Columbia University
MAILMAN SCHOOL
OF PUBLIC HEALTH

Epidemiology and Forecast of the Current West African Ebola Outbreak

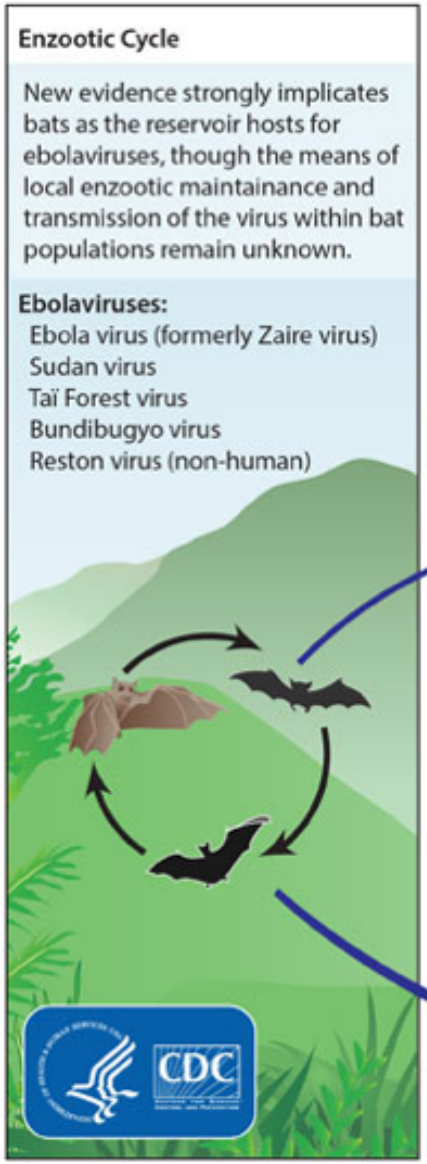
Models of Infectious
Disease Agent Study

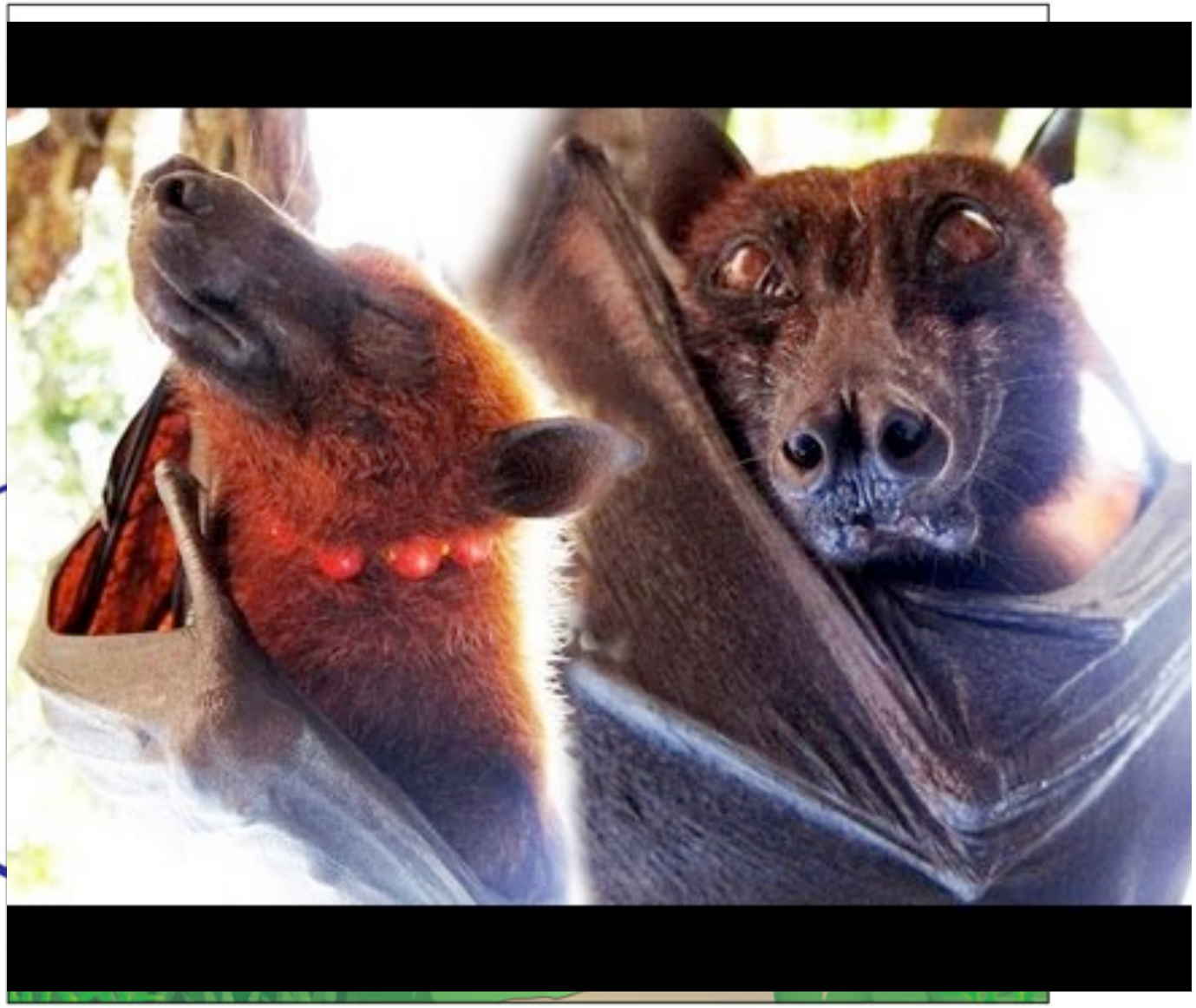
Funded by the National Institutes of Health

