THE 2014 EBOLA OUTBREAK
Lessons for DH from the Hot Zone

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Division of Public Health Services
October **2014**

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I have no conflict of interest.

Patient Zero

12-6-2013 2yo child died in Meliandou in Guéckédou after contact with bat

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The Timeline

- March 10 2014: 2 Guinean jurisdictions
  - In Guéckédou, 8 patients; 3 died
    - Families!
  - In Macenta, high mortality
    - HCWs!
  - March 14 investigation; EVD identified
- Spread recognized
  - March 10 Liberia
  - May 25 Sierra Leone
  - Introduced and controlled Nigeria, Senegal

Baize et al. NEJM April 2014

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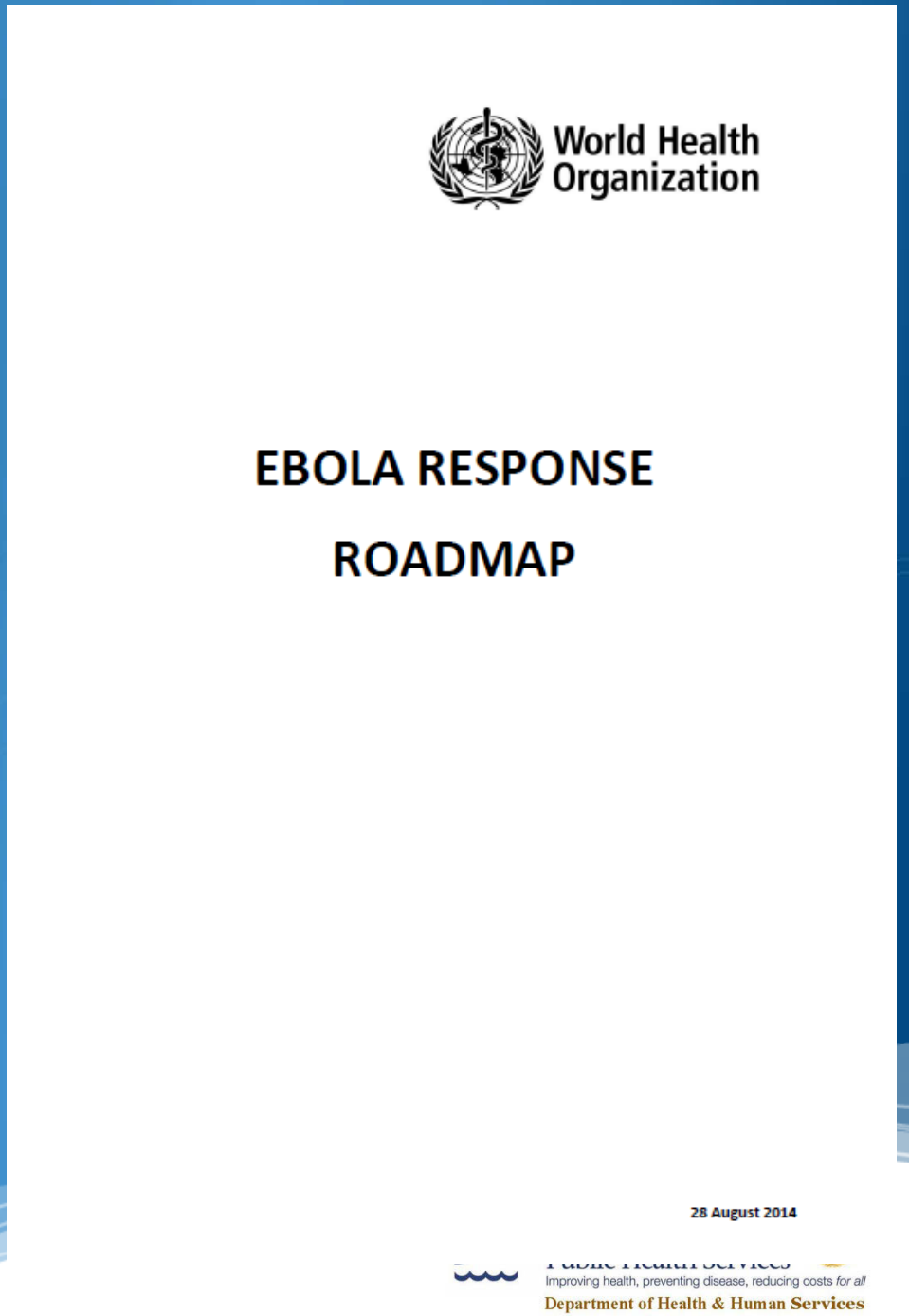
Aug 8 "Public Health Emergency of International Concern" Announced

- Health systems are fragile and resource limited
- Inexperience in dealing with Ebola outbreaks
- Misperceptions about disease and transmission
- High population mobility
  - Cross-border movement of travelers with infection
- Generations of transmission in 3 capital cities
- Many infections among HCWs
  - Inadequate infection control practices in many facilities

http://www.who.int/mediacentre/news/statements/2014/ebola-20140808/en/#

Global Control Strategy

- Early diagnosis
- Contact tracing
- Patient isolation and care
- Infection control
- Safe burial
  - 60% cases in Guinea



Ebola Virus Disease in West Africa — No Early End to the Outbreak

Margaret Chan, M.D.

Many people have asked me why the outbreak of Ebola virus disease in West Africa is so large, so severe, and so difficult to contain. These questions can be answered with a single word: poverty.

Global Epidemiologic Summary

- Outbreak in Guinea, Liberia, and Sierra Leone continues to worsen with widespread transmission and recent spread to previously unaffected Guinean prefecture of Kankan
  - Borders Cote d'Ivoire and on major trade route with Mali
- Intense transmission continues in 3 capital cities
- Global total exceeds 10,000 cases
  - Approximate 50% mortality

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Mali is Sixth West African Country with EVD

