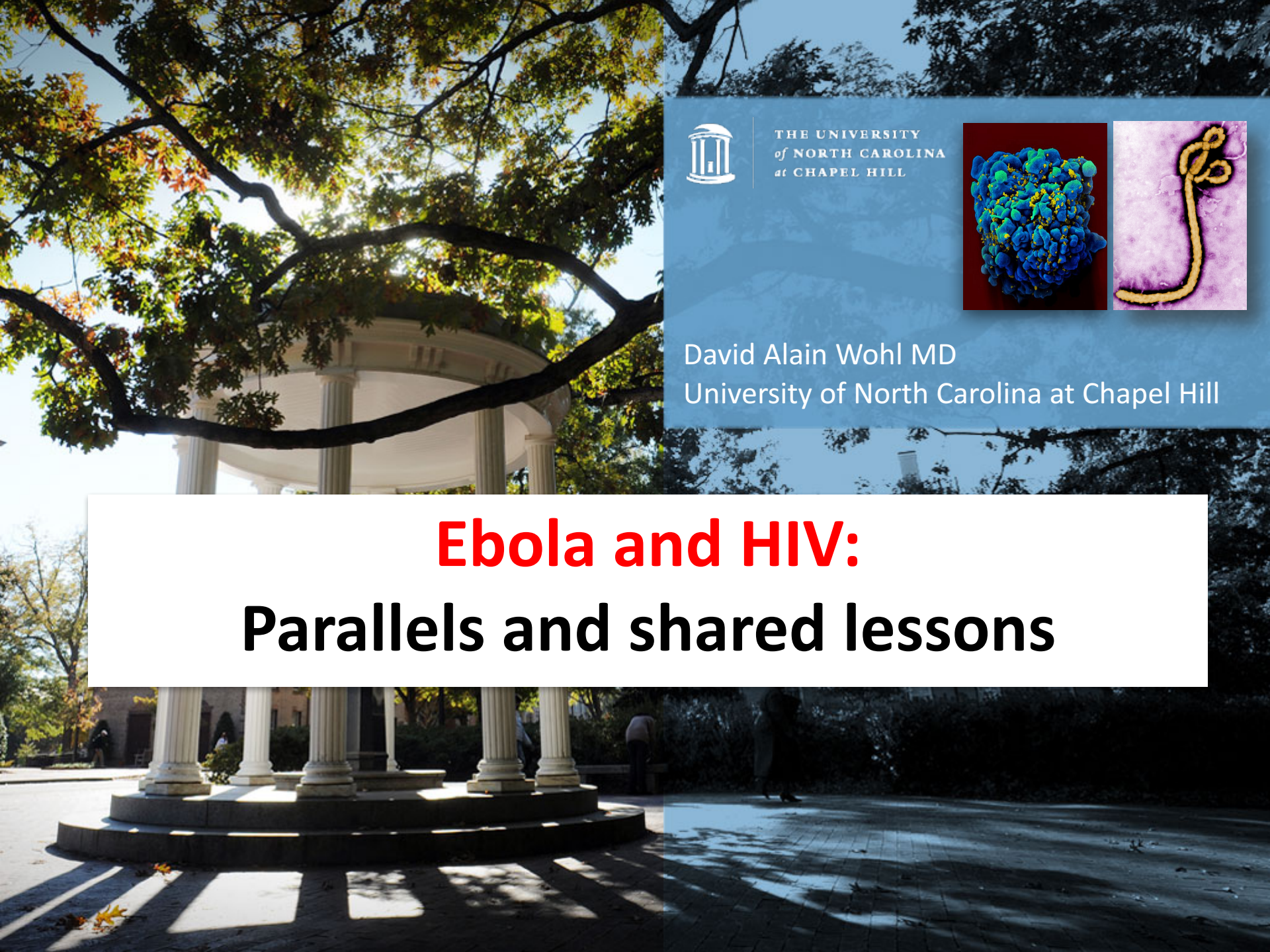
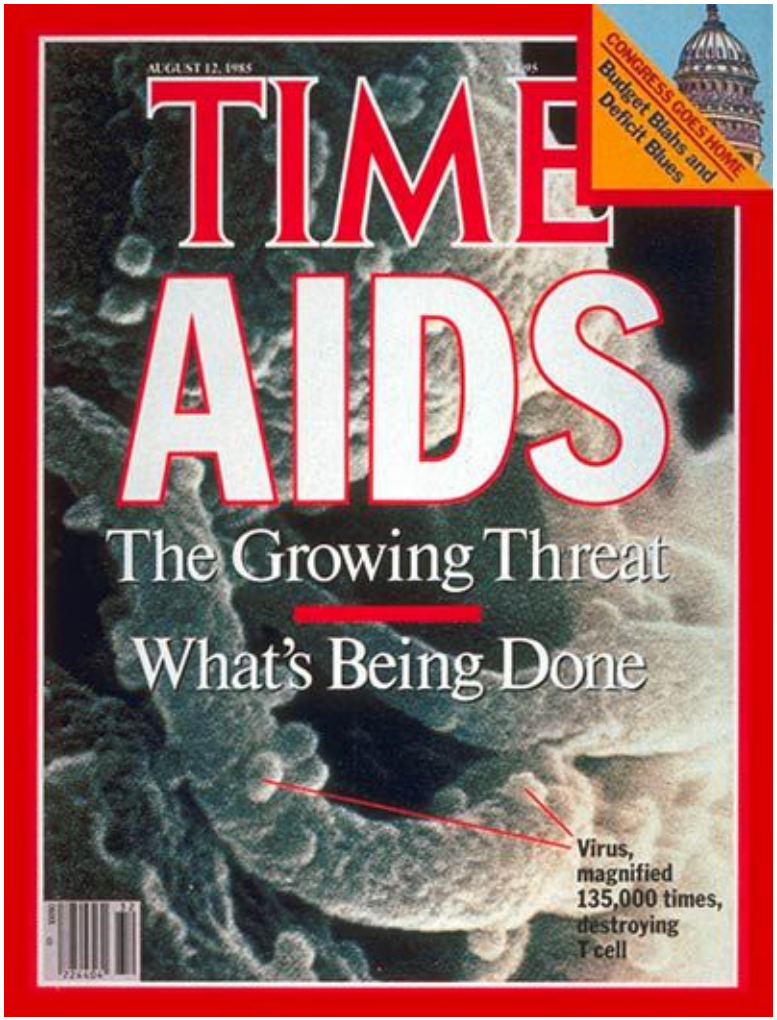


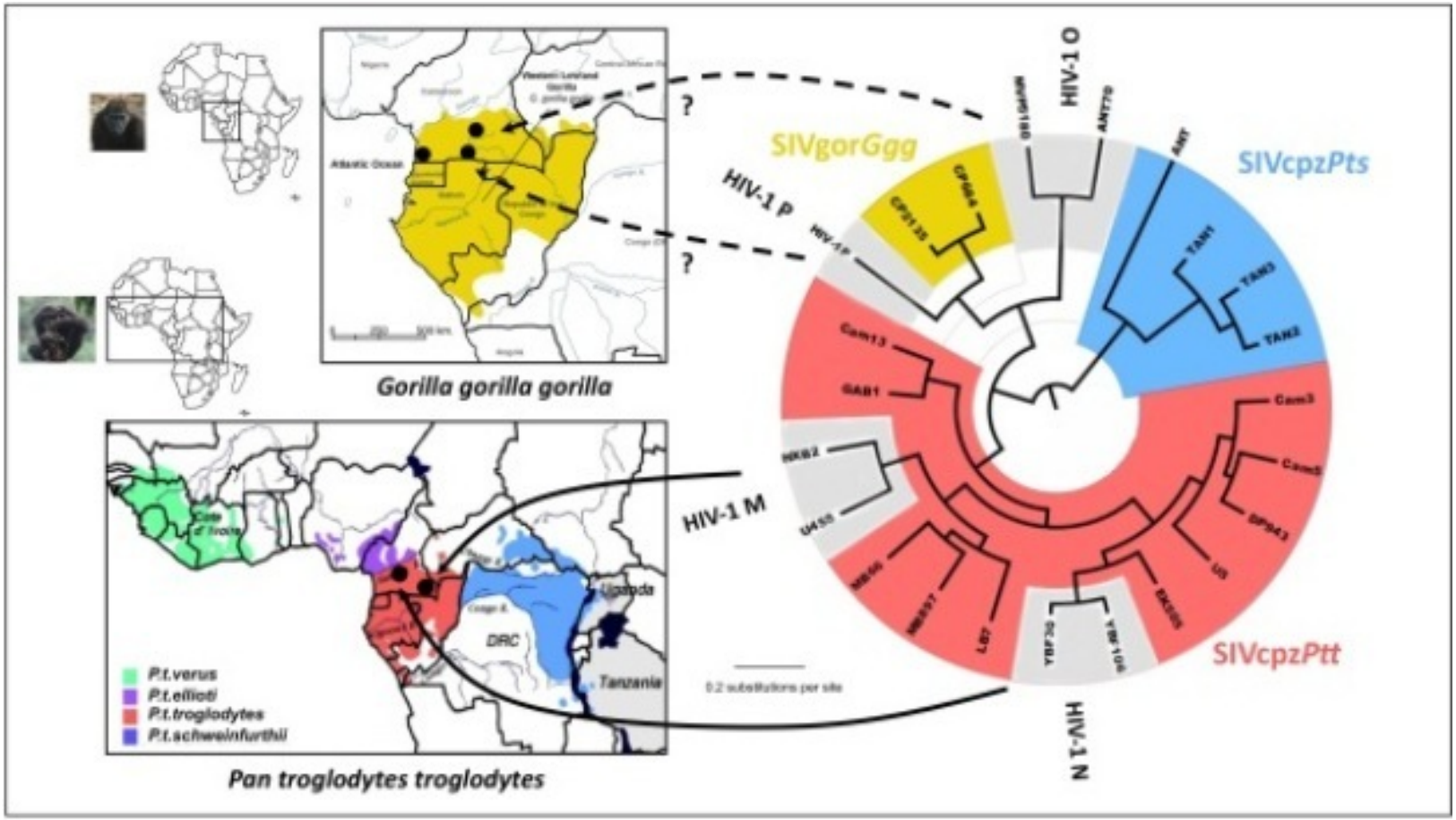
THE UNIVERSITY of NORTH CAROLINA at CHAPEL HILL

