EBOLA RISK ASSESSMENT AND CONTROL IN THE FIELD: *UNDERSTANDING THE TRUE VALUE OF DYNAMIC RISK ASSESSMENTS*

IAN GOODFELLOW

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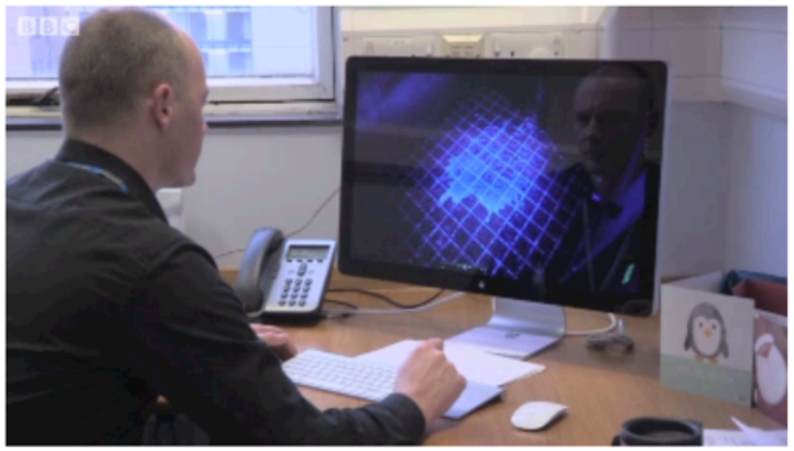
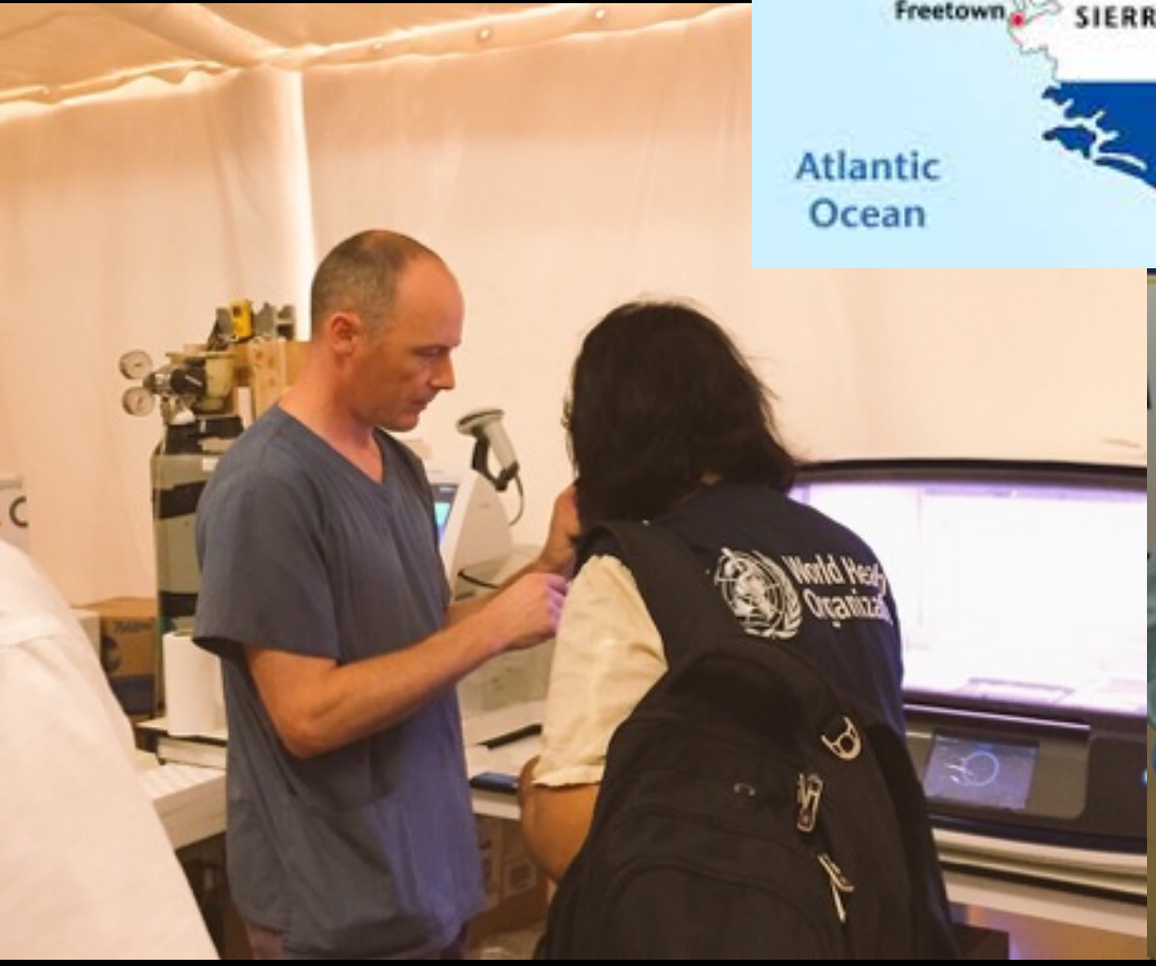


Norovirus: Winter vomiting bug 'impressing' scientists

24 December 2012 Last updated at 23:59 GMT

"Norovirus is the Ferrari of the virus world," says Professor Ian Goodfellow, a Wellcome Trust fellow, who has been studying the virus for 10 years.

NOVEMBER ’14 ONWARDS



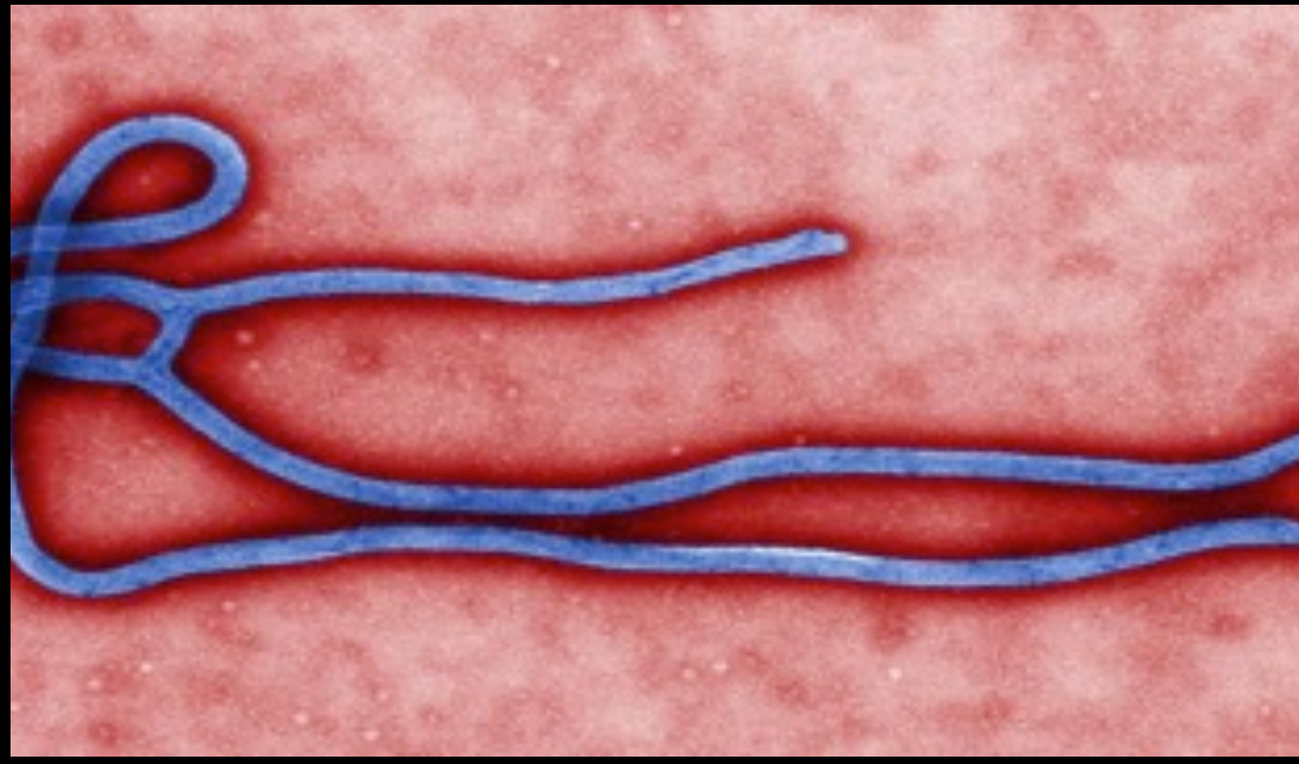
CAMBRIDGE STAFF INVOLVED IN THE RESPONSE

- Numerous staff from the University and associated institutes were involved
  - Biomedical scientists
  - Researchers
  - Academics
- *List not complete*

