Introduction to Infectious Disease Data

Clinic on the Meaningful Modeling of Epidemiological Data, 2018
African Institute for Mathematical Sciences
Muizenberg, South Africa
May-June, 2019

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Slide set citation: https://doi.org/10.6084/m9.figshare.5044603.v4

Goals

- Understand case definitions - infection, disease, infectious diseases
- Understand approaches to collection of infection and disease data
- Metrics to measure presence and spread of infectious diseases

How would you define:

- Infection?

- Disease?

- Infectious disease?

Disease

A deviation from the normal physiological status of an organism that negatively affects its survival or reproduction

What kills East African Zebu calves during their first year of life?

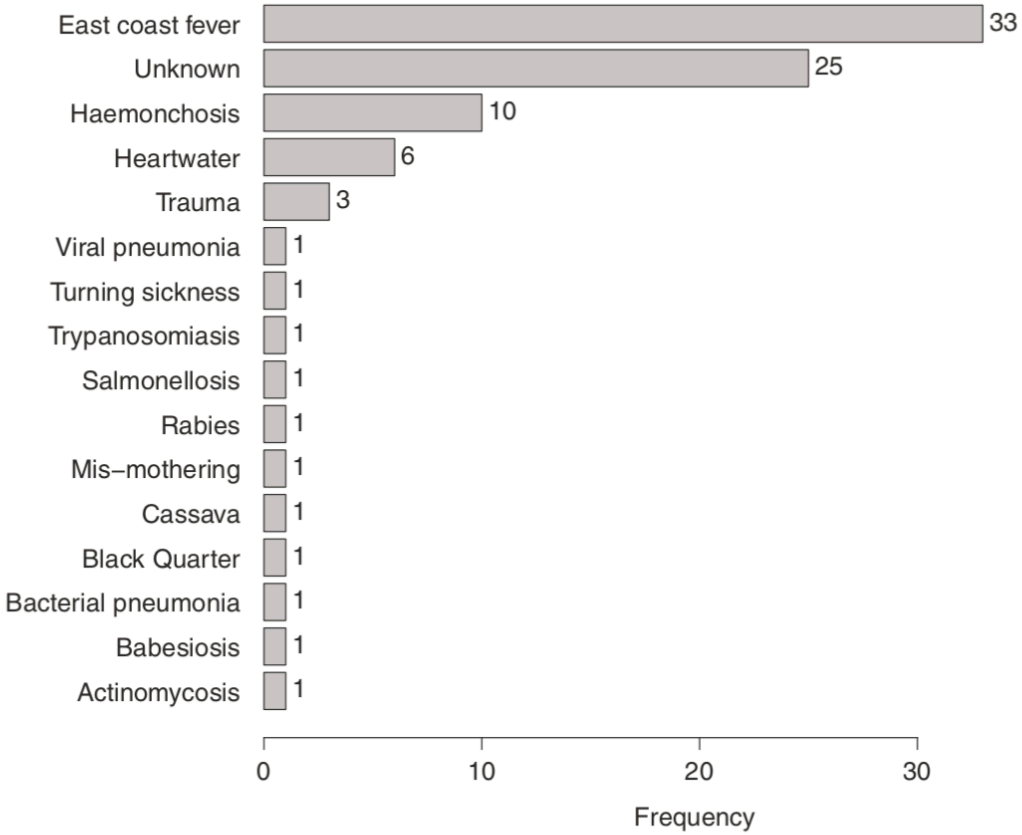
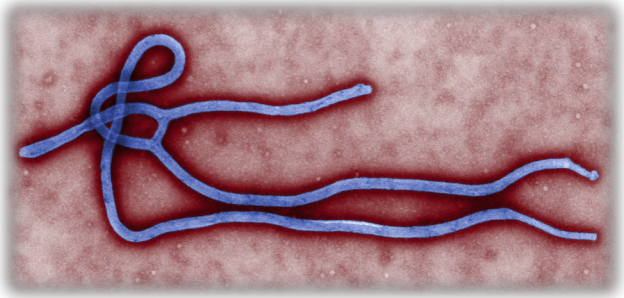


Figure 6 Definitive aetiological causes of death. A total of 88 deaths occurred during the study. Five of these were attributed to non-infectious causes (trauma, mis-mothering and cassava poisoning). East Coast Fever was the main cause of death, followed by haemonchosis and heartwater disease. For 25 deaths, a definitive aetiological cause of death could not be determined.

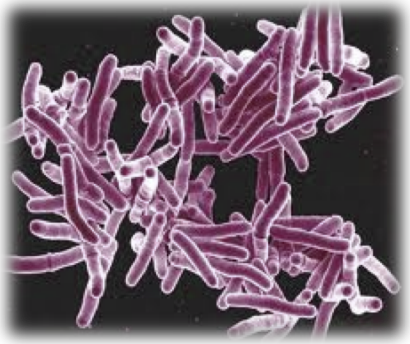
Thumbi *et al. BMC Veterinary Research* 2013, **9**:175
http://www.biomedcentral.com/1746-6148/9/175

Infectious Disease

A disease in one organism (the host) that is caused by another organism (pathogen or parasite) which has entered the host's body



Ebola Virus



Tuberculosis Bacteria

HIV

Pathogen: Microorganism that causes disease

(virus, bacteria, parasite)

- **Unravel patterns of disease**
- **Identify the risk factors for disease (host factors and non-host factors)**
- **Control options**

Image source: https://vimeo.com/user3106917

…from infection to disease….

What is the difference between:

- Incubation period?

- Latent period?

- Infectious period?

Infection to disease

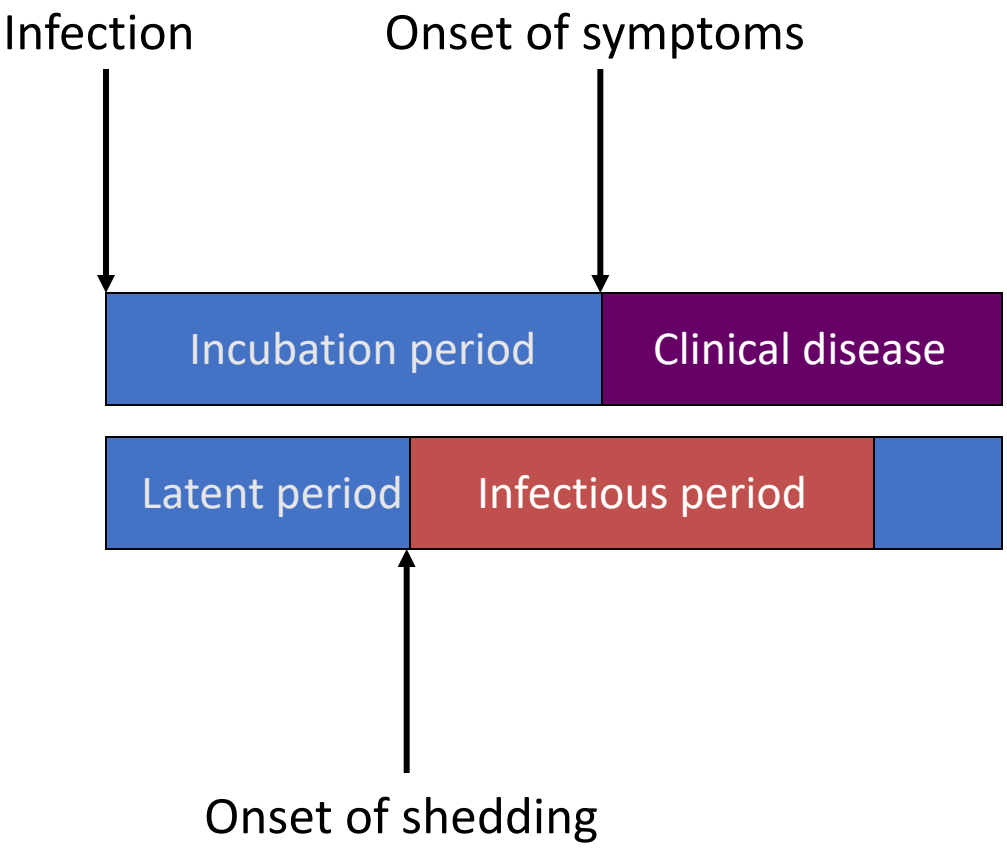


Table 5.3. Overview of relevant outcomes from all other data sources: World Health Organization (WHO, Centers for Disease Control and Prevention (CDC), Red Book (RB), Quick Reference guide (RG), Richardson 2001 (R2001)

Disease/agent	Incubation period	Period of infectiousness	Period of shedding	Exclusion period	Reference
Vaccine preventable diseases					
Measles	**WHO**: 7–18 (often, 10-12) days from exposure to the onset of fever [121]; **RB**: Generally 8–12 days from exposure to onset of symptoms; **CDC**:7–21 (14) days to a rash [122-124];10–12 days to prodrome [123, 125] **R2001**:6–19 (13) days	**WHO**: 4 days before the rash until 1–2 days after a rash [121]; **RB**: 4 days before the rash to 4 days after a rash; **CDC**:4 days before to 4 days after a rash onset [123-125] **R2001**:ND (but at least 1–2 days before a rash)	**WHO**: Following a rash onset, measles excretes for very short period (about 5 days) [126]; **CDC**: Beginning with the prodrome until 3-4 days after a rash onset ; **R2001**:-2 to +3 days	**RB**: Until 24 hours after treatment has been initiated; **RG:** At least 2 weeks after a rash in the last case for unimmunised people who have been exempted from measles immunised within 72 hr of exposure; **CDC**: 4 days after a rash for cases; 21 days after a rash in the last case for persons who have been exempted from measles vaccination within the appropriate time; **R2001**:5 days from onset of a rash	[121-126]
Seasonal influenza	**WHO:** 1–4 (average, 2) days(170); **RB:** 1–4 (average, 2) days; **CDC:** 1–4 (average, 2) days [123, 124, 130]; **R2001:** 1–3 (median, 1.5) days	**WHO:** Shortly before onset of symptoms and last into the second week [170]; **RG:** From the day before symptoms appear until at least 7 days after the onset of flu, although virus shedding can be longer; **CDC**: Adults can transmit 1 day before and 5–7 days after symptoms [124], Children can transmit for over 10 days [123]	**WHO:** Young children: up to 21 days [171]; **CDC:** 5–10 days [123], Children: >10 days after symptom onset [124], Peak usually occurs from 1 day before onset of symptoms to 3 days after [130]; **R2001:** 7–12 days, mean 9 days	**RG:** No need to exclude, unless the child is unable to participate, meets other exclusion criteria such as fever with behaviour change	[123, 124, 130, 170, 171]

Reference: European Centre for Disease Prevention and Control. Systematic review on the incubation and infectiousness/shedding period of communicable diseases in children. Stockholm: ECDC; 2016

Science
AAAS
REPORTS

Relationship Between Clinical Signs and Transmission of an Infectious Disease and the Implications for Control
Bryan Charleston, *et al.*
Science **332**, 726 (2011);
DOI: 10.1126/science.1199884

Relationship Between Clinical Signs and Transmission of an Infectious Disease and the Implications for Control

Bryan Charleston,[1]* Bartlomies M. Bankowski,[1] Simon Gubbins,[1] Margo E. Chase-Topping,[2] David Schley,[1] Richard Howey,[2] Paul V. Barnett,[1] Debi Gibson,[1] Nicholas D. Juleff,[1] Mark E. J. Woolhouse[2]

Control of many infectious diseases relies on the detection of clinical cases and the isolation, removal, or treatment of cases and their contacts. The success of such "reactive" strategies is influenced by the fraction of transmission occurring before signs appear. We performed experimental studies of foot-and-mouth disease transmission in cattle and estimated this fraction at less than half the value expected from detecting virus in body fluids, the standard proxy measure of infectiousness. This is because the infectious period is shorter (mean 1.7 days) than currently realized, and animals are not infectious until, on average, 0.5 days after clinical signs appear. These results imply that controversial preemptive control measures may be unnecessary; instead, efforts should be directed at early detection of infection and rapid intervention.

