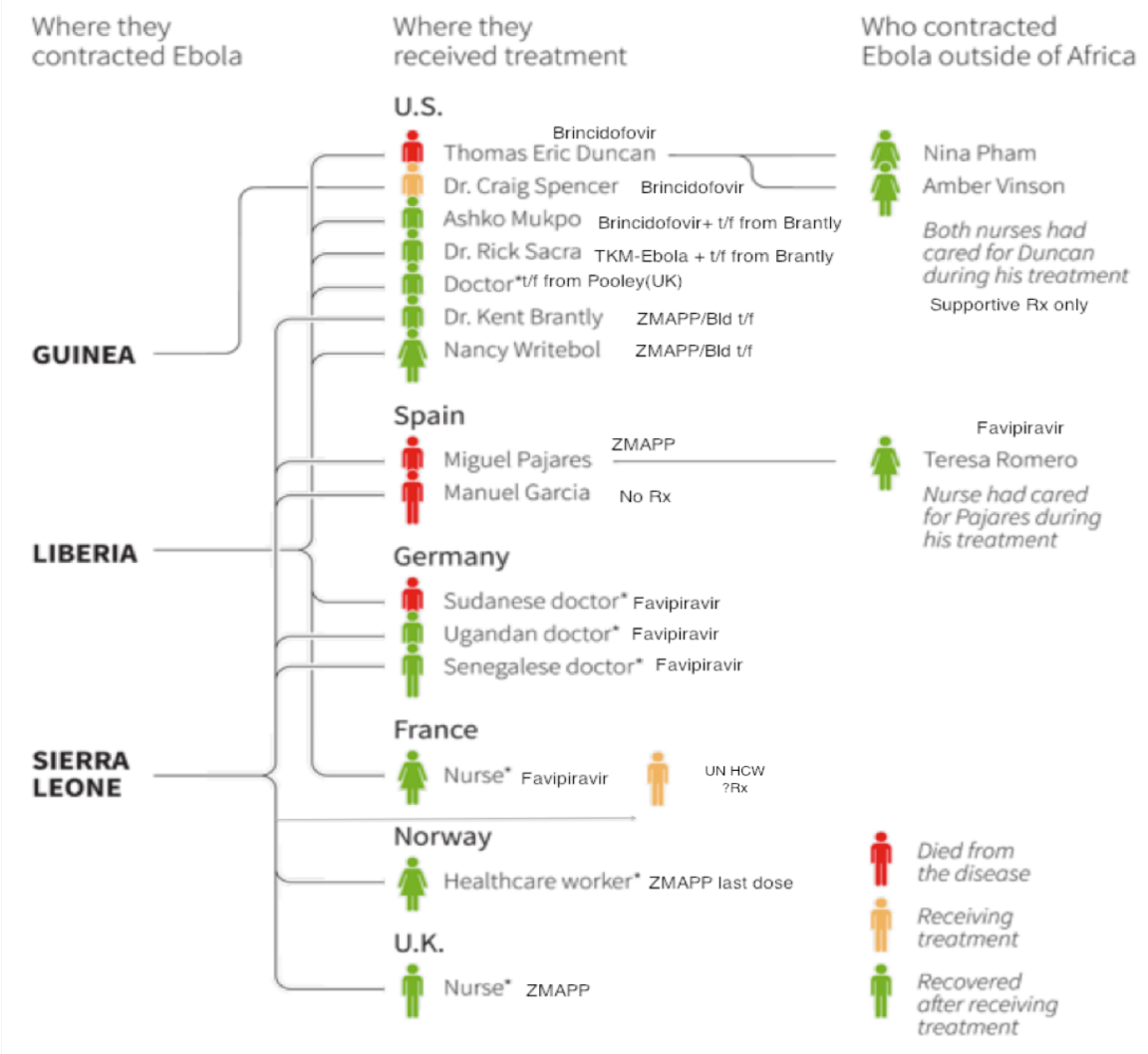
District level analysis, Ebola transmission, West Africa 2014