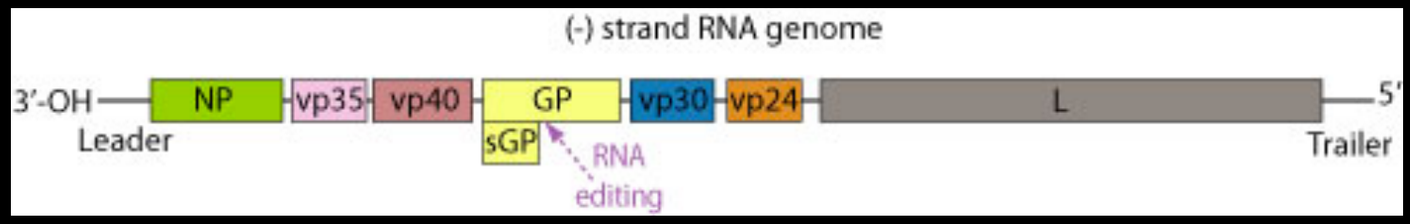
NAME	DEPARTMENT/DIVISION	ROLE
PROF. IAN GOODFELLOW	PATHOLOGY/VIROLOGY	DIAGNOSTICS/SEQUENCING TEAM
DR ARMANDO ARIAS	PATHOLOGY/VIROLOGY	SEQUENCING TEAM
DR LUCY THORNE	PATHOLOGY/VIROLOGY	SEQUENCING TEAM
MR JIA LU	PATHOLOGY/VIROLOGY	SEQUENCING TEAM
DR SARAH CADDY	PATHOLOGY/VIROLOGY	DIAGNOSTICS/SEQUENCING TEAM
DR GARETH EVANS	PATHOLOGY/VIROLOGY	DIAGNOSTICS
DR LUKE MEREDITH	PATHOLOGY/VIROLOGY	DIAGNOSTICS/SEQUENCING TEAM
DR BO MENG	MEDICINE	DIAGNOSTICS
DR JONATHAN ASHCROFT	MEDICINE	DIAGNOSTICS
DR AXEL FUN	MEDICINE	DIAGNOSTICS
DR ANDRZEJ RUTKOWSKI	MEDICINE	DIAGNOSTICS
DR JANE GREATOREX	MEDICINE/PHE CAMBRIDGE	DIAGNOSTICS
MARIE BLACKMAN-NORTHWOOD	PHE CAMBRIDGE	DIAGNOSTICS
SWEETY TULCIDAS	PHE CAMBRIDGE	DIAGNOSTICS
CLARE ETHERIDGE	PHE CAMBRIDGE	DIAGNOSTICS
BARRIE BAILEY	PHE CAMBRIDGE	DIAGNOSTICS
MARK WARE	PHE CAMBRIDGE	DIAGNOSTICS
BRIAN KOEHN	PHE CAMBRIDGE	DIAGNOSTICS
SHANE BRECKENRIDGE	PHE CAMBRIDGE	DIAGNOSTICS
JULIA YELLOLY	PHE CAMBRIDGE	DIAGNOSTICS
KIRSTIN SHAND	PHE CAMBRIDGE	DIAGNOSTICS
CHRISTIANA ADESANWO	PHE CAMBRIDGE	DIAGNOSTICS
FRAN LUDWIG	PHE CAMBRIDGE	DIAGNOSTICS
DR MATT COTTON	WELLCOME SANGER CENTRE	SEQUENCING TEAM
DR MY PHAN	WELLCOME SANGER CENTRE	SEQUENCING TEAM
DR RUTH WATKINSON	MRC LMB	DIAGNOSTICS

EBOLA VIRUS

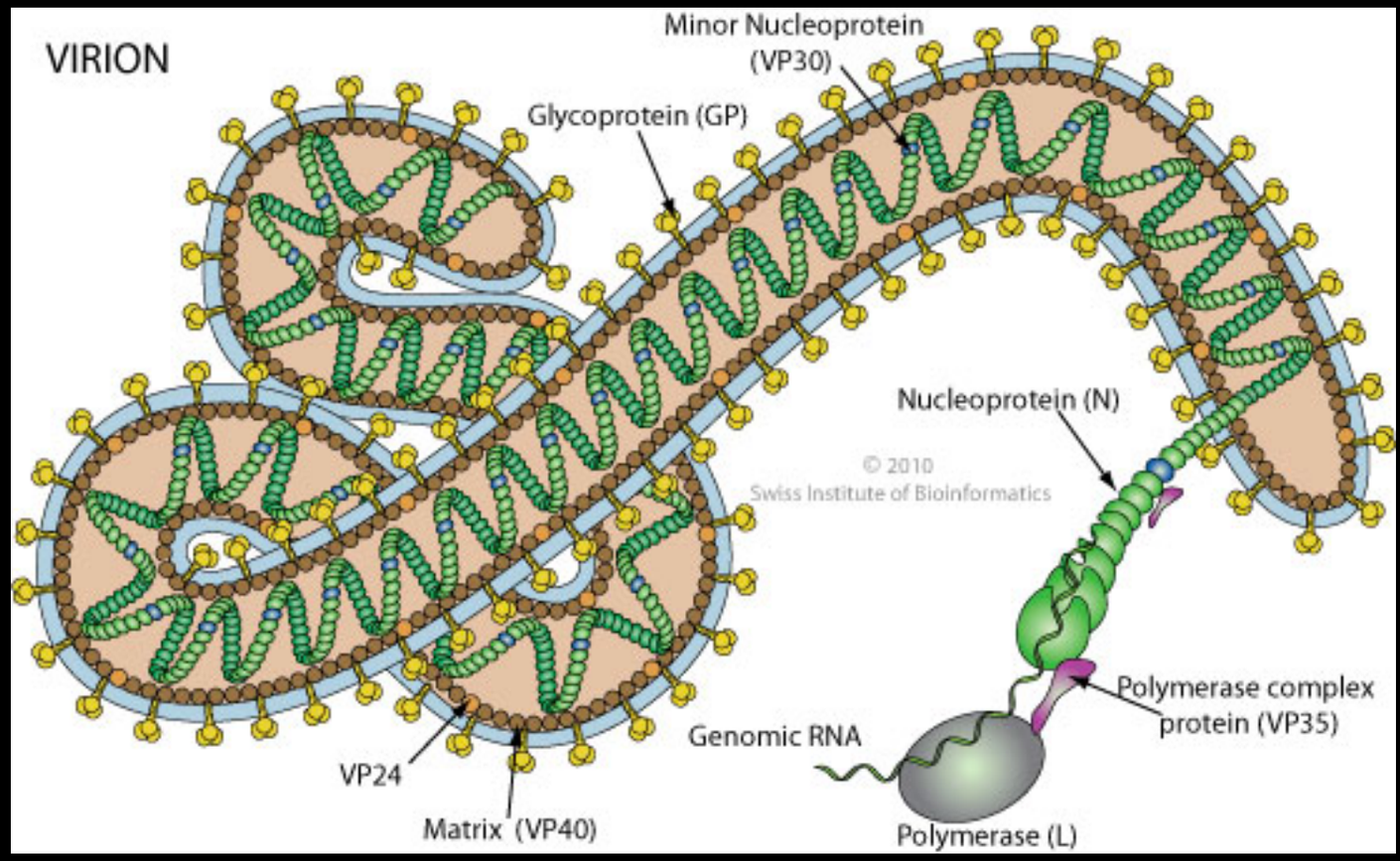
- EVD first appeared in 1976 in Nzara, Sudan, and in Yambuku, Congo (prev Zaire).
- Yambuku village near the Ebola River
- Family: *Filoviridae*
- Genus: *Ebolavirus*
- Species: 5 types
  - Zaire ebolavirus (EBOV)
  - Sudan ebolavirus (SUDV)
  - Bundibugyo ebolavirus (BDBV)
  - Taï Forest ebolavirus (TAFV).
  - Reston ebolavirus (RESTV) (Philippines & China)