Case definition

“a set of standard criteria for deciding whether a person has a particular disease [or infection]”

2001 Foot & Mouth Disease outbreak in the UK

Image source: https://www.bbc.com/news/17818367

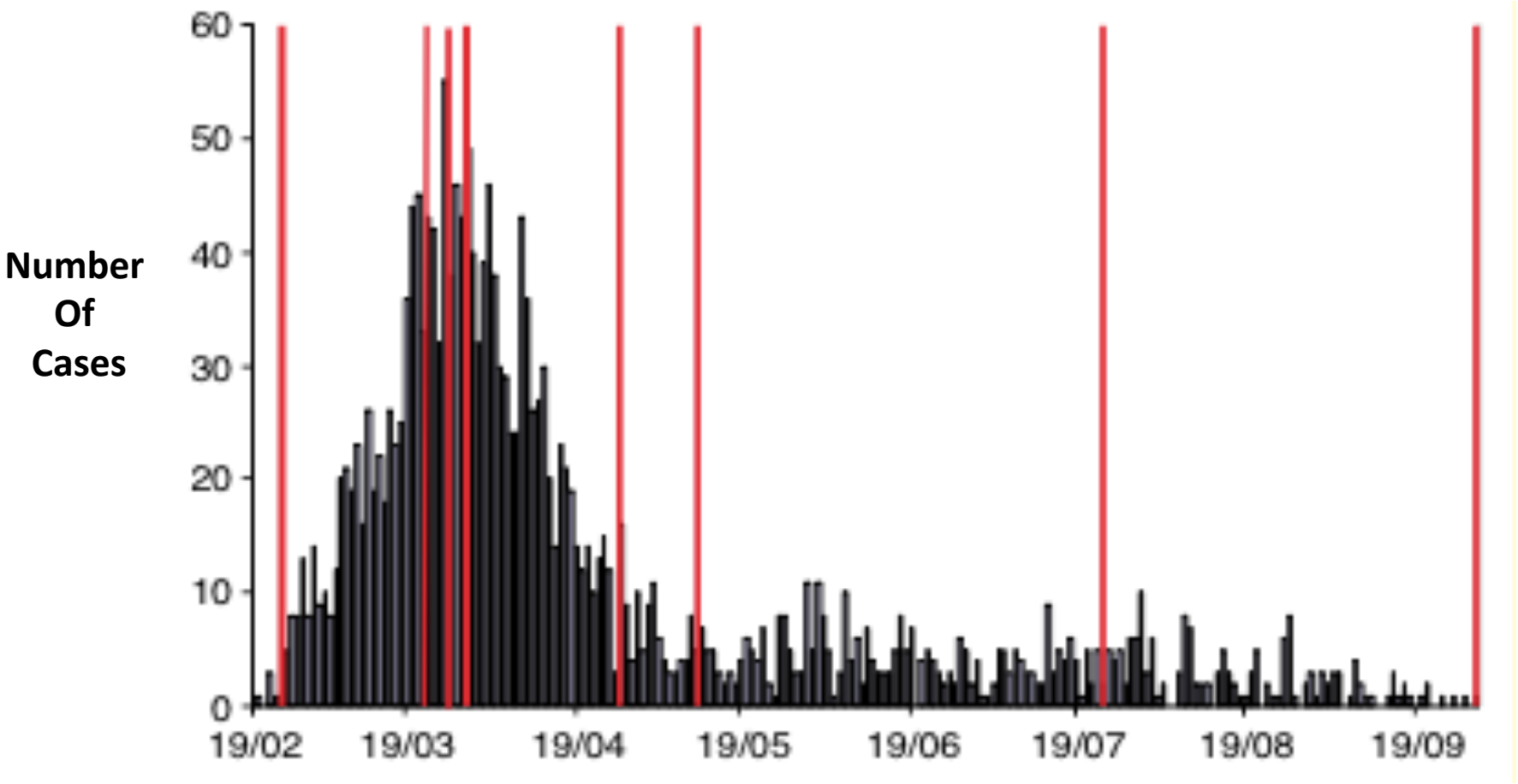
Person:

Place:

Time:

Clinical description:

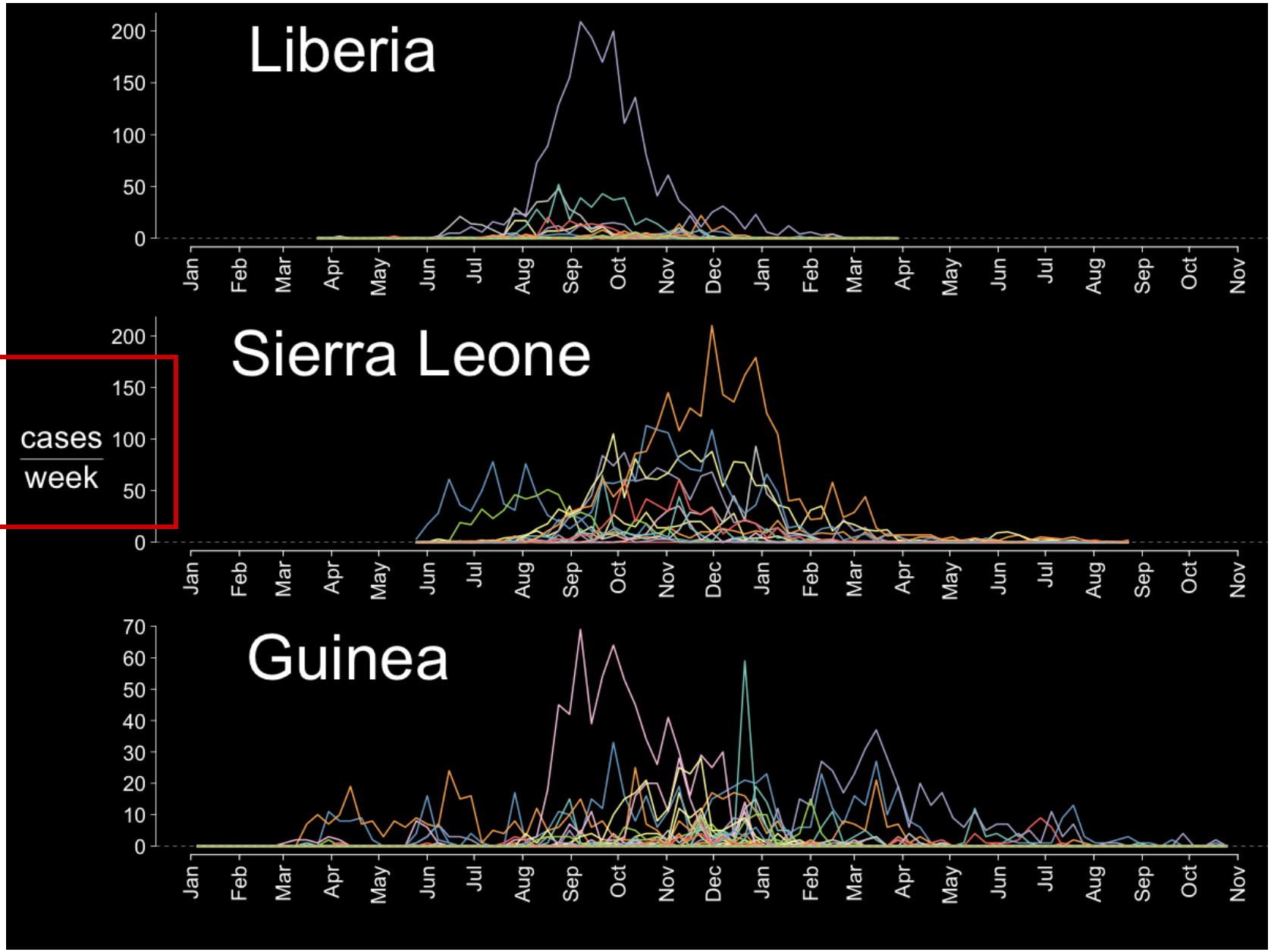
- First case – 19th February, 2001 – ante-mortem examination of pigs in an abattoir in Essex
- 21st Feb, 2001 – European Union ban on all British exports of livestock, meat and animal products
- 23rd Feb, 2001 – case confirmed in pig from Northumberland –case definition**)
- 24th Feb, 2001 – case in Devon, then Cornwall, and Scotland
- By 16th March, 2001 - the number of cases was at 240



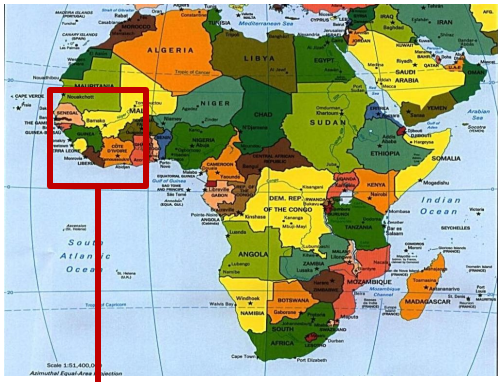
23/02 – movement restrictions
22/03 – welfare cull
23/03 – 3km cull policy
29/03 – 24/48hour slaughter on suspicion policy and contiguous premises (<3km from infected premises) cull