Jeffrey Shaman

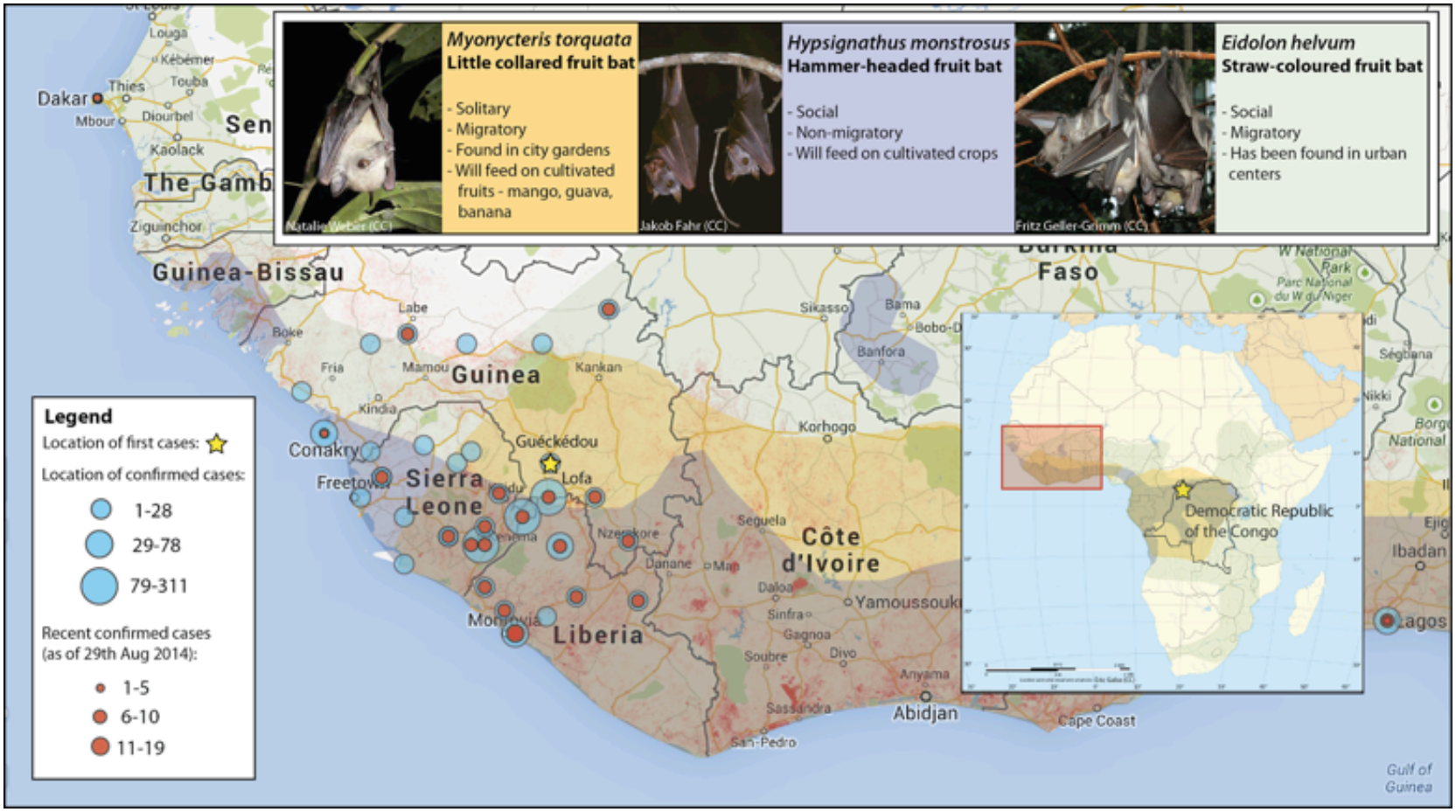
16 October 2014

Bats Believed to be Natural Reservoir





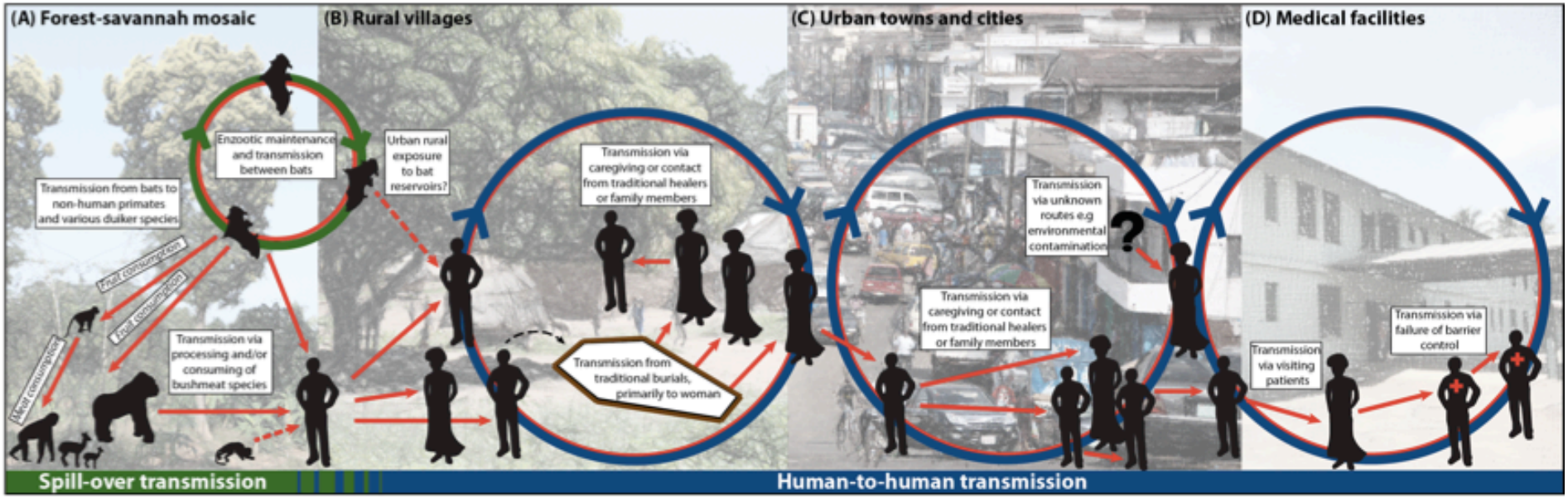
Ebola Transmission Cycle



Range of putative EBOV reservoir species, the little collared fruit bat (yellow), hammer-headed fruit bat (blue), and straw-colored fruit bat (green) -- thought to be associated with previous Central African EBOV outbreaks

Alexander et al., in review

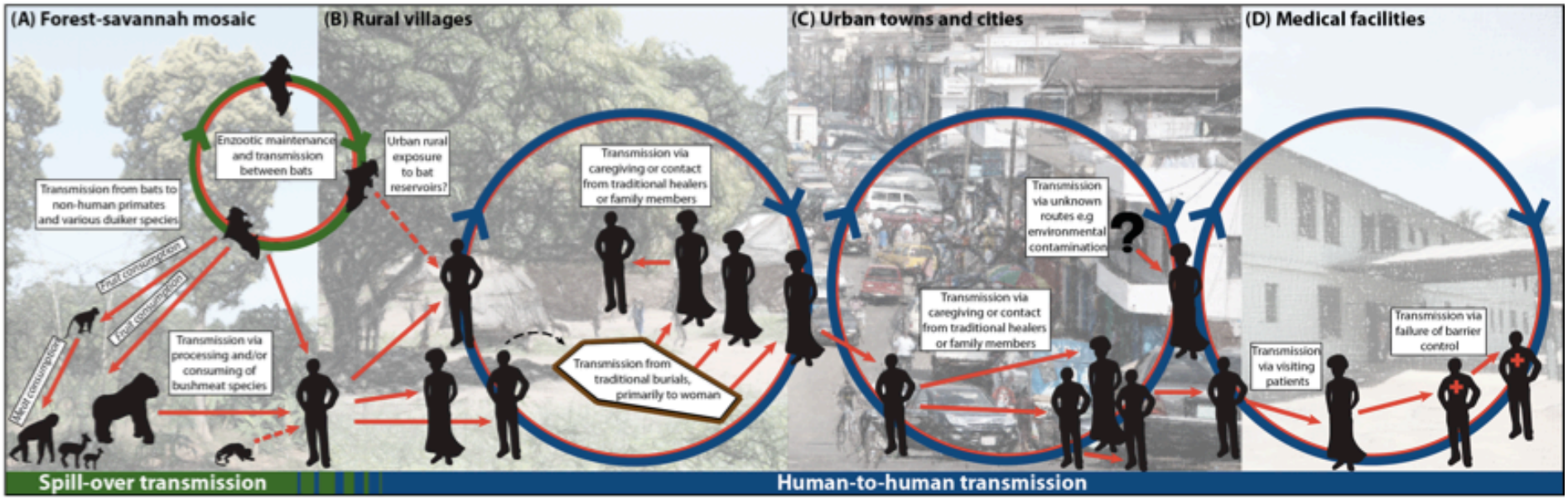
Ebola Transmission Cycle



Alexander et al., in review

- Pathogen spillover to humans is typically associated with the use of bush meat and direct contact with tissues or bodily fluids through handling and eating of infected animals (e.g. duiker, primates, or fruit bats).
- Predation and consumption of a red colobus monkey by chimpanzees has also been linked to an outbreak of Ebola among chimpanzees and one researcher in Côte d'Ivoire.

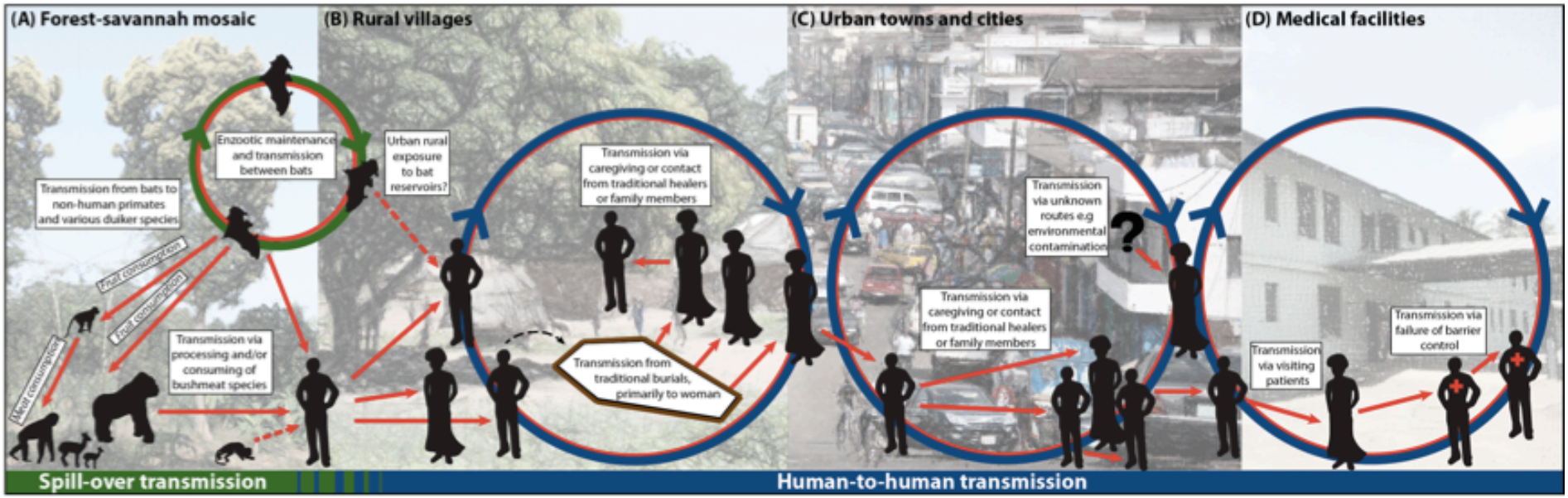
Ebola Transmission Cycle



Alexander et al., in review

- Ingestion of fruit contaminated with Ebola infected bat saliva or feces may be another mechanism by which bats infect other species (e.g., duiker, non-human primates), including humans.
- Human-to-human transmission associated with traditional burial practices, caregiving, or other forms of direct physical contact with infected individuals or bodily fluids.

Ebola Transmission Cycle



Alexander et al., in review

- Transmission dynamics in high-density urban centers (C) will differ importantly from rural villages (B) influencing outbreak progression and control efforts.
- Transmission in the hospital setting is largely associated with failures in infection control procedures and standard barrier precautions (D).

Ebola in Humans is Novel to West Africa

FIGURE 1

Geographical distribution of human ebolavirus disease outbreaks included in analyses of monthly temperature and absolute humidity, 1976–2014

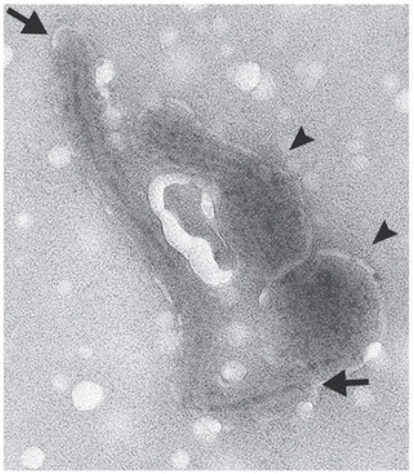
The red circles represent the outbreak areas.