David Alain Wohl MD
University of North Carolina at Chapel Hill

Ebola and HIV:
Parallels and shared lessons


AUGUST 12, 1985
TIME
CONGRESS GOES HOME
Budget Blahs and Deficit Blues
AIDS
The Growing Threat
What's Being Done
Virus, magnified 135,000 times, destroying T cell


TIME
STOPPING EBOLA
THE RISKS AND REALITIES OF THE OUTBREAK

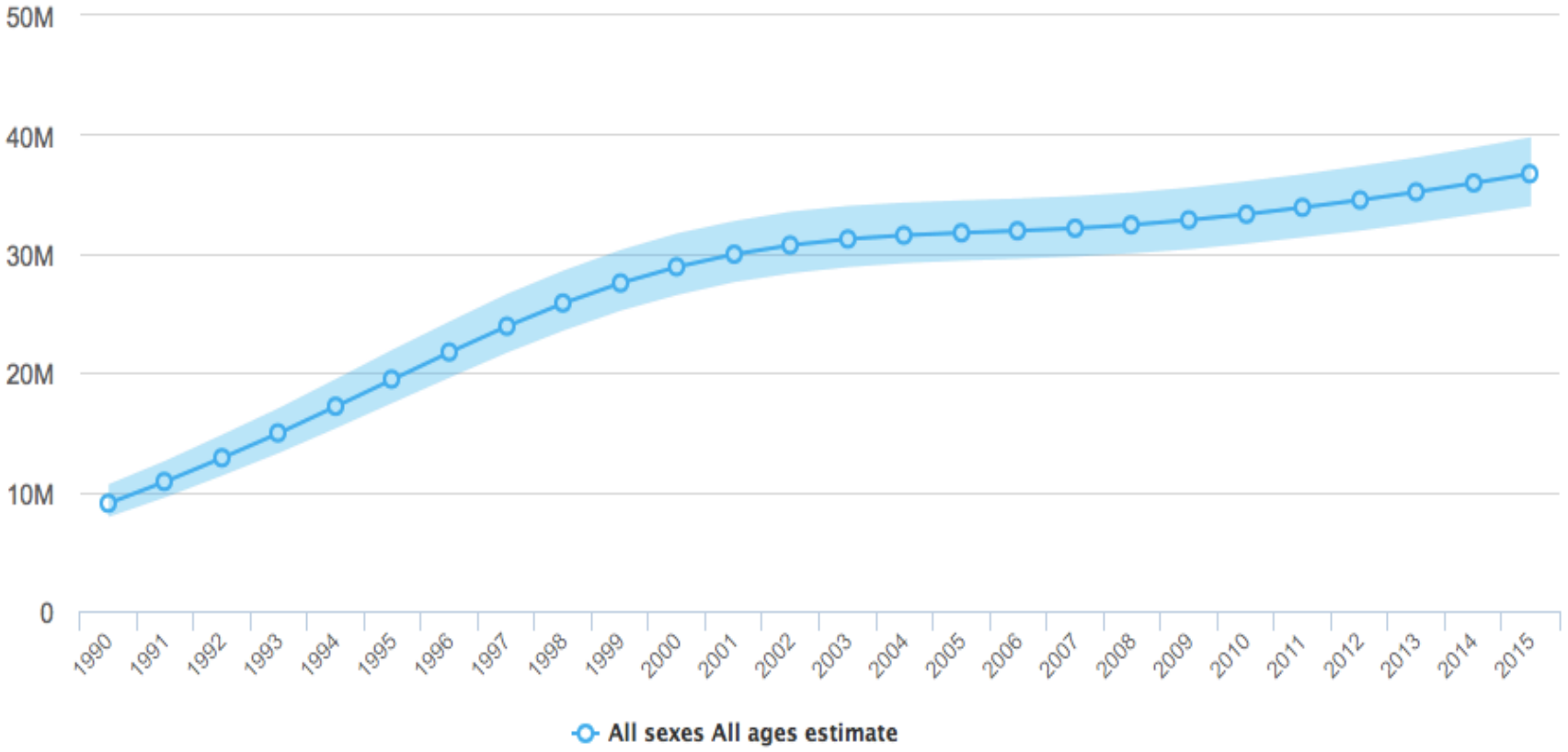


Non-Human Primates, Retroviruses, and Zoonotic Infection Risks in the Human Population

By: Sabrina Locatelli (*Institut de Recherceh pour le Developpment (IRD) and Uni. of Montpellier 1, Montpellier, France*) & Martine Peeters (*Institut de Recherche pour le Developpement (IRD) and Uni. of Montpellier 1, Monpellier, France*)

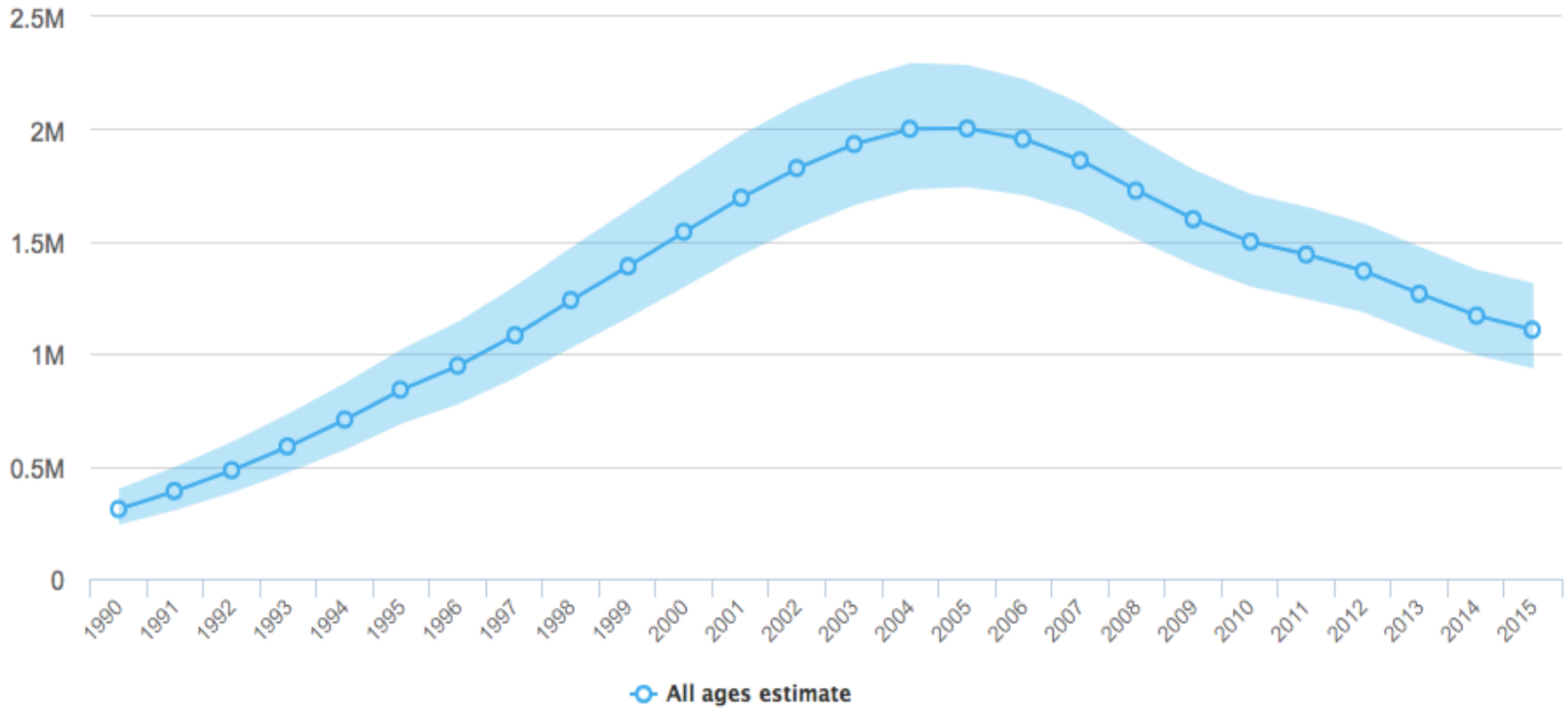
Citation: Locatelli, S. & Peeters, M. (2012) Non-Human Primates, Retroviruses, and Zoonotic Infection Risks in the Human Population. *Nature Education Knowledge* 3(10):62

People living with HIV (all ages)



