Infectious Diseases
2017

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STAMFORD HOSPITAL

Disclosure

Research support from

- Cidara Pharmaceuticals
- Glaxo/Smith-Kline

Newly identified infectious diseases

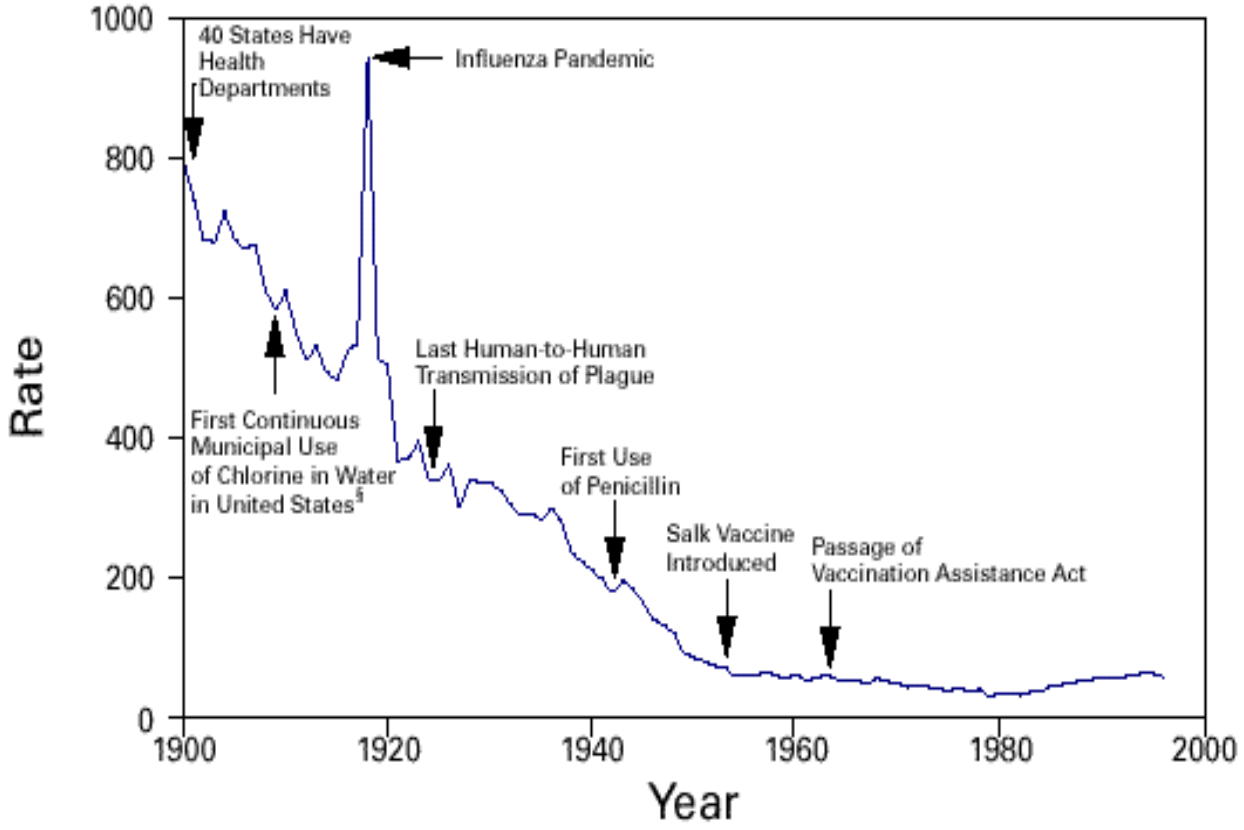
2017	**Candida auris**
2016	**Colistin resistance (mcr-1 gene)**
2015	**Zika virus**
2014	**Powassan, Heartland, Bourbon virus, etc**
2014	**Enterovirus D68**
2013	**Chikungunya**
2012	**MERS**
2009	**H1N1pdm influenza**
2008	**CRE (KPC, NDM-1, etc) infections**
2007	**Parechovirus**
2005	**H7N9 and H9N2 influenza**
2004	**ESBL 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**

Outline

- Antibiotic resistance
- Zika
- Candida auris
- Influenza

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.

