Conducting research during outbreaks: from Guinea to Democratic Republic of Congo

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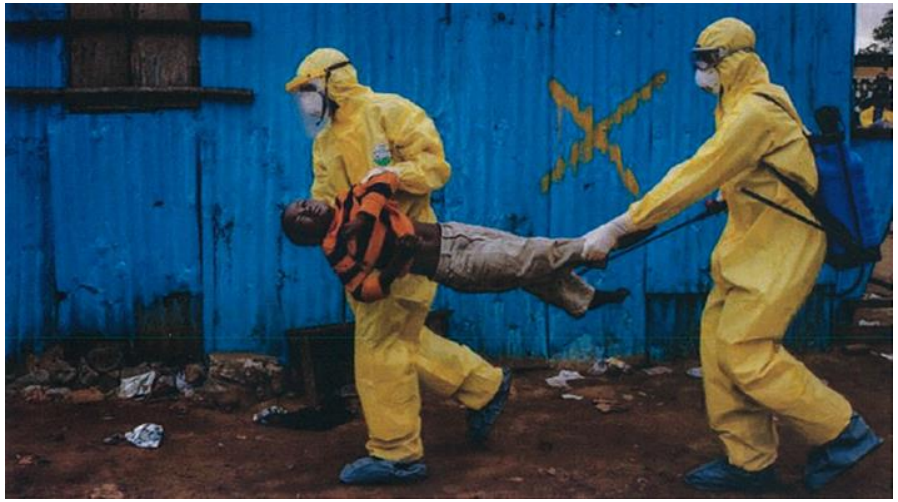
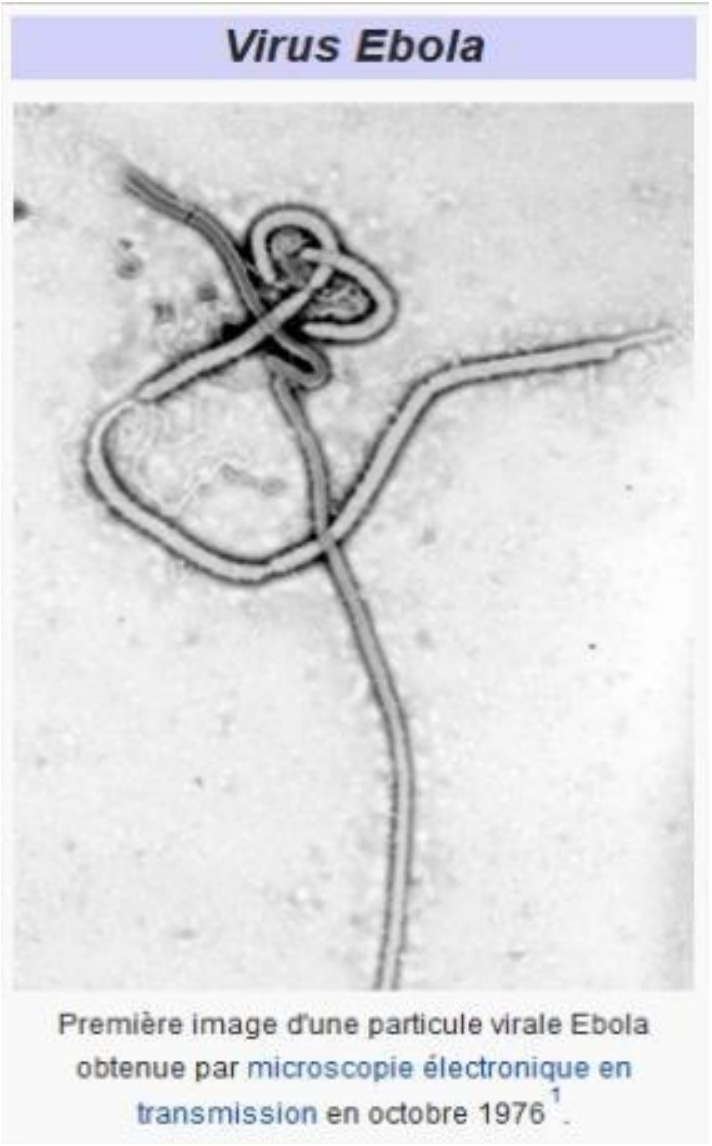
Dpt des Maladies Infectieuses, CHU Montpellier

THE EBOLA CRISIS



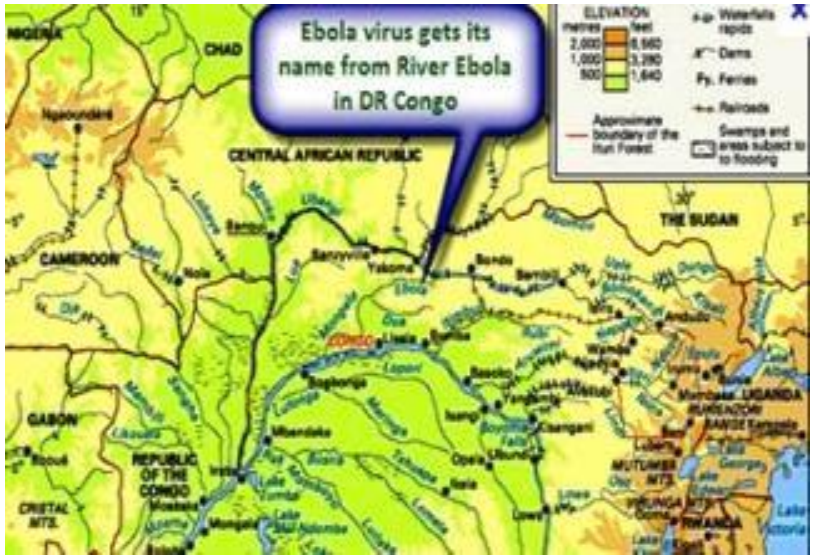
AUGUST – SEPTEMBER 2014

Virus Ebola : Premiere identification en 1976 en RDC



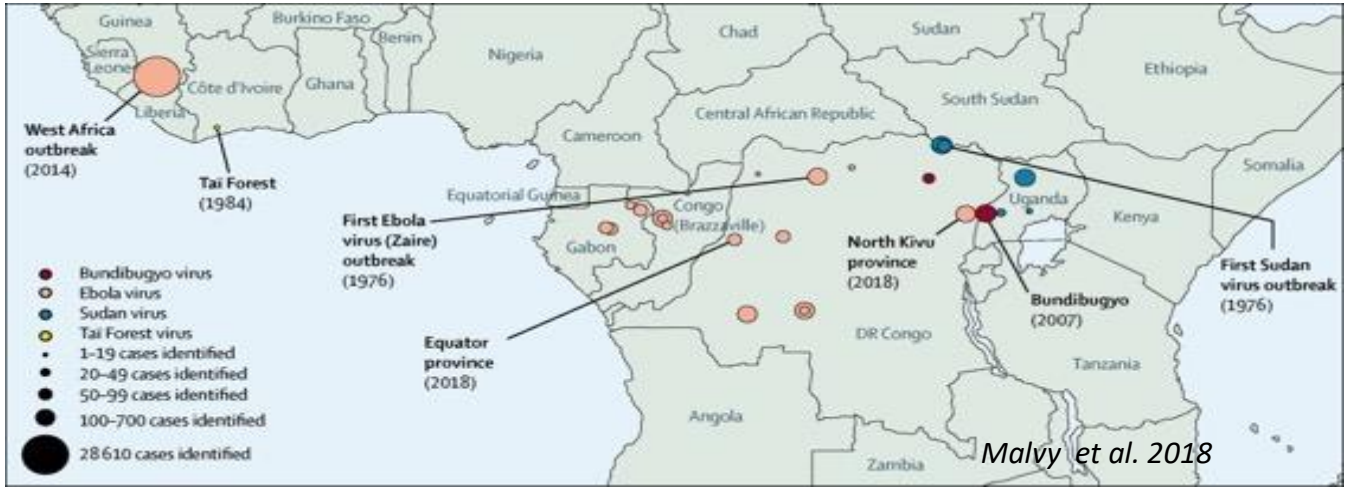
Première image d'une particule virale Ebola obtenue par microscopie électronique en transmission en octobre 1976 [1].

- 1ere épidémie à Yambuku en 1976
- 318 cas et 88% de décès
- Contamination par contact direct et utilisation des seringues dans les hôpitaux
- Investigations internationales: ITM, CDC, WHO, INRB,…



Rivière Ebola près de la mission catholique de Yambuku

Ebola: 30 outbreaks since 1976



1976-1978: 3 outbreaks

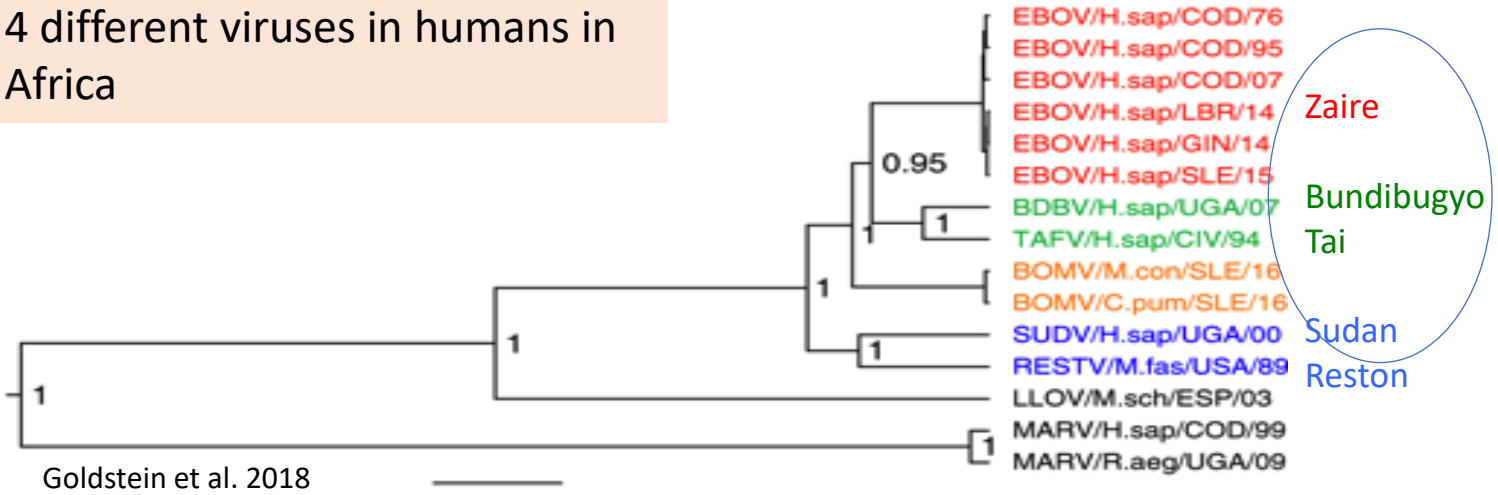
1994-1996: Ivory Coast, DRC, Gabon

rural/semi-rural areas
Limited number of victims

2014-2016:
Major outbreak in West Africa
10 X victims than all previous outbreaks

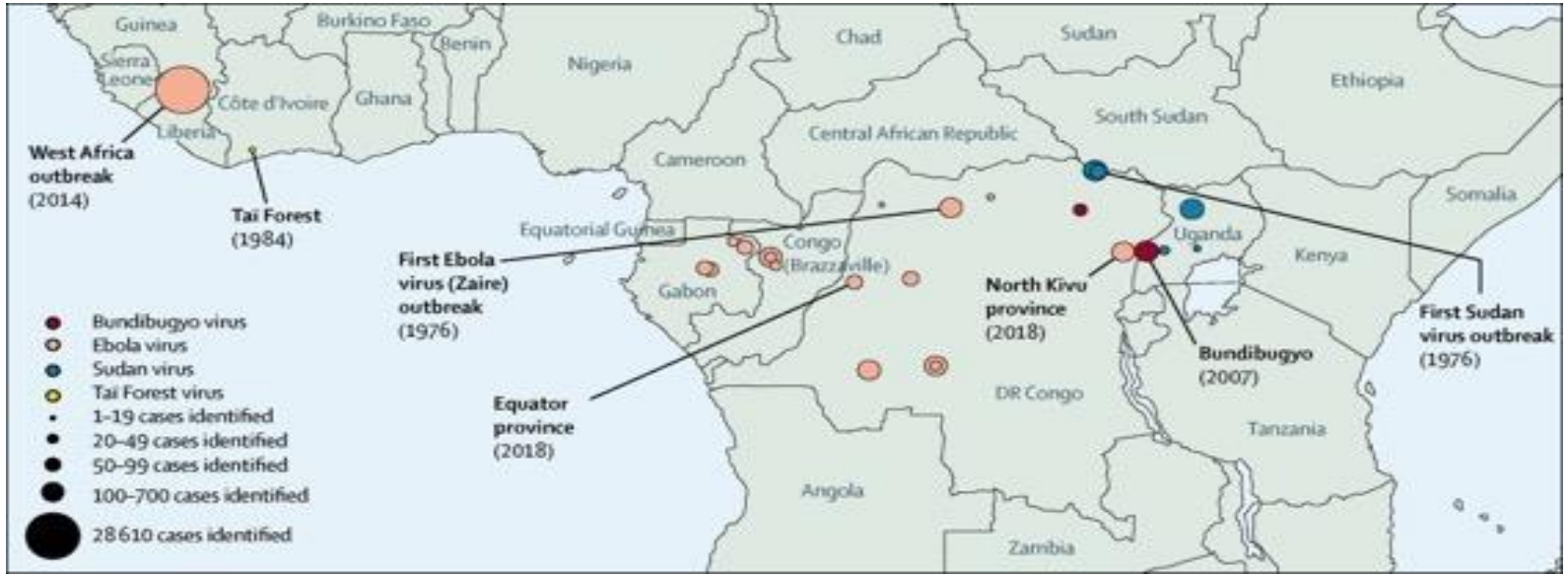
Increasing frequency
4 outbreaks in DRC (5/2017-8/2019-2020)
Major Outbreak in North Kivu & Ituri

4 different viruses in humans in Africa



Goldstein et al. 2018

2014 Ebola: 28 outbreaks since 1976



The West Africa outbreak with 10 X victims than all previous outbreaks represented a paradigm shift in particular for research

Treatment: O
Vaccin: O
Diagnosis: home-based
Clinical consequences : « death »

2014: International mobilization

Ebola: time to act

Governments and research organizations must mobilize to end the West African outbreak.

11 SEPTEMBER 2014 | VOL 513 | NATURE | 143

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RÉPUBLIQUE FRANÇAISE

EBOLA
TASK FORCE
INTERMINISTERIELLE

Head JF Delfraissy and Y Lévy for Research

A large porfolio of projects : Clinical Trial (« Jiki »), Vaccine (« PREVAC »), Social Sciences, Diagnosis,…

Focus on The POSTEBOGUI Project

BRIEF REPORT

Emergence of Zaire Ebola Virus Disease in Guinea

Sylvain Baize, Ph.D., Delphine Pannetier, Ph.D., Pharm.D., Lisa Oestereich
Toni Rieger, Ph.D., Lamine Koivogui, Ph.D., N'Faly Magassouba, Ph.
Barrè Soropogui, M.Sc., Mamadou Saliou Sow, M.D., Sakoba Keïta, M
Hilde De Clerck, M.D., Amanda Tiffany, M.P.H., Gemma Dominguez, E
Mathieu Loua, M.D., Alexis Traoré, M.D., Moussa Kolié, M.D.,
Emmanuel Roland Malano, M.D., Emmanuel Heleze, M.D., Anne Bocquin
Stephane Mély, M.Sc., Hervé Raoul, Ph.D., Valérie Caro, Ph.D.,
Dániel Cadar, D.V.M., Ph.D., Martin Gabriel, M.D., Meike Pahlmann, P
Dennis Tappe, M.D., Jonas Schmidt-Chanasit, M.D., Benido Impouma,
Abdoul Karim Diallo, M.D., Pierre Formenty, D.V.M., M.P.H.,
Michel Van Herp, M.D., M.P.H., and Stephan Günther, M.D.

- Epicentre en Guinée (Guéckédou, Macenta) début 2014
- Fin mars, l'épidémie s'est propagée au Libéria et au Sierra Leone voisins
- Fin juillet, le Nigéria est le 4ème pays de la région à rapporter des cas
- Puis le Sénégal , le Mali, les USA….

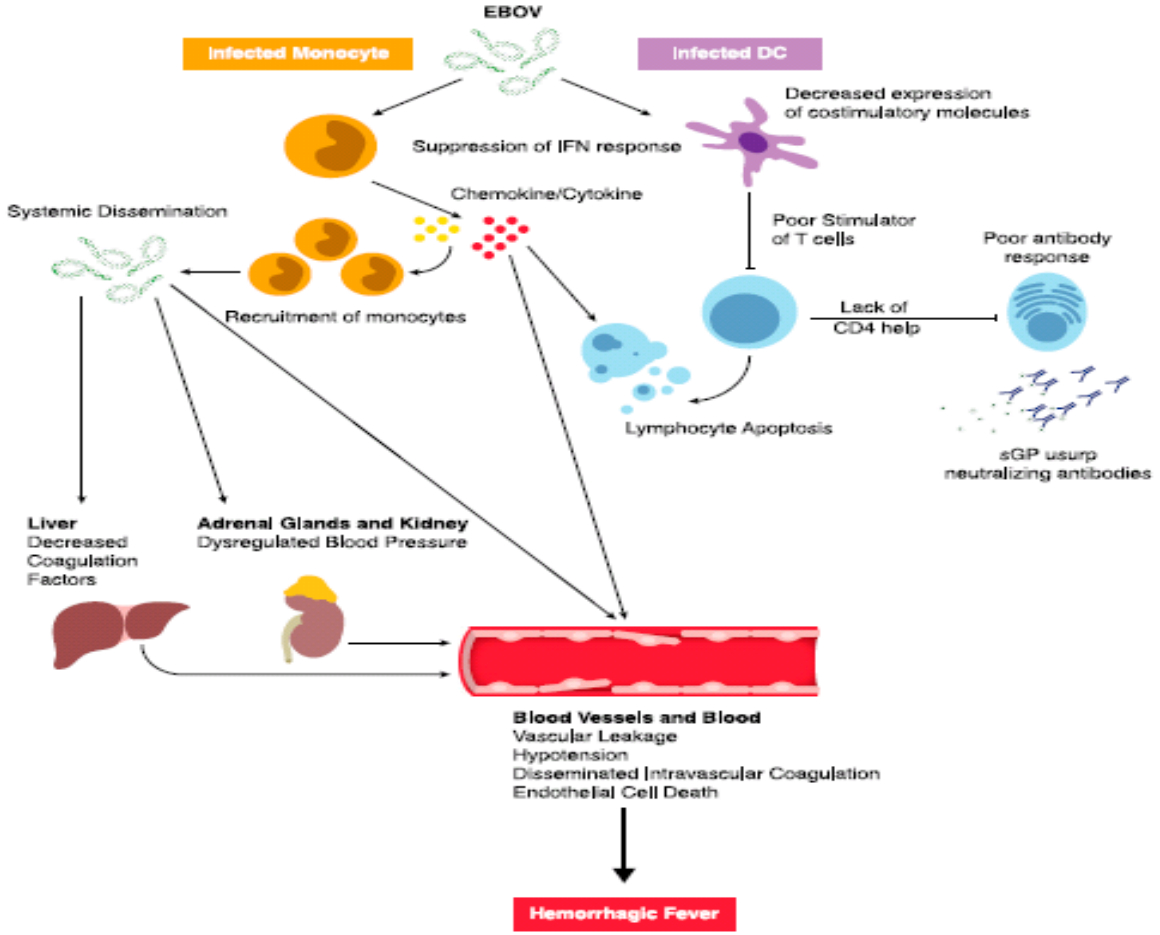
Crainte d'une pandémie…

Figure 1. Map of Guinea Showing Initial Locations of the Outbreak of Ebola Virus Disease.