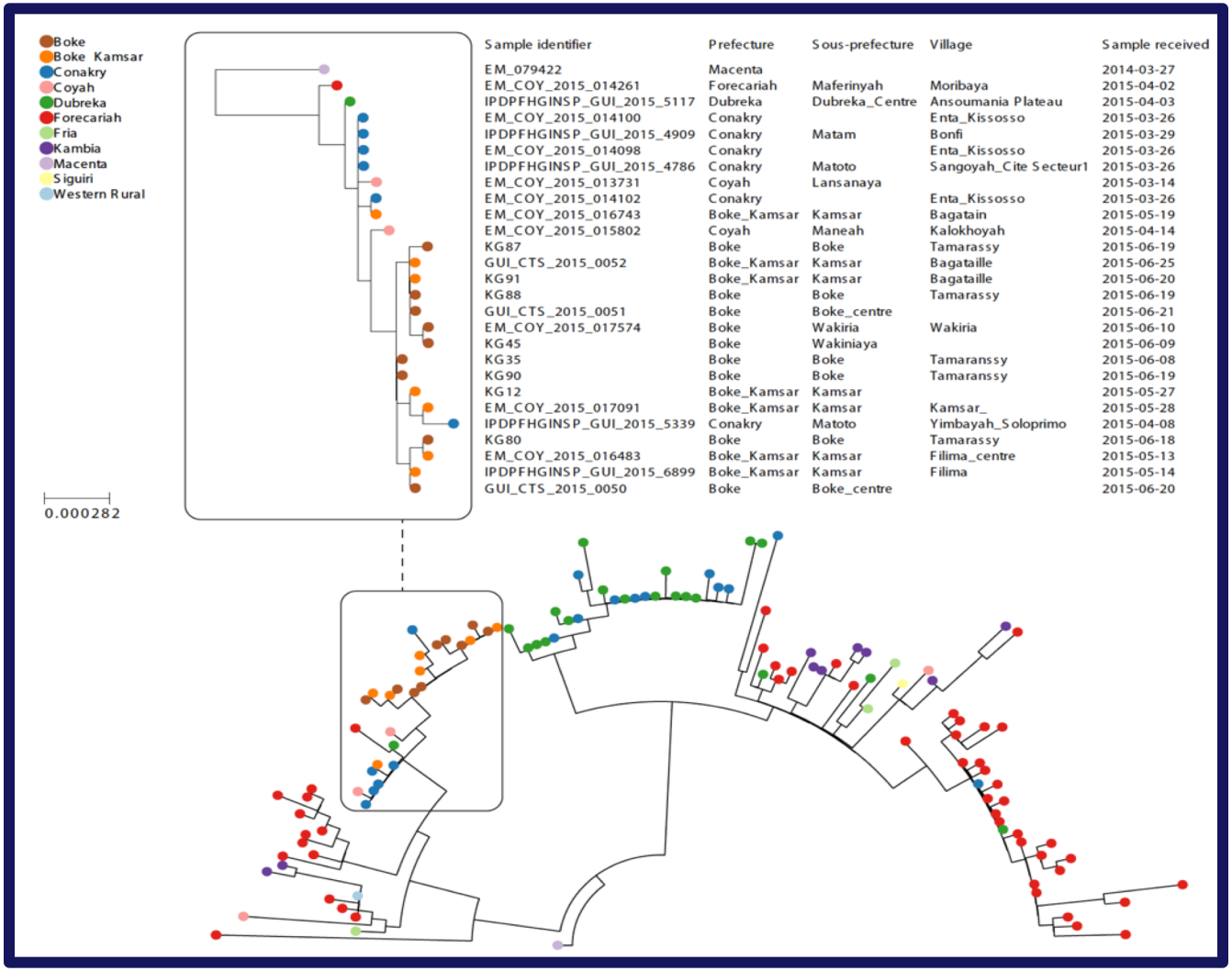
Source: Ebola Response Team, Imperial College, *PLoS Med, 2016*

Correlation between R(t) and the proportion of cases who reported funeral exposure amongst those reporting any exposure (top), and between R(t) and the proportion of hospitalised cases who are hospitalised within <=3 days (bottom). Each point represents a district-month and the size of a point is proportional to its weight – a larger point has more weight (less uncertainty). Points are shown in blue for districts in Guinea, in green for Liberia and red for Sierra Leone.

