Infectious Diseases 2015

Michael F. Parry, M.D.

Professor of Clinical Medicine, Columbia University

Director of Infectious Diseases & Microbiology

The Stamford Hospital

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STAMFORD HOSPITAL

Outline

- Overview
- Antibiotic resistant infections
- New Enterovirus infections
- Ebola
- MERS
- Arbovirus infections

Complexity of human infectious diseases on a global scale:

(*pity the infectious diseases specialist!)*

- 342 human infectious diseases
- 2000 pathogens
- 240 diagnostic tools
- 65 vaccines
- 269 anti-infective drugs
- 9979 drug trade names
- 220 countries

Newly identified infectious diseases

2014	Powassan, Heartland, Bourbon virus
2014	Enterovirus D68
2013	Chikungunya
2012	MERS
2009	H1N1pdm influenza
2005	H7N9 and H9N2 influenza
2004	ESBL / CRE infections
2003	SARS
2002	VRSA
1999	Nipah virus
1999	West Nile Virus (new world)
1997	H5N1 influenza
1996	nCJD (mad cow disease)
1995	HHV-8 (Kaposi sarcoma virus)
1994	Hantavirus
1992	MDR-Tuberculosis
1989	Hepatitis C
1988	Hepatitis E, HHV-6
1983	HIV/AIDS, Helicobacter
1983	E. coli O157:H7, Lyme disease
1980	HTLV I, II
1978	Clostridium difficile colitis
1976	Ebola, Legionnaires disease

A Historical Perspective

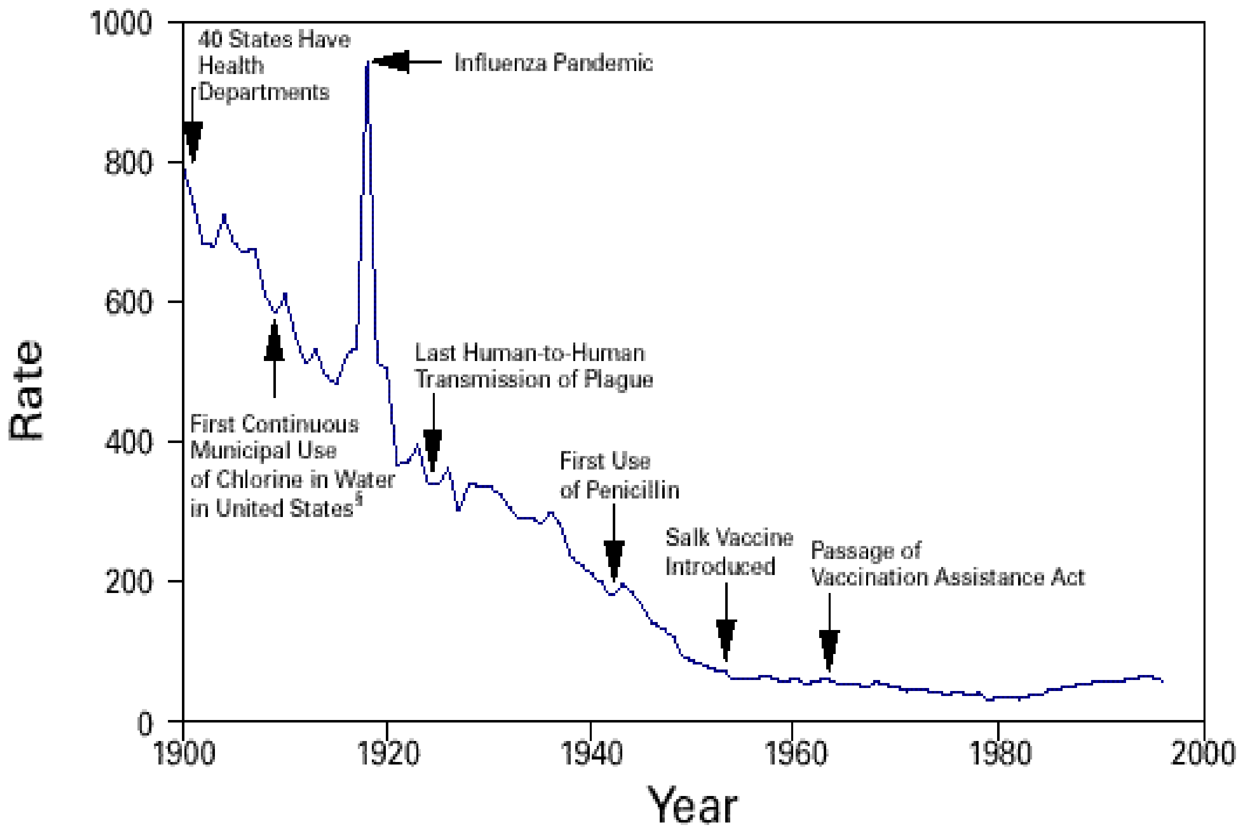
- Greece and Egypt accounts describe epidemics of smallpox, leprosy, tuberculosis, meningococcal infections and diphtheria prior to 1000 BC.
- Smallpox and plague killed 25% to 90% of naïve populations from Athens to Europe to North and South America from 400BC to 1600 AD
- These plagues contributed greatly to collapse of Spartans, Roman Empire, Aztec civilization.
- Although the epidemiology of infectious diseases was well described by John Snow (cholera in London) and Ignatz Semmelweiss (puerperal fever in Vienna) microbial causes were not apparent.
- It remained for Louis Pasteur in 1857 and Robert Koch in 1867 to introduce the concept that microorganisms were pathogens and could cause disease.

A Historical Perspective

- In the 18th and 19th century, TB (“consumption”) was the leading cause of death in the US, the life expectancy was 40 years, and infant mortality was astronomical.
- There were no effective medicinal treatments
- There were epidemics related to impure foods, contaminated water supplies, inadequate sewage disposal, and poor housing conditions.
- Yellow fever, malaria and smallpox were common in the Northeast U.S.
- Infectious diseases, poverty and squalor became the subjects of great literary works (*The Jungle, Cannery Row*).
- Such ravages led to the “quarantine” system of public health which was instituted in 1873.

Dramatic decline in infectious disease mortality preceded the antibiotic era

FIGURE 1. Crude death rate* for infectious diseases — United States, 1900–1996†



*Per 100,000 population per year.
†Adapted from Armstrong GL, Conn LA, Pinner RW. Trends in infectious disease mortality in the United States during the 20th century. JAMA 1999:281;61–6.
§American Water Works Association. Water chlorination principles and practices: AWWA manual M20. Denver, Colorado: American Water Works Association, 1973.

EVOLUTION OF ANTIBIOTIC RESISTANCE: Rate of Development

Antibiotic	Year Deployed	Resistance Observed
Sulfonamides	1930s	1940s
Penicillin	1943	1946
Streptomycin	1943	1959
Chloramphenicol	1947	1959
Tetracycline	1948	1953
Erythromycin	1952	1988
Vancomycin	1956	1988
Methicillin	1960	1961
Ampicillin	1961	1973
Cephalosporins	1960s	late 1960s

Table 20.2 Microbiology: A Clinical Approach (© Garland Science)

Factors known to increase prevalence of resistance

- Appropriate antibiotic prescribing
- Inappropriate antibiotic prescribing
- Excessive treatment
  - Chronic treatment
  - Repeated courses of rx
- Overuse, particularly in a health care facility
- Inadequate dosing
- Inadequate surgery / drainage
- Poor infection control practices
- Antibiotic use in animal feed

The crisis in antibiotic resistance **1992**

The synthesis of large numbers of antibiotics over the past three decades has caused complacency about the threat of bacterial resistance. Bacteria have become resistant to antimicrobial agents as a result of chromosomal changes or the exchange of genetic material via plasmids and transposons.

Streptococcus pneumoniae, *Staphylococcus aureus*, organisms that cause respiratory and cutaneous infections; and members of the *Enterobacteriaceae* and Pseudomonas families, organisms that cause diarrhea, urinary infection, and sepsis, are now resistant to virtually all of the older antibiotics.

The extensive use of antibiotics in the community and hospitals has fueled this crisis. Mechanisms such as antibiotic control programs….and better hygiene….need to be adopted in order to limit bacterial resistance.

Harold C. Neu, M.D. Science. 1992 Aug 21;257:1064-73.
Columbia University, New York, NY

Bad Bugs, No Drugs

As Antibiotic Discovery Stagnates …
A Public Health Crisis Brews

2004

ID Physicians Warn of Brewing "Superbug" Crisis

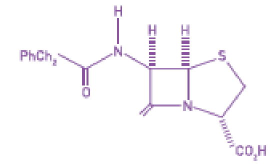
Infectious Diseases Society of America Proposes Federal Measures to Spur Antibiotic Development

IDSA
Infectious Diseases Society of America

http://www.idsociety.org

2014

ANTIMICROBIAL RESISTANCE
Global Report on surveillance 2014



What you need to know
WHO's first global report on antimicrobial resistance, with a focus on antibiotic resistance, reveals that it is no longer a prediction for the future. Antibiotic resistance - when bacteria change and antibiotics fail - is happening **right now**, across the world

The report is the most comprehensive picture to date, with data provided by 114 countries

Looking at 7 common bacteria that cause serious diseases from bloodstream infections to gonorrhoea

High levels of resistance found in all regions of the world

Significant gaps exist in tracking of antibiotic resistance

Over the last 30 years, no major new types of antibiotics have been developed

1910 1920 1930 1940 1950 1960 1970 1980 1990 2000 2010

Penicillin · Cephalosporin · Carbapenem · Fluoroquinolones · Discovery void

What does this mean?
Without urgent action we are heading for a post-antibiotic era, in which common infections and minor injuries can once again kill

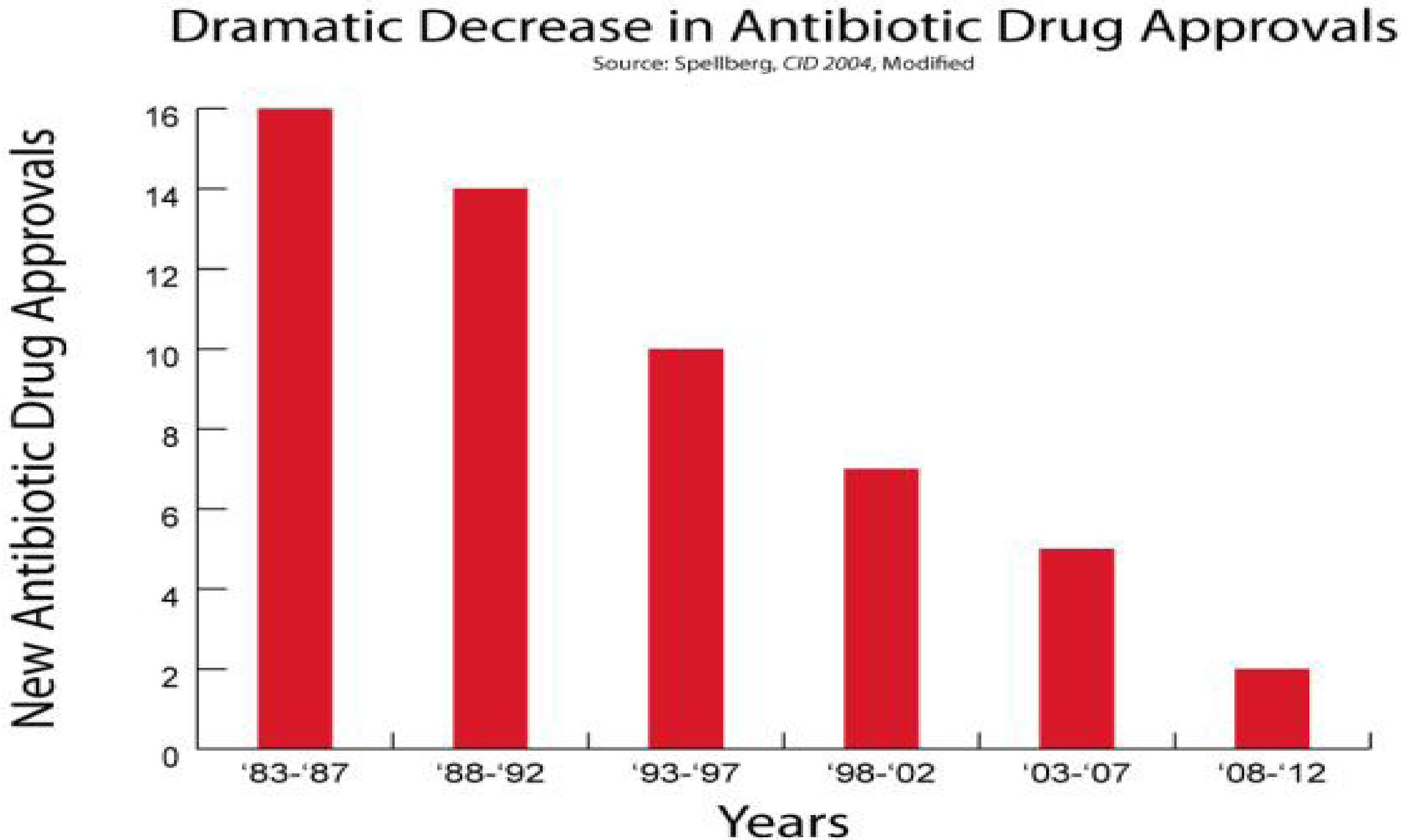
How can infections be prevented in the first place to reduce the need for antibiotics?

- Better hygiene
- Access to clean water and sanitation
- Infection control in healthcare facilities
- Vaccination

What you can do
- Use antibiotics only when prescribed by a health professional
- Complete the full prescription, even if you feel better
- Never share antibiotics with others or use leftover prescriptions

World Health Organization

Crisis in Antimicrobial Drug Development



Combating Antimicrobial Resistance: Policy Recommendations to Save Lives. IDSA 2011.

Trends in Antimicrobial Resistance 2015: *ESCAPE pathogens*

- ***E****nterococcus* (VRE)
- ***S****taphylococcus aureus* (MRSA and VISA)
- ***C****arbapenem resistant Enbterobacteriaceae (CRE) E coli, Klebsiella, Enterobacter* (and others: NDM-1, etc)
- ***A***cinetobacter (multi-drug resistant)
- ***P***seudomonas (FQ resistant)
- ***E***xtended spectrum beta-lactamase producing GNR (ESBL positive *E. coli, Klebsiella, Enterobacter*)

  plus

- *Clostridium difficile* (NAP-1 strains, and others)

Staphylococcal Infections


INFECTIOUS DISEASE
A Nasty Bug Breaks Out
Drug-resistant staph bacteria now stalk even students
By Lindsay Lyon
PATRIK GIARDINO—GETTY IMAGES
MEDICAL DEVICES
HEALTH
Surviving the New KILLER BUG
A nasty, drug-resistant staph infection—the kind usually seen in hospitals—is racing across the U.S.
BY CHRISTINE GORMAN
WHAT YOU CAN DO
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By BETSY McCAUGHEY
Published: November 14, 2006
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Dead Student Had Infection, Officials Say
By WINNIE HU and SARAH KERSHAW
Published: October 26, 2007
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HP Thin Clients starting at only $199
PRECAUTION A Chicago school where officials thought a student might have a staph infection ordered a heavy-duty cleanup.
Jerry Lai/Associated Press
By KEVIN SACK
Published: October 28, 2007
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The ADVOCATE
STAMFORD
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Stamford student has staph infection
Officials: Northeast school disinfected
By Natasha Lee
Staff Writer
LogOn
To read the letter that was sent by Stamford Public Schools to alert students, visit www.stamfordadvocate.com.
Experts' advice
Stamford health officials said the best way to prevent staph infections is to:
· Wash hands frequently
· Cover open sores with bandages
· Avoid sharing personal items such as towels, soap and clothes
For more information on staph infections, contact Dr. Tsung-Wen Kuo, epidemiologist at the Stamford Health Department, at 977-4390; your child's school nurse; or the state Health Department information line at (800) 830-9426.

