

Challenges & Opportunities of Vaccination for Ebola in Africa

Seminar on Infectious Diseases and Infection Control Management

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**LIBERIA:
BRIEF COUNTRY PROFILE**



Liberians: Harness Local Expertise



Dr. Fatorma K. Bolay



Dr. Garfee Williams



Dr. Moses Massaquoi



Dr. Mosoka Fallah



Dr. Tolbert Nyenswah



Dr. Joel Jones



Dr. Eugene Dolopei



Dr. Stephen B. Kennedy



Dr. Emmet Dennis



Mr. Luke Bawo



Dr. Saye Bawo



Cllr. Abia G. Williams



Dr. Rev. Tijli Tye



Dr. Francis Kateh



Mrs. Gloria Mason-Ross



EBOLA IN LIBERIA

Chronology of Key Events in Liberia

First case of confirmed EVD	30 March 2014
First District affected by EVD	Foya, Lofa County
Presidential Declaration /Launch	State of Public Health Emergency Declared in May 2014
Month with the highest number of cases	October 2014 (Cases 2,200 / Death 1,101)
Cases & (deaths) in Health Workers	378 (192): First Responders
Ebola Free Declaration & Certification by WHO	May 9, 2015

30 March 2014: EVD Confirmed in Liberia



EBOLA OUTBREAK LEADS LIBERIA TO WAR; 90-DAYS SUSPENSION OF RIGHTS AND PRIVILEGES

STATE OF EMERGENCY

"The Ebola virus disease the ramifications and consequences thereof now constitute an unrest affecting the existing security and well being of the republic, amounting to a clear and present danger. The government and people of Liberia require extraordinary measures for the very survival of our state and for the protection of the rights of our people. Therefore, and by virtue of the power vested in me, as President of the Republic of Liberia, I, Ellen Johnson Sirleaf, President of the Republic of Liberia in keeping with Article 80 a and b of the constitution of the Republic of Liberia, hereby declare a state of emergency throughout the Republic of Liberia effective as of August 8, 2014 for period of 90 days".
President Ellen Johnson-Sirleaf.