The area of the outbreak is highlighted in red. The main road between the outbreak area and Conakry, the capital of Guinea, is also shown. The map was modified from a United Nations map.

La maladie à virus Ébola (avant 2014…)

- La maladie aiguë
- Forme sévère



Incubation: 2à 21J le plus souvent de 4 à 9 jours
CRF: >80%...

	Time since symptom onset	Clinical features	Typical patient
Early febrile or mild stage	0–3 days	Non-specific features: fever, weakness, lethargy, and myalgia	Ambulatory, able to compensate for fluid losses; no indication for intravenous fluid administration
Gastrointestinal involvement	3–10 days	Same as early stage plus diarrhoea, vomiting, or both, or abdominal pain	Unable to compensate for fluid losses because of emesis or large volume losses; indication for intravenous fluid administration
Complicated stage	7–12 days	Same as gastrointestinal involvement stage plus haemorrhage, shock, organ failure, and neurological complications	Critically ill, usually hypovolaemic, often with confusion or seizures

Adapted from Chertow and colleagues[63] and Hunt and colleagues.[64]

Table 1: **Ebola virus disease presentation by stage**

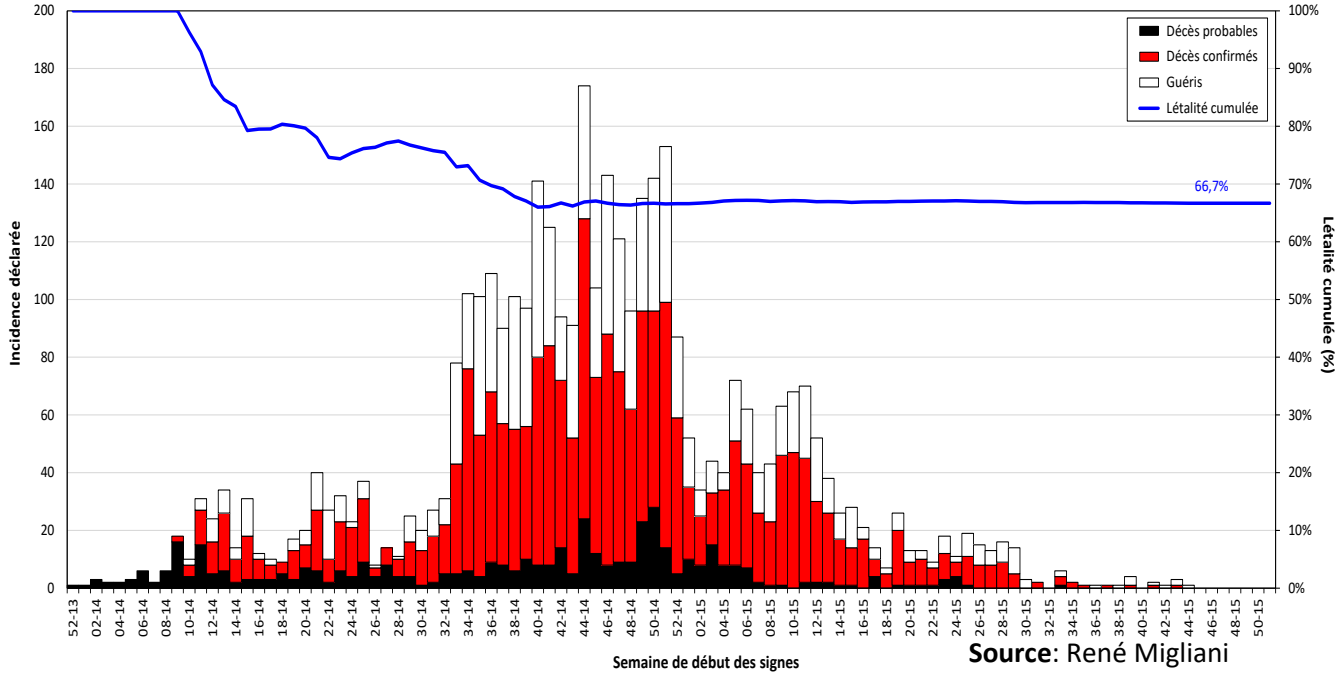
Les soignants ++

Table 1. Demographic Characteristics and Signs and Symptoms in Confirmed and Probable Ebola Case Patients with a Definitive Clinical Outcome in Guinea, Liberia, Nigeria, and Sierra Leone.*

Variable	All Patients	Patients Who Died	Patients Who Recovered	Odds Ratio (95% CI)†
		no./total no. (%)		
Demographic characteristics				
Male sex	685/1415 (48.4)	515/1056 (48.8)	170/359 (47.4)	0.93 (0.73–1.19)
Age group				
<15 yr	190/1378 (13.8)	145/1021 (14.2)	45/357 (12.6)	1.18 (0.83–1.71)
15–44 yr	838/1378 (60.8)	577/1021 (56.5)	261/357 (73.1)	0.48 (0.36–0.62)
≥45 yr	350/1378 (25.4)	299/1021 (29.3)	51/357 (14.3)	2.47 (1.79–3.46)
Health care worker	158/1429 (11.1)	112/1067 (10.5)	46/362 (12.7)	0.86 (0.60–1.27)

Ebola in Guinea

- Guinea declared Ebola-free on May 31, 2016
- 3811 cases, 2536 deaths
- 1270 survivors (33%)
  - Children < 15: 16%
  - Female: 55%
  - Health workers: 8%



Source: René Migliani

Multidiciplinary assessment of post-Ebola sequelae: an obsevational cohort study

The « order »: The convalescents

Why?: Initially for a therapeutic objective

After a field assessment: A priority the care fo survivors (at that time nothing was proposed)

With scientifc questions based on few data from previous outbreaks suggesting sequellae and persistence of the virus in body fluid

How?: No previous collaboration in Guinée but contacts through training

Mamadou Saliou Sow : Infectious Diseases Specialist (CHU Donka)

Abdoulaye Toure: Public Health specialist

Alpha Kabinet Keita: Microbiologist (former PhD in Montpellier)

Plus scientits from my group and Medical students

JF Etard, Ph Msellati, S Izard, M Peeters, A Ayouba, A Desclaux, B Taverne, N Vidal

Postebogui Project

- **Research projects**
  - Postebogui cohort (PI M Barry, E Delaporte)
  - Contactebogui (PI S Sow, JF Etard)
  - Reservoir (PI S Ahuka-Mundeke,E Mpoudi, AC Keita, M Peeters)
- **Public Health support**
  - Care of survivors
  - Capacity building
  - Training

Rationale

Few data on survivors from previous outbreaks, limited cases

New questions : clinical sequels, reactivation, reservoir

- Long-term medical problems
- Psychosocial consequences
- Viral clearance in the body compartments

Which package of care to respond to the survivors' needs?

« (Re) Vivre après Ebola »

Accompagnement et évaluation des patients déclarés guéris d'une infection par le virus Ebola en Guinée

« POSTEBOGUI »

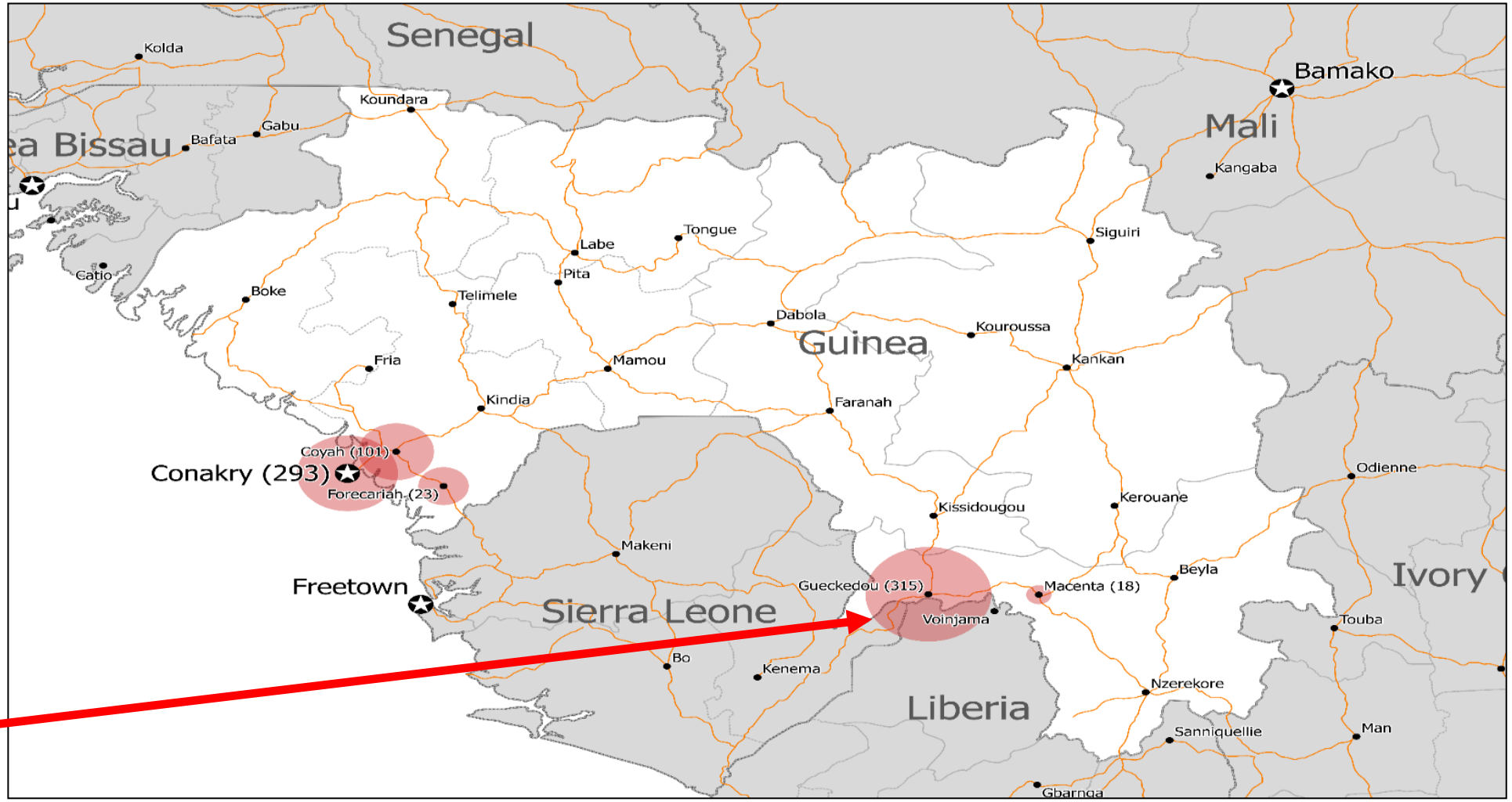
- Principaux Investigateurs : Dr Mounié Barry
  Pr Eric Delaporte
- Objectif général : Améliorer les connaissances sur les conséquences cliniques, biologiques et sociales de la maladie
- Méthode : Etude de cohorte multicentrique (Conakry, Macenta) pluridisciplinaire chez des enfants et des adultes
- Paquet d'accompagnement :
  - Renforcement des infrastructures avec un service dédié à la prise en charge pluridisciplinaire des patients
  - Renforcement des capacités des associations de patients guéris
  - Mise en place d'un continuum des soins gratuits et de prise en charge des complications éventuelles

Package of care and capacity building

- Continuum of care after discharge from an ETC:
  - Free reference to specialised medical advices if needed
  - Psycho-social support
  - Free access to complementary diagnostics and treatment if needed
  - Training medical and lab staff, GCP
- Rehabilitation of the existing infrastructure in Donka
- Building of a clinical and research center in Donka with the support of the French Ebola Task force

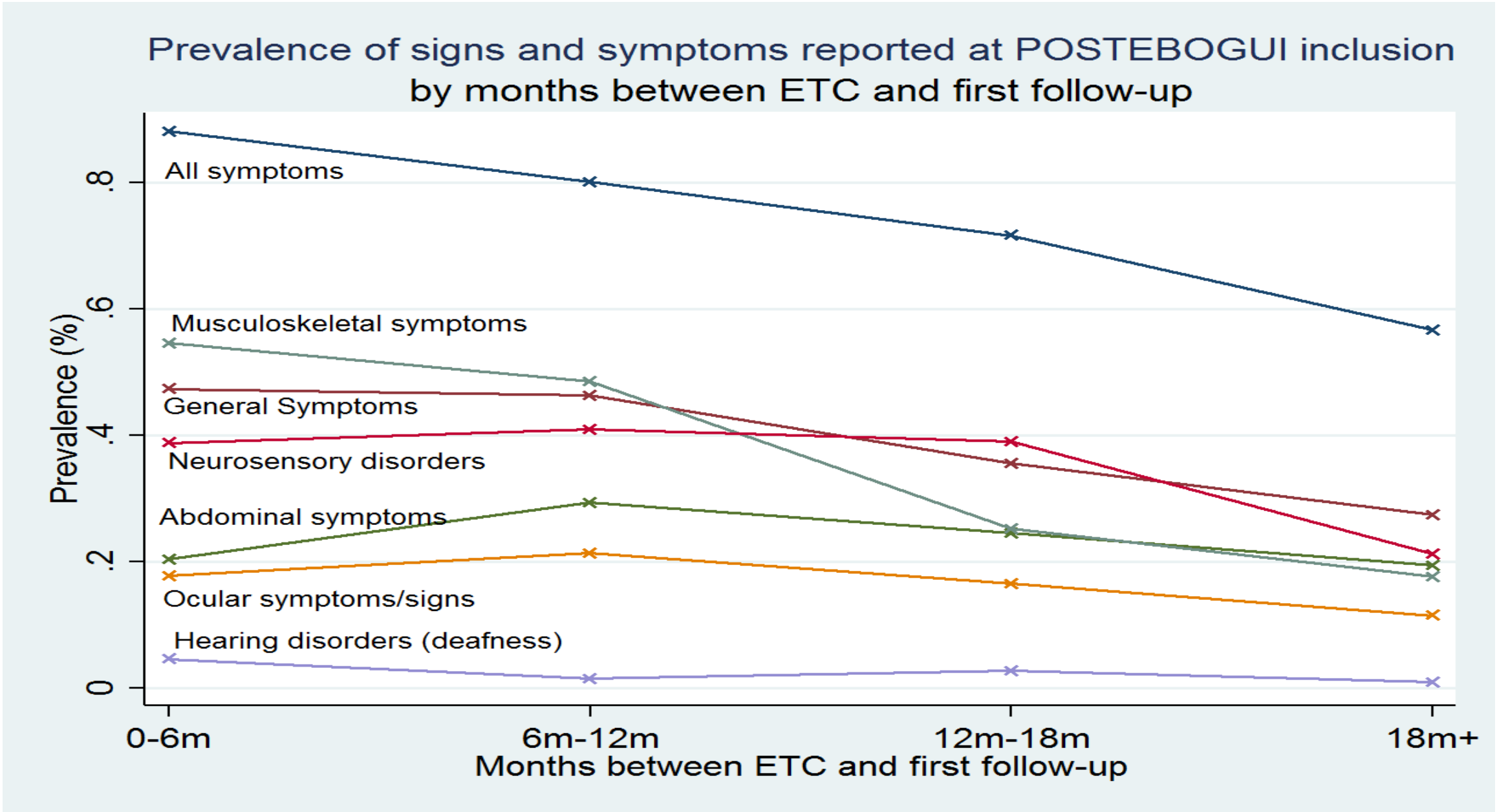
Ebola Treatment Centers of the survivors included in Postebogui

802 survivors included in 4 sites
Conakry
Forecarhia
Macenta
Nzérékoré



In collaboration with ALIMA

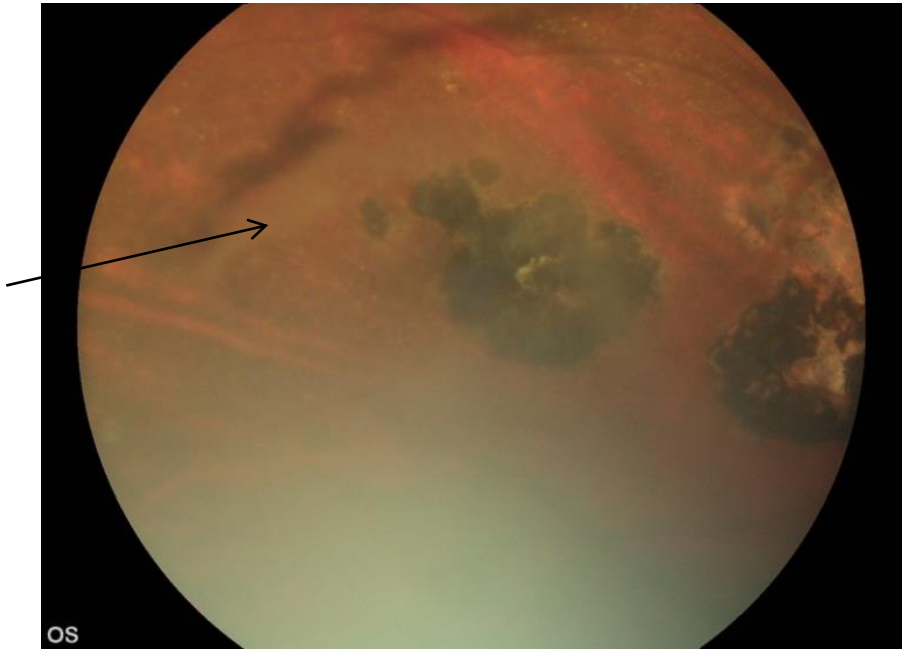
REACTing


Prevalence of signs and symptoms reported at POSTEBOGUI inclusion
by months between ETC and first follow-up
All symptoms
Musculoskeletal symptoms
General Symptoms
Neurosensory disorders
Abdominal symptoms
Ocular symptoms/signs
Hearing disorders (deafness)
Prevalence (%)
0
.2
.4
.6
.8
0-6m
6m-12m
12m-18m
18m+
Months between ETC and first follow-up

Focus on ophthalmology

- 157 patients examined (slit lamp, dilated fundoscopy):
  - 24 uveitis (48% ant, 76% unilat)
  - 4 episcleritis
  - 2 keratitis