MRSA
(methicillin-resistant *Staphylococcus aureus*

- First appeared in 1959
- Hospital-acquired (HA-MRSA)
  - Patients in the hospital
- Healthcare associated (HA-MRSA)
  - Patients who have visited the hospital
  - Nursing home
  - Infusion Center or dialysis outpatients
  - Visited relatives or friends in hospital
  - Discharged from the hospital
- Community acquired (CA-MRSA)
  - Patients with none of the above risk factors

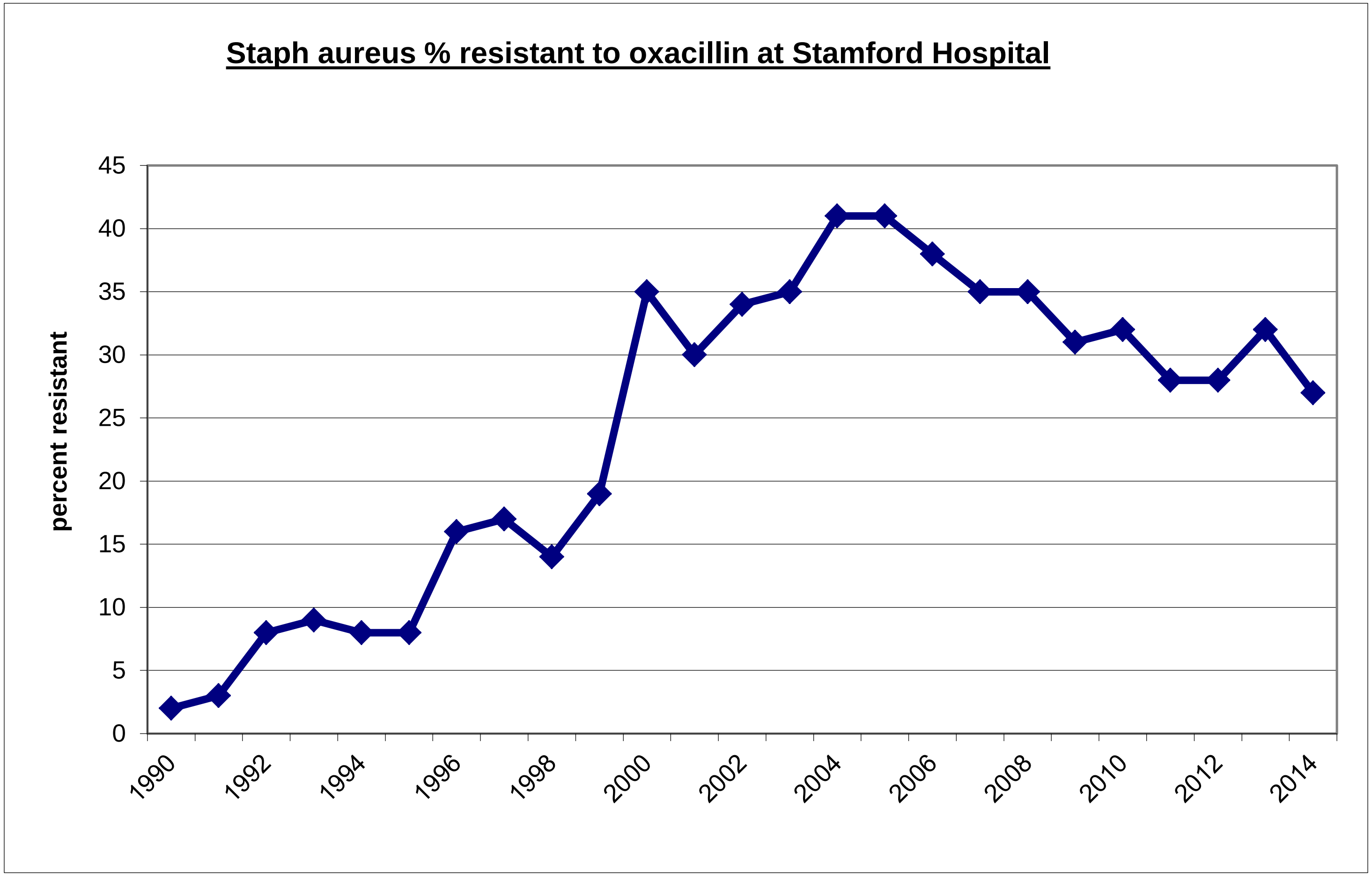
Burden of *Staphylococcus aureus* Infections in the United States

- 292,045 inpatient stays per year in US due to Staph infections (CDC)
  - 0.8% of all inpatients
  - 120,000 cases MRSA per year
- MRSA accounts for up to 70% of hospital-acquired Staph. aureus infections
- Patients with MRSA infection have
  - 3 times length of hospital stay (14.3 vs 4.5 days)
  - 3 times total charges ($48,824 vs $14,141)
  - 5 times risk of hospital death (11.2% vs 2.3%)

After *Noskin et al. Arch Intern Med. 2005;165:1756-1761*

Emergence of MRSA over 20 years Stamford Hospital Microbiology Lab data

(community and hospital strains)




INCHES
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made in
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Community Acquired MRSA in athletes

- Football, rugby, wrestling
- Towel, soap, razor sharing
- Turf burns, other sites of abrasion
- Body shaving
- Suboptimal hygiene in players, trainers
- High BMI (e.g. linemen)
- Prior antibiotic use
- Poor maintenance of equipment (e.g. whirlpools)

Outpatient purulent cellulitis: Empiric Rx for CA-MRSA

Drug	**Adult Dose**	**Evidence / Grade**
TMP-SMX	1-2 DS BID	AII
Doxycycline, Minocycline	100 BID	AII
Clindamycin	300-450 TID	AII
Linezolid	600 BID	AII

Infectious Diseases Society of America (IDSA) Guidelines 2014

Recurrent MRSA SSTI: Decolonization Regimens

- Mupirocin (Bactroban) nasal + any other colonized site
  - twice daily x 10 days
- Chlorhexidine bathing or wipes
  - Daily x 10 days
- Systemic antibiotic active at skin surface
  - Rifampin, TMP/SMX, minocycline x 10 days
- 70% response rate
  - Risk of recolonization

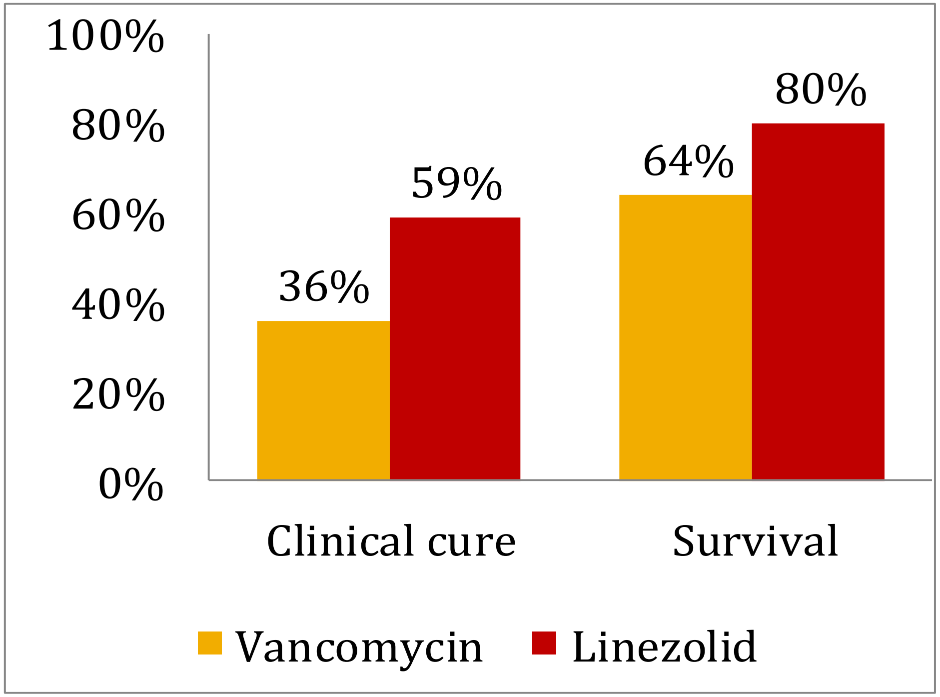
Predictive Value of MRSA Nasal Swab PCR Assay for MRSA Pneumonia

Benjamin Dangerfield, Andrew Chung, Brandon Webb, and Maria Teresa Seville
Mayo Clinic and University of Utah. AAC *February 2014 vol. 58 no. 2 859-864*

ABSTRACT

Pneumonia due to methicillin-resistant Staphylococcus aureus (MRSA) is associated with poor outcomes and frequently merits empirical antibiotic consideration despite its relatively low incidence. Nasal colonization with MRSA is associated with clinical MRSA infection and can be reliably detected using the nasal swab PCR assay. In this study, we evaluated the performance of the nasal swab MRSA PCR in predicting MRSA pneumonia. A retrospective cohort study was performed in a tertiary care center from January 2009 to July 2011. All patients with confirmed pneumonia who had both a nasal swab MRSA PCR test and a bacterial culture within predefined time intervals were included in the study. These data were used to calculate sensitivity, specificity, positive predictive value, and negative predictive value for clinically confirmed MRSA pneumonia. Four hundred thirty-five patients met inclusion criteria. The majority of cases were classified as either health care-associated (HCAP) (54.7%) or community-acquired (CAP) (34%) pneumonia. MRSA nasal PCR was positive in 62 (14.3%) cases. MRSA pneumonia was confirmed by culture in 25 (5.7%) cases. The MRSA PCR assay demonstrated 88.0% sensitivity and 90.1% specificity, with a positive predictive value of 35.4% and a negative predictive value of 99.2%. In patients with pneumonia, the MRSA PCR nasal swab has a poor positive predictive value but an excellent negative predictive value for MRSA pneumonia in populations with low MRSA pneumonia incidence. In cases of culture-negative pneumonia where initial empirical antibiotics include an MRSA-active agent, a negative MRSA PCR swab can be reasonably used to guide antibiotic de-escalation.

MRSA pneumonia: Vancomycin vs. Linezolid?



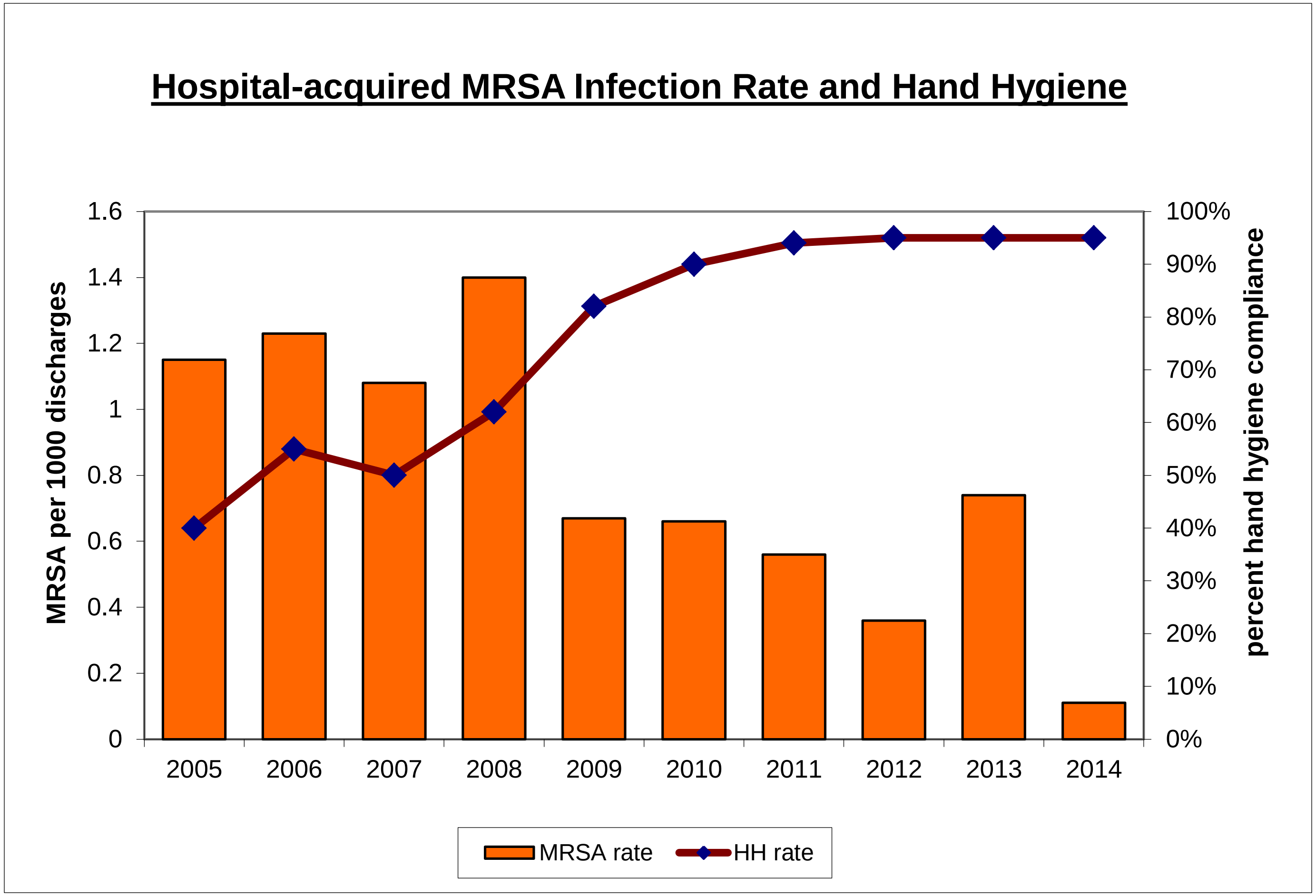
Rubinstein CID 2001;32:402-12; Wunderink Clin Therap 2003;25:980-92;

Infectious Diseases Society of America (IDSA) Guidelines 2014

Hospital Isolation Process for Patients with MRSA

- Contact precautions – whether infected or colonized
  - Hand hygiene, gown, gloves
  - Soap and water or alcohol gel
- Remove from isolation if two negative screening cultures at least 48 hours apart
  - Must be off topical and systemic abx
  - Nasal culture (or PCR) plus previously positive sites
- Isolate on readmission if previously positive
  - Flagging system in admissions office
  - Remove from isolation if new screening cultures are negative
- Reason for isolation is to prevent spread to health care workers and transmission within the hospital

Hospital-acquired MRSA Infections
Stamford Hospital Overall



Multi-drug resistant organisms MDRO Infections

Gram-negative infections

Enterobacteriaceae

- Family of bacteria -- primarily of intestinal origin
- Common causes of community and healthcare acquired infections.
- *E. coli* is the most common cause of outpatient urinary tract infections.
- Penicillins and cephalosporins have been the mainstay of treating infections caused by *Enterobacteriaceae.*
- However, resistance to many beta-lactams emerged several years ago and has continued to rise, due to enzymes which destroy the drugs
- These resistance enzymes are called beta-lactamases.

Beta-lactamases

- Beta-lactamases destroy penicillin and cephalosporin antibiotics
- Found in all types of bacteria
- More than 700 chemical types are described to date
  - Varying structures with complex epidemiology
  - Preference for different beta-lactam antibiotics
- Extended spectrum beta-lactamases (ESBLs)
  - Broad spectrum of activity
  - ESBLs confer resistance to all penicillins and cephalosporins including the newest and most potent agents
  - Increasingly prevalent in hospitals and SNFs

Infection Control Issues for ESBL-producing bacteria

- Evidence indicates that patients acquire ESBL-producing organisms while in hospital
- Treatment failures occur due to resistance to primary treatment regimen and comorbidities
- These organisms transiently colonize the hands of hospital staff members
- The intestinal tract constitutes the main reservoir for ESBL-producing *Enterobactericeae*
- Environmental sources are rarely found
- Growing prevalence in the community