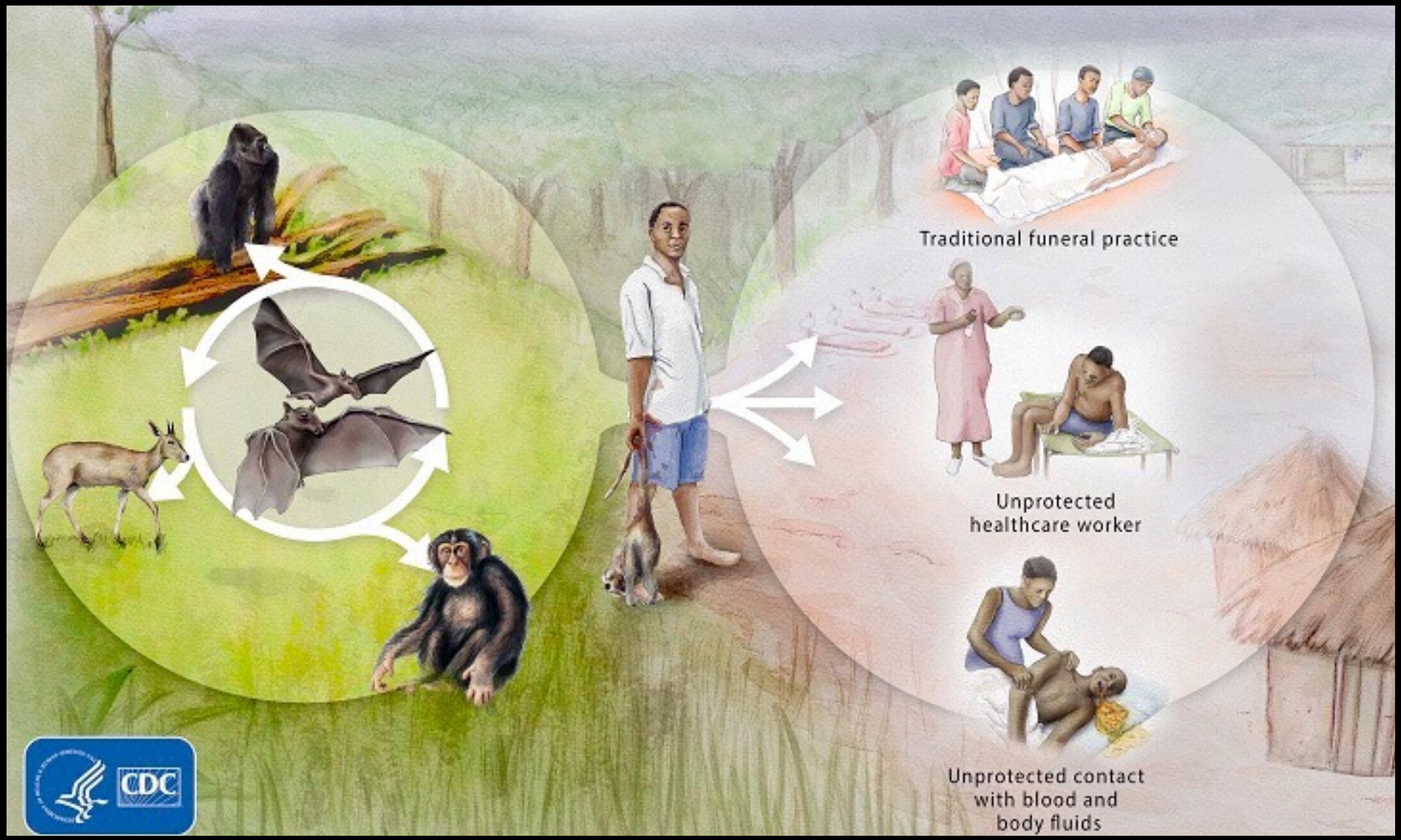
THE ANATOMY OF EBOLA VIRUS



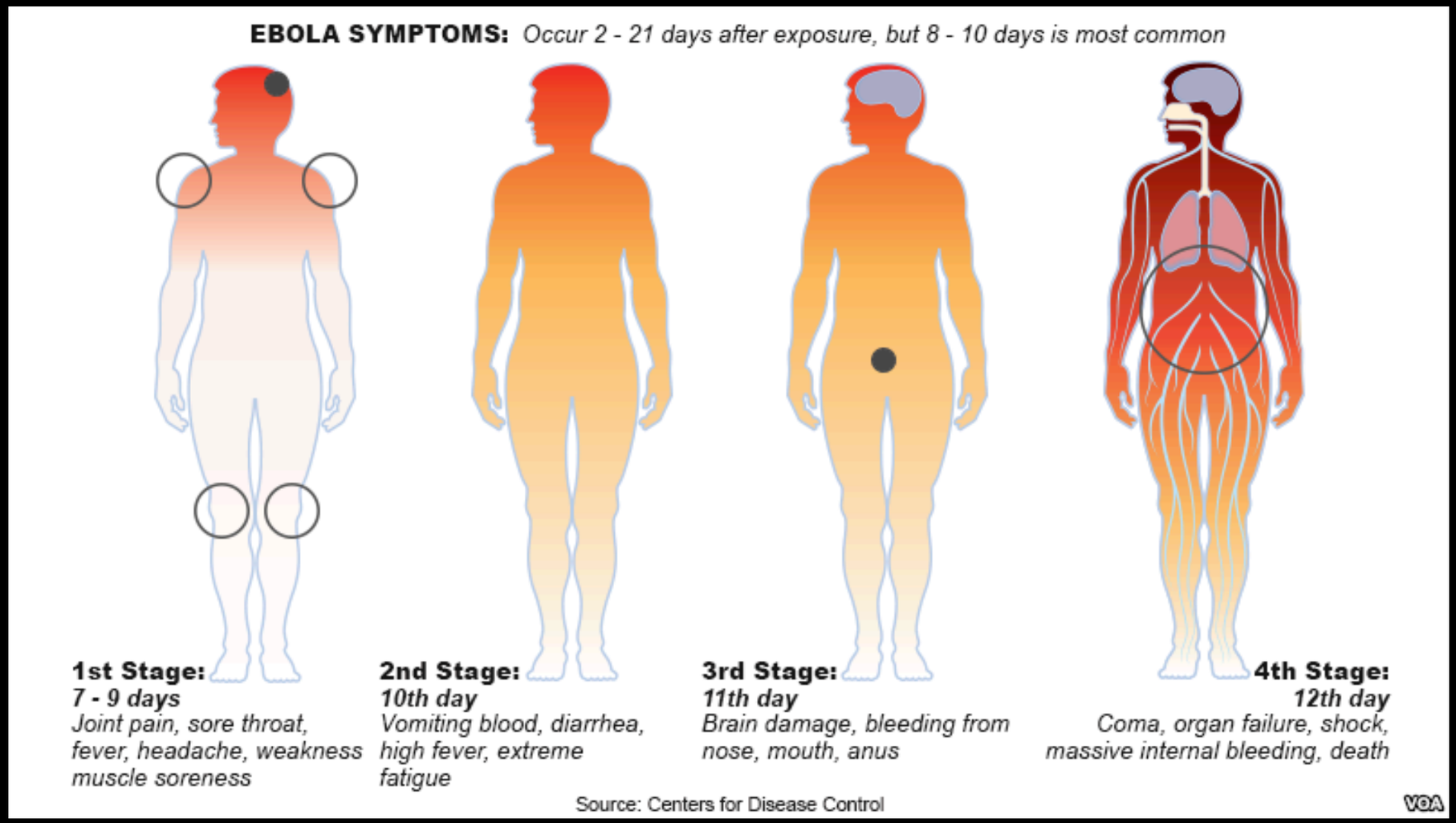
- **Negative Sense RNA virus**
- Enveloped
- ~19Kb - 7 ORFs
- Filamentous
- *Relatively easy to inactivate*



EBOLA VIRUS ECOLOGY



EBOLA VIRUS - EFFECTS AND TRANSMISSION

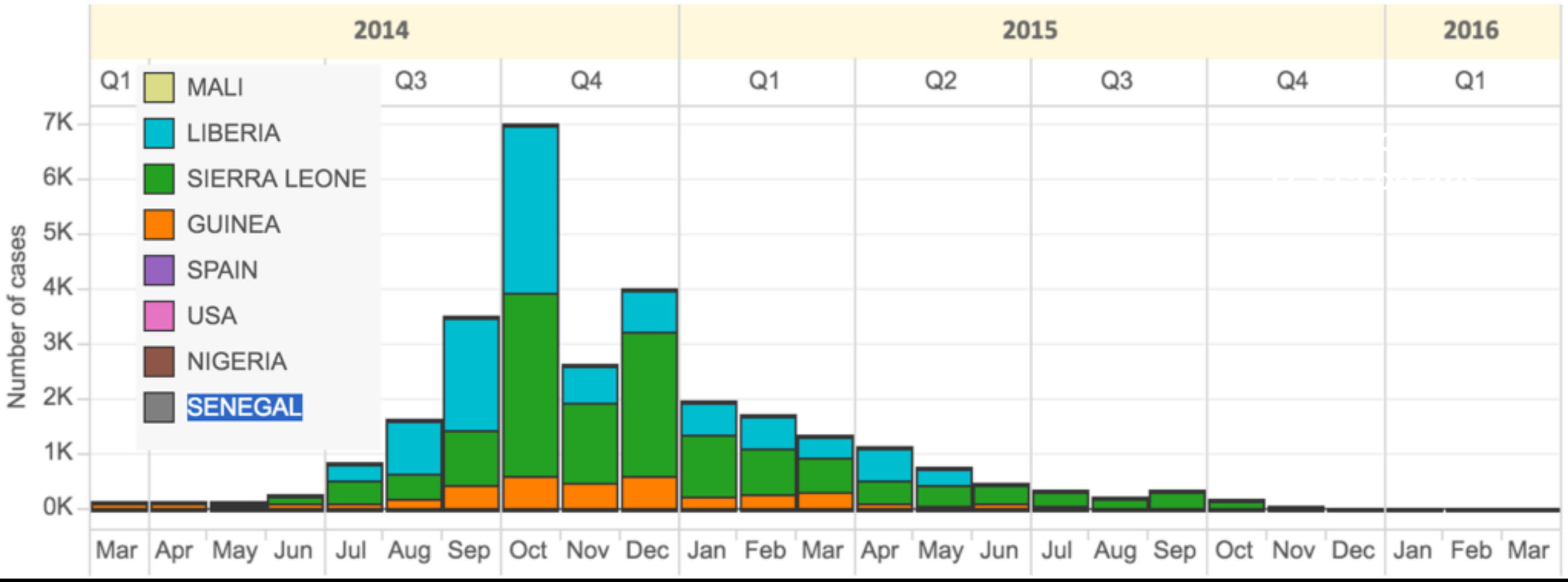


- Transmission occurs by contact with an infected person or bodily fluids
- Transmission can ONLY occur during the symptomatic phase
- At the final stages of the disease patient have high viral loads in all bodily fluids
- Sexual contact
- Breast Milk?
- Persistence in survivors has caused sporadic cases

THE ORIGINS OF THE EBOLA EPIDEMIC

EPIDEMIOLOGICAL EVIDENCE SUGGESTS PATIENT ZERO WAS EMILE OUAMOUNO (2 YR BOY) FROM MELIANDOU VILLAGE IN GUINEA

EBOLA EPIDEMIC – MAR 2016



~30,000 cases
>15,000 deaths
Significant underreporting of cases - sometimes as high as 3X

WHY WAS THIS EPIDEMIC SO BAD?