Ng et al., 2014

Emergence of the West African Epidemic

Suspected first case a 2-year old infected in early December 2013 in Guéckédou, Guinea

The Guinean Ministry of Health was alerted in early March 2014 by local hospitals and public health officials of the appearance of a new disease with high case fatality

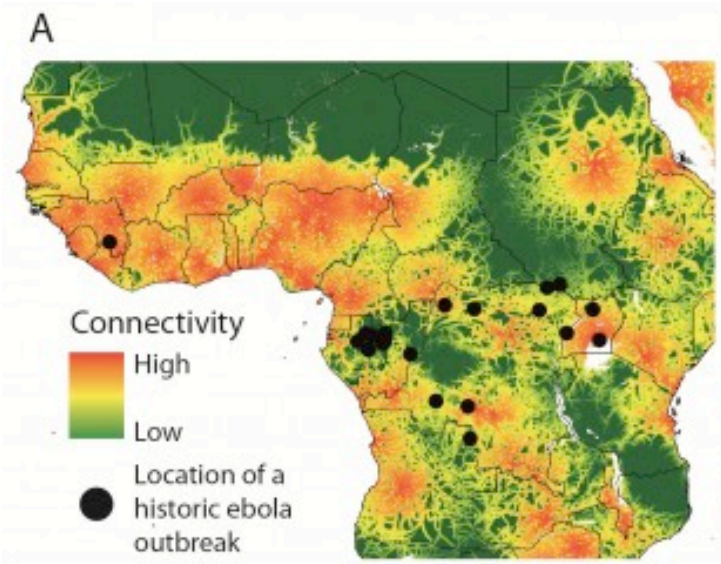


Baize et al., 2014

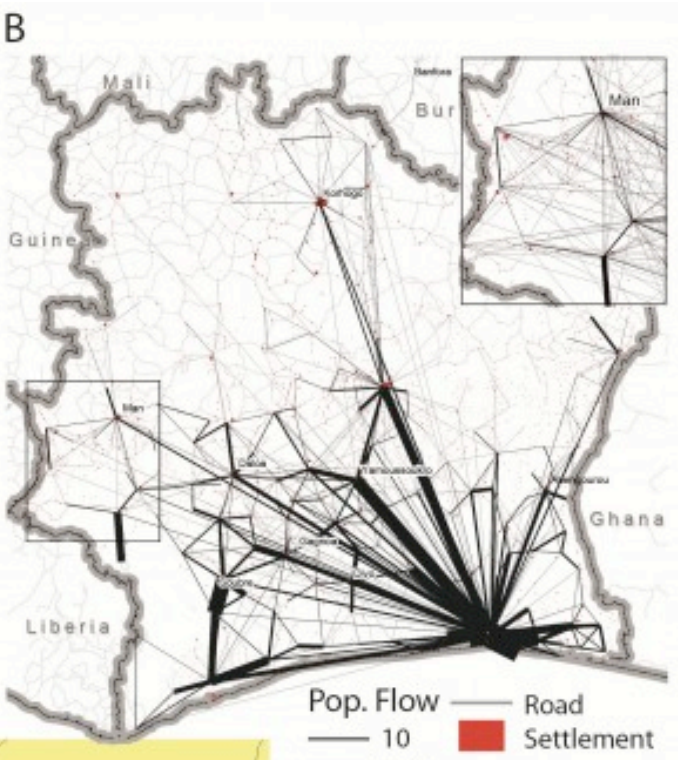
Prior Outbreaks in Isolated Rural Communities

Monrovia

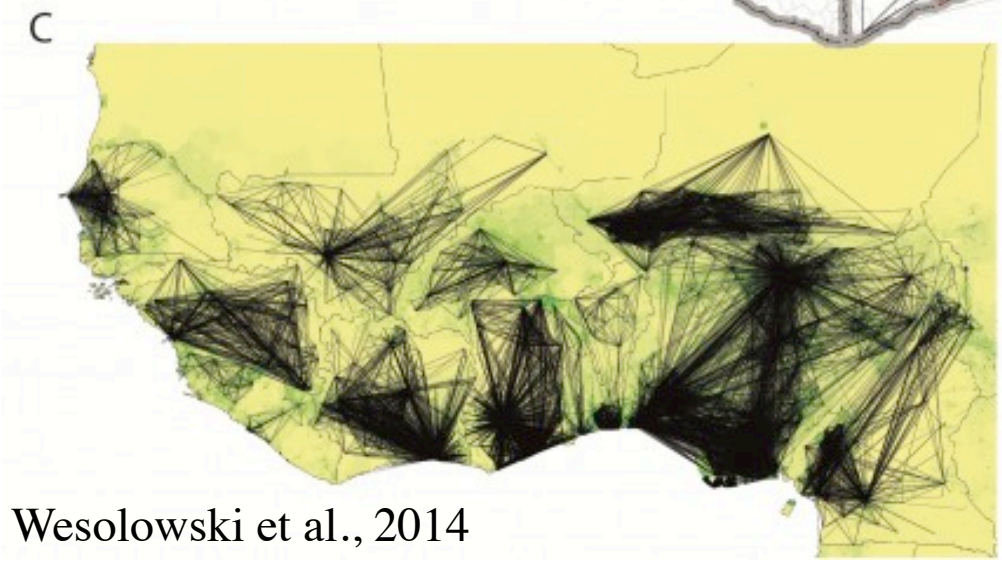
West Africa an Area of High Connectivity



Based on travel time to nearest settlement of 500,000+



Flow of 500,000 mobile phone users in Cote d'Ivoire



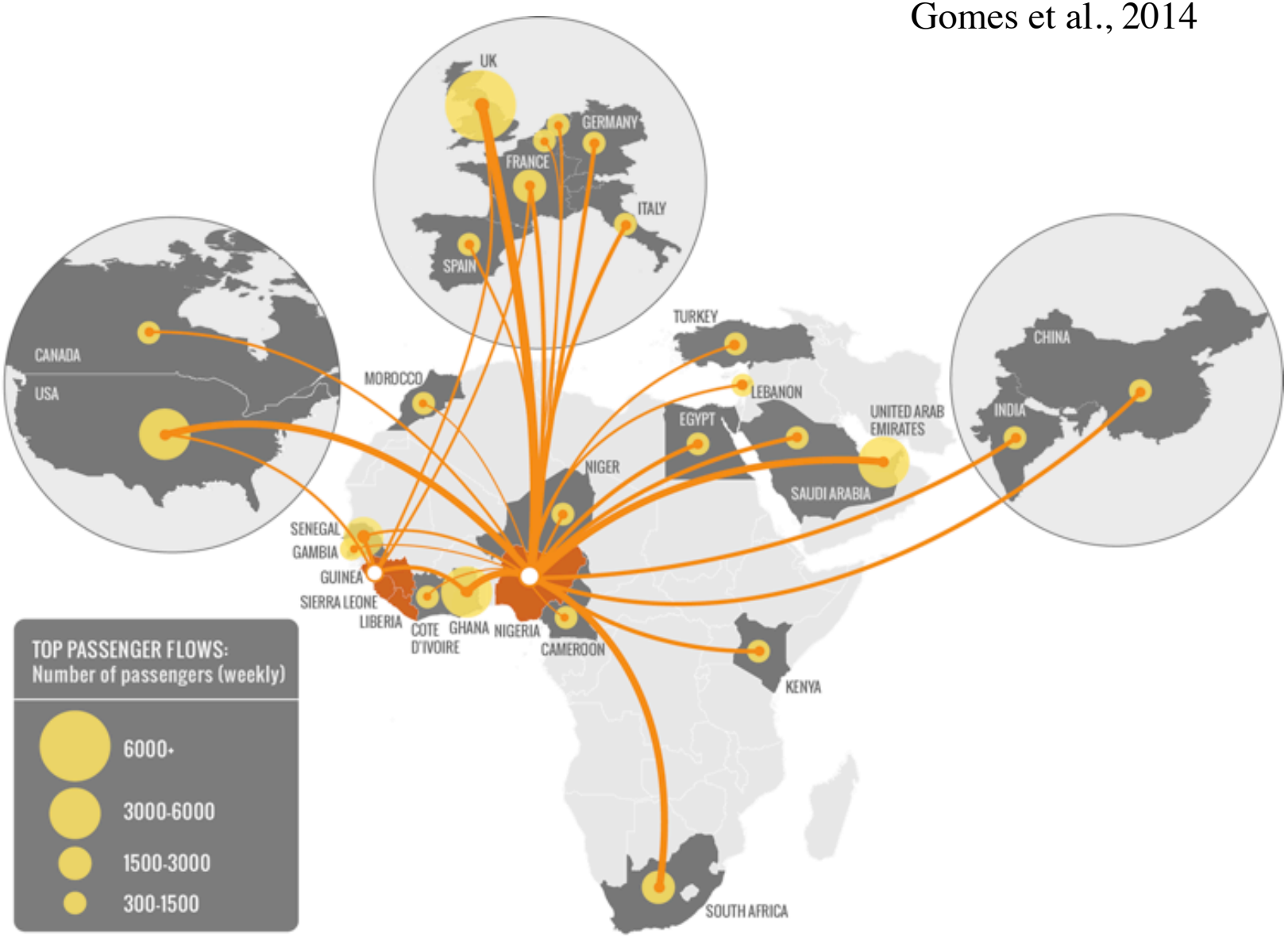
Wesolowski et al., 2014

Model estimated flow built using mobile phone data

No previous recorded outbreak in an area of such population density or connectivity