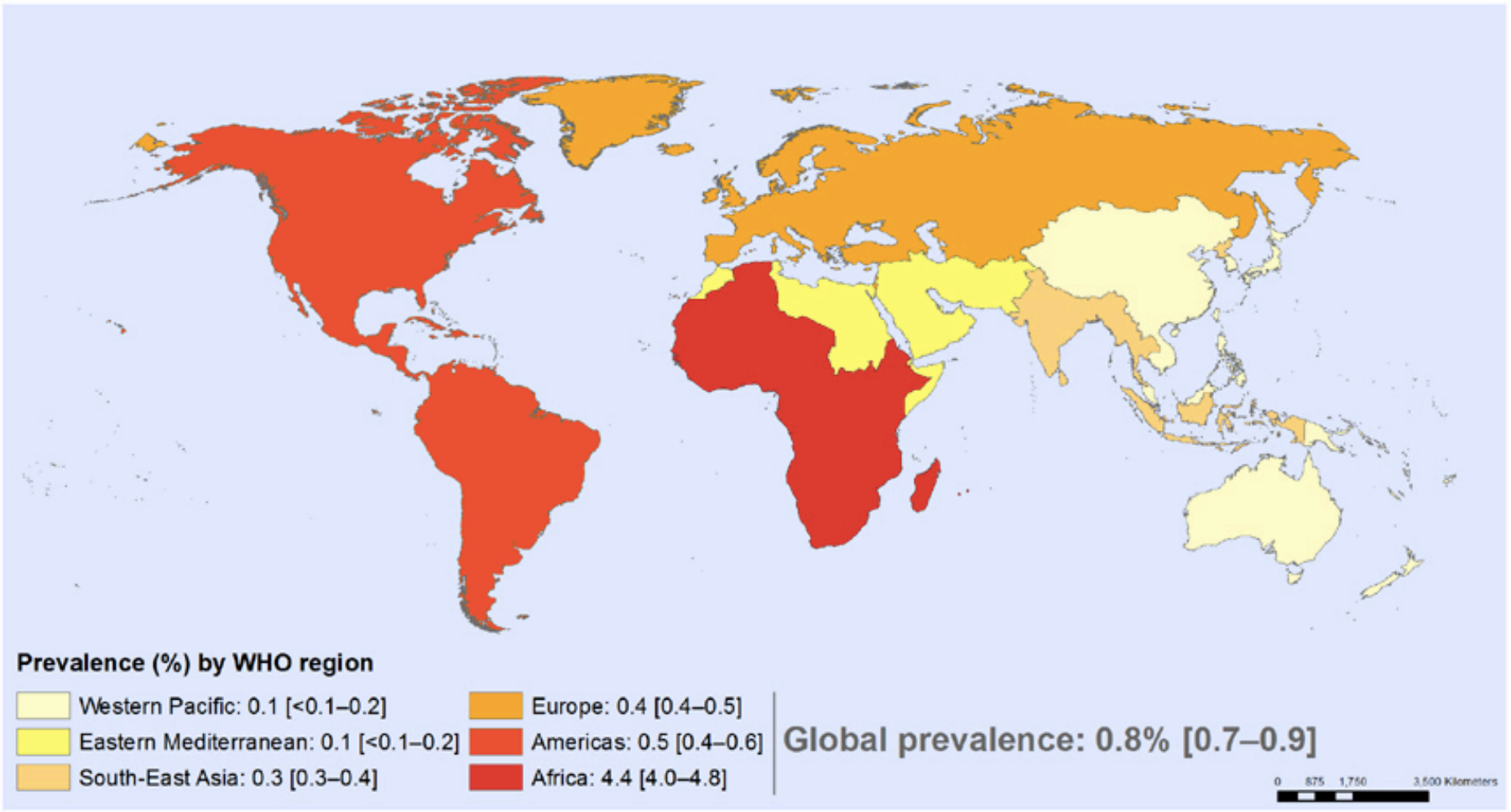
Source: UNAIDS Estimates 2016

AIDS-related deaths (all ages)



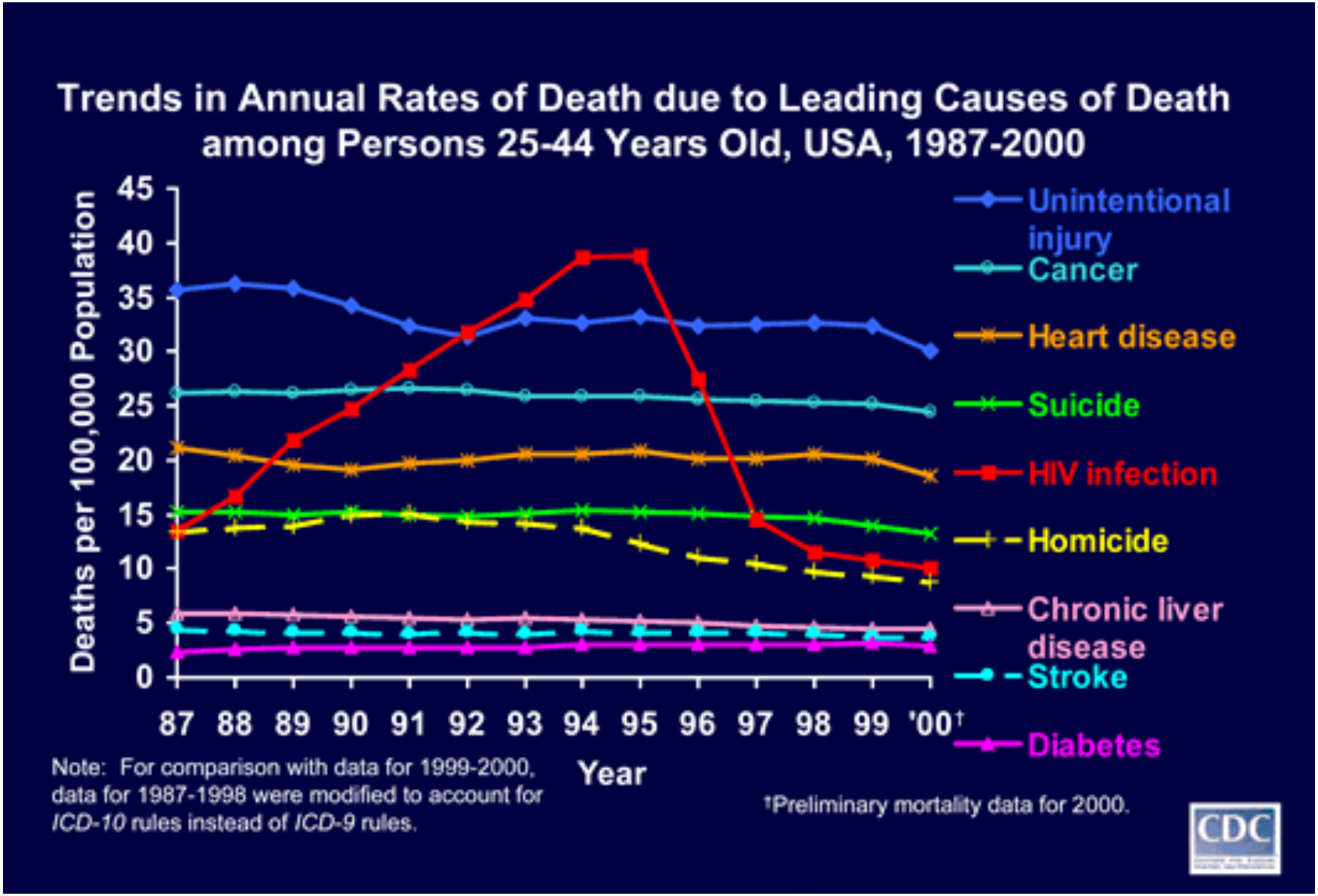
Source: UNAIDS Estimates 2016

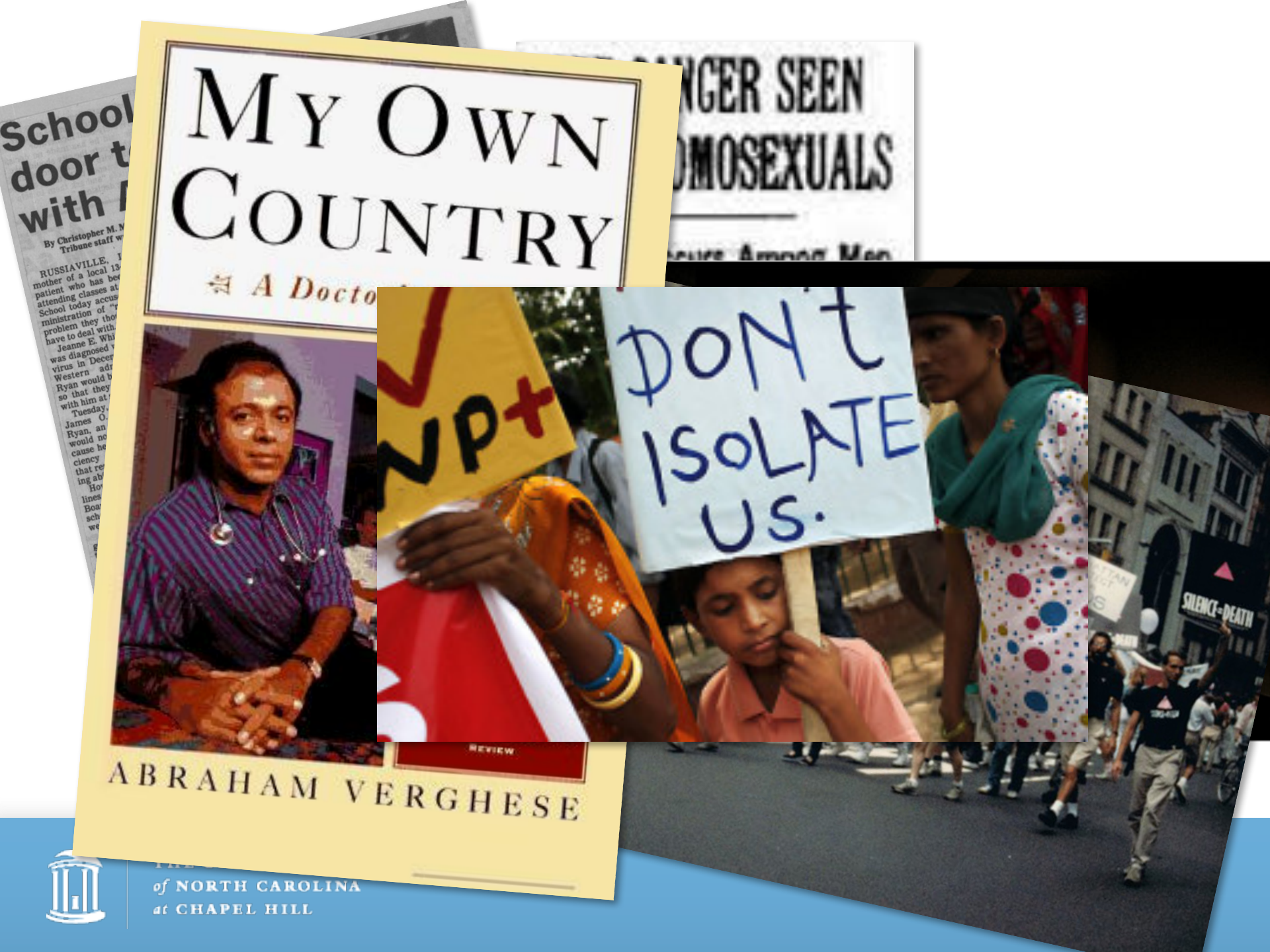
Adult HIV prevalence (15–49 years), 2015
By WHO region