- Densely populated areas
- Poor hygiene
- Lack of easy access to clean water

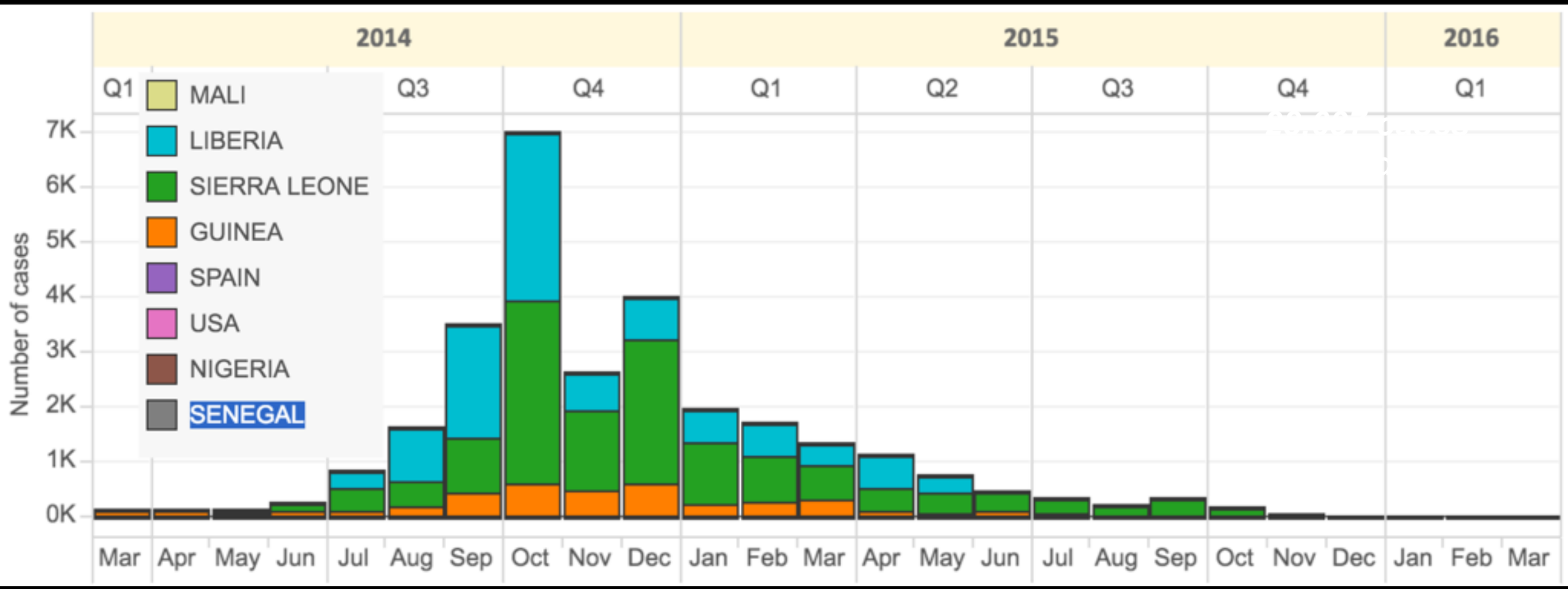
WHY WAS THIS EPIDEMIC SO BAD?

- Inadequate healthcare
- Sierra Leone: Population: ~6 million
- Pre EVD epidemic:
  - 136 doctors
  - 1017 nurses and midwives
- London: 8.3 million
  - ~22,400 doctors alone

WHY WAS THIS EPIDEMIC SO BAD?

- Burial Practices

EBOLA EPIDEMIC – MAR 2016



ESTABLISH & RUN DIAGNOSTIC LAB

PHE

ESTABLISH & RUN SEQUENCING LAB/RESEARCH LAB

University of Cambridge

http://virologydownunder.blogspot.com.au/

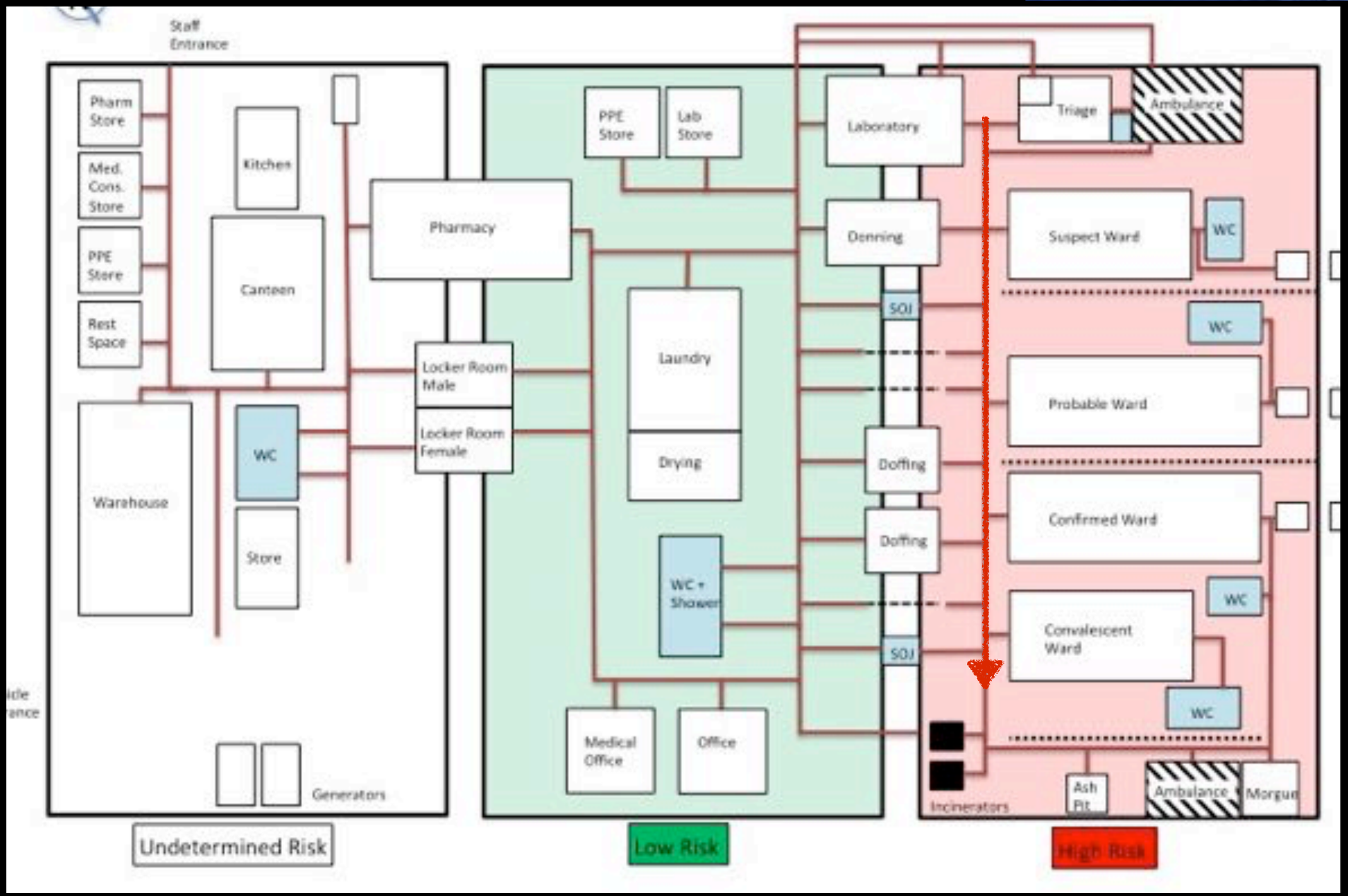
PRE-DEPLOYMENT TRAINING

- Health & psychological screening (Interhealth)
- Vaccinations (and more vaccinations)
- Porton Down (5 days)
- Training in:
  - Use of flexible film isolators
  - Standard operating procedures
  - Emergency procedures

"SELECTION" OF VOLUNTEERS

- Once volunteers started flowing a more rigorous "selection" process was established:
    - Reference from their line manager
    - More formal assessment during training
    - Practical ability and suitability to work in a team in a stressful environment
- *However - there was still limited numbers so the skill requirements were low*

