

## PHARMACOMETRICS IN EPIDEMICS

Modeling with minimal information to identify effective therapies: lessons learned from Ebola



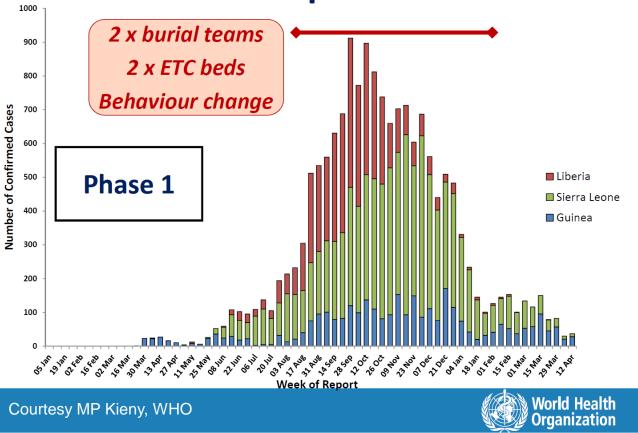
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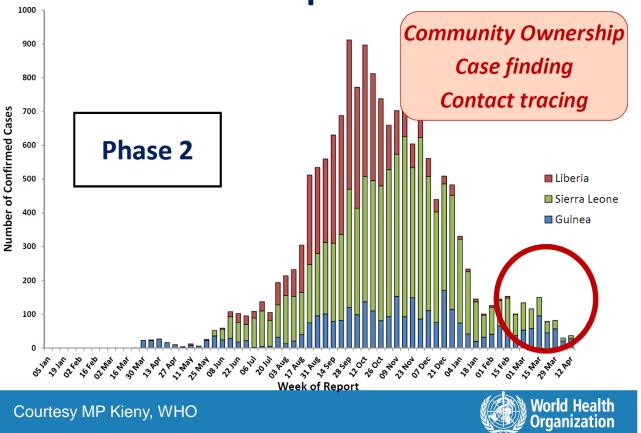
#### PHARMACOMETRIC IN EPIDEMICS

- Dosing a repurposed therapeutic based on data from its primary indication
- Determining the dose of a new therapeutic with minimal clinical data
- Creating a study design that minimizes exposure to ineffective options
- Opportunity for pharmacometics in GH Disease Modeling

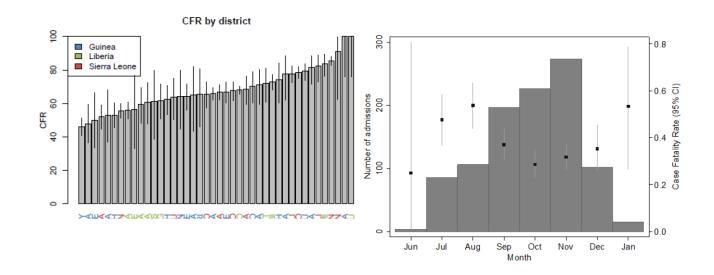
### **West Africa Epidemic Curve**



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### Case-fatality case is variable: between treatment centers - within individual ETCs



Courtesy MP Kieny, WHO



### PATIENT ACCESS DURING DISEASE PROGRESSION IS DIFFICULT

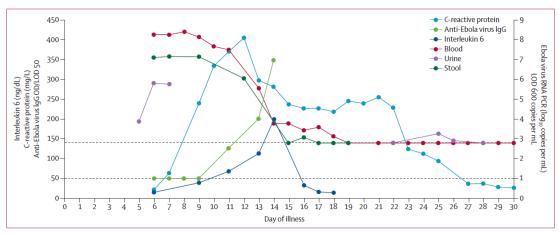


Figure 2: Ebola virus RNA PCR, anti-Ebola-virus IgG, and inflammatory parameters over the course of the illness Interleukin 6, C-reactive protein, Ebola virus RNA PCR (plasma, stool, and urine), and anti-Ebola-virus IgG titres are shown as a function of the days of disease. The patient was anuric from day 7 to 22, therefore the line for the urine PCR is interrupted. LOD=limit of detection.