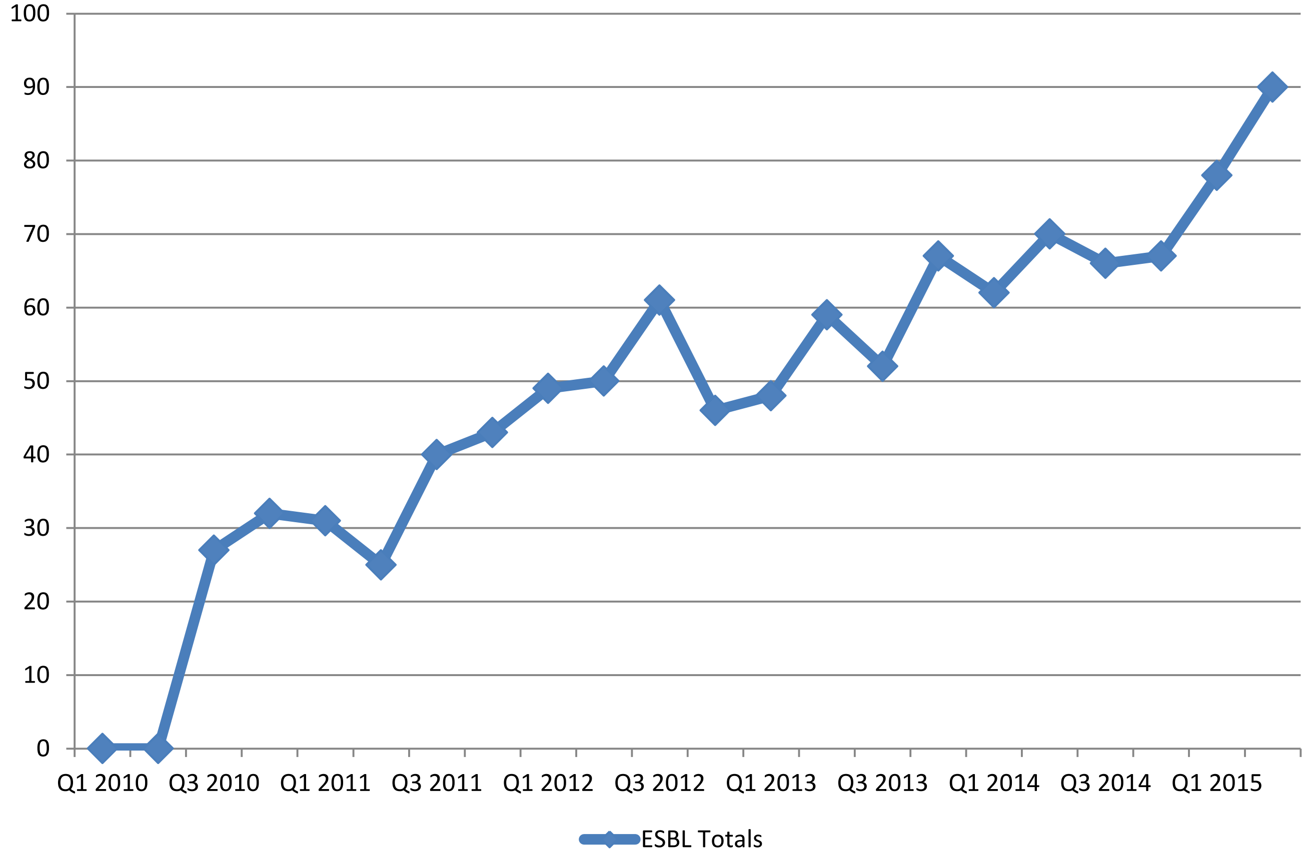
Infection due to ESBL+ Klebsiella

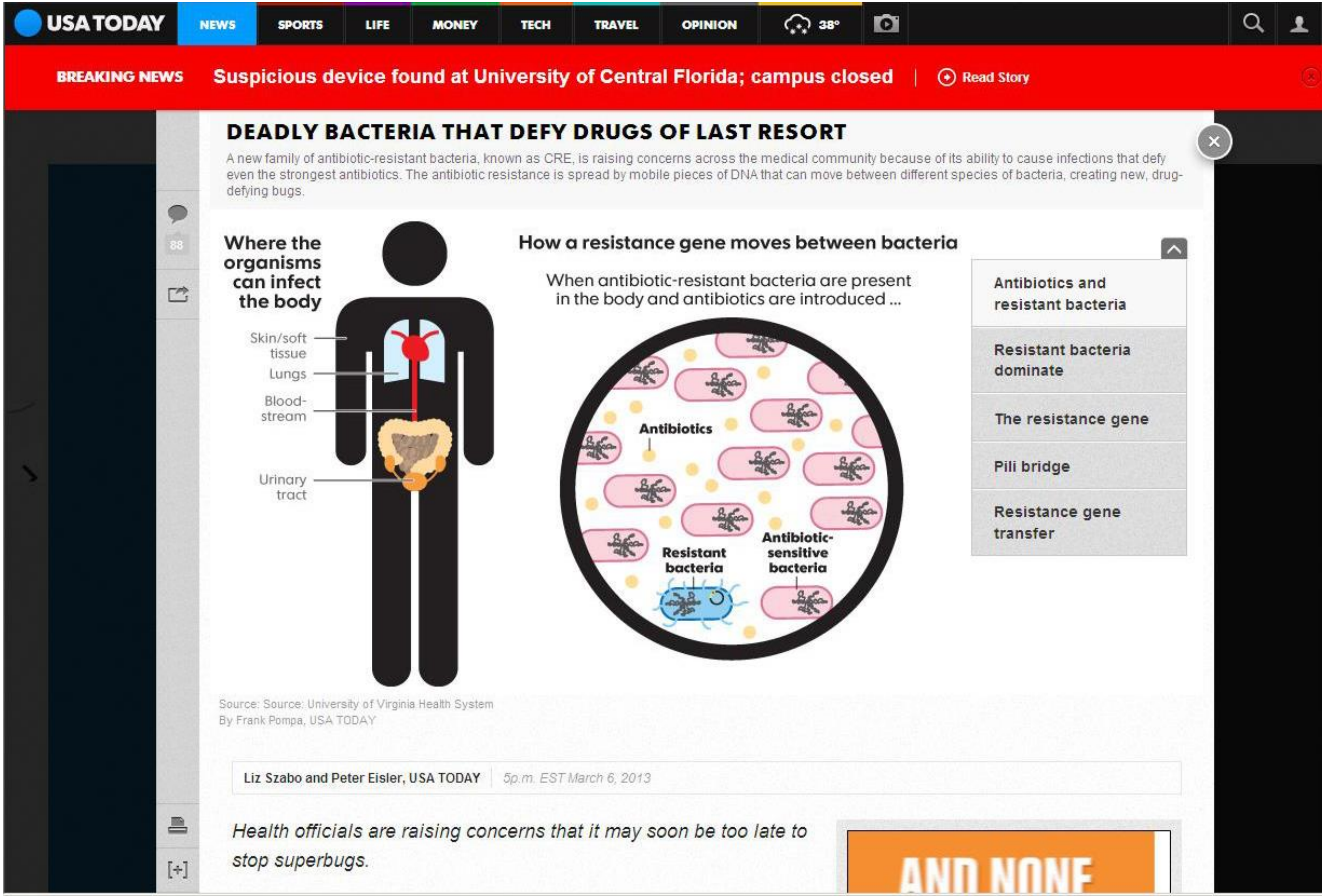
URINE CULTURE Final Verified 03/06/12-0845
Source: URINE CATH FOLEY
This organism exhibits extendend spectrum beta lactamase (**ESBL**) activity. In vitro susceptibility testing may be unreliable. Consider Infectious Diseases consultation.

Organism 1 KLEBSIELLA PNEUMONIAE **ESBL**
Colony Count: >100,000 COL./CC.

	KLEB PNEU*	
	MIC	RX
TRIMET/SULFA	>2/38	R
AMPICILLIN	>16	R*
CEFAZOLIN	>16	R*
CIPROFLOXACIN	>2	R
GENTAMICIN	>8	R
NITROFURANTOIN	>64	R
TETRACYCLINE	>8	R

ESBL-positive isolates at Stamford

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DEADLY BACTERIA THAT DEFY DRUGS OF LAST RESORT

A new family of antibiotic-resistant bacteria, known as CRE, is raising concerns across the medical community because of its ability to cause infections that defy even the strongest antibiotics. The antibiotic resistance is spread by mobile pieces of DNA that can move between different species of bacteria, creating new, drug-defying bugs.

Source: Source: University of Virginia Health System
By Frank Pompa, USA TODAY

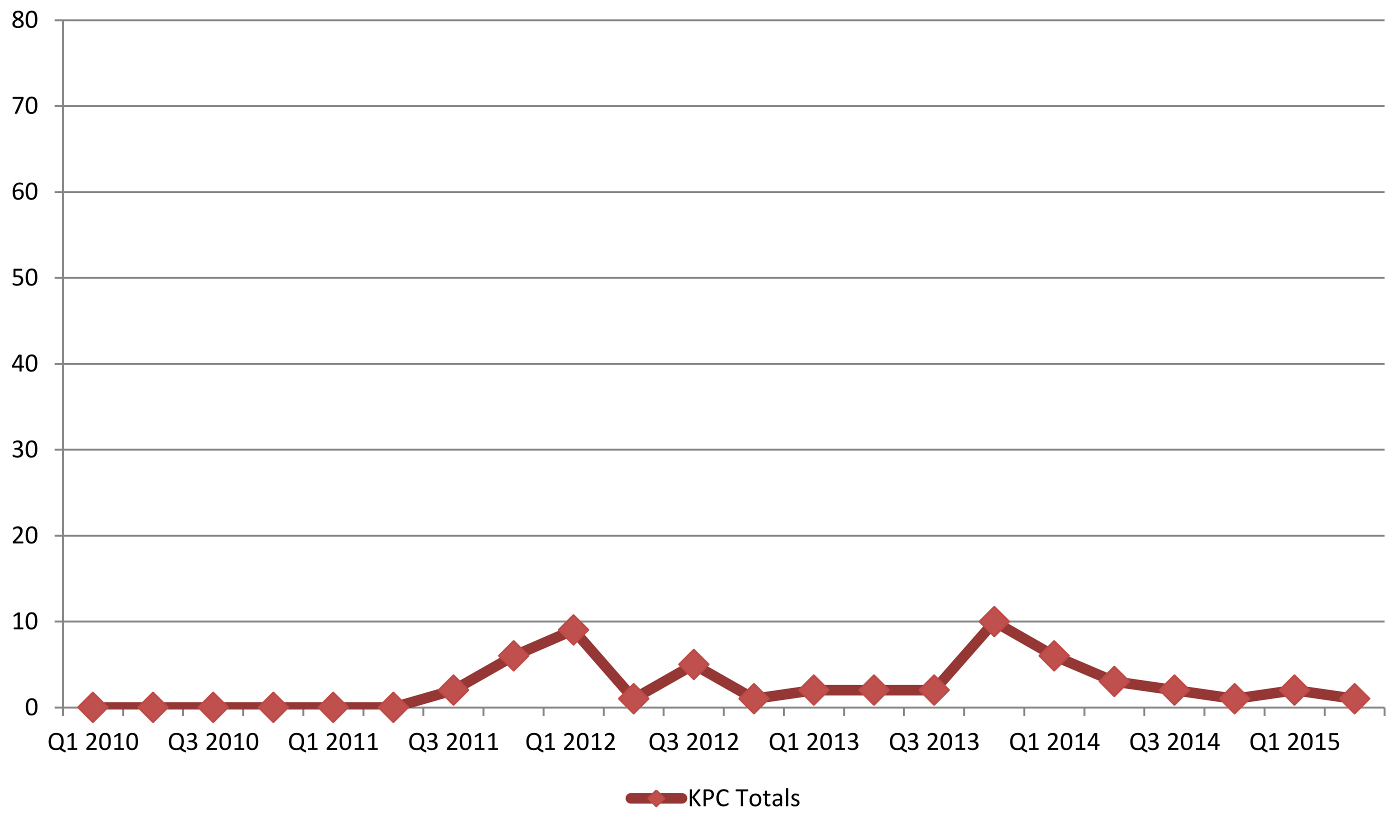
Liz Szabo and Peter Eisler, USA TODAY | 5p.m. EST March 6, 2013

Health officials are raising concerns that it may soon be too late to stop superbugs.

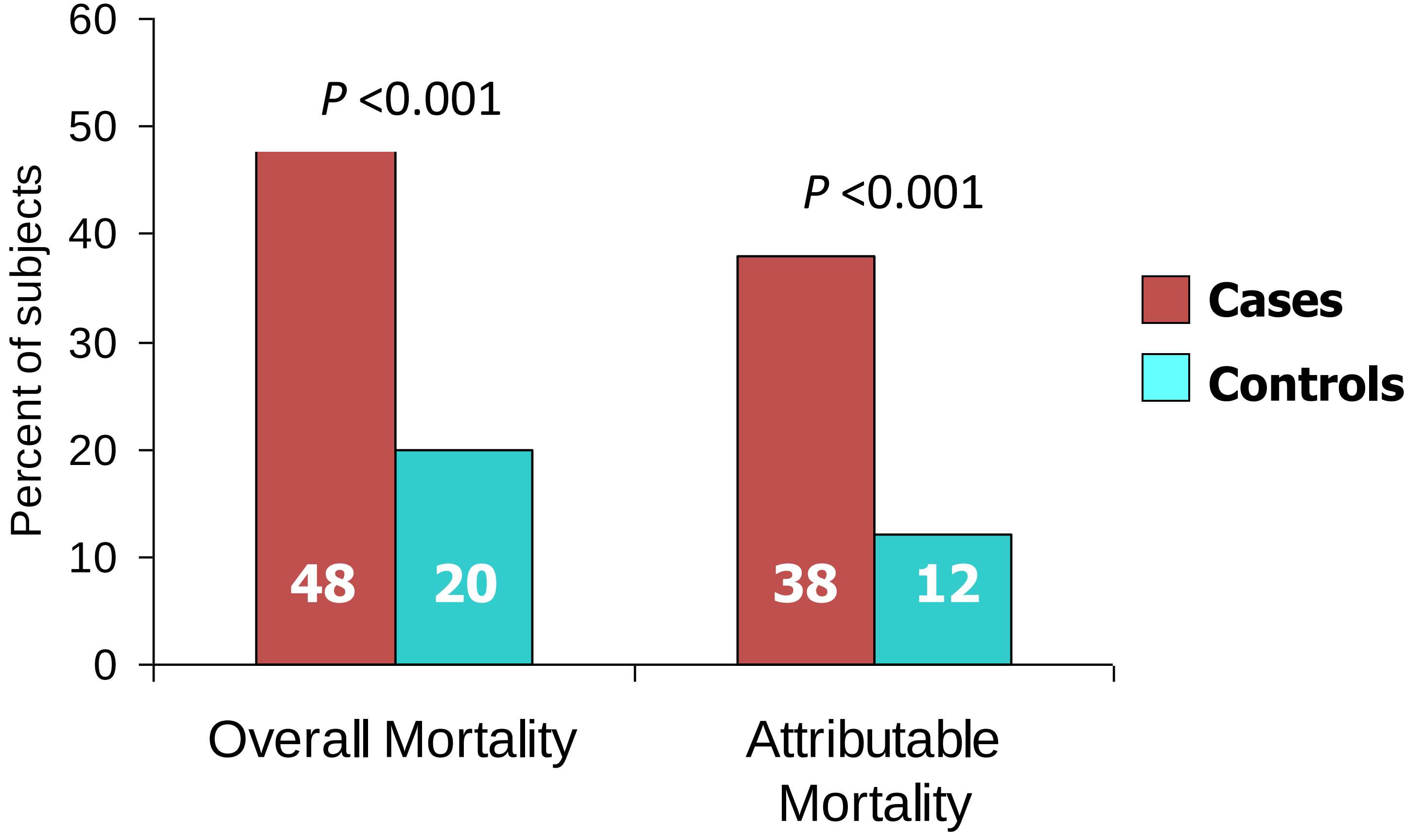
CRE (Carbapenem resistant *Enterobacteriaceae*)

- Newest concern
  - 2006 described in NYC
  - 2009 described in India (NDM)
  - Numerous cases associated with medical tourism
- Clusters now occurring in hospitals in most states
  - NIH outbreaks; ERCP associated
  - Transmitted on the hands of personnel > environmental
  - Very difficult to treat
- Resistant to all beta-lactams including carbapenems
  - Usually co-resistant to multiple other classes
- Stamford experience
  - Sporadic single cases
  - 2/3 outpatients
  - No spread or trend yet

CRE isolates at Stamford



CRE Infections
Outcome data from NYC



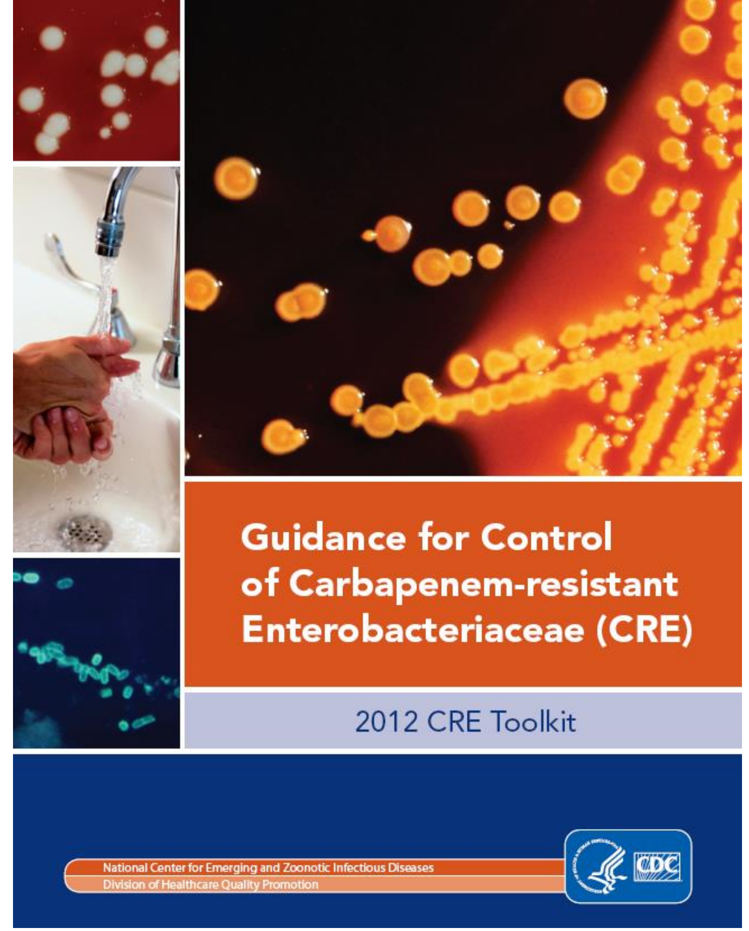
Patel G et al. *Infect Control Hosp Epidemiol* 2008;29:1099-1106.