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

A 'slow catastrophe' unfolds as the golden age of antibiotics comes to an end

2016

Research scientist Rosslyn Mayback was part of the team that identified a strain of E. coli bacteria with a gene that could spread antibiotic resistance. (Walter Reed Army Institute of Research)

By Melissa Healy

JULY 11, 2016, 10:05 AM | REPORTING FROM BETHESDA, MD.

In early April, experts at a military lab outside Washington intensified their search for evidence that a dangerous new biological threat had penetrated the nation's borders.

NATIONAL ACTION PLAN FOR COMBATING ANTIBIOTIC-RESISTANT BACTERIA

MARCH 2015

THE WHITE HOUSE
WASHINGTON

The Joint Commission

• Issued June 22, 2016 •

Prepublication Requirements

The Joint Commission has approved the following revisions for prepublication. While revised requirements are published in the semiannual updates to the print manuals (as well as in the online E-dition®), accredited organizations and paid subscribers can also view them in the monthly periodical *The Joint Commission Perspectives®*. To begin your subscription, call 877-223-6866 or visit http://www.jcrinc.com.

Joint Commission Requirement

New Antimicrobial Stewardship Standard

APPLICABLE TO HOSPITALS AND CRITICAL ACCESS HOSPITALS

Effective January 1, 2017

Medication Management (MM)

Standard MM.09.01.01
The [critical access] hospital has an antimicrobial stewardship program based on current scientific literature.

Elements of Performance for MM.09.01.01

1. Leaders establish antimicrobial stewardship as an organizational priority. (*See also* LD.01.03.01, EP 5)

   Note: *Examples of leadership commitment to an antimicrobial stewardship program are as follows:*

   - *Accountability documents*
   - *Budget plans*

Note: *An example of an educational tool that can be used for patients and families includes the Centers for Disease Control and Prevention's Get Smart document, "Viruses or Bacteria—What's got you sick? at http://www.cdc.gov/getsmart/community/downloads/getsmart-chart.pdf.*

4. The [critical access] hospital has an antimicrobial stewardship multidisciplinary team that includes the following members, when available in the setting:

   - Infectious disease physician
   - Infection preventionist(s)
   - Pharmacist(s)
   - Practitioner

   Note 1: *Part-time or consultant staff are acceptable as members of the antimicrobial stewardship multidisciplinary team.*

   Note 2: *Telehealth staff are acceptable as members of [illegible]timicrobial stewardship multidisciplinary team.*

Proposed CMS rule on infection control and inappropriate antibiotic use

CMS

Today, the Centers for Medicare and Medicaid Services (CMS) proposed new standards to advance healthcare quality and equity in our nation's hospitals. In a proposed rule open for public comment, CMS recommends strengthening Conditions of Participation (CoPs) related to infection prevention and antibiotic prescribing in U.S. hospitals and critical-access hospitals (CAHs).

The rule includes provisions for preventing healthcare-associated infections, stopping spread of antibiotic-resistant germs and reducing inappropriate antibiotic prescribing. Hospitals and CAHs would be required to have and demonstrate adherence to facility-wide infection prevention and control programs, as well as antibiotic stewardship programs.

The proposed rule builds on the Department of Health and Human Services (HHS) quality initiatives, including the National Quality Strategy, the Centers for Disease Control's Antibiotic Resistance Solutions Initiative and the Partnership for Patients.