Data Source: World Health Organization
Map Production: Information Evidence and Research (IER)
World Health Organization

World Health Organization


Trends in Annual Rates of Death due to Leading Causes of Death among Persons 25-44 Years Old, USA, 1987-2000
Deaths per 100,000 Population
45
40
35
30
25
20
15
10
5
0
87 88 89 90 91 92 93 94 95 96 97 98 99 '00†
Year
Unintentional injury
Cancer
Heart disease
Suicide
HIV infection
Homicide
Chronic liver disease
Stroke
Diabetes
Note: For comparison with data for 1999-2000, data for 1987-1998 were modified to account for ICD-10 rules instead of ICD-9 rules.
†Preliminary mortality data for 2000.
CDC


School
door t
with
By Christopher M. N
Tribune staff w
RUSSIAVILLE,
mother of a local 13
patient who has be
attending classes at
School today accus
ministration of "
problem they tho
have to deal with.
Jeanne E. Whi
was diagnosed
virus in Decer
Western ad
Ryan would b
so that they
with him at
Tuesday,
James O.
Ryan, an
would no
cause he
ciency
that re
ing ab
Ho
lines
Boa
sch
we
NCER SEEN
OMOSEXUALS
MY OWN
COUNTRY
A Docto
NP+
DON't
ISOLATE
US.
SILENCE=DEATH
REVIEW
ABRAHAM VERGHESE
of NORTH CAROLINA
at CHAPEL HILL

HIV/AIDS Timeline


RARE CANCER SEEN IN 41 HOMOSEXUALS

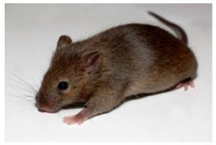
Outbreak Occurs Among Men in New York and California —8 Died Inside 2 Years