Ebola: where treated may make a difference



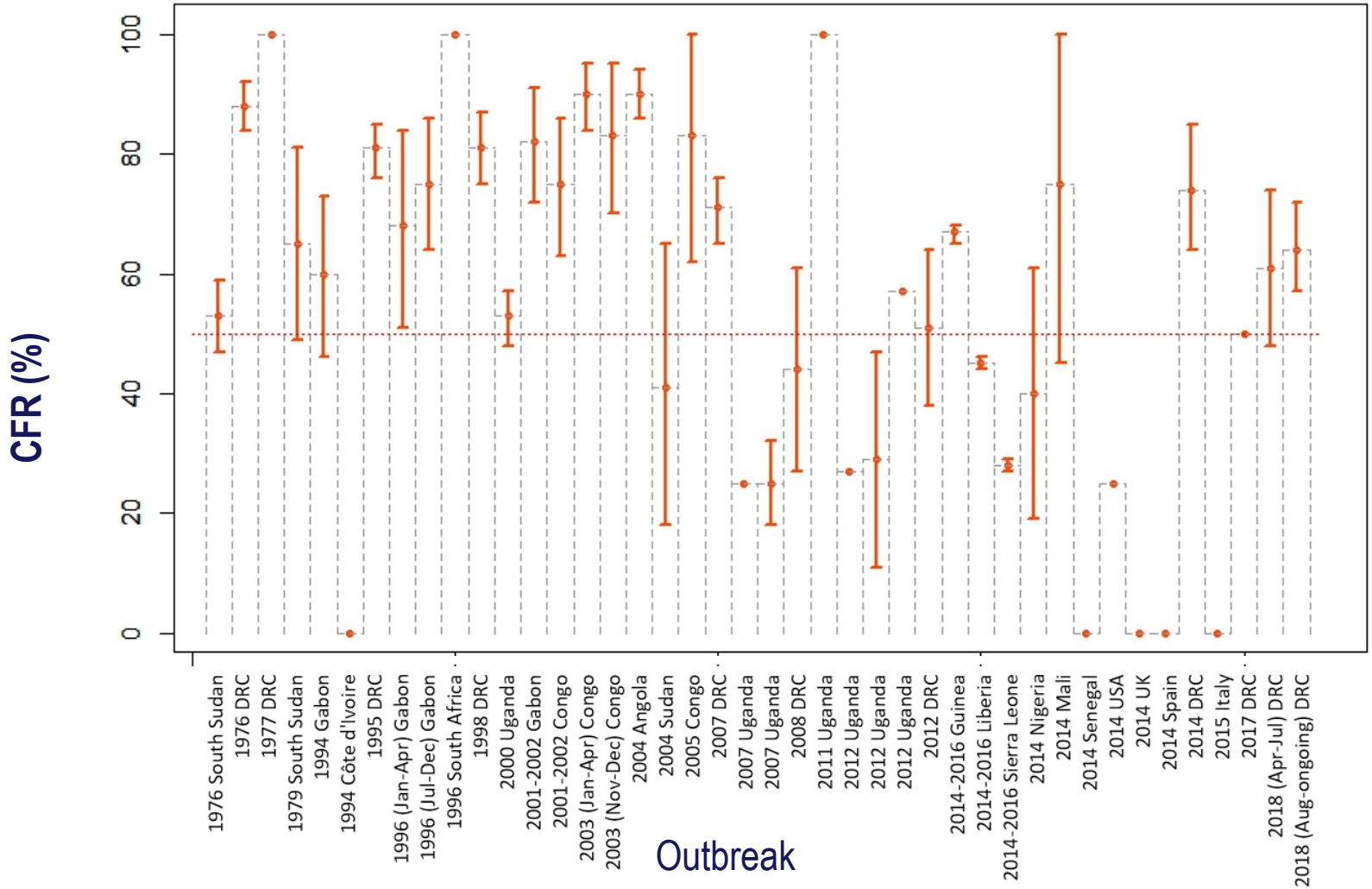
Ebola surveillance and contact tracing across prefectures, Guinea, 2014 - 2016