Trends in Antimicrobial Resistance 2017: *ESCAPE pathogens*

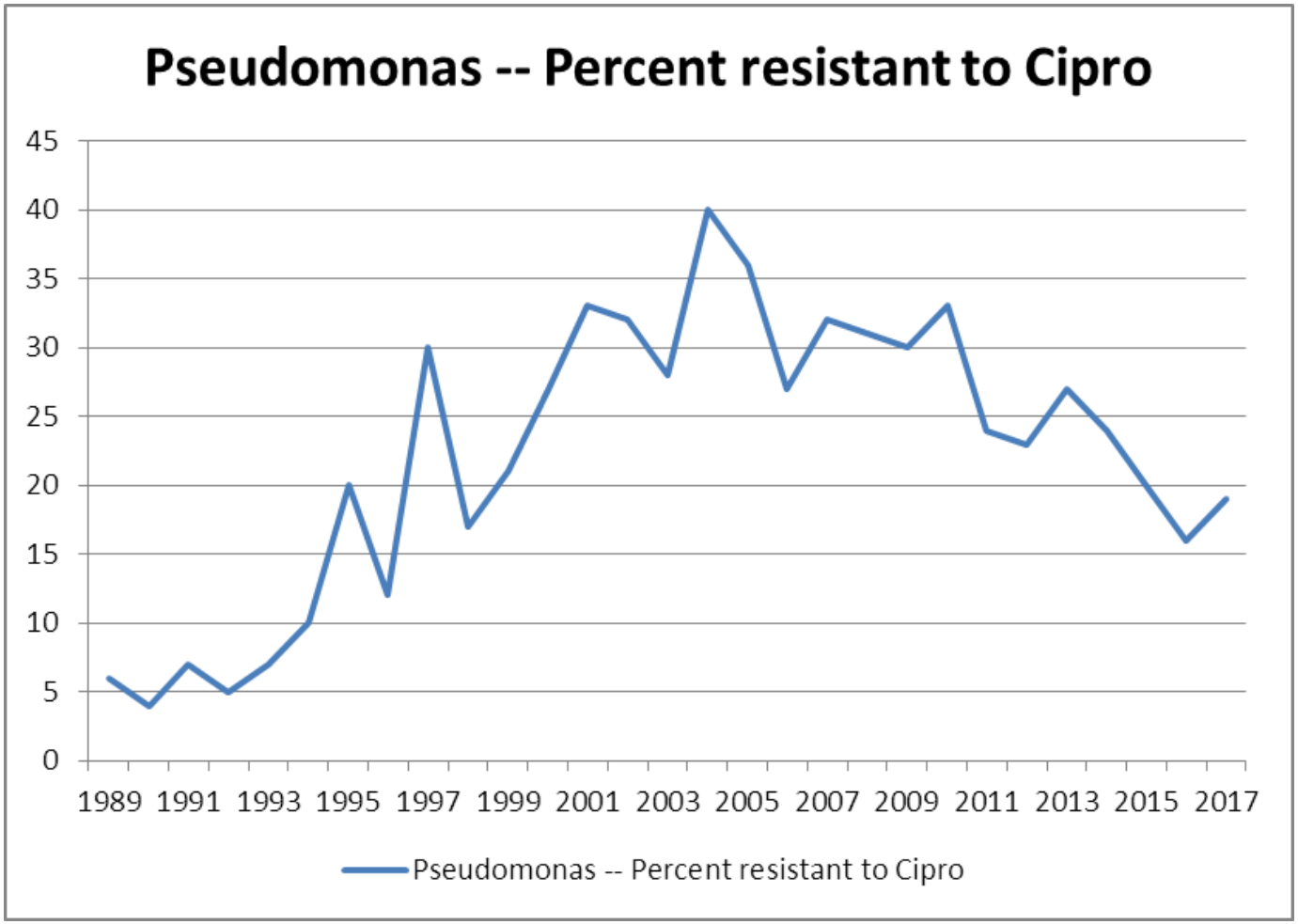
- ***E****nterococcus* (VRE)
- ***S****taphylococcus aureus* (MRSA and VISA)
- ***C****arbapenem resistant Enbterobacteriaceae (CRE) E coli, Klebsiella, Enterobacter* (and others: NDM-1, etc)
- ***A***cinetobacter (multi-drug resistant)
- ***P***seudomonas (FQ resistant)
- ***E***xtended spectrum beta-lactamase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