NOV '14 - MATENEH EBOLA TREATMENT CENTRE, MAKENI SIERRA LEONE



Mateneh Ebola Treatment Centre

MAKENI, SIERRA LEONE

Makeni October 2014

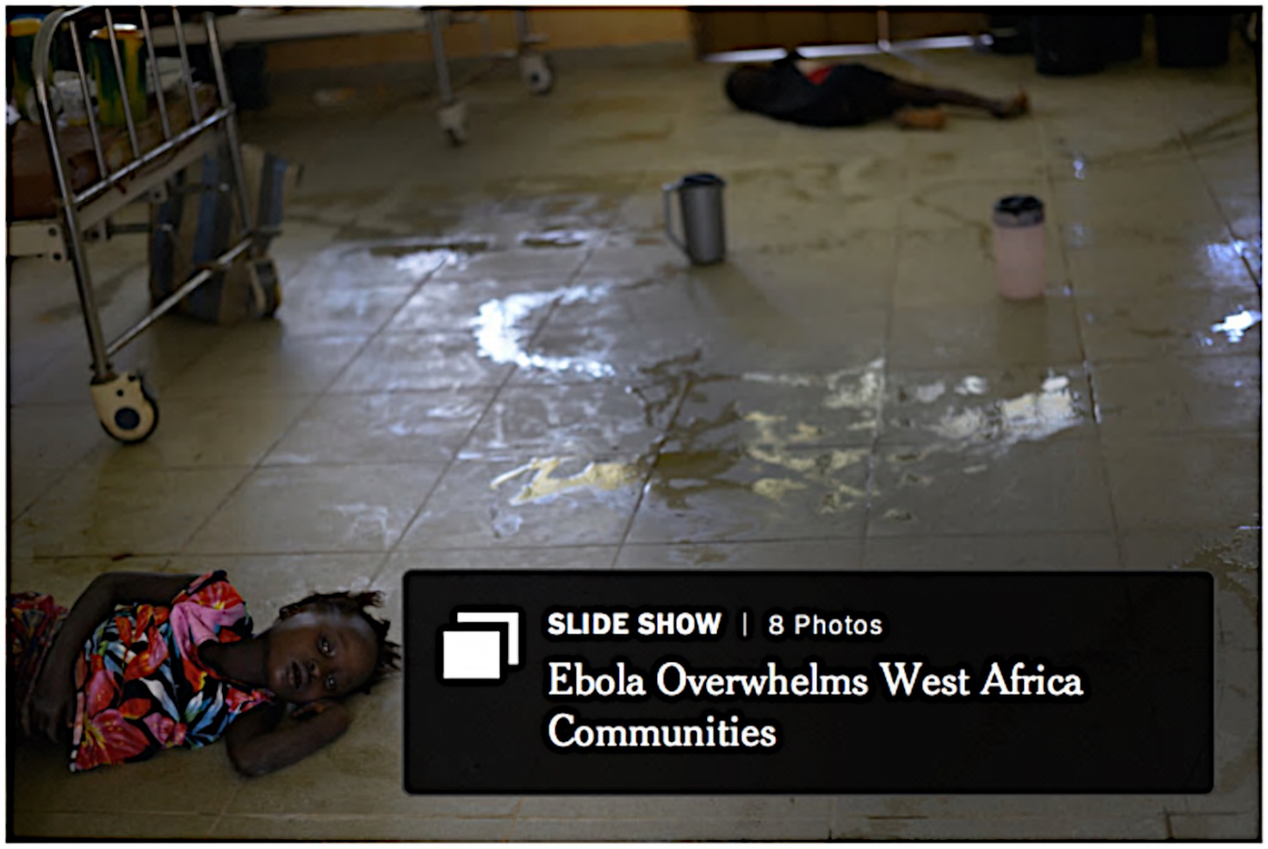
–NEW YORK TIMES

A Hospital From Hell, in a City Swamped by Ebola

By ADAM NOSSITER OCT. 1, 2014

MAKENI, Sierra Leone — "Where's the corpse?" the burial-team worker shouted, kicking open the door of the isolation ward at the government hospital here. The body was right in front of him, a solidly built young man sprawled out on the floor all night, his right hand twisted in an awkward clench.

The other patients, normally padlocked inside, were too sick to look up as the body was hauled away. Nurses, some not wearing gloves and others in street clothes, clustered by the door as pools of the patients' bodily fluids spread to the threshold. A worker kicked another man on the floor to see if he was still alive. The man's foot moved and the team kept going. It was 1:30 in the afternoon.



Samuel Aranda for The New York Times

In the next ward, a 4-year-old girl lay on the floor in urine, motionless, bleeding from her mouth, her eyes open. A corpse lay in the corner — a young woman, legs akimbo, who had died overnight. A small child stood on a cot watching as the team took the body away, stepping around a little boy lying immobile next to black buckets of vomit. They sprayed the body, and the little girl on

FEATURED COMMENT

Hannah Brooklyn
"To see a four-year-old girl ... alone, scared, bleeding and dying in the remnants of other patients' fluids, is so unacceptable, inhumane and shocking

Makeni October 2014

–NEW YORK TIMES

Ebola Overwhelms West Africa Communities

A burial team removing a body last week from Makeni Regional Hospital. The Ebola epidemic has intensified across parts of West Africa, sweeping into areas that had been largely spared the onslaught and are not in the least prepared for it.