Sample identifier	Prefecture	Sous-prefecture	Village	Sample received
EM_079422	Macenta			2014-03-27
EM_COY_2015_014261	Forecariah	Maferinyah	Moribaya	2015-04-02
IPDPFHGINSP_GUI_2015_5117	Dubreka	Dubreka_Centre	Ansoumania Plateau	2015-04-03
EM_COY_2015_014100	Conakry		Enta_Kissosso	2015-03-26
IPDPFHGINSP_GUI_2015_4909	Conakry	Matam	Bonfi	2015-03-29
EM_COY_2015_014098	Conakry		Enta_Kissosso	2015-03-26
IPDPFHGINSP_GUI_2015_4786	Conakry	Matoto	Sangoyah_Cite Secteur1	2015-03-26
EM_COY_2015_013731	Coyah	Lansanaya		2015-03-14
EM_COY_2015_014102	Conakry		Enta_Kissosso	2015-03-26
EM_COY_2015_016743	Boke_Kamsar	Kamsar	Bagatain	2015-05-19
EM_COY_2015_015802	Coyah	Maneah	Kalokhoyah	2015-04-14
KG87	Boke	Boke	Tamarassy	2015-06-19
GUI_CTS_2015_0052	Boke_Kamsar	Kamsar	Bagataille	2015-06-25
KG91	Boke_Kamsar	Kamsar	Bagataille	2015-06-20
KG88	Boke	Boke	Tamarassy	2015-06-19
GUI_CTS_2015_0051	Boke	Boke_centre		2015-06-21
EM_COY_2015_017574	Boke	Wakiria	Wakiria	2015-06-10
KG45	Boke	Wakiniaya		2015-06-09
KG35	Boke	Boke	Tamaranssy	2015-06-08
KG90	Boke	Boke	Tamaranssy	2015-06-19
KG12	Boke_Kamsar	Kamsar		2015-05-27
EM_COY_2015_017091	Boke_Kamsar	Kamsar	Kamsar_	2015-05-28
IPDPFHGINSP_GUI_2015_5339	Conakry	Matoto	Yimbayah_Soloprimo	2015-04-08
KG80	Boke	Boke	Tamarassy	2015-06-18
EM_COY_2015_016483	Boke_Kamsar	Kamsar	Filima_centre	2015-05-13
IPDPFHGINSP_GUI_2015_6899	Boke_Kamsar	Kamsar	Filima	2015-05-14
GUI_CTS_2015_0050	Boke	Boke_centre		2015-06-20

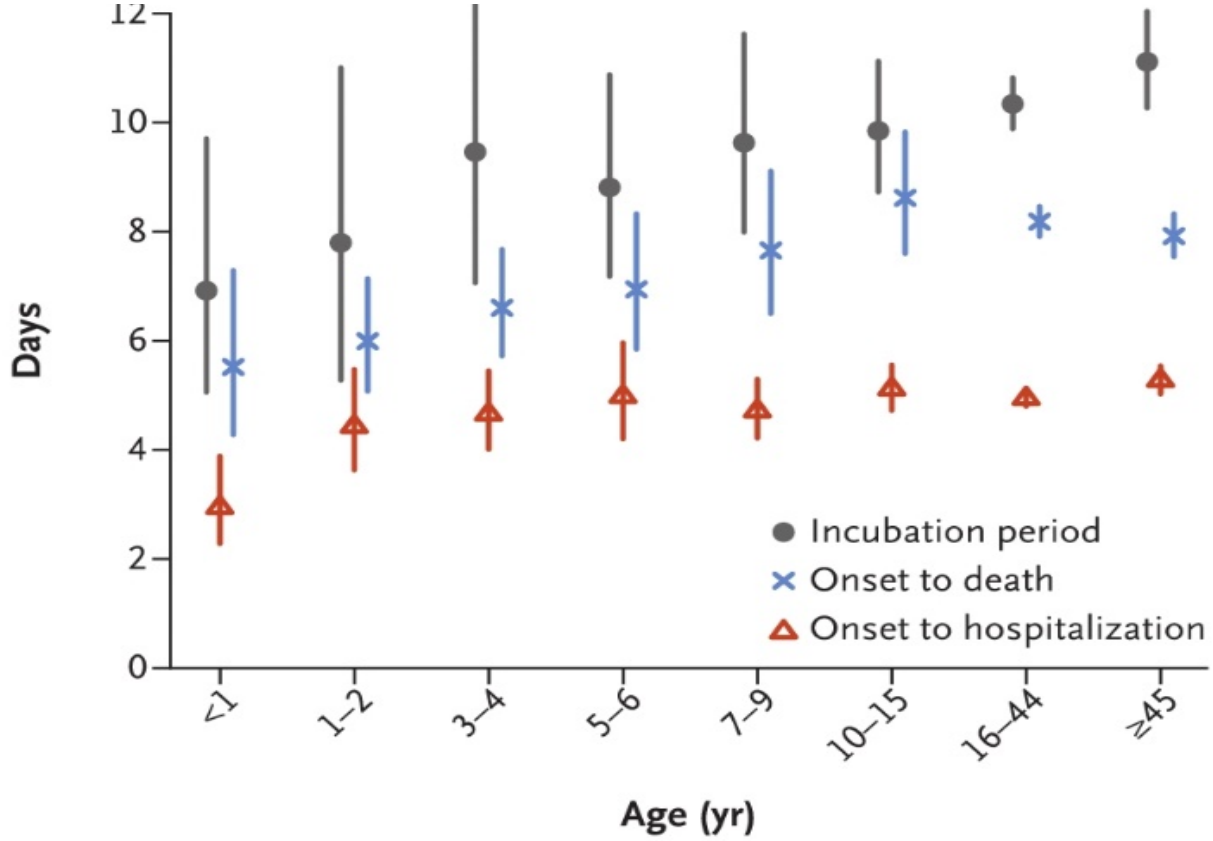
Source: Carroll M, et al Nature 2016

Case fatality rate (CFR), Ebola: possible, probable and confirmed cases, 1976-2018