International Travel

Gomes et al., 2014



Traditional Intervention in Remote Settings

1. ISOLATION FACILITY/CASE MANAGEMENT/LAB
2. CONTACT TRACING
3. EPIDEMIOLOGICAL SURVEILLANCE
4. ALERT SYSTEM/REFERRALS
5. EPI INVESTIGATION & RUMOR CHECKING
6. HEALTH PROMOTION
7. INFECTION CONTROL
8. BURIAL TEAMS
9. PSYCHOSOCIAL SUPPORT
10. TRAINING

Courtesy: Estrella Lasry, MSF

West African Cases thru October 12 (October 11 for Liberia)

Table 1: Probable, confirmed, and suspected cases in Guinea, Liberia, and Sierra Leone

Country	Case definition	Cases	Cases in past 21 days	Cases in past 21 days/total cases (%)	Deaths
Guinea	Confirmed	1184	289	24%	653
	Probable	190	19	10%	190
	Suspected	98	89	91%	0
	All	**1472**	**397**	**27%**	**843**
Liberia	Confirmed	950	66	7%	*
	Probable	1923	468	24%	*
	Suspected	1376	555	40%	*
	All	**4249**	**1089**	**26%**	**2458**
Sierra Leone	Confirmed	2849	1110	39%	926
	Probable	37**	0	0%	157**
	Suspected	366	220	60%	100
	All	**3252**	**1330**	**41%**	**1183**
Total		**8973**	**2816**	**31%**	**4484**

**No available data. **For Sierra Leone, 120 more probable deaths have been reported than have probable cases. Data are based on official information reported by Ministries of Health. These numbers are subject to change due to ongoing reclassification, retrospective investigation and availability of laboratory results.*

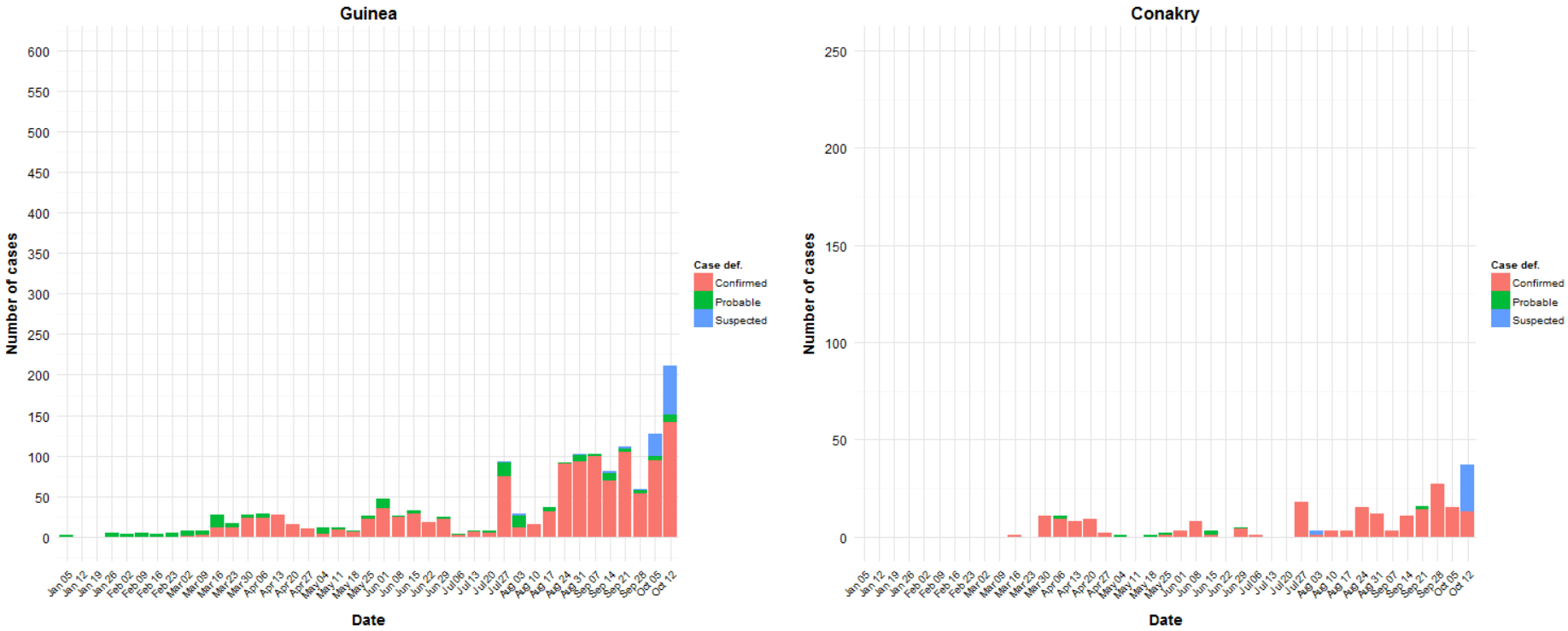
Ebola Epidemiology

Based on detailed records from 4010 cases.

- 11.4 day mean incubation period (time from infection to symptom onset)
- 15.3 (+/- 9.3) day serial interval
- 5.0 (+/- 4.7) day time from symptom onset to hospitalization
- 4.2 (+/- 6.4) day time from admission to death
- 11.8 (+/- 6.1) day time to discharge
- 70.8% case fatality rate
- Doubling time (as of September 14) ~ 16, 24 and 30 days in Guinea, Liberia and Sierra Leone, respectively.

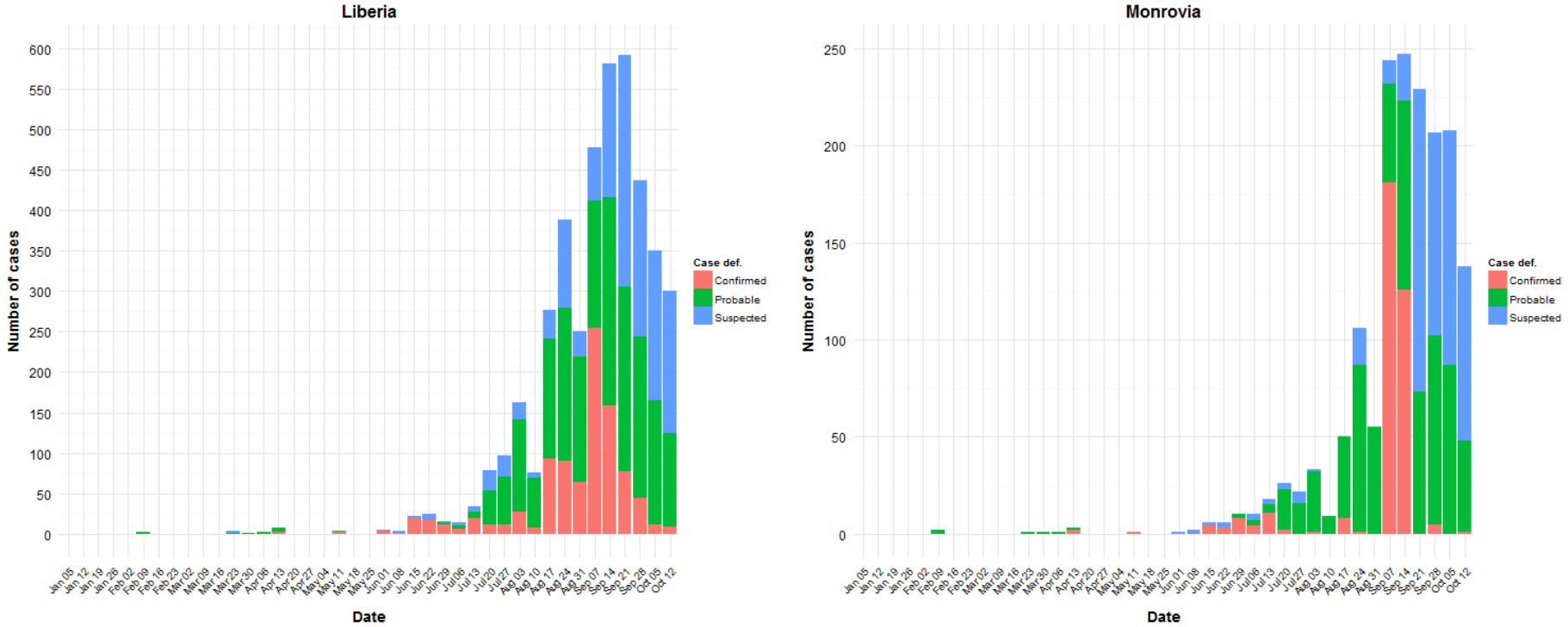
WHO Ebola Response Team, 2014

Figure 1: Ebola virus disease cases reported each week from Guinea and Conakry



Data are based on official information reported by Ministries of Health up to the end of 12 October for Guinea and Sierra Leone, and 11 October for Liberia. These numbers are subject to change due to ongoing reclassification, retrospective investigation and availability of laboratory results.