Infection due to CRE + Klebsiella

```
 Procedure                         Result                         Verified
---------------------------------------------------------------------------------------------

 URINE CULTURE  Final                                   Verified 01/03/15-1124
    Source: URINE NEPHROSTOMY LEFT

       The Klebsiella pneumoniae **ESBL** activity cannot be
       determined due to increased resistance of this organism.

       The Klebsiells pnemoniae exhibits carbapenemase **KPC**
       production. The clinical efficacy of the carbapenems and
       other beta lactams has not been established for treating
       infections caused by Enterobacteriaceae that demonstrate
       carbapenemase production in vitro.  Consider Infectious
       Diseases consultation.

    Organism 1                  KLEBSIELLA PNEUMONIAE **KPC**
       Colony Count:            >100,000 COL./CC.
    Organism 2                  ESCHERICHIA COLI
       Colony Count:            <5,000 COL./CC.
    Organism 3                  DIPHTHEROID
       Colony Count:            10,000 - 20,000 COL./CC.
```

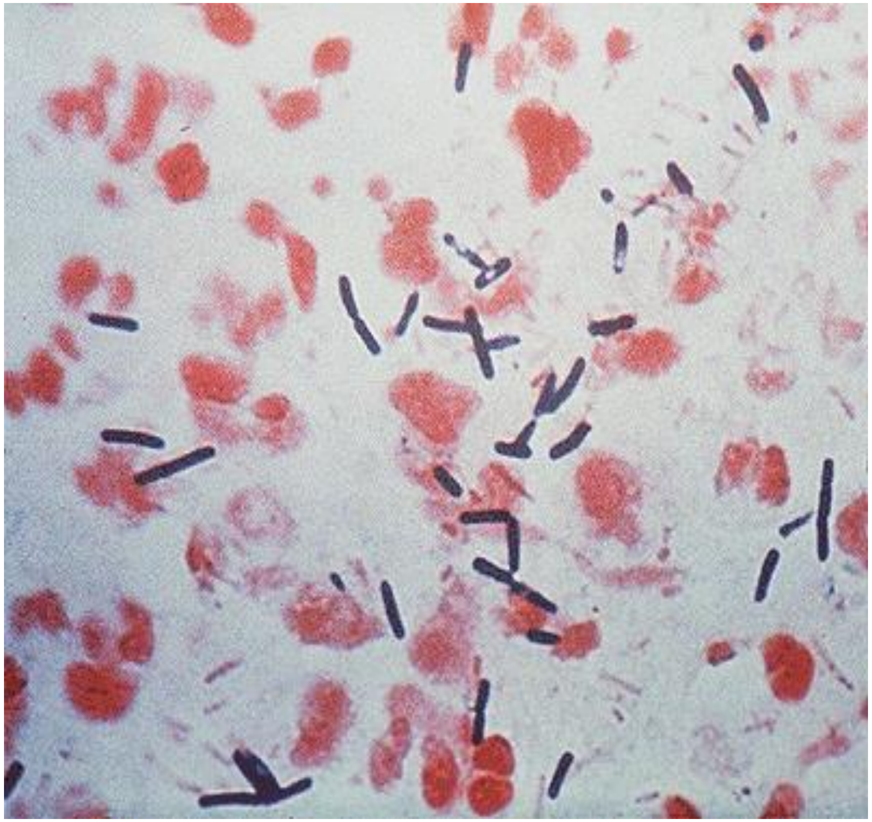
	KLEB KPC MIC	RX	ESC COLI MIC	RX
TRIMET/SULFA	>2/38	R	<=2/38	S
AMPICILLIN	>16	R	>16	R
AMP/SUL	>16/8	R	>16/8	R
CEFAZOLIN	>16	R	<=8	S
CEFOTAXIME	>32	R		
CEFOTETAN	>32	R		
CEFUROXIME	>16	R		
CIPROFLOXACIN	>2	R	>2	R
GENTAMICIN	<=4	S	<=4	S
NITROFURANTOIN	>64	R	<=32	S
TETRACYCLINE	>8	R	>8	R
PIP/TAZO	>64	R	64	I

CDC Action Plan for CRE



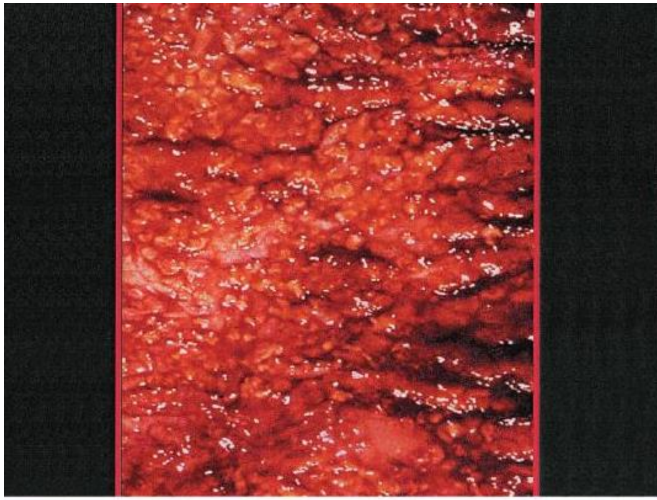
- Surveillance
  - ICP education
- Laboratory detection
  - Lab education
- Mandatory Reporting
- Rigid isolation / contact tracing / screening
- Antibiotic stewardship
- Controlled use of rx: polymixin, fosfomycin, tigecycline, ceftazidime + avibactam (Avycaz®)

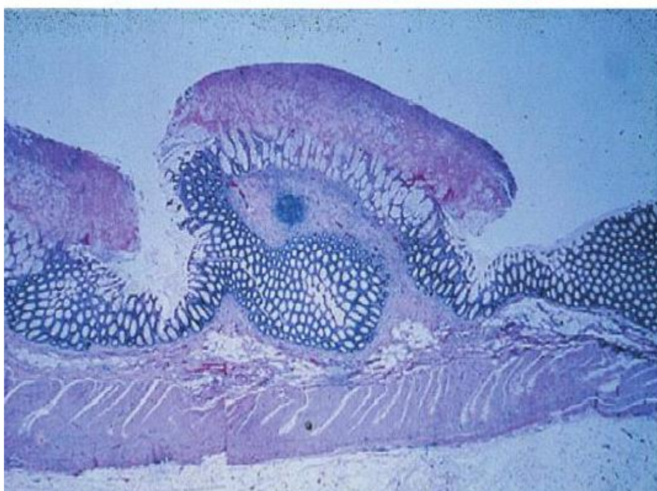
Clostridium difficile

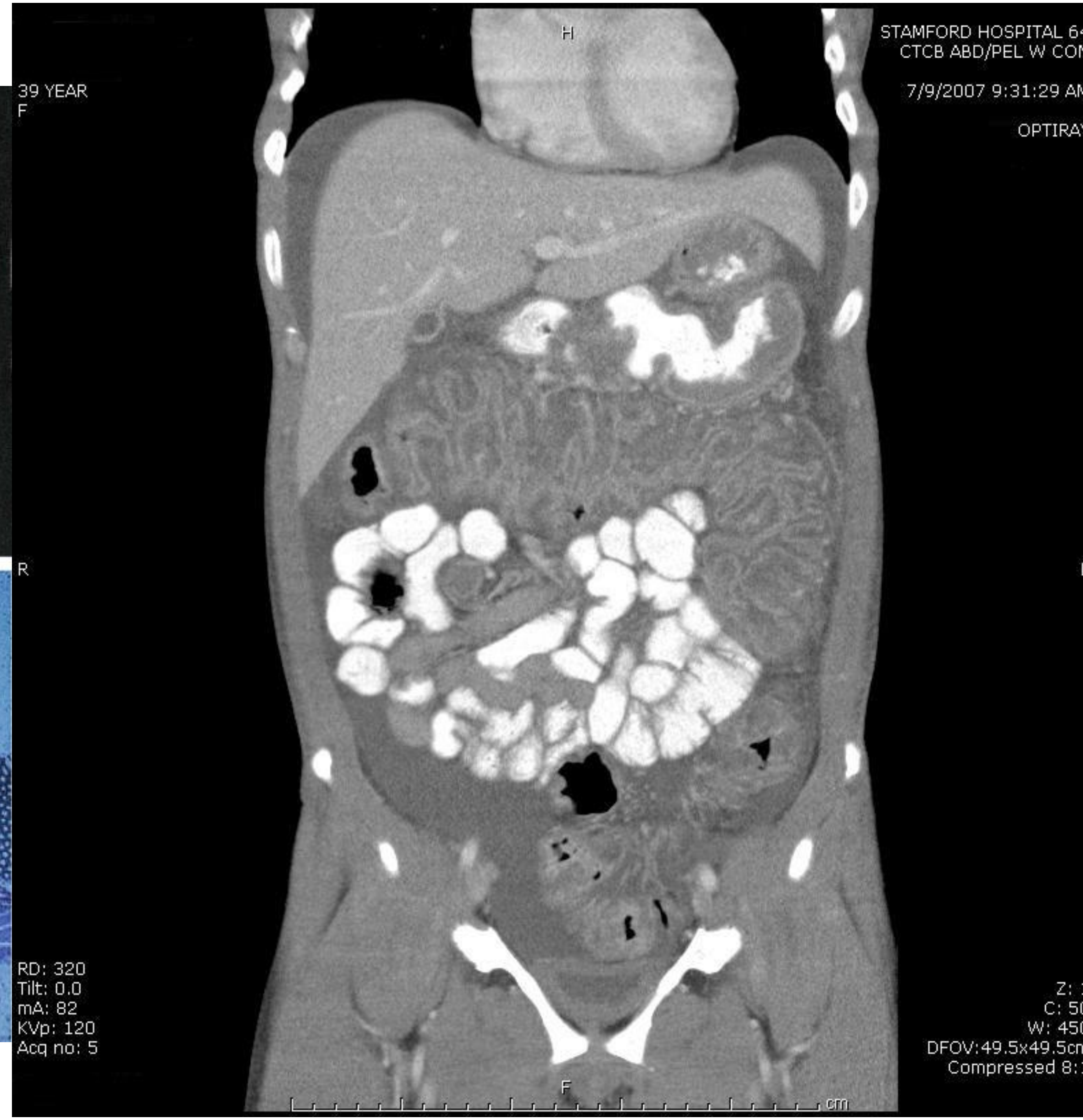


Changing Epidemiology of C. diff

- Recent outbreaks of severe disease caused by new epidemic strain of *C. difficile* with increased virulence, antibiotic resistance (NAP-1)
- ≥95% CDI pts have received antibiotic therapy
  - Fluoroquinolones>cephalosporins>penicillins
  - PPIs an important risk factor
- Although elderly (over 75) are still most greatly affected, more disease reported in “low-risk” persons
  - Healthy persons, pregnant women
- Community-acquired cases becoming more common
- High relapse rate -- 20% (importance of microbiome)
- C. difficile carried on hands and skin and persists in the environment
- Asymptomatic patients carry *C. difficile*
  - Community 5-10%
  - SNF and LTAC 50%



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CTCB ABD/PEL W CON
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OPTIRAY
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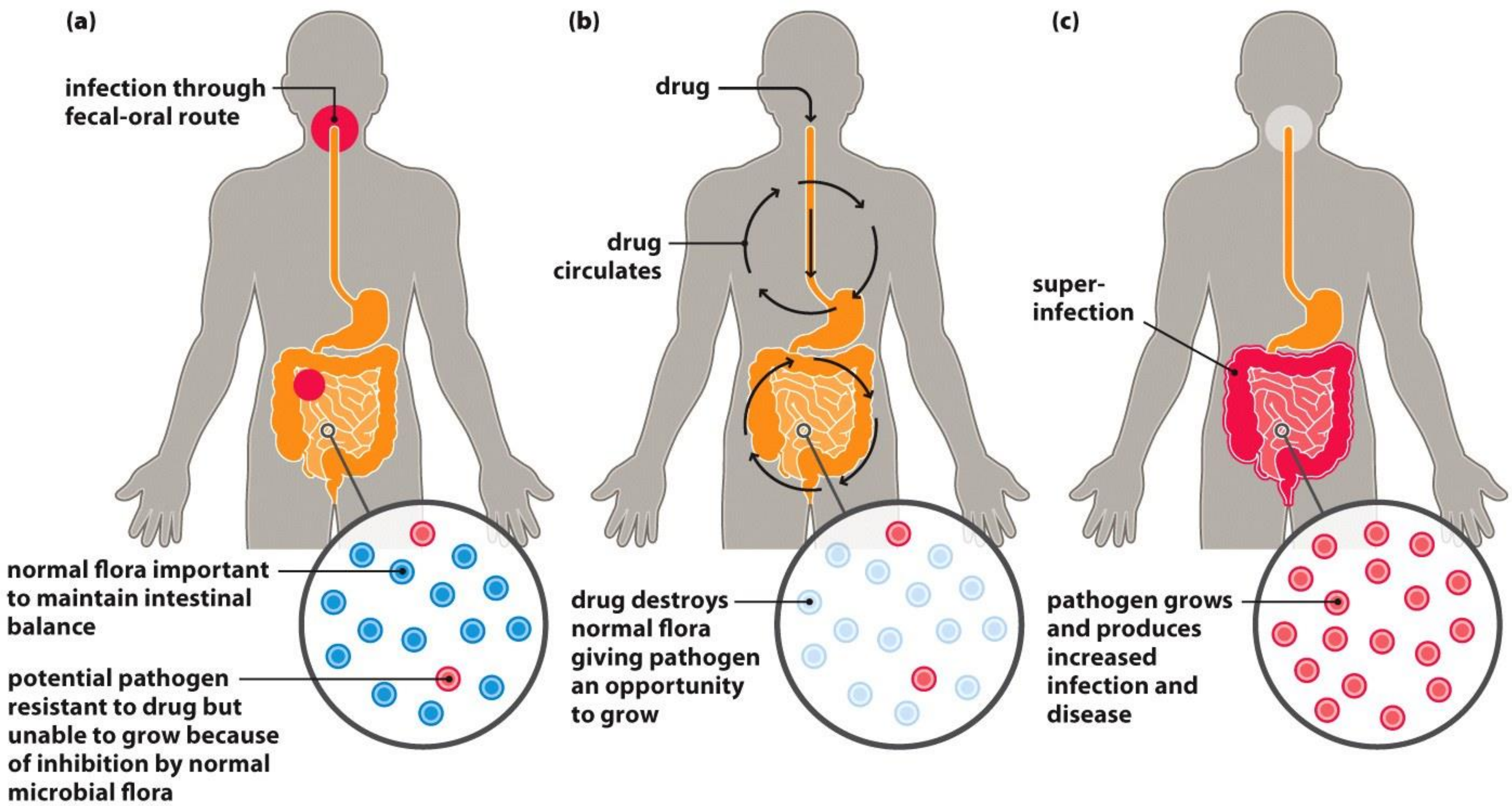
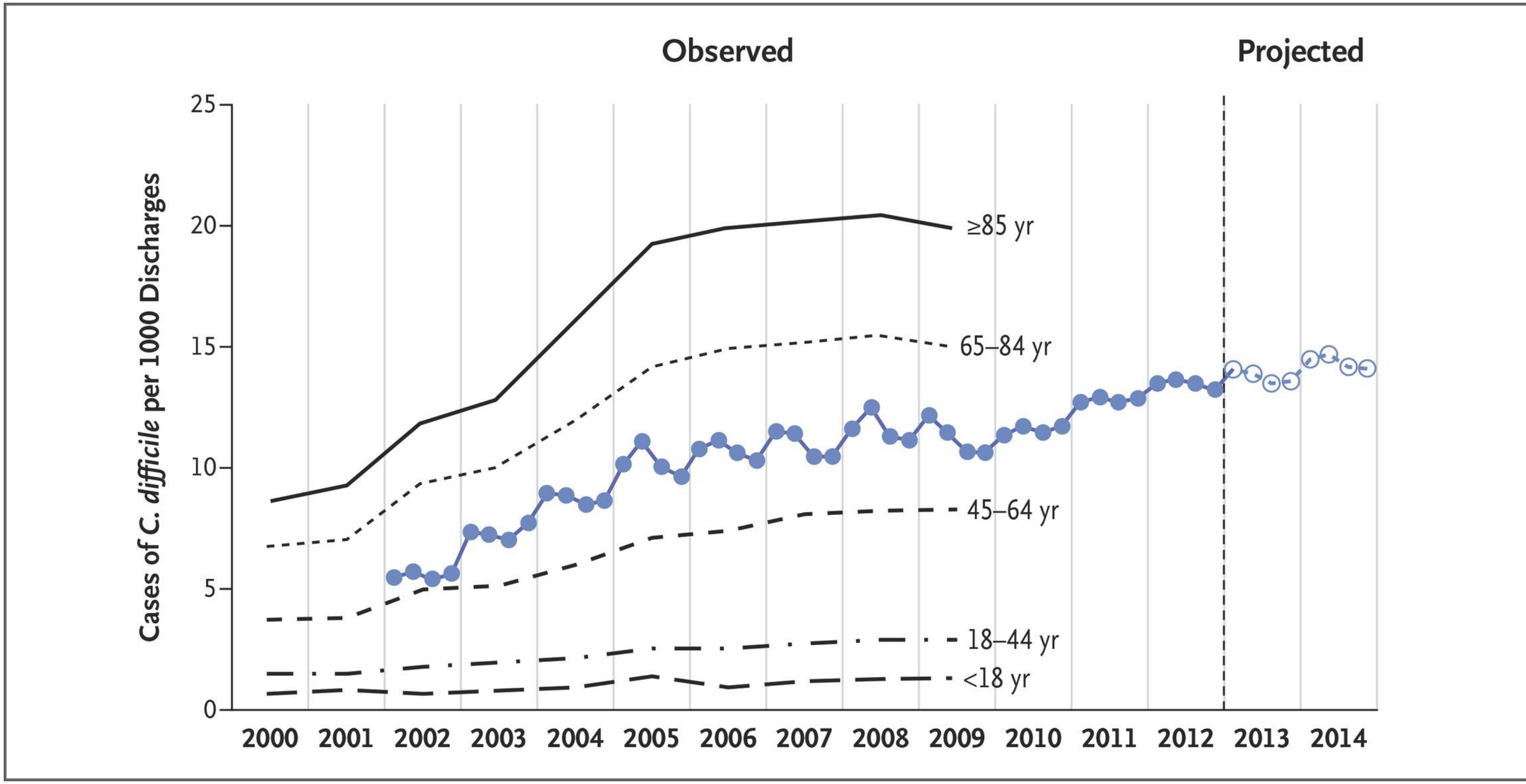
RD: 320
Tilt: 0.0
mA: 82
KVp: 120
Acq no: 5
Z: 1
C: 50
W: 450
DFOV:49.5x49.5cm
Compressed 8:1
F
cm