Source: WHO

Estimated epidemiological parameters, Ebola West Africa, 2014-2015



Source: WHO Ebola Response Team, 2015

Ebola haemorrhagic fever surveillance, Zaire, 1981–1985: antibody among symptomatic contacts and asymptomatic community controls

Age group, years	No. of contacts tested/no. with titers ⩾1:64 (%)	No. of controls tested/no. with titers ⩾1:64 (%)	*P*
0–14	61/4 (7)	43/2 (5)	
15–19	13/2 (15)	10/0	
⩾20	114/22 (19)	84/0	
Total	188/28 (15)	137/2 (<1)	<.0001

Source: Jezek Z. The Journal of Infectious Diseases, Volume 179, Issue Supplement_1, 1 February 1999

IgG in Ebola survivors, household contacts and community controls, Sierra Leone, 2015

	Total	Positive			Negative				Indeterminate	IgG positive/total*	IgG positive (95% CI)
		RR	R	RUR	RUU	UUU	UU	U	RRUU		
Community controls	339	0	0	0	1	0	25	313	0	0/339	0·0% (0–1·08)
Kerry Town survivor	116	92	19	1	1	2	1	0	0	93/97	95·9% (89·8–98·9)
Household member: survivor from other Ebola treatment centre	36	29	2	0	0	2	3	0	0	29/34	85·3% (68·9–95·0)
Household member: asymptomatic	389	10	0	0	17	8	76	277	1†	10/388	2·6% (1·2–4·7)
Household member: symptomatic	92	10	0	1	1	2	8	70	0	11/92	12·0% (6·1–20·4)
Symptoms fitting case definition/no PCR test	40	3	0	1	1	1	3	31	0	4/40	10·0% (2·8–23·7)
Symptoms fitting case definition/PCR negative	19	0	0	0	0	1	0	18	0	0/19	0·0% (0–17·6)
Symptomatic not fitting case definition	33	7	0	0	0	0	5	21	0	7/33	21·2% (9·0–38·9)

Because of limited availability of kits, not all samples could be retested. We retested all positives (except some from known survivors of Ebola virus disease but including all those nearer the cutoff), all negatives from EVD survivors, and a sample of other negatives, prioritising those nearer the cutoff. We did third tests on any samples with discrepant results after two tests. For those samples with only one previous result, which were retested on the last available plate, we retested in duplicate in case any discrepancies arose. R=reactive. U=unreactive. *Total individuals; those with only a single reactive test available or indeterminate results excluded. †Retested because of borderline results; mean of all normalised optical densities 1·0 (SD 0·4; appendix p 5).

Table 1: **Prevalence of Ebola IgG positivity in samples from Ebola virus disease survivors, household contacts, and community controls, Sierra Leone, 2015**

Persistent Ebola Virus post infection, seminal fluid, Ebola laboratory accident UK, 1976

Day of sample (from onset of illness)	Details and remarks	Activity of circulating antibody (Fluorescent antibody titre)	Recovery of infective virus (guinea-pig intraperitoneal infective units/ml or g of sample tested)	
			Positive	Negative
1			Blood, $10^{4.5}$	
2	Before transfusion of 450 ml convalescent plasma	<1/2	Blood, $10^{4.5}$	
3	11 am, 6 pm, 11 pm	1/16	Blood, 3–10	
4	Morning	1/16	Blood, 3–10	
5	Morning	1/16	Blood, 3–10	
6	Before transfusion of 330 ml convalescent plasma	1/16	Blood, 3–10	
7	Morning and afternoon	1/16	Blood, 3–10	
8	Morning	1/8	Blood, 3–10	
9	Morning	1/16		Blood
10, 11, 12, 13	Morning	1/32		Blood
14, 16, 20	Morning	1/64		Blood, faeces, urine, throat swab
23, 27	Morning	Not done		Blood, faeces, urine, throat swab
34	Morning	1/128		Blood
39	Morning	Not done	Seminal fluid, 3–10	
61	Morning	1/128	Seminal fluid, 3–10	
76	Morning	1/128		Blood, urine
92, 110	Morning	Not done		Blood, urine, seminal fluid
				Urine, seminal fluid