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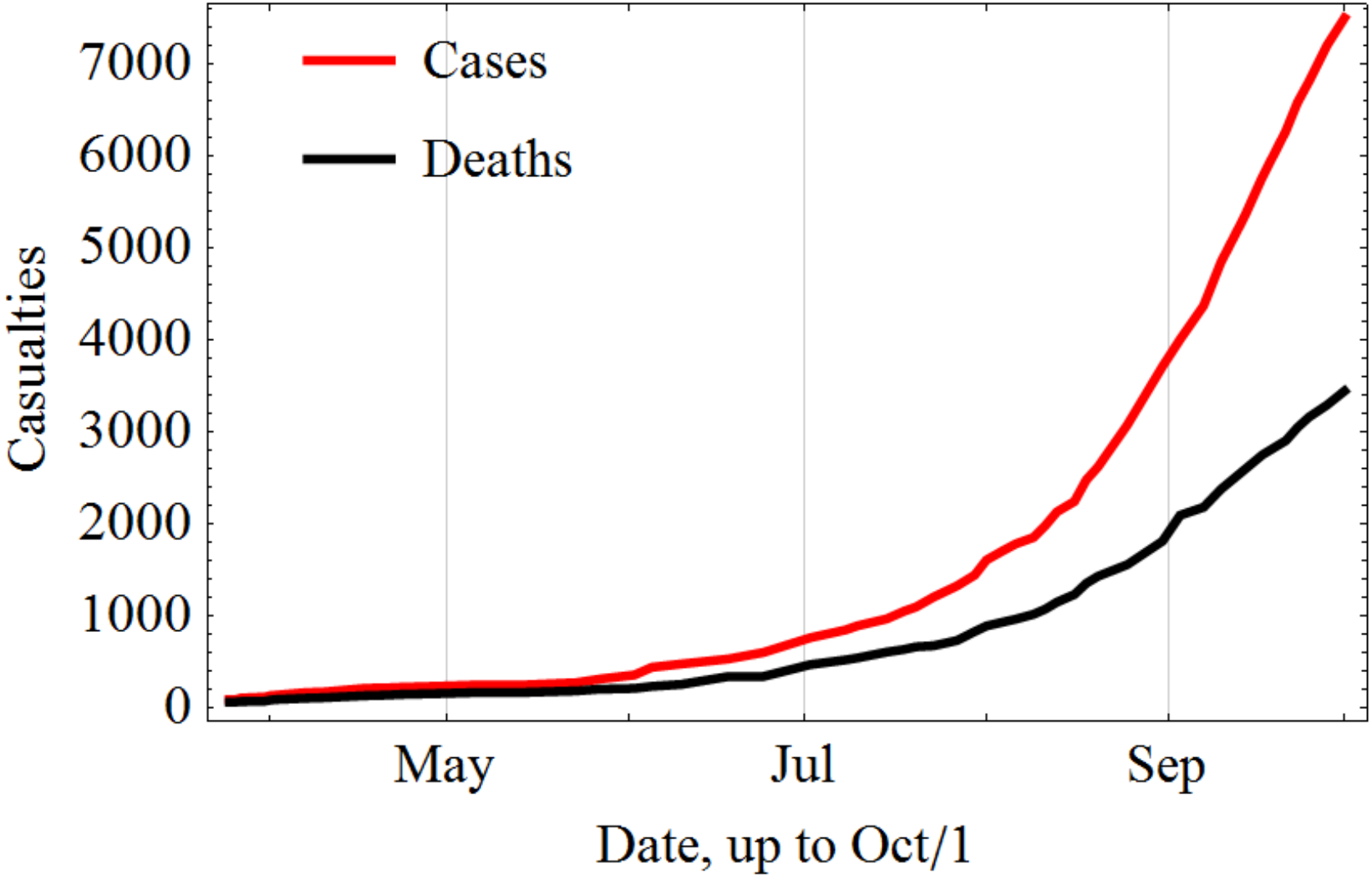
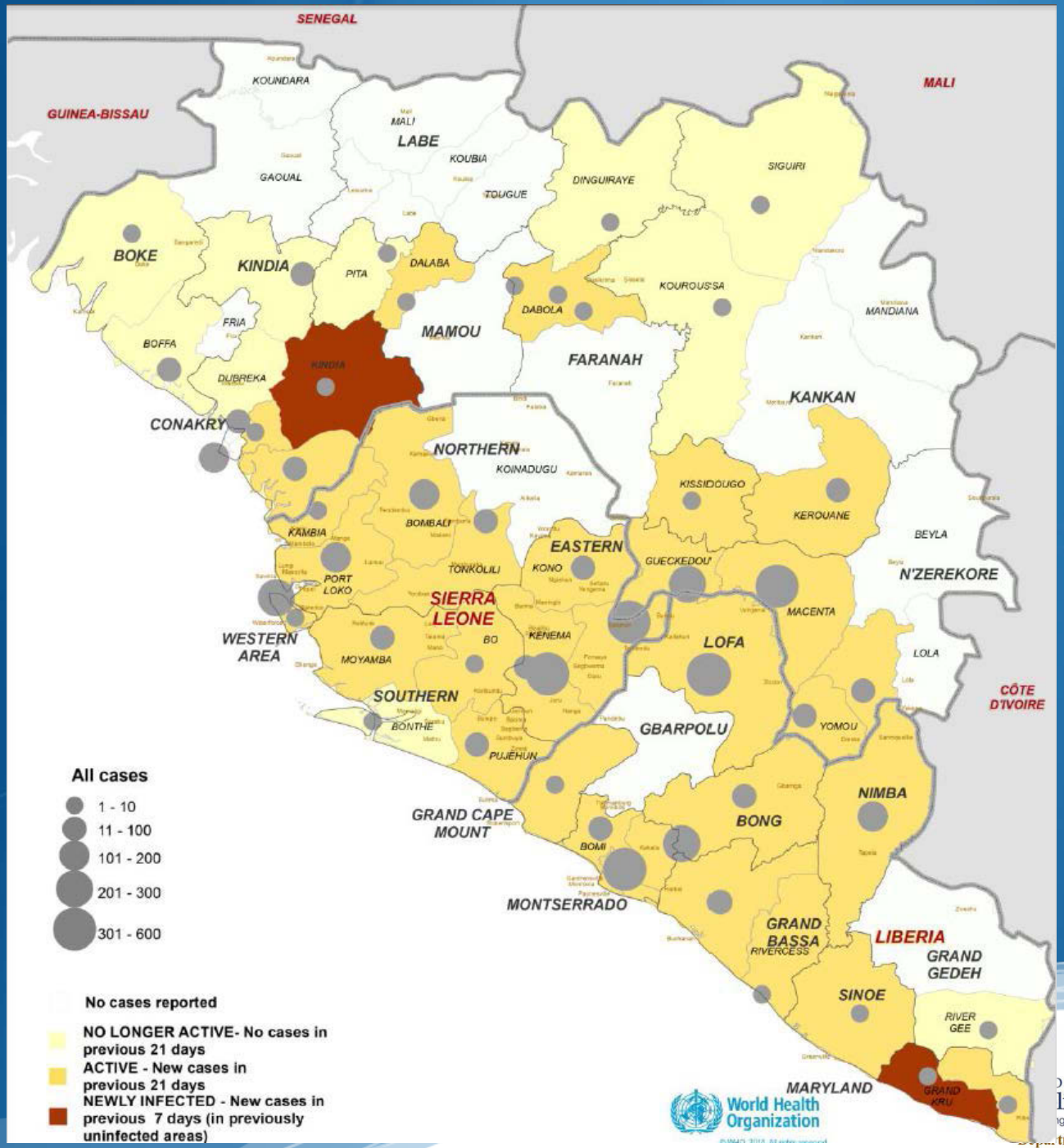
Mali Vulnerable with Porous Borders with Guinea

- 2yo's father died in Guinea; grandmother took her by circuitous route to Mali
  - Nosebleeding and bloody vomiting
  - Died in Mali on Oct 24
- WHO reports "The child's symptomatic state during the bus journey is especially concerning, as it presented multiple opportunities for exposures - including high-risk exposures - involving many people"
- 43 people quarantined
- UN humanitarian flight service airlifted about 1 ton of medical supplies to Mali


Cases
Deaths
7000
6000
5000
4000
3000
2000
1000
0
Casualties
May
Jul
Sep
Date, up to Oct/1



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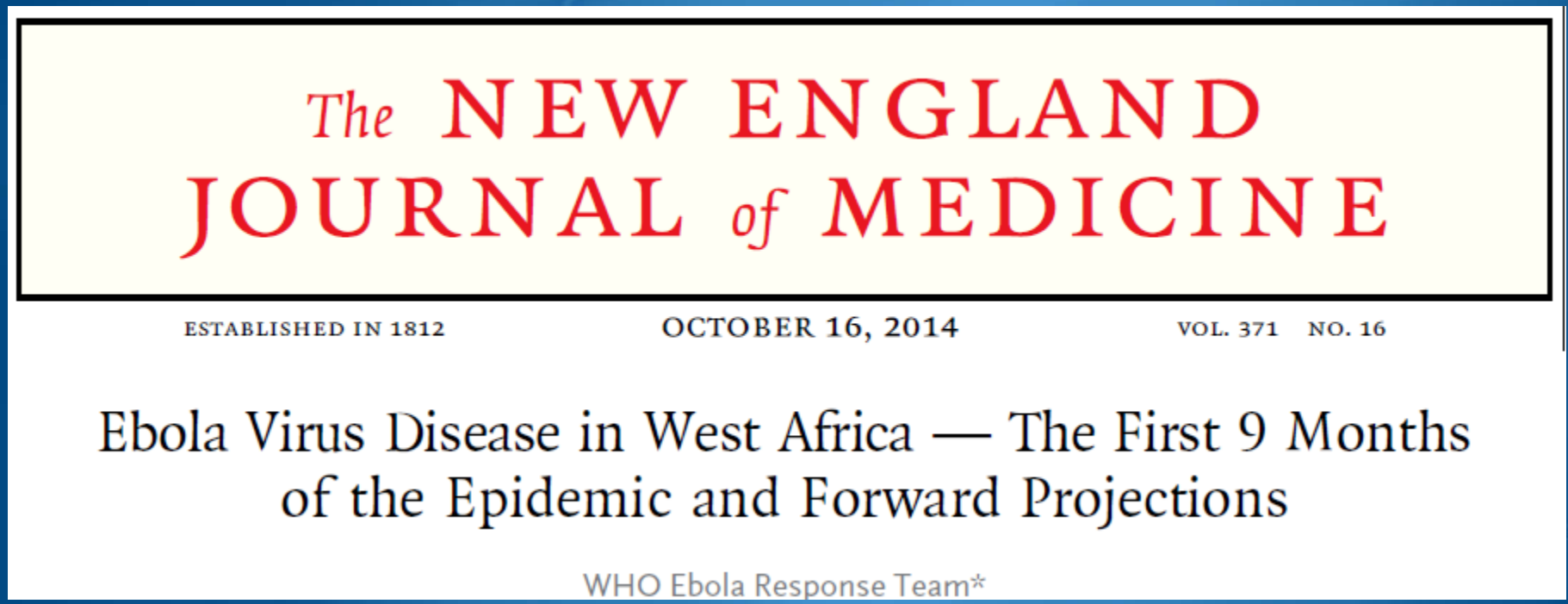
Genomic Surveillance

- Sequenced 137 EVD samples
- Compared to previous strains, current outbreak strain has 341 fixed substitutions
- Comparing strains within current outbreak
  - Single transmission from animal then H2H
  - 55 single nucleotide polymorphisms
    - "Continual mutations could generate more lethal or more easily transmitted strain"
      - No evidence or historic precedent

Gire SK, Goba A, Andersen KG, et al. *Science* 2014; 345(6202):1369-72



The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 OCTOBER 16, 2014 VOL. 371 NO. 16

Ebola Virus Disease in West Africa — The First 9 Months of the Epidemic and Forward Projections

WHO Ebola Response Team*

- Analysis of 3343 confirmed and 667 probable Ebola cases through Sept 14
- Key clinical features and time intervals
  - Predict timeline
  - Improve control efforts