Sub-Regional Spread of EVD Outbreak

December 2013

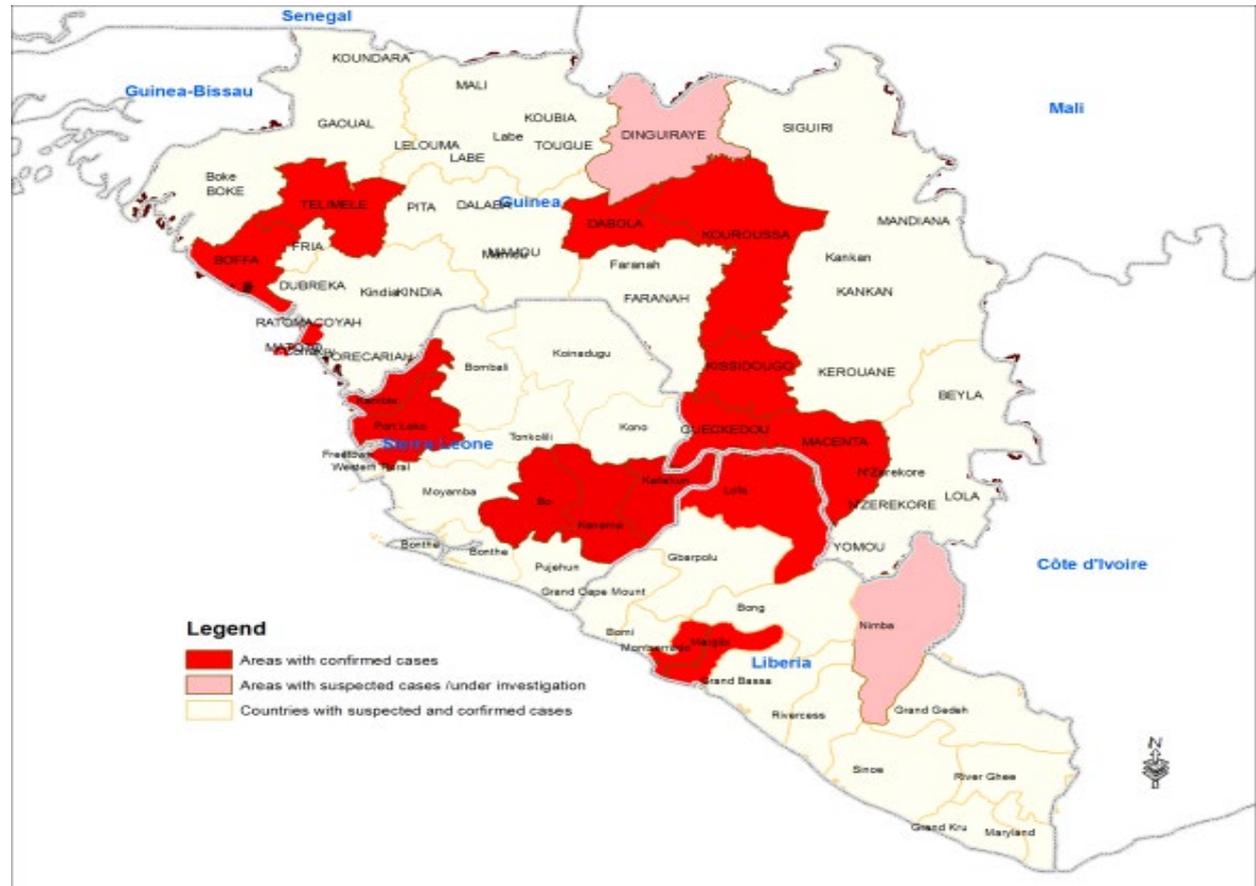
Guekedou, Guinea

March 2014

Liberia

May 2014

Sierra Leone



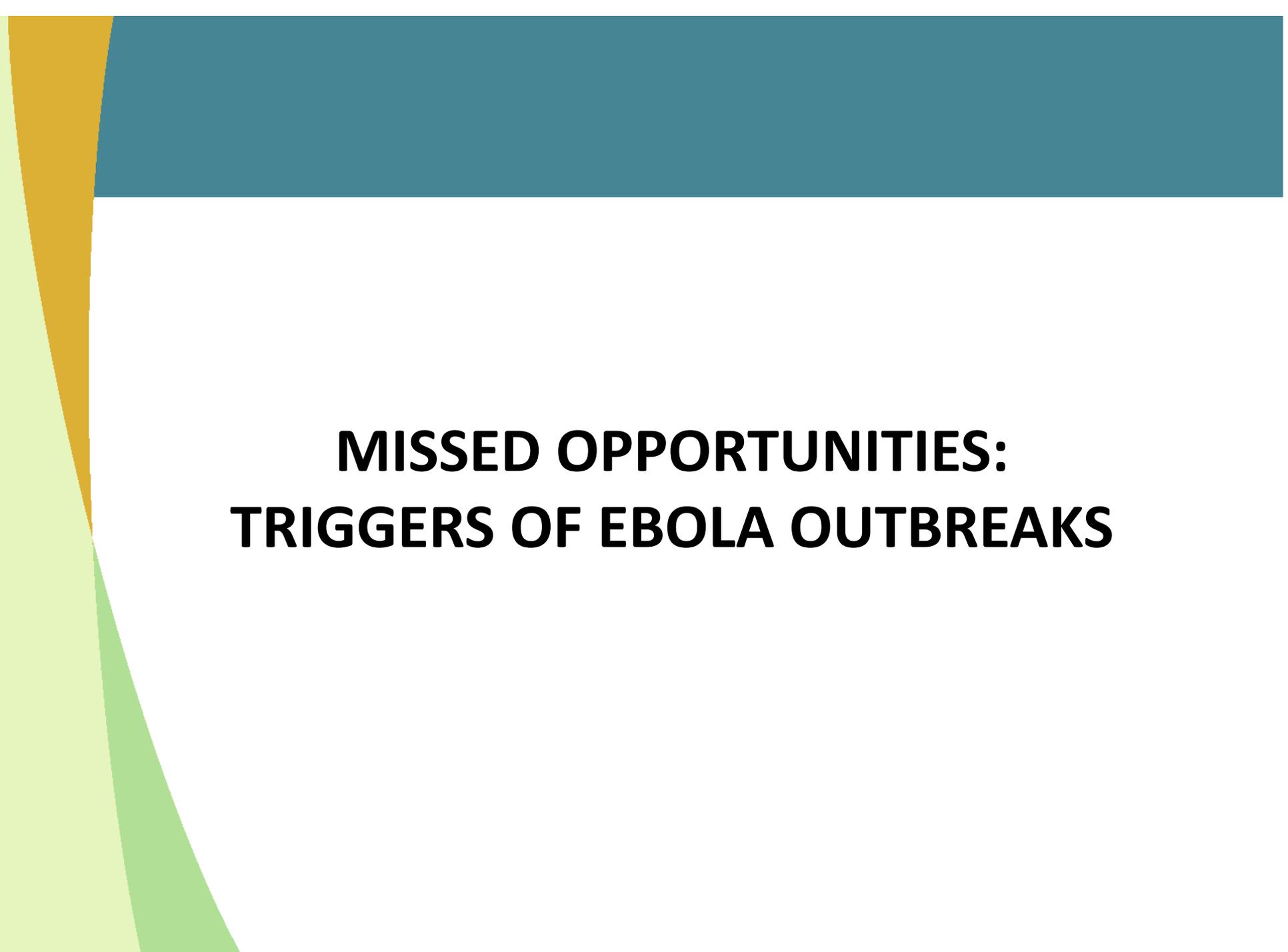
**60 sites
within 6
months**

Vast Spatial Distribution

Contexts for Sub-Region Ebola Outbreak

- Post conflict environment in affected countries
 - civil wars in Sierra Leone and Liberia
 - Internal conflict in Guinea
- Porous borders between countries
- Inefficient healthcare system
- No institutional memory of Ebola in West Africa
- Health workers not trained to respond and protect themselves
- High level of community resistance to the Ebola outbreak response





MISSED OPPORTUNITIES: TRIGGERS OF EBOLA OUTBREAKS

Bulletin of the World Health Organization

Editorials

The Ebola epidemic: a transformative moment for global health

Stephen B Kennedy^a & Richard A Nisbett^b

- “This region is characterized by weak system of government and health care delivery, high rates of illiteracy, poverty, and distrust of the government, and extreme population mobility across porous, artificial boundaries”.
