Case study: Nubia's mother

Experimental drugs and pregnancy in the 2014-2016 Ebola epidemic West-Africa

3-4 nov 2016

Buenos Aires Argentina

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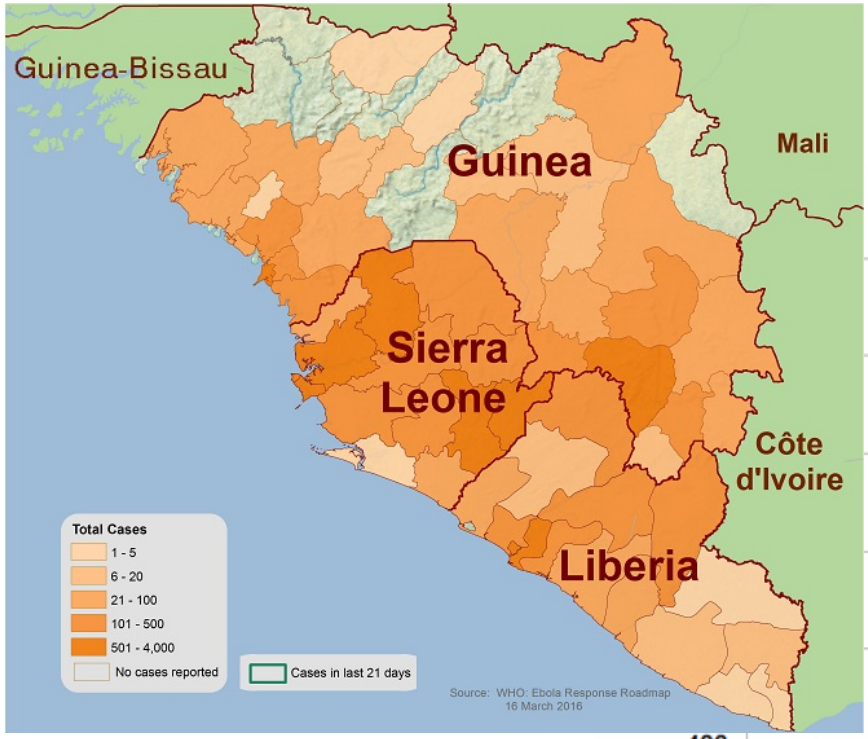
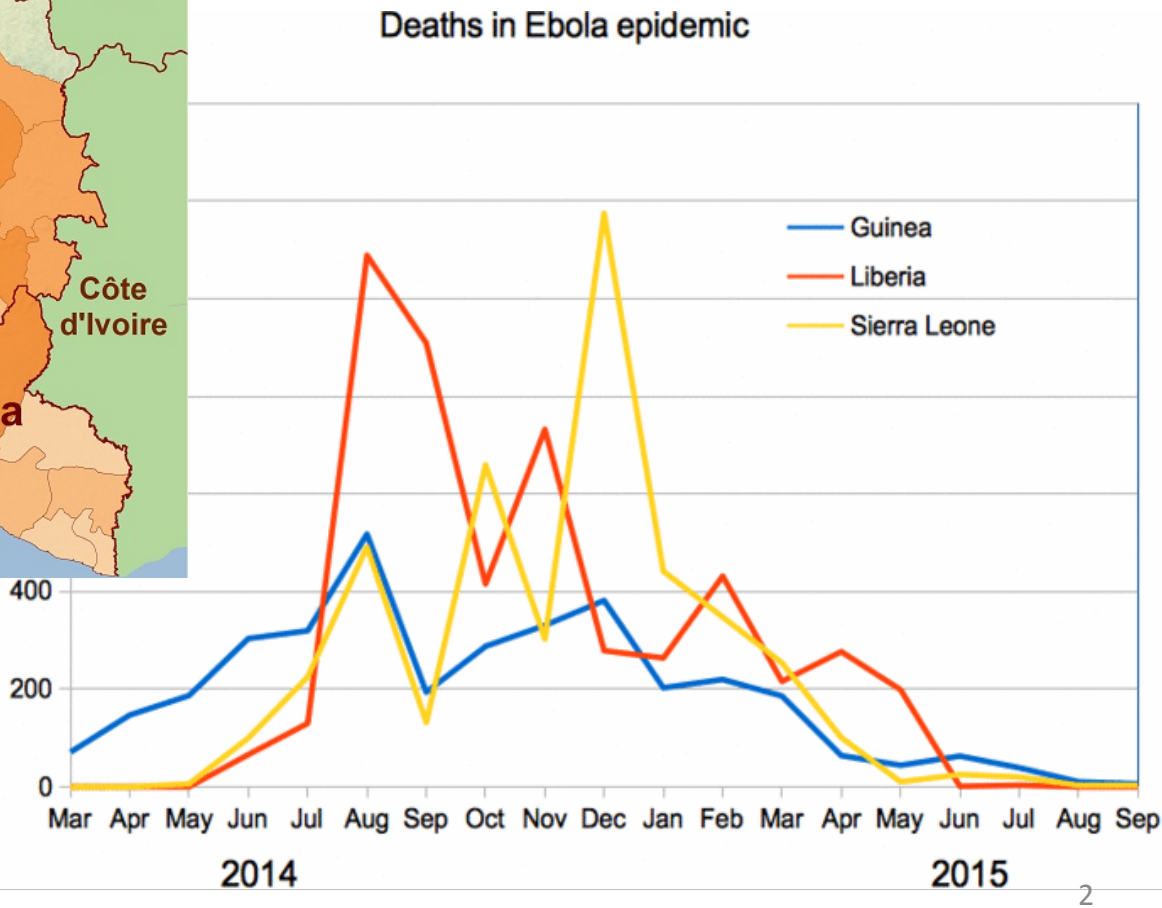
The setting : 2014-2016 Ebola epidemic Guinea West-Africa Oct 2015





