
Global Clinical Research Networks

The NIAID/NIH Experience

Definition of a Clinical Research Network

- **Clinical Research:** Research relating to the observation and treatment of actual patients rather than theoretical or laboratory studies.
- **Network:** A group or system of interconnected people or things.

Value of a Clinical Research Network

- **Provides a forum for sharing infrastructure, ideas and expertise**
- **Is able to accomplish what no single site can do on their own**
 - **Large, Simple Trials**
 - **Studies of rare diseases**

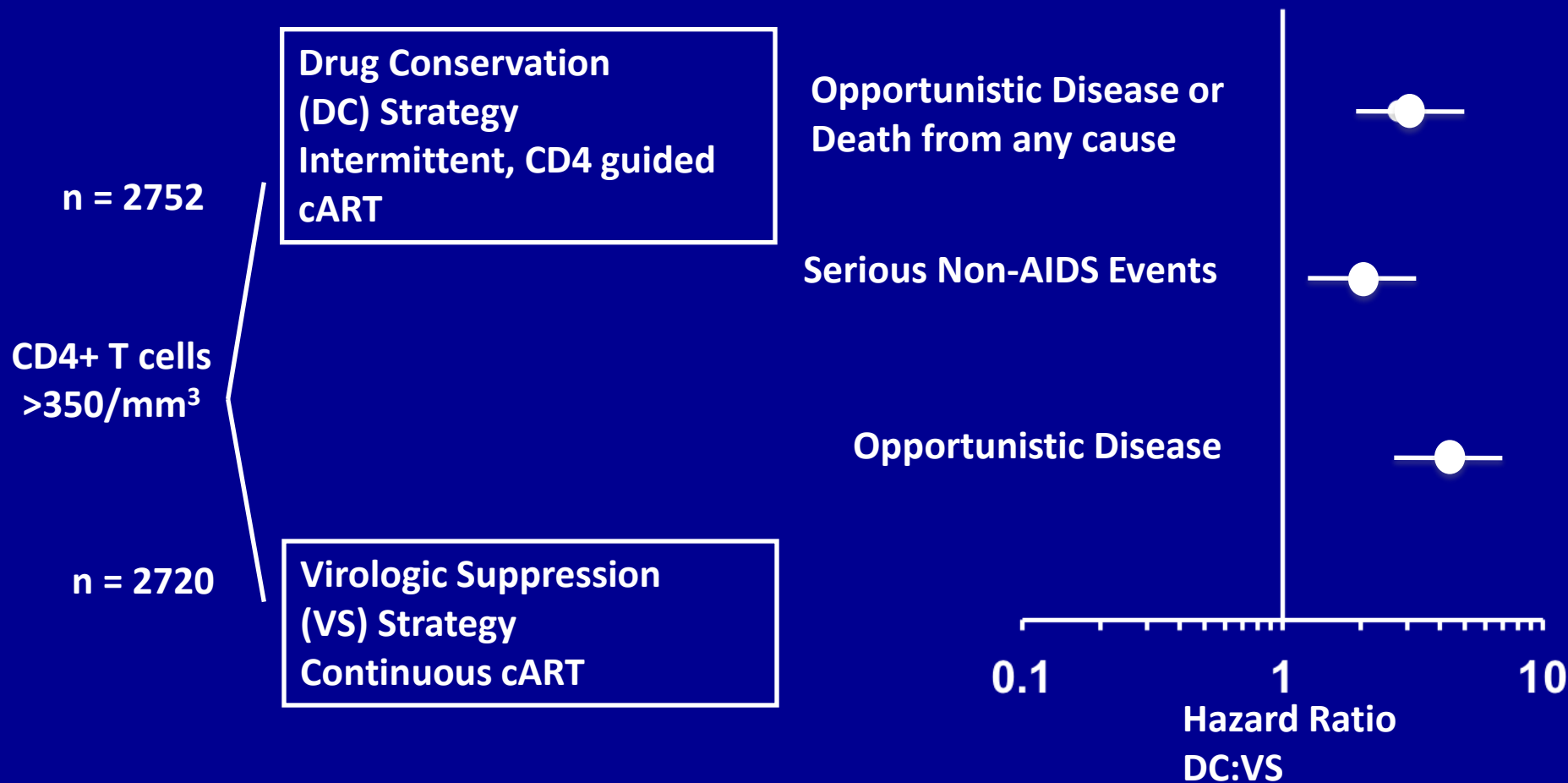
Global Clinical Research Partnerships with NIAID