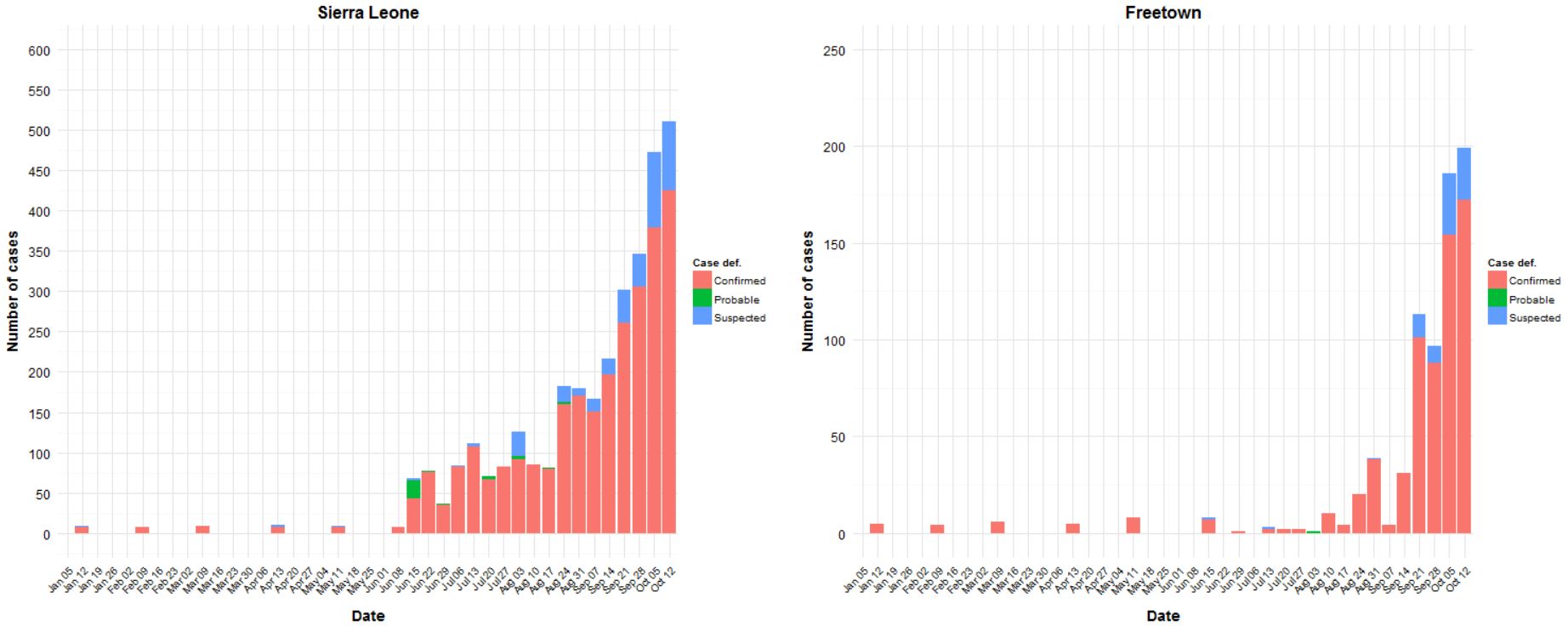
Figure 2: Ebola virus disease cases reported each week from Liberia and Monrovia



Data are based on official information reported by Ministries of Health up to the end of 12 October for Guinea and Sierra Leone, and 11 October Liberia. These numbers are subject to change due to ongoing reclassification, retrospective investigation and availability of laboratory results.

Growing number of Suspected Cases may be indicative of overwhelmed medical infrastructure

Figure 3: Ebola virus disease cases reported each week from Sierra Leone and Freetown



Data are based on official information reported by Ministries of Health up to the end of 12 October for Guinea and Sierra Leone, and 11 October for Liberia. These numbers are subject to change due to ongoing reclassification, retrospective investigation and availability of laboratory results.

Data Quality in an Unfolding Crisis

'We knew the ~350 confirmed cases last week were an undercount….we now think there are 7-900 in reality.'
Les Roberts, Blog: Day 7 (Oct. 11), Sierra Leone.

Under-reporting, particularly as systems are overwhelmed, is a huge concern.

The large spatial extent of the outbreak within country may mean that areas of activity go unreported

Few cases in Liberia are confirmed

Large, Complicated Geographic Element

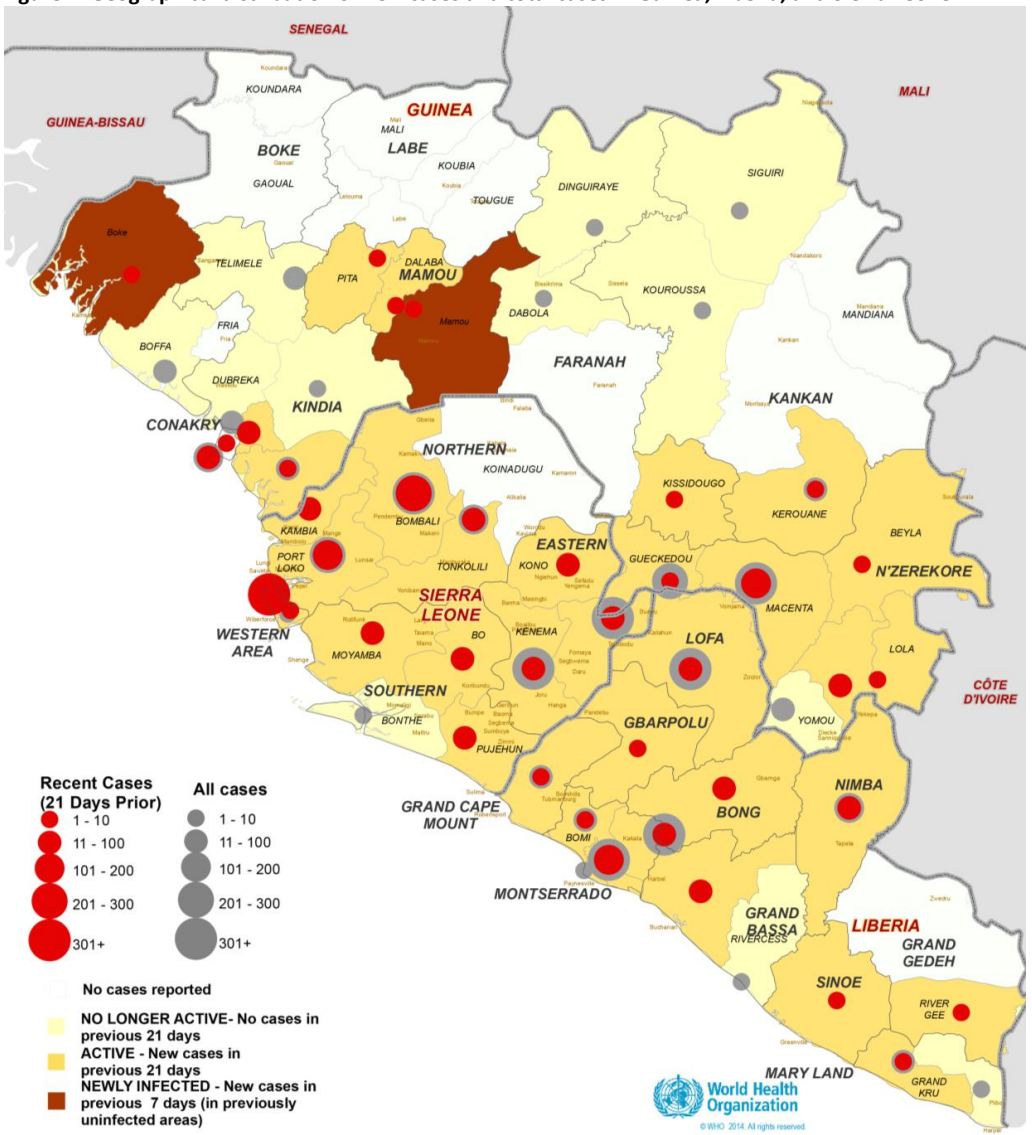
The outbreak is unprecedented.

The data are poor

The transmission dynamics are under-resolved

How will it progress? How does this all end?

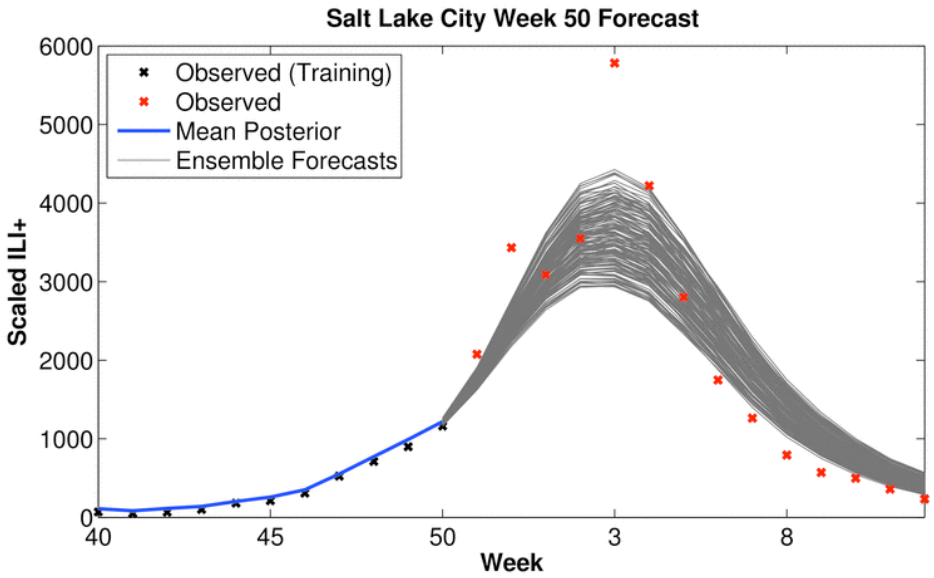
Figure 4: Geographical distribution of new cases and total cases in Guinea, Liberia, and Sierra Leone



Data are based on official information reported by Ministries of Health up to the end of 12 October for Guinea and Sierra Leone, and 11 October for Liberia. The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any

Ebola Modeling and Forecast

Forecasting approach based on our work with influenza



To predict Ebola, we mimic strategies used in numerical weather prediction

Requires 3 ingredients:

1) Real-time estimates of Ebola incidence and mortality (i.e. observations)

2) Model of Ebola transmission dynamics

3) Data assimilation method to rigorously combine #1 and #2.