- “Such epidemics threaten not just the world’s most resource-poor settings, but also the entire global community”.

Vulnerability Zone

Pre-EVD Laboratory System and related challenges in Liberia - Kennedy, SB et al, Afr J Lab Med, 2016

“...laboratory system was duplicative, fragmented and minimally coordinated”.

“...challenges included limited trained human resource capacity, inadequate infrastructure & a lack of coordination.”

Ebola virus & malaria parasite positivity: a febrile illness quagmire - Massaquoi, MBF & Kennedy, SB Lancet Infect. Dis, 2017

“...differential diagnoses and management of febrile illnesses will remain a crucial challenge in west Africa”.

The New York Times

The Opinion Pages | OP-ED CONTRIBUTORS

Yes, We Were Warned About Ebola

By BERNICE DAHN, VERA MUSSAH and CAMERON NUTT APRIL 7, 2015

“The conventional wisdom among public health authorities is that the ebola virus... was a new phenomenon, not seen in West Africa before 2013”.

“The conventional wisdom was wrong”.

1978-1979

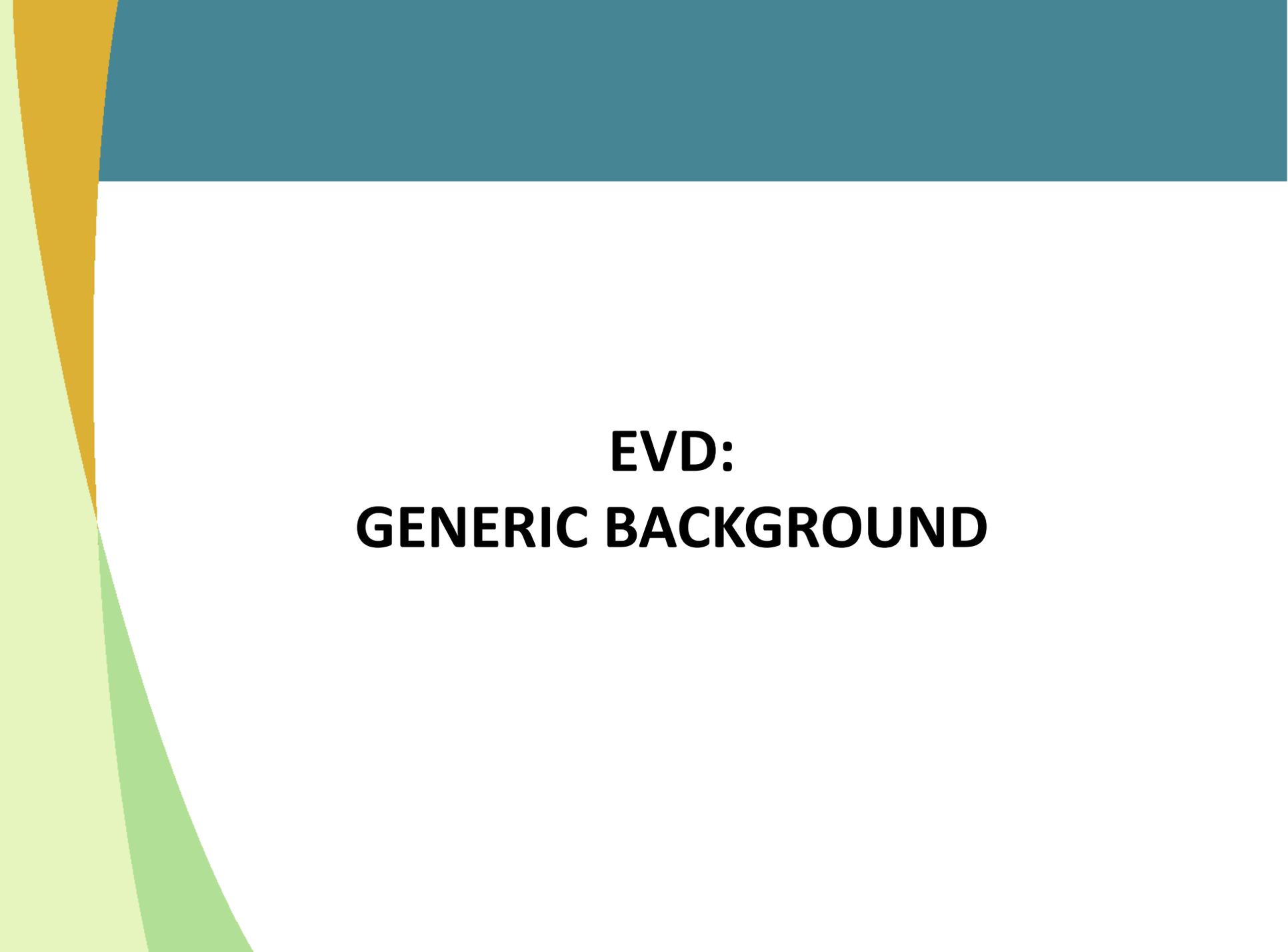
- 433 Liberian samples collected
- Retrospectively analyzed
- 6% (26) had antibodies to EVD