1981 The New York Times reports a mysterious illness

1982 The name "AIDS" – Acquired Immune Deficiency Syndrome – is created

1984 Françoise Barré-Sinoussi and Luc Montagnier discover HIV as the cause of AIDS and later win the Nobel Prize

1985 A test for screening blood donations is developed through chimpanzee research



1987 AZT, developed in mice, becomes the first drug approved for treating AIDS

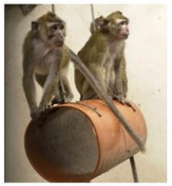
1990 8 million people have HIV

1994 Infant HIV infections begin to fall due to AZT treatment

1996 Combination treatment of antiretrovirals developed

1997 AIDS-related deaths fall in developed countries due to combination treatments

22 million people have HIV



2010 After tests in mice and macaques, Truvada is shown to reduce the risk of HIV infection

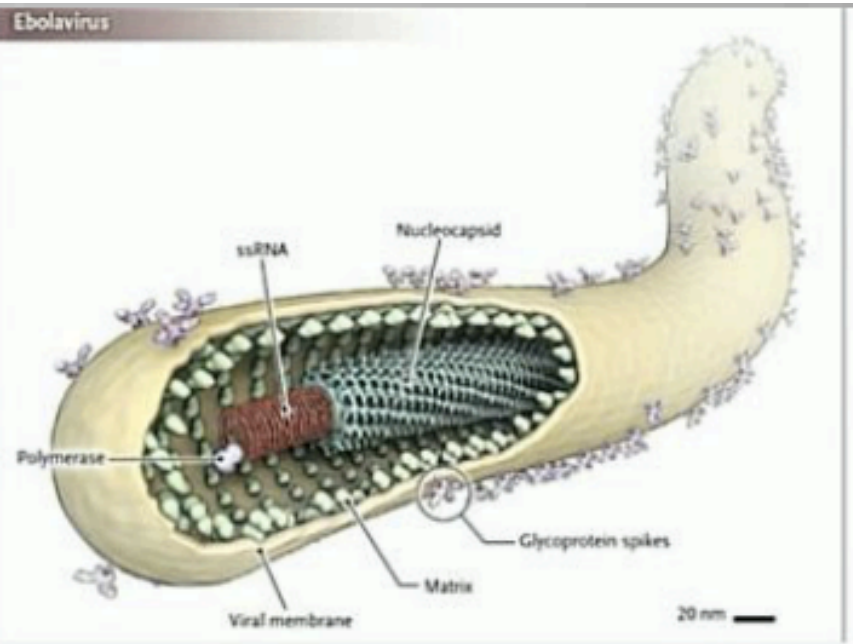
2007 33 million people have HIV

2012 The majority of people worldwide eligible for antiretrovirals are now receiving them

2011 Antiretrovirals are shown to reduce the risk of transmitting HIV by 96%

Image credits: Trocaire, Gates Foundation, iStock/LordRunar, Harwell

Understanding ANIMAL RESEARCH

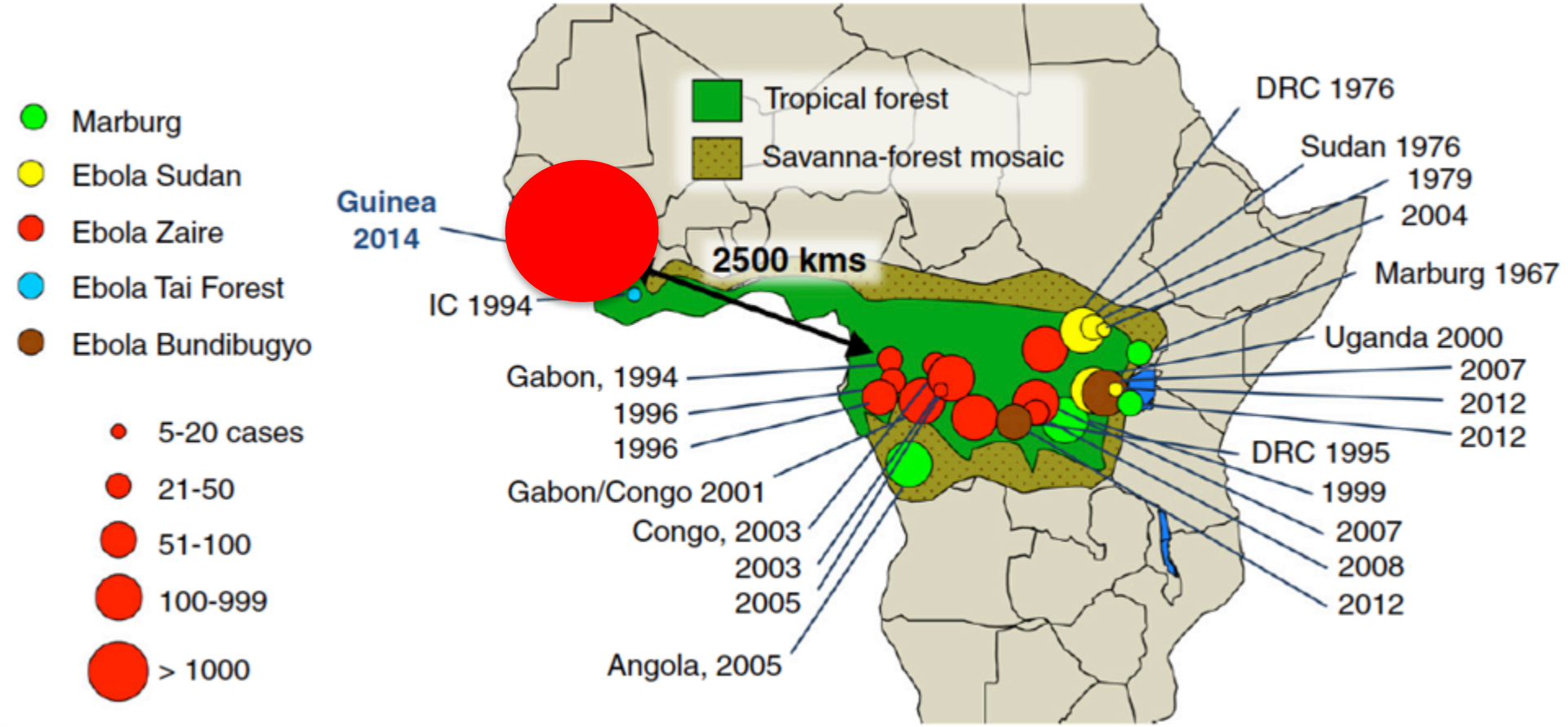


Feldmann, NEJM, 2014

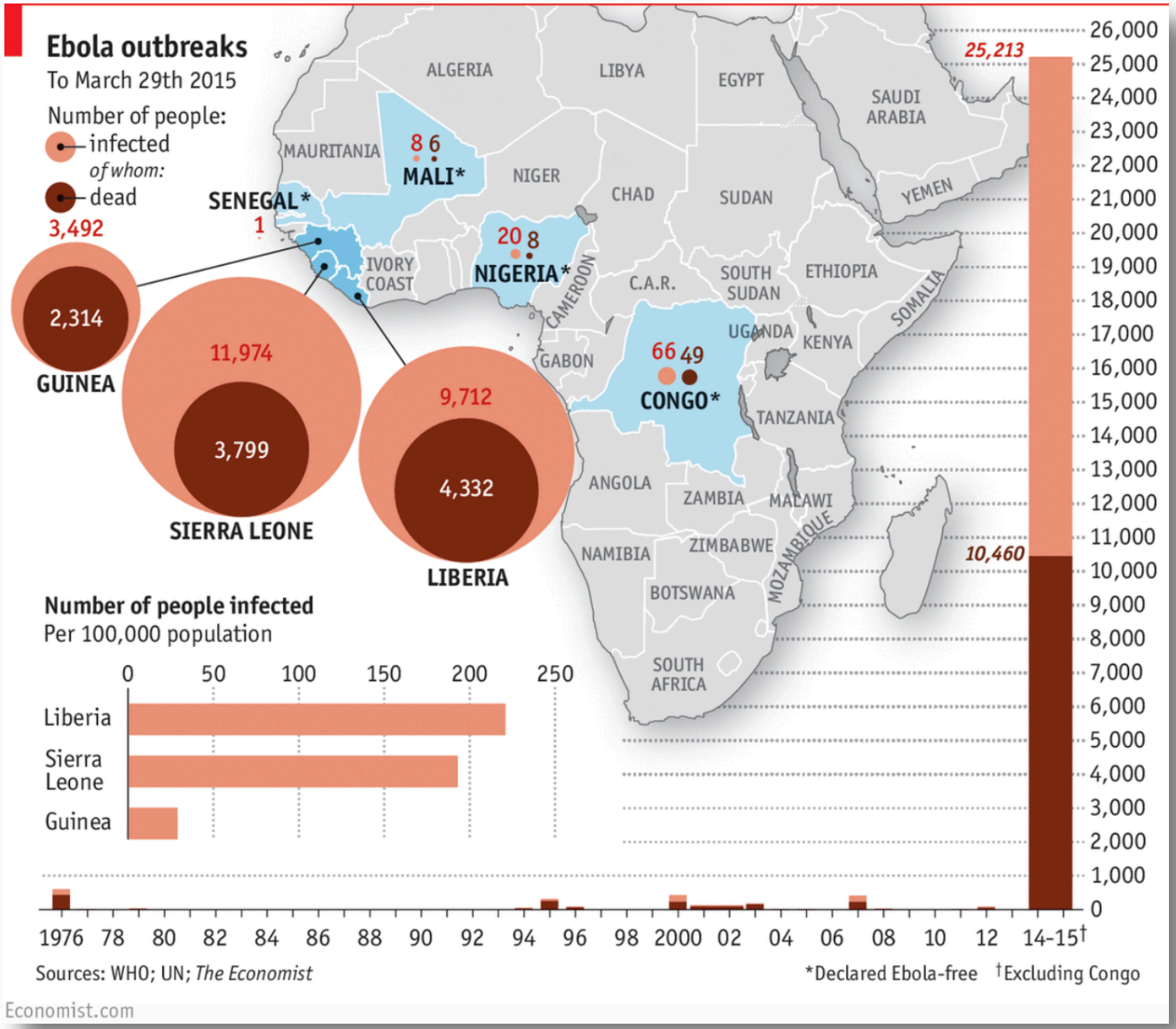
"The feeling was overpowering. Ebola is like a sickness from a different planet. It comes with so much pain." -
SALOME KARWAH, EBOLA SURVIVOR

- Ebolavirus, family Filovirus
- Enveloped, negative stranded RNA virus
- 5 species of varying virulence and disease progression (Zaire, Sudan, Bundibugyo, Tai Forest and Reston)
- Incubation 2-21 days
- Clinical progression in 4 phases: early febrile, gastrointestinal, shock or recovery, late complications.
- Case fatality 30-90%
- Transmission: human to human; contact with body fluids of symptomatic or dead; social networks, nosocomial, unsafe burials.

2013-15- Unprecedented Ebola Epidemic



Adapted from: Baize S. Current Opin Virol, 2015


Ebola outbreaks
To March 29th 2015
Number of people:
infected
of whom:
dead
SENEGAL*
1
3,492
2,314
GUINEA
11,974
3,799
SIERRA LEONE
9,712
4,332
LIBERIA
8 6
MALI*
20 8
NIGERIA*
66 49
CONGO*
ALGERIA
LIBYA
EGYPT
SAUDI ARABIA
MAURITANIA
NIGER
CHAD
SUDAN
YEMEN
IVORY COAST
CAMEROON
C.A.R.
SOUTH SUDAN
ETHIOPIA
SOMALIA
UGANDA
KENYA
GABON
TANZANIA
ANGOLA
ZAMBIA
MALAWI
MOZAMBIQUE
NAMIBIA
ZIMBABWE
BOTSWANA
SOUTH AFRICA
Number of people infected
Per 100,000 population
0 50 100 150 200 250
Liberia
Sierra Leone
Guinea
25,213
10,460
26,000 25,000 24,000 23,000 22,000 21,000 20,000 19,000 18,000 17,000 16,000 15,000 14,000 13,000 12,000 11,000 10,000 9,000 8,000 7,000 6,000 5,000 4,000 3,000 2,000 1,000 0
1976 78 80 82 84 86 88 90 92 94 96 98 2000 02 04 06 08 10 12 14-15†
Sources: WHO; UN; The Economist
*Declared Ebola-free †Excluding Congo
Economist.com

Saez M, et al . EMBO Mol Med, 2014

(S1) Child, 2 yr of age
Fever, black stool, vomiting
Onset Dec. 2, 2013; died Dec. 6, 2013

Conakry

S14 Health care worker at **Guéckédou** hospital
Fever, diarrhea, vomiting
Onset Feb. 5, 2014
Went to **Macenta** hospital; died Feb. 10, 2014

Macenta

Sierra Leone

Liberia

Baize, S et al. NEJM 2014

Ebolavirus Ecology

Enzootic Cycle

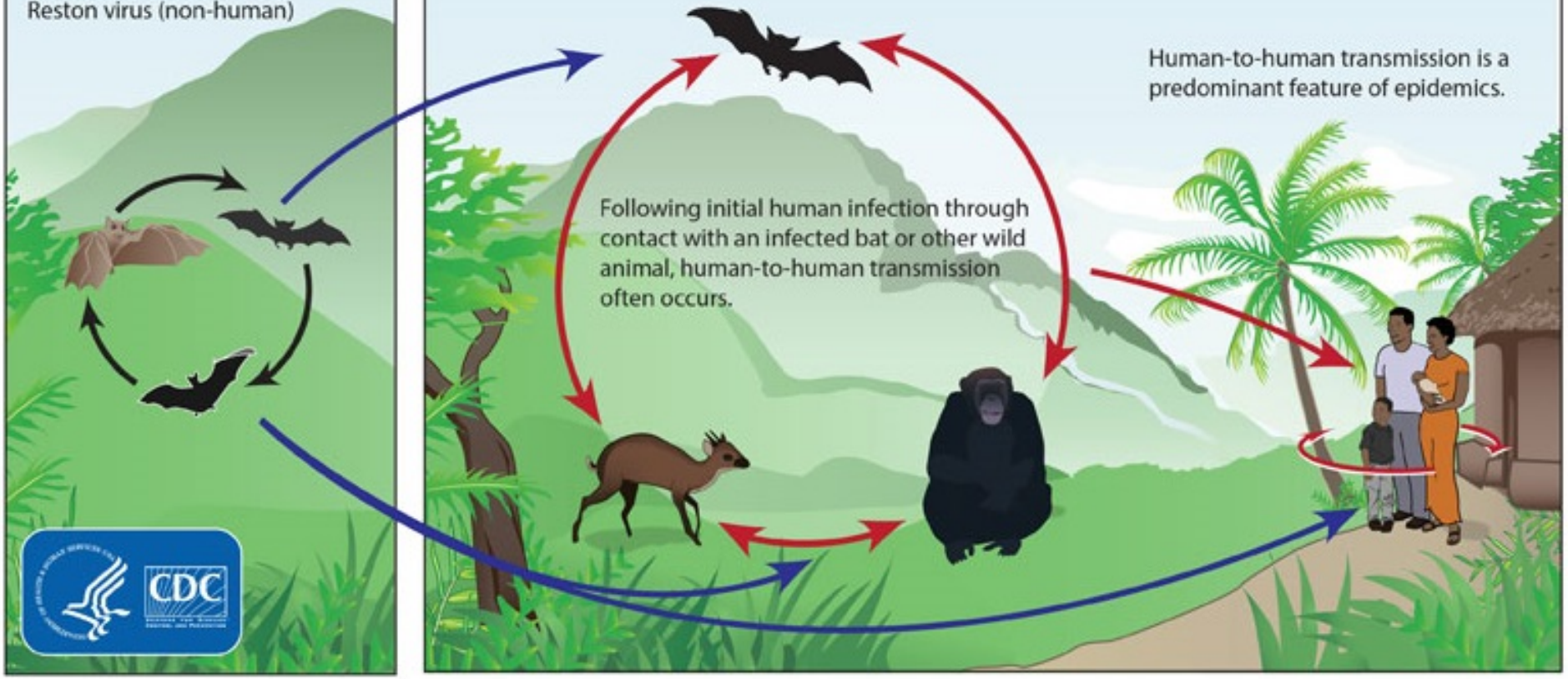
New evidence strongly implicates bats as the reservoir hosts for ebolaviruses, though the means of local enzootic maintainance and transmission of the virus within bat populations remain unknown.