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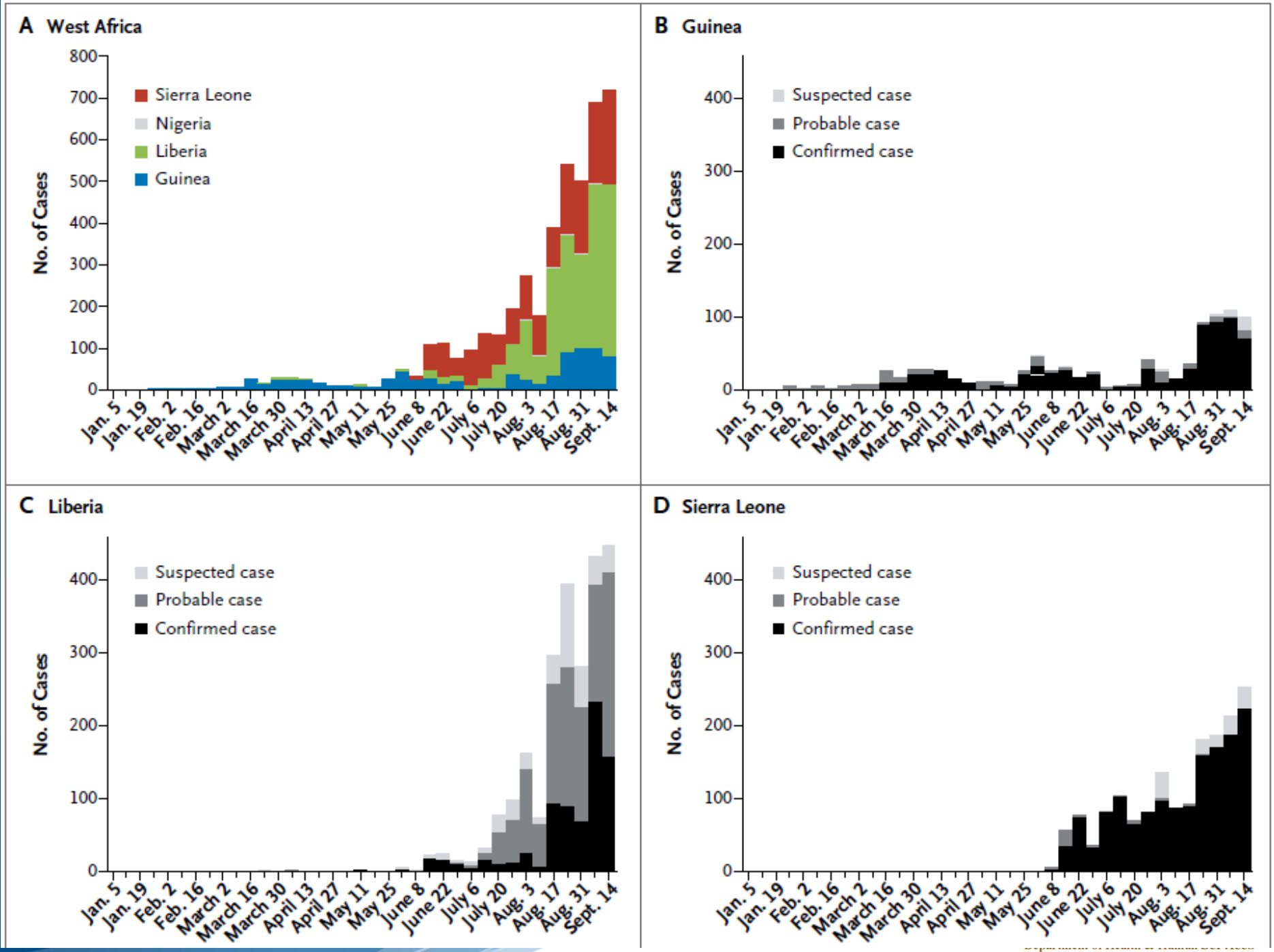
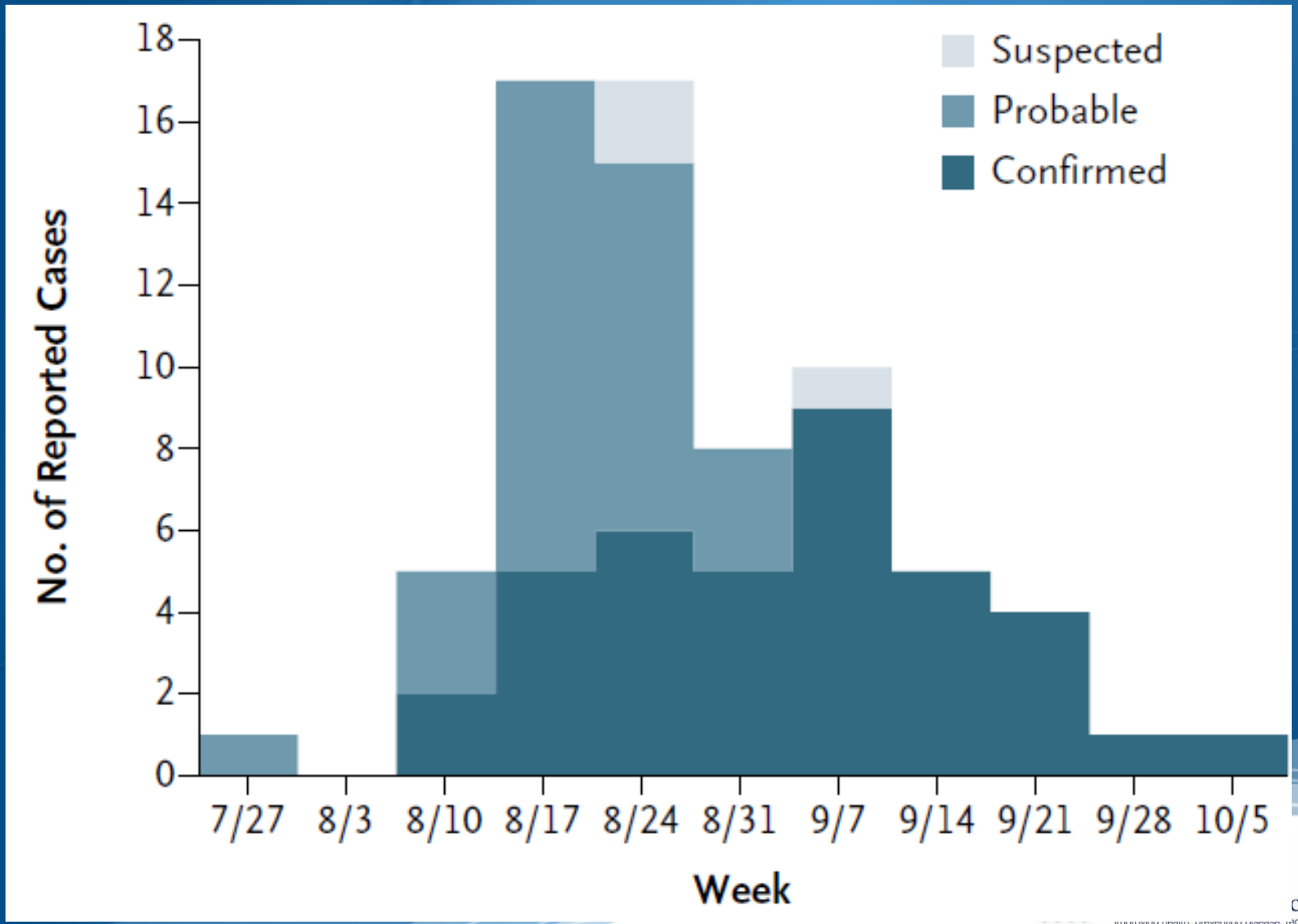

A West Africa
No. of Cases
800
700
600
500
400
300
200
100
0
Sierra Leone
Nigeria
Liberia
Guinea
Jan. 5
Jan. 19
Feb. 2
Feb. 16
March 2
March 16
March 30
April 13
April 27
May 11
May 25
June 8
June 22
July 6
July 20
Aug. 3
Aug. 17
Aug. 31
Sept. 14
B Guinea
No. of Cases
400
300
200
100
0
Suspected case
Probable case
Confirmed case
C Liberia
No. of Cases
400
300
200
100
0
Suspected case
Probable case
Confirmed case
D Sierra Leone
No. of Cases
400
300
200
100
0
Suspected case
Probable case
Confirmed case