Source: Emond RTD, British Medical Journal, 1977, 2, 541-544

Real Time RT-PCR testing of seminal fluid samples, Ebola survivors West Africa, 2014-2016

Study	Program	Location	Total no. of participants*	Positive real-time RT-PCR, by interval since disease onset	Virus isolated
Deen GF (New Eng J Med)	Unnamed pilot study	Sierra Leone	93	2–3 months: 9/9 (100%) 4–6 months: 26/40 (65%) 7–9 months: 11/43 (26%)	Ongoing
Fallah M (CROI)	Partnership for Research on Ebola Virus in Liberia (PREVAIL)	Liberia	76	Any (≥1 positive finding): 28/76 (37%)	No
Knust B (ASTMH)	Sierra Leone Ebola Virus Persistence Study	Sierra Leone	92	Any (≥1 positive finding): 15/92 (16%)	Yes
Keita AK (Clin Microbiol Infect)	Postebogui cohort	Guinea	188	Any (≥1 positive finding): 15/188 (8%)	No
Soka MJ (Lance Global Health)	Men's Health Screening Program	Liberia	429	Any (≥1 positive finding): 38/429 (9%) Of which >12 months: 24/38 (63%)	No
Sissoko D (Lancet Global Health)	Unnamed longitudinal study	Guinea	26	Initial sample (median 55 days post-onset): 19/26 (73%)	Yes

Clusters of Ebola infection occurring by the country, after outbreak had been declared over

Study	Location	Date cluster identified	Cluster size	Estimated interval from disease onset in survivor to contact with index case (days)
Alpren C ,et al (MMWR, 2016)	Sierra Leone	January 2016	2	Unknown‡
Arias A, et al (Vir Evol 2016)	Sierra Leone	August 2015	7	14–55*
Blackley DJ, et al (Sci Adv 2016)	Liberia	June 2015	6	Unknown‡
Christie A, et al (MMWR, 2015)	Liberia	March 2015	1	199*
Diallo B, et al (Clin Infect Disease, 2016)	Guinea	March 2016	13§	482*

Ebola virus in body fluids during illness

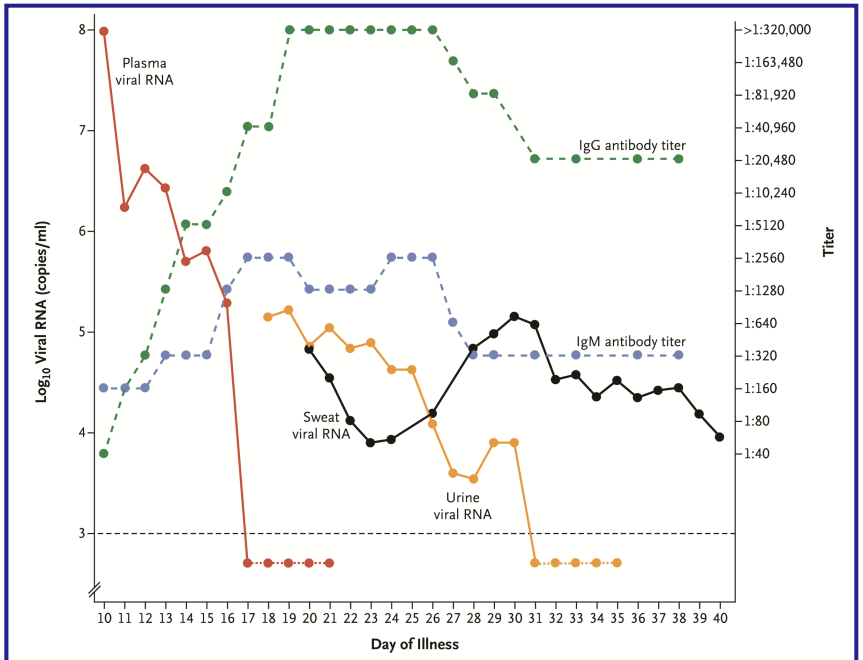


Figure 2. Timeline of Viral RNA Load in Plasma, Sweat, and Urine and Antibody Titers in Plasma.
The y axis on the left side of the graph shows the viral RNA load (solid lines). Owing to strong fluctuations in single measurements, line plots for urine and sweat are shown as moving averages over a period of 3 days. The y axis on the right side of the graph shows the antibody titers (dashed lines). The horizontal dashed line indicates the lower limit of detection of viral RNA on reverse-transcriptase–polymerase-chain-reaction assay.