Ebolaviruses:

Ebola virus (formerly Zaire virus)
Sudan virus
Taï Forest virus
Bundibugyo virus
Reston virus (non-human)

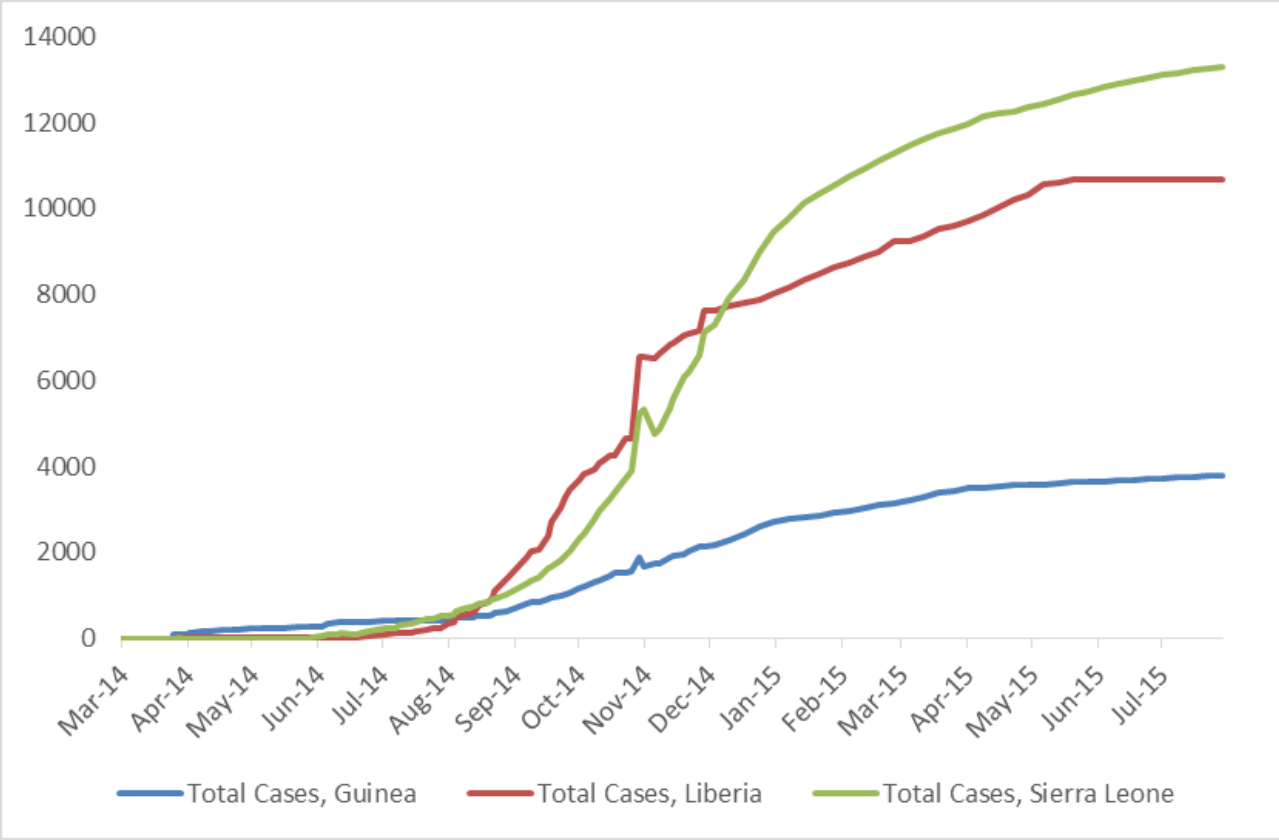
Epizootic Cycle

Epizootics caused by ebolaviruses appear sporadically, producing high mortality among non-human primates and duikers and may precede human outbreaks. Epidemics caused by ebolaviruses produce acute disease among humans, with the exception of Reston virus which does not produce detectable disease in humans. Little is known about how the virus first passes to humans, triggering waves of human-to-human transmission, and an epidemic.



Spreads Fast: 2014 Ebola Outbreak

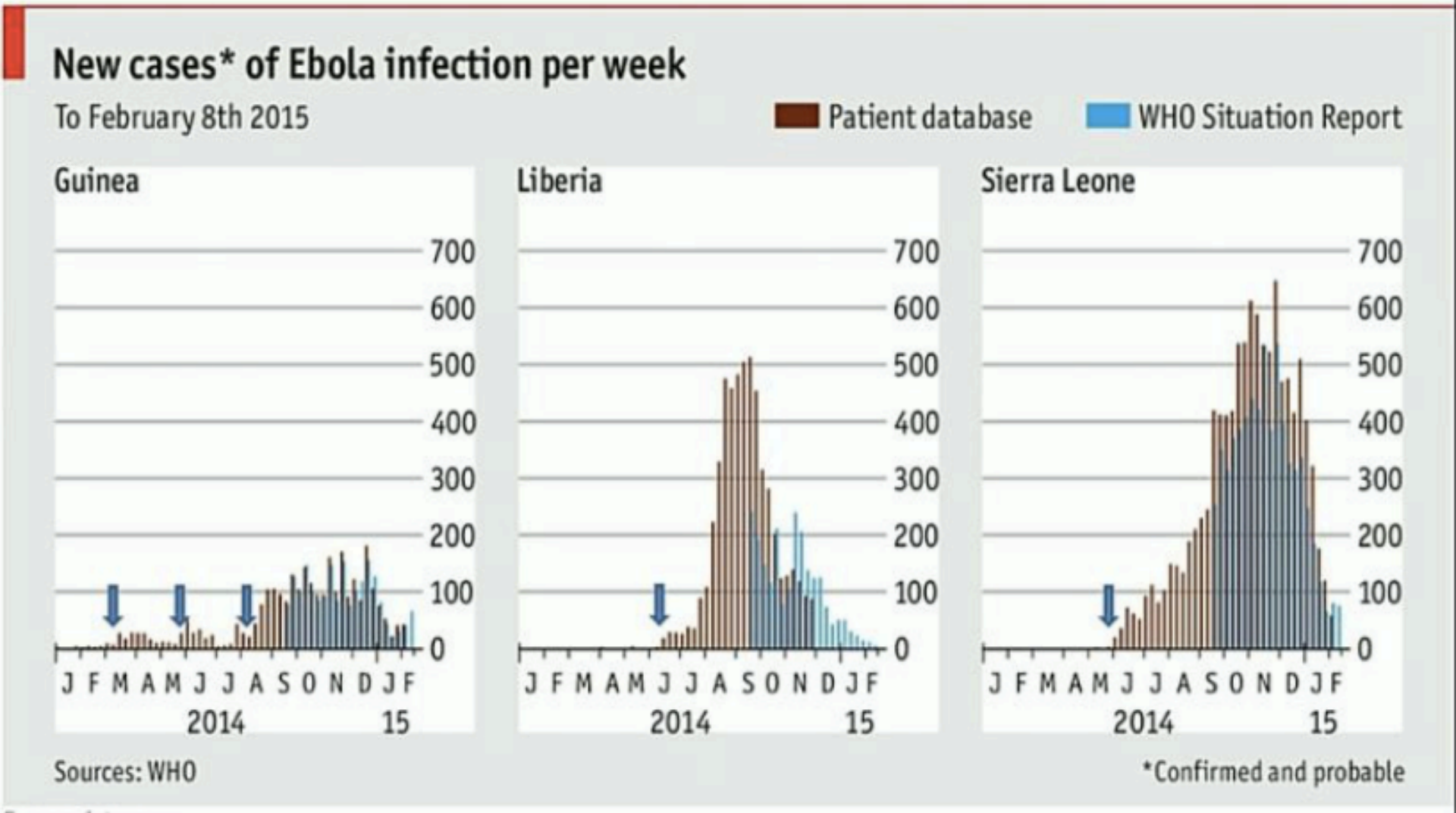
Reported Cases (Suspected, Probable, and Confirmed) in Guinea, Liberia, and Sierra Leone



This graph shows the total reported cases (suspected, probable, and confirmed) in Guinea, Liberia, and Sierra Leone provided in WHO situation reports beginning on March 25, 2014, through the most recent situation report on July 29, 2015.


NORWAY
UK
NETHERLANDS
GERMANY
FRANCE
SWITZERLAND
SPAIN
USA
MALI
SENEGAL
NIGERIA

3 waves = 3 missed opportunities




UNKNOWN MAN

What have we learned

- Humanitarian/Political
  - Response by those charged with responding to emerging infectious diseases was slow
  - Conditions that allowed this epidemic to happen are rooted in poverty and threadbare healthcare infrastructures
  - To contain this outbreak and prevent the next one will require long term commitment to this region

This **Will** Happen Again

Poverty Increases Interaction with Potential Reservoirs

Inadequate Basic Healthcare Infrastructure

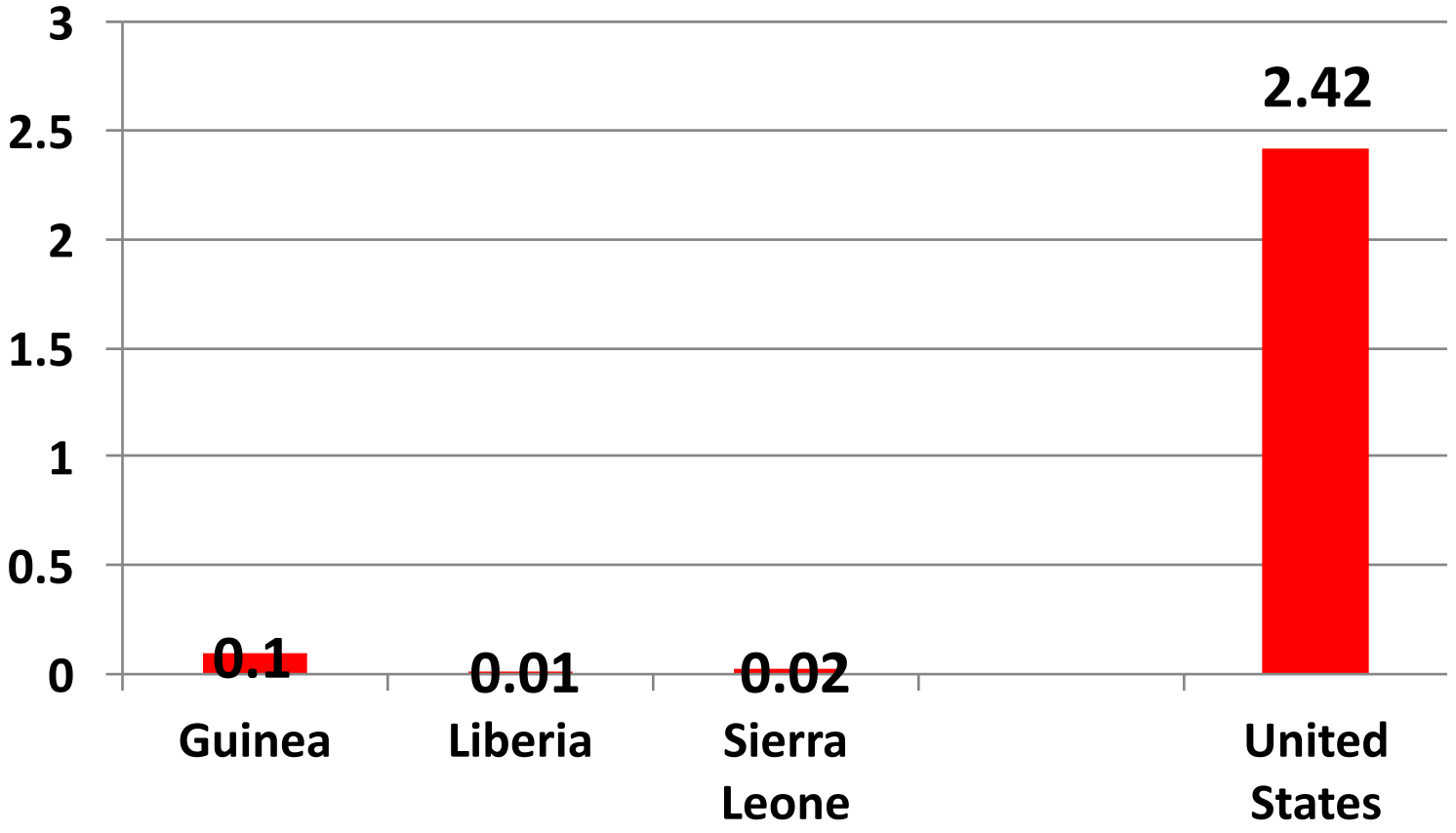
Higher Level of Care + Investigational Therapies