Simultaneous DRC Outbreak



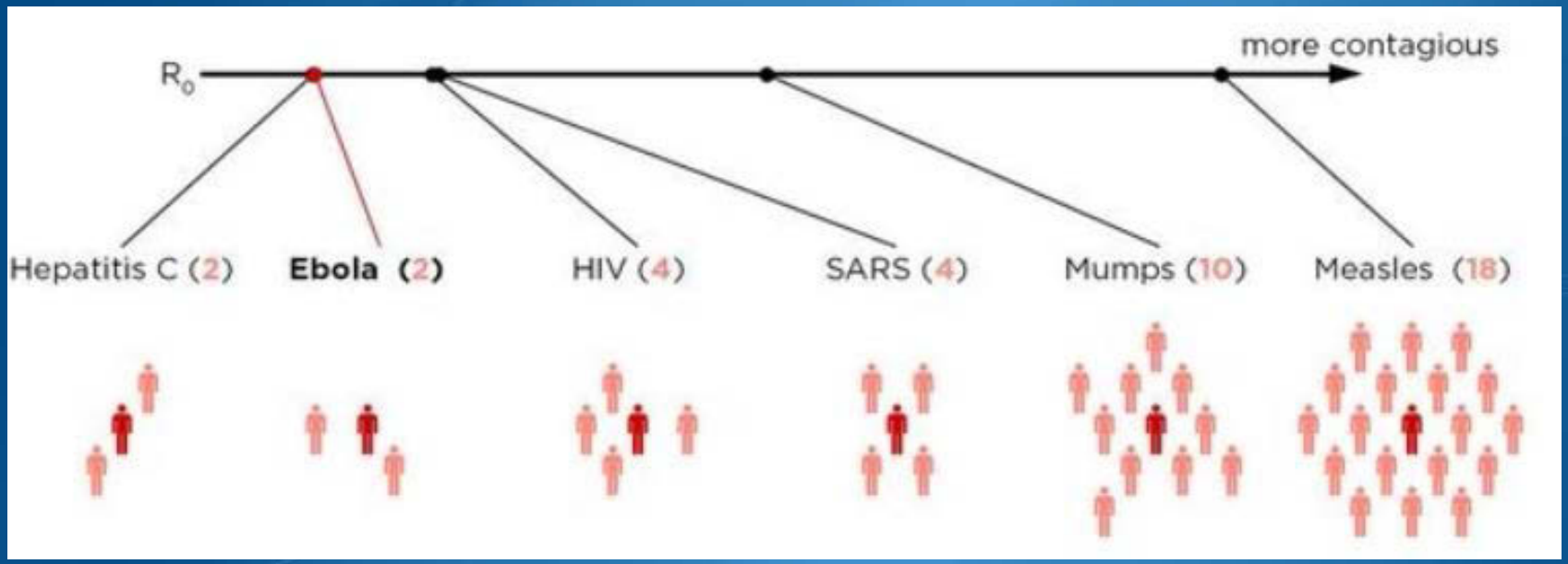
Key Numbers

- Incubation period: time between infection and the onset of symptoms
  - Suggests quarantine
- Infectious period: symptom onset to hospitalization
  - Suggests community impact
- Serial interval: time between disease onset in source patient and contact
- Generation time: time between infection in an source patient and contact

- Incubation period: time between infection and the onset of symptoms = 11.4d
- Infectious period: symptom onset to hospitalization = 5d
- Serial interval: time between disease onset in source patient and contact = 15.3d
- Generation time: time between infection in an source patient and contact = 15.3d

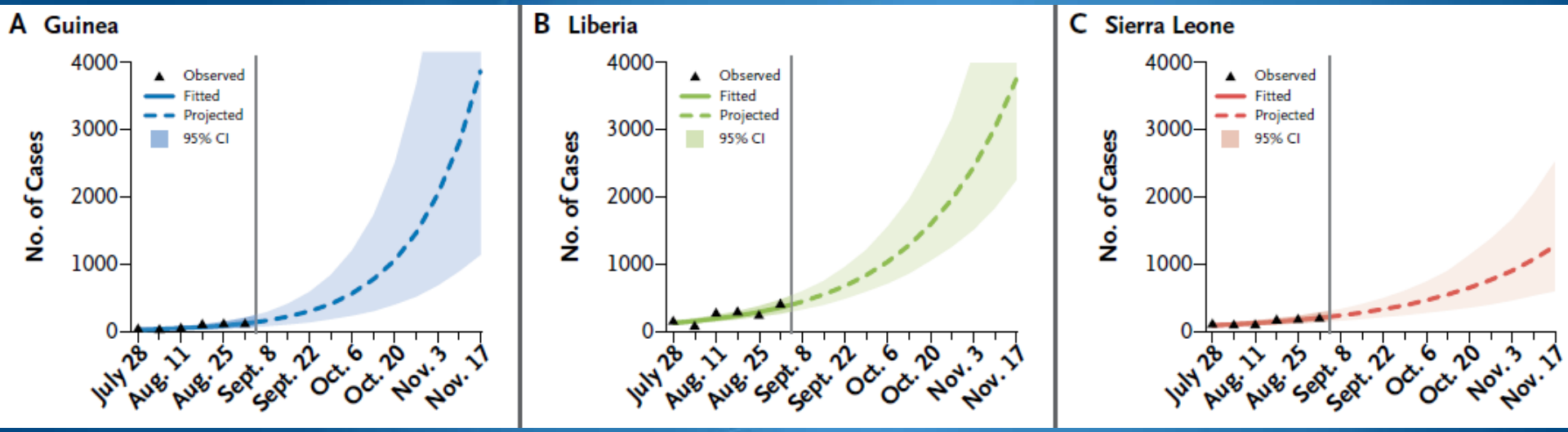
These Numbers Inform R

- R_0: # of secondary cases from one case in uninfected population (max)



- R_t: # of secondary cases during epidemic
  - Changes
  - When <1, epidemic not sustainable
    - Predicts need

Bleak



- Unless control measures (contact tracing, case isolation and management, safe burials, vaccine/drugs) improve quickly, thousands of cases and deaths each week
- “Endemic in Africa”??

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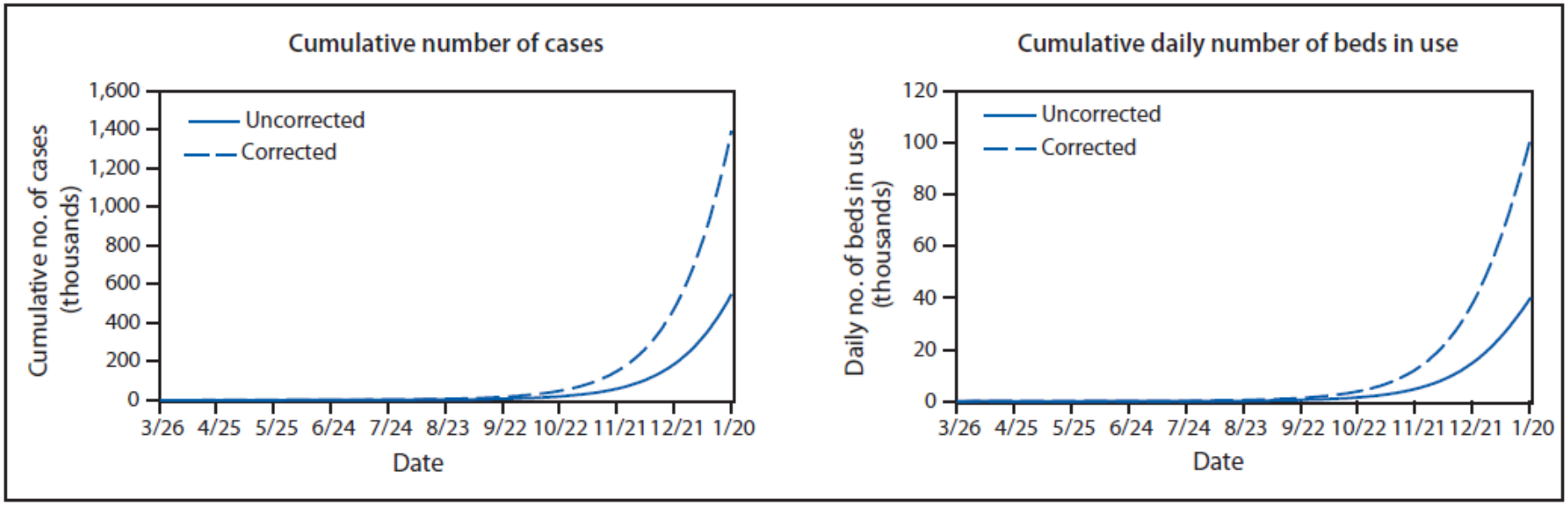
CDC's Projections

FIGURE 2. Estimated number of Ebola cases and daily number of beds in use,* with and without correction for underreporting† — EbolaResponse modeling tool, Liberia and Sierra Leone combined, 2014–2015



* Corrected for potential underreporting by multiplying reported cases by a factor of 2.5 (Table 4).
† Estimates of daily number of beds in use are calculated using estimates of likelihood of going to an Ebola treatment unit (ETU) and days in the ETU (Table 3).

MMWR Vol 63, Sept 26 2014.