- **International Network for Strategic Initiatives in Global HIV Trials (INSIGHT)**
- **Project Phidisa (South African Military)**
- **South East Asia Infectious Diseases Clinical Research Network (SEAICRN)**
- **INA-RESPOND**
- **La Red (Mexico Ministry of Health)**
- **Liberian-US Clinical Research Partnership (Liberian Ministry of Health)**

Insight Network

- **Began in 1995 as a consortium of sites involved in a phase 3 trial of IL-2**
- **Has become the world's leading Network for Strategic Trials in HIV**
 - **SMART**
 - **START**
- **Has recently expanded to include studies of influenza**

Uncontrolled HIV Replication is Associated with More than Opportunistic Diseases



The Strategies for Management of Antiretroviral Therapy (SMART) Study Group. NEJM 355:2283, 2006

SMART: Baseline Biomarkers and All-Cause Mortality

Biomarker	Un-adjusted		Adjusted	
	OR (4 th /1 st)	P-value	OR (4 th /1 st)	P-value
Hs-CRP	2.0	0.05	2.8	0.03
IL-6	8.3	<0.0001	11.8	<0.0001
sCD14	6.0	<0.001	8.0	0.003
D-dimer	12.4	<0.0001	26.5	<0.0001

Kuller, PLoS Med, 2008; Sandler, JID, 2011

Phidisa

- **A South African word meaning: Make better, save lives.**
- **Established in 2002 as a way to get cART to soldiers and their families.**
- **Codified in formal agreements between the US and RSA governments**
- **Provided data that led to a change in HIV health policy in South Africa**

Signing of Formal Agreements between US and RSA by US Embassy and South African Officials



**Amb. Frasier and Minister Lakota
April 26, 2005**



**DCM La Lime and MG Motumi
October 5, 2010**



South Africa's war on AIDS

A slow march

PRETORIA

Soldiers get AIDS drugs, civilians wait

SOLDIERS jostled camera crews, doctors beamed and the deputy defence minister snipped a red ribbon to open South Africa's first clinic for soldiers with HIV. This ceremony in Pretoria was the first sign of progress in implementing a long-delayed plan, announced in November, to distribute anti-AIDS drugs nationwide.

The army had cause to act early. At least one in five of all soldiers, sailors and airmen is infected. Aspiring recruits who test HIV-positive are now (controversially) turned away, on the ground that they make less effective soldiers. Besides their tendency to fall ill, they are barred from UN peacekeeping operations. They are expensive, too, partly because their families often need treatment. Helpfully, America will provide \$30m-35m to the new clinic in Pretoria over five years. This week the first five soldiers registered for a course of anti-retroviral drugs.

As well as treating the troops, the clinic will conduct research on how best to use the available medicine. If that helps speed the national distribution of drugs, it is welcome, say campaigners. But Eric Goemaere of Médecins Sans Frontières, a group that dishes out anti-AIDS drugs in townships near Cape Town, notes "little sense of hurry" in the health ministry. Though the neighbouring Eastern Cape province has asked his group to train nurses in drug distribution, he sees few signs of the national programme starting.

An official at the health ministry counters that staff are "working flat out" on the drug plan; by 2007 state clinics should be



Some Phidisa Findings to Date

- AZT/ddI was inferior to d4T/3TC in a clinical endpoint study. (A Ratsela, et al. *JID* 202:1529, 2010)
- Peri-partum single dose nevirapine did not affect virologic outcomes after 6 months of an efavirenz-based regimen. (J Dlamini, et al. *Pharmacotherapy* 31:158, 2011)
- Twenty percent of patients with unexplained cough were culture positive for TB. Of these only 1/3 were smear positive and 20% had MDR strains. (S Hassim, et al. *CID* 50:1053, 2010).