Samuel Aranda for The New York Times


MAE
UK
MOD
LAB 2

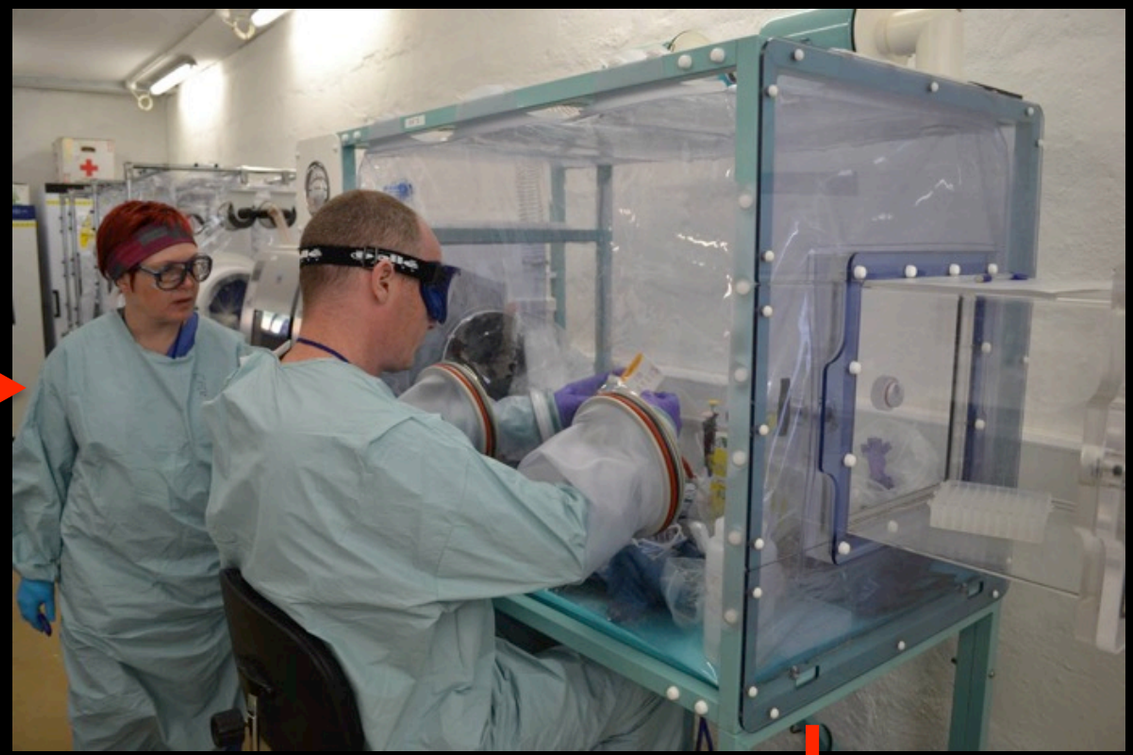

LAB 2

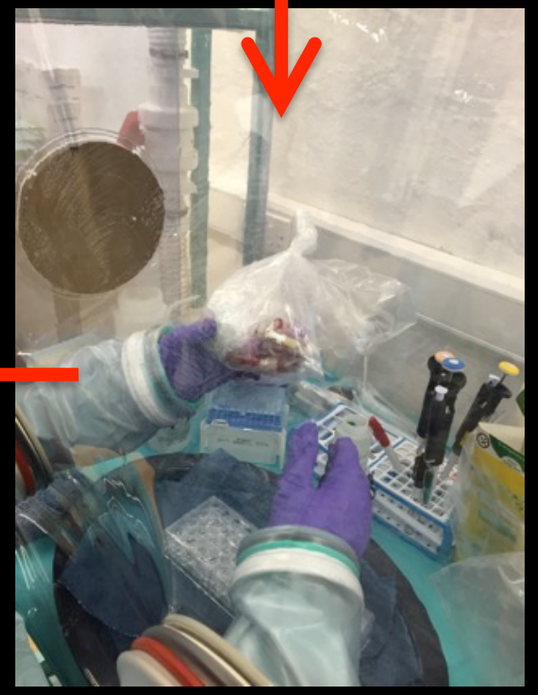

dawnus


SAMSUNG

DEC 13TH – OPENING DAY

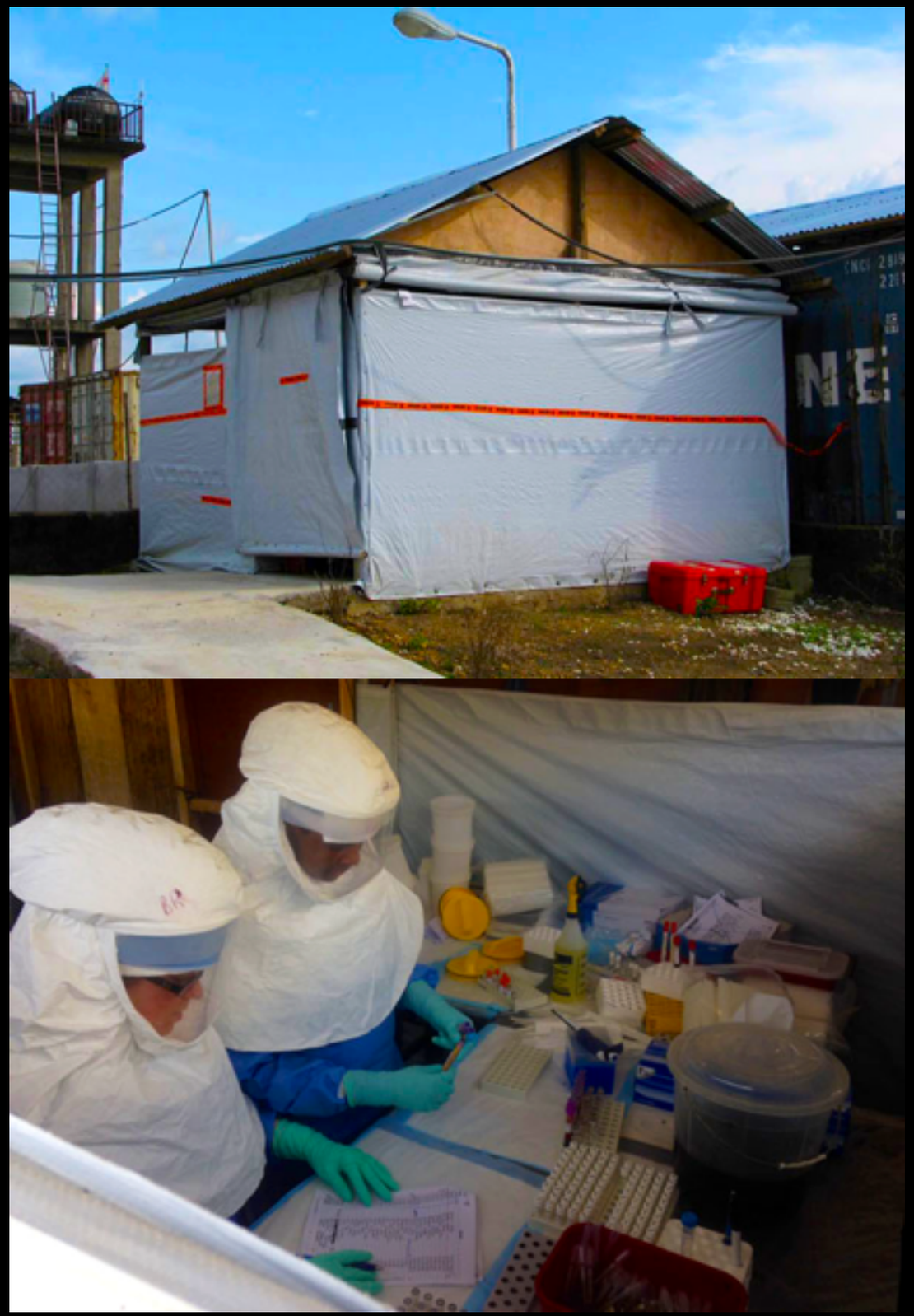
Sample workflow





UK VS US APPROACH

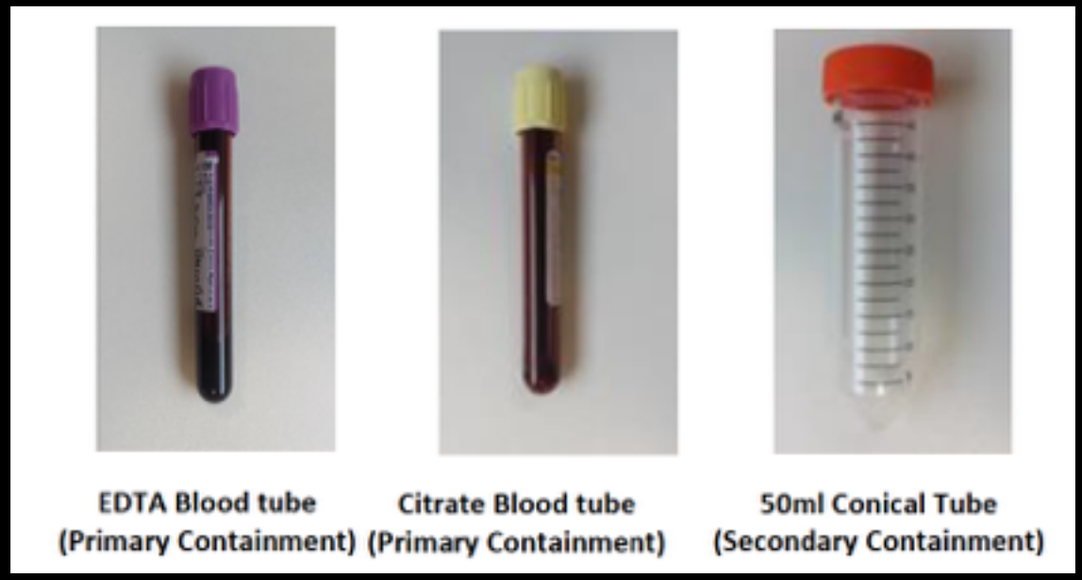
- Isolation of the worker
- Faster approach
- More user dependent
- Staff typically experienced BSL4 workers

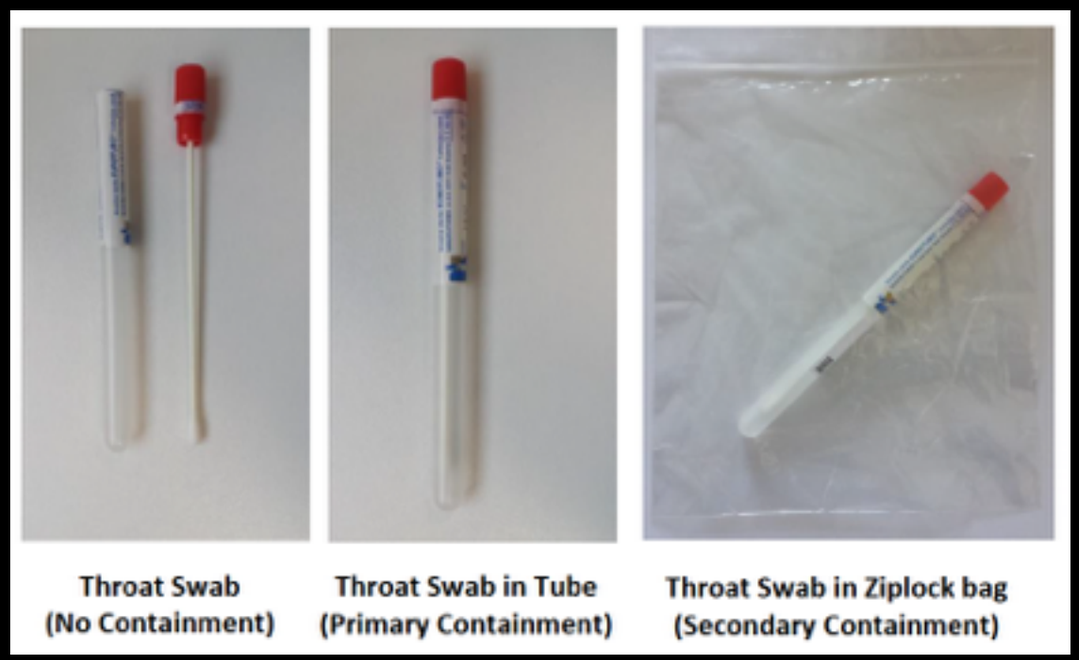


CDC Lab Bo, Sierra Leone

SAMPLE PROCESSING

- Blood and swabs
- Primary container and typically double zip-lock
- Samples sometimes not correctly packaged
  - *Needles*
  - *Lack of secondary containment*
  - *Leaking samples*





SOPs and more SOPs!

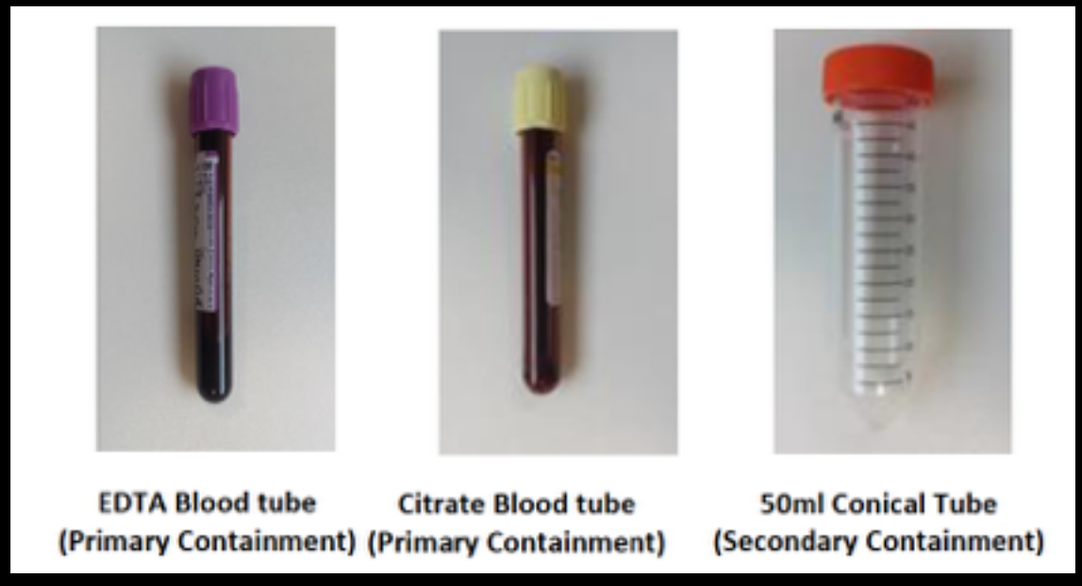
- Risk Assessment Draft5.pdf
- SD EDL 001 Sample tracking form v1 0.pdf
- SD EDL 002 Guidance Sample tracking form v1 0.pdf
- SD EDL 003 Sample referral form v1 0.pdf
- Signed top sheets of v1 0 SOPs.pdf
- SOP EDL 001 Sample Reception v1 2.pdf
- SOP EDL 002 Maintenance Use of flexible film isolator SOP v1 1.pdf
- SOP EDL 003 Sample handling in flexible film isolator v1 0.pdf
- SOP EDL 004 diagnostic lab Malaria BinaxNOW test v1 1.pdf
- SOP EDL 005 Manual extraction of viral RNA using QIAamp kit v1 1.pdf
- SOP EDL 006 Automated RNA extraction using EZ1 v1 0.pdf
- SOP EDL 007 UK EVD diagnostic lab Altona assay on SmartCycler v1 0.pdf
- SOP EDL 008 Isolator fumigation v1 1.pdf