Underreporting

- Conservative 2.5 factor
- Symptomatic persons evade diagnosis and treatment
- Laboratory diagnoses not been included in national databases
- Deaths from suspected EVD buried without diagnosis

Ebolaviruses

CLINICAL FEATURES

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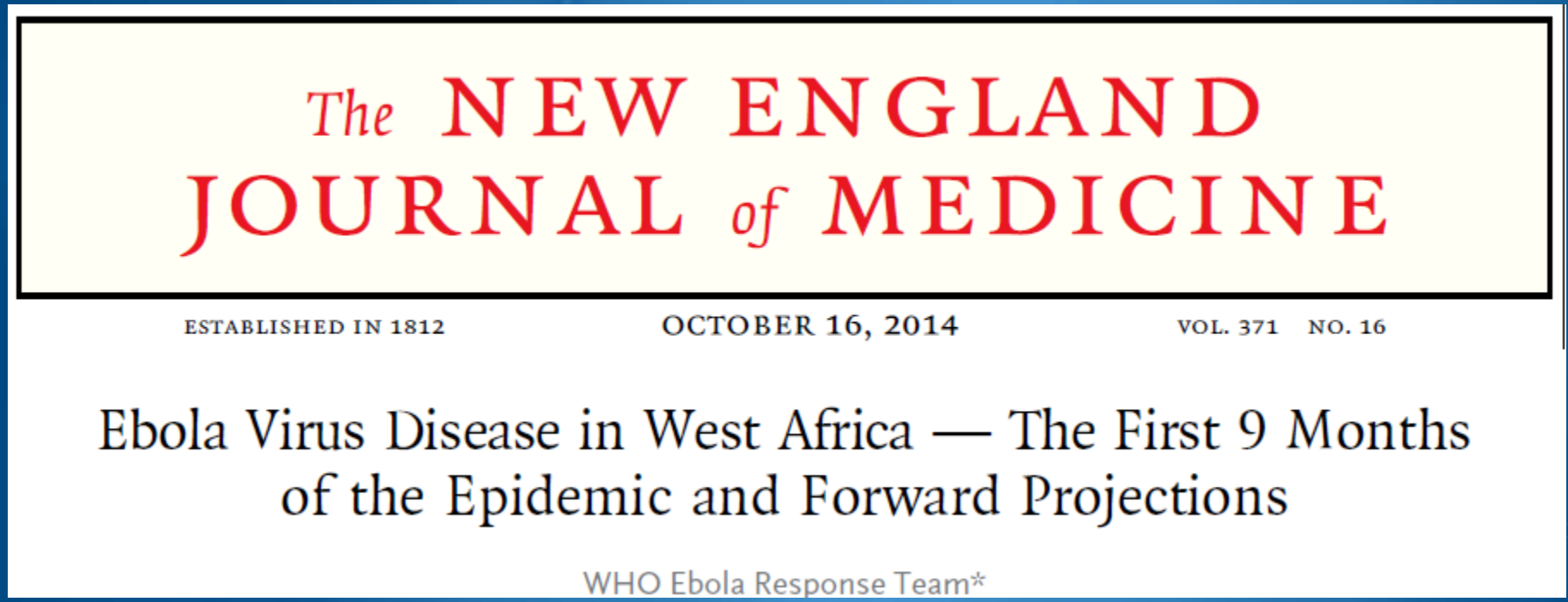

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Variable	All Patients	Patients Who Died	Patients Who Recovered	Odds Ratio (95% CI)†
		no./total no. (%)		
Demographic characteristics				
Male sex	685/1415 (48.4)	515/1056 (48.8)	170/359 (47.4)	0.93 (0.73–1.19)
Age group				
<15 yr	190/1378 (13.8)	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)
Signs and symptoms				
General symptoms				
Fever‡	1002/1151 (87.1)	746/846 (88.2)	256/305 (83.9)	1.34 (0.92–1.95)
Fatigue	866/1133 (76.4)	633/829 (76.4)	233/304 (76.6)	0.94 (0.68–1.28)
Loss of appetite	681/1055 (64.5)	498/778 (64.0)	183/277 (66.1)	0.92 (0.69–1.23)
Vomiting	753/1114 (67.6)	566/816 (69.4)	187/298 (62.8)	1.19 (0.89–1.59)
Diarrhea	721/1099 (65.6)	555/813 (68.3)	166/286 (58.0)	1.42 (1.06–1.89)
Headache	553/1035 (53.4)	407/757 (53.8)	146/278 (52.5)	1.03 (0.78–1.36)
Abdominal pain	439/992 (44.3)	311/715 (43.5)	128/277 (46.2)	0.85 (0.64–1.13)
Muscle pain	385/990 (38.9)	293/728 (40.2)	92/262 (35.1)	1.24 (0.92–1.67)
Joint pain	374/950 (39.4)	283/695 (40.7)	91/255 (35.7)	1.32 (0.98–1.80)
Chest pain	254/686 (37.0)	196/488 (40.2)	58/198 (29.3)	1.53 (1.07–2.20)
Cough	194/655 (29.6)	150/462 (32.5)	44/193 (22.8)	1.74 (1.18–2.61)
Difficulty breathing	155/665 (23.3)	123/472 (26.1)	32/193 (16.6)	1.68 (1.10–2.63)
Difficulty swallowing	169/514 (32.9)	138/375 (36.8)	31/139 (22.3)	2.22 (1.41–3.59)
Conjunctivitis	137/658 (20.8)	109/465 (23.4)	28/193 (14.5)	2.03 (1.29–3.29)
Sore throat	102/467 (21.8)	82/339 (24.2)	20/128 (15.6)	1.94 (1.13–3.46)
Confusion	84/631 (13.3)	68/446 (15.2)	16/185 (8.6)	2.00 (1.14–3.71)
Hiccups	108/947 (11.4)	91/699 (13.0)	17/248 (6.9)	2.15 (1.27–3.82)

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Bleeding Less Common than Most Anticipate

Variable	All Patients	Patients Who Died	Patients Who Recovered	Odds Ratio (95% CI)†
		no./total no. (%)		
Unexplained bleeding	168/932 (18.0)	140/693 (20.2)	28/239 (11.7)	1.83 (1.20–2.90)
Hematemesis	26/670 (3.9)	20/503 (4.0)	6/167 (3.6)	1.07 (0.44–3.01)
Blood in stool	48/843 (5.7)	35/614 (5.7)	13/229 (5.7)	0.98 (0.52–1.96)
Bleeding gums	19/837 (2.3)	18/608 (3.0)	1/229 (0.4)	6.69 (1.35–121.32)
Bloody nose	16/836 (1.9)	15/610 (2.5)	1/226 (0.4)	8.02 (1.54–148.62)
Bloody cough	20/831 (2.4)	16/605 (2.6)	4/226 (1.8)	1.63 (0.58–5.82)
Other bleeding	8/657 (1.2)	5/493 (1.0)	3/164 (1.8)	0.45 (0.11–2.23)
Bleeding at injection site	20/833 (2.4)	19/605 (3.1)	1/228 (0.4)	6.51 (1.32–118.04)
Blood from vagina§	14/431 (3.2)	13/290 (4.5)	1/126 (0.8)	6.0 (1.11–112.4)
Blood in urine	10/827 (1.2)	9/601 (1.5)	1/226 (0.4)	5.14 (0.90–98.73)
Bleeding under skin	5/827 (0.6)	5/604 (0.8)	0/223	NA

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Simultaneous DRC Outbreak

Sign or Symptom	Non-EVD Cases (N=60)	Probable EVD Cases (N=28)	Odds Ratio of Probable EVD (95% CI)†	Confirmed EVD Cases (N=38)	Odds Ratio of Confirmed EVD (95% CI)†
	no. of patients (%)			*no. of patients (%)*	
Fever	41 (68)	28 (100)	NA	35 (92)	5.4 (1.7 to 9.1)
Headache	7 (12)	7 (25)	2.5 (–0.7 to 5.7)	17 (45)	6.1 (3.4 to 8.9)
Diarrhea	22 (37)	23 (82)	7.9 (4.7 to 11.1)	26 (68)	3.7 (1.4 to 8.9)
Abdominal pain	12 (20)	7 (25)	1.3 (–1.9 to –4.5)	18 (47)	3.6 (1.1 to 6.1)
Vomiting or nausea	18 (30)	22 (79)	8.6 (5.4 to 11.8)	26 (68)	5.1 (2.6 to 7.5)
Intense fatigue or general weakness	11 (18)	11 (39)	2.9 (–0.3 to 6.1)	27 (71)	10.9 (8.3 to 13.5)
Anorexia	9 (15)	11 (39)	3.7 (0.5 to 6.9)	15 (39)	3.7 (1.1 to 6.3)
Muscle pain	3 (5)	7 (25)	6.3 (3.1 to 9.5)	17 (45)	15.4 (11.6 to 19.1)
Difficulty swallowing	3 (5)	6 (21)	5.2 (2.0 to 8.4)	10 (26)	6.8 (2.9 to 10.7)
Difficulty breathing	5 (8)	6 (21)	3.0 (–0.2 to 6.2)	6 (16)	2.1 (–1.5 to 5.6)
Cough	5 (8)	5 (18)	2.4 (–0.8 to 5.6)	2 (5)	0.6 (–4.8 to 6.0)
Rash	1 (2)	2 (7)	4.5 (1.3 to 7.7)	3 (8)	5.1 (–4.9 to 15.0)
Bleeding from injection site	0	2 (7)	NA	3 (8)	NA
Gingivitis	1 (2)	3 (11)	7.1 (3.9 to 10.3)	3 (8)	5.1 (–4.9 to 15.0)
Conjunctivitis	1 (2)	4 (14)	9.8 (6.6 to 13.0)	6 (16)	11.0 (2.4 to 19.7)
Bloody or black stools	4 (7)	12 (43)	10.5 (7.3 to 13.7)	8 (21)	3.7 (0.1 to 7.3)
Vomiting blood	3 (5)	10 (36)	10.6 (7.4 to 13.8)	6 (16)	3.6 (–0.7 to 7.8)