26/04 – CP cull relaxed
23/07 – hotspots targeted
30/07 – last reported case

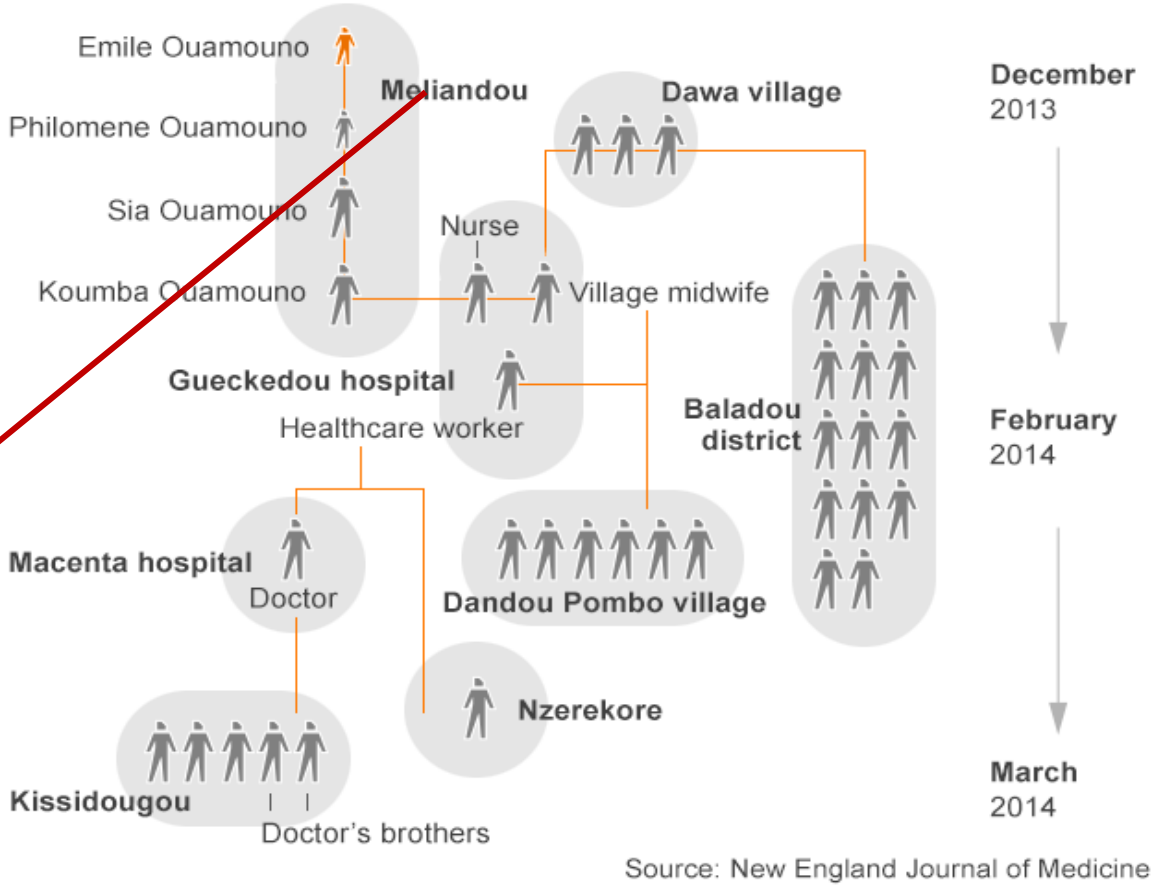
Shanafelt et al 2018 EcoHealth 15, 338–347


Liberia
Sierra Leone
Guinea
cases
week
0
50
100
150
200
10
20
30
40
60
70
Jan
Feb
Mar
Apr
May
Jun
Jul
Aug
Sep
Oct
Nov
Dec

A “case” study



West Africa



Case definition

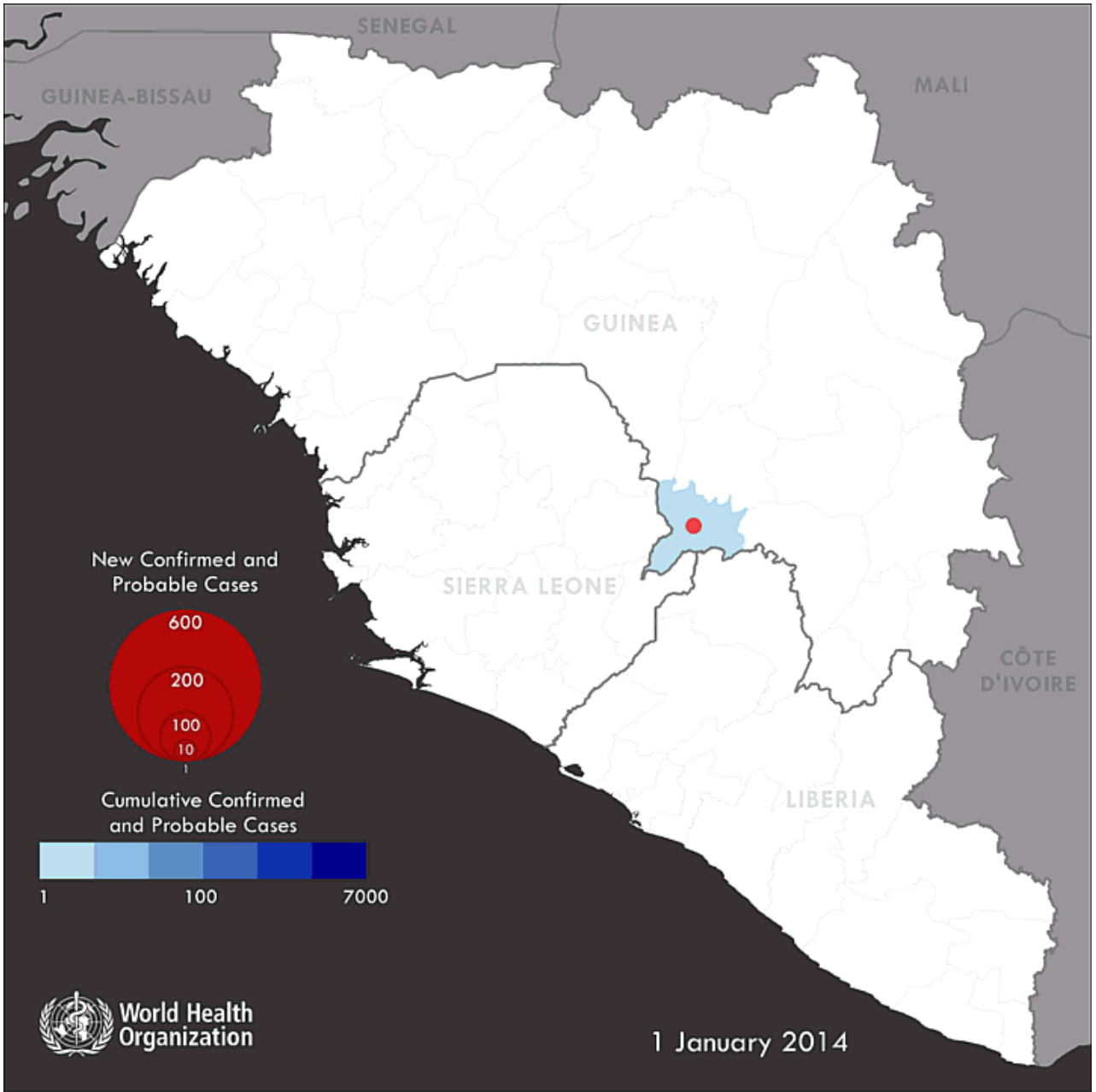
"a set of standard criteria for deciding whether a person has a particular disease [or infection]"

Person: Residents of Meliandou, recent visitors to Meliandou

Place: West Africa, Guinea

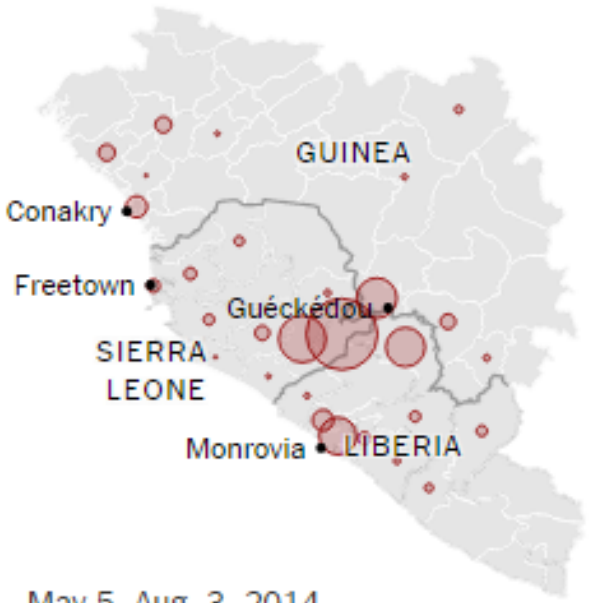
Time: On or after November 15, 2013

Clinical description: Elevated body temperature or subjective fever or symptoms, including severe headache, fatigue, muscle pain, vomiting, diarrhea, abdominal pain, or unexplained hemorrhage


SENEGAL
GUINEA-BISSAU
MALI
GUINEA
SIERRA LEONE
LIBERIA
CÔTE D'IVOIRE
New Confirmed and Probable Cases
600
200
100
10
1
Cumulative Confirmed and Probable Cases
1
100
7000
World Health Organization
1 January 2014