  plus

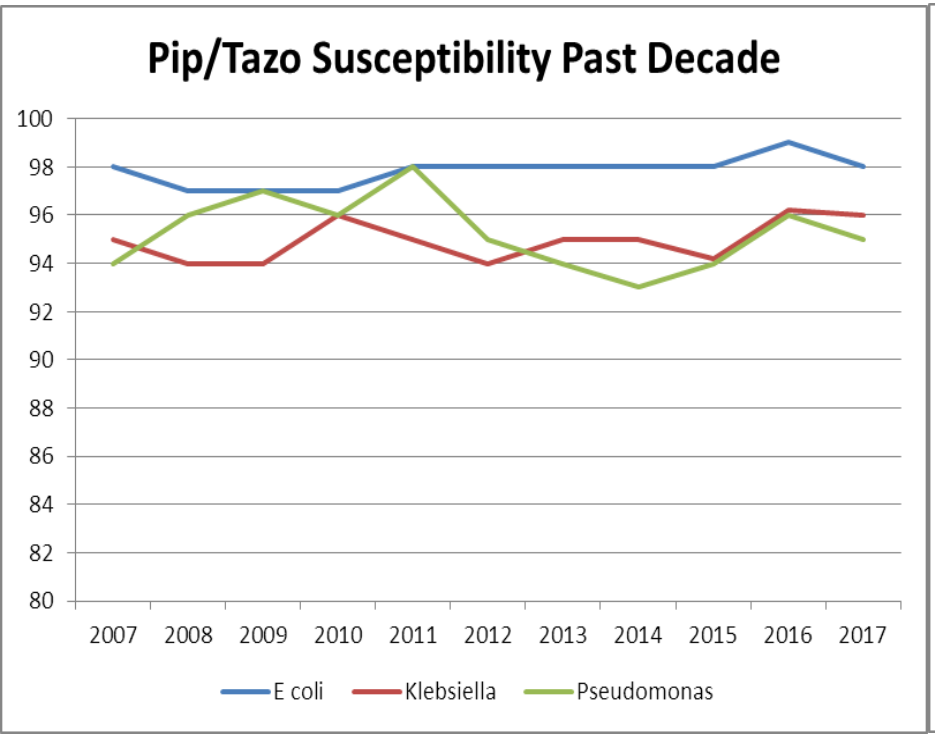
- *Clostridium difficile* (NAP-1 strains, and others)

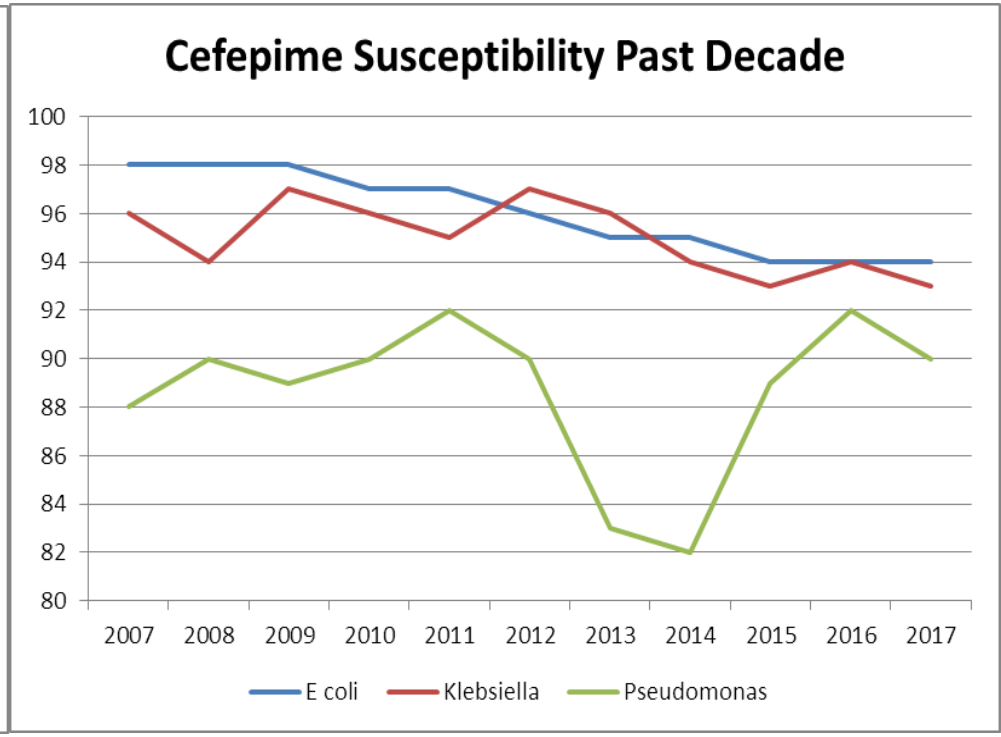
Multi-drug resistant organisms MDRO Infections

Fluoroquinolone resistance Stamford



Are our work-horse agents in the hospital eroding in value due to emerging resistance?