Ebolaviruses
MANAGEMENT

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Diagnosis

- Culture
- Real-time RT-PCR detects virus in symptomatic patients
  - Blood best

- Salivary swabs when blood is difficult to obtain

Therapy

- Supportive
  - Adequate tissue delivery of oxygen
  - Nutritional support
  - Hydration
- Replace blood, platelets, and clotting factors if hemorrhage
- Hyperimmune globulin*
  - Prophylaxis in lab or nosocomial accidents
  - Used for

*Qiu X et al. Sci Transl Med. 2012;4:138ra81

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Pipeline for Therapy

- Zmapp
- TkM-Ebola: interfering RNAs target EV RNA polymerase L
- AVI-7537 targets EV protein VP24 through RNA interference
- BCX-4430: adenosine analogue

Warren TK, et al. Nature. 2014;508:402-5

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Patients Treated in West

- Dr. Kent Brantly, Nancy Writebol and Dr. Rick Sacra contracted in Liberia and survived

- Nina Pham is one of 2 nurses infected after treating Thomas Eric Duncan
  - Discharged from NIH
- Amber Vinson, second nurse
  - Doing well at Emory

Vaccines

- Phase 1 pre-licensure clinical trials
  - cAd3-ZEBOV (GSK/NIAID)
    - Chimpanzee-derived adenovirus vector with Ebola virus gene inserted
  - rVSV-ZEBOV (Public Health Agency of Canada, license held by NewLink Genetics, IA)
    - Attenuated vesicular stomatitis virus with one gene replaced by Ebola gene
- WHO et al facilitating expedited evaluation of these for safety and immunogenicity data
  - January?

Ebolaviruses
TRANSMISSION IN US?

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What Do We Know?

- Direct contact with blood through broken skin or mucous membranes
- Indirect contact with environments contaminated with fluids
  - HCWs infected through close contact with patients when infection control precautions are not strictly practiced
- Burial ceremonies
  - 60% of cases in Guinea

Table 1. Ebola virus detection by reverse-transcription polymerase chain reaction (RT-PCR) in body fluids collected from EVD patients during an outbreak in Gulu, Uganda14 and the maximum described persistence after symptom onset described in the literature[16,18-20]

Body Fluid	Acute phase of illness number detected/number tested (percent)	Convalescent phase of illness number detected/number tested (percent)	Last day detected after symptom onset described in the literature	Comments
Skin	1/8 (13%)	0/4 (0%)	6	
Saliva	8/12 (67%)	0/4 (0%)	8	
Urine	0/7 (0%)	0/4 (0%)	23	Ebola virus antigen has been detected in the urine in other studies[20]
Stool / Feces	2/4 (50%)	n/d	29	
Breast milk	1/1 (100%)	1/1 (100%)	15	Ebola infects circulating macrophages which are present in breast milk[16]
Semen	n/d	1/2 (50%)	101	Sexual transmission of Marburg virus (but not Ebola virus) has been described[36]
Vaginal fluid	n/d	n/d	33	

First Nosocomial Spread Outside Africa

- Nurse's assistant cared for both priests repatriated morbidly ill from Sierra Leone
  - These 2 were among 10 evacuations to EU or US
  - 1 of 30 who cared for these 2 patients
- Sept 30-Oct 6 she had fever before becoming so ill she called EMS while on vacation
- No transmission identified

Tough Questions for Spain

- Why did they repatriate moribund patients?
- Why was nurse not quarantined or at least better informed re: significance of fever?
- What went wrong with the PPE??
  - Doffing, training

First Case Diagnosed in US

- Sept 15, 2014 Liberian cared for EVD patient
- Sept 19 traveled from Liberia to Dallas
- Sept 23-24 became ill: F, N/V, abd pain
- Sept 25 10pm ED, reported from Africa, discharged with antibiotics
- Sept 28 worse, transported by EMS
- Sept 30 diagnosed
- Two nurses acquired disease

Tough Questions for Dallas

- Why was first patient not recognized?
- Why were two nurses infected?
  - Doffing again implicated
- Why was nurse not better quarantined?

After second nurse, Obama said his administration will respond to new Ebola cases "in a much more aggressive way,”

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In US 9 Adults Confirmed

- 5 medically evacuated
- 2 identified in US
  - Duncan from Liberia
  - Physician from Columbia working in Guinea with MSF
- 2 nurses exposed to imported case
- 4 discharged, 1 died, 3 still hospitalized
  - 3 survivors received plasma donations from Brantly, Zmapp and other experimental treatments

Message Evolution

"The initial guidelines used by the CDC worked well for many, many years in approaching patients who have Ebola in the African setting. … With patients here [in the US], we do things that are much more aggressive, such as intubation. Under those original guidelines, [HCWs] had a mask, but their skin and hair were exposed. … We want to [eliminate those vulnerabilities] and have essentially everything covered."

Dr. Anthony Fauci,

How much confidence do you have in federal government to prevent a major outbreak of Ebola virus in U.S.? (%)

How worried are you that you or someone in your family will be exposed to the Ebola virus? (%)

Survey conducted Oct. 2-5, 2014.
Figures may not add to 100% because of rounding.

PEW RESEARCH CENTER

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Fear-bola

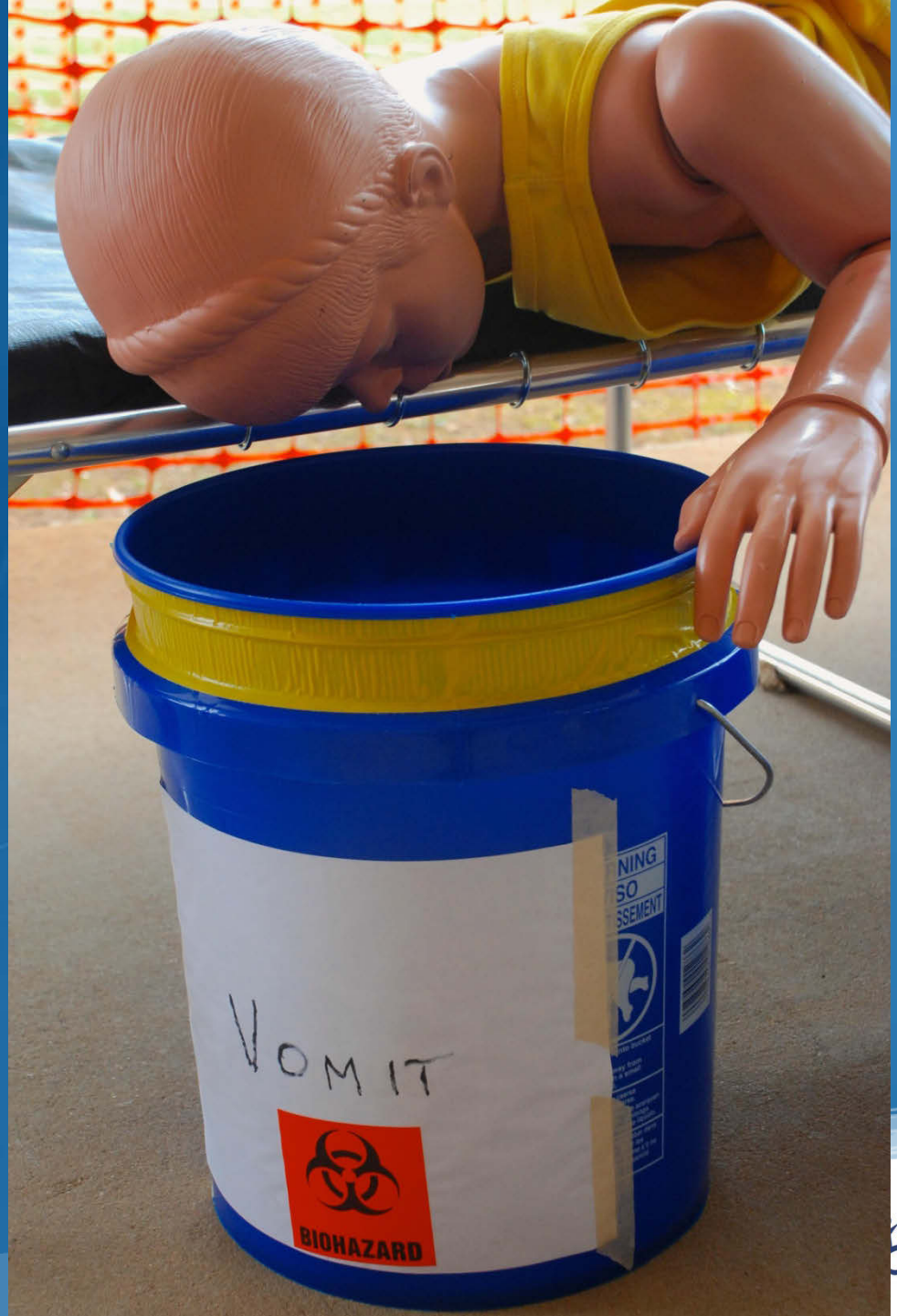
- Mel Robbins, a CNN commentator and legal analyst, coined the US hysteria as “Fear-bola”
- "Fear-bola attacks the part of the brain responsible for rational thinking. It starts with a low-grade concern about the two health care workers diagnosed with Ebola in Dallas and slowly builds into fear of a widespread epidemic in the United States."
- Treatment may be education

Military Medical Strike Team

- Defense Secretary Hagel, responding to an HHS request, ordered the Northern Command “to compile a team of five doctors, five trainers and 20 nurses to head to Fort Sam Houston in Texas for high-level preparations to respond to any additional Ebola cases [in the US].”