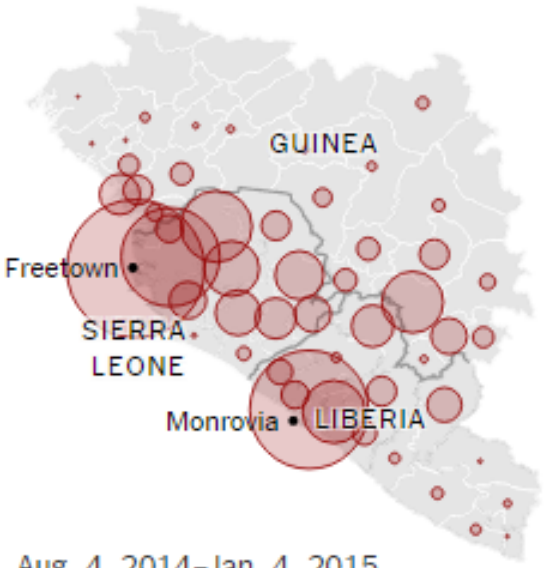
Dec. 30, 2013–May 4, 2014

The Outbreak Begins



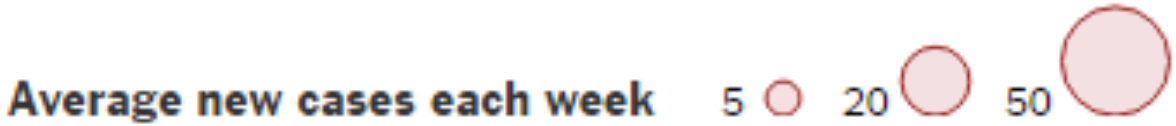
May 5–Aug. 3, 2014

New Cases Rise Rapidly



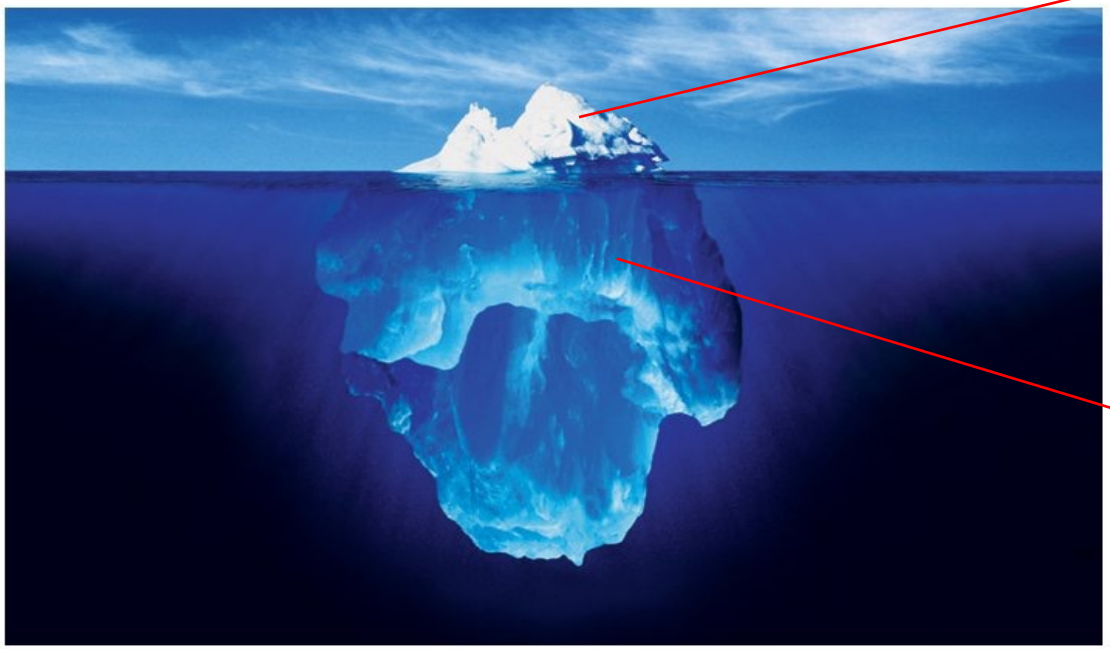
Aug. 4, 2014–Jan. 4, 2015

W.H.O. Sounds the Alarm



Source: World Health Organization

Clinical epidemiology

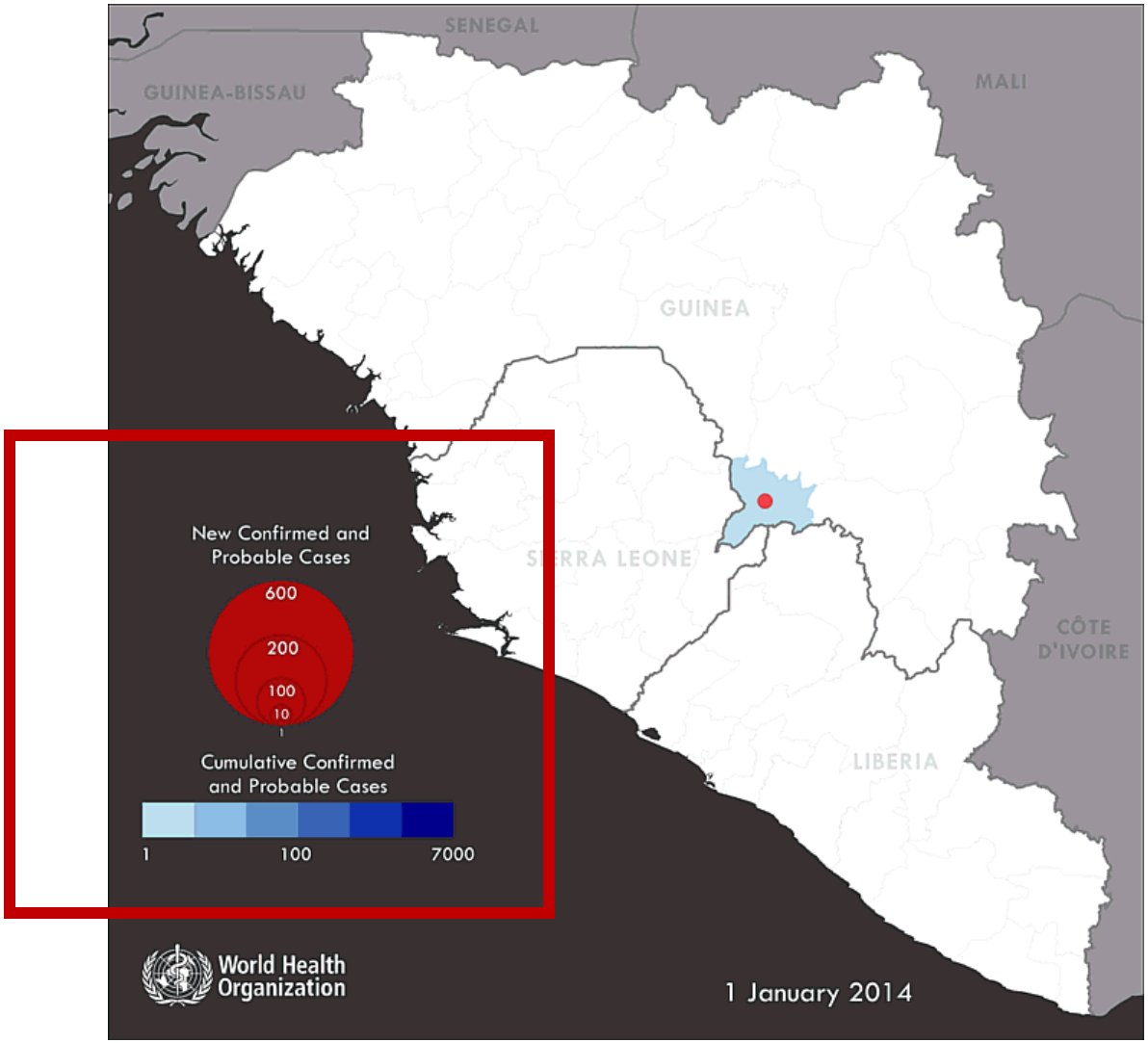


Population-based epidemiology

Clinical disease (that which comes to the attention of the clinician) is often only a 'tip of the iceberg' compared to the number of 'submerged' cases that go undiagnosed and unreported

John M. Last

Iceberg image source: https://octavianreport.com/rostrum/why-icebergs-are-still-dangerous/


SENEGAL
GUINEA-BISSAU
MALI
GUINEA
SIERRA LEONE
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CÔTE D'IVOIRE
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World Health Organization
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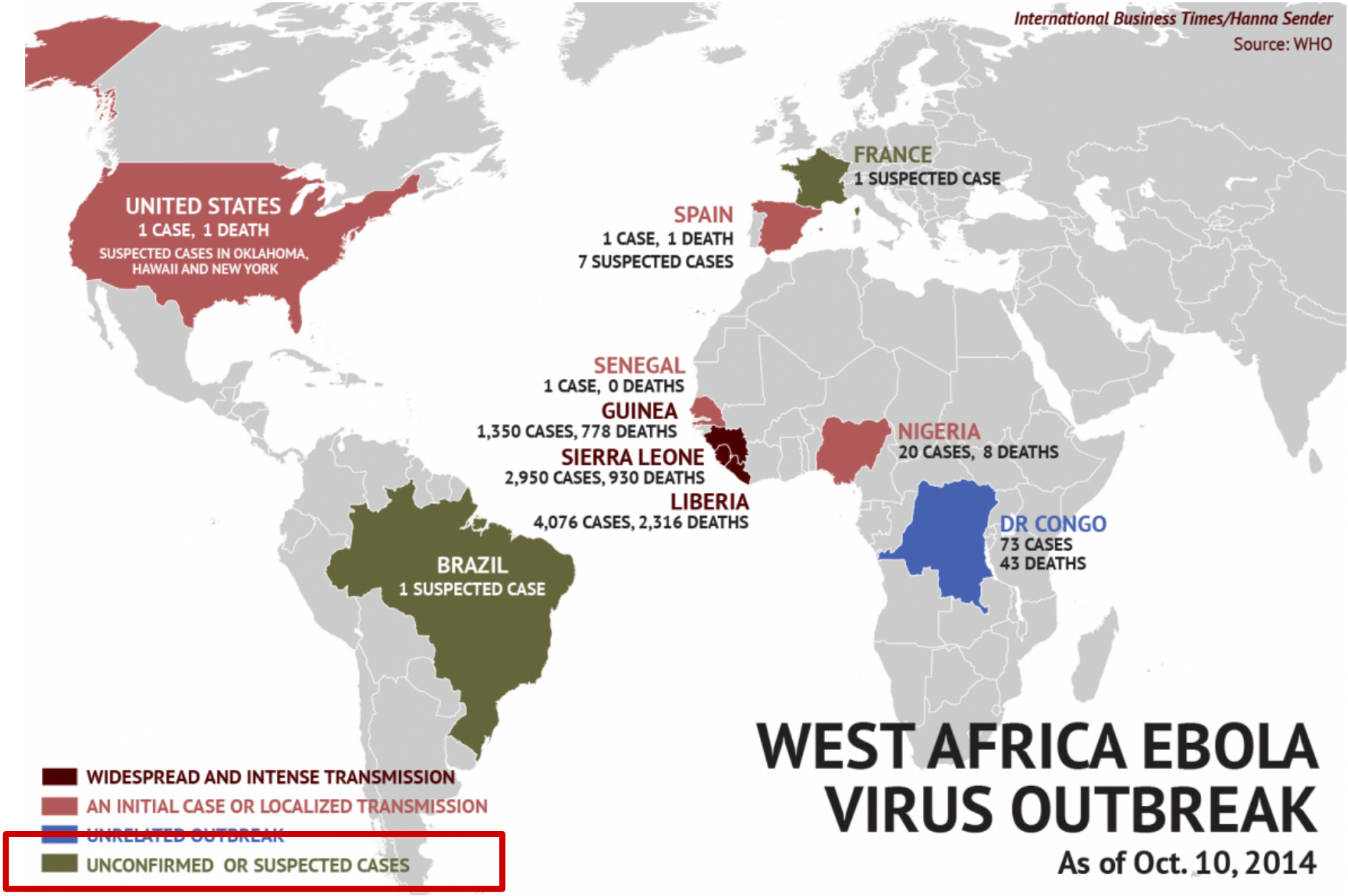