http://news.emory.edu/stories/2014/10/ehc_ebola_protocols_website/campus.html

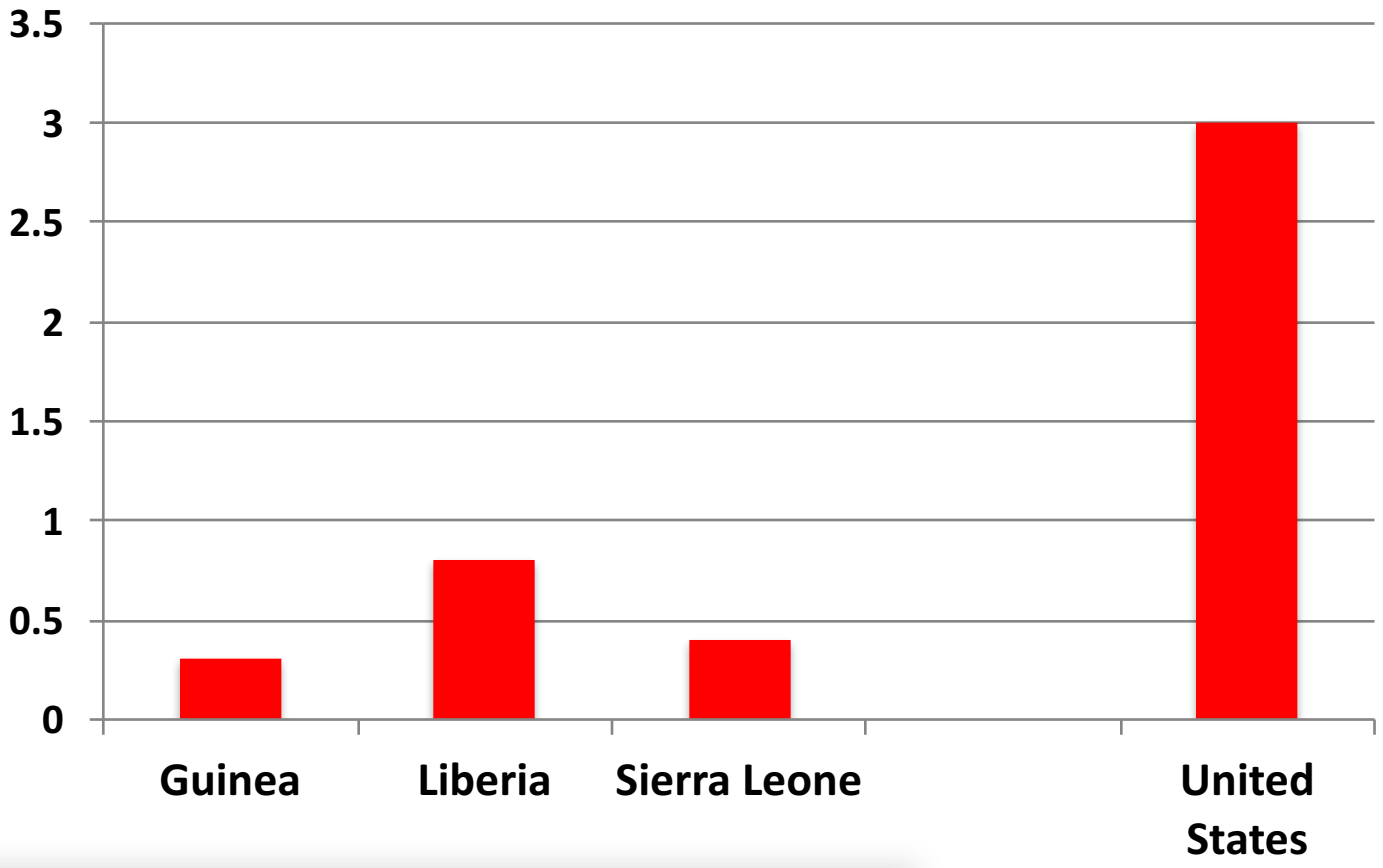
http://www.emoryhealthcare.org/ebola-protocol/videos.html

Critical Care Medicine Is Possible in West Africa

Physicians/1000 Population



Hospital Beds/1000 Population



Distrust from Decades of Civil Conflict

Courtesy of Meredith Dixon


DONT TOUCH
IS
THE KEY MESSAGE
ABOUT EBOLA


FOX
NEWS
SUNDAY
EXCLUSIVE
ON STA


CELEBRATE
EBOLA
SURVIVORS
Aminata Kanjbo is a hero.
She faced Ebola and beat it.
Learn more at
WALLACE JOHNSON STREET

Increasing Access by UNC

Launch of Convalescent plasma trial

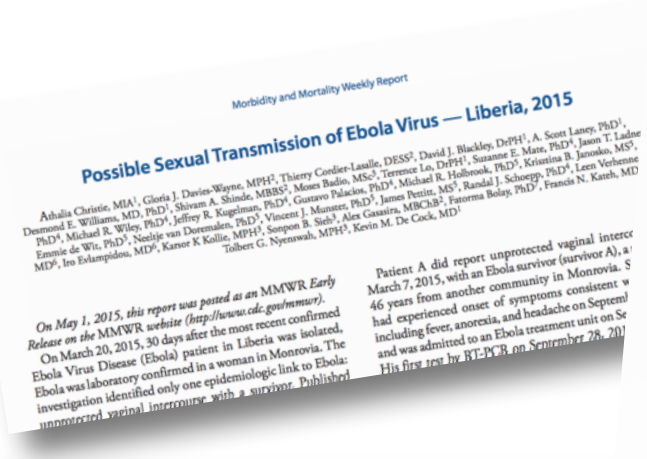
Launch of Longitudinal Survivor Study

Launch of NIH GS-5734 Phase II Trial

Dec 2014

Aug 2015

May 2016


Morbidity and Mortality Weekly Report

Possible Sexual Transmission of Ebola Virus — Liberia, 2015

at CHAPEL HILL

Clinical Response

- A UNC physician was deployed to the epicenter to improve care for patients with Ebola Virus Disease (EVD)
  - Along with team from WHO demonstrated that aggressive supportive care could improve outcomes
- Dr. Fischer partnered with Dr. Wohl to bring enhanced care to patients in West Africa
  - Convalescent Plasma
  - Care for EVD Survivors
  - Evaluation of novel therapeutics


3. Suit
4. N-95
5. Hood
6. Surgi
over n
7. Apron
8. Goggl
9. Outer
10. Partne

ELWA Hospital

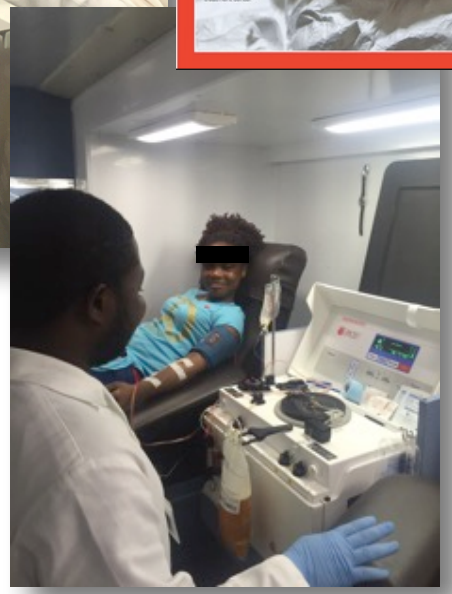
- Location: Paynesville, 30 minutes from Monrovia
- Facilities:
  - Private medical center with ~50 beds
  - For study (tentative): 2 in-patient beds and outpatient space
  - Out-patient clinics including dedicated Ebola Survivor Clinic
  - Site for convalescent plasma trial and longitudinal Ebola survivor cohort study
  - Basic clinical laboratory
  - On-site pharmacy

Ebola Convalescent Plasma – Clinical Trials

Liberia – UNC – CRM Trial

(Gates Funded)

- First ever trial of Ebola therapeutic intervention
- Plasma collected from survivors and given to pts with acute EVD
- Provided diagnostic labs to enhance patient care
- Replicated in Sierra Leone
- Plasma collection (>100 donors)



“Even When its Over – Its Not Over”