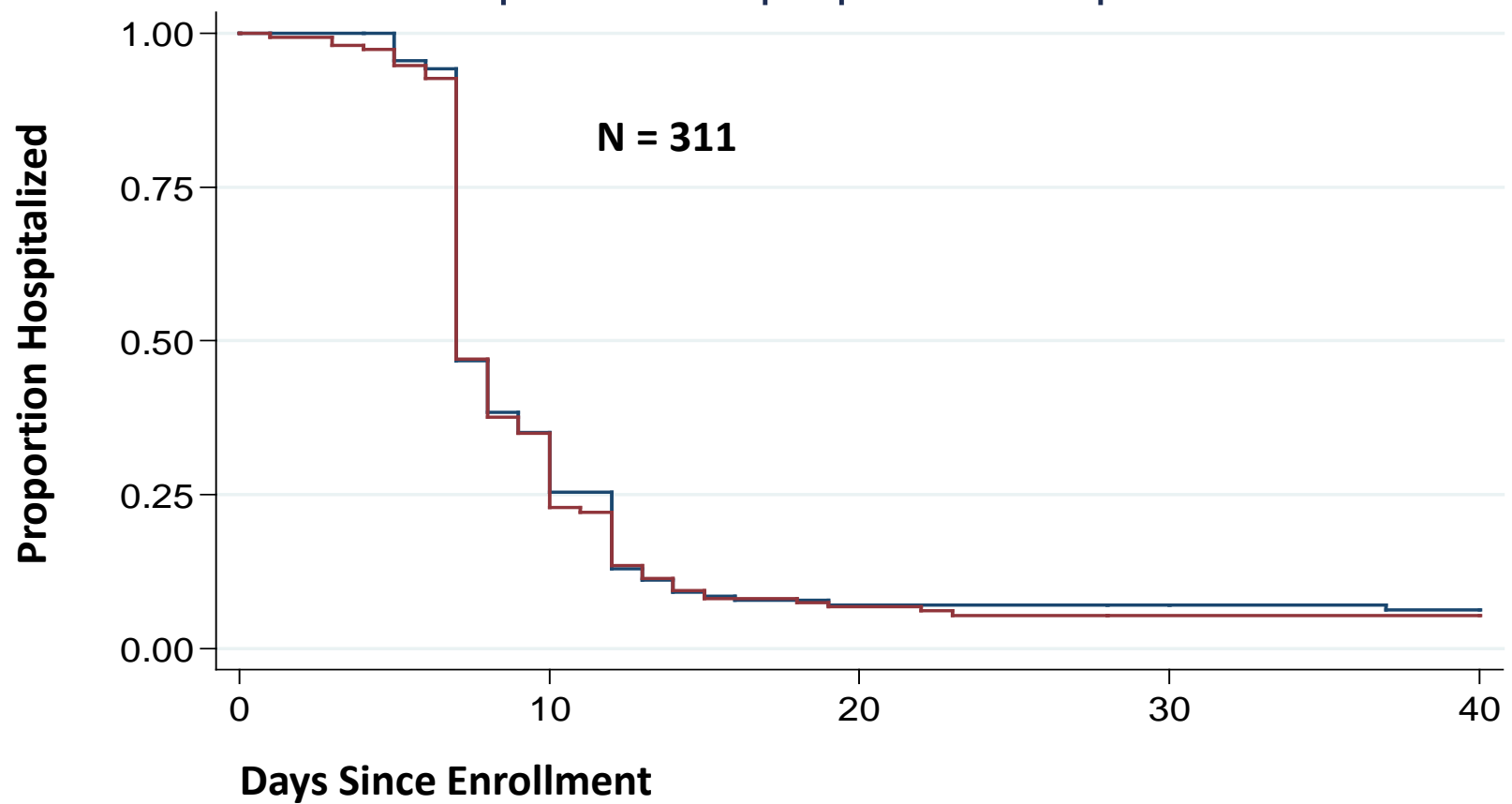
SEAICRN

- **Formed in 2005 as a collaborative partnership between hospitals and research institutions within Thailand, Viet Nam and Indonesia, the National Institutes of Allergy and Infectious Diseases (USA) and the Wellcome Trust (UK) in response to concerns about H5N1.**
- **Has demonstrated that double dose oseltamavir is equivalent to single dose in treating severe influenza**

SEAICRN (con't.)

- **At next Governing Board Meeting discussions will take place regarding the future of this Network.**
 - **Degree of capacity building**
 - **Degree of contribution to the medical literature**
 - **Impact on public health policy**

High vs. Standard Dose Oseltamivir in Hospitalized Patients with Influenza



INA-RESPOND

- **Discussions between US and Indonesia began in 2007 in the aftermath of the closing of NAMRU-2.**
- **Formally established in 2011 under the auspices of the US-Indonesia Science and Technology Agreement with a vision of becoming the premier research network in the region providing evidence to inform policy making, minimize the impact of infectious diseases, and improve human well-being.**
- **Is well on its way to accomplishing that vision!**