SOP EDL 001, APPENDIX 1: **SAMI**

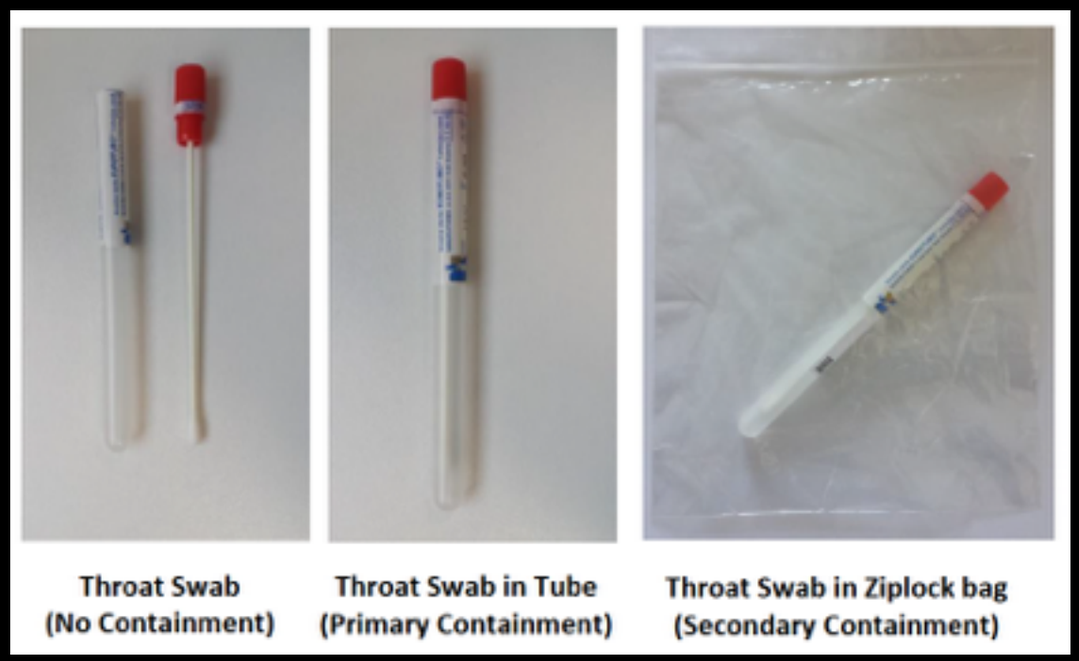
CHECK	ACTION	
Is there evidence of contamination e.g. obvious spill or spots of blood on referral form?	No Continue to next step	Yes Return referral form (in red plastic wallet) and the zip-lock bag containing the samples to the referring ETU. Request fresh form.
On visual inspection of each zip-lock bag is there evidence of leakage from the primary container?	No Continue to next step	Yes Return zip-lock bags containing any leaking samples together **with the relevant referral form** to the referring ETU for disposal. Request fresh samples.
Does zip-lock bag of samples have a corresponding referral form?	Yes Continue to next step	No Return bag of samples to referring treatment unit for correction. All samples need a referral form and vice versa
Does zip–lock bag contain the correct number and type of clinical samples as indicated on the accompanying sample request form?	Yes Continue to next step	No Keep samples that have been sent & COPY of referral form. On reverse of original form, note the missing samples and send back with the carrier/porter to request the missing sample(s).
Are all the samples in a primary AND secondary container (screw-top tube OR sealed plastic bag) inside the zip-lock bag?	Yes Continue to next step	No Incorrectly packed samples should be returned with the relevant referral form to the referring treatment centre for re-packaging.
Does the patient name and patient ID on the sample referral form **exactly match** what is written on the secondary sample tube(s)?	Yes Continue to next step	No Return all the samples from this patient together with the referral form, to the referring treatment unit, asking for clarification.
Is **each** primary sample in a separate secondary container within the zip-lock bag OR are samples for different workstreams in the same secondary container?	Yes Continue to next step. Samples can be sorted at sample reception.	No: continue to next step BUT Samples will have to be sorted in the flexible film isolator and transferred to the relevant workstream.

SAMPLE PROCESSING

- Secondary container wiped prior to opening in a FFI for sorting



- 10 minute contact time 5,000 ppm chlorine



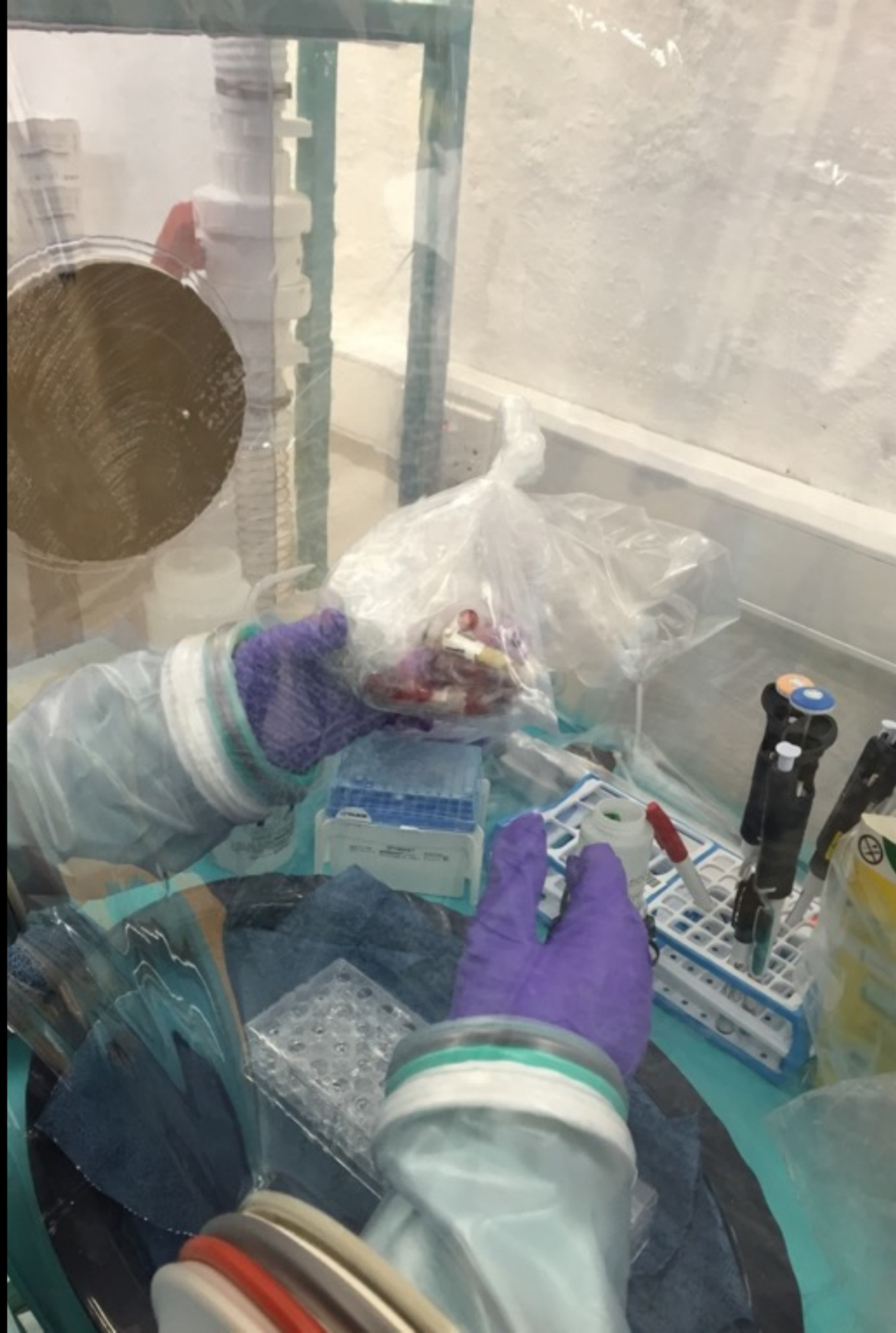
CONTROL MEASURES

- Isolation
  - Multiple layers of containment of primary samples
  - Use of flexible film isolators

- Chlorine (and plenty of it)
  - 5,000 ppm for dunk buckets and floor washing
  - 10,000 ppm for inside isolators
  - 500 ppm for hand wash

SAMPLE INACTIVATION

- Qiagen viral RNA mini preparation kit
- Guanidinium thiocyanate and ethanol
- Automated extractions included heat treatment 15 minutes
- Removal from FFI following inactivation and 10 minute contact with 10,000 ppm for external surfaces of tubes



CHALLENGES

- Logistics
- Lack of water
- Haztabs stopped working - provided with powder but no weighing scales and no way to measure ppm
- Impact of chlorine on individuals
  - floor washing
  - piped chlorine
  - revision of SOP
- Stress, tiredness

IN HINDSIGHT - WHAT WERE THE SIGNIFICANT HAZARDS?