- 2 blindness due to cataract among two children → surgery



Source: Esther Hereth

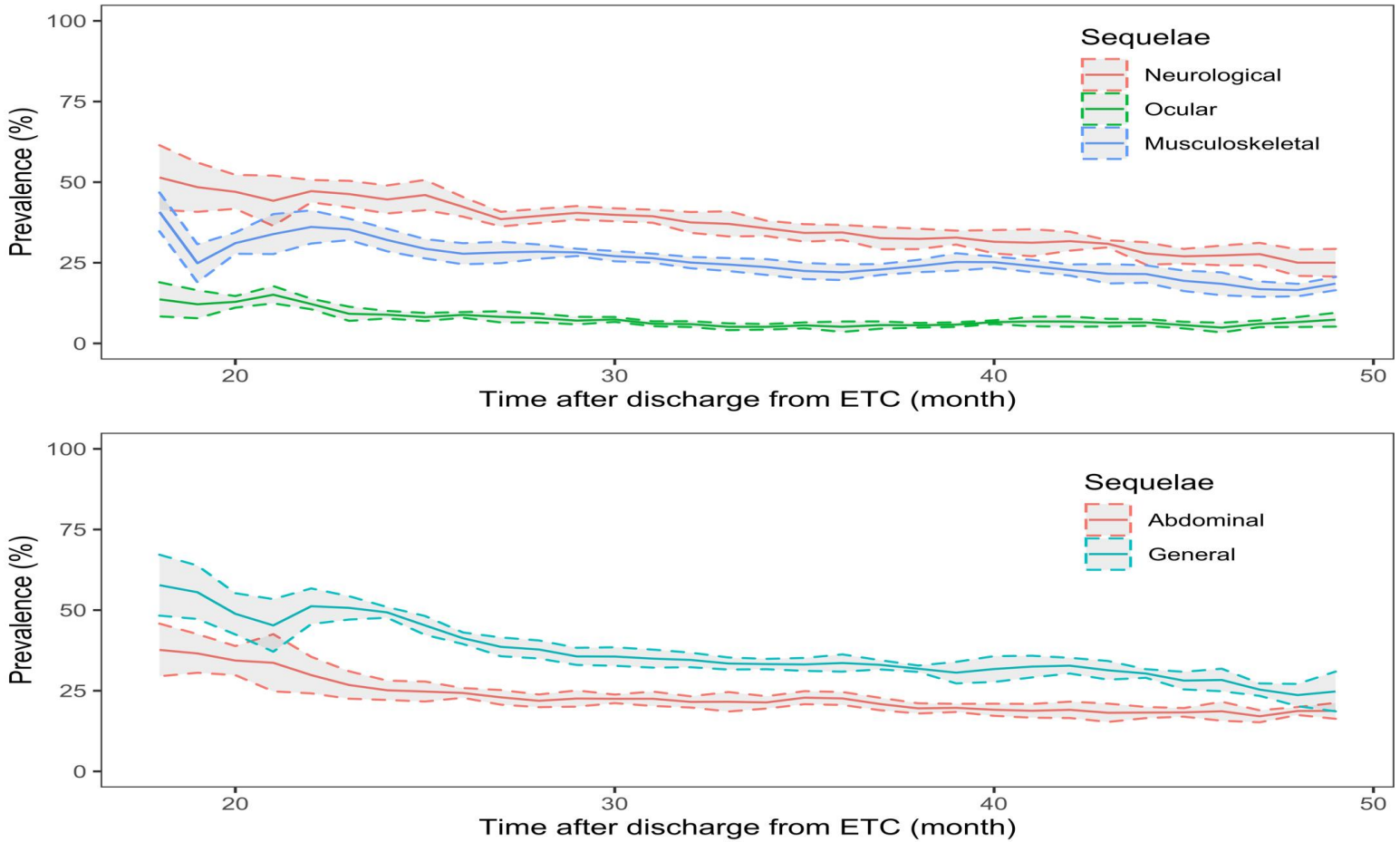
→ Overall abnormal examination = 19 %

Ebola-long …..

- **Understanding the long-term evolution and predictors of sequelae of Ebola virus disease survivors in Guinea: A 48-month prospective, longitudinal cohort study (PostEboGui)**

Mamadou Saliou Kalifa Diallo[1,2], Abdoulaye Toure[2,3], Mamadou Saliou Sow[4], Cécé Kpamou[2], Alpha Kabinet Keita[1,2], Bernard Taverne[1], Martine Peeters[1], Philippe Msellati[1], Thierno Alimou Barry[2], Jean-Francois Etard[1], René Ecochard[5,6,7,8], Eric Delaporte[1] for the PostEboGui Study Group

Clinical Infectious Diseases, 2021



POSTEBOGUI: Clinical follow-up

Lancet Infect Dis 2017

Articles

Multidisciplinary assessment of post-Ebola sequelae in Guinea (Postebogui): an observational cohort study

Jean-François Etard*, Mamadou Saliou Sow*, Sandrine Leroy*, Abdoulaye Touré*, Bernard Taverne, Alpha Kabinet Keita, Philippe Msellati, N'Fally Magassouba, Sylvain Baize, Hervé Raoul, Suzanne Izard, Cécé Kpamou, Laura March, Ibrahima Savane, Moumié Barry, Eric Delaporte, and the Postebogui Study Group†

Summary

Background The high number of survivors from the 2013–16 west African outbreak of Ebola virus disease (EVD) has raised several new issues: long-term clinical complications, psychosocial consequences, risks of EVD reactivation, and secondary transmission due to viral persistence in body fluids. We aimed to assess long-term clinical, psychosocial, and viral outcomes in EVD survivors in Guinea.

Lancet Infect Dis 2017; 17: 545–52

Published Online January 13, 2017 http://dx.doi.org/10.1016/S1473-3099(16)30516-3

Prevalence of infection among asymptomatic and paucisymptomatic contact persons exposed to Ebola virus in Guinea: a retrospective, cross-sectional observational study

Lancet Infect Dis 2019; 19: 308–16

Published Online February 11, 2019

Mamadou Saliou Kalifa Diallo, Muriel Rabilloud*, Ahidjo Ayouba*, Abdoulaye Touré*, Guillaume Thaurignac, Alpha Kabinet Keita, Christelle Butel, Cécé Kpamou, Thierno Alimou Barry, Mariama Djouldé Sall, Ibrahima Camara, Sandrine Leroy, Philippe Msellati, René Ecochard, Martine Peeters, Mamadou Saliou Sow, Eric Delaporte, Jean-François Etard, on behalf of the Contactebogui Study Group†*

Mise en évidence de formes cliniques a-et pauci-symtomatiques avec une séroconversion chez les contacts selon le degré d'exposition aux risque de 3 à 8 %

Ocular Complications in Survivors of the Ebola Outbreak in Guinea

ESTHER HERETH-HEBERT, MAMADOU OURY BAH, JEAN FRANÇOIS ETARD, MAMADOU SALIOU SOW, SERGE RESNIKOFF, CHRISTINE FARDEAU, ABDOULAYE TOURE, ALEXIS NIOUMA OUENDENO, ISAAC CEOUGNA SAGNO, LAURA MARCH, SUZANNE IZARD, PIERRE LOUIS LAMA, MOUMIÉ BARRY, AND ERIC DELAPORTE, FOR THE POSTEBOGUI STUDY GROUP

RESEARCH ARTICLE

Depressive symptoms among survivors of Ebola virus disease in Conakry (Guinea): preliminary results of the PostEboGui cohort

Mamady Mory Keita, Bernard Taverne, Sékou Sy Savané, Laura March, Monfodé Doukouré, Mamadou Saliou Sow, Abdoulaye Touré, Jean François Etard, Moumié Barry, Eric Delaporte and the PostEboGui Study Group

BMC Psychiatry (BMC series – open, inclusive and trusted) 2017 17:127 | DOI: 10.1186/s12888-017-1280-8 | © The Author(s) 2017

Received: 1 July 2016 | Accepted: 22 March 2017 | Published: 4 April 2017

RHEUMATOLOGY

Concise report

Characteristics of the musculoskeletal symptoms observed among survivors of Ebola virus disease in the Postebogui cohort in Guinea

Yves-Marie Pers[1], Mamadou Saliou Sow[2], Bernard Taverne[3], Laura March[3], Suzanne Izard[3], Jean François Étard[3], Moumié Barry[4], Abdoulaye Touré[5] and Eric Delaporte[3]

Follow-up 26·2 months (IQR 23-30)
Persistent chronic MS pain: 69%
Older age and female gender are two main risk

Develop serological and molecular assays for large scale screening

AMERICAN SOCIETY FOR MICROBIOLOGY | Journal of Clinical Microbiology®

Development of a Sensitive and Specific Serological Assay Based on Luminex Technology for Detection of Antibodies to Zaire Ebola Virus

Ahidjo Ayouba,[a] Abdoulaye Touré,[b] Christelle Butel,[a] Alpha Kabinet Keita,[a] Florian Binetruy,[a] Mamadou S. Sow,[c] Vincent Foulongne,[d] Eric Delaporte,[a] Martine Peeters,[a] for the PostEboGui Study Group

IRD UMI 233-INSERM U1175-Montpellier University, Montpellier, France[a]; Chaire de santé publique, Département de Pharmacie, Université de Conakry, Conakry, Guinea[b]; Donka National Hospital, Conakry, Guinea[c]; INSERM U1058-Montpellier University, Montpellier, France[d]

Test that can detect the 4 EBV species in Africa

Simultaneous screening to >10 antigens

Optimized with samples from survivors

Adapted for screening of wildlife

Plasma, whole blood, dried blood spots, fecal samples,..

Adapted for Bats, monkeys, antelopes, rodents,

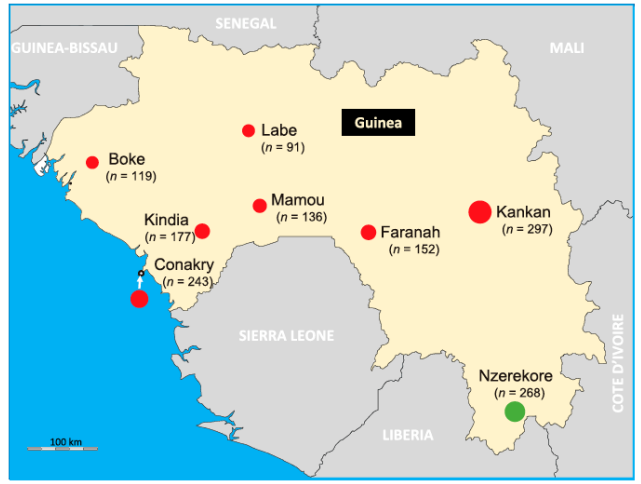
ASTMH AMERICAN SOCIETY OF TROPICAL MEDICINE & HYGIENE

THE AMERICAN JOURNAL OF TROPICAL MEDICINE AND HYGIENE
official Journal of the American Society of Tropical Medicine and Hygiene

Serological Evidence of Ebola Virus Infection in Rural Guinea before the 2014 West African Epidemic Outbreak

Alpha K. Keita,[1,2,3] Christelle Butel,[1] Guillaume Thaurignac,[1] Aminata Diallo,[4] Talla Nioke,[4] Falaye Traoré,[4] Lamine Koivogui,[4] Martine Peeters,[1] Eric Delaporte,[1] and Ahidjo Ayouba[1]*

[1]Institut de Recherche pour le Développement, IRD-UMI 233/INSERM U 1175, Montpellier University, Montpellier, France; [2]OneHealth Laboratory, Institut National de Santé Publique, Conakry, Guinea; [3]Centre de Recherche et de Formation en Infectiologie de Guinée (CERFIG), Conakry, Guinea; [4]Institut National de Santé Publique, Conakry, Guinea



Immunological study on EVD survivors in Guinea

2 years after EVD, Ebola Survivors exhibit:

- Increased **activation/inflammation** markers in blood
- Increased activated CD8 T cells, activated/exhausted B cells, non-classical NK cells and activated DC
- Up-regulation of pathways implicated in **antiviral response** (IFN signaling, Complement System and PRR signaling pathways)

EBOV-associated immune activation

- **Microbial translocation** from a leaky gut
- **Ab responses** and robust and polyfunctional memory **EBOV-specific T cell responses**

"Chronic Ebola Virus Disease"

Possible maintenance of EBOV in immune-privileged sites

(Wiedemann et al., under revision)

VACCINE RESEARCH INSTITUTE

POSTEBOGUI : Research in Social sciences

Taverne, Diop, Desclaux

THEY'LL INJECT YOU AND YOU'LL DIE": FROM MEDICATION NON-COMPLIANCE TO ACCEPTANCE IN GUINEA'S EBOLA TREATMENT UNITS

Sams K., Desclaux A., Postebogui Research Group

Accepted Anthropology & Medicine


Bull. Soc. Pathol. Exot. (2016) 109:309-313
DOI 10.1007/s13149-016-0510-5

ANTHROPOLOGIE MÉDICALE / *MEDICAL ANTHROPOLOGY*

Ebola en Guinée : formes de la stigmatisation des acteurs de santé survivants

Ebola in Guinea: Experience of Stigma among Health Professional Survivors

S. Sow · A. Desclaux · B. Taverne · Groupe d'étude PostEboGui

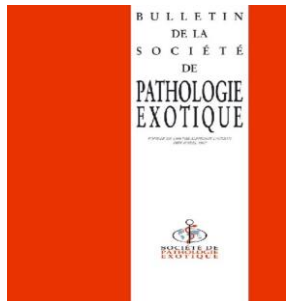
Survivant-e-s d'Ebola et silence réconciliateur

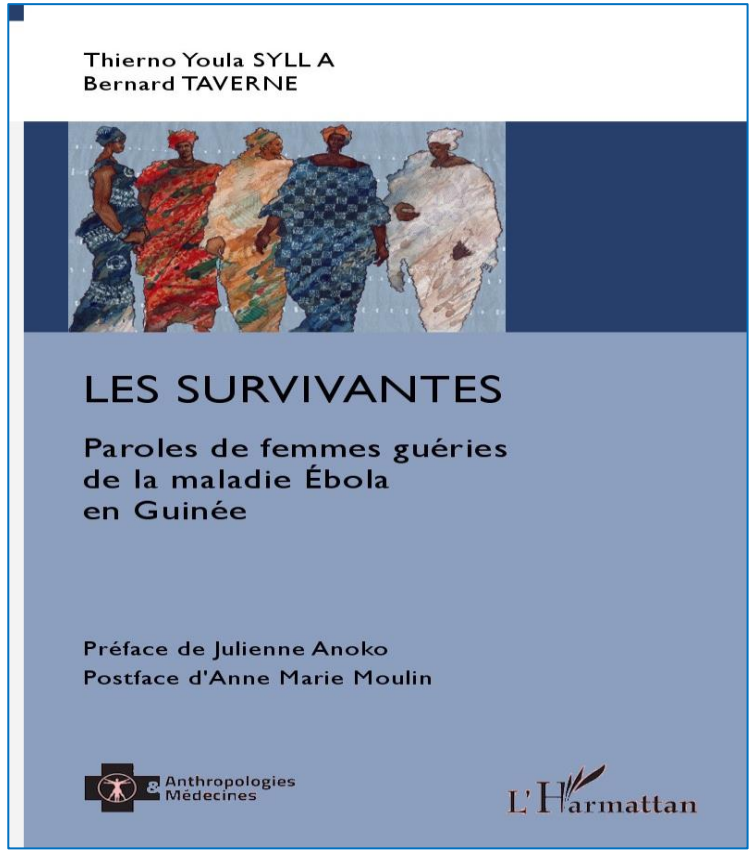
Paix sociale, consensus, fracture entre survivants et population

M. Fribault

Des « vrais » et « faux » survivants d'Ebola ?
Traces biologiques et conflits de preuves en Guinée

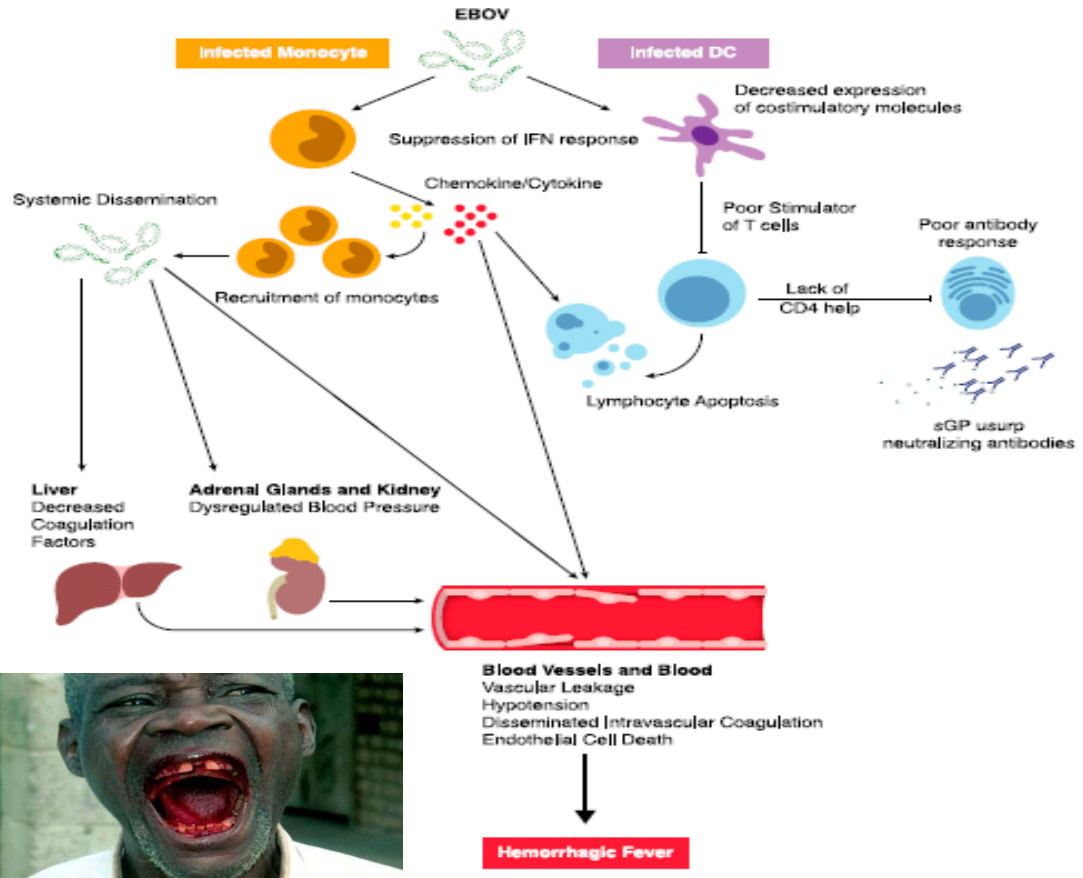
Desclaux A., Barranca E. *Ethnologie Française*



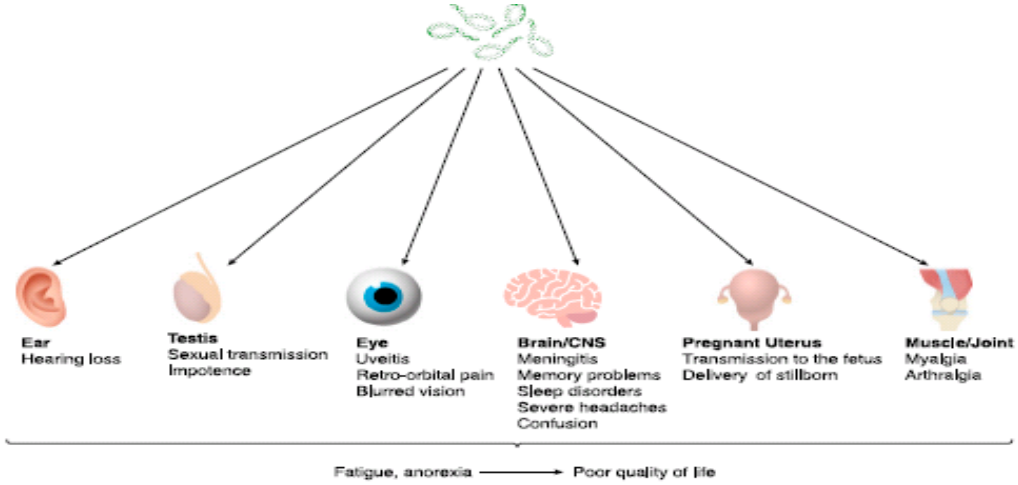


La maladie à virus Ébola après 2014

- La maladie aiguë
- Forme sévère († 6-10j)