1986

- 3 Studies published
- Increased prevalence of EVD antibodies
- 10.6%, 13.4% & 14%, respectively



CLINICAL RESEARCH: REGIONAL INEQUALITY

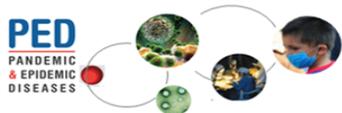


**EVD:
GENERIC BACKGROUND**

Viral Hemorrhagic Fevers (VHFs)

Arenaviridae	Bunyaviridae	Filoviridae	Flaviviridae
Lassa HF	Hantavirus Genus	Ebola	Dengue
Junin Virus	Congo-Crimean HF	Marburg	Yellow fever
Machupo Virus	Rift Valley Fever	Lloviu	Kyasanur
Guanarito Virus			Omsk
Sabia Virus			

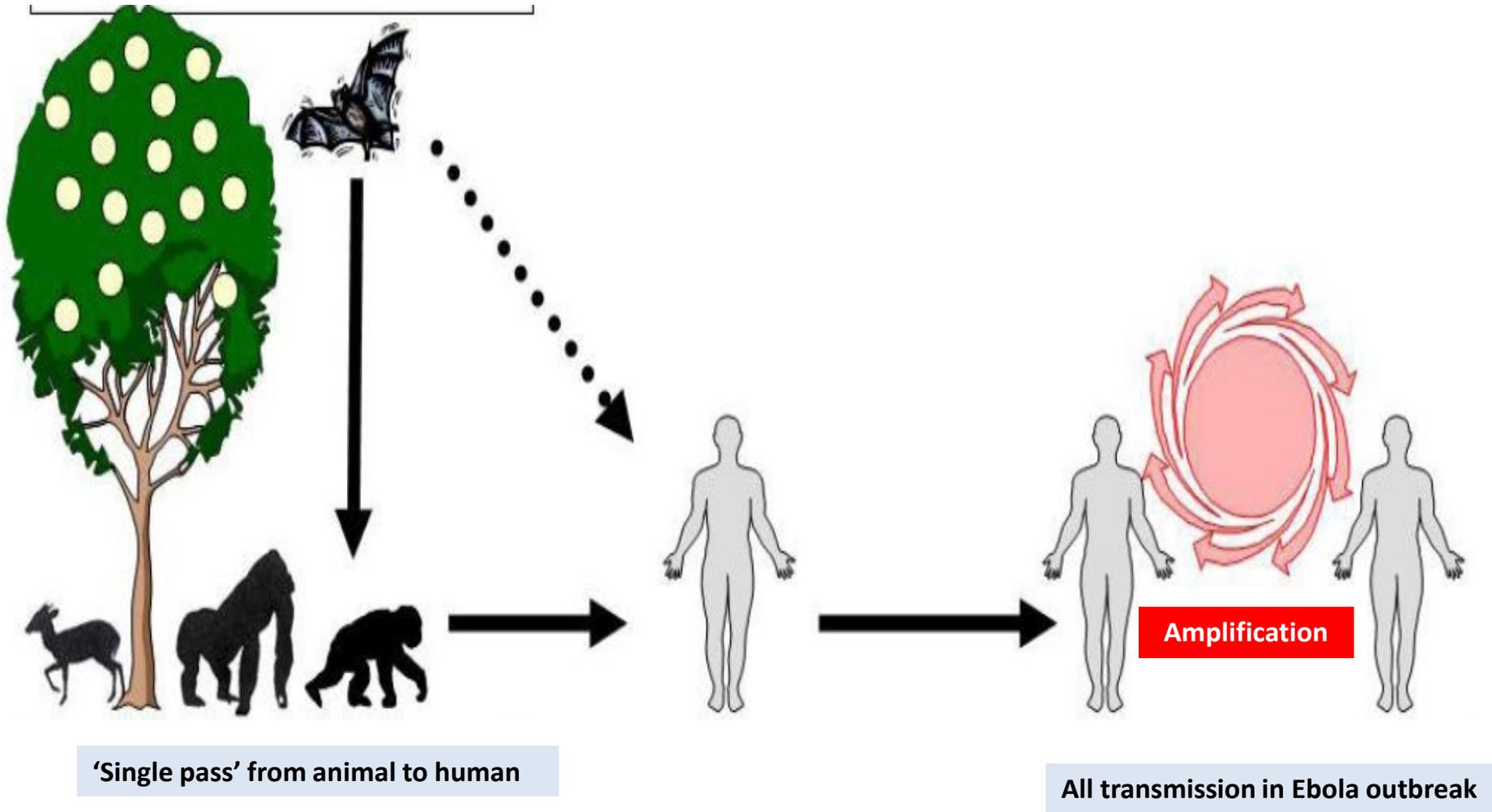
Category A Priority Pathogens



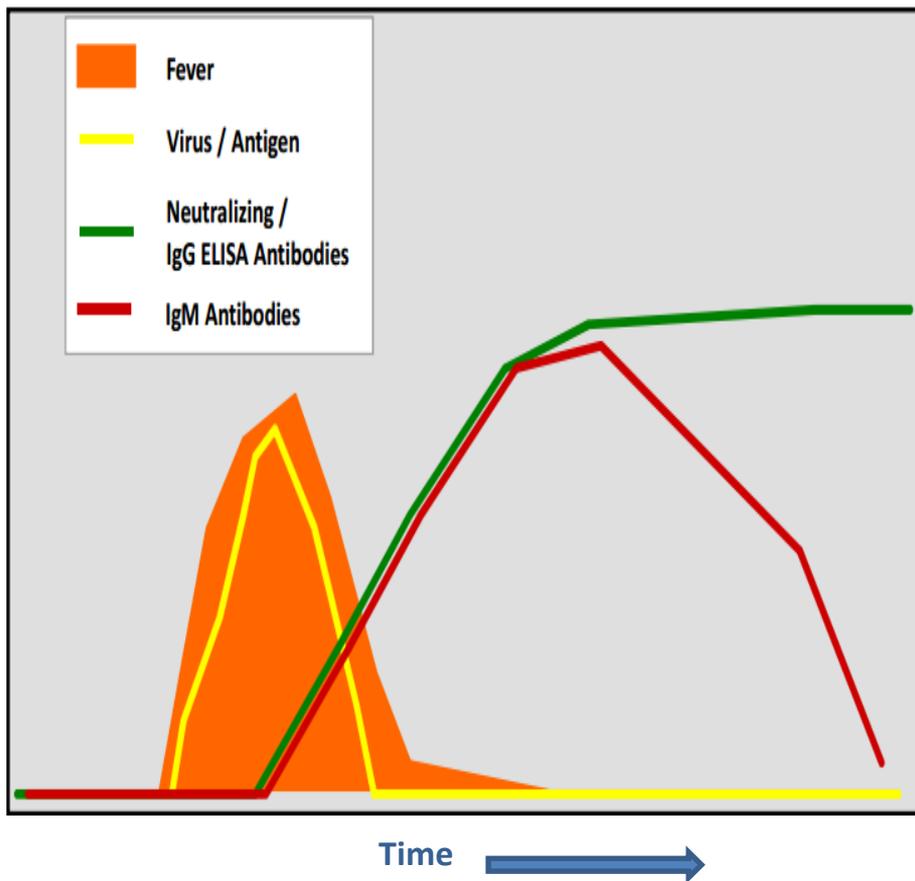
Strains of Ebola Virus

- Ebola Zaire
- Ebola Sudan
- Ebola Bundibugyo
- Ebola Ivory Coast (Tai Forest)
- Ebola Reston
- Ebola Bombali (Angolan free tailed bats)

Filovirus Cycle of Transmission



Ebola Symptoms & Immune Response



Adapted from T Ksiazek, CDC

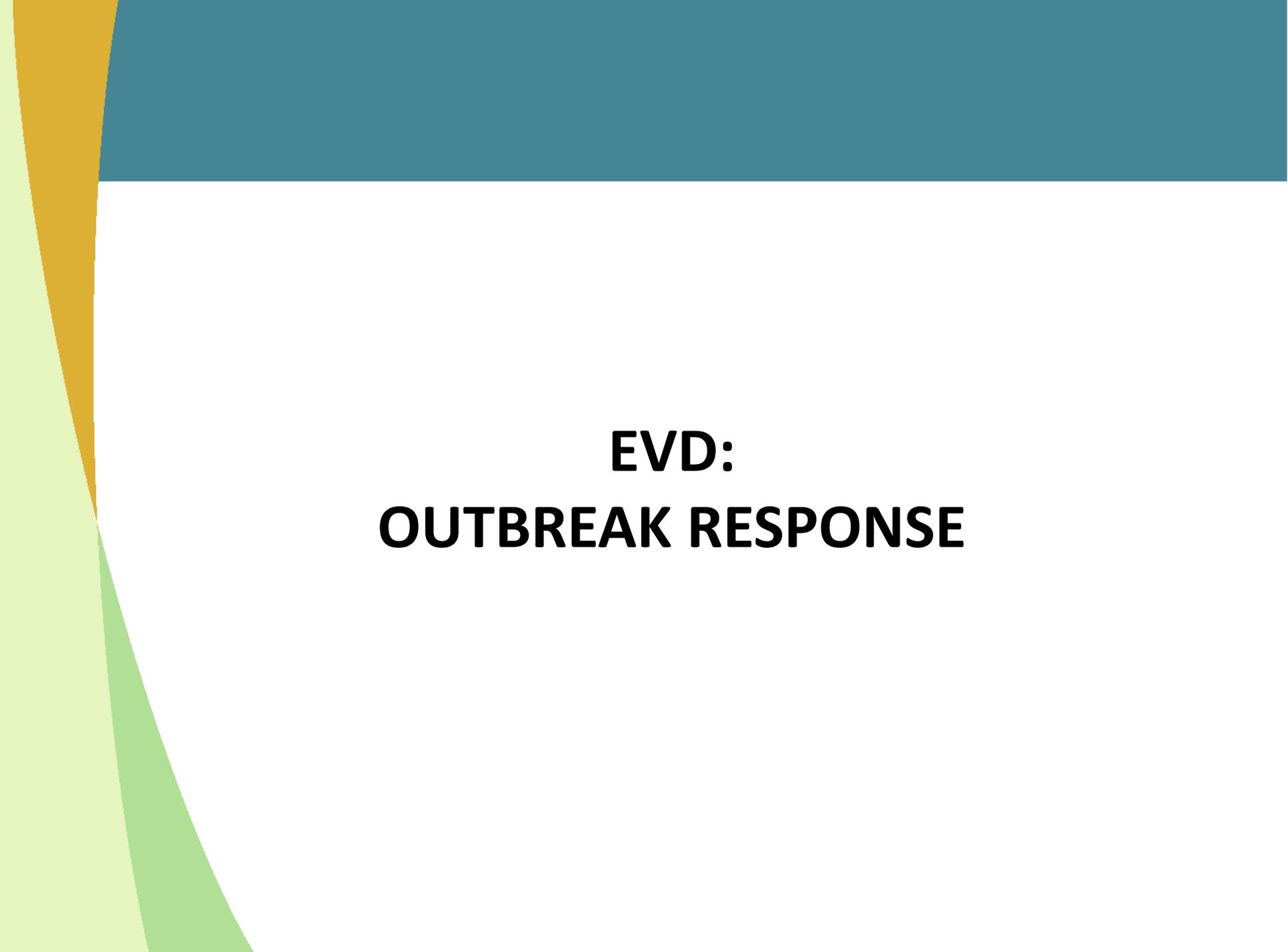
- Subclinical period for 1-3 days before symptoms arise
- Peak of viral load tracks with peak of fever
- Persistent positive PCR can occur despite resolution of symptoms
- Immune response
 - Robust IgG response seen in patients with more severe disease
 - Detection can take several weeks after onset of symptoms
- Ebola diagnosis depends on:
 - Detecting the virus during the acute phase of the diseaseOR
 - Measuring the host's specific immunological response during illness and convalescence

How is Ebola Virus Diagnosed in the Laboratory?

1. **RT-PCR:** rapid, more sensitive than antigen detection ELISA, and provides specific identification of genetic fragments of the virus
2. **ELISA:** allows the detection of the viral **antigen or antibody** on inactivated specimens, such as blood, serum, or tissue suspensions
3. **Virus isolation:** requires a Biosafety Level-4 laboratory and can take several days
4. **Immuno-histochemical staining and histopathology:** On collected tissue or dead animals, localizes viral antigen

EXPANDED TESTING FOR SUSPECTED CASES AND DEAD BODIES
The timing for specimen collection, testing and disclosure of Lab results improved with the establishment of mobile labs at strategic locations in the country