- Road Travel

- Electrocution/Fire

- Malaria

- Psychosocial

- Food poising

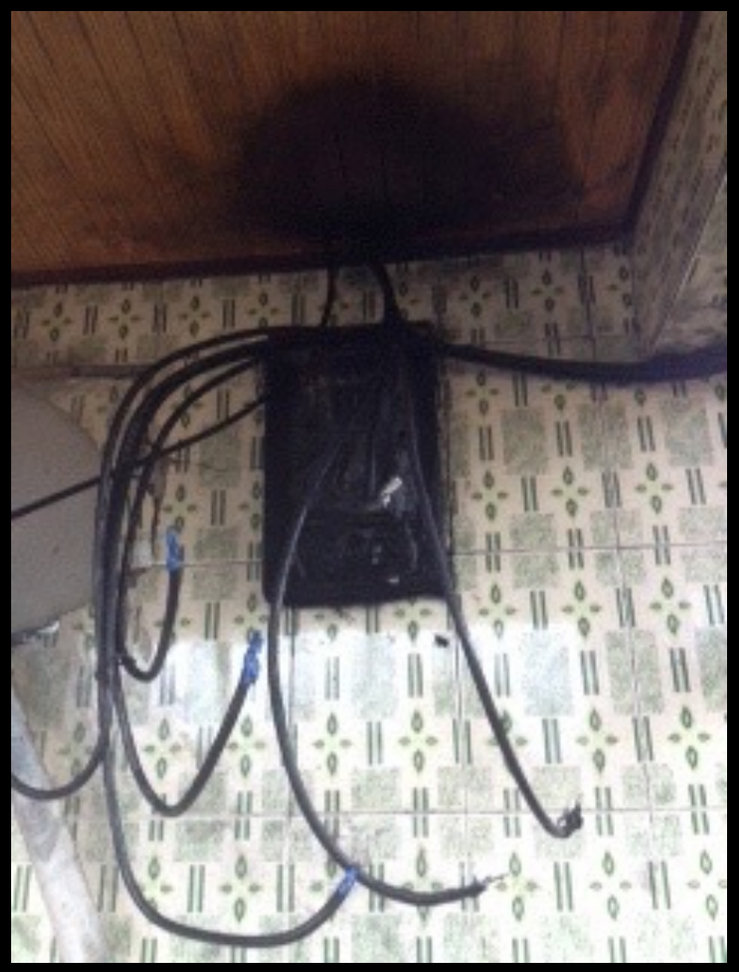
- Ebola

ROAD TRAVEL

- Poorly maintained vehicles
- Poorly maintained roads
- No lighting
- *No rules!*
- *Control measures:*
  - *Limited travel at night*
  - *Use of local drivers*
  - *Use of "well-maintained" vehicles*

ELECTROCUTION & FIRE

- Most electricians not “classically trained”
- Nothing is earthed correctly
- Control measures
  - Common sense
  - Always wear shoes
  - Provision of fire alarms
  - Identification of hazards



IN HINDSIGHT - WHAT WERE THE SIGNIFICANT HAZARDS?

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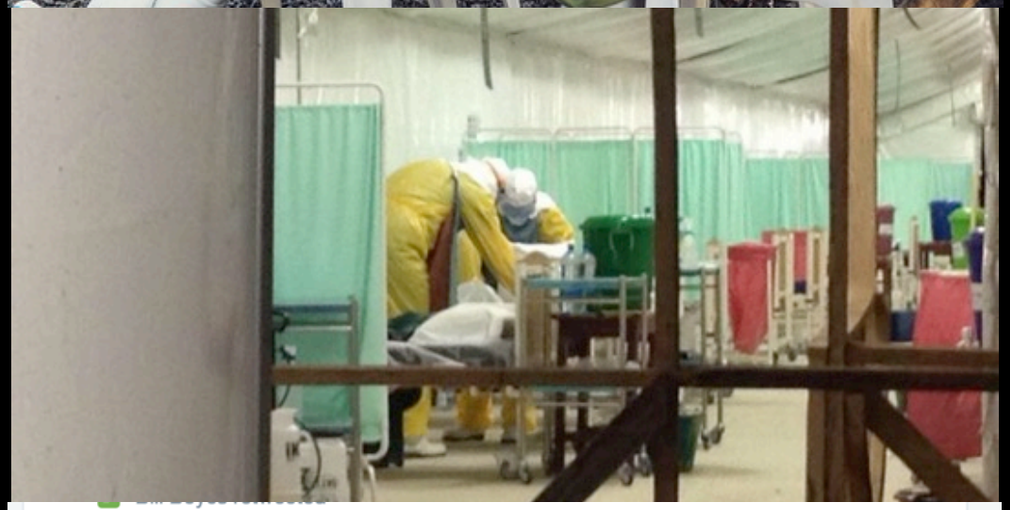

SUMMARY

- The UK provided invaluable lab support during the response
- Staff came from varied background so strict SOPs were vital
- Risk management in the field was challenging given the changing environment
- Ebola was probably the least hazardous thing we had to deal with
- Having recently established a research facility - we are encountering an entire new set of challenges

CREDITS

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WHO

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Clinicians, nurses, scientists, PHE volunteers who helped run diagnostic and care facilities

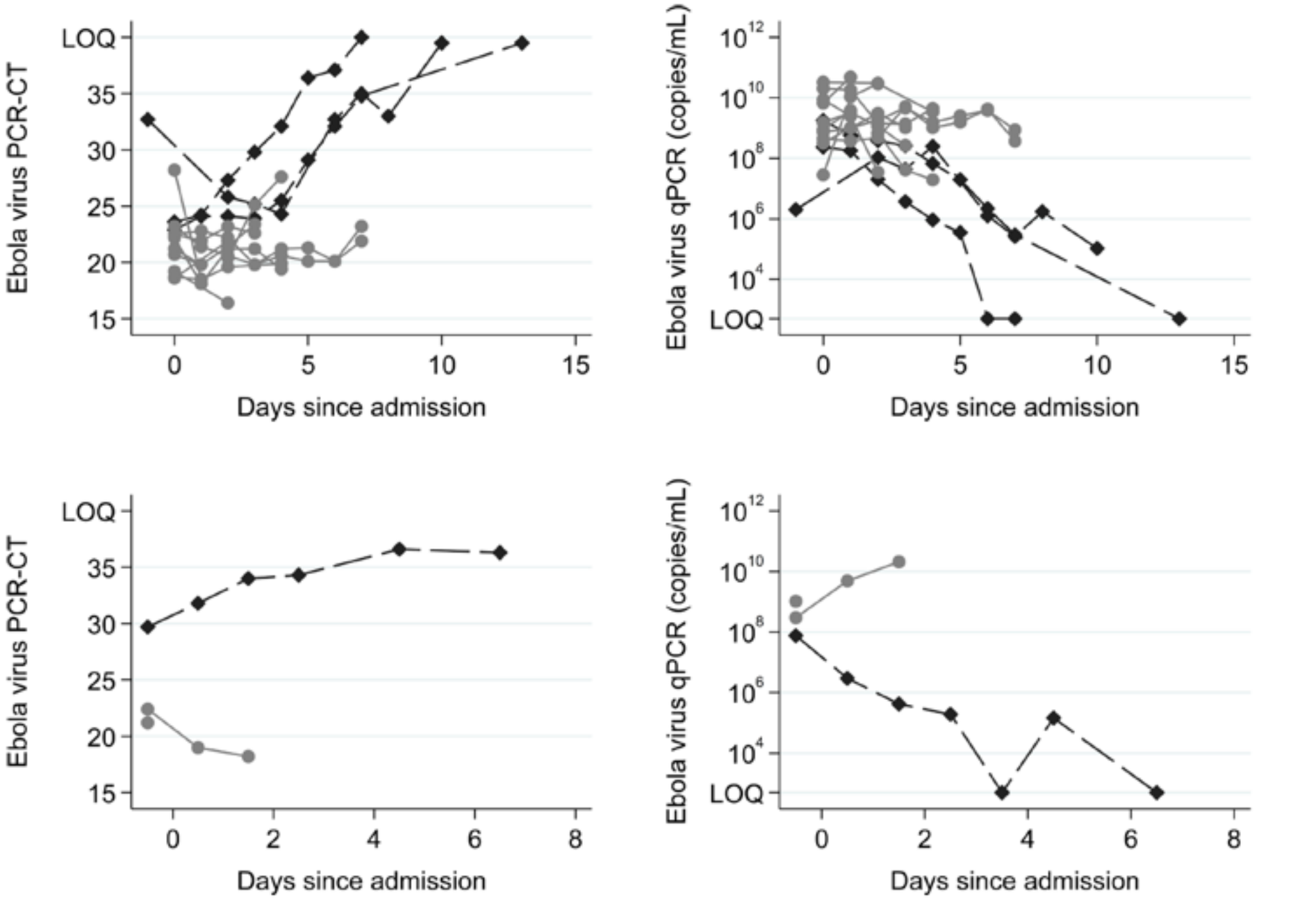

Fig 3. Ebola virus RT-PCR cycle threshold values and RNA copies/ml over time. Top row: TKM-130803 recipients. Bottom row: Observational patients. RT-PCR Ct upper limit of quantitation (LOQ) = 40. RT-qPCR lower limit of quantitation = 1,000 genome copies. The Ebola virus RT-qPCR quantification is expressed as the number of genome copies/millilitre of plasma. Black diamonds denote results for survivors. Grey circles denote results for non-survivors.

doi:10.1371/journal.pmed.1001997.g003

DUNNING J, SAHR F, ROJEK A, GANNON F, CARSON G, IDRISS B, ET AL. (2016) EXPERIMENTAL TREATMENT OF EBOLA VIRUS DISEASE WITH TKM-130803: A SINGLE-ARM PHASE 2 CLINICAL TRIAL. PLOS MED 13(4): E1001997. DOI:10.1371/JOURNAL.PMED.1001997