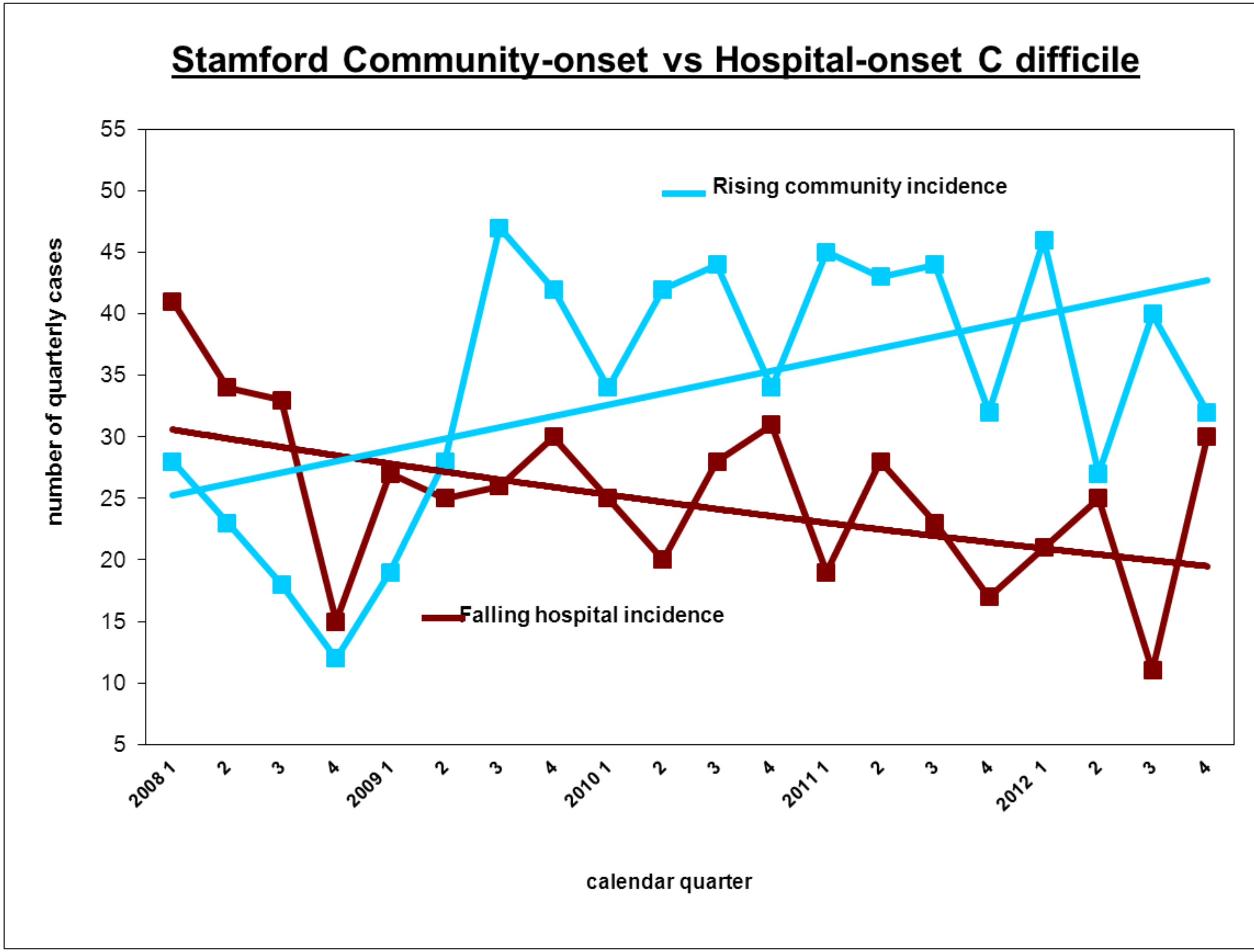
CONTRIBUTING FACTORS



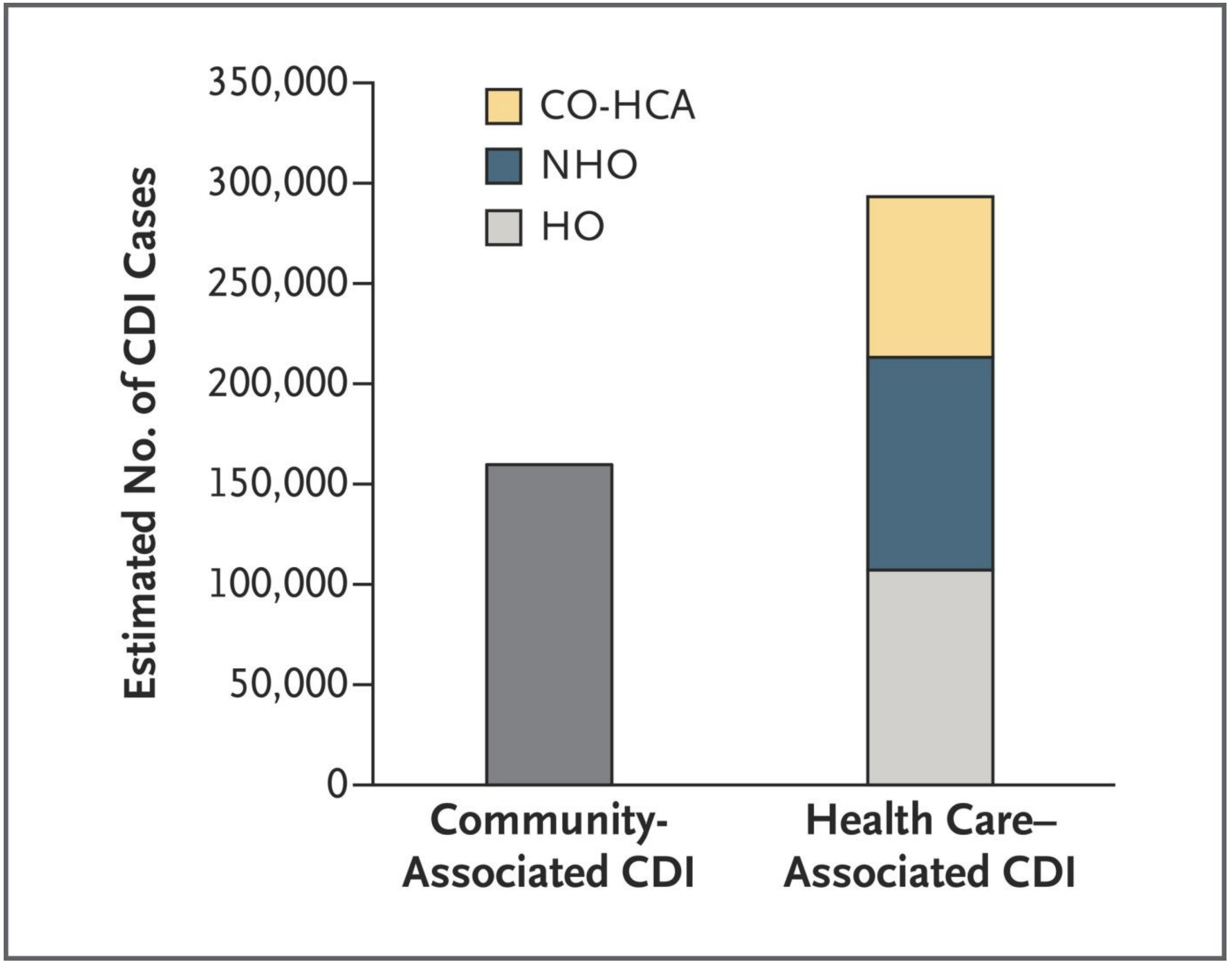
Incidence of Hospital acquired *Clostridium difficile* Infection.



Leffler DA, Lamont JT. N Engl J Med 2015;372:1539-1548


Stamford Community-onset vs Hospital-onset C difficile
Rising community incidence
Falling hospital incidence
number of quarterly cases
55
50
45
40
35
30
25
20
15
10
5
2008 1
2
3
4
2009 1
2
3
4
2010 1
2
3
4
2011 1
2
3
4
2012 1
2
3
4
calendar quarter

Estimated U.S. Burden of *Clostridium difficile* Infection (CDI), According to the Location of Stool Collection and Inpatient Health Care Exposure, 2011.



Lessa FC et al. N Engl J Med 2015;372:825-834

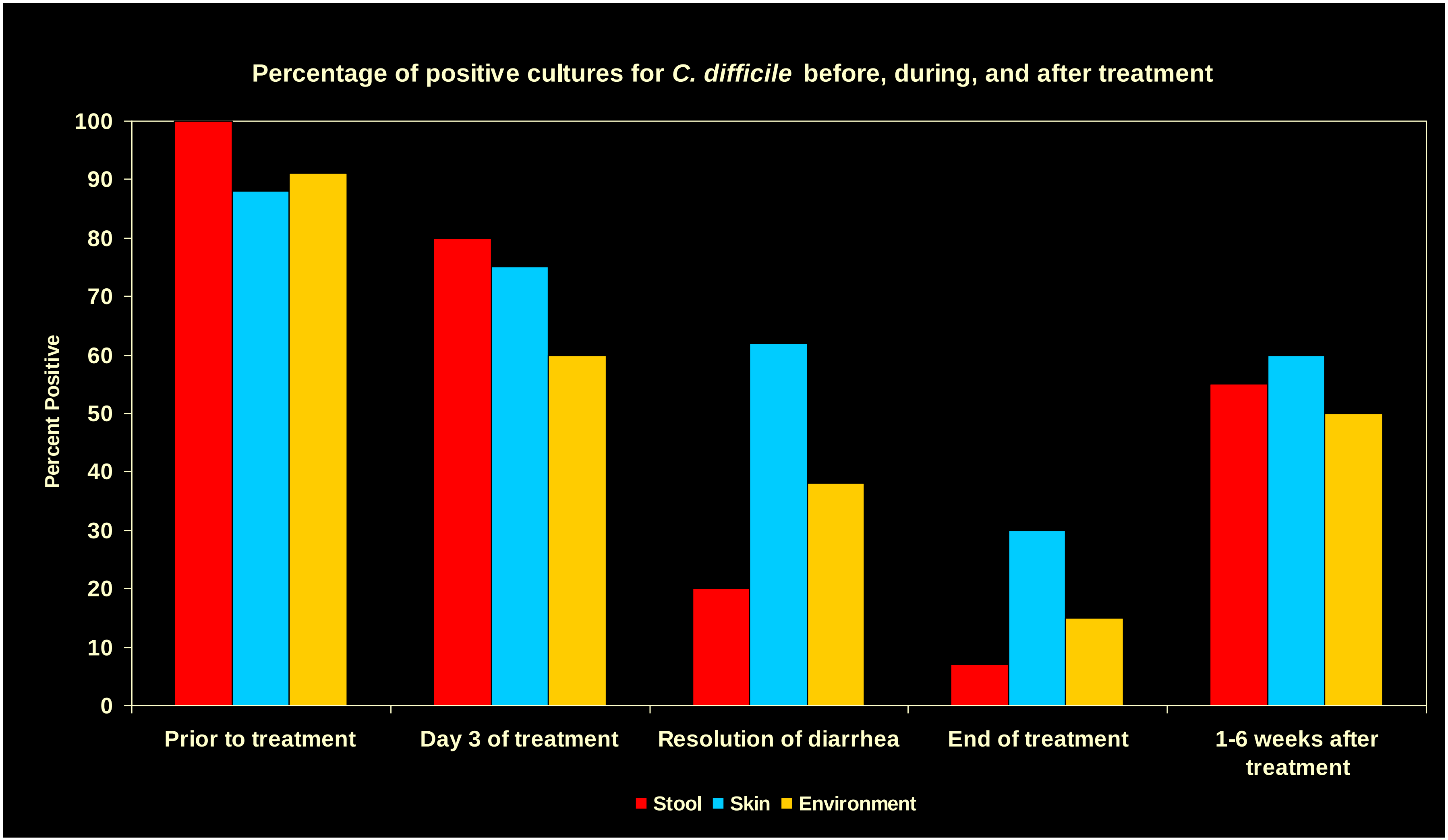
Risk of *C. difficile* with Antibiotics Given for Surgical Prevention

Carignan, Sherbrooke Hospital, Quebec. SHEA abstract 001, 2007

- 7256 class 1 and 2 surgeries
- CDAD rate 9.2/1000 cases
  - 5.1 / 1000 cases after only PAP
  - 21.8 / 1000 cases after treatment
- Equivalent rates for cefazolin, cefoxitin, other PAP
  - No cases after vancomycin prophylaxis
- Risk increased with hip surgery, higher Charlson score, case since 2003
- Risk related to number of antibiotic doses received

0 doses	**0 cases**
1 dose	**1.6/1000 days**
2 doses – 48 hours	**3.4/1000 days**
>48 hours	**13.0/1000 days**

Persistence of *C. difficile* During and After Treatment



Wafa Al Nassir, et al. Cleveland VA. 2008

C. difficile “bundle”
Hospital Methods to Attempt Control

- ✓ Barrier Precautions
  - Handwashing with soap and water, gloves, gowns
  - Duration of hospitalization
- ✓ Single room isolation or patient cohorting
- ✓ Patient bathing with chlorhexidine
- ✓ Environmental cleaning and disinfection
  - Patient room disinfection
  - Bleach
- ✓ Disposables
  - Disposable rectal thermometers, etc
- ✓ Antibiotic use – restriction policies
  - Use probiotics
  - Creative regimens: prolonged, taper, pulse, fidaxomycin
  - Fecal transplantation for multiple recurrences
  - Avoid antibiotics for 6-12 months

Executive Order -- Combating Antibiotic-Resistant Bacteria

EXECUTIVE ORDER

\- - - - - - -

COMBATING ANTIBIOTIC-RESISTANT BACTERIA

By the authority vested in me as President by the Constitution and the laws of the United States of America, I hereby order as follows:

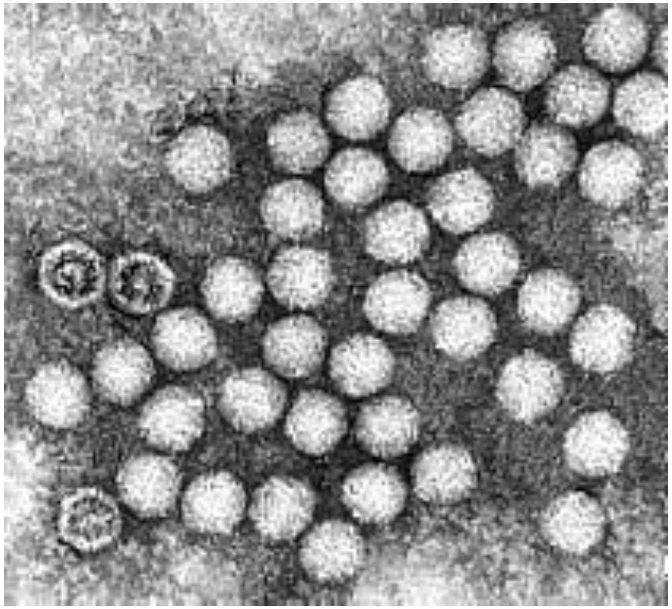
Sec. 5. Improved Antibiotic Stewardship. (a) By the end of calendar year 2016, HHS shall review existing regulations and propose new regulations or other actions, as appropriate, that require hospitals and other inpatient healthcare delivery facilities to implement robust antibiotic stewardship programs that adhere to best practices, such as those identified by the CDC. HHS shall also take steps to encourage other healthcare facilities, such as ambulatory surgery centers and dialysis facilities, to adopt antibiotic stewardship programs.

BARACK OBAMA

THE WHITE HOUSE,
September 18, 2014.

Enteroviruses

- Family Picornavirus
- RNA Viruses
- Include
  - Coxsackie viruses
  - Polio viruses
  - Echo viruses
  - Other enteroviruses



Clinical manifestation of Enterovirus Infections

- Aseptic meningitis
- Nonspecific febrile illness
- Colds
- Conjunctivitis
- Pharyngitis
- Herpangina
- Hepatitis
- Exanthems
- Encephalitis
- Paralytic polio
- Vomiting
- Diarrhea
- Pericarditis
- Myocarditis
- Hand-foot-mouth syndrome

Epidemiology

- Transmission from person to person
  - Fecal-Oral
  - Respiratory
  - Food and water
- Peak incidence : Summer & Fall
- Male = Female
- Age: Young children
- Incubation period: 3-6 Days

Hand-foot-mouth syndrome

Small intraoral ulcers and macular or vesicular lesion on hands and feet & buttock

Neurologic complications described

Enterovirus D68

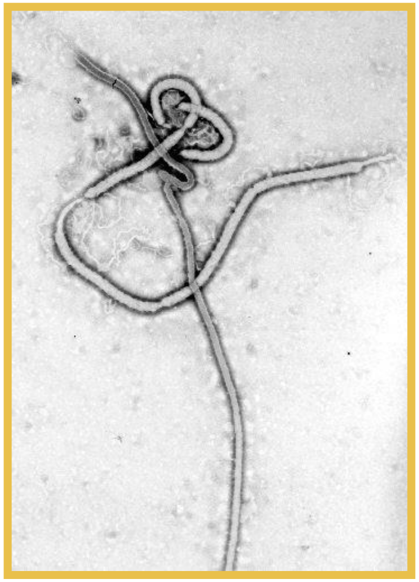
- Outbreak started in Midwest in 2014
  - Missouri, Illinois, Kansas; nationwide , including CT
- Children with severe respiratory illness
  - Runny nose, cough, sneezing, SOB
  - Age range 10 months to 18 years
  - Up to 15% require PICU care
  - Usually afebrile (80%)
  - Many have predisposing asthma
  - Spread by droplet and contact with secretions
- Diagnosis by viral culture/PCR from NP sample
  - EV-D68 confirmation by CDC
- Supportive care