Table 1.
Maximum Interval Between Onset of Ebola Virus Disease (EVD) and Last Detection of *Ebolavirus* RNA by Reverse Transcription–Polymerase Chain Reaction (RT-PCR) and Last Detection of *Ebolavirus* by Culture, by Human Body Fluid Specimen

Specimen(s)	Last Positive RT-PCR Result, d	Last Positive Culture Result, d
Saliva	22	4
Tears/conjunctival swab	28	…[a]
Rectal swab/stool	29	…[b]
Vaginal swab	33	…[c]
Amniotic fluid/placenta	38	NA
Skin swab/sweat	44	NA
Urine	64	26
Aqueous humor	101	101
Cerebrospinal fluid	283	NA
Breast milk	486[d]	15
Semen	488	82

Abbreviation: NA, no report available in the literature.
[a] No data on final positive results are available. Culture results were negative 6 days after EVD onset.
[b] No data on final positive results are available. Culture results were negative 4–12 days after EVD onset.
[c] No data on final positive results are available. Culture results were negative 22, 25, and 33 days after EVD onset.
[d] The time was specified as 16 months in the literature but is converted here to days for parallelism with units specified elsewhere in the column. This sample was *Ebolavirus* RNA positive at low levels, making interpretation difficult. Further testing is necessary to confirm these results.

Source: Vetter P et al. *The Journal of Infectious Diseases*, Volume 214, Issue suppl_3, 15 October 2016, Pages S177–S184,

Modelling: intervention benefits and cost of inaction, Ebola outbreak West Africa, 2014

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Modeling tool shows intervention benefits, cost of inaction

In the *MMWR* report, the projection of possible EVD cases for Liberia and Sierra Leone comes from a modeling tool constructed by CDC experts. Based on previous EVD models and data from August in the countries, the tool is designed to help outbreak response planners make decisions about response steps such as isolation and safer burials; it will be freely available in a Microsoft Excel spreadsheet. CDC officials said multiple separate waves of EVD activity in Guinea made it impossible to include that country in the modeling tool.

By the end of September, cases could reach a range between 8,000 and 21,000, according to the CDC model. It calculates that by the middle of January, barring more interventions or changes in community behavior, the total in the two countries could reach about 550,000 reported cases or 1.4 million total cases, including reported and unreported ones. The higher number assumes that there are 2.5 unreported cases for each reported case.

The CDC team included several caveats with its estimate, including that the estimate reflects only what was known in August and doesn't consider ongoing US response efforts.

Modeling calculations suggest that cases in Liberia are doubling every 15 to 20 days and that in Guinea and Sierra Leone, cases are doubling every 30 to 40 days, the CDC said.

At a media briefing today, CDC Director Tom Frieden, MD, MPH, downplayed the estimate's use as a projection, because it is based on already outdated numbers and doesn't consider response efforts, which he said have started to improve over the past few weeks. Rather, the model and estimates are designed to illustrate that the interventions are likely to have an important impact and send the message that the human cost of delaying the response would be very high.

"The bottom line is that the model shows a surge now can break the back of the epidemic," he said.

Gayle Smith, special assistant to President Barack Obama and senior director with the National Security Council, told reporters that the data suggest how to bend the epidemic curve but don't take into account the response surge over the past few weeks. The United States and other key groups that are leading the response need to keep the pressure on the international community to do more, and she added that with 700 treatment unit beds being added by the United Kingdom and significant contributions from Asian countries, the African Union, and other groups, "We are starting to see a significant (response) surge."

Model show 70% isolation 'sweet spot'

The CDC team that published the modeling report said stopping the epidemic requires isolating up to 70% of patients in treatment centers or other settings that reduce transmission, assuming that

A figure in the new CDC paper shows that delaying intensified control measures will lead to vastly more new cases later. (For the full paper, click here.) MMWR

WHO, CDC publish grim new Ebola projections

By Kai Kupferschmidt | Sep. 23, 2014 , 6:30 PM

Six months after the World Health Organization (WHO) was notified of the Ebola outbreak in West Africa, its experts have released a new study warning that the situation is quickly growing worse and that Ebola may even "become endemic among the human population of West Africa, a prospect that has never previously been contemplated."