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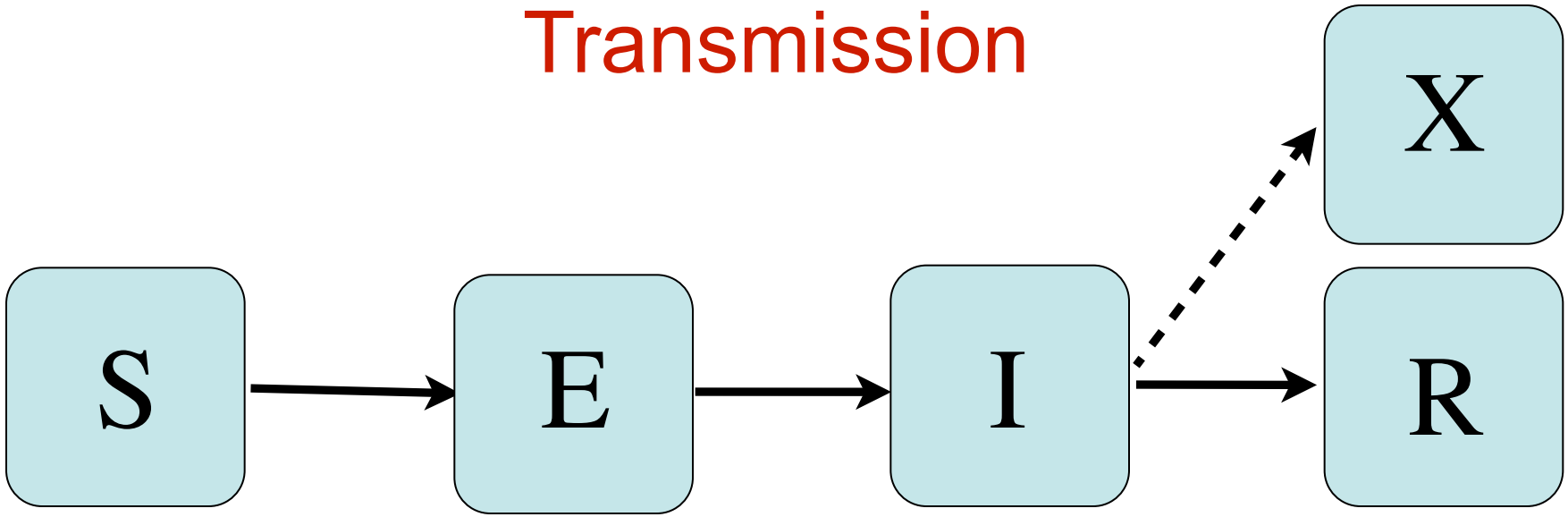
Compartmental Models of Ebola Transmission

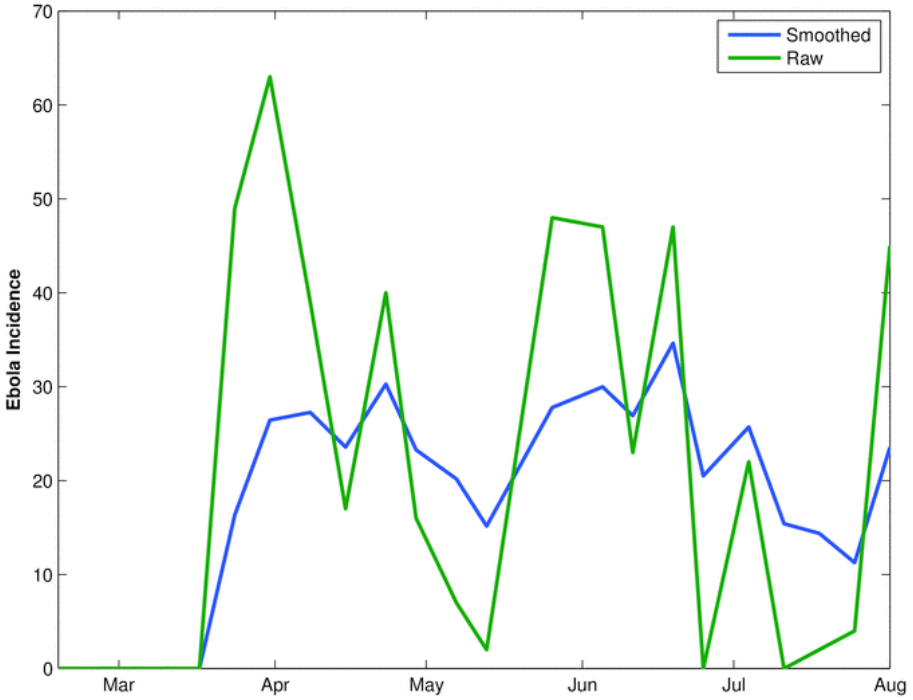


We use basic compartmental models run at the country level

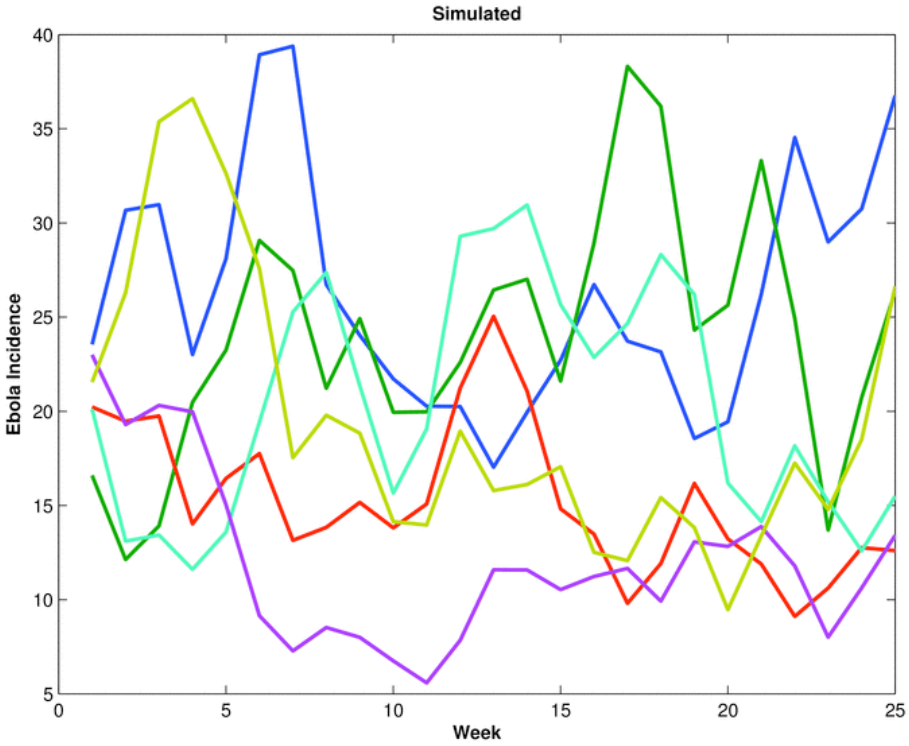
We impose some features, including a stochastic component in the force of transmission, that enable simulation of time series (by the model alone) similar to observed incidence time series.