Acute Limb Weakness complicating Enterovirus D68 infection

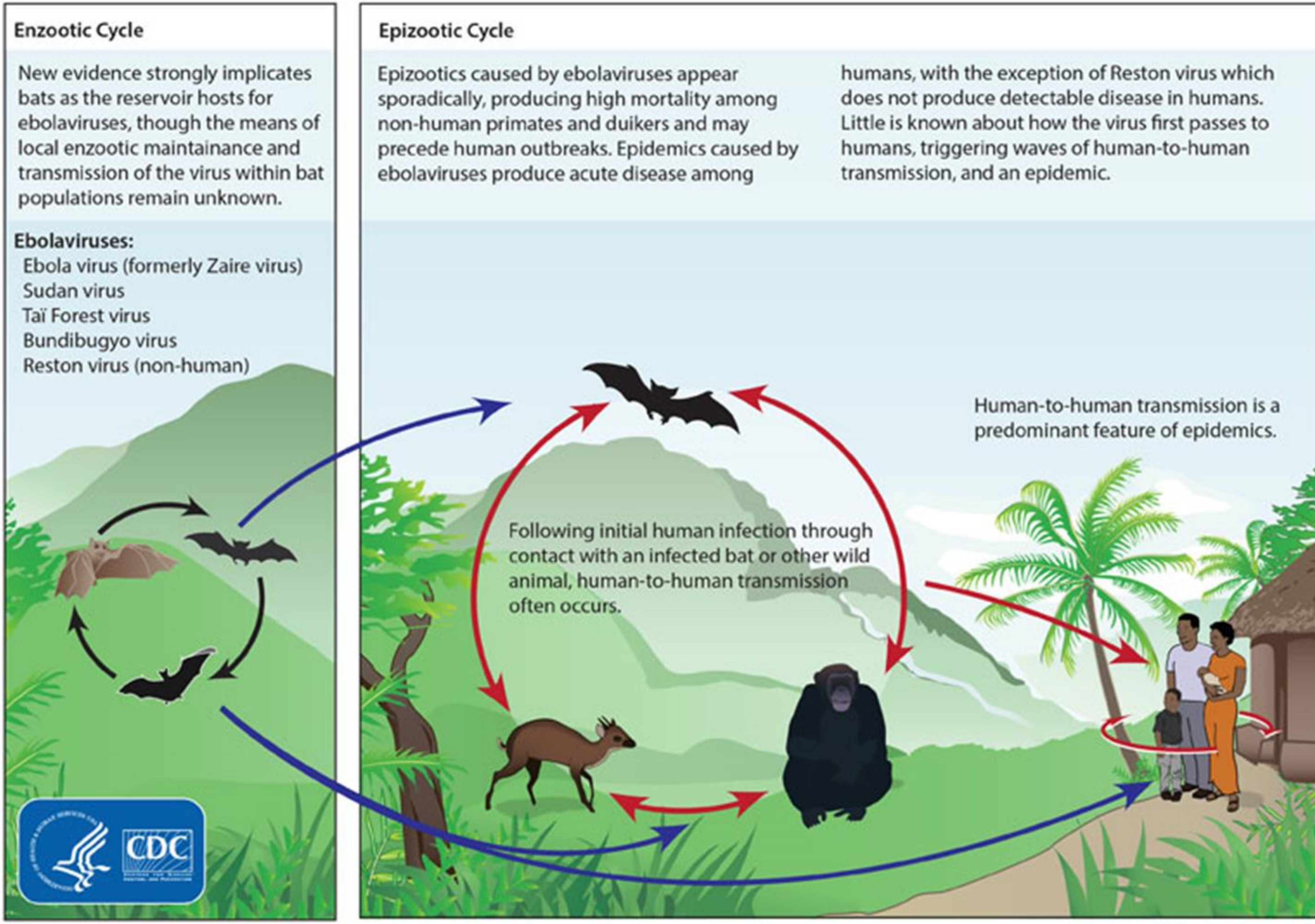
- Children, age range 1-18 years
- URI followed 2 weeks later with focal limb weakness or cranial nerve palsies
- MRI and CSF c/w spinal cord infection
- CSF samples negative for virus
- Residual weakness and atrophy – like polio

Viral Hemorrhagic Fever

- Viruses of four distinct families
  - Arenaviruses (Lassa)
  - Filoviruses (Ebola)
  - Bunyaviruses (Hantavirus)
  - Flaviviruses (Dengue)
- RNA viruses
  - Enveloped in lipid coating
- Animal or insect host is the natural reservoir



Ebolavirus Ecology




CENTRE DE TRAITEMENT
EBOLA

Pathogenesis - how does Ebola cause disease?

- Virus enters the body through infected blood/body fluid in contact with a mucus membranes or a break in skin.
- Virus multiplies in monocytes/macrophages which facilitate dissemination of the virus throughout the body
- Rapid viral growth in hepatocytes, endothelial and epithelial tissues.
- Strong cytokine/inflammatory mediators; release of TNF-α.
- Leads to endothelial damage, increased vascular permeability and shock.
- This results in the multi-organ failure
- Diffuse intravascular coagulopathy (DIC) leads to hemorrhage.

Ebola Symptoms

- Incubation period, is 2 to 21 days; average is 8 to 10 days.
- Onset: Abrupt – Fever, Headache, Myalgia
- Soon Thereafter:
  - Rash,
  - Nausea, Vomiting, Abdominal Pain, Diarrhea
- Ongoing:
  - Jaundice, Pancreatitis
  - CNS – Somnolence, Delirium, Coma
  - Bleeding (1/3) – Petechiae, Hemorrhages
- Laboratory
  - Electrolyte abnormalities – sodium and potassium loss
  - Liver failure → low serum protein → edema
  - Bleeding from low platelets
- Fatality rate, current outbreak: ~50%

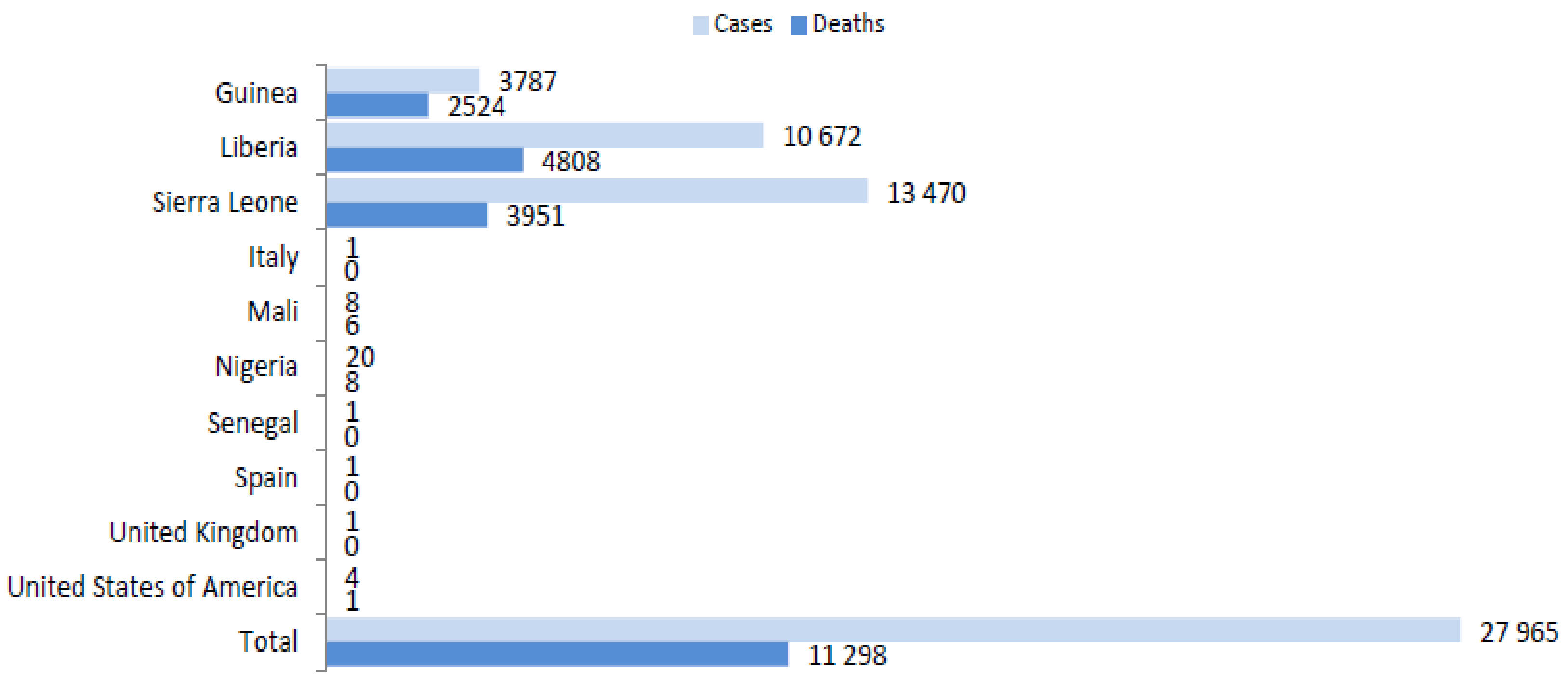
Ebola Awareness

- >27,000 cases, >11,000 deaths
- Border closures, airport closures, martial law, curfews, country lockdown
- Ongoing cases
- Supportive treatment
- Prevention by PPE / avoiding high risk contact
- Cultural barriers to infection control
- Travelers still arriving

WHO Epidemiologic Histogram (8/9/15)

EBOLA SITUATION REPORT

Figure 1: Confirmed, probable, and suspected EVD cases worldwide (data up to 9 August 2015)



Ebola Response

- Ebola preparation meetings
- Screening questionnaire
  - Registration, EMS, ED triage physicians
- Rapid triage plan
- Patient management flow algorithm
- High risk isolation signage
- High risk isolation cart
- Upgraded fluid impermeable PPE
- Process for safe laboratory management
- Ongoing training and competency program for staff

Have you travelled outside of the country in the last 3 weeks?

If "yes", please alert medical personnel upon arrival

SCREENING FOR EBOLA

Patient presentation

- Fever >101.5 (>38.6)
- Headache
- Muscle aches
- Vomiting or diarrhea
- Abd pain
- Hemorrhage

Travel History

West Africa within 21 days:

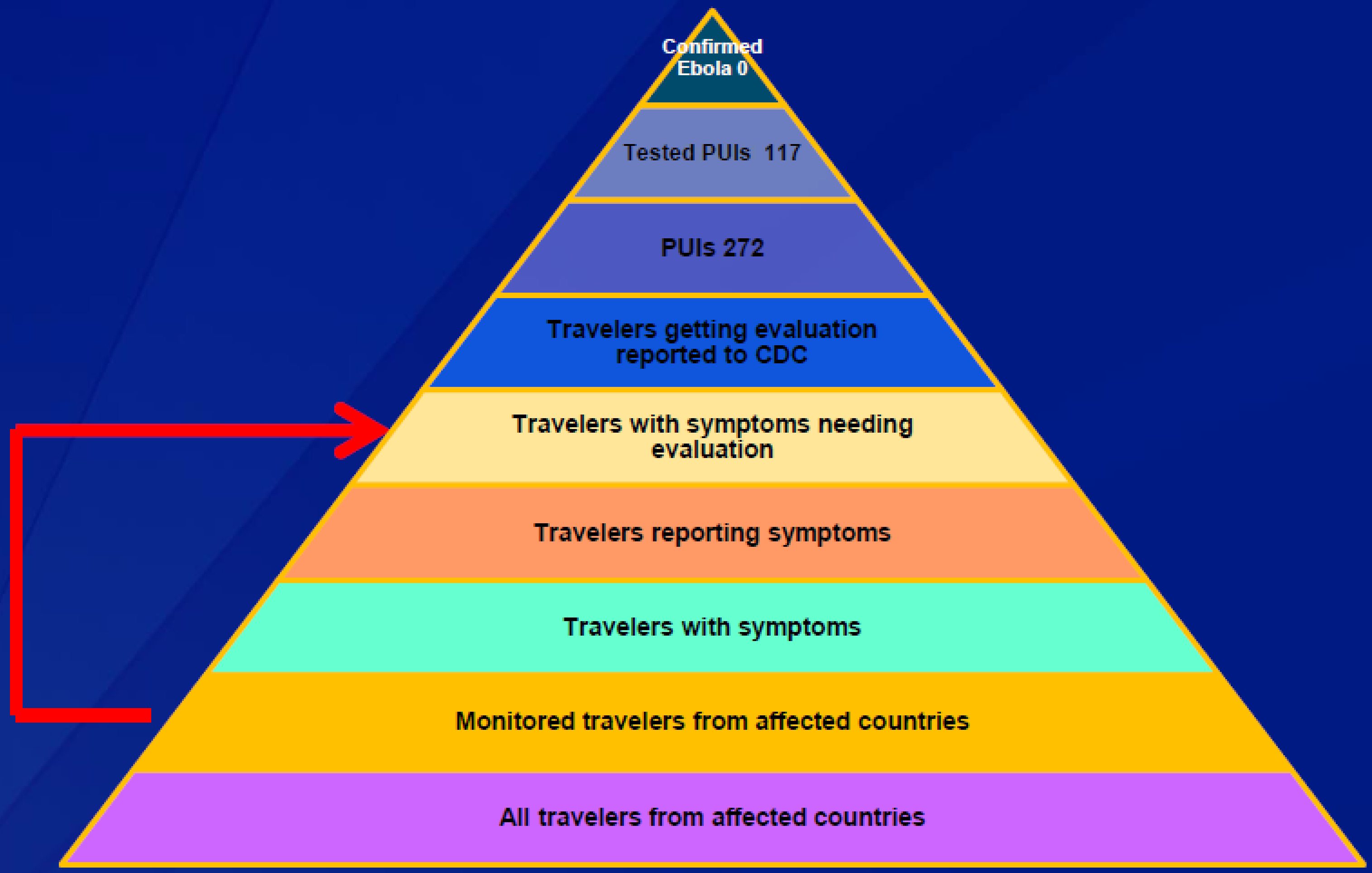
- Guinea
- Liberia
- Sierra Leone

Close Contact

- With anyone sick with Ebola or suspect?
- With blood or body fluids of a person sick with Ebola?
- With remains of a person who died of Ebola?


Exam Rooms
G 199 D

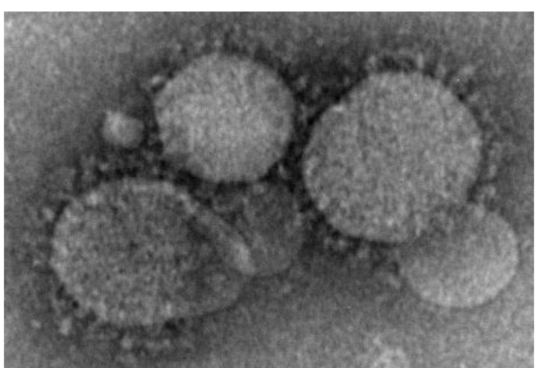
Number of persons traveling, monitored, and reported to CDC as PUIs with concerns about Ebola -- United States, 2014-15

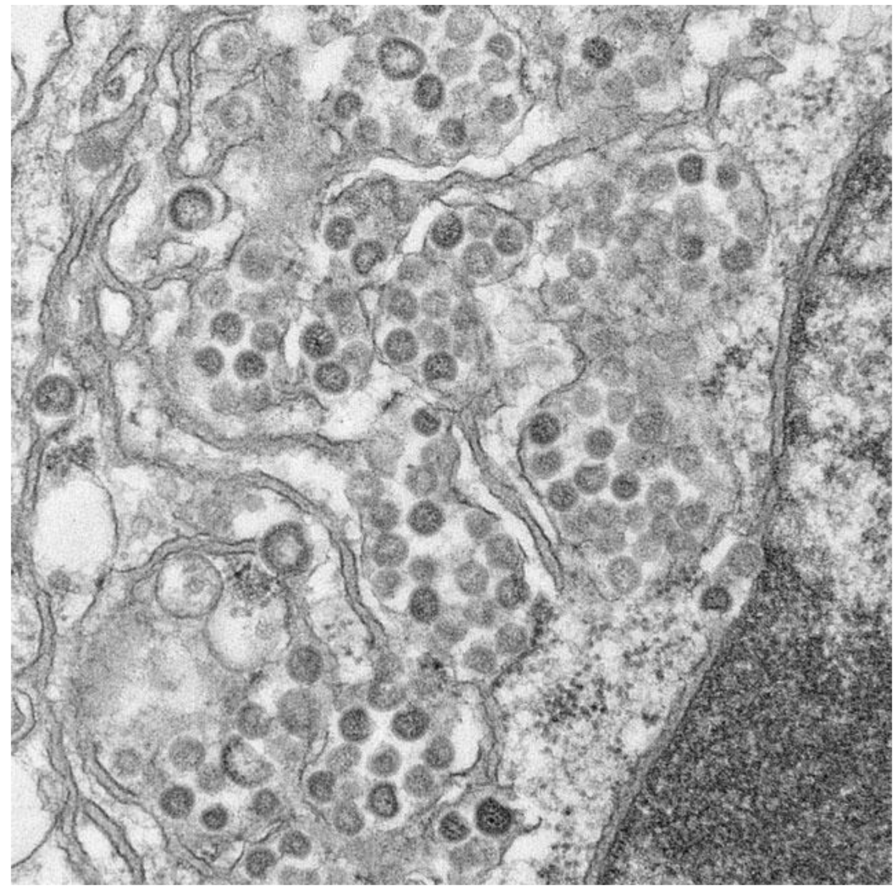


Source: CDC Domestic Clinical Inquiries Team

Middle East Respiratory Syndrome Coronavirus (MERS-CoV)

- Novel coronavirus that emerged in 2012
- Epicenter in Saudi Arabia
- Causes severe acute respiratory illness
- 1368 cases
- 37% fatality rate