International Business Times/Hanna Sender
Source: WHO
UNITED STATES
1 CASE, 1 DEATH
SUSPECTED CASES IN OKLAHOMA, HAWAII AND NEW YORK
FRANCE
1 SUSPECTED CASE
SPAIN
1 CASE, 1 DEATH
7 SUSPECTED CASES
SENEGAL
1 CASE, 0 DEATHS
GUINEA
1,350 CASES, 778 DEATHS
SIERRA LEONE
2,950 CASES, 930 DEATHS
LIBERIA
4,076 CASES, 2,316 DEATHS
NIGERIA
20 CASES, 8 DEATHS
DR CONGO
73 CASES
43 DEATHS
BRAZIL
1 SUSPECTED CASE
WIDESPREAD AND INTENSE TRANSMISSION
AN INITIAL CASE OR LOCALIZED TRANSMISSION
UNRELATED OUTBREAK
UNCONFIRMED OR SUSPECTED CASES
WEST AFRICA EBOLA VIRUS OUTBREAK
As of Oct. 10, 2014

Confirmed case: signs and symptoms *plus* laboratory confirmation

Probable case: signs and symptoms in an individual meeting person, place, and time criteria *plus* contact with a known case *or* more specific clinical signs

Possible case: signs and symptoms in an individual meeting person, place, and time criteria *plus* a physician diagnosis

Suspect case: signs and symptoms in an individual meeting person, place, and time criteria

Not a case: failure to fulfill the criteria for a confirmed, probable, possible, or suspect case

Case definition

"a set of standard criteria for deciding whether a person has a particular disease [or infection]"

Person:

Place:

Time:

Clinical description:

Case definition

"a set of standard criteria for deciding whether a person has a particular disease [or infection]"

Person: Residents of Meliandou, recent visitors to Meliandou

Place: West Africa, Guinea

Time: On or after November 15, 2013

Clinical description: Elevated body temperature or subjective fever or symptoms, including severe headache, fatigue, muscle pain, vomiting, diarrhea, abdominal pain, or unexplained hemorrhage

Case definition for Ebola

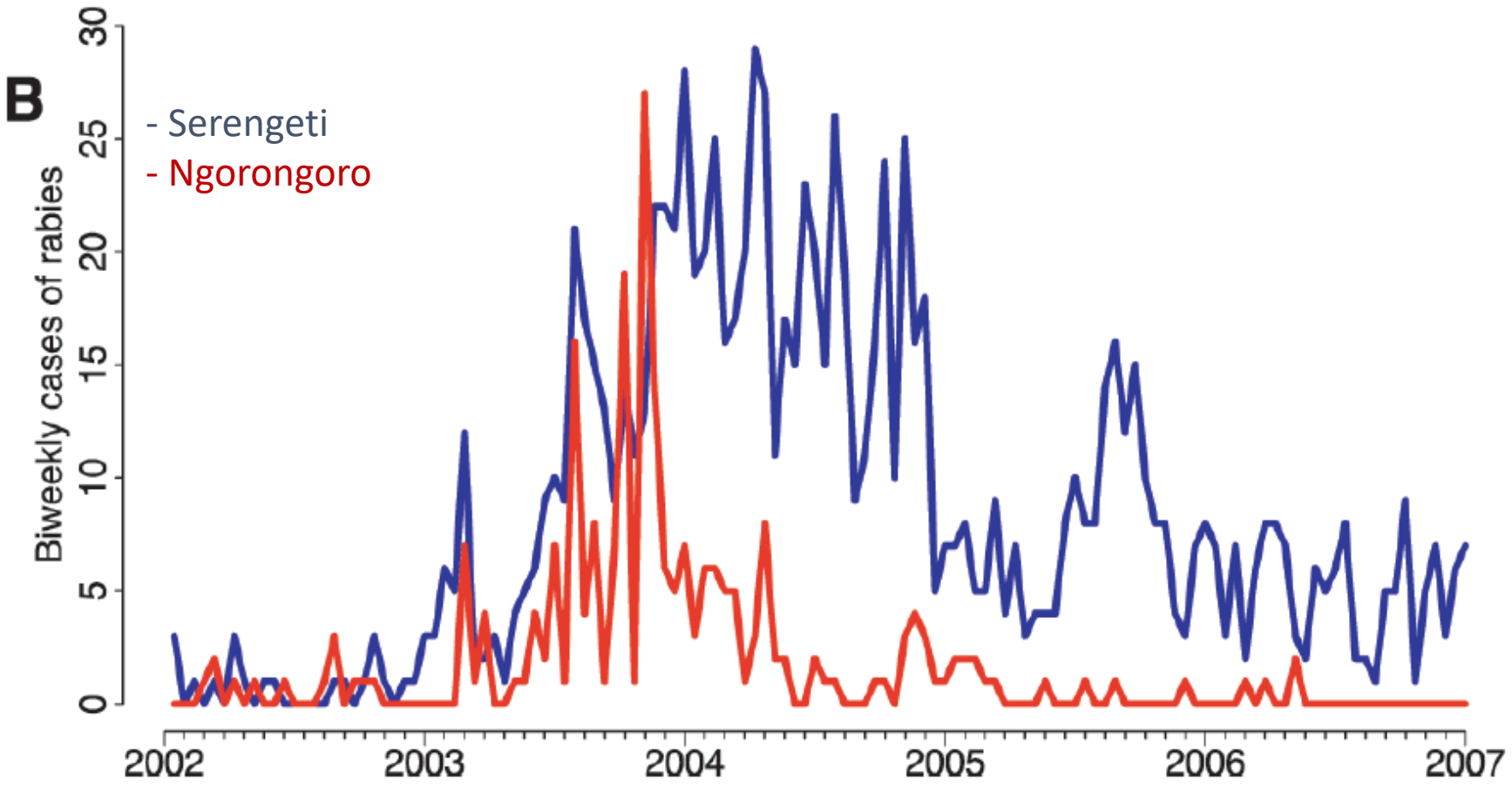
Person:	Residents of and recent visitors to West Africa, including Senegal, Guinea, Sierra Leone and Liberia, as well as their close contacts or others in their community
Place:	Worldwide
Time:	On or after November 15, 2013
Clinical Description:	Illness with onset of fever and no response to treatment for usual causes of fever in the area, and at least one of the following signs: bloody diarrhoea, bleeding from gums, bleeding into skin (purpura), bleeding into eyes and urine.

Goals

- Defining a case
- Different approaches to data collection and presentation.
- Metrics to describe the spread of the disease

Ways of collecting data on cases

Surveillance + Contact Tracing/Outbreak investigation



Hampson et al. 2009

Ways of collecting data on cases

- Passive
- Active

Epidemiological studies

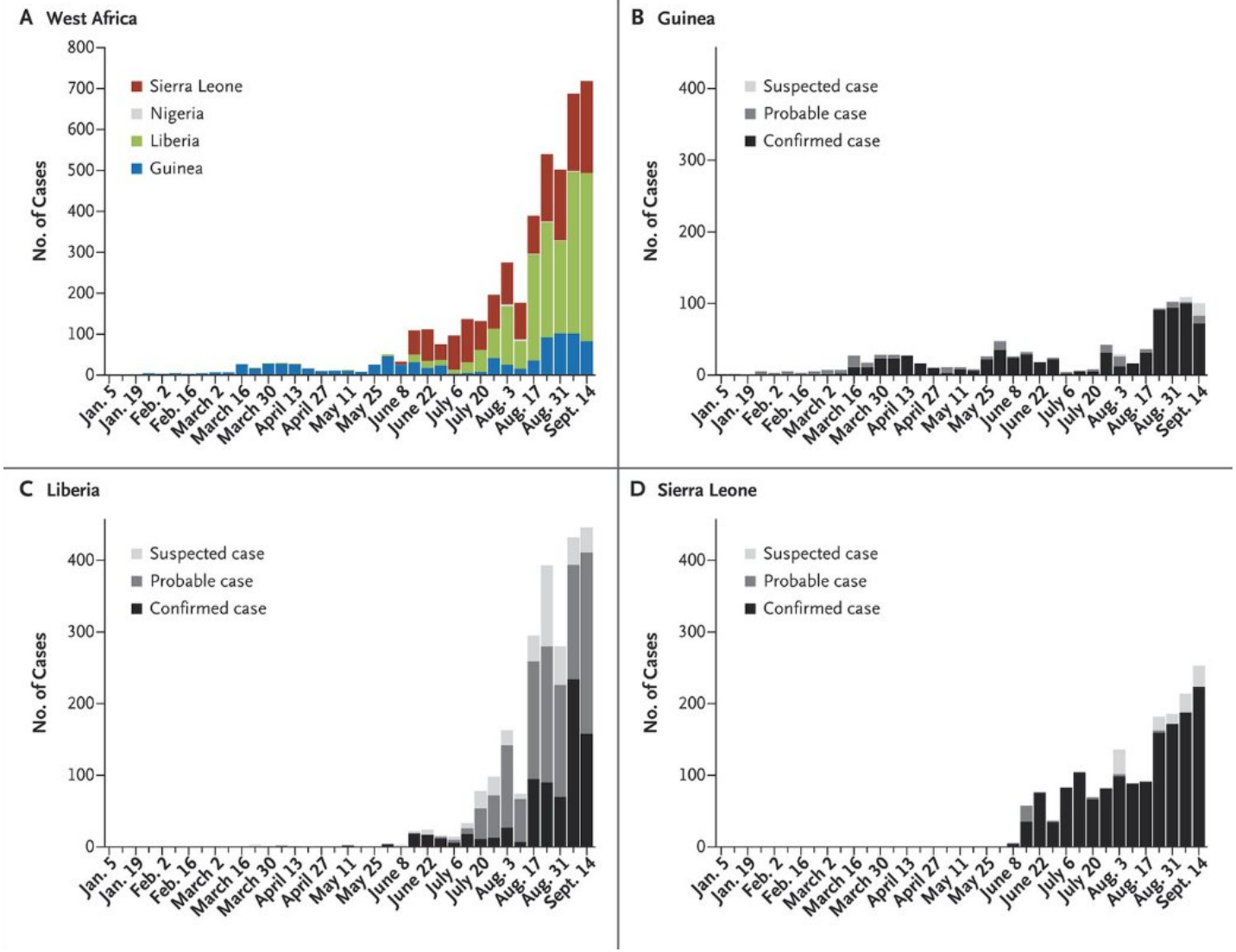
- Case-series
- Case-control
- Cohort
- Outbreak investigations