- Forme résolutive
- La maladie chronique et le syndrome post-Ébola



Multidisciplinary assessment of post-Ebola sequelae in Guinea (Postebogui): an observational cohort study

Jean-François Etard*, Mamadou Saliou Sow*, Sandrine Leroy*, Abdoulaye Touré*, Bernard Taverne, Alpha Kabinet Keita, Philippe Msellati, N'Faly Magassouba, Sylvain Baize, Hervé Raoul, Suzanne Izard, Cécé Kpamou, Laure Morel, Ibrahima Savane, Mauriel Barry, Eric Delaporte, and the Postebogui Study Group†

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Prevalence of infection among asymptomatic and paucisymptomatic contact persons exposed to Ebola virus in Guinea: a retrospective, cross-sectional observational study

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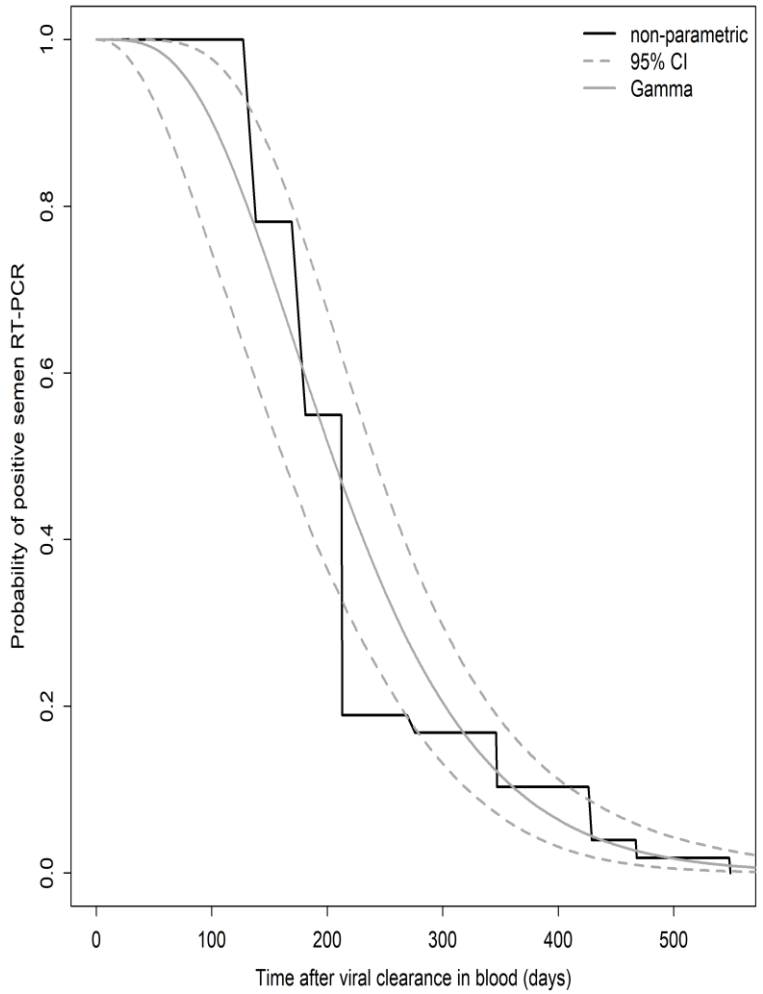
POSTEBOGUI: biological follow up



ACCEPTED MANUSCRIPT EDITOR'S CHOICE

A 40 months follow-up of Ebola virus disease survivors in Guinea (Postebogui) reveals longterm detection of Ebola viral RNA in semen and breast milk

Alpha Kabinet Keita, Nicole Vidal, Abdoulaye Toure, Mamadou Saliou Kalifa Diallo, N'Fally Magassouba, Sylvain Baize, Mathieu Mateo, Herve Raoul, Stephane Mely, Fabien Subtil ... Show more

Author Notes

Open Forum Infectious Diseases, ofz482, https://doi.org/10.1093/ofid/ofz482

Clinical Infectious Diseases

BRIEF REPORT

Dynamics of Ebola RNA Persistence in Semen: A Report From the Postebogui Cohort in Guinea

Fabien Subtil,[1,2,3,a] Charlotte Delaunay,[1,2,3,a] Alpha Kabinet Keita,[1] Mamadou Saliou Sow,[4] Abdoulaye Touré,[1,5] Sandrine Leroy,[1] Philippe Msellati,[1] N'Fally Magassouba,[5] Sylvain

The Journal of Infectious Diseases

BRIEF REPORT

New Evidence of Long-lasting Persistence of Ebola Virus Genetic Material in Semen of Survivors

Mamadou S. Sow,[1] Jean-François Etard,[6] Sylvain Baize,[7] N'Fally Magassouba,[2] Ousmane Faye,[8] Philippe Msellati,[6] Abdoulaye Il Touré,[3,4] Ibrahima Savane,[5] Moumié Barry,[1] and Eric Delaporte[6]; for the Postebogui Study Group[a]

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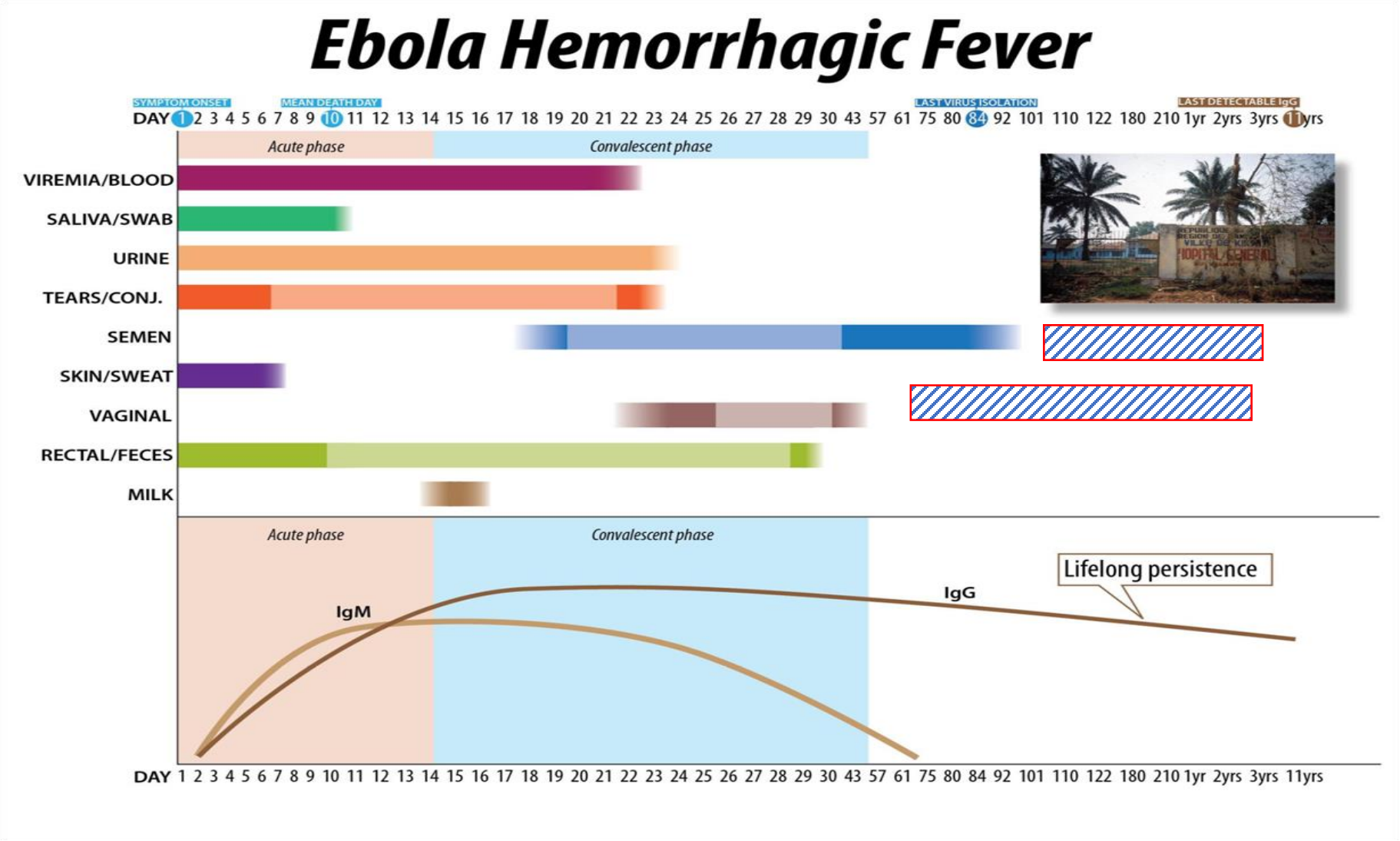
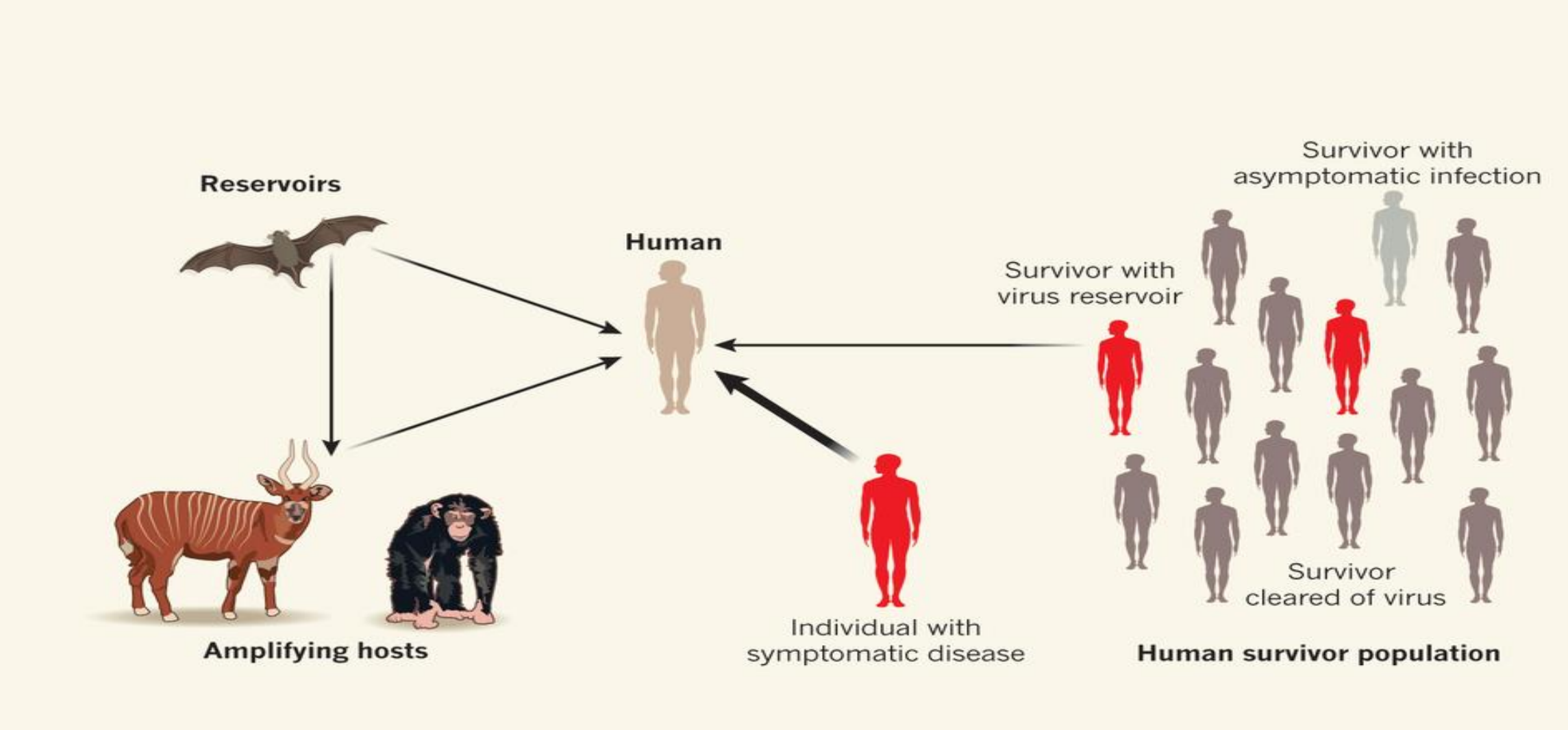
Letter to the Editor

Extraordinary long-term and fluctuating persistence of Ebola virus RNA in semen of survivors in Guinea: implications for public health

Portage d'EBOV dans les fluides : Etat des connaissances



Un réservoir humain…..



Ebola infection dynamics in animals and humans.

Creation of a clinical center for Care, Research and Training

GUINEA: A center for Research, Care and Training

Centre de Recherche et de Formation en Infectiologie de Guinée

LMI RESPIRE: Abdoulaye Toure, Directeur INSP et Cerfig , Agrégé en Biostatistique Santé Publique
Alpha Keita , Directeur adjoint CERFIG , NEF Fellow, chercheur Université de Montpellier
Saliou Sow, 1° Professeur en infectiologie , Chef de service CHU Donka

Clinical research center with Classroom

Lab Facilities

Computer server

Clinical Consultation rooms

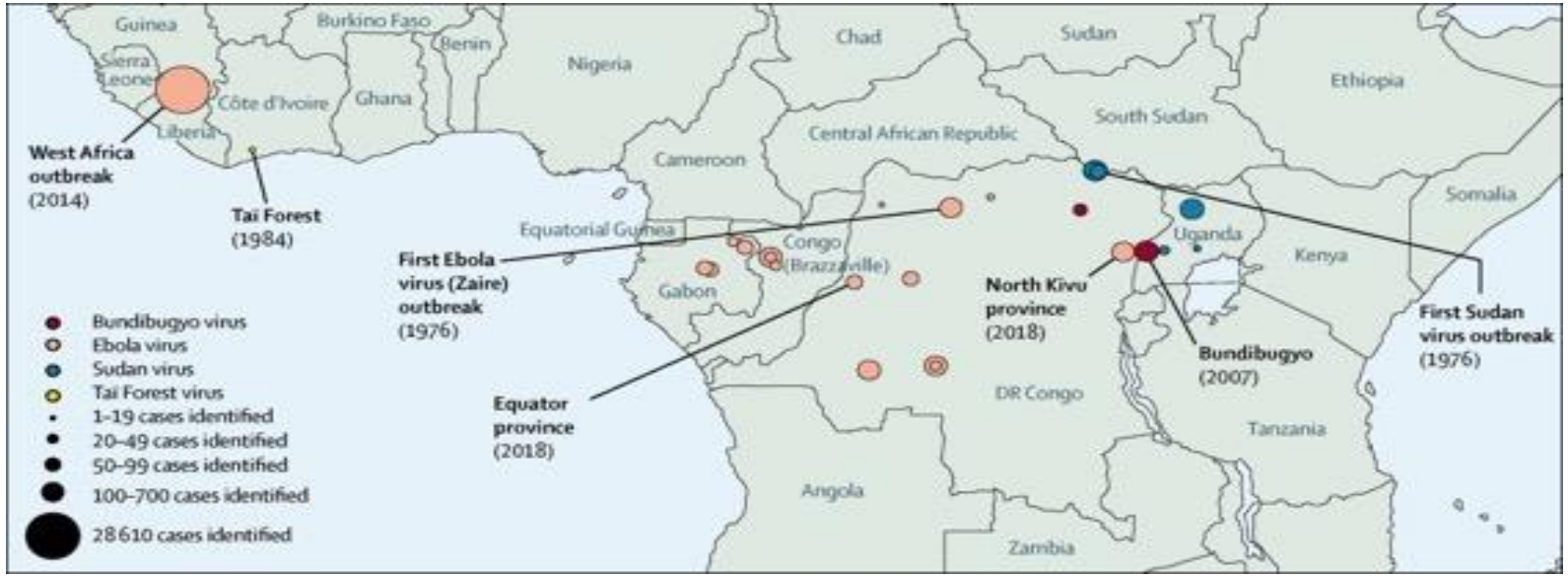
MONTPELLIER UNIVERSITE D'EXCELLENCE

Academic Courses

Diplôme Inter-universitaire ; **Santé Globale,** PhD students co-supervised

RAEE
Réseau Anthropologie des Epidémies Emergentes

Ebola: 28 outbreaks since 1976



The West Africa outbreak with 10 X victims than all previous outbreaks represented a paradigm shift in particular for research

Treatment: From Favipiravir , ZmApp to the Palm Study in RDC

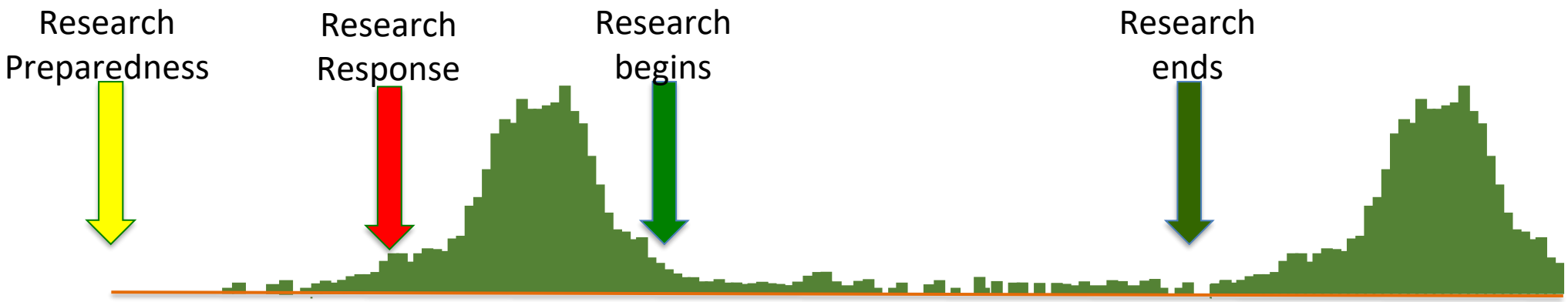
Vaccin: Validation of the Merck vaccin and its use to control the outbreak in RDC, evaluation of the J& J vaccin also (PREVAC study)

Diagnosis: Developpement of operationnal real time PCR tests, NGS, Luminex serology, ..

Clinical consequences : Asymptomatic, acute and standard of care, « chronic »

To conduct research during an outbreak : To solve antagonist points !