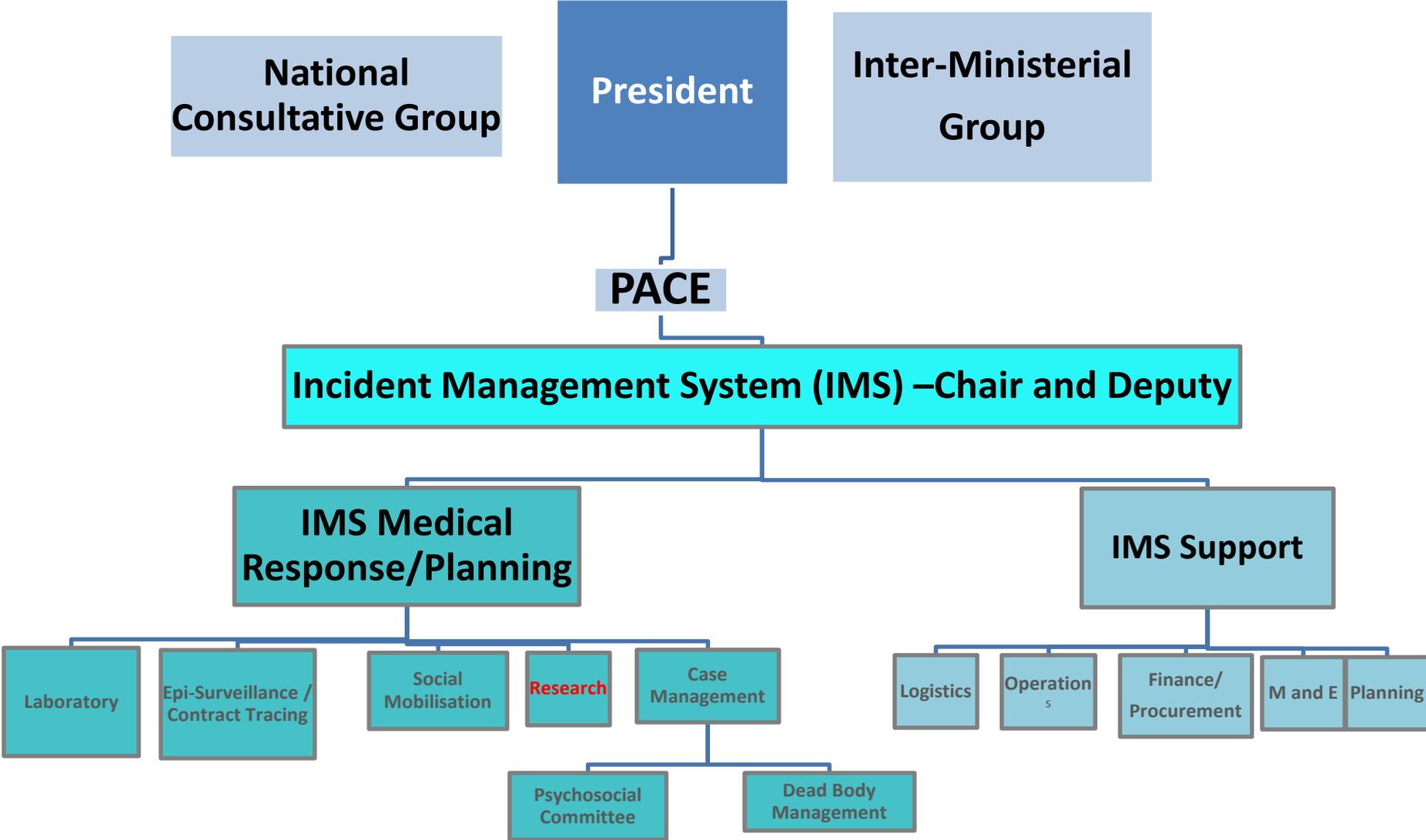


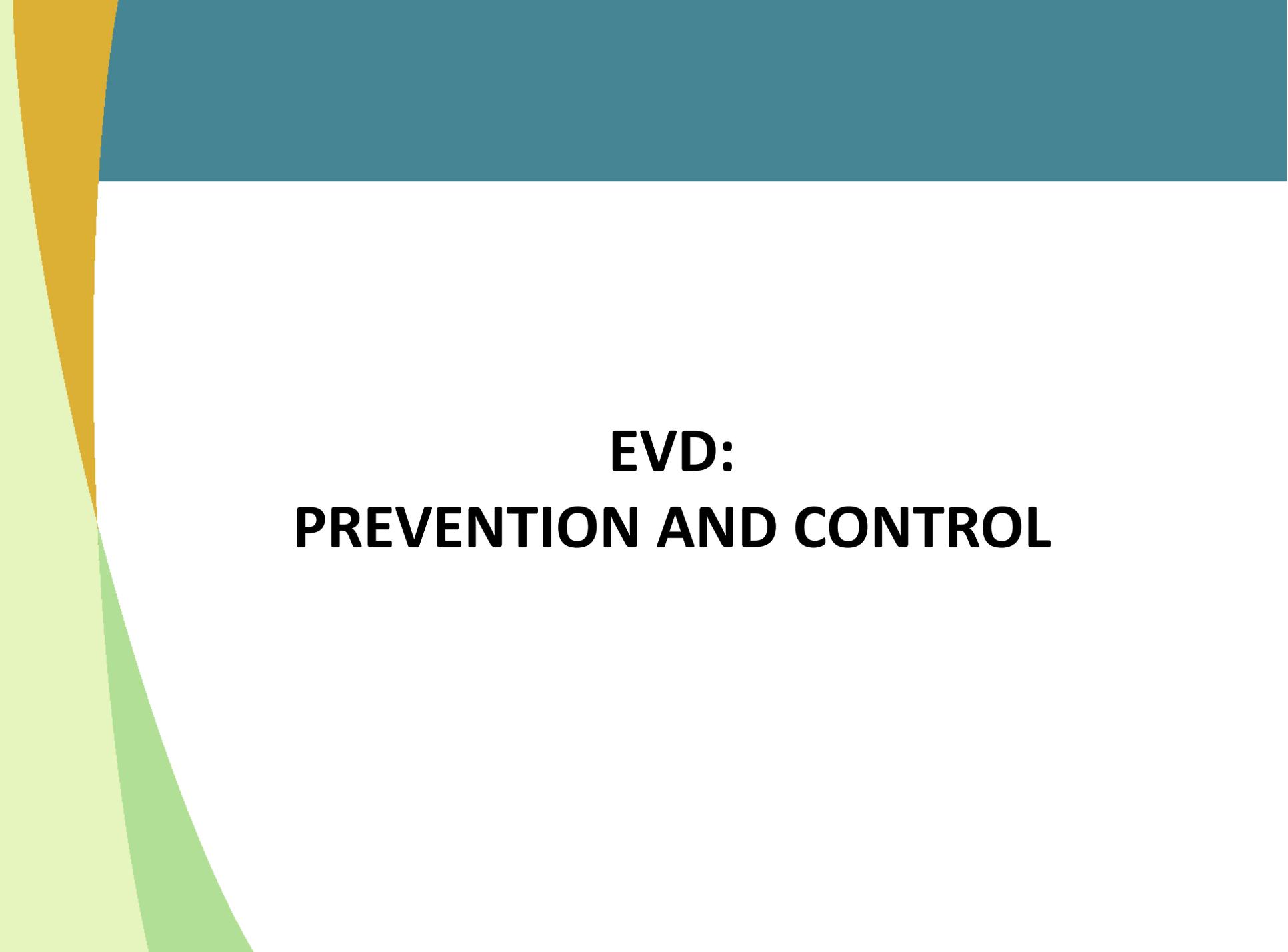
**EVD:
OUTBREAK RESPONSE**

Coordination

- Ebola outbreak response is **complex** with many interdependent activities.
- Different organizations doing case investigation, contact tracing, case management, care of the sick, surveillance, health structure support, safe burials, health promotion, laboratory diagnostics, and household decontamination
- Must ensure that everything is done, and done well.
- Frequent coordination meetings needed.