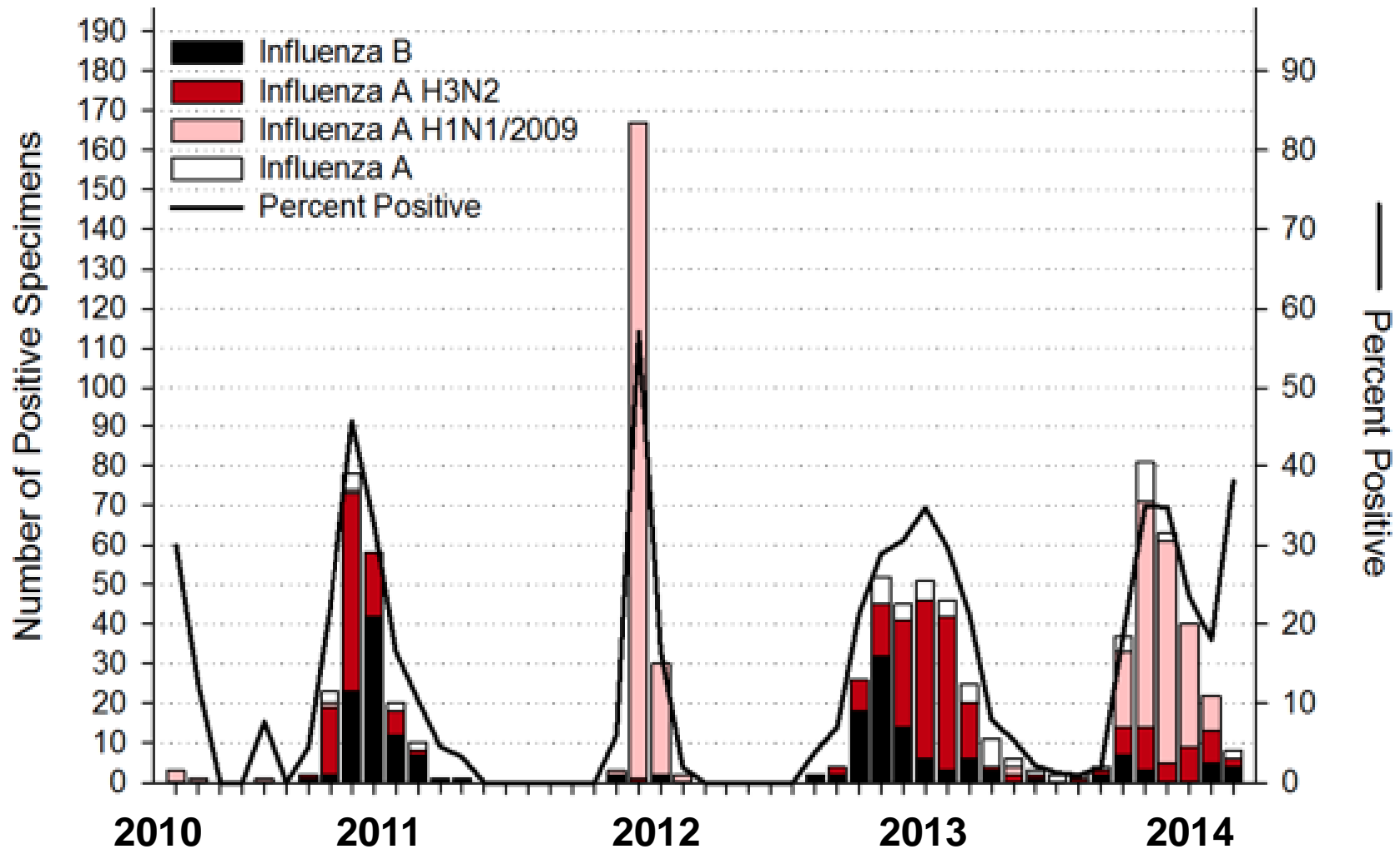
La Red

- **Translates to “The Network”.**
- **Initiated in September 2009 a part of the response to the H1N1 pandemic as a partnership between NIAID and the Mexican MoH.**
- **Vision is to a be a global leader in clinically relevant research on influenza, other respiratory viruses, and other emerging infectious diseases that will impact public health policy and practice.**

La Red (con't)

- **Has completed an observational cohort study of influenza-like illness in children and adults.**
- **Has initiated a randomized, controlled trial of Nitazoxanide in patients with influenza-like illness.**
- **Has been a leading site in a multi-network study designed to validate a symptom score for staging influenza illness.**