Severe Ebola virus disease with vascular leakage and multiorgan failure: treatment of a patient in intensive care

Timo Wolf, Gerrit Kann, Stephan Becker, Christoph Stephan, Hans-Reinhardt Brodt, Philipp de Leuw, Thomas Grünewald, Thomas Vogl, Volkhard A I Kempf, Oliver T Keppler, Kai Zacharowski

Lancet 2015; 385: 1428-35

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### RUNNING A CLINICAL STUDY IN AN ETC IS CHALLENGING



Courtesy of Peter Horby, MBBS, PhD. Oxford ISARIC Trial Centre

### PAPER IS INCINERATED – PHOTO IS THE RECORD





Courtesy of Peter Horby, MBBS, PhD. Oxford ISARIC Trial Centre

### DATA IS LIMITED - PK SPARSE IF ANY, PD CLINICAL SIGNS

"Filling out a form on 300 patients when you have just two nurses and a doctor is just not realistic." cohort (lick): TKM Observational (OBS) Date (DOMM?????) DRUG INFUSION DAY (If in TKM cohort) End Other Enter any additional comments

Courtesy of Peter Horby, MBBS, PhD. Oxford ISARIC Trial Centre

### DATA AND RESULTS SHARING IN A PUBLIC HEALTH EMERGENCY

Priorities and motivations:

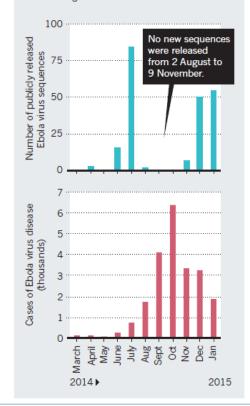
Healthcare providers
Government agencies
Private companies
Academic investigators
"...data owners, ...my trial site"

# Make outbreak research open access

Establish principles for rapid and responsible data sharing in epidemics, urge Nathan L. Yozwiak, Stephen F. Schaffner and Pardis C. Sabeti.

#### **GAPS IN THE DATA**

Genome sequences from the West Africa outbreak of Ebola virus were first made publicly available in April 2014. Since 99 genomes were released in July, data sets have been shared sporadically, even though more are known to have been generated.



#### OPPORTUNITY FOR THE PHARMACOMETICS COMMUNITY



The NEW ENGLAND JOURNAL of MEDICINE

### The Next Epidemic — Lessons from Ebola

Bill Gates

Perhaps the only good news from the tragic Ebola epidemic in Guinea, Sierra Leone, and Liberia is that it may serve as a wake-up call: we must prepare for future epidemics of diseases that may spread

more effectively than Ebola.

This article was published on March 18, 2015, at NEJM.org.

### Recommendations for Preparing for Future Epidemics

The world needs to build a warning and response system for outbreaks. This system should

- be coordinated by a global institution that is given enough authority and funding to be effective.
- enable fast decision making at a global level,
- expand investment in research and development and clarify regulatory pathways for developing new tools and approaches,
- improve early warning and detection systems, including scalable everyday systems that can be expanded during an epidemic,
- involve a reserve corps of trained personnel and volunteers,
- strengthen health systems in low- and middle-income countries, and
- incorporate preparedness exercises to identify the ways in which the response system needs to improve.

#### **BMGF Global Organization**

Reporting line Global Health Global Development

**Global Health Functional Areas** 

> Discovery & Translational Sciences

> Vaccine **Development**

Integrated **Development** Chem, Manu, Cont

**Quantitative Science** 

**Regulatory Science** 

**Diagnostics** 

Strategy, Planning & Management

Global **Program Strategy Teams** 

HIV

ТВ **Enteric and Diarrheal Diseases** 

Malaria

**Neglected Infectious Diseases** 

Pneumonia

Polio

Maternal, Neonatal & Child Health

**Family Planning** 

Water, Sanitation & Hygiene

Agriculture

**Financial Services for the Poor** 

Nutrition

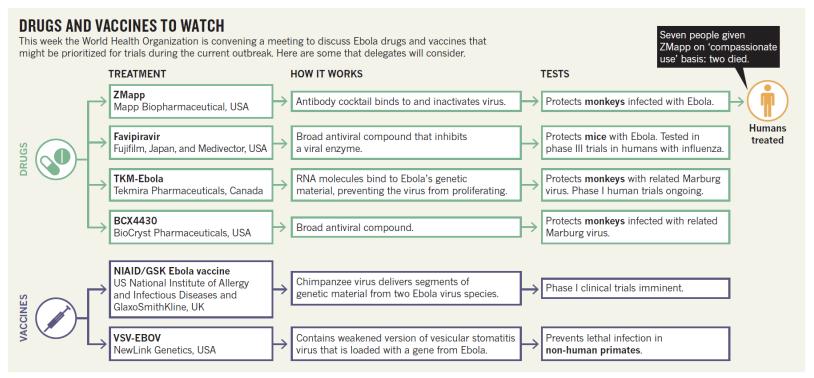
**Global Development Functional Areas** 

**Vaccine Delivery** 

**Integrated Delivery** 

Strategy, Planning & Management

### IN TODAY'S SESSION...



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