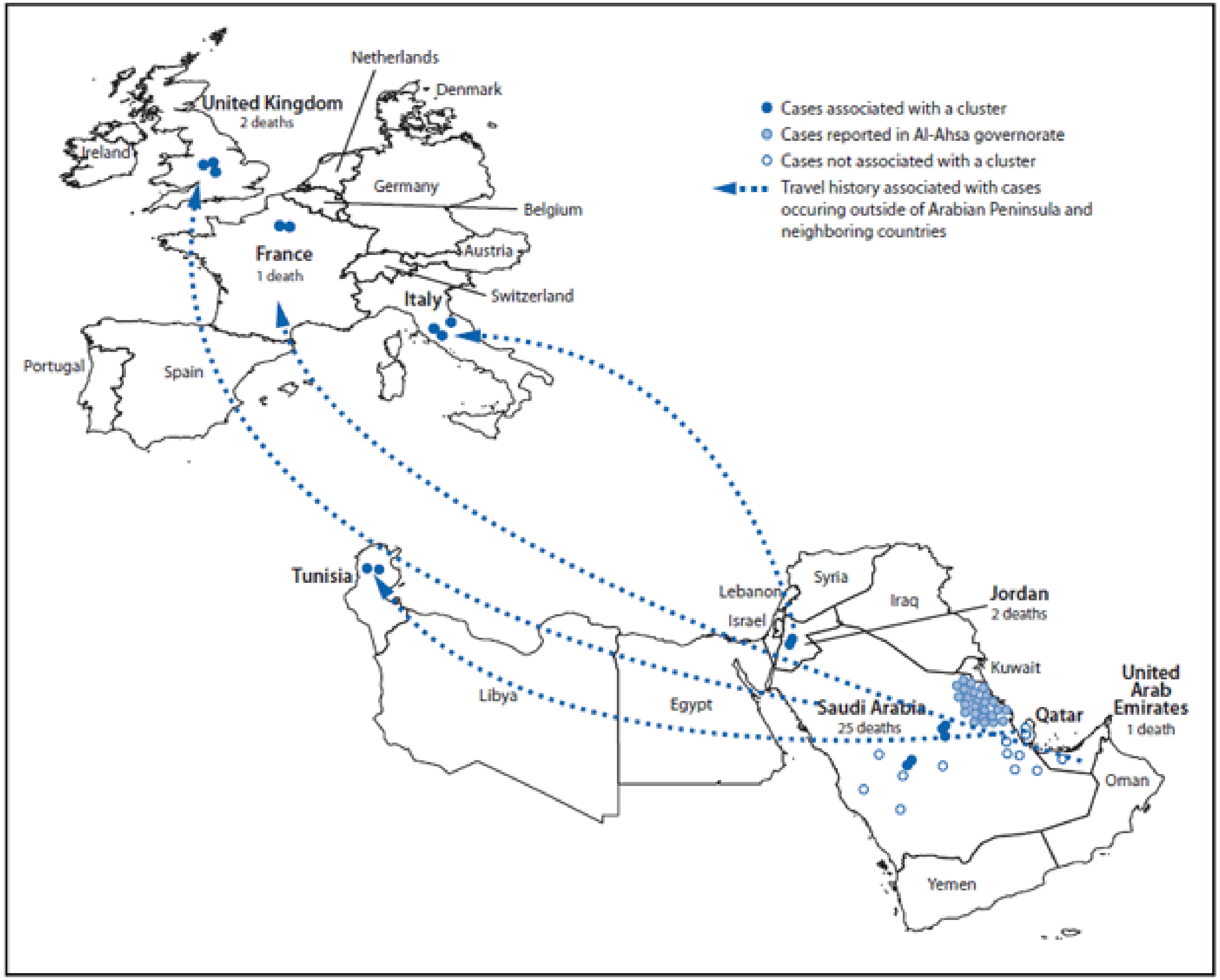




MERS-CoV Symptoms

- Severe acute respiratory illness:
  - Fever, cough, shortness of breath
  - ARDS with multiorgan failure
- Incubation period is 10-14 days
- 65% male, mean age 50 (range 9-99)
- Illness initially sporadic, family clusters, HCW, then epidemic peaks in S Korea and Saudi Arabia.
- Some cases have had atypical presentations:
  - Initially presented with abdominal pain and diarrhea and later developed respiratory complications
- Reservoir potential camels, bats
- Healthcare exposure

Confirmed cases of Middle East Respiratory Syndrome Coronavirus (MERS-CoV) (N =55) reported as of June 7, 2013, to the World Health Organization, and history of travel from the Arabian Peninsula or neighboring countries



MMWR. June 14, 2013 / 62(23);480-483

Patient Under Investigation (PUI)

PUI Criteria:

1. Persons who develop severe acute lower respiratory illness of known etiology within 14 days after traveling from the Arabian Peninsula or neighboring countries
2. Persons who develop severe acute lower respiratory illness who are close contacts of a symptomatic traveler who developed fever and acute respiratory illness within 14 days of traveling from the Arabian Peninsula or neighboring countries
3. Acute respiratory infection, may include fever ≥ 100.4°F and cough
4. Suspicion of pneumonia or acute respiratory distress syndrome based on clinical or radiological evidence
5. Symptoms not already explained by any other infection or etiology

MERS-CoV Transmission

- Airborne / droplet
    - Gowns, gloves, N-95 mask, eye protection
- Transmission:
    - Transmission between close contacts
    - Transmission from infected patients to healthcare personnel
    - Clusters of illnesses have been reported by six countries

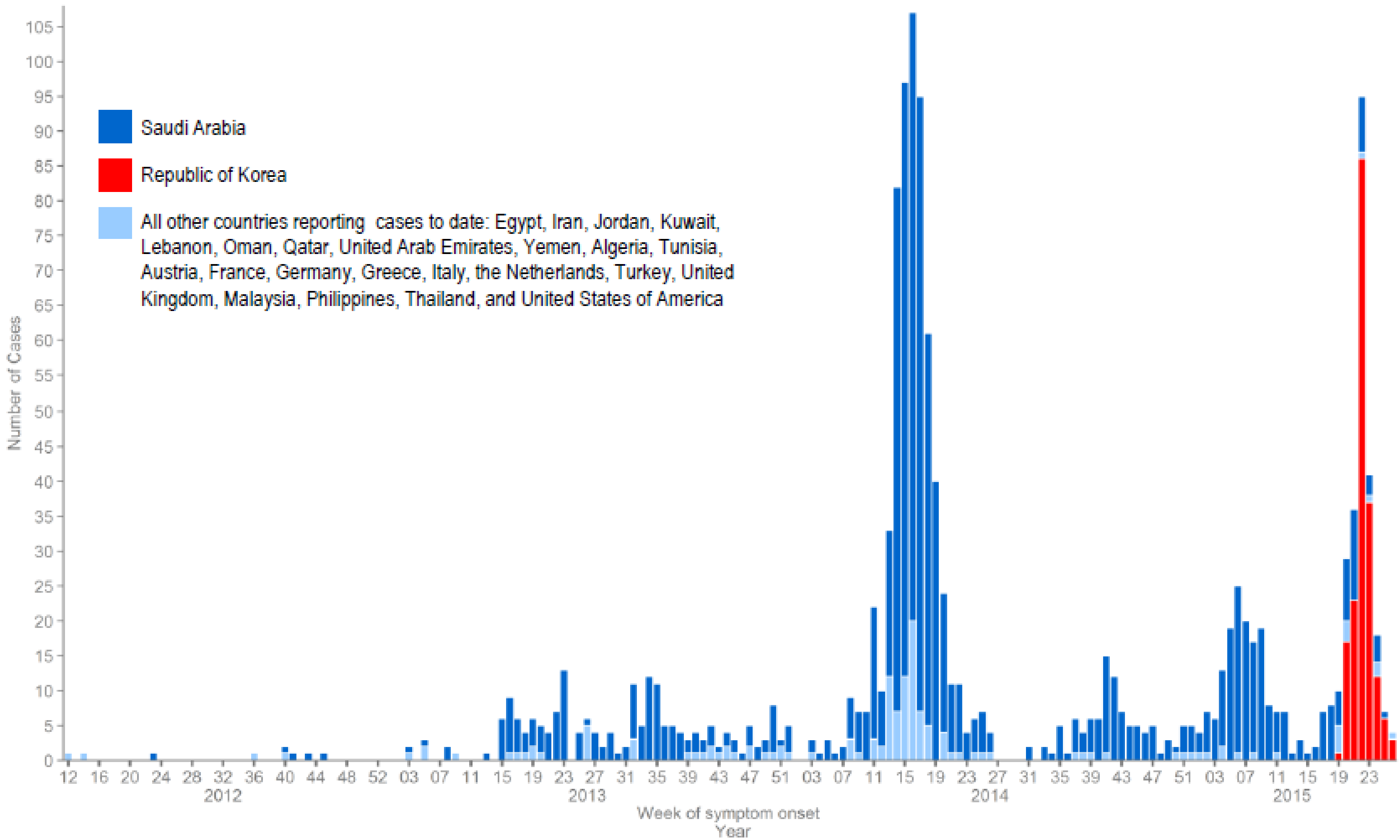


Figure 1. Epidemic curve of MERS-CoV cases (n=1368) (as of 7 July 2015)

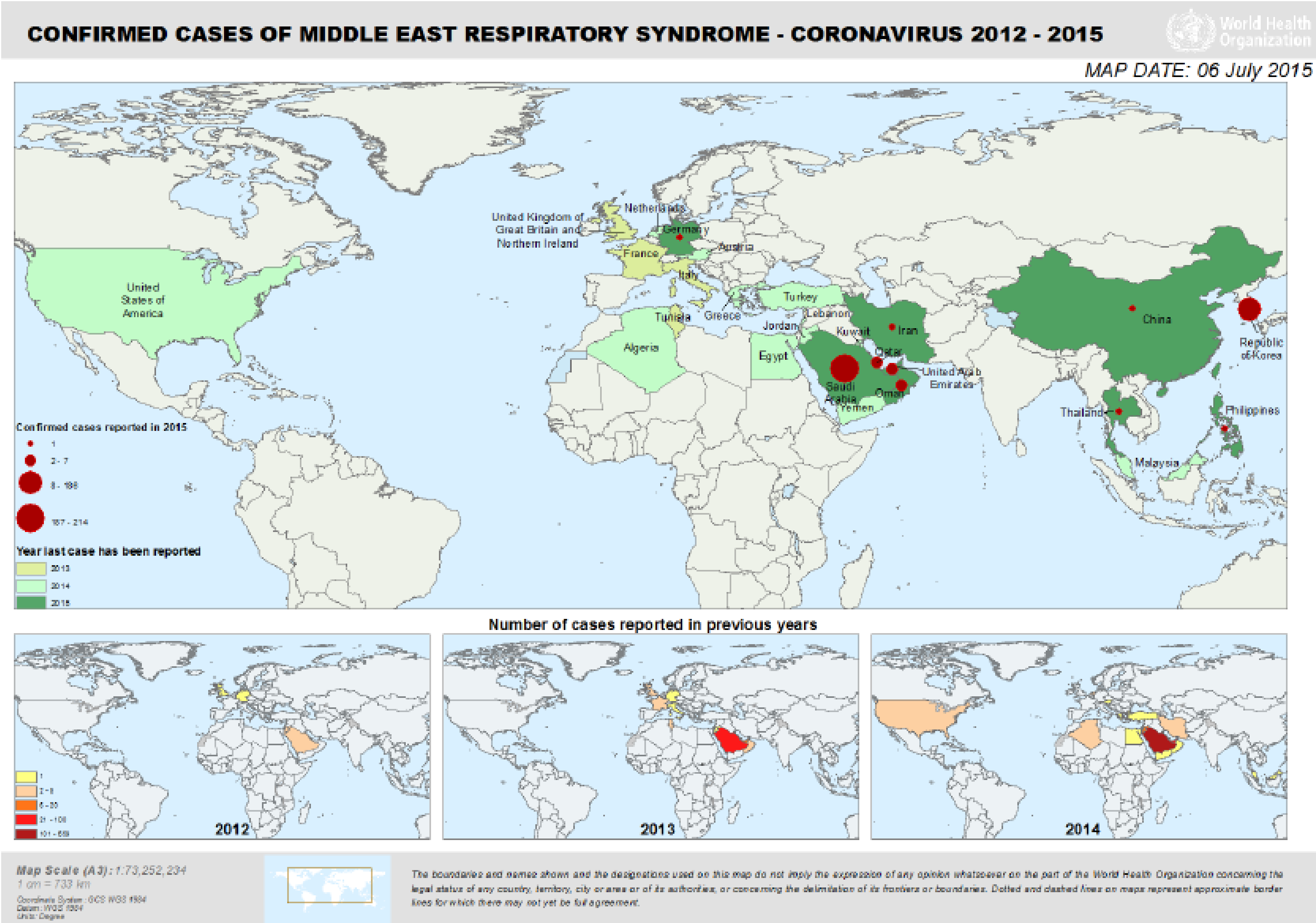
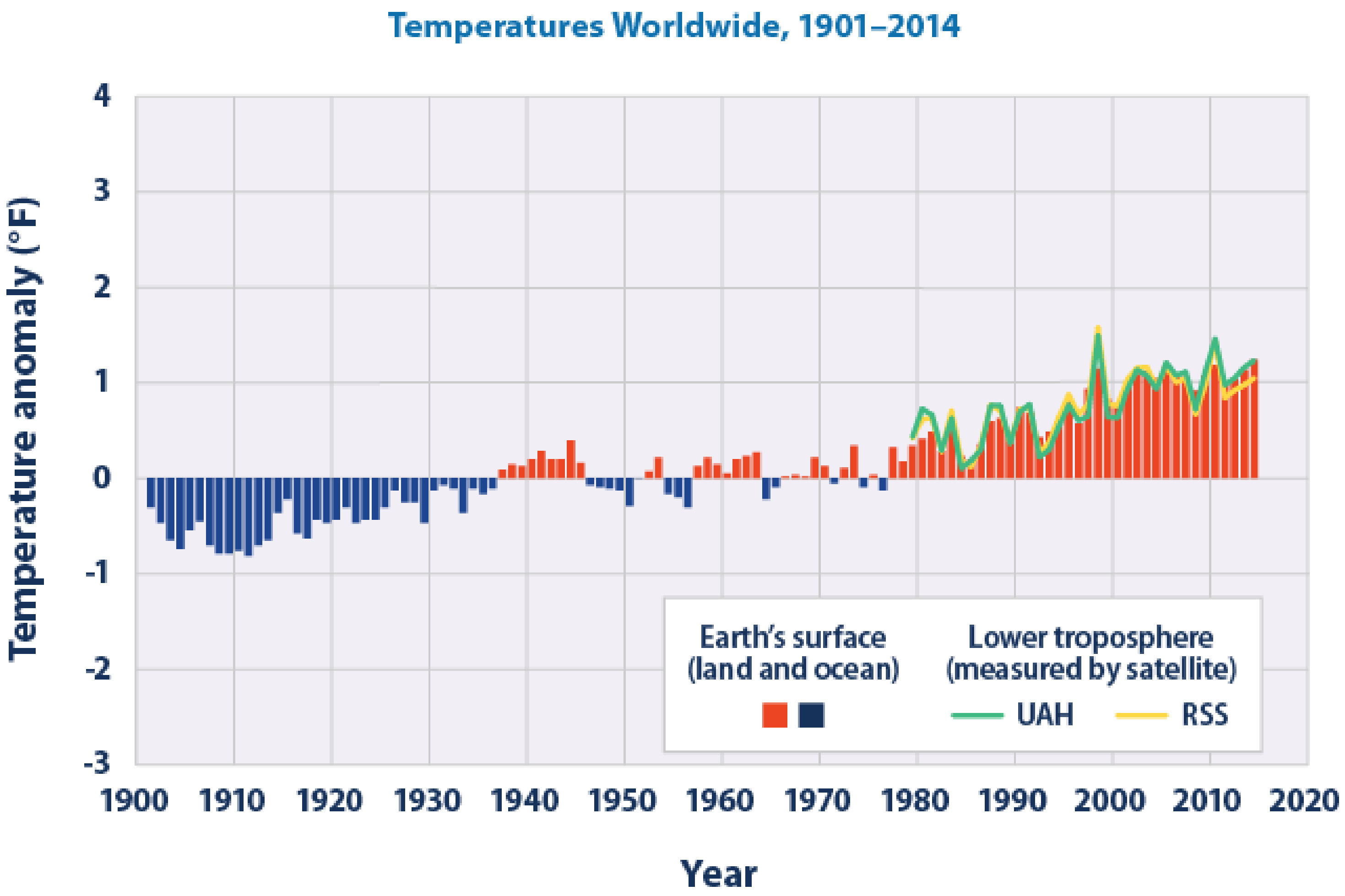


Figure 2. Number of laboratory-confirmed MERS-CoV cases reported by countries by year since 2012