Causes of Influenza-like Illness as a Function of Time (La Red)

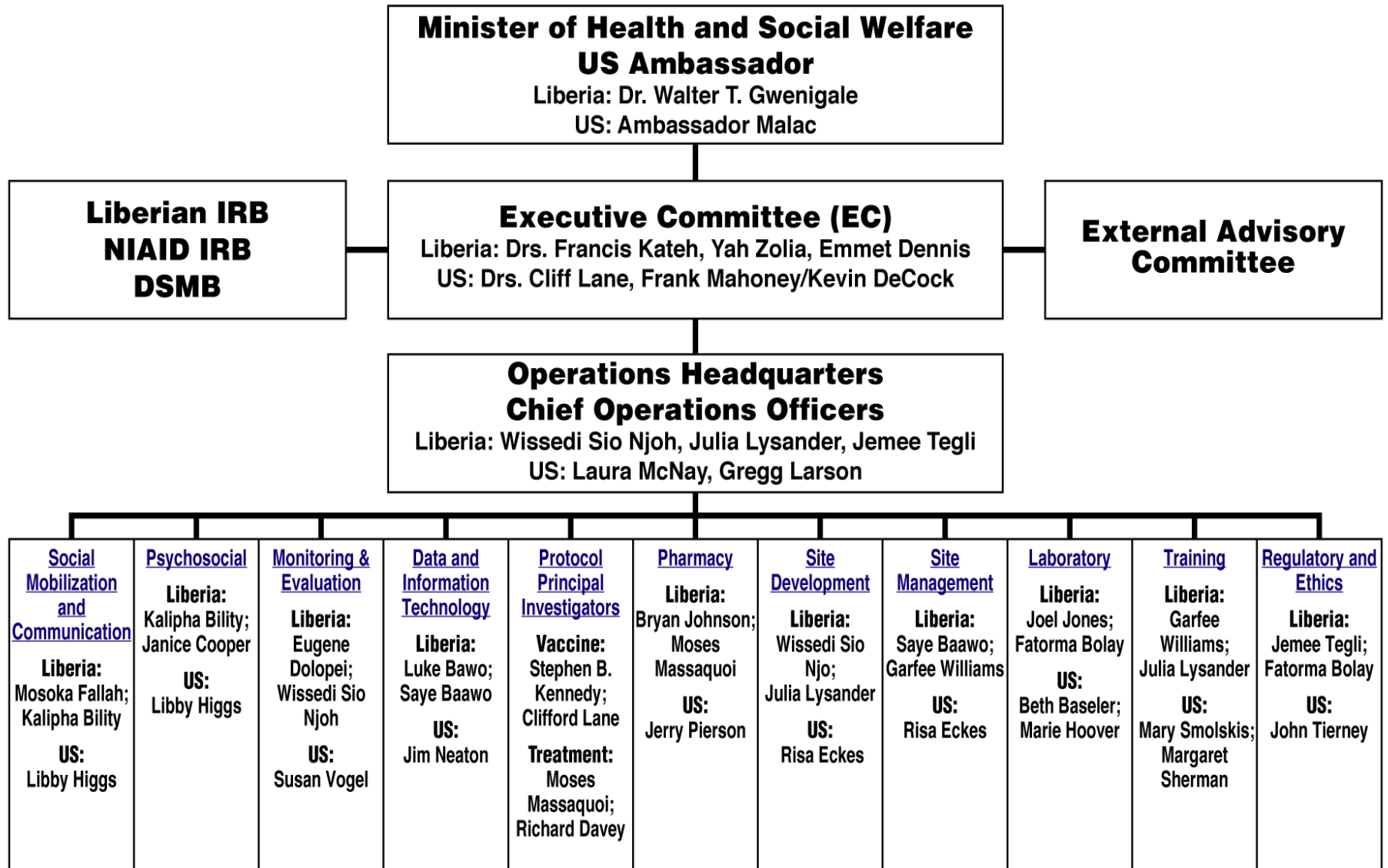


Liberian-US Clinical Research Partnership

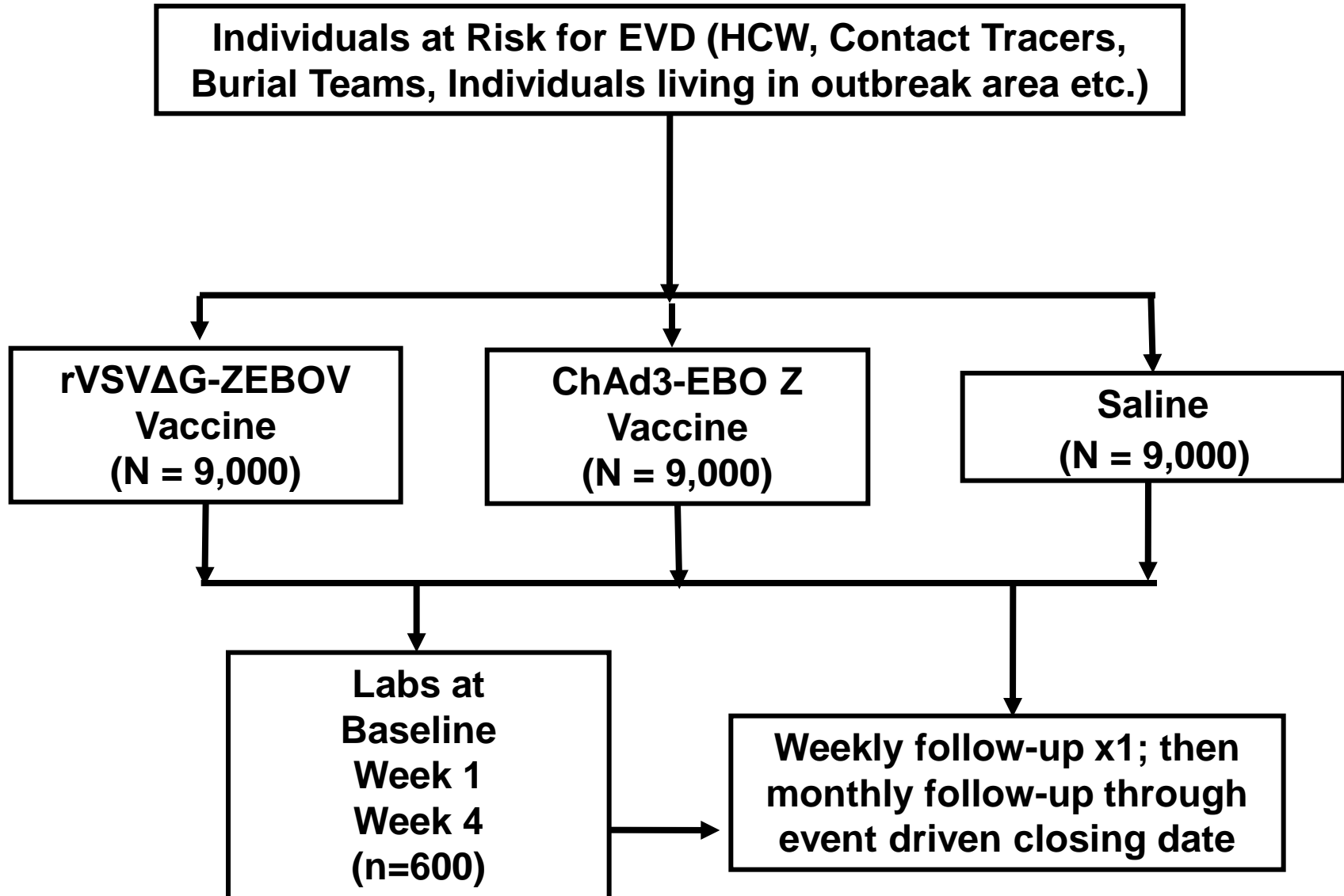
- **Formed in October, 2014 at the invitation of Liberian Minister of Health to bring research to the Ebola response.**
- **Has initiated two randomized controlled trials of countermeasures:**
 - **A placebo-controlled trial of two different candidate Ebola vaccines**
 - **A randomized, controlled trial of the Zmapp monoclonal antibody cocktail**

Organizational Structure

Liberian - US Joint Clinical Research Partnership



Prevail Study Design Overview



Screening Volunteers for Participation in the Prevail Vaccine Study at Redemption Hospital



Summary

- **Clinical Research Networks provide an opportunity to accomplish something no site can accomplish on their own.**
- **To be successful they must represent true partnerships and be driven by the public health needs of the population they serve.**

*“Coming together is a beginning;
keeping together is progress;
working together is success.”*

Henry Ford
Detroit, Michigan USA