Coordination, Control and Command Center





**EVD:
PREVENTION AND CONTROL**

Outbreak Control Interventions

Prevent Transmission = prevent new cases

1. Find and identify cases
2. Separate them in treatment center
3. Contact Tracing & early referral (Surveillance)
4. Community mobilization
5. Reduce viral exposures

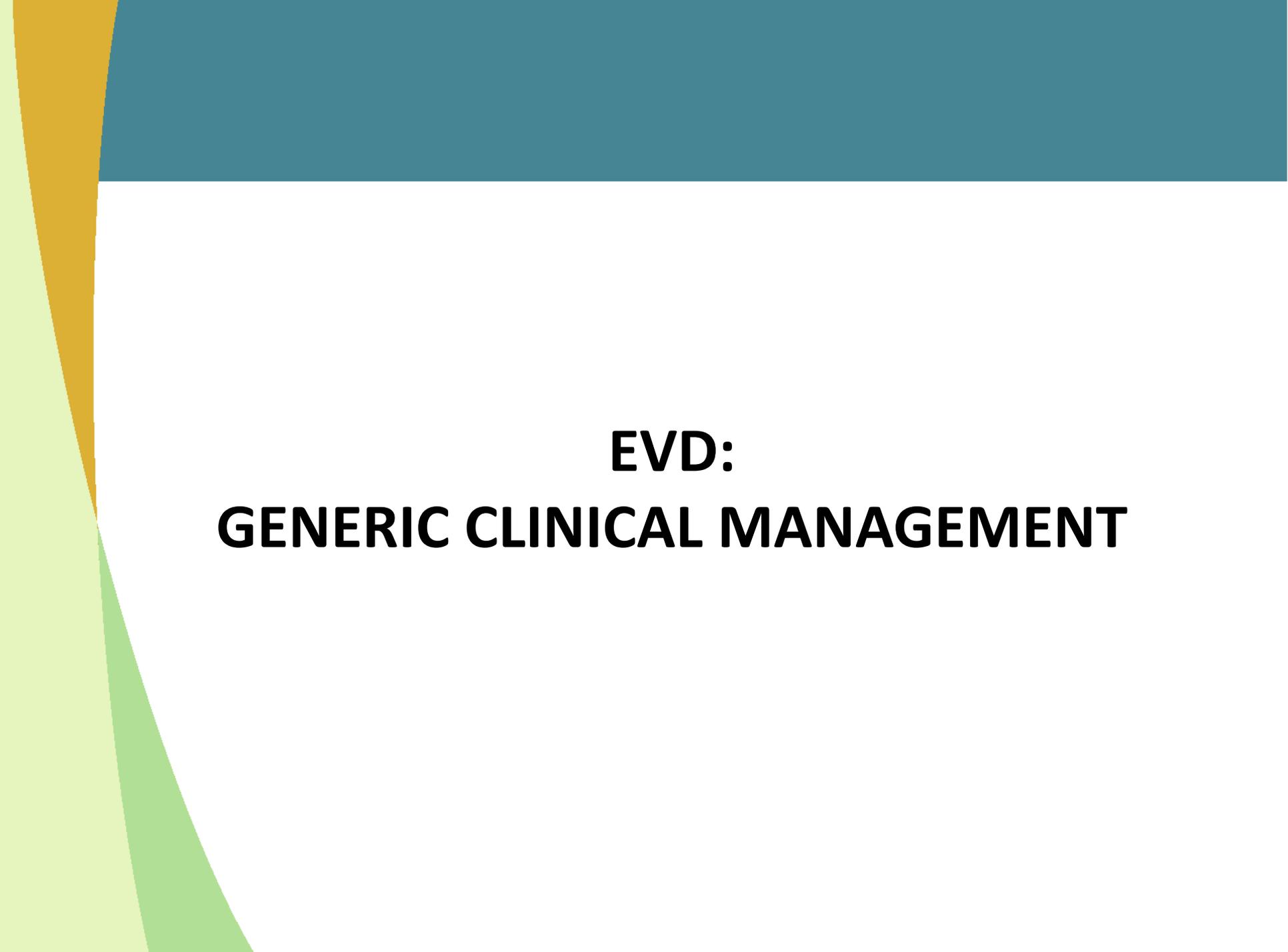
Personal Protective Equipment Policies and Equipment Vary by Organization and Site



MSF PPD: Used in Guinea



WHO PPD: Used in Liberia



**EVD:
GENERIC CLINICAL MANAGEMENT**

Case Management: Ebola Treatment Units (ETUs)

- Comfortable ETUs: beds, Fans, Tables, Televisions, Toiletries, etc.
- Documentation: Scanners for patient records.
- Build Trust: Families see sick relatives from distance and talk.
- Laboratory support: linked to ETU for EVD Testing.
- Staff support: Empathy, identification, medical support, etc.



- **Clinical management → supportive, but intensive**
- **Especially important:** Fluid and electrolyte replacement for diarrhoea and vomiting
- Altered mental status in some patients leads to challenges in care