Goals

- Defining a case
- Different approaches to data collection and presentation.
- Metrics to describe the spread of the disease

Incidence of disease

Weekly incidence of confirmed, probable and suspected Ebola cases in West Africa

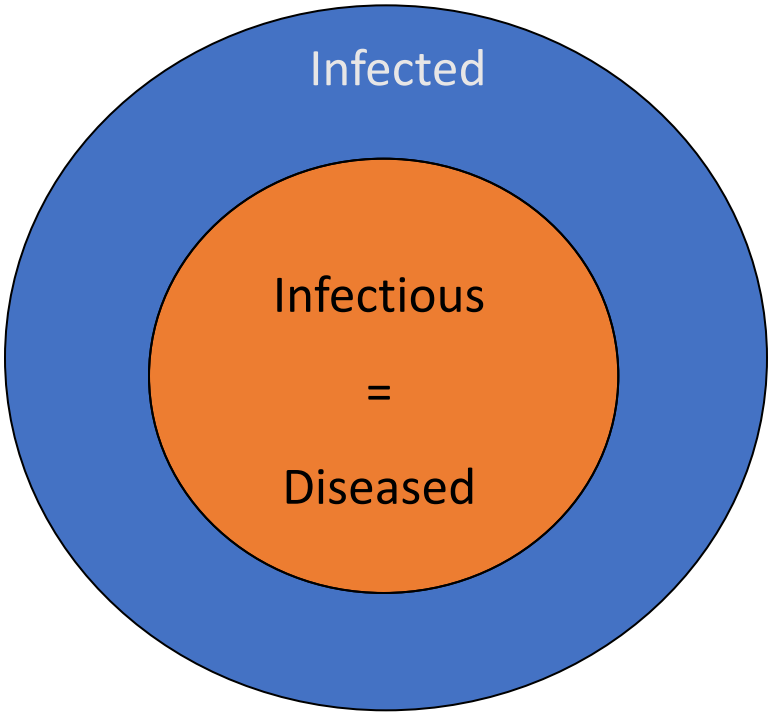


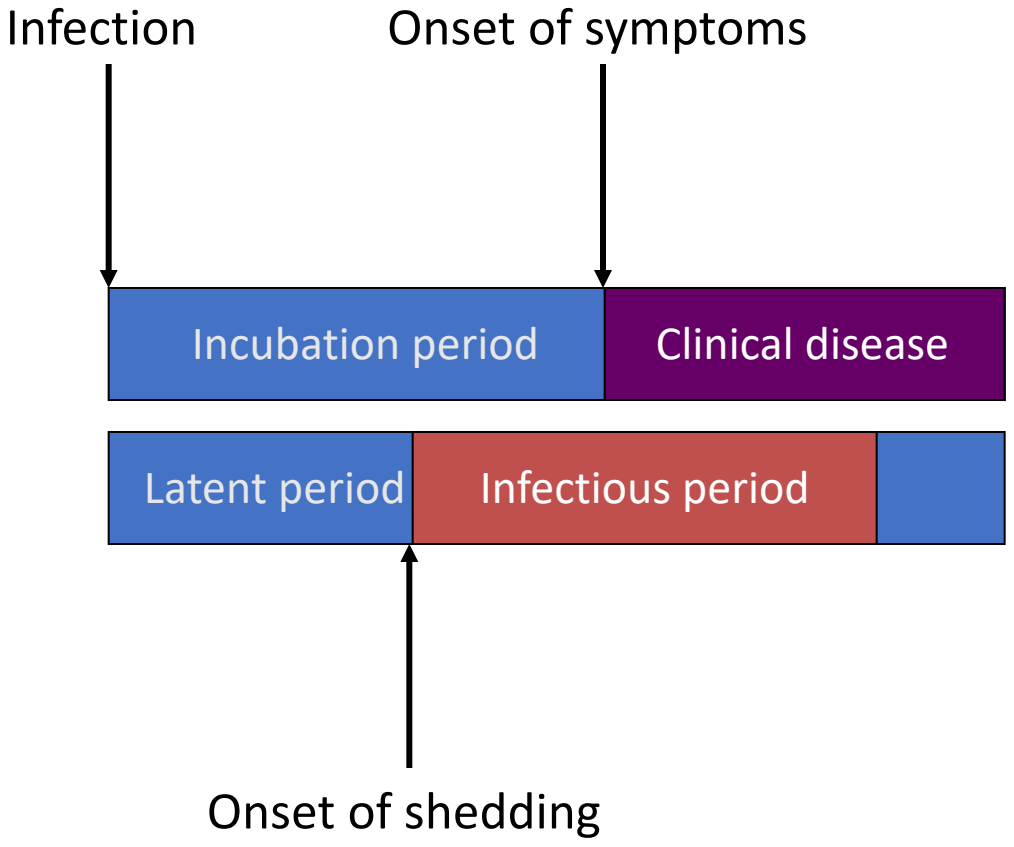
Source: WHO Ebola Response Team N Engl J Med 2014; 371:1481-1495; DOI: 10.1056/NEJMoa1411100

Incidence of Infection

Infectivity = 1

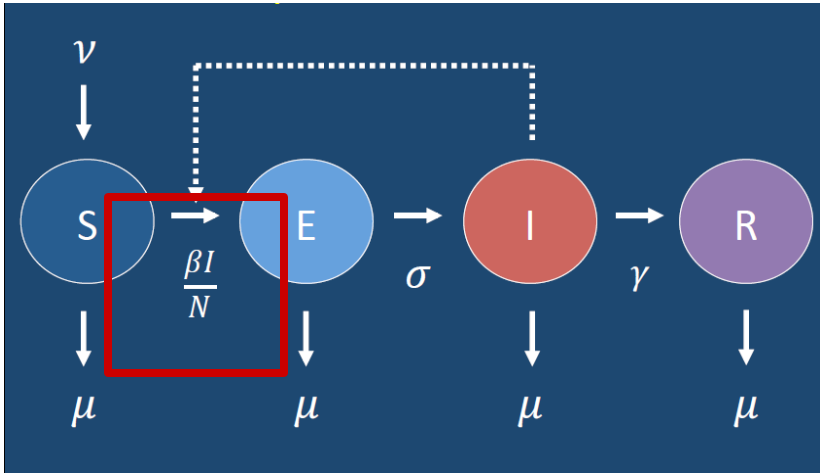
(everyone exposed becomes infected)





Incidence of infection

Mathematical expression?



SEIR Model

$$\frac{dS}{dt} = \nu - \frac{\beta SI}{N} - \mu S$$

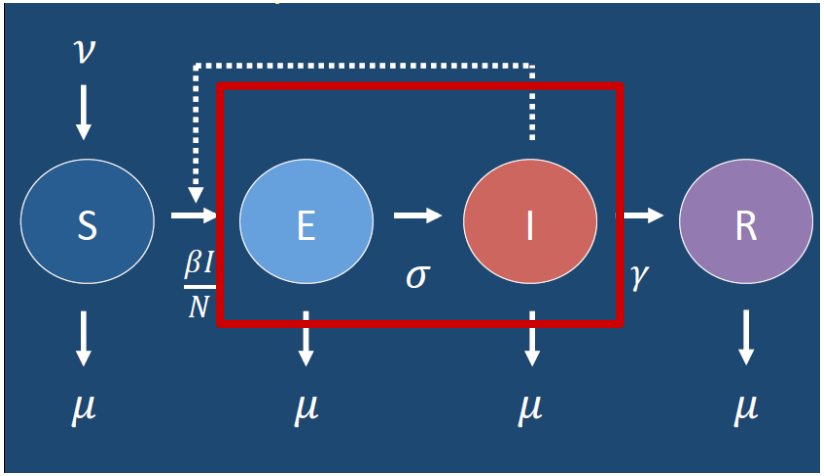
$$\frac{dE}{dt} = \frac{\beta SI}{N} - \sigma E - \mu E$$

$$\frac{dI}{dt} = \sigma E - \gamma I - \mu I$$

$$\frac{dR}{dt} = \gamma I - \mu R$$

ν	birth rate
μ	mortality rate
σ	1 / latent period
γ	1 / infectious period
β	transmission coefficient

Prevalence



$$\frac{E+I}{N}$$

Mathematical expression?