Mortality?

Ebola deaths

Figures up to 20 December 2015

11,315

Deaths - probable, confirmed and suspected

(Includes one in the US and six in Mali)

4,809 Liberia

3,955 Sierra Leone

2,536 Guinea

8 Nigeria

Source: WHO

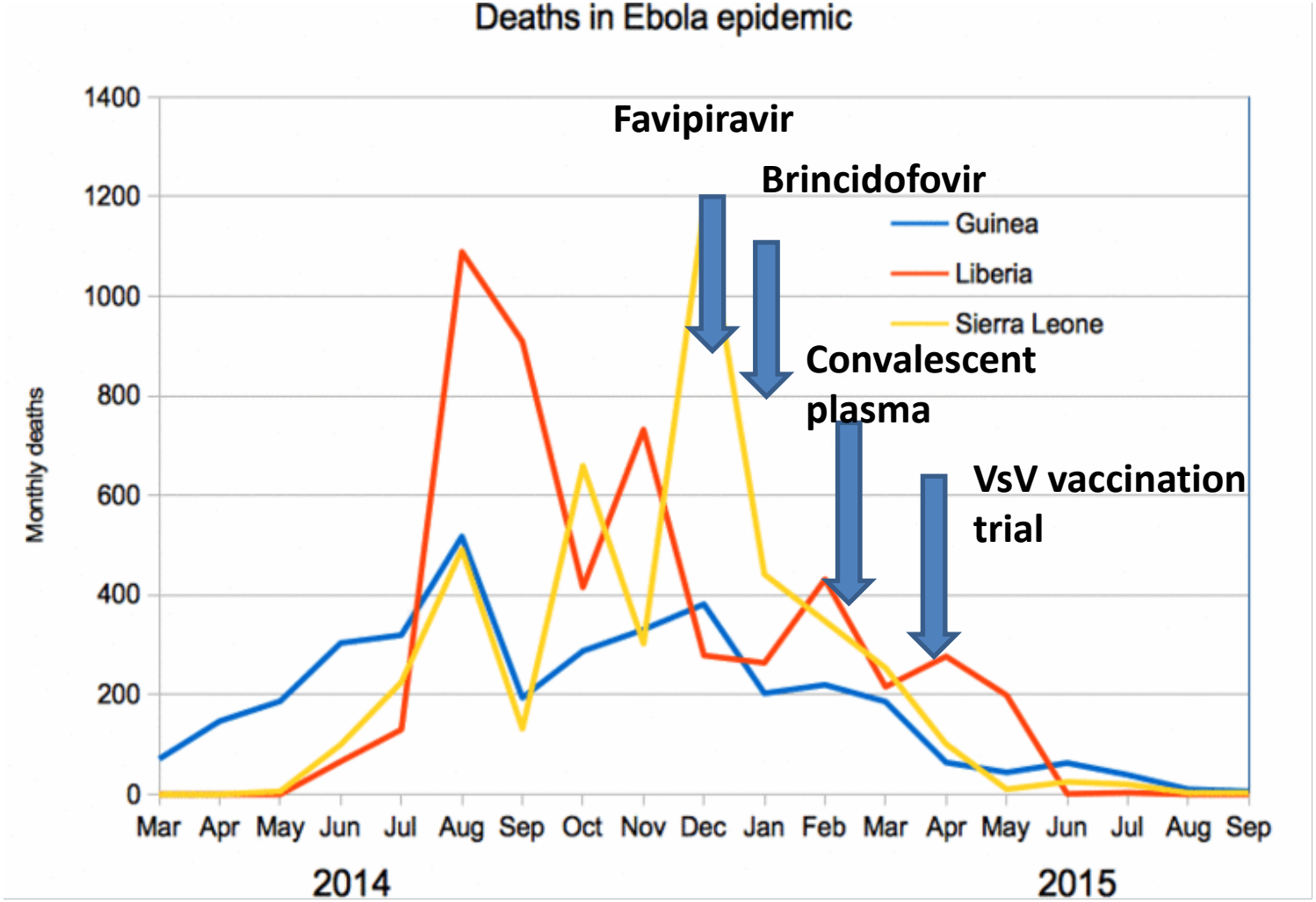
Clinical trials in Ebola:

Ethical considerations for use of unregistered interventions for Ebola viral disease.