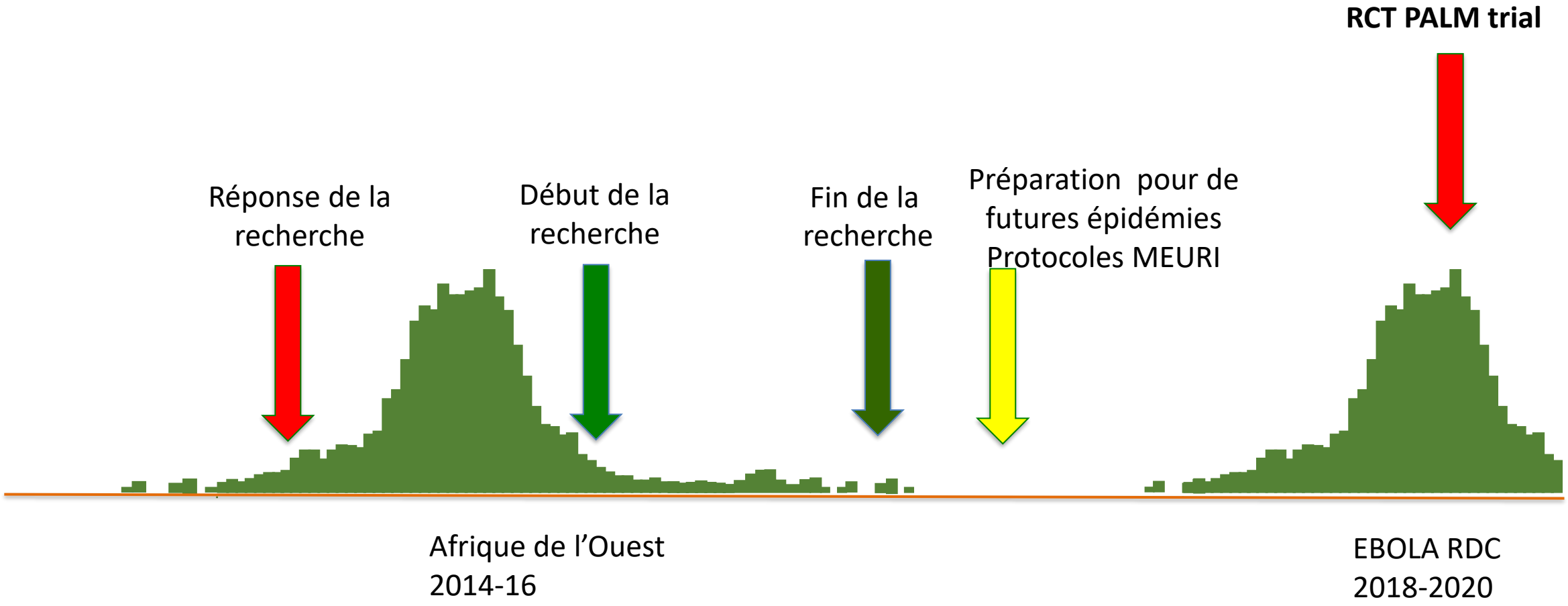
Emergency and Research procedures:



Research and Intervention:
Links with National Program and institutions, NGO's, International Agencies

To anticipate the end of the outbreak and the prevention of futur outbreaks
Implications of researchers of National Institution, long term collaborations
Training , capacity building

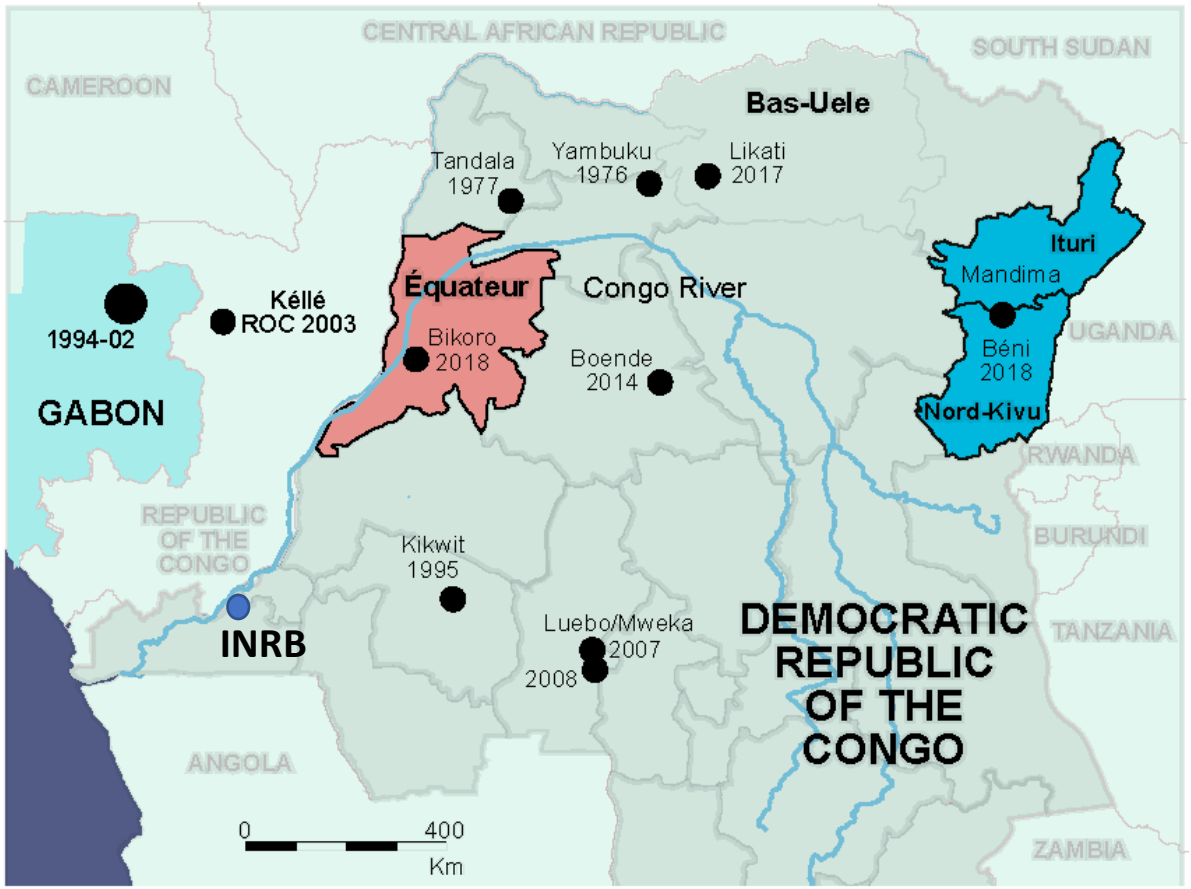
Recherche thérapeutique en situation de crise aigue: Exemple Ebola



La préparation d'une future crise et la capitalisation de l'expérience a permi la mise en place d'un essai randomisé avec 4 stratégies!

Monitored Emergency Use of Unregistered and Experimental Interventions' (**MEURI**) protocol

Ebola Virus Disease Outbreaks in the DRC 2018-19



The 9th DRC Ebola outbreak occurred in Bikoro, Equateur province

- Outbreak close to Mbandaka, a large city with about 500 000 inhabitants and connected to Kinshasa and other cities.

- Vaccine available and effective against Zaire ebolavirus.

Technical support to virology laboratory of INRB

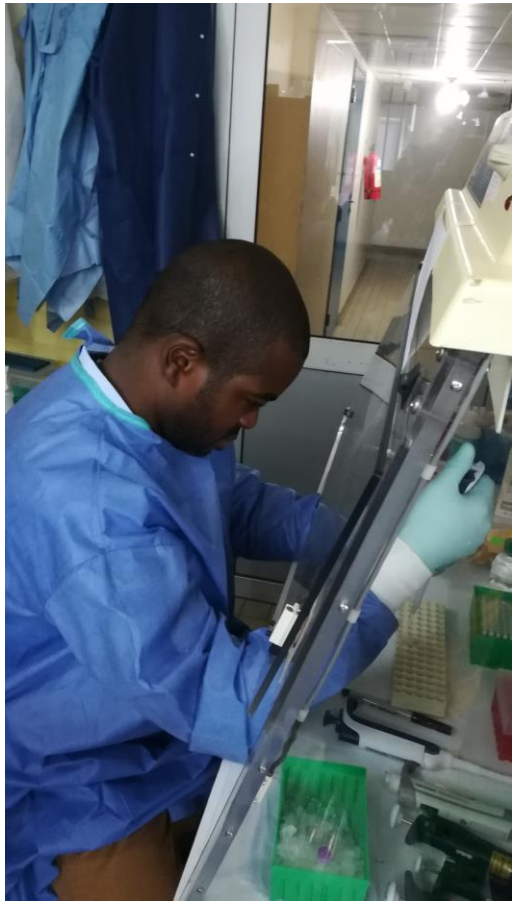
(A.Ayouba, C.Butel, A. Lacroix, M Peeters, L.Serrano)

- **New diagnostic tools**
  - **MagPix** (High throughput serology)
  - NGS sequencing « **MinIon** »
- **Training of laboratory staff**
  - Aziza Amouri
  - Junior Bulabula
  - Placide Mbala
- **Implementation of new tools**
  - Antibody screening of clinical suspect cases neg with Xpert
  - Antibody screening of contacts
  - Amplicon sequencing of Ebola strains from the outbreak with Minlon

Installation des laboratoires de terrain pour la detection et caractérisation rapide des virus Ebola (Bikoro, Itipo, Mbandaka)

Séquençage de Nouvelle Génération

Préparation de la librairie



1. Nanopore (Minion)

2. Hiseq

3. Miseq

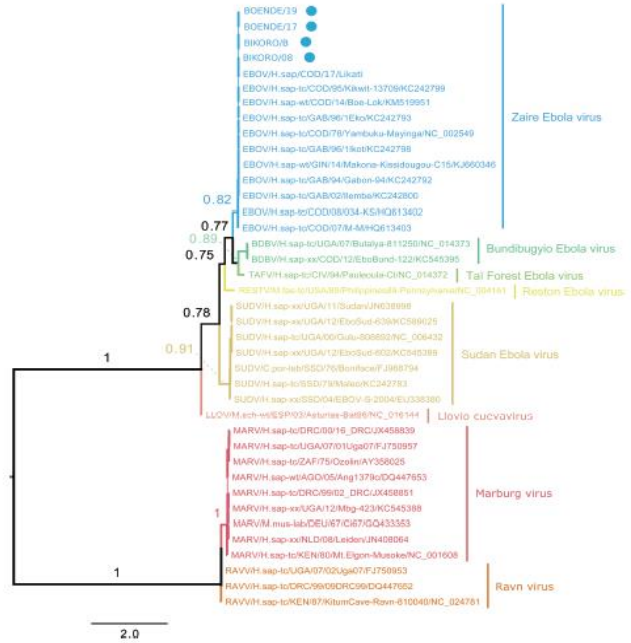
Séquençage sur terrain : caractérisation rapide des souches virales

Clinical Infectious Diseases

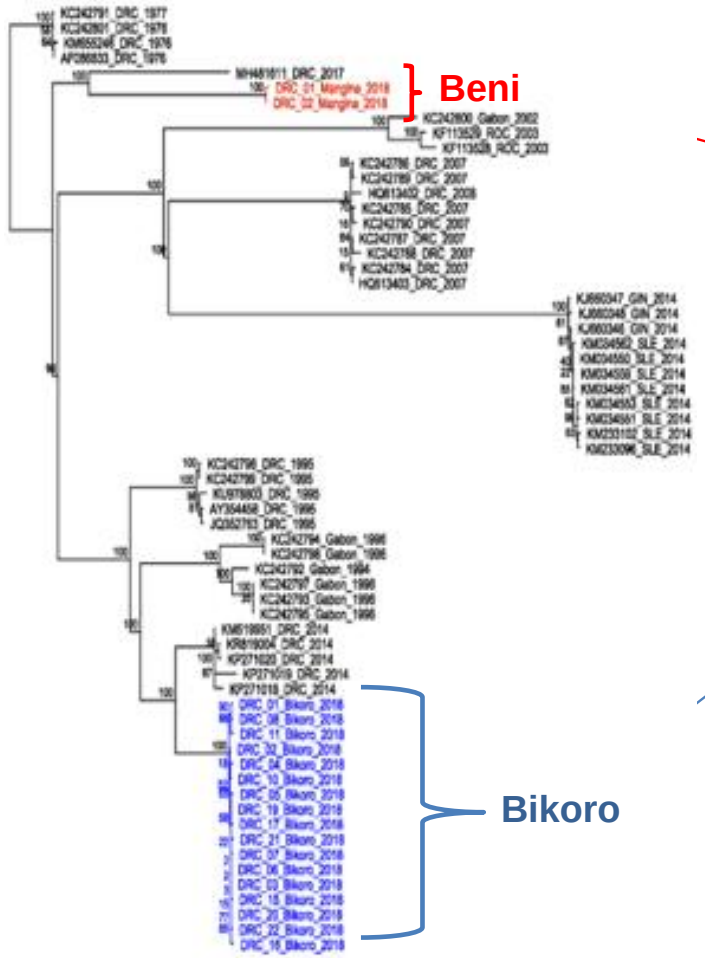
BRIEF REPORT

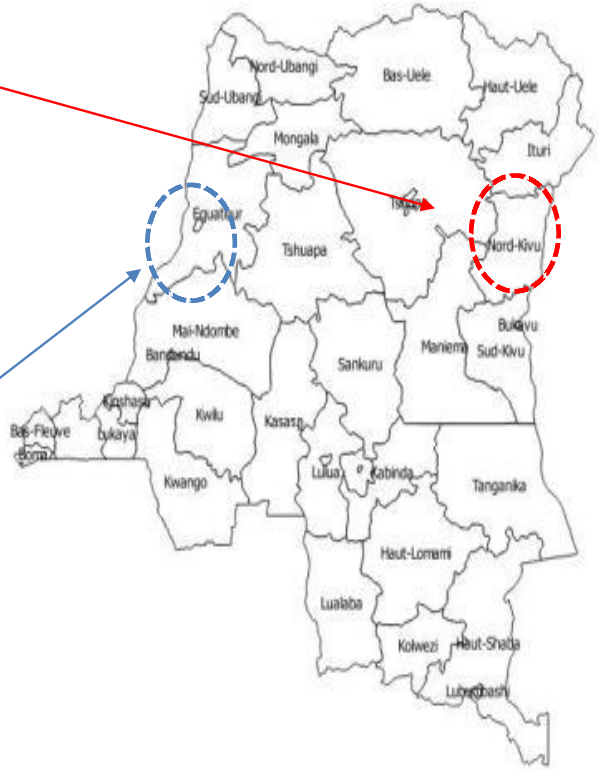
Rapid Confirmation of the Zaire Ebola Virus in the Outbreak of the Equateur Province in the Democratic Republic of Congo: Implications for Public Health Interventions

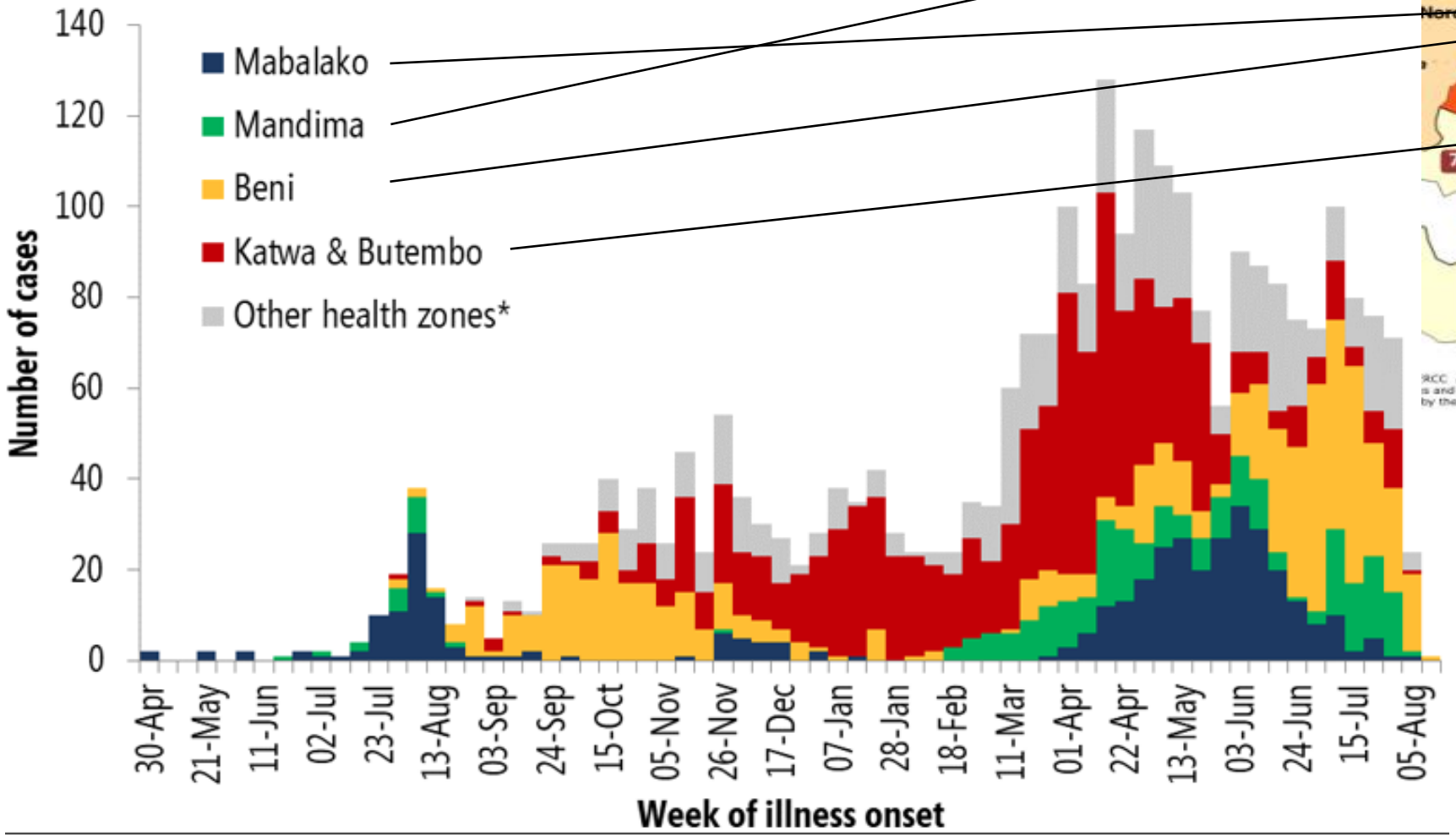
Placide Mbala-Kingebeni,[1,2,3] Christian-Julian Villabona-Arenas,[3] Nicole Vidal,[3] Jacques Likofata,[4] Justus Nsio-Mbeta,[5] Sheila Makiala-Mandanda,[1,2] Daniel Mukadi,[1,2] Patrick Mukadi,[1,2] Charles Kumakamba,[1,6] Bathe Djokolo,[5] Ahidjo Ayouba,[3] Eric Delaporte,[3] Martine Peeters,[3] Jean-Jacques Muyembe Tamfum,[1,2] and Steve Ahuka-Mundeke[1,2]