Model Emulation of Observed Characteristics at the Country Level

Guinea through End of July

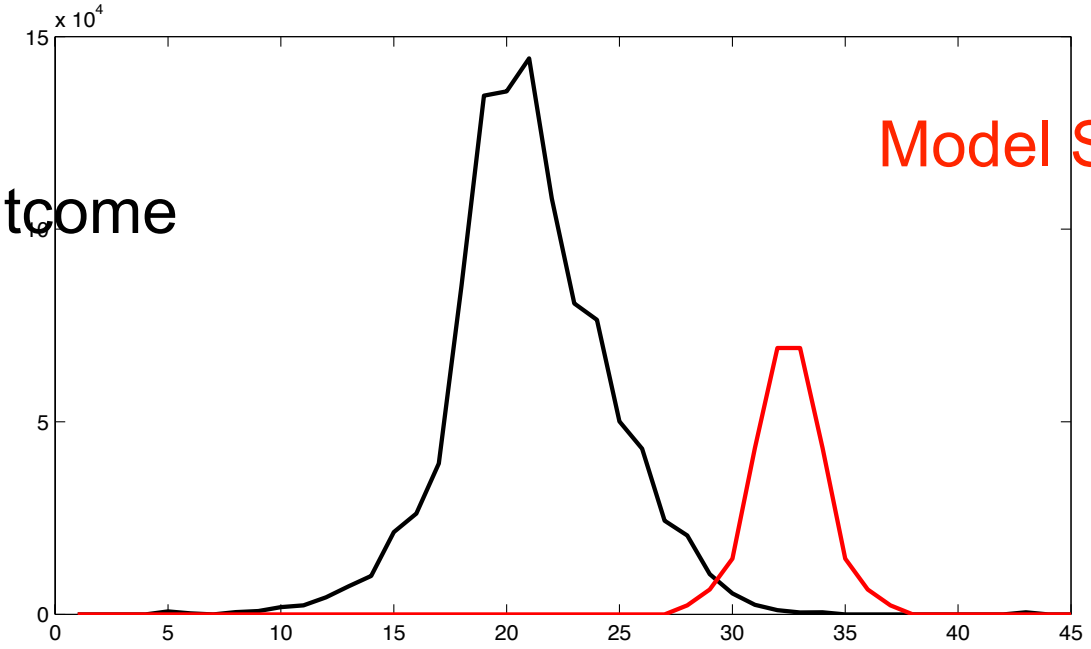


SEIRX Free Simulation

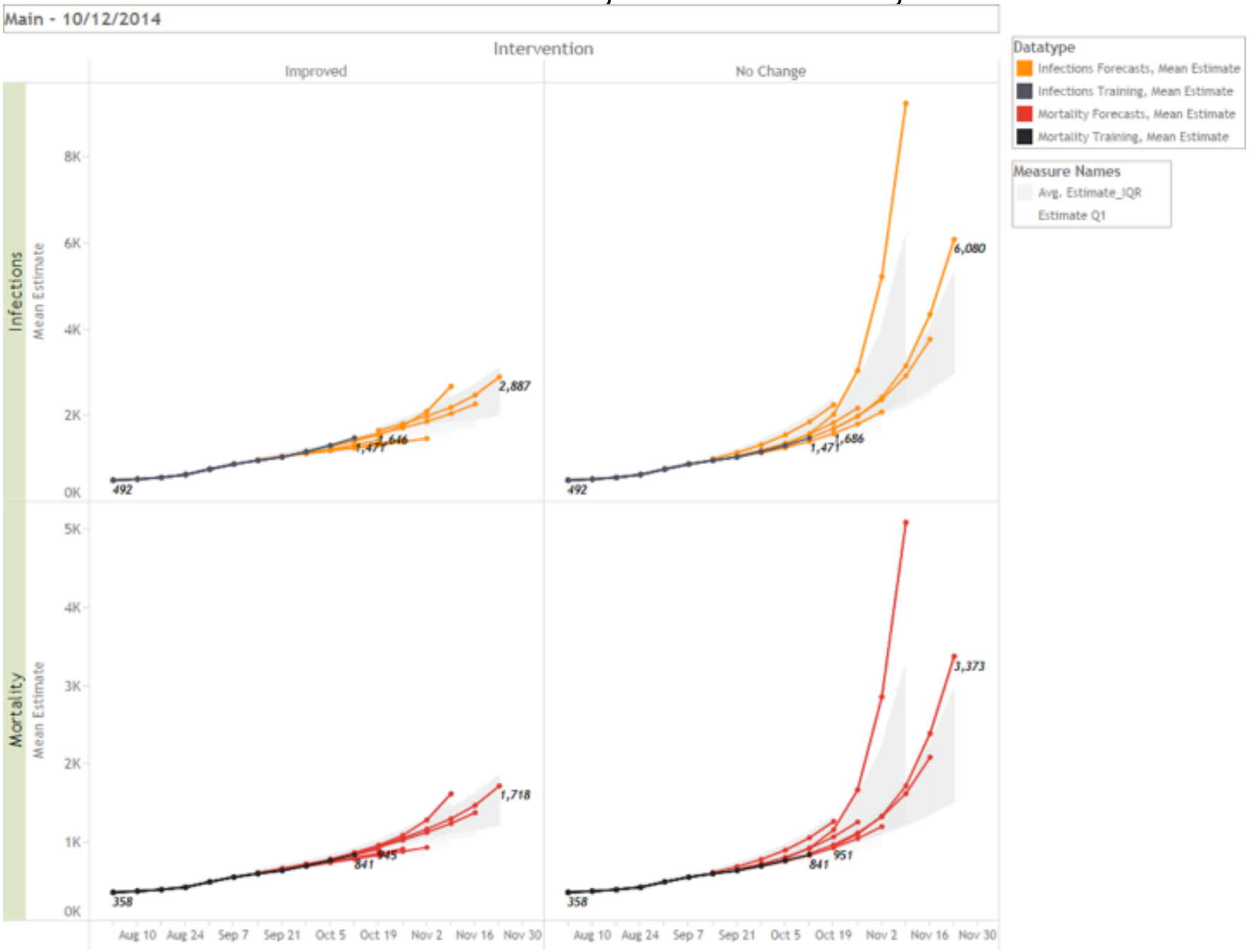


Prior to Forecast: Training the Model

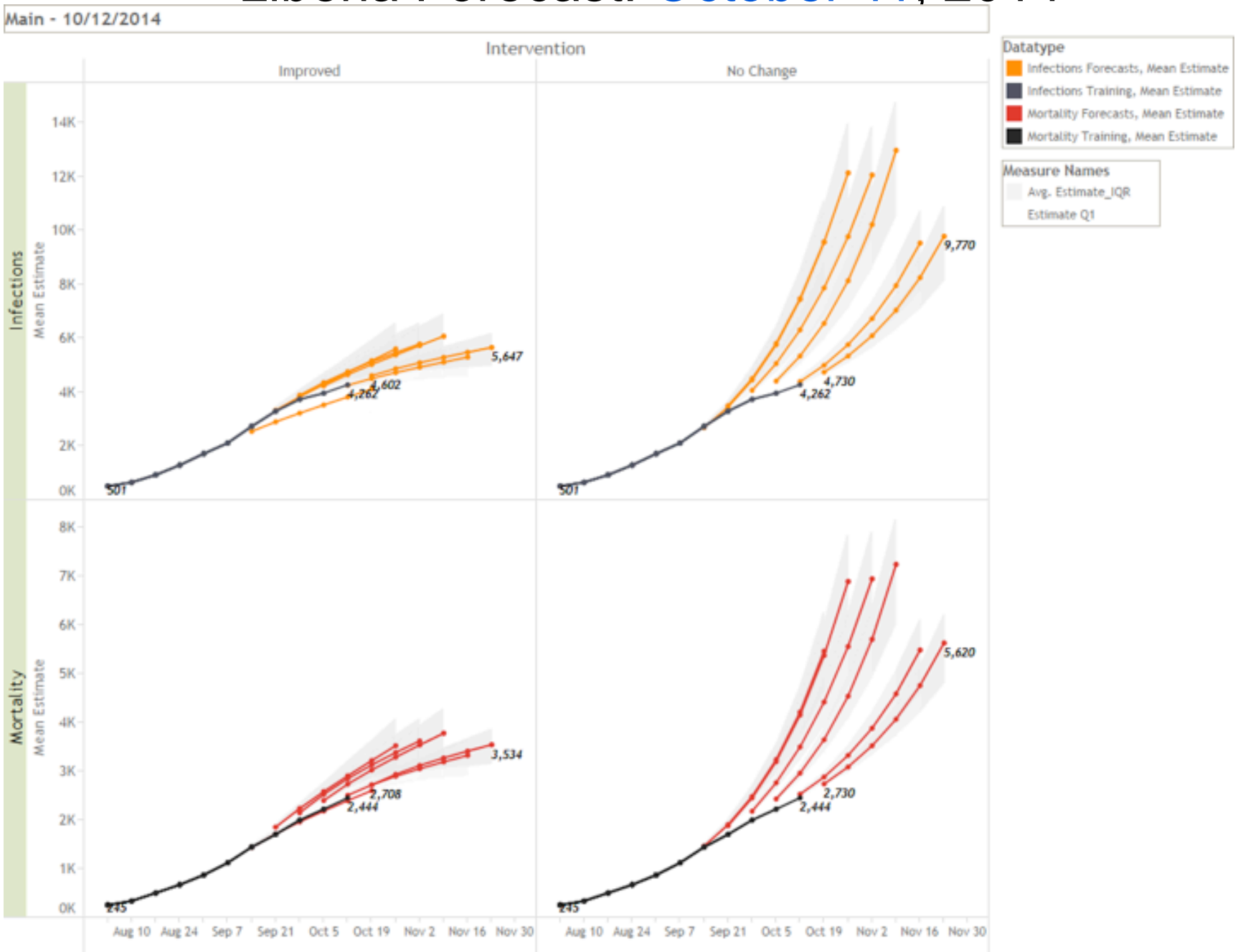
- Errors in the model structure, model parameters and initial model state amplify through time
- Left to its own devices the model forecast will deviate from reality