WHO 11 August 2014

*'In the **particular context** of the current Ebola outbreak in West Africa, it is **ethically acceptable** to offer **unproven interventions** that have shown promising results in the laboratory and in animal models but have not yet been evaluated for **safety and efficacy** in humans **as potential treatment or prevention**.'*

MSF and Clinical Ebola trials?



Drug Choice?

- MSF and partners selected 3 therapeutic interventions (Favipiravir/Brincidofovir/convalescent plasma) based on:
  - Efficacy and safety data
  - Antiviral preferred over host support
  - Availability and post trial access possibilities
  - Way of administration

  - Option not to randomise (comparison with historical controls)

  - **Pregnant women?**

  Favipiravir: no insurance in trial,Monitored Emergency use allowed
  Brincidofovir: never allowed (refusal by manufacturer)
  Convalescent plasma: no problem

Vsv Vaccine trial (March-June 2015) (WHO promotor)

Not allowed in pregnant women /children under 6

(vaccine given to family members/contacts of confirmed Ebola positive patients and to health care workers)

Bút: no pregnancy testing before administration =>

+/- 20 women were vaccinated while pregnant!

http://www.who.int/mediacentre/news/releases/2015/effective-ebola-vaccine/en/

Lancet, August 2016

Editorial

An Ebola vaccine: first results and promising opportunities

Cellou Binani/Stringer

Published Online
July 31, 2015
http://dx.doi.org/10.1016/
S0140-6736(15)61177-1

See Articles page 857

Today, *The Lancet* publishes the first results from a phase 3 cluster randomised trial of a novel Ebola virus vaccine. The study, sponsored and led by WHO, is a remarkable scientific and logistical achievement. In the midst of an extreme public health emergency, researchers, health workers, and community facilitators in Guinea included 7651 people in a trial to test the efficacy of a recombinant, replication-competent vesicular stomatitis virus-based vaccine expressing a surface glycoprotein of Ebola (Zaire). The authors conclude that their interim analysis indicates the vaccine "might be highly efficacious and safe".

The technique used in the trial was "ring vaccination". This method involves identifying a newly diagnosed

study's staff were from Guinea. Before this work, no clinical trial on this scale had ever been performed in the country.

This study will be the subject of intense scientific scrutiny and debate. But what do the results mean for those most at risk of Ebola virus infection in west Africa? The vaccine is not yet licensed. More data on efficacy are needed before it can be widely deployed. But if the evidence proves sufficient for licensing, a Global Ebola Vaccine Implementation Team, also under WHO's leadership, has been preparing the ground for its introduction—creating guidelines for the vaccine's use, strategies for community engagement, and mechanisms to expand country capacity for the vaccine's distribution and delivery. In addition, the

Nubia's mother

- Forécariah, Guinea, oct 2015
- 25 yr old, third trimester pregnancy

- Cared for woman in same household who died of Ebola

- Everyone in the household vaccinated except for her and a 3-month old baby

- Developed fever and tested Ebola postive after a few days => referred to MSF

Nubia's mother

- Patient was in poor clinical condition and had very high viral load
- Baby apparently alive (mother reported fetal movements)

- MSF wanted Zmapp for her (Zmapp trial ongoing in centre near by, promotor NIH) => refusal Zmapp outside clinical trial

=> Pt could enter clinical trial but 50% chance of receiving placebo – negotiations ongoing

Nubia's mother

- Favipiravir administered
- Mother went into labour and delivered baby 4 days after admission, Nubia, 3 kg and alive and well

- Mother died 7 hours after birth of haemorrhage and diffuse intravascular coagulation (complication Ebola)

- Nubia received without delay first Zmapp within 24 hours after birth, after some days GS5734 and buffy coat survivor , she survived

Issues for discussion (1)

- 1. Availability **experimental drugs for pregnant women was complicated** in Ebola (Brincidofovir: impossible – Favipiravir: lengthy process)

=> Potentially pregnancy could be a negative prognostic factor, no access to experimental drugs

Issues for discussion(2)

- 2. Zmapp once the baby was born was obtained immediately, for the mother the centre where the trial was managed insisted on randomisation

=> The baby seems to have been « privileged » compared to her mother

- 3. **Ebola vaccination access for pregnant women**:

=> Ebola is a condition with > 50% mortality, Nubia's mother was at high risk to contract the disease but **she was not eligible for vaccination**

Issues for discussion (3)

- 4. Nubia's mother herself was **never involved** in the discussion process

All pictures MSF, 2015

Acknowledgements
to **Frontline workers**
and **communities**

THANK YOU