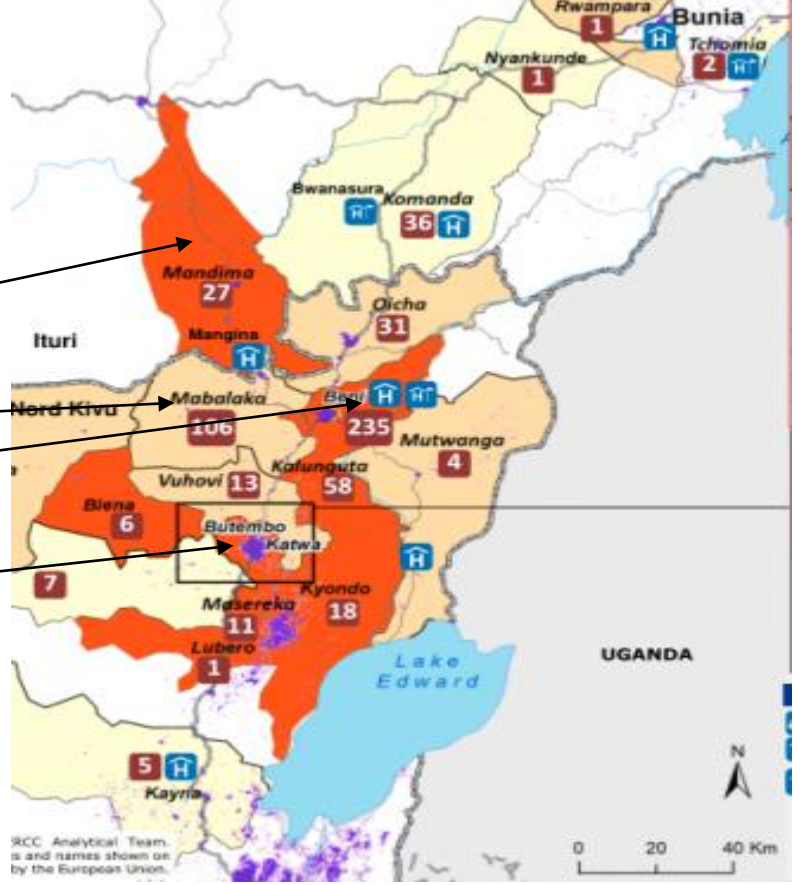


2 épidémies différentes causées par le virus Ebola






Mabalako
Mandima
Beni
Katwa & Butembo
Other health zones*
Number of cases
140
120
100
80
60
40
20
0
30-Apr
21-May
11-Jun
02-Jul
23-Jul
13-Aug
03-Sep
24-Sep
15-Oct
05-Nov
26-Nov
17-Dec
07-Jan
28-Jan
18-Feb
11-Mar
01-Apr
22-Apr
13-May
03-Jun
24-Jun
15-Jul
05-Aug
Week of illness onset


Rwampara
1
Bunia
Tchomia
2
Nyankunde
1
Bwanasura
Komanda
36
Mandima
27
Oicha
31
Ituri
Mangina
Nord Kivu
Mabalaka
106
Beni
235
Mutwanga
4
Kalunguta
58
Vuhovi
13
Biena
6
Butembo
Katwa
7
Kyondo
18
Masereka
11
Lubero
1
Lake Edward
UGANDA
5
Kayna
N
0
20
40 Km

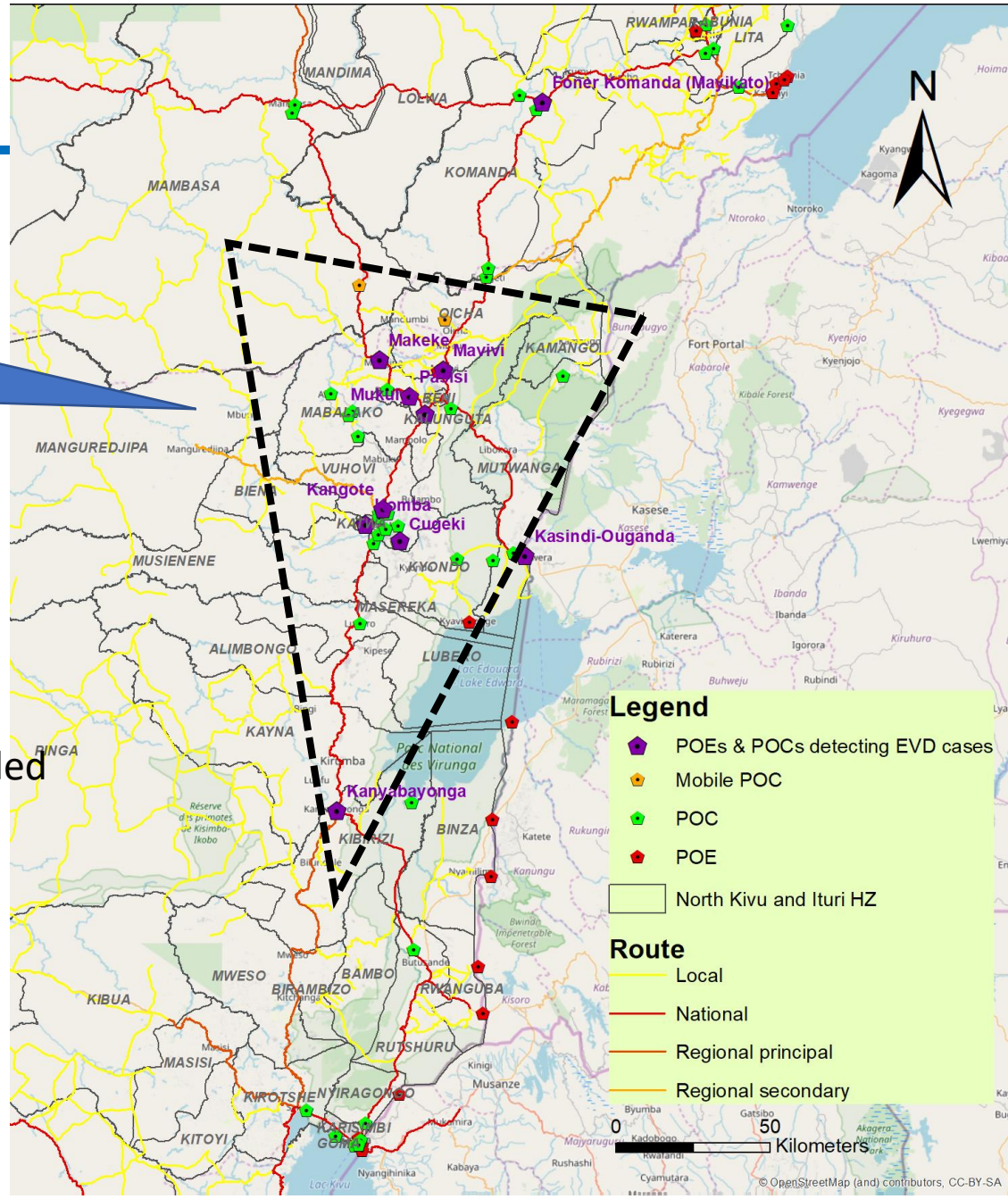
Cases Movements and PoC/PoE

- Nowadays:
  - 72 PoC et 26PoE : >80 millions of movements
  - 24 cases of suspect EVD detected at the PoE/PoC were confirmed by lab test

Transport of a corpse concealed as baggage, Byakato, ZS of Mandima, Ituri,

72 POC

26POE



Défis à relever : épidémie au Nord-Kivu et Ituri, RDC

- Epidémie en milieu semi-urbains et urbains (mouvement important de la population entre les différentes zones)
- Résistance de la communauté et violence contre les équipes de riposte (paralysie des activités sur terrain)

Contexte d'insécurité dans la région avec la présence des plusieurs groupes armés rebelles.

Destruction du CTE de ButemboDEs

Destruction du CTE de la ZS BIENA

Destruction du CTE de Katwa

Séquençage sur terrain : suivi des chaines de transmission

2018 Ebola virus disease outbreak in Équateur Province, Democratic Republic of the Congo: a retrospective genomic characterisation

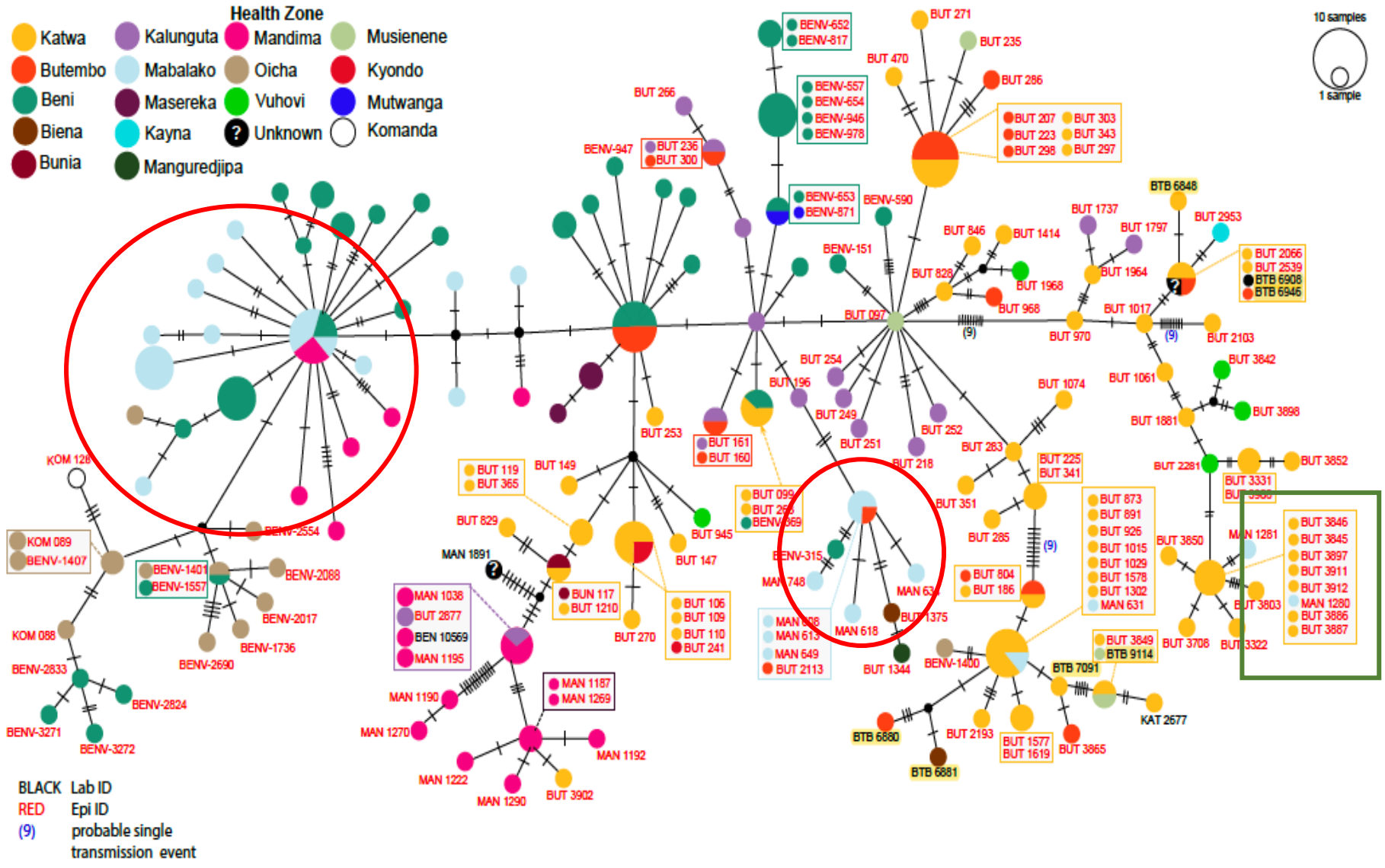
Placide Mbala-Kingebeni*, Catherine B Pratt*, Michael R Wiley*, Moussa M Diagne*, Sheila Makiala-Mandanda, Amuri Aziza, Nicholas Di Paola, Joseph A Chitty, Mamadou Diop, Ahidjo Ayouba, Nicole Vidal, Ousmane Faye, Oumar Faye, Stormy Karhemere, Aaron Aruna, Justus Nsio, Felix Mulangu, Daniel Mukadi, Patrick Mukadi, John Kombe, Anastasie Mulumba, Sophie Duraffour, Jacques Likofata, Elisabeth Pukuta, Katie Caviness, Maggie L Bartlett, Jeanette Gonzalez, Timothy Minogue, Shanmuga Sozhamannan, Stephen M Gross, Gary P Schroth, Jens H Kuhn, Eric F Donaldson, Eric Delaporte, Mariano Sanchez-Lockhart, Martine Peeters, Jean-Jacques Muyembe-Tamfum, Amadou Alpha Sall†, Gustavo Palacios†, Steve Ahuka-Mundeke†

Medical countermeasures during the 2018 Ebola virus disease outbreak in the North Kivu and Ituri Provinces of the Democratic Republic of the Congo: a rapid genomic assessment

Placide Mbala-Kingebeni*, Amuri Aziza*, Nicholas Di Paola*, Michael R Wiley*, Sheila Makiala-Mandanda, Katie Caviness, Catherine B Pratt, Jason T Ladner, Jeffrey R Kugelman, Karla Prieto, Joseph A Chitty, Peter A Larson, Brett Beitzel, Ahidjo Ayouba, Nicole Vidal, Stormy Karhemere, Mamadou Diop, Moussa M Diagne, Martin Faye, Ousmane Faye, Aaron Aruna, Justus Nsio, Felix Mulangu, Daniel Mukadi, Patrick Mukadi, John Kombe, Anastasie Mulumba, Christian-Julian Villabona-Arenas, Elisabeth Pukuta, Jeanette Gonzalez, Maggie L Bartlett, Shanmuga Sozhamannan, Stephen M Gross, Gary P Schroth, Roger Tim, Junhua J Zhao, Jens H Kuhn, Boubacar Diallo, Michel Yao, Ibrahima S Fall, Bathe Ndjakoko, Mathias Mossoko, Audrey Lacroix, Eric Delaporte, Mariano Sanchez-Lockhart, Amadou A Sall, Jean-Jacques Muyembe-Tamfum, Martine Peeters†, Gustavo Palacios†, Steve Ahuka-Mundeke†

Réintroduction de la maladie à Mangina

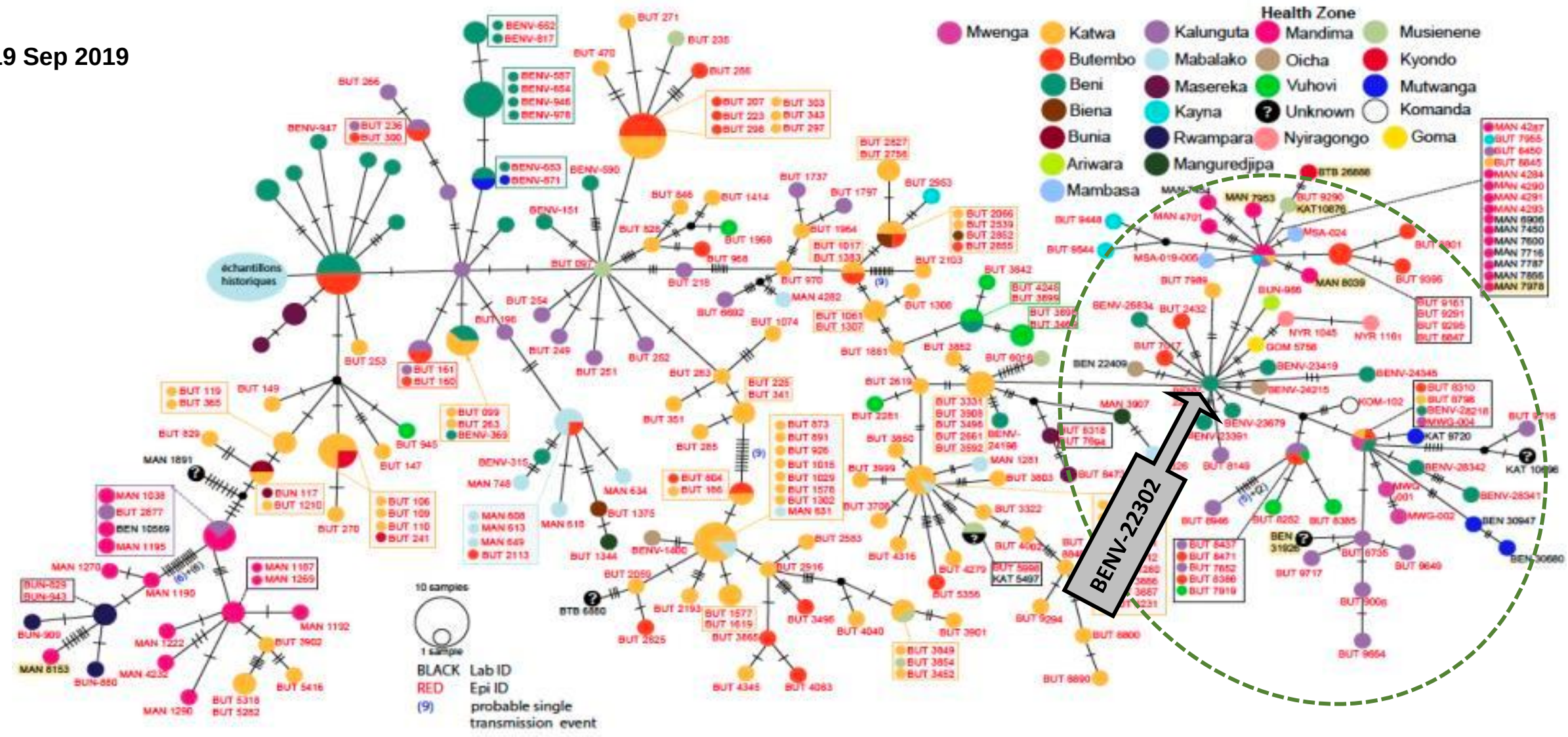
Une nouvelle chaine à partir d'un chauffeur de taxi moto



Using genomics to identify super spreading

BENV-22302 was a pastor who died. 53 subsequent cases from 16 health zones were exposed at the funeral.

19 Sep 2019



Défis pour assurer un enterrement à la fois sécurisé et humanisé

Transport d'un cadavre dissimulé comme bagage, Byakato, ZS de Mandima, Ituri, RD Congo

Membres de famille portant des gants participent à l'enterrement.