Climate Change

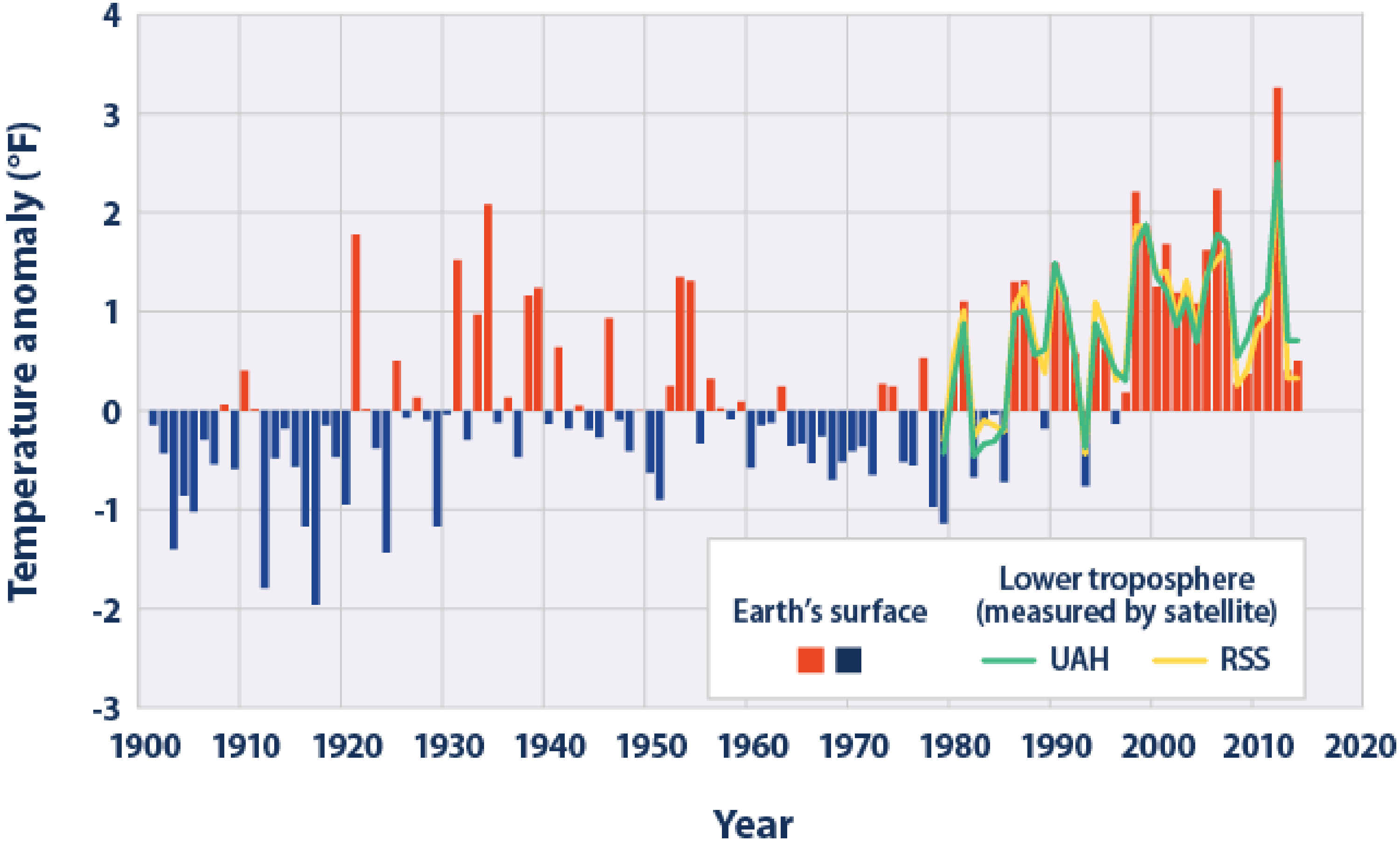
- Global average surface temperature has risen at an average rate of 0.15°F per decade since 1901. Average temperatures have risen more quickly since the late 1970s (0.26 to 0.43°F per decade).
- Worldwide, 2014 was the warmest year on record and 2005–2014 was the warmest decade on record since thermometer-based observations began.
- Similar to the rate of warming within the contiguous 48 states. Seven of the top 10 warmest years on record for the contiguous 48 states have occurred since 1998, and 2012 was the warmest year on record.
- Concentrations of heat-trapping greenhouse gases are increasing in the Earth's atmosphere. In response, average temperatures at the Earth's surface are expected to continue rising.
- Annual and seasonal temperature patterns determine the types of animals and plants and insects that can survive in particular locations. Changes in temperature can disrupt a wide range of natural processes, particularly if these changes occur more quickly than species can adapt.



Data source: NOAA (National Oceanic and Atmospheric Administration). 2015. National Centers for Environmental Information. Accessed April 2015. www.ncei.noaa.gov.

For more information, visit U.S. EPA's "Climate Change Indicators in the United States" at www.epa.gov/climatechange/indicators.

Temperatures in the Contiguous 48 States, 1901–2014



Data source: NOAA (National Oceanic and Atmospheric Administration). 2015. National Centers for Environmental Information. Accessed April 2015. www.ncei.noaa.gov.

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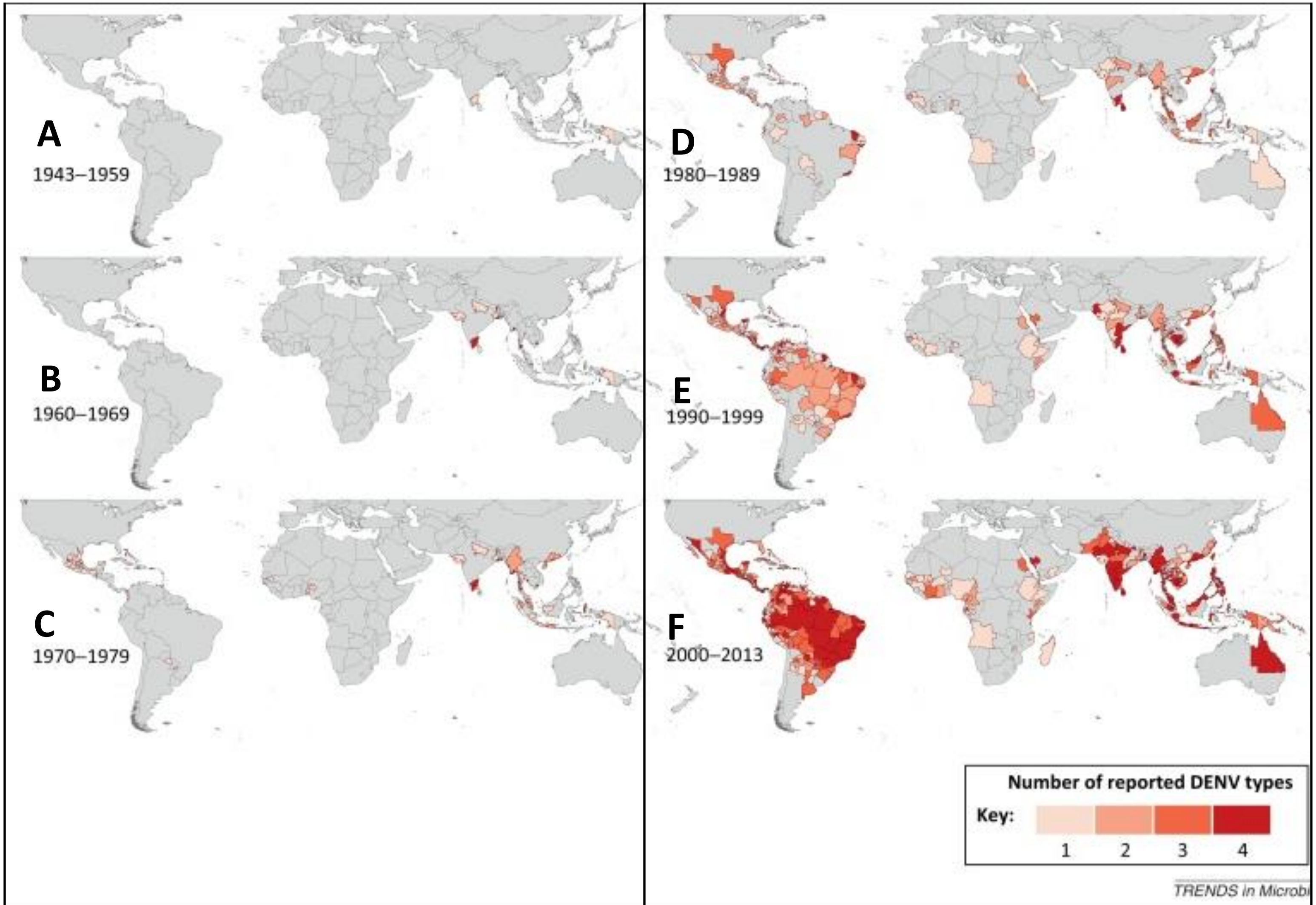
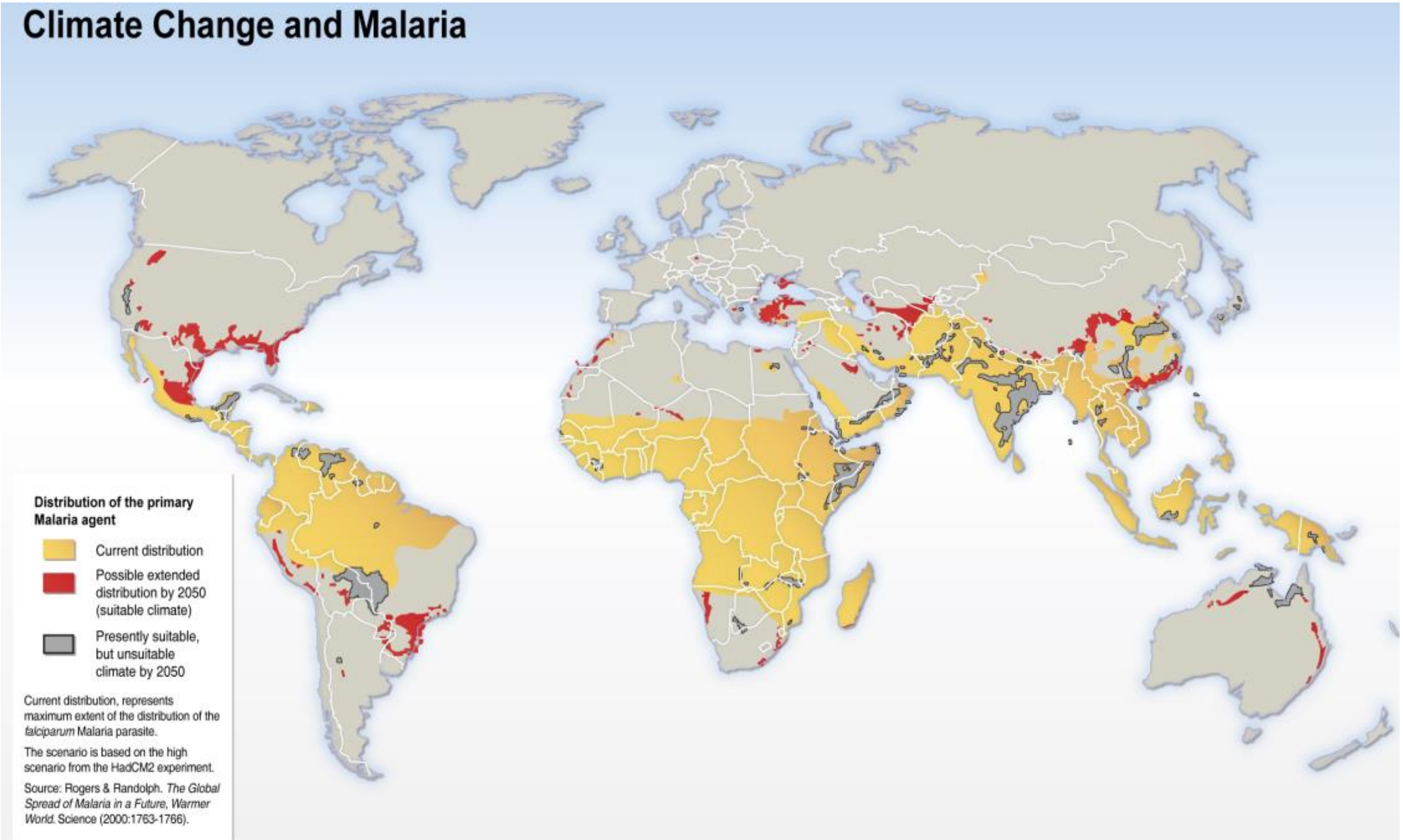
Jane P. Messina, et al. Trends Microbiol. 2014 Mar; 22(3): 138–146.

Global spread of dengue virus types: mapping the 70 year history



Spread of Arthropod-borne Infections due to Climate Change



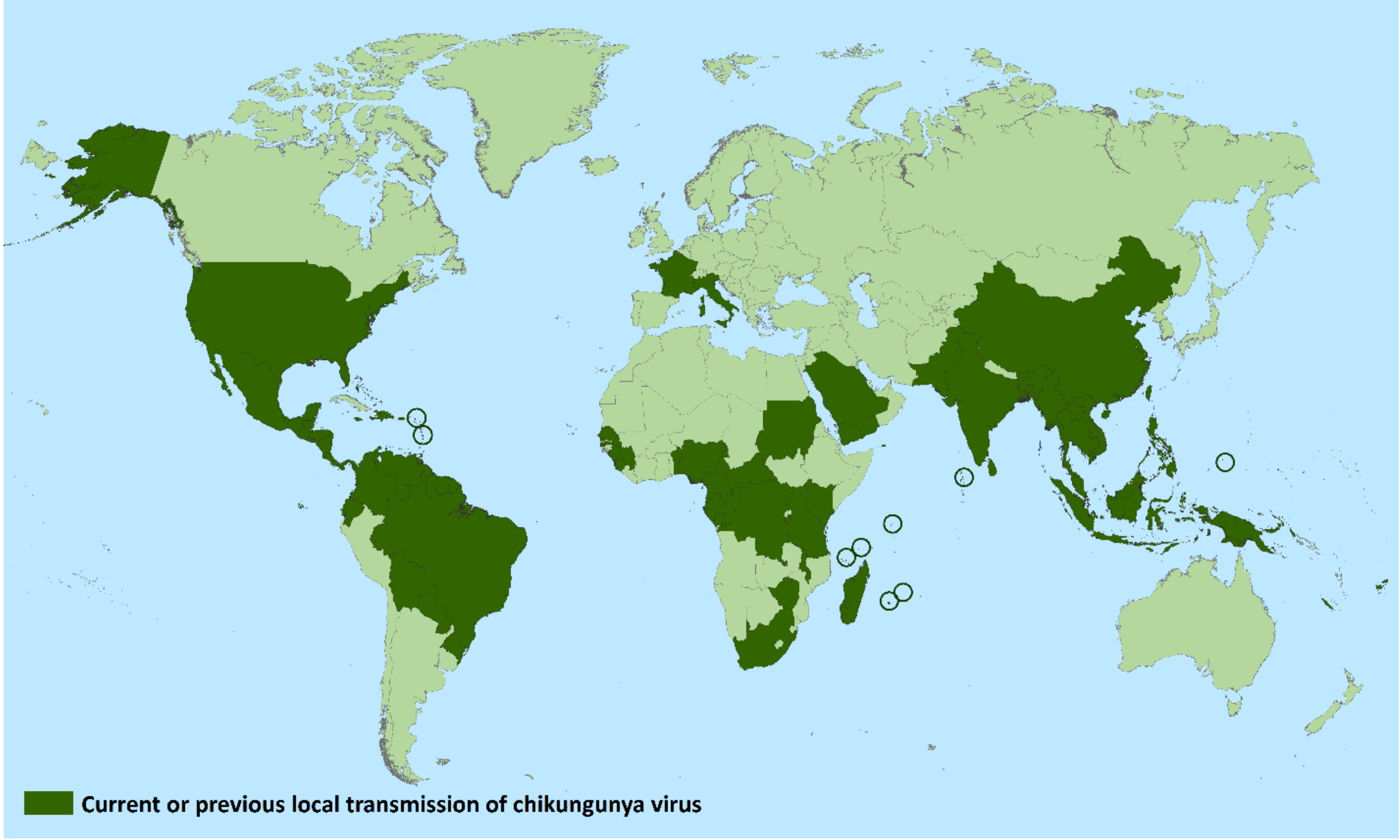
Aedes mosquito vector distribution in United States

2014 map of the U.S. showing the areas at risk of dengue outbreaks, based on the approximate distribution of dengue mosquito vectors *Aedes aegypti* and *Aedes albopictus*.

Aedes species transmit:

- Dengue
- Yellow fever
- West Nile
- Eastern Equine Encephalitis
- Zika virus
- Chikungunya

Chikungunya Prevalence



Chikungunya

- Transmitted by Aedes sp. mosquitos
- Incubation period 3-7 days
- Acute onset of fever and polyarthralgia, bilateral, symmetrical
- Debilitating, severe arthritis may occur
- Headache, myalgia, conjunctivitis, rash
- Lymphopenia, thrombytopenia, elevated SCr and ALT
- Complications (rare): uveitis, retinitis, myocarditis, nephritis, encephalitis, hepatitis, bullous skin lesions
- Symptoms typically resolve in 10 days but may persist for months
- Serologic diagnosis (PCR or IgG/IgM)
- Supportive treatment: NSAIDs, corticosteroids

Chikungunya Arthritis

Tick Borne Diseases in the US -- 2015

- Anaplasmosis
- Babesiosis
- *Borrelia burgorferi* (Lyme Disease)
- *Borrelia miyamotoi* infection
- Colorado tick fever
- Ehrlichiosis
- Heartland virus
- Powassan virus
- Bourbon virus
- Rocky Mountain Spotted fever (*Rickettsia rickettsii)*
- Southern tick-associate rash illness (STARI)
- Tick borne relapsing fever
- Tularemia
- *Rickettsia parkeri*
- Rickettsia species 364D

Powassan, Heartland, Bourbon viruses

- Powassan virus (phlebovirus)
  - Fever, headache, vomiting, confusion, seizures
  - CSF pleocytosis (viral meningoencephalitis)
  - Northeast and Great Lakes
  - Ixodes
- Heartland virus (phlebovirus)
  - Fever, myalgias, HA
  - Leukopenia, thrombocytopenia
  - Missouri & Tennessee
  - Lone star tick
- Bourbon virus (orthomyxovirus)
  - Fever, rash, nausea & vomiting, encephalitis
  - Leukopenia, thrombocytopenia
  - Kansas
  - Tick type unclear

New infectious diseases

2015	??
2014	Powassan, Heartland, Bourbon virus
2014	Enterovirus D68
2013	Chikungunya
2012	MERS
2009	H1N1pdm influenza
2005	H7N9 and H9N2 influenza
2004	ESBL / CRE infections
2003	SARS
2002	VRSA
1999	Nipah virus
1999	West Nile Virus (new world)
1997	H5N1 influenza
1996	nCJD (mad cow disease)
1995	HHV-8 (Kaposi sarcoma virus)
1994	Hantavirus
1992	MDR-Tuberculosis
1989	Hepatitis C
1988	Hepatitis E, HHV-6
1983	HIV/AIDS, Helicobacter
1983	E. coli O157:H7, Lyme disease
1980	HTLV I, II
1978	Clostridium difficile colitis
1976	Ebola, Legionnaires disease

Thank You!

Questions?