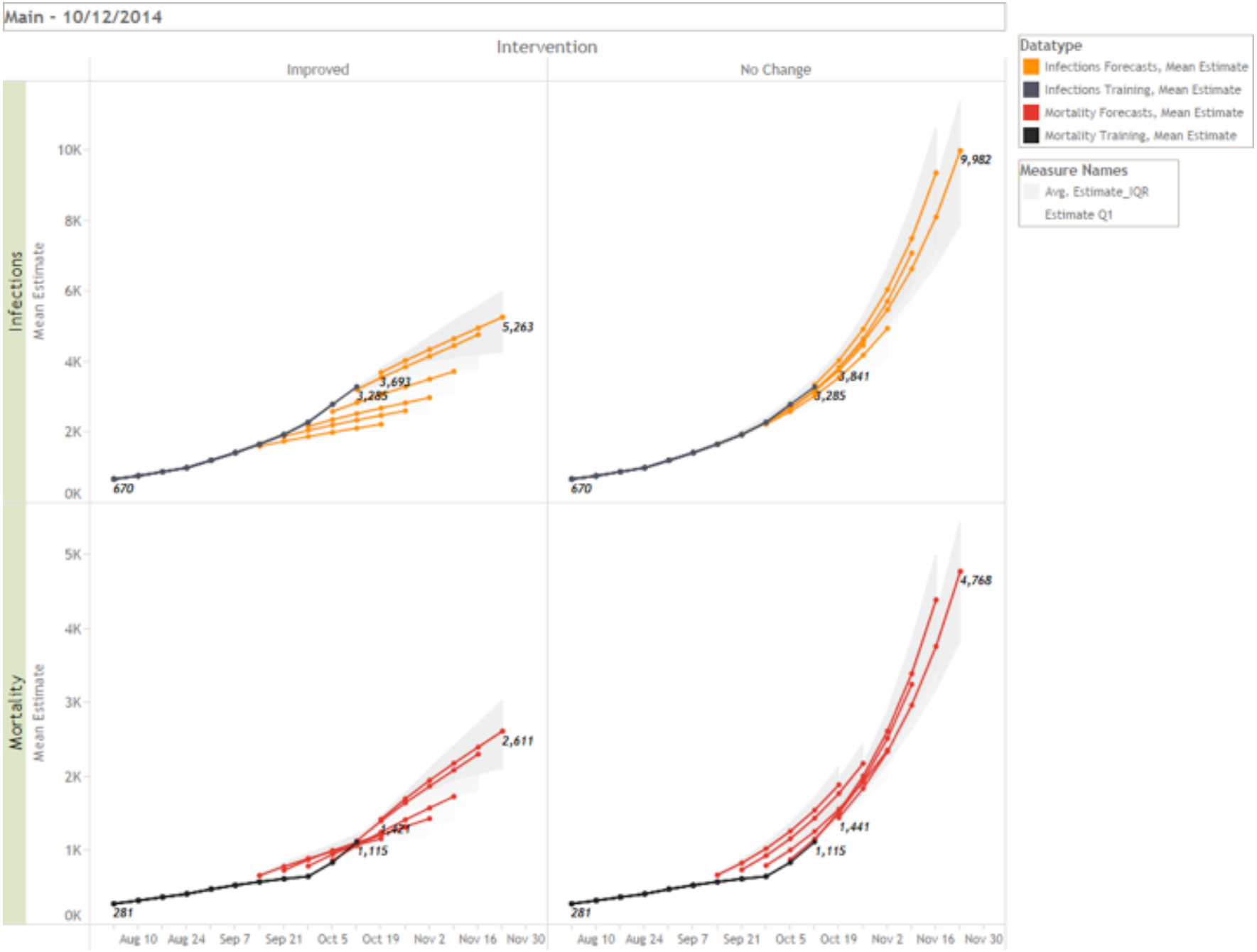
Guinea Forecast, October 12, 2014



Liberia Forecast: October 11, 2014



Sierra Leone Forecast: October 12, 2014



Why are the Liberia forecasts consistently high?

1) Model is mis-specified or not well optimized; hence the ‘no change’ predictions consistently over-predict new case levels;

2) Data are biased low—under-reporting; delays in reporting such that some of those new cases and deaths belong to earlier weeks;

3) Virus has changed, against evolutionary theory, and is less transmissible;

Why are the forecasts consistently high?

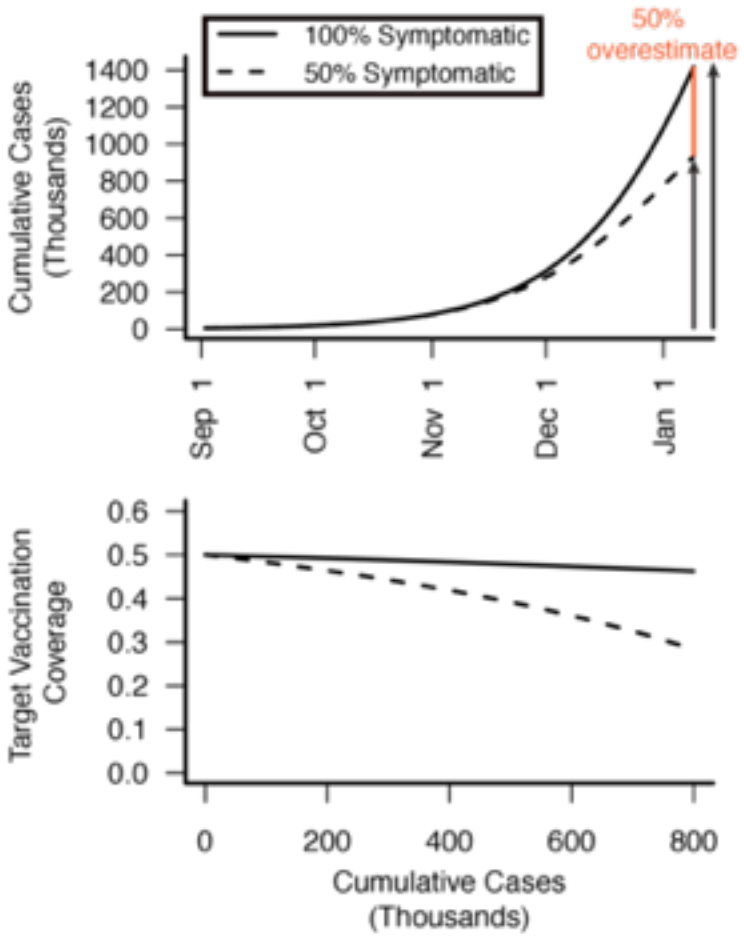
4) Virus is in areas where the effects of localized herd immunity are evident and transmission is slowing;

5) There has been an improvement in intervention and control.

Asymptomatic Infection

Is asymptomatic infection common?

Will herd immunity become a factor in the current outbreak?



Need different levels of vaccine coverage

Bellan et al., 2014 The Lancet

Asymptomatic Infection in NE Gabon

Within general population in area with multiple Ebola outbreaks, 1% positive, suggesting low general levels of asymptomatic infection

Heffernan et al., 1997, JID

Asymptomatic Infection in Northern Gabon

Found IgG and IgM response to Ebola antigens in 11 of 24 close asymptomatic contacts of symptomatic patients.

Leroy et al., 2000, The Lancet

Cameroon

Evidence of antibodies to Ebola found in 9.7% of the 1517 tested. Highest in Pygmies, young adults and rain forest farmers

Bouree and Bergmann, 1983, AJTMH

Central African Republic

Evidence of antibodies to Ebola found in 5.3% of the 240 tested. Higher in Pygmies than Bantu

Gonzalez et al., 2000, Microbes and Infection

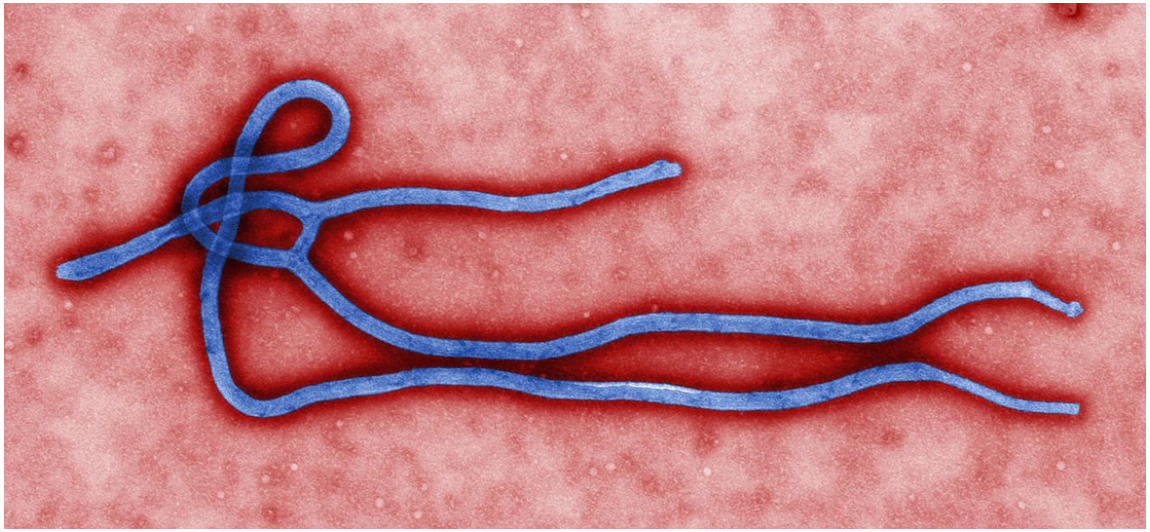
Evidence of antibodies to Ebola found in 17.6% of the 427 tested. Higher in Pygmies

Johnson et al., 1993, TRSTMH

Selection of a More Transmissible Virus?

Humans are not the natural host for Ebola

Evolutionary theory indicates that with repeated serial passage in the human host less virulent but more transmissible virus phenotypes will be selected



Collaborators

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