SEIR Model

$$\frac{dS}{dt} = \nu - \frac{\beta SI}{N} - \mu S$$

$$\frac{dE}{dt} = \frac{\beta SI}{N} - \sigma E - \mu E$$

$$\frac{dI}{dt} = \sigma E - \gamma I - \mu I$$

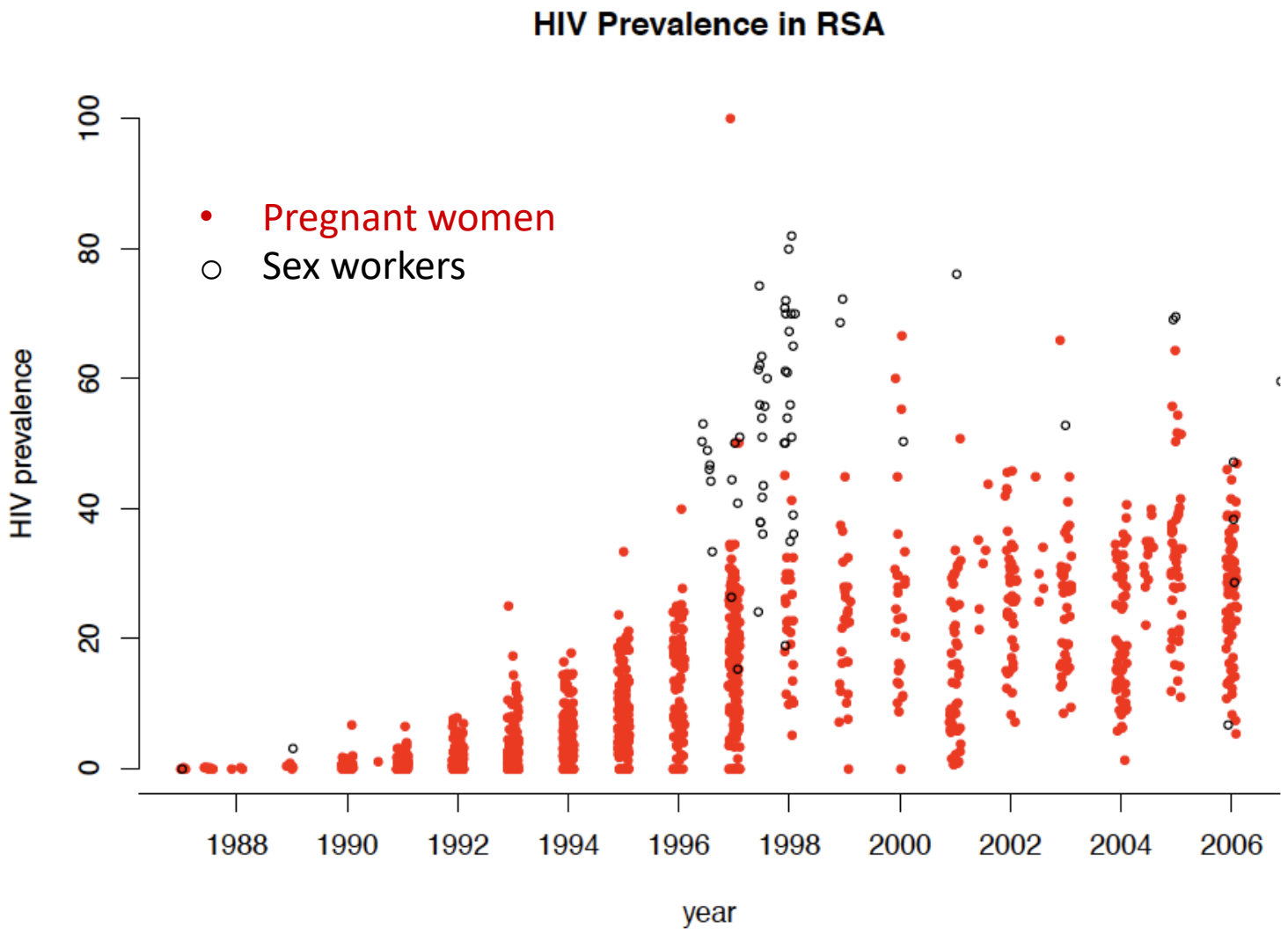
$$\frac{dR}{dt} = \gamma I - \mu R$$

ν	birth rate
μ	mortality rate
σ	1 / latent period
γ	1 / infectious period
β	transmission coefficient

Prevalence of infection

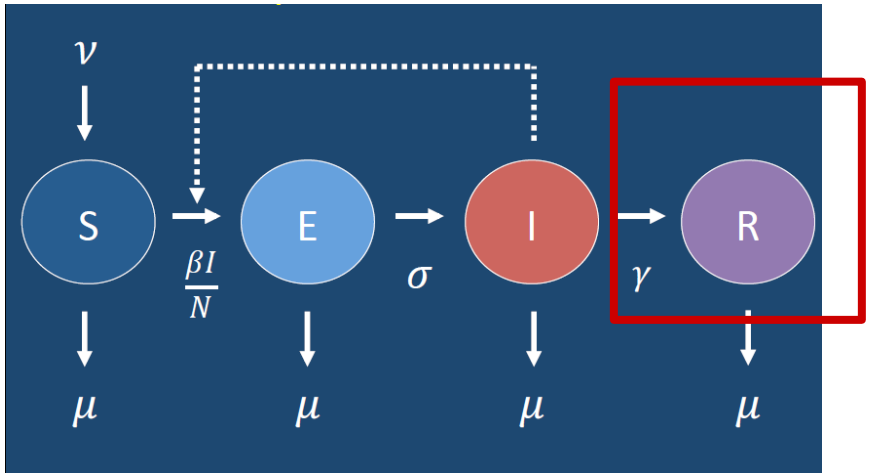
Prevalence of antibodies (seroprevalence)

Prevalence



Source: UNAIDS HIV Surveillance Database

Seroprevalence



$$\frac{R}{N}$$

SEIR Model

$$\frac{dS}{dt} = \nu - \frac{\beta SI}{N} - \mu S$$

$$\frac{dE}{dt} = \frac{\beta SI}{N} - \sigma E - \mu E$$

$$\frac{dI}{dt} = \sigma E - \gamma I - \mu I$$

$$\frac{dR}{dt} = \gamma I - \mu R$$

ν	birth rate
μ	mortality rate
σ	1 / latent period
γ	1 / infectious period
β	transmission coefficient

Mathematical expression?

Prevalence of infection

Prevalence of antibodies (seroprevalence)

Seroprevalence

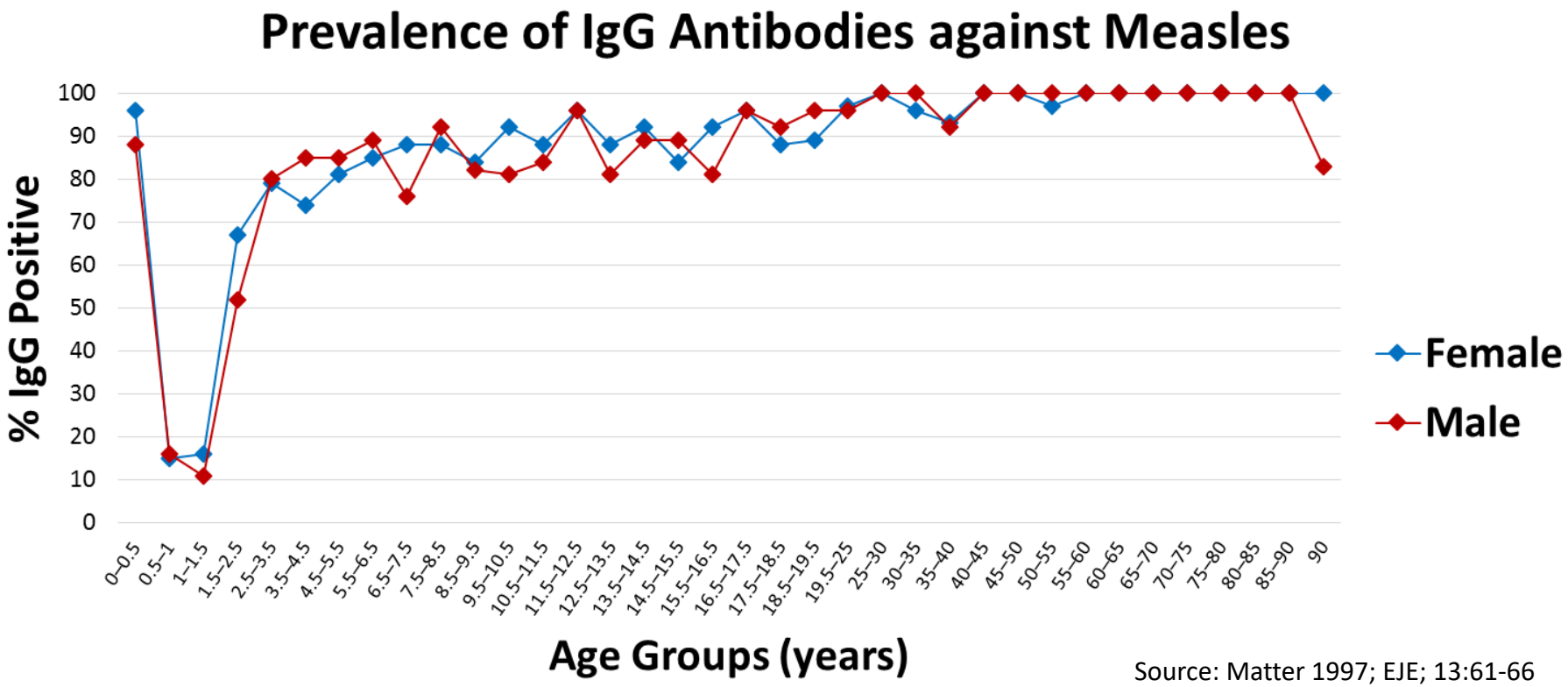
Can be related to:

* Prevalence of infection
* Past exposure

May or may not be:

* Prevalence of resistance
* Specific to infection of interest

Seroprevalence



Source: Matter 1997; EJE; 13:61-66

Can be related to:

- Prevalence of infection
- Past exposure

May or may not be:

- Prevalence of resistance
- Specific to infection

Levels of data aggregation

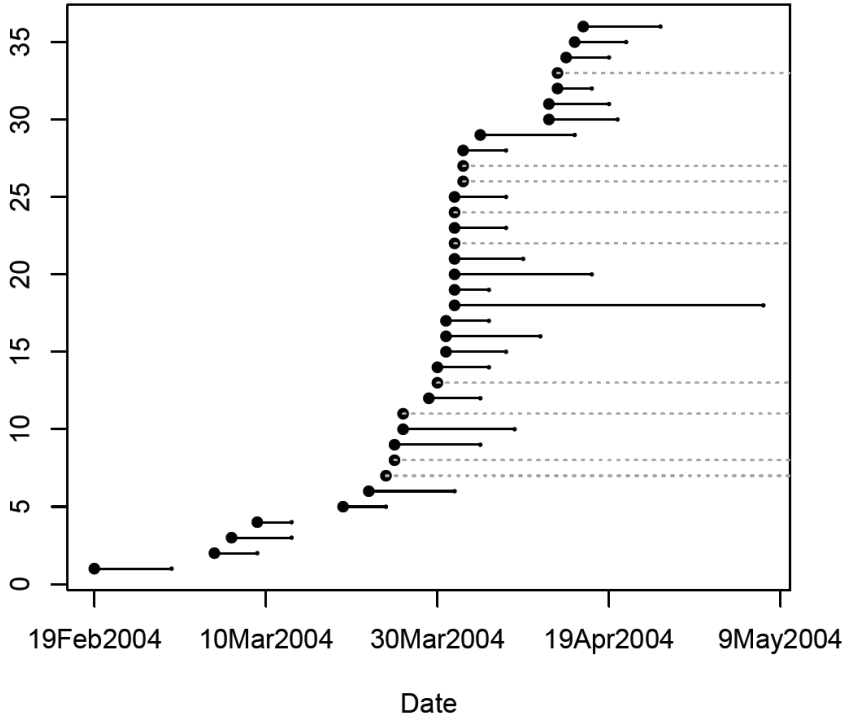
Aggregated data

De-identified data

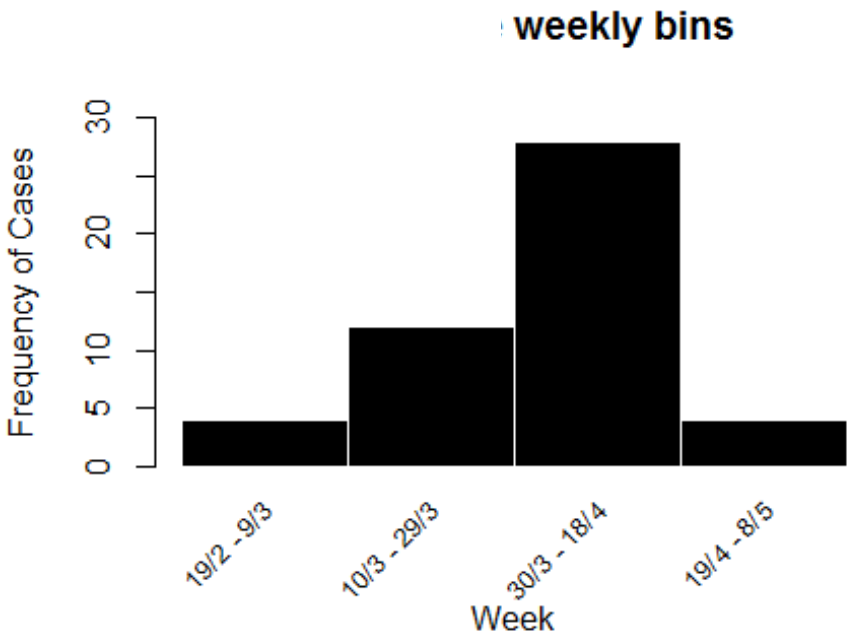
Personally identifying data

Levels of data aggregation

De-identified data



Aggregated data



Data from ICDDR,B and Gurley *et al*. 2007

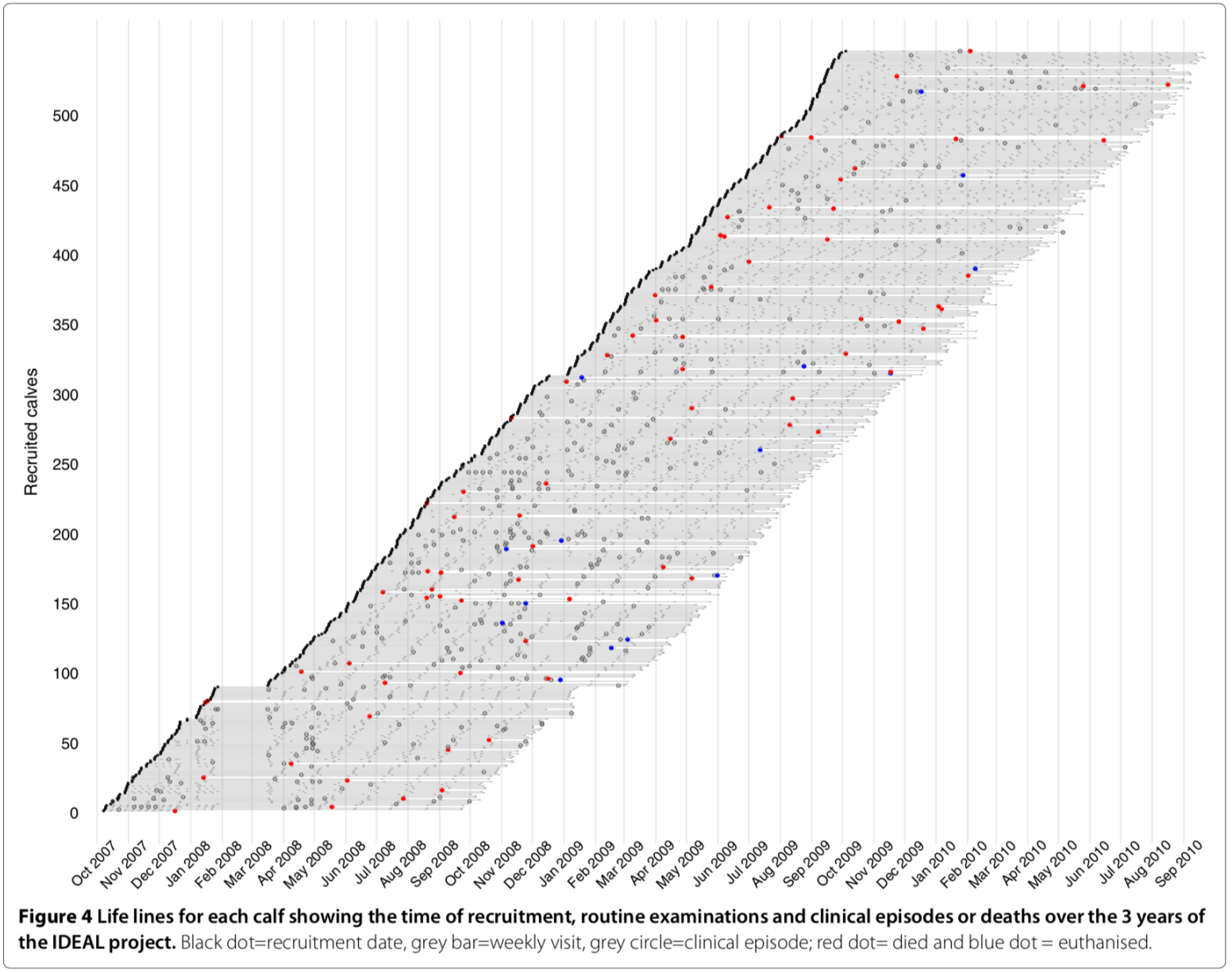


Figure 4 Life lines for each calf showing the time of recruitment, routine examinations and clinical episodes or deaths over the 3 years of the IDEAL project. Black dot=recruitment date, grey bar=weekly visit, grey circle=clinical episode; red dot= died and blue dot = euthanised.

Bronsvoort, Thumbi *et al. BMC Veterinary Research* 2013, **9**:171

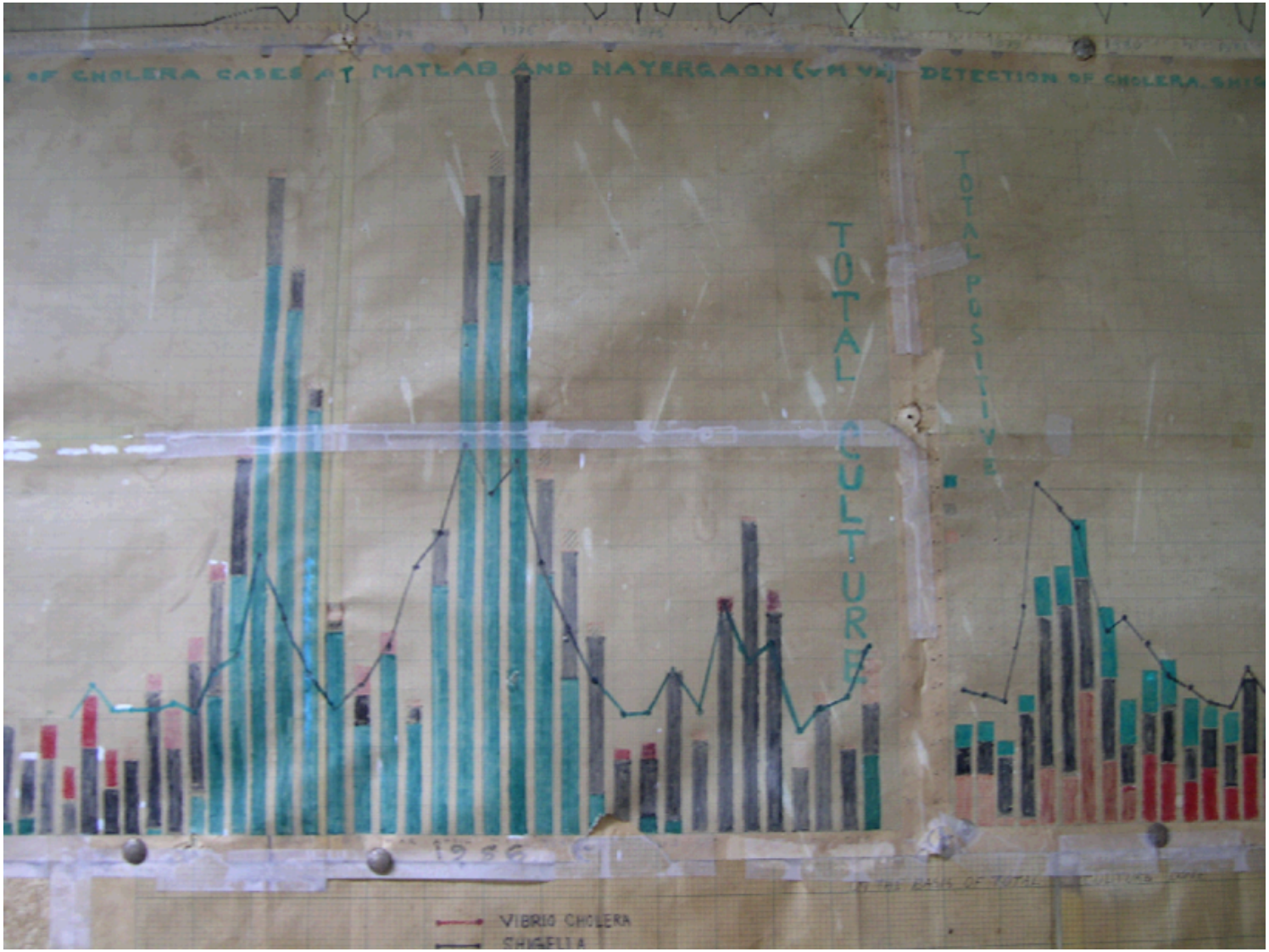
Investigation line-list

Case ID	Age (Yrs)	Gender	Symptoms onset	Symptoms	Lab sample collected	Date sample collection	Date Hospitalized	Date discharged	Fatal case	Date of death
Case 1	7	Male	2/18/14	papule/ edema	X	x	2/20/14	2/24/14	x	x
Case 2	31	Male	2/20/14	papule	X	x	2/20/14	2/24/14	x	x
Case 3	65	Female	2/21/14	papule	Skin swab	2/28/14	x	x	x	x
Case 4	32	Male	2/18/14	diarrhea	X	x	2/21/14	x	Yes	2/21/14
Case 5	24	Male	2/17/14	diarrhea/ vomiting	X	x	x	x	Yes	2/18/14
Case 6	48	Male	2/16/14	vomiting/ painful swallowing	Oropharyngeal swab	2/28/14	x	x	x	x

Anthrax outbreak – Kenya 2014

Muturi et al 2018 Am. J. Trop. Med. Hyg., 99(4), pp. 833–839

Visualizing data before R…



Thumbi SM, Bruce F, Bellan SE, Pulliam JRCP. "Introduction to Infectious Disease Data" Clinic on the Meaningful Modeling of Epidemiological Data. https://doi.org/10.6084/m9.figshare.5044603.v4

Attribution:

Thumbi SM, Bruce F, Bellan SE, Pulliam JRCP

Clinic on the Meaningful Modeling of Epidemiological Data

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