Center for Domestic Preparedness in Anniston AL


LOWE
LOWE



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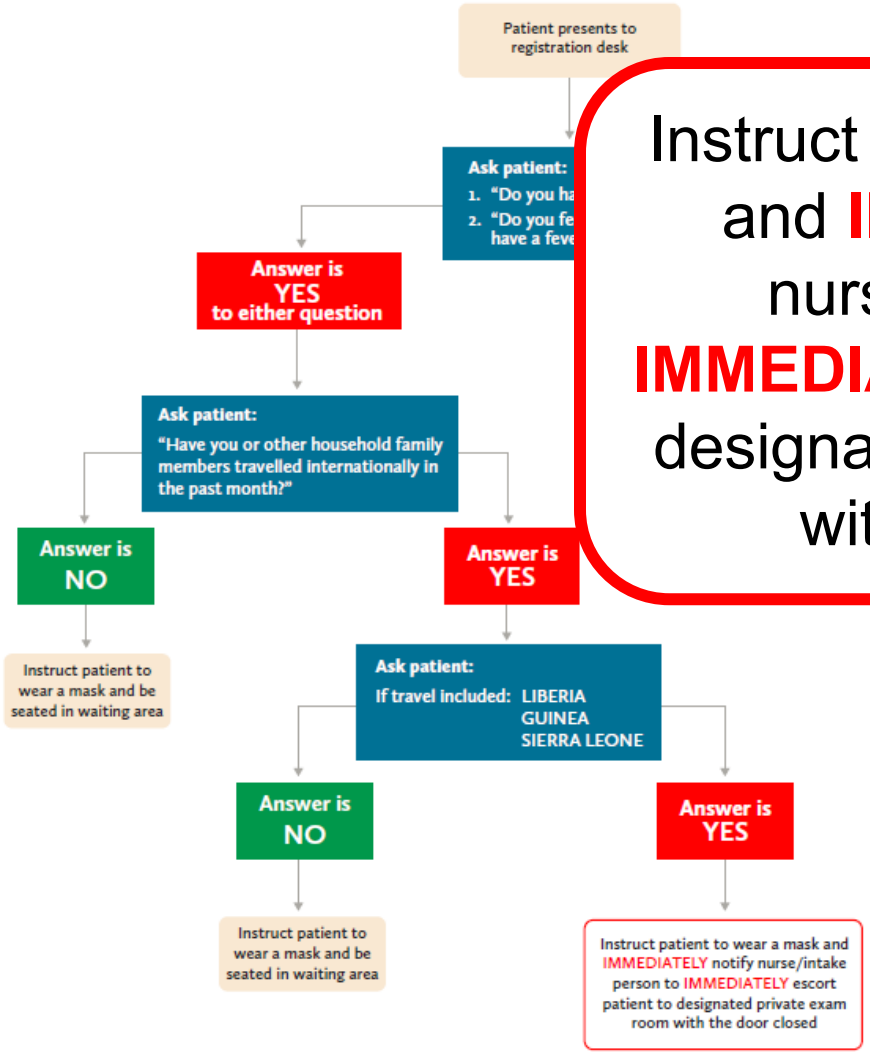
Ebola Screening Flow Chart for Reception Desks

October 20, 2014



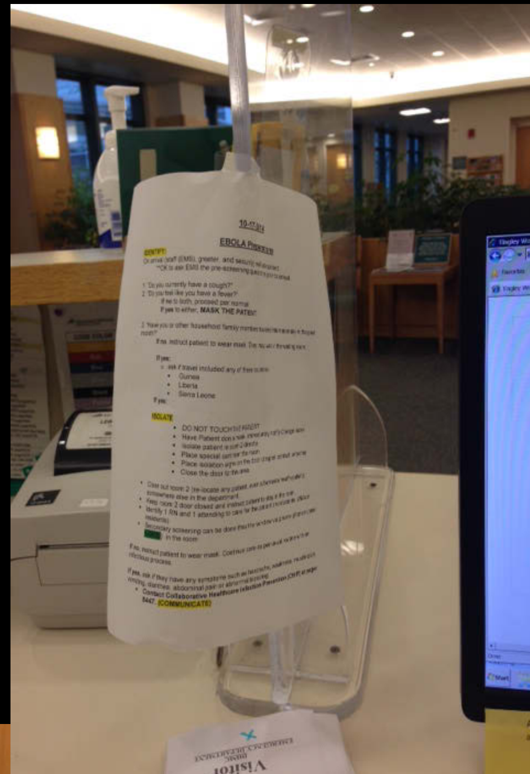
If you have questions following the actions on this script contact
Collaborative Healthcare Infection Prevention (CHIP) at pager 8447 or call extension 3-3800

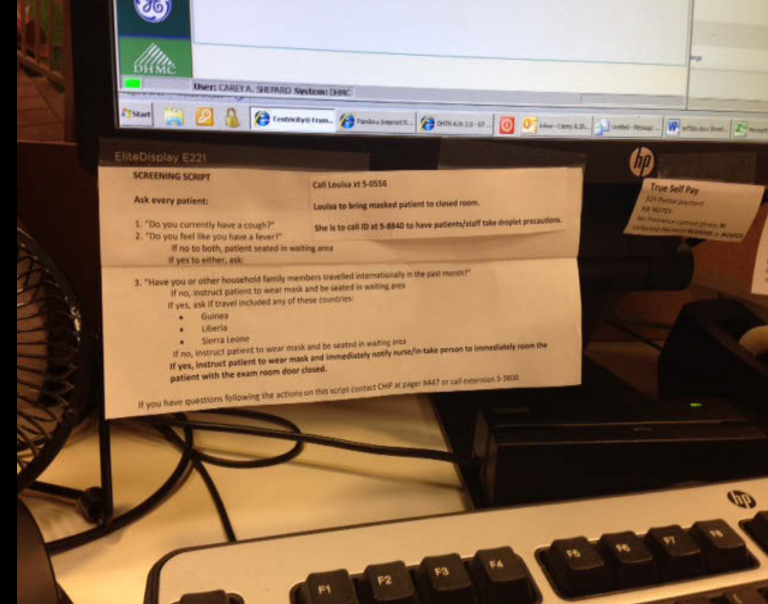
Dartmouth-Hitchcock

Instruct patient to wear a mask and **IMMEDIATELY** notify nurse/intake person to **IMMEDIATELY** escort patient to designated private exam room with the door closed

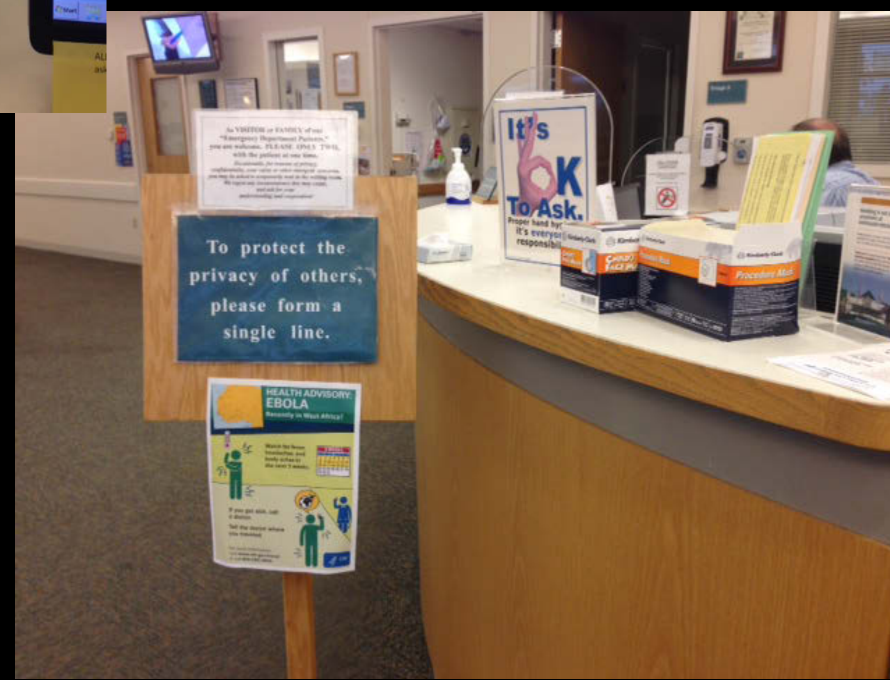
Page CHIP (8447)


HEALTH ADVISORY:
EBOLA
Recently in West Africa?
Watch for fever, headaches, and body aches in the next 3 weeks.
3 WEEKS
If you get sick, call a doctor.
Tell the doctor where you traveled.
Stay healthy.
Take the time to get vaccinated.
Public Flu Vaccination Clinics
Dartmouth-Hitchcock