**Clinical Management of Patients
with Viral Haemorrhagic Fever:**

A Pocket Guide for the Front-line Health Worker
30 MARCH 2014

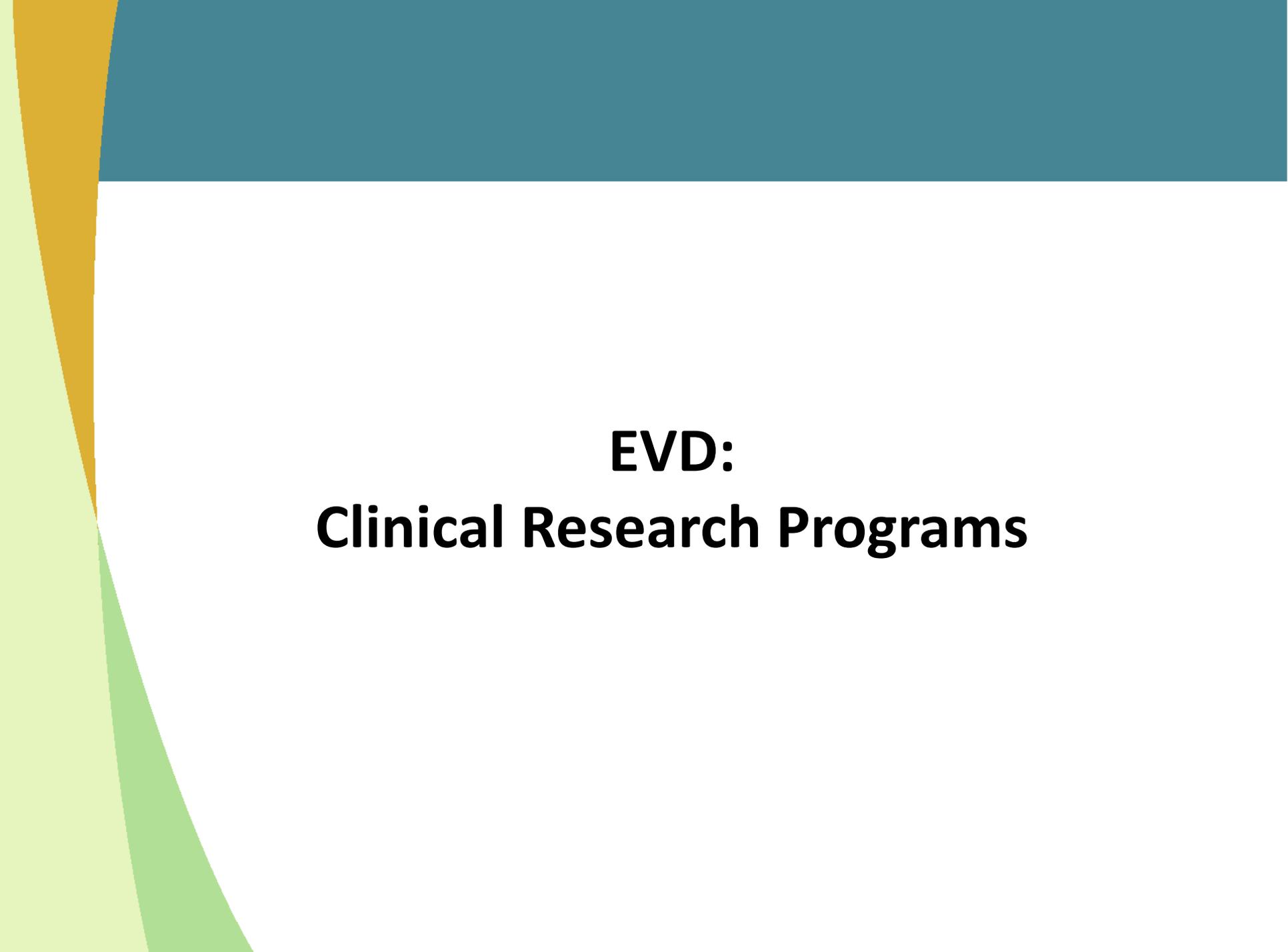


Interim emergency guidance- generic draft
for West African adaptation



Specific Ebola Treatments

- Convalescent plasma as post exposure prophylaxis:
 - Results mixed, unclear benefits
- Monoclonal Antibodies (MAb)
 - ZMAPP: Triple Monoclonal Antibody
 - Remdesivir: Antiviral Agent
 - MAb114: Single Monoclonal Antibody
 - REGN-EB3: Triple Monoclonal Antibody



**EVD:
Clinical Research Programs**

BIRTH OF PREVAIL

PREVAIL began in mid-2014 at the request of Liberia's former Minister of Health (MoH), Dr. Walter T. Gwenigale.

Key was to develop partnership between the US DHHS and GoL's MoH for clinical research on promising therapeutic, diagnostic & vaccine products.

US Sec DHHS Sylvia Burwell, responded favorably and committed to "combat the epidemic".

Dr. H. Clifford Lane, Deputy Director, NIAID represented the US DHHS research efforts.

Dr. Stephen B. Kennedy, PI, UL-PIRE Africa Center, represented Liberia's MoH research efforts.

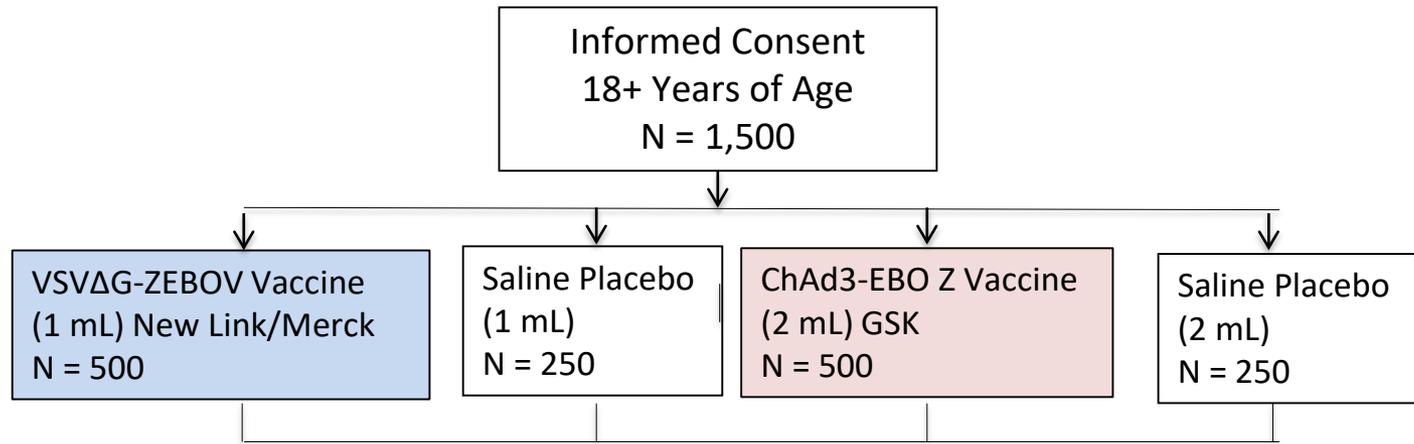
Partnership for Research on Ebola Virus in Liberia

- PREVAIL I: Phase 2 EVD Vaccine RCT
- PREVAIL II: ZMAPP RCT
- PREVAIL III: Natural History of EVD Survivors
 - Birth Cohorts
 - Semen
 - Vagina
 - Neurological
- PREVAIL IV: Gilead Viral Persistence RCT
- PREVAIL V: Multi-Country EVD Vaccine RCT
- PREVAIL VI: Genomic Study
- PREVAIL VII: Ophthalmology Study
- PREVAIL VIII: HIV+ Observational Cohort Study

PREVAIL I Team



PREVAIL I Design



Antibody testing at Vaccination, Week 1, Month 1, Month 6 and Month 12; also visits at Months 2, 4, 8, and 10.

Vaccinations for Phase 2 began 2 February and ended 30 April 2015
Long-term follow-up for immunogenicity testing.

SB Kennedy et al., Clinical Trials, 2016
SB Kennedy et al., N Engl J Med, 2017

ORIGINAL ARTICLE

Phase 2 Placebo-Controlled Trial of Two Vaccines to Prevent Ebola in Liberia

S.B. Kennedy, F. Bolay, M. Kieh, G. Grandits, M. Badio, R. Ballou, R. Eckes, M. Feinberg, D. Follmann, B. Grund, S. Gupta, L. Hensley, E. Higgs, K. Janosko, M. Johnson, F. Kateh, J. Logue, J. Marchand, T. Monath, M. Nason, T. Nyenswah, F. Roman, E. Stavale, J. Wolfson, J.D. Neaton, and H.C. Lane, for the PREVAIL I Study Group*

PLOS ONE

RESEARCH ARTICLE

The impact of the 2014 Ebola epidemic on HIV disease burden and outcomes in Liberia West Africa

Soka J. Moses^{1*}, Ian Wachekwa^{2*}, Collin Van Ryn³, Greg Grandits³, Alice Pau⁴, Moses Badio¹, Stephen B. Kennedy¹, Michael C. Sneller⁵, Elizabeth S. Higgs⁴, H. Clifford Lane⁶, Mosoka Fallah⁴, Stephen A. Migueles⁴, Cavan Reilly^{6*}