Evaluation et accompagnement des patients déclarés guéris d'une infection par le virus Ebola et de leurs contacts en République Démocratique du Congo

« Les Vainqueurs d'Ebola »

S. Ahuka-Mundeke

R. Kitenge

A MoH program dedicated to survivors

- Three clinics
- Three components : clinic, laboratory and psychosocial
- A 12 months follow-up
- With the supports of WHO and NG0's

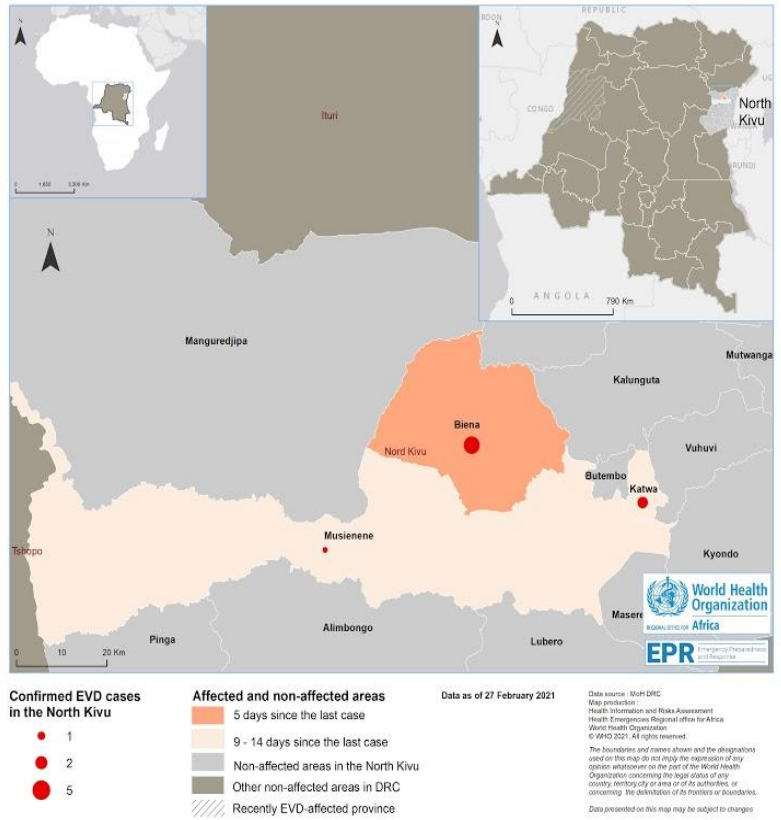
Site de Beni

Site de Mangina

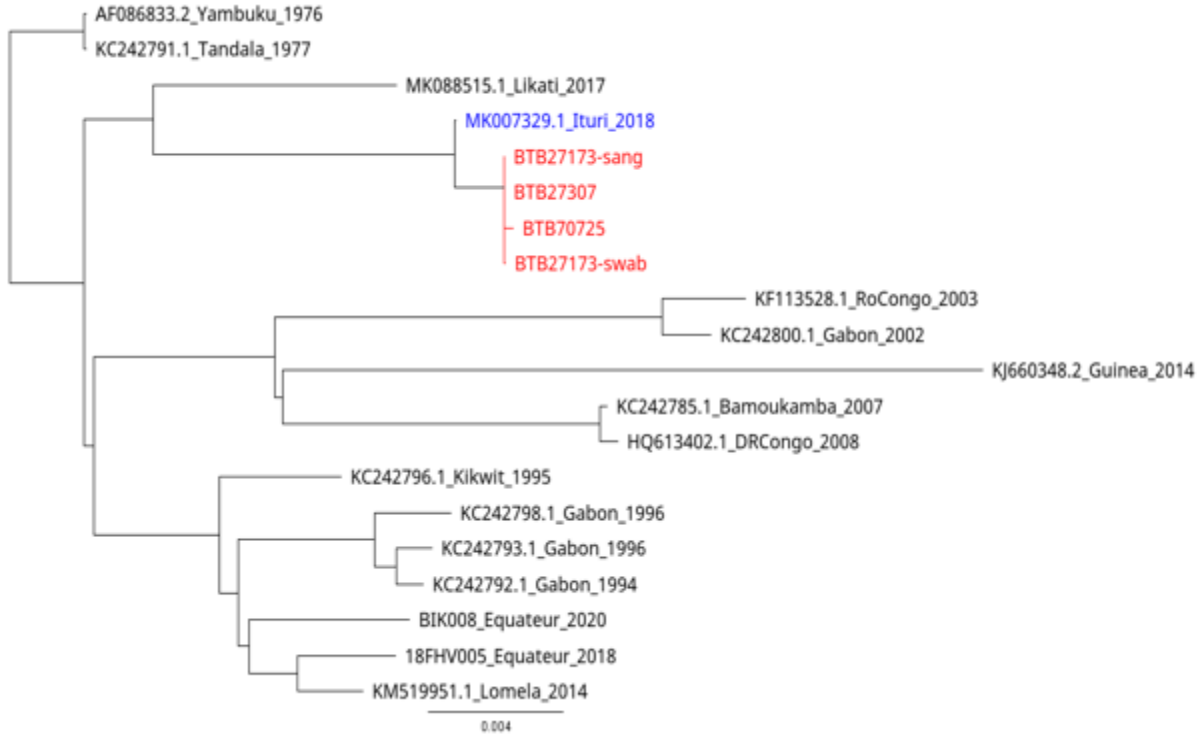
Resurgence of Ebola Cases

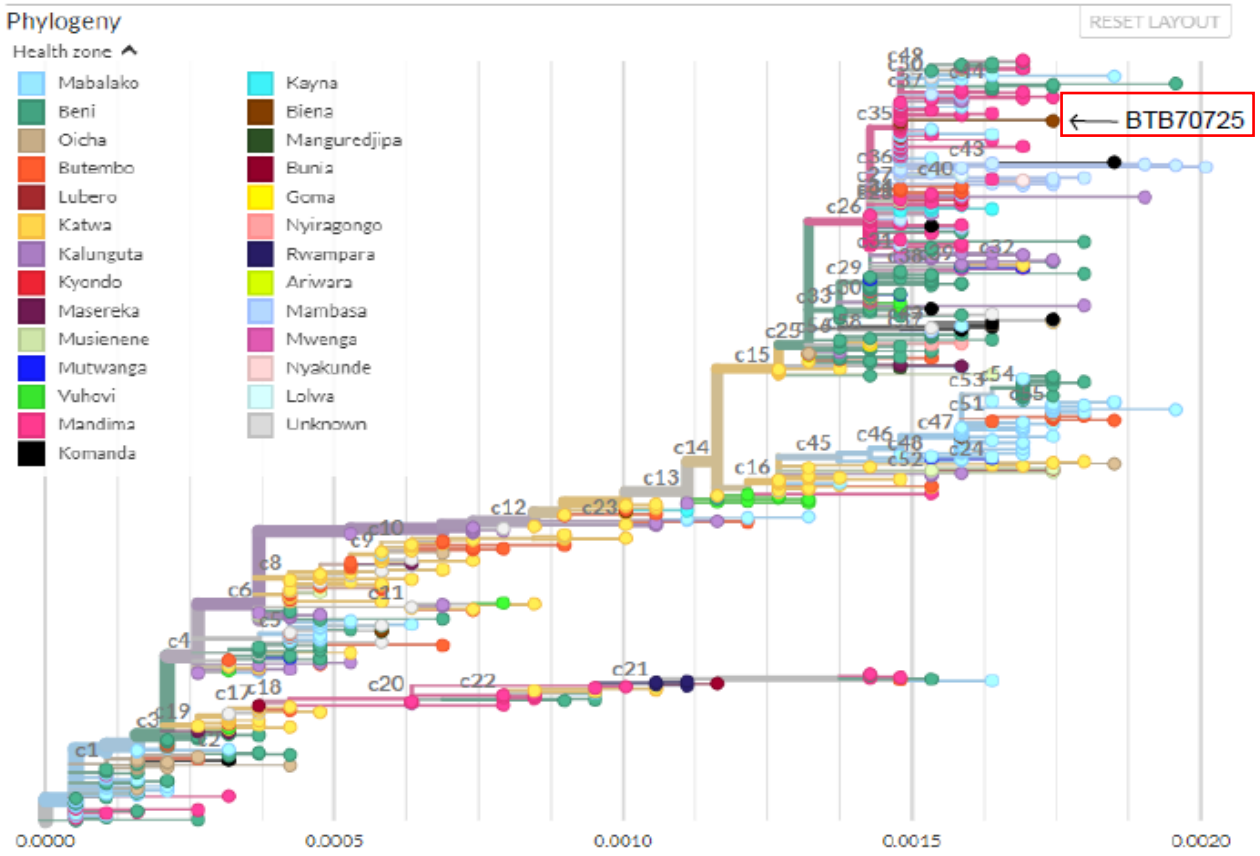
- Resurgence of Ebola cases in North Kivu on February 07, 2021
- 8 confirmed cases around the Butembo ZS including 4 deaths, 746 contacts (28/02/2021): no new cases since 5 days
- Index case: 42-year-old patient wife

of a survivor followed at the Butembo site.



The new case is descended from the Ituri variant and therefore **does not represent a new spillover event**, but indicates this variant is from the Nord Kivu/Ituri EVD outbreak.





Resurgence of Ebola Cases

- Le survivant avait un résultat de PCR EBOV négatif dans le sperme en Septembre et Novembre 2020! Et était sorti du CTE un an avant
- L'épouse avait été vaccinée
- La stigmatisation des survivants est encore plus importante

Guinée Ebola 2021

- Au 27/02 13 cas (3décès) confirmés et 4 probables (dcd)

Implication dans la riposte

- Diagnostic de référence et plate-forme de séquençage
- Investigation de l'épidémie :

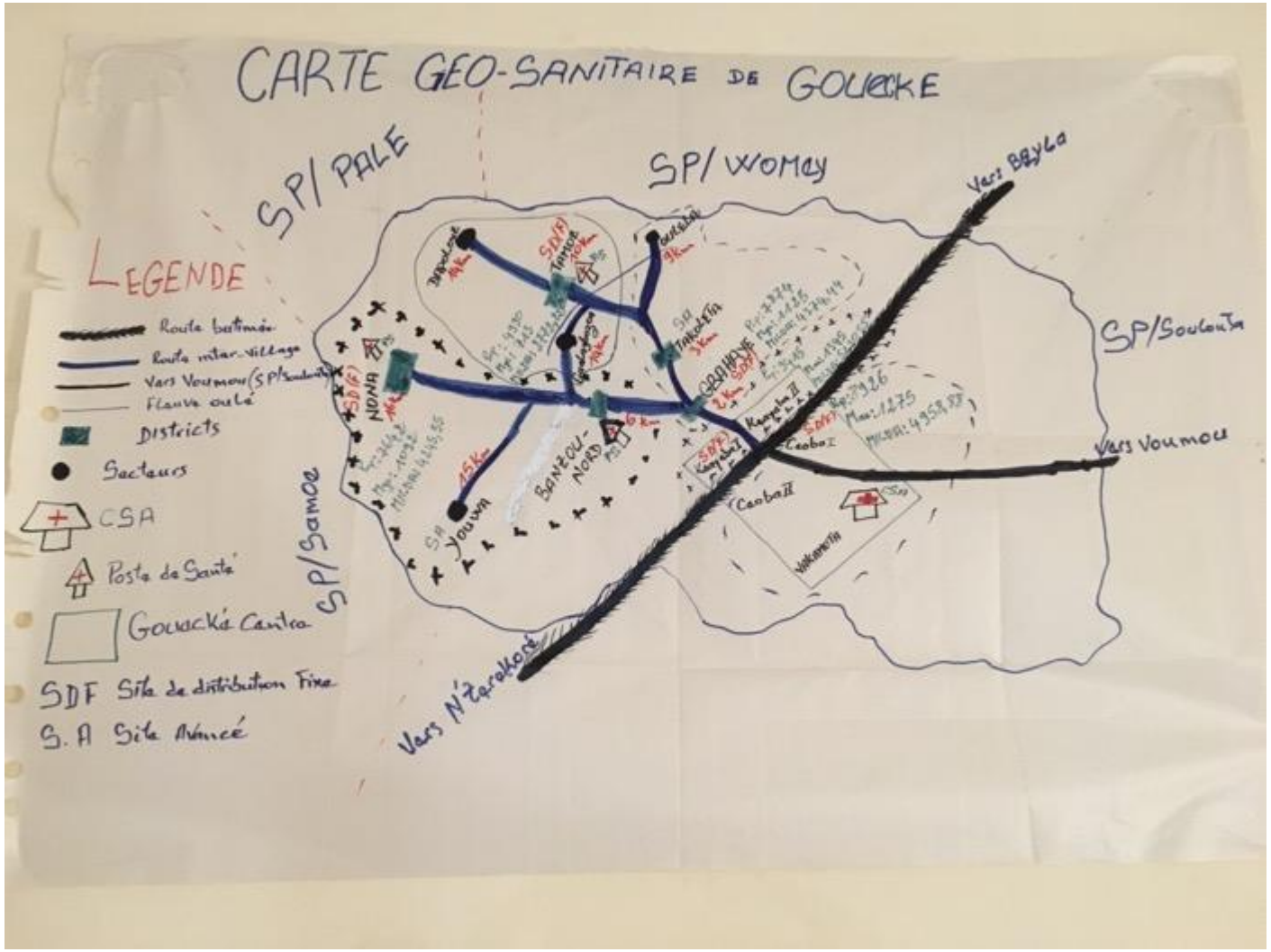
Mission conjointe:

Infectiologues-Ecologues-Anthropologues-Epidémiologistes

Valorisation des projets Post Ebola

Implication dans la riposte:
Investigation de l'origine approche anthropologique

Retour de mission de Fr Le Marcis



Jardin de Lucie le cas index

Implication dans la riposte: « Faune »

Collaboration: CERFIG/TransVIHMI, CIRAD, Robert Koch Institute (F. Leendertz) et Wild Chimpanzee Organization (WCF, Guinee)

Expertises compléméntaires

3 équipes sur le terrain

2 équipes petit mammifères (Chauves souris, rongeurs, .. Viande de brousse)

-prospection autour de l'habitation du cas index
- prospection autour des zones de chasse

1 équipe grands mammifères: chimpanzés, antilopes, etc..

- prospections de la densité et diversité dans les forets classés de la région

Prélèvements organes chauves souris, rongeurs..
Prélèvements sur les carcasses d'animaux trouvé mort en foret (expertise RKI)

Implication dans la riposte: Laboratoire

- Confirmation du 1° cas d'infection EBOV : déclaration de l'épidémie
- Caractérisation par séquençage de la nature Ebola-Zaire de la souche:

Implication dans la riposte:
Investigation de l'origine approche virologique

- Analyse phylogénétique des souches

identité (sans évolution) avec la souche de 2014-16

Nouvelle épidémie liée à une résurgence à partir d'un survivant.. Et non pas liée à un spillover…

Epidémie Ebola Guinée 2021

- **Bilan**
  - ✓Guinea
    - ✓ 23 cas (16 confirmés, 7 probables)
    - ✓ **12 décès (52%)**
    - ✓Fin de l'épidémie le 19 juin 2021

Article

Resurgence of Ebola virus in 2021 in Guinea suggests a new paradigm for outbreaks

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Check for updates

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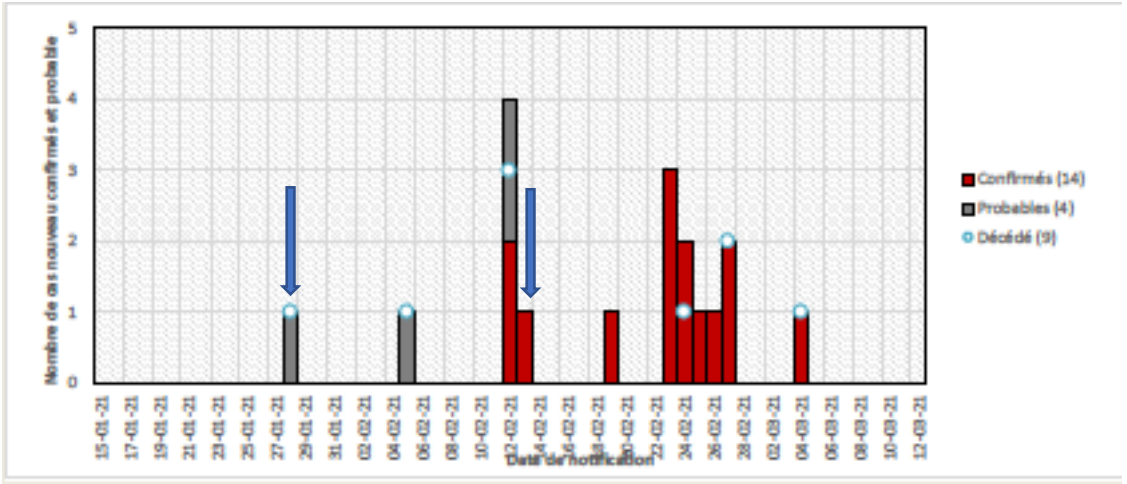
Seven years after the declaration of the first epidemic of Ebola virus disease in Guinea, the country faced a new outbreak—between 14 February and 19 June 2021—near the epicentre of the previous epidemic[1,2]. Here we use next-generation sequencing to generate complete or near-complete genomes of *Zaire ebolavirus* from samples obtained from 12 different patients. These genomes form a well-supported phylogenetic cluster with genomes from the previous outbreak, which indicates that the new outbreak was not the result of a new spillover event from an animal reservoir. The 2021 lineage shows considerably lower divergence than would be expected during sustained human-to-human transmission, which suggests a persistent infection with reduced replication or a period of latency. The resurgence of *Zaire ebolavirus* from humans five years after the end of the previous outbreak of Ebola virus disease reinforces the need for long-term medical and social care for patients who survive the disease, to reduce the risk of re-emergence and to prevent further stigmatization.

nature



Epidémie Ebola 2013-2016

- **> 28000 cas / > 11000 déces**
  - ✓Guinea
    - ✓ 3811 cas d'Ebola survenus
    - ✓ **1270 survivants (+33%)**

The NEW ENGLAND JOURNAL of MEDICINE

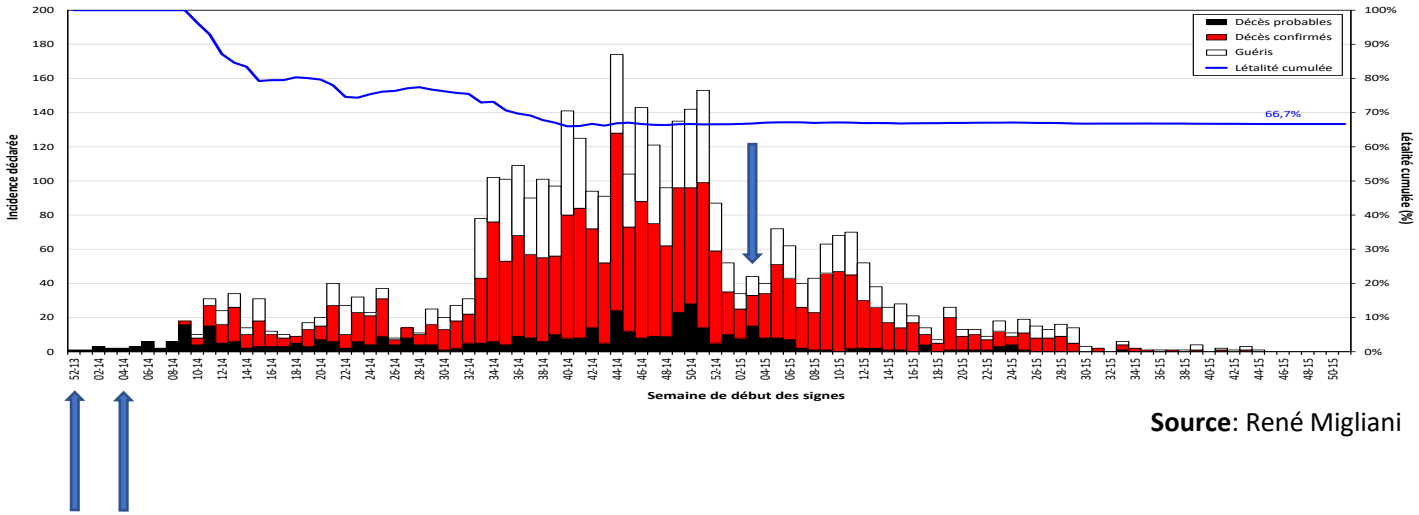
BRIEF REPORT

Emergence of Zaire Ebola Virus Disease in Guinea

Sylvain Baize, Ph.D., Delphine Pannetier, Ph.D., Pharm.D., Lisa Oestereich, M.Sc., Toni Rieger, Ph.D., Lamine Koivogui, Ph.D., N'Faly Magassouba, Ph.D., Barrè Soropogui, M.Sc., Mamadou Saliou Sow, M.D., Sakoba Keïta, M.D., Hilde De Clerck, M.D., Amanda Tiffany, M.P.H., Gemma Dominguez, B.Sc., Mathieu Loua, M.D., Alexis Traoré, M.D., Moussa Kolié, M.D., Emmanuel Roland Malano, M.D., Emmanuel Heleze, M.D., Anne Bocquin, M.Sc., Stephane Mély, M.Sc., Hervé Raoul, Ph.D., Valérie Caro, Ph.D., Dániel Cadar, D.V.M., Ph.D., Martin Gabriel, M.D., Meike Pahlmann, Ph.D., Dennis Tappe, M.D., Jonas Schmidt-Chanasit, M.D., Benido Impouma, M.D., Abdoul Karim Diallo, M.D., Pierre Formenty, D.V.M., M.P.H., Michel Van Herp, M.D., M.P.H., and Stephan Günther, M.D.