EBOLA Process
Guinea
Liberia
Sierra Leone
DO NOT TOUCH PATIENT

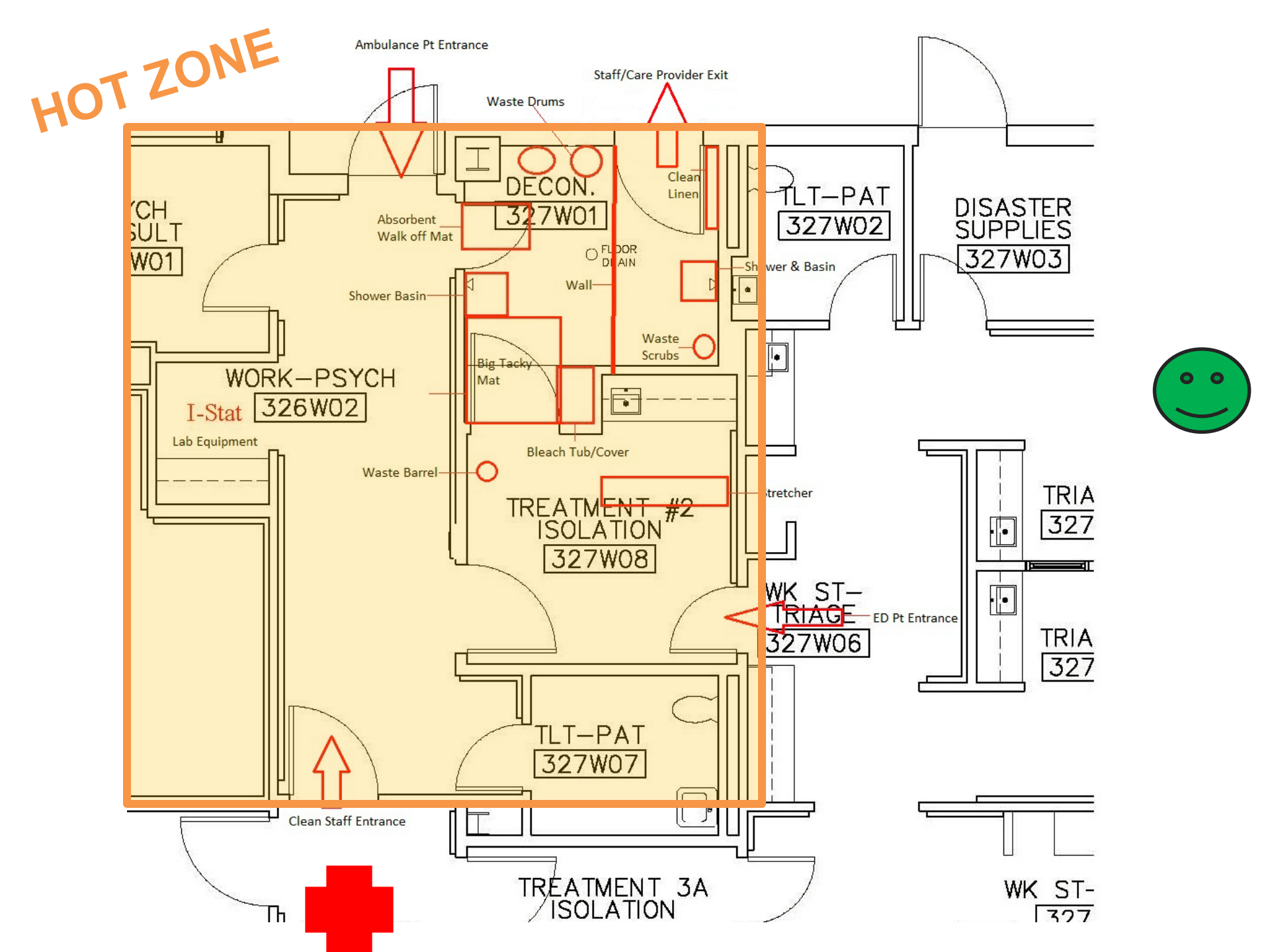

EliteDisplay E221
SCREENING SCRIPT
Call Louisa at 5-0556
Ask every patient:
Louisa to bring masked patient to closed room.
1. "Do you currently have a cough?"
2. "Do you feel like you have a fever?"
If no to both, patient seated in waiting area
If yes to either, ask:
3. "Have you or other household family members travelled internationally in the past month?"
If no, instruct patient to wear mask and be seated in waiting area
If yes, ask if travel included any of these countries:
Guinea
Liberia
Sierra Leone
If no, instruct patient to wear mask and be seated in waiting area
If yes, instruct patient to wear mask and immediately notify nurse/in-take person to immediately room the patient with the exam room door closed.
True Self Pay


Please form a single line and wait to be called by the next available representative.
HEALTH ADVISORY:
EBOLA
Recently in West Africa?
Watch for fever, headaches, and body aches in the next 3 weeks.
3 WEEKS
If you get sick, call a doctor.
Tell the doctor where you traveled.


To protect the privacy of others, please form a single line.
It's OK To Ask.
HEALTH ADVISORY:
EBOLA
Procedure Mask

PROTECT
#1 priority is to protect our staff

- Personal Protective Equipment (PPE)
  - Determining the ensemble
  - Training and Drills
  - 2 person “buddy system” plus 3rd person observer
- Limiting access to the patient


HOT ZONE
Ambulance Pt Entrance
Staff/Care Provider Exit
Waste Drums
DECON.
327W01
Clean Linen
TLT–PAT
327W02
DISASTER SUPPLIES
327W03
Absorbent Walk off Mat
FLOOR DRAIN
Shower & Basin
Wall
Shower Basin
Waste Scrubs
Big Tacky Mat
WORK–PSYCH
I-Stat
326W02
Lab Equipment
Bleach Tub/Cover
Waste Barrel
Stretcher
TREATMENT #2 ISOLATION
327W08
TRIA
327
WK ST–TRIAGE
327W06
ED Pt Entrance
TRIA
327
TLT–PAT
327W07
Clean Staff Entrance
TREATMENT 3A ISOLATION
WK ST-

PROTECT

#1 priority is to protect our staff

- Detailed procedures
  - Laboratory specimen handling
  - Cleaning and disinfection
  - Waste management

RESPOND

- Ebola Response Team (ERT)
  - Critical Care/Anesthesia and Emergency Medicine (MD/RN)
  - Respiratory therapy
  - DHART
  - Laboratory
- Orientation
- Training (PPE and waste management)
- Team activation system

RESPOND

- Employee Expectations
  - Human Resource FAQs
- Safety and Medical Monitoring
  - Occupational Medicine protocols
- Patient care ethical questions
  - CPR
  - Hemodialysis
  - Intubation

INJURIES & SAFETY
Workers' Compensation
Occurrence Reporting System
Injuries, Illnesses, & Exposures
Safety Resources
Health and Safety Manual
Material Safety Data Sheets (MSDS)
Emergency Management (Lebanon)
Preparedness for Ebola
Frequently Asked Questions about Ebola

Preparedness for Ebola

Updated on Tuesday, October 21, 2014

Dartmouth-Hitchcock and all New Hampshire hospitals are working closely with the NH Department of Health and Human Services (NH DHHS) and other agencies to ensure we are prepared in the unlikely event a patient with symptoms of Ebola presents in one of our practices.

We are confident in Dartmouth-Hitchcock's ability to identify potential patients who would be suspect for Ebola, and we are actively preparing for Ebola patients who could potentially arrive at any D-H facility.

A message from Dartmouth-Hitchcock CEO and President Dr. James N. Weinstein

This page is a clearinghouse for information on D-H's preparations, as well as resources from other sources including DHHS, the Centers for Disease Control and Prevention (CDC), the World Health Organization, and Medecins san Frontieres (MSF, also known in the United States as "Doctors Without Borders")

A special Ebola Preparation Group, made up of leaders and experts from around D-H, is putting into place plans and protocols for managing the care of a potential Ebola patient, as well as the safety of our staff in the treatment of such a patient.

Already we've shared screening scripts and a flow chart for patients arriving at all clinics and departments, one of the first steps to detect, protect, and respond to the possibility of a case of Ebola at D-H. We are now in the process of pulling together a specialized, multidisciplinary Ebola Response Team of clinicians, highly trained to manage suspected cases.

All of our health care professionals and all D-H staff are contributing to our preparedness for Ebola by being ready to detect a potentially infected person; protect yourself, your colleagues, and other patients; and respond with appropriate patient care.

A reminder that Ebola is primarily transmitted through direct contact with an infected person's body fluids – blood, vomit, stools, sweat, urine or sputum. It is NOT transmitted through the air.

D-H Ebola Preparation Group Updates

- In Liberia, US forces have been building desperately needed treatment centers and helping to bring in aid
- Maj. Gen. Gary J. Volesky in charge of troops assigned to Ebola response: "I've been told by a number of people that the task we face is extremely hard. Well, a fairly famous person once said *hard is not impossible*. Together, we're going to beat it."