ORIGINAL ARTICLE

A Randomized, Controlled Trial of ZMapp for Ebola Virus Infection

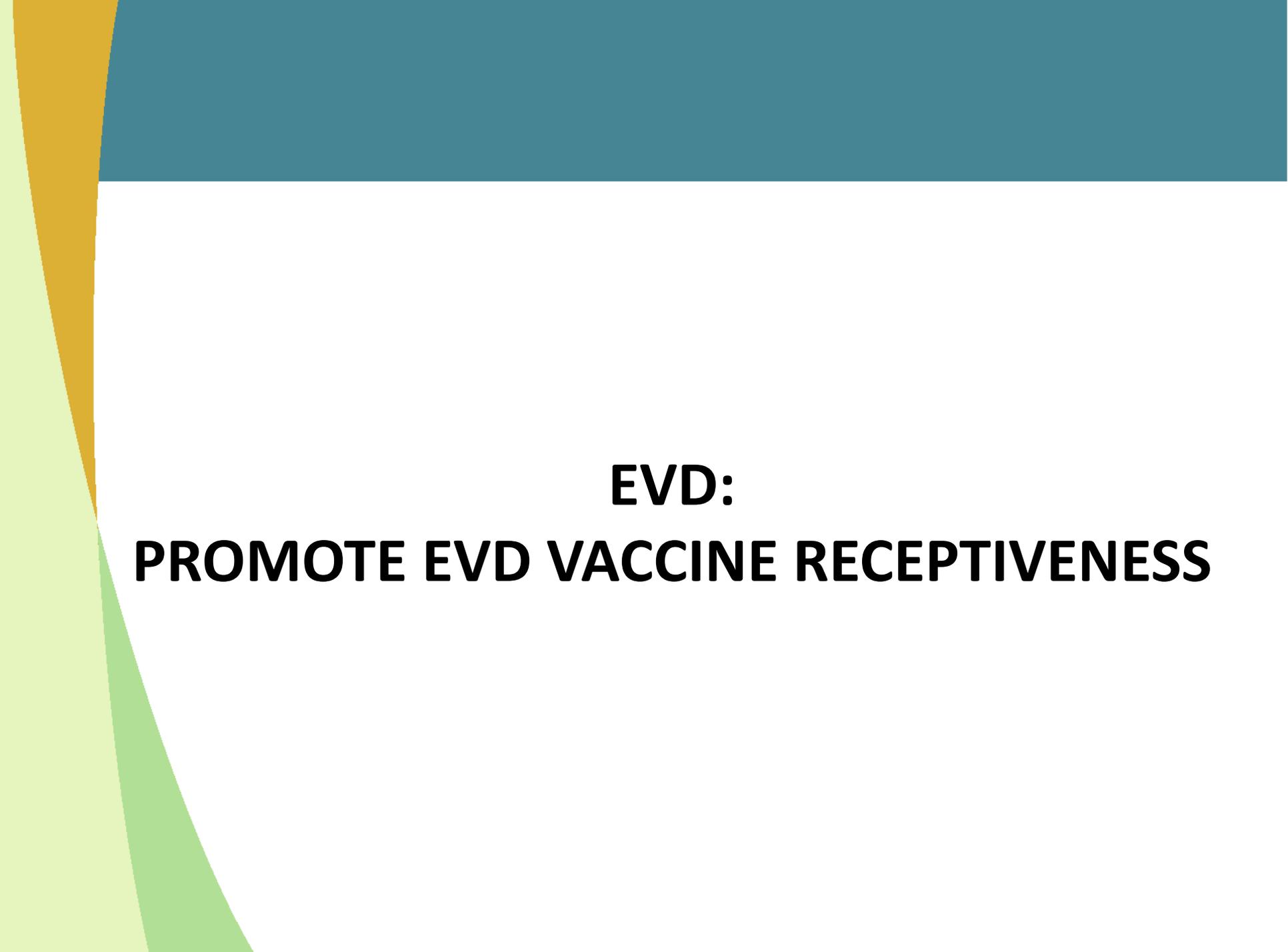
The PREVAIL II Writing Group, for the Multi-National PREVAIL II Study Team*

The Lancet Microbe

Estimation of the correlates of protection of the rVSVΔG-ZEBOV-GP Zaire ebolavirus vaccine: a post-hoc analysis of data from phase 2/3 clinical trials

Rebecca F Grais, Stephen B Kennedy, Barbara E Mahon, Sheri A Dubey, Rebecca J Grant-Klein, Ken Liu, Jonathan Hartzel, Beth-Ann Collier, Carolee Welebob, Mary E Hanson, Jakub K Simon





**EVD:
PROMOTE EVD VACCINE RECEPTIVENESS**

EVD Vaccines

- **ERVEBO: rVSV-ZEBOV EVD Vaccine: Merck**
 - Licensed for aged 1 year and above
 - Replication-competent, live, attenuated, recombinant vesicular stomatitis virus
 - Pre-exposure vaccination (Outbreak Response)
- **Zabdeno (Ad26.ZEBOV) & Mvabea (MVA-BN-Filo): J&J**
 - Licensed for aged 1 year and above
 - Prophylactic (Preventive) 2-dose regimen 8 weeks apart
 - Non-replicating viral vector

Address Public Perceptions

News Headlines

After heated "zoo-room" talks at S/Court & Executive Mansion, Verney Sherman certificated finally.

About 800,000 Fula people are in Lib., says report.

MRU states vow to make sub-region Ebola-free in 60 days.

Whistle blower Michael body found on 5th St. beach in Mon. Details to come.

Prepare for until departure in Lib. says UNMIL Boss but fails to talk on UN peace-keeper kidnapping a 16 yr. old Lib. child.

Gov't announces March 2, 2015 final date set for reopening of schools, but yet to distribute anti-Ebola materials to schools in Lib. promised of the 2.2 Million USD.

"War Memory" Year: 2013 - After looting & eating in this house in Bomi Co., these LURD robbers posted for Peace

EBOLA Experimental Vaccine Suffering - Due To Corruption, Public Fear In Lib.

666

Health

Health News: From survey done by Daily Talk & some news media institutions in Lib., there is an increasing public fear and

EBOLA Vaccine vs Public Fear

1

4

Date: Feb 23-24, 2015.

"News Headlines"

Pres. Siaka "I'm afraid that Ebola could come back here again like before due to high cases in countries around Liberia."

Pres. Siaka gives 51,000 USD to lawmakers at Capitol Building as "cold water" for quick passage of oil block in "Da Stealing!"

Judiciary breaks ground for new court in Bomi Co. with public outcry of corrupt court system in Lib.

2015 County Meet may not hold due to Ebola.

Gov't dismantle Ebola treatment Unit in Lib. says report.

Healthworkers president calls on Gov't to pay salary & benefits of health workers across the country despite being on the run.

Gov't announces curfew lifted finally despite public condemnation of the Ebola curfew as Pres. Siaka orders all borders open.

"Governor Siaka" to make Ebola report to US Pres. Obama this week.

Community Engagement & Empowerment: Critical Steps for Outbreak Response & Vaccine Receptiveness



Public, Traditional & Parliamentary Engagement



Demonstrate
Local Vaccine
Leadership





CONCLUSION

Experiences on Liberia's Response

- **High political commitment (PACE)**
- **Formation of Incident Management System (IMS)**
- **Scaled up in number of ETU beds geographically**
- **Cremation to deal with high number of dead bodies**
- **Increased in number of safe burial teams**
- **Community Intervention / Community-Related Activities**
- **Enforced quarantine in “trouble spots”**
- **Clinical Research: e.g., EVD Vaccines, Therapeutics, etc.**

Young Girl from Western Liberia





Q&A