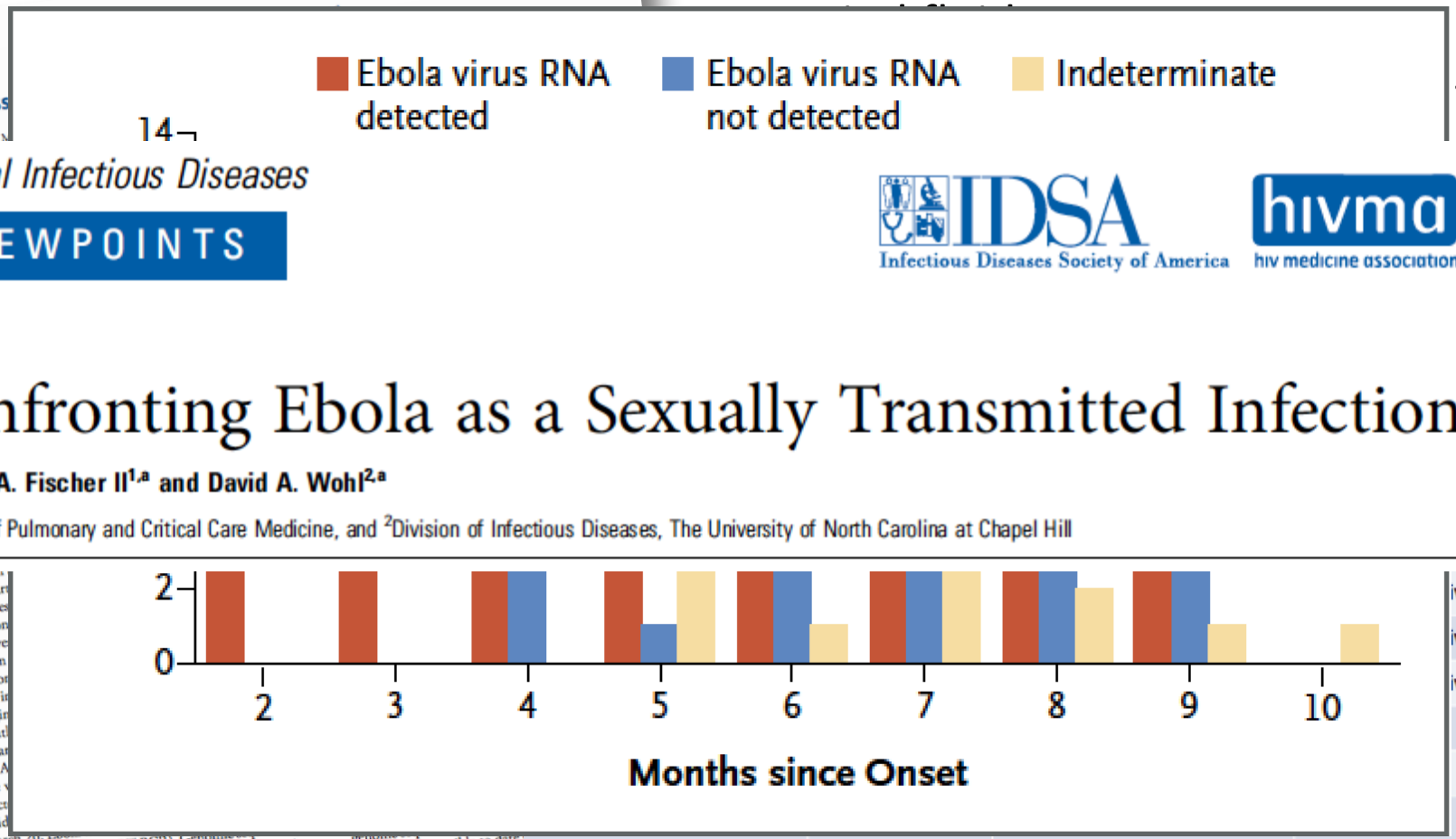
Post Ebola Syndrome

Table 2. Symptoms associated with Post-Ebola Syndrome (14,21)		
Symptom	**Survivors (%)**	**Household Contacts (%)**
Arthralgia	48	3
Ocular Disease	16-39	NA
Hearing Loss or Tinnitus	11-27	NA
Myalgias	24	3
Extreme Fatigue	8	3
Anorexia	7	3

Rowe AK, et al JID 1999

Persistence of Ebola Virus After "Cure"

- Evidence of persistence of EBOV in



the

Clinical Infectious Diseases

VIEWPOINTS

IDSA Infectious Diseases Society of America

hivma hiv medicine association

OXFORD

Confronting Ebola as a Sexually Transmitted Infection

William A. Fischer II[1,a] and David A. Wohl[2,a]

[1]Division of Pulmonary and Critical Care Medicine, and [2]Division of Infectious Diseases, The University of North Carolina at Chapel Hill

Rodriguez, L. et al	Semen	97	NA
Rodriguez, L. et al	Semen	63	NA
Christie, A. et al	Semen	199	NA
Bausch, D et al	Semen	40	40 *

* Culture Positive

Longitudinal Survivor Study

- 300 survivors in Liberia
- Followed every 3-6 months
  - Clinical status
  - Psychosocial/Stigma
  - Sexual behavior
  - Blood for immune and inflammatory markers
  - Semen and vagina fluid for Ebola virus shedding
    - Results provided directly to survivors
    - 1st ever Ebola PCR platform validated for genital fluids

PREVAIL IV – Trial of GS-5734

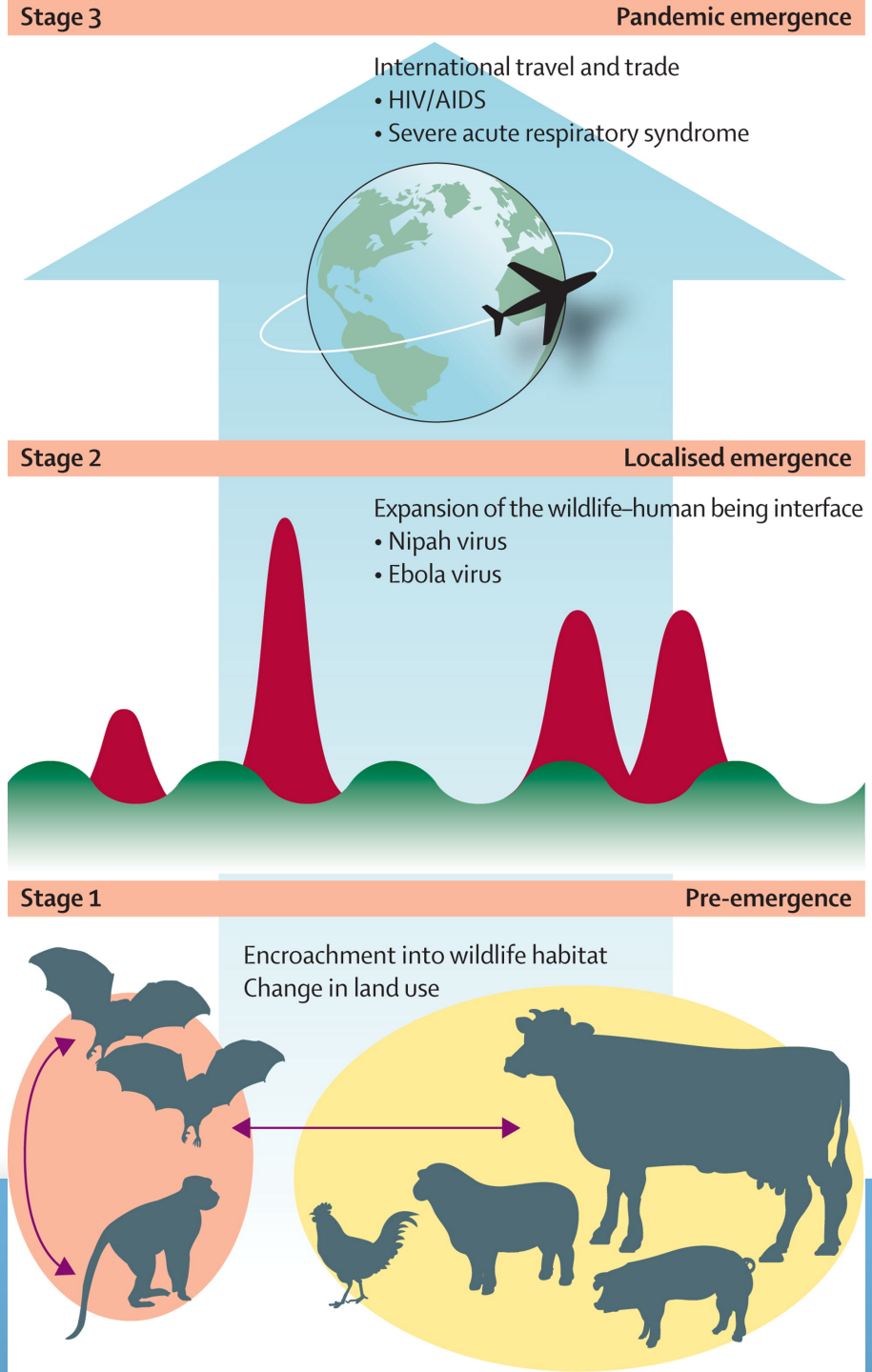
- Phase II trial of a novel anti-Ebola agent
- Male Ebola survivors with active seminal shedding of EBOV

Capacity Building

- Stand up point of care of care chemistry diagnostics for use during and following the active outbreak
- Support of plasma collection for Ebola concentrated immunoglobulin production
- Training of clinical staff in high quality clinical research
- Setting up of 3 clinical research sites in Liberia
- Developing validated, high quality Ebola PCR (blood, semen, cervico-vaginal fluid) testing at national reference laboratory

Relationship Building

- Survivor advocacy groups
- Medical community
- Regulatory authorities
- Community service orgs



Acknowledgements

- The many survivors of Ebola who have taught us much about overcoming unimaginable horrors with dignity and resolve.
- Hero healthcare providers & researchers
- My work partner & friend Billy Fischer
- Our families