The U.S. Centers for Disease Control and Prevention (CDC) in Atlanta, meanwhile, released a new model for the spread of the deadly virus. Its worst-case scenario estimates that up to 1.4 million people could be infected by the end of January. If control efforts are stepped up in a truly dramatic fashion and prove a stunning success, however, the epidemic could be almost over by that time. "Delay is extremely costly in terms of lives and efforts," CDC Director Tom Frieden said at a press conference today.

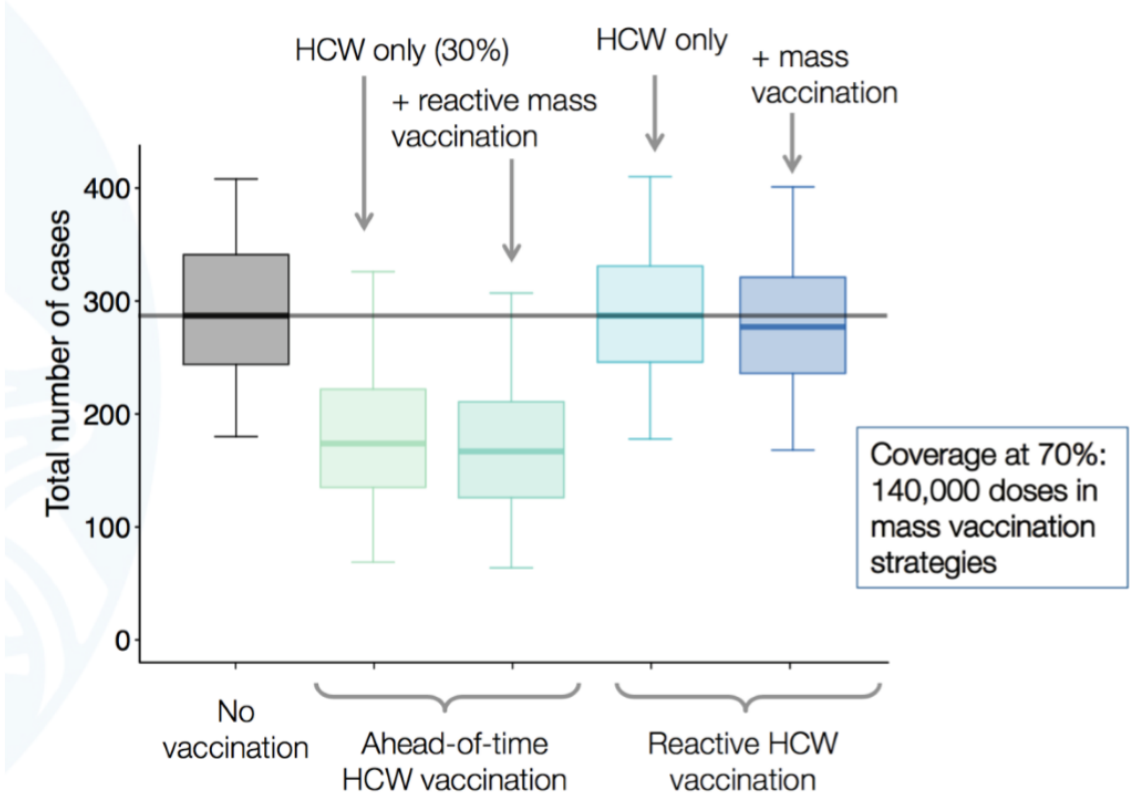
The Ebola outbreak, which probably started in Guinea in December last year, has already sickened at least 5843 people, according to the latest WHO figures—more than twice as many as all known previous outbreaks combined—and killed 2803. Epidemiologists expect the real numbers to be two or three times that, however, because only a fraction of cases is reported. And the spread of the disease keeps accelerating.

The new study by WHO experts and scientists at Imperial College London, **published today by *The New England Journal of Medicine***, is "excellent" because it fills some important gaps, says Preben Aavitsland, a Norwegian epidemiologist. "For instance, the study gives an average length of hospital stay of 6.4 days," he says. That is important to know, because it means that about as many beds are needed as there are new Ebola cases every week. It also means that tens of thousands of beds will be needed by the end of November, Aavitsland says. "It's completely

Field Hospital 22 Sierra Leone

rVSV-ZEBOV vaccine efficacy trials, Guinea, 2015

WHO/LSHTM
model of effectiveness of various vaccine strategies



Source: WHO