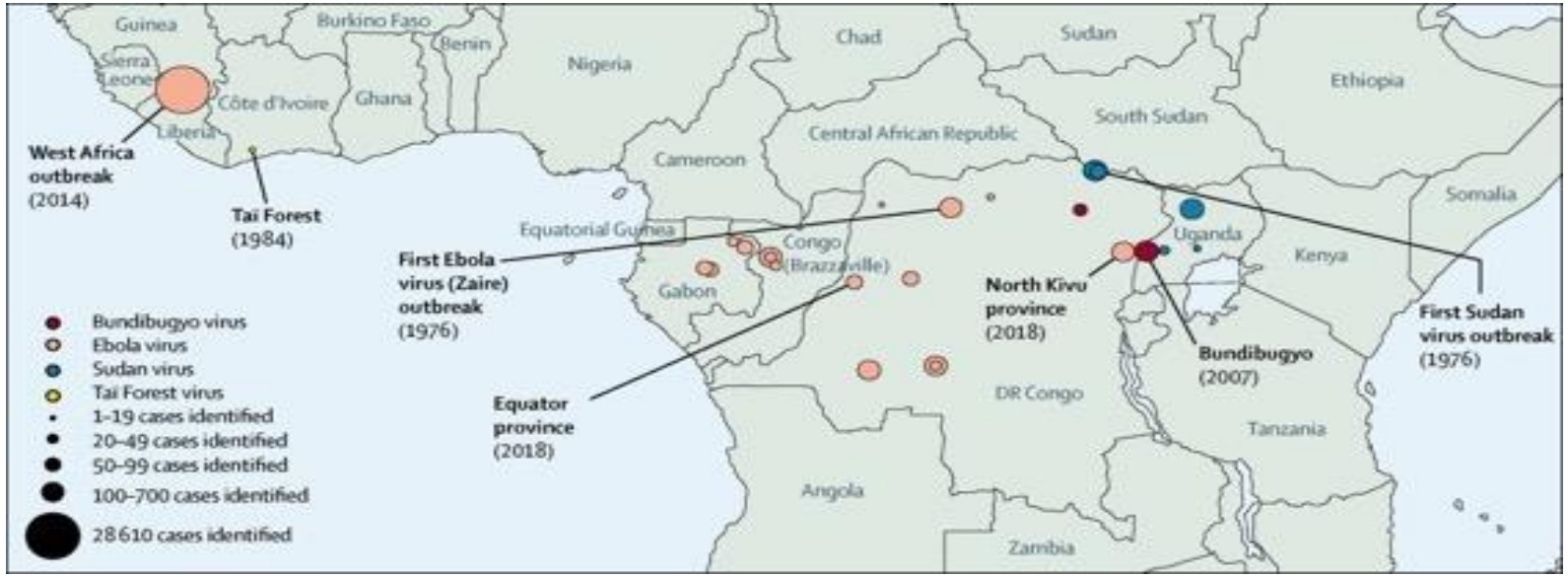
SUMMARY

In March 2014, the World Health Organization was notified of an outbreak of a communicable disease characterized by fever, severe diarrhea, vomiting, and a high fatality rate in Guinea. Virologic investigation identified *Zaire ebolavirus* (EBOV) as the causative agent. Full-length genome sequencing and phylogenetic analysis showed that EBOV from Guinea forms a separate clade in relationship to the known EBOV strains from the Democratic Republic of Congo and Gabon. Epidemiologic investigation linked the laboratory-confirmed cases with the presumed first fatality of the outbreak in December 2013. This study demonstrates the emergence of a new EBOV strain in Guinea.



Source: René Migliani

Ebola: 2021



Treatment: Palm Study in RDC (Ab onlyl)
Vaccin: Merck and J&J
Diagnosis: Developpement of operationnal real time PCR tests, NGS, Luminex serology, ..
Clinical consequences : Asymptomatic, acute and standard of care, « chronic »
Reservoir: not only animal…
Preparadness…

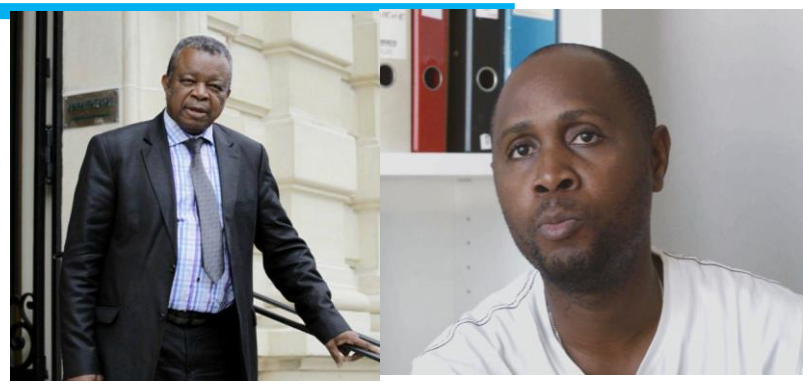
Acknowledgements

UMI233, Montpellier

Martine Peeters, Eric Delaporte, Ahidjo Ayouba, …

PRESICA, Cameroon

Eitel Mpoudi Ngole,
Innocent, Aime, Jozef, Thomas



INRB, RDC

JJ Muyembe, Steve Ahuka Mundeke

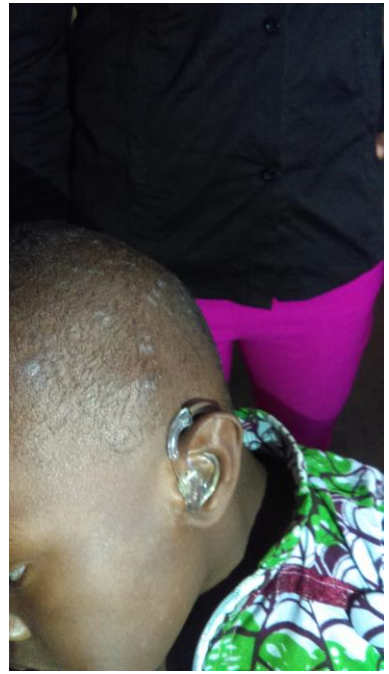
CERFIG
Centre de Recherche et de Formation en Infectiologie de Guinée

A Touré, A Keita, S Sow

anrs France REcherche Nord & sud Sida-hiv Hépatites
Agence autonome de l'Inserm

Points clefs

- **Savoir pourquoi on s'investit , protocole , financement , rôle**
- **Recherche = Soins + Formation + Renforcement des capacités =Ethique**
- **Importance du partenariat++++++++++++++**
- **« Durabilité »**

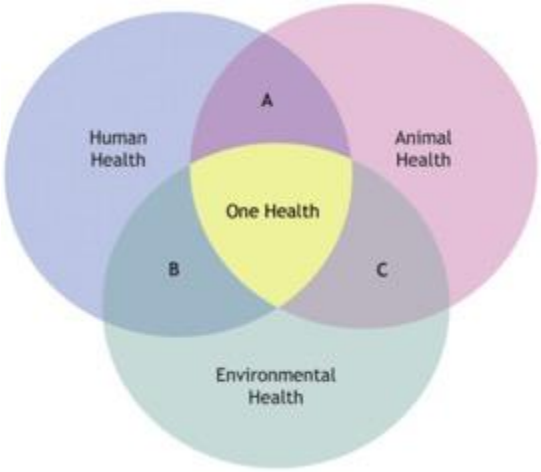


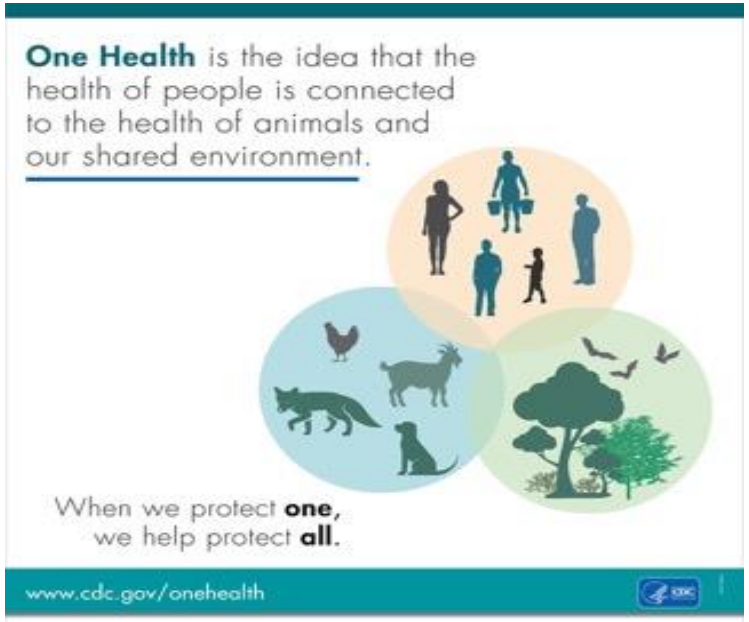
Centre de Recherche Clinique et de Formation sur les Maladies Infectieuses (CERFIG)

One Health approach

- Multi-disciplinary approach
  - animal, human, and environmental health
  - **understand the ecology of each emerging zoonotic diseases**

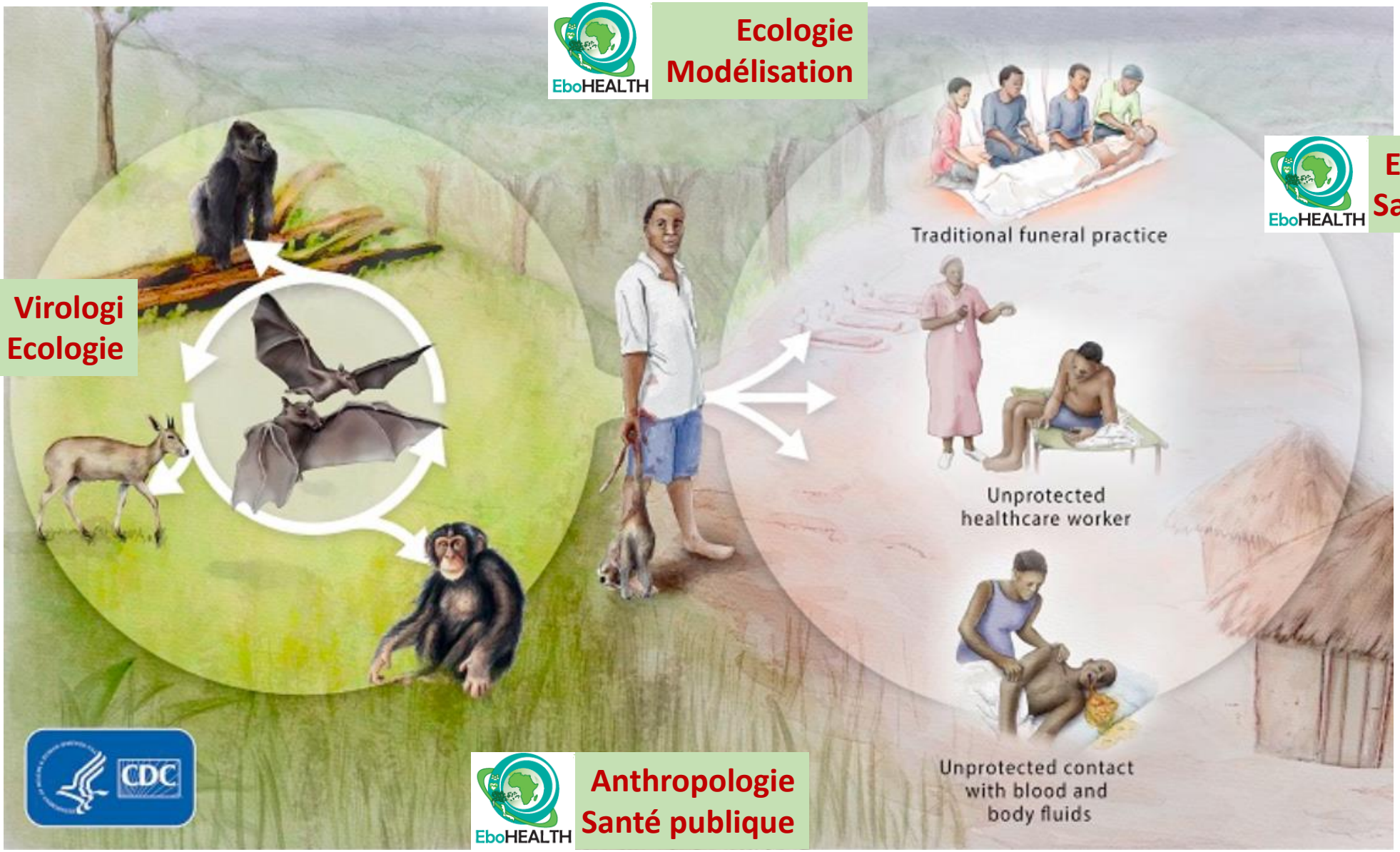
    (>70% of Human Emerging Diseases)
  - risk assessment, and develop plans for response and control.





Ecologie et transmission d'EBOV

Disciplines engagées dans EboHEALTH



EboHEALTH **Ecologie Modélisation**

EboHEALTH **Epidemiologie Santé publique**

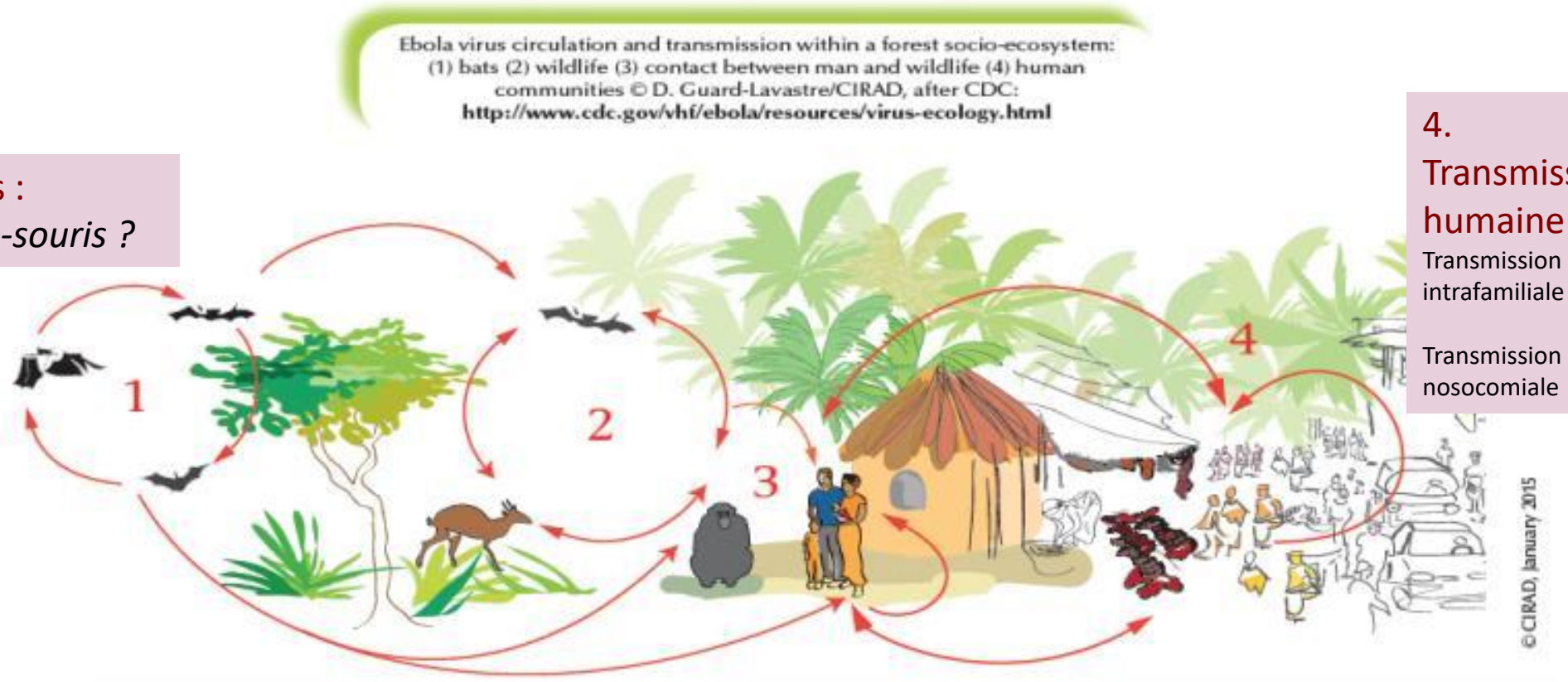
EboHEALTH **Virologie Ecologie**

EboHEALTH **Anthropologie Santé publique**

Origine des épidémies

Chaque épidémie chez les humains = événement de transmission zoonotique indépendant

1. réservoirs :
   Chauves-souris ?



4. Transmission humaine
   Transmission intrafamiliale

   Transmission nosocomiale

2. Hôtes intermédiaires ou amplificateur:
   Primates non-humains, antilopes, autres

3. Transmission inter-espèces
   de la faune sauvage a l'homme

cirad
AGRICULTURAL RESEARCH FOR DEVELOPMENT

Projet EboHEALTH: Comprendre et prévenir l'émergence d'Ebola

- CERFIG (Conakry) TransVIHMI (IRD, INSERM, Univ Montpellier)
- IP Pr Eric Delaporte, Dr Abdoulaye Touré (2019-2021) Fint MUSE
- 4 angles pour aborder l'émergence / objectifs de recherche:
  - **Santé animale**: Explorer le portage du virus Ebola par les chauves-souris, comprendre l'écologie et la dynamique du virus de l'espèce réservoir
  - **Santé humaine**: Explorer le portage d'anticorps Ebola, comprendre les épisodes épidémiques antérieurs et leurs déterminants
  - **Environnement**: Comprendre les facteurs climatiques et environnementaux des émergences, cartographier les risques
  - **Sociétés**: Connaître les rappports entre humains et chauves-souris, comprendre les facteurs sociaux de la surveillance communautaire

One Health