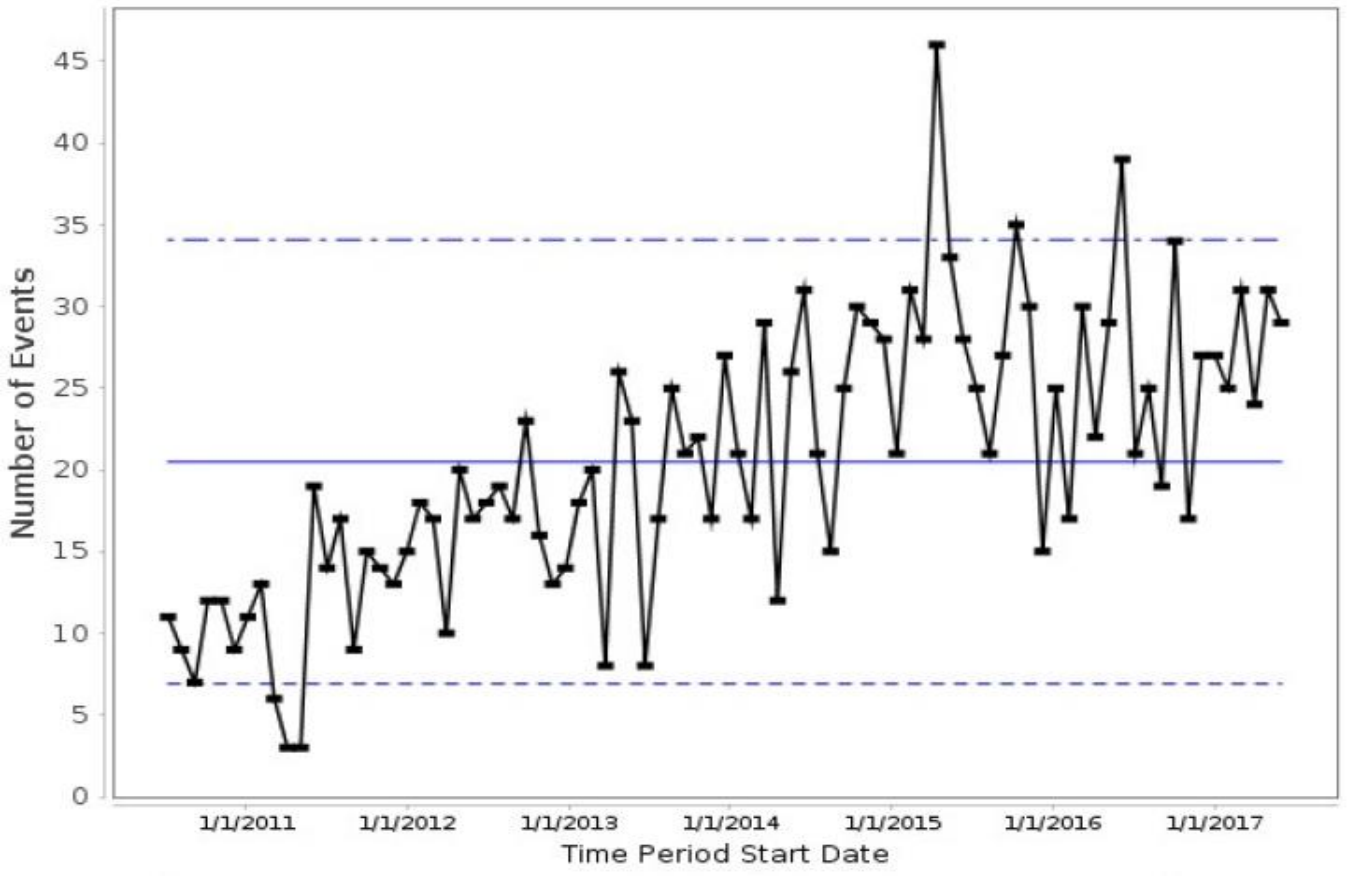


Growing Resistance in *Enterobacteriaceae*

*Extended Spectrum Beta-lactamases (**ESBL**)*

- Enzymes confer resistance to cephalosporins and penicillins, including third generations
  - Gram negative bacilli (E coli, Klebsiella, etc)
  - Varying phenotypes
  - 700 different profiles
- Prevalence of ESBLs is unappreciated
  - Laboratories fail to detect ESBL in 25% of instances depending on the type of enzyme present (Tenover, CDC, 2009)
- Chronic intestinal carriage for months / years
- High rate of treatment failure
- Inpatient and community prevalence
  - 80% outpatient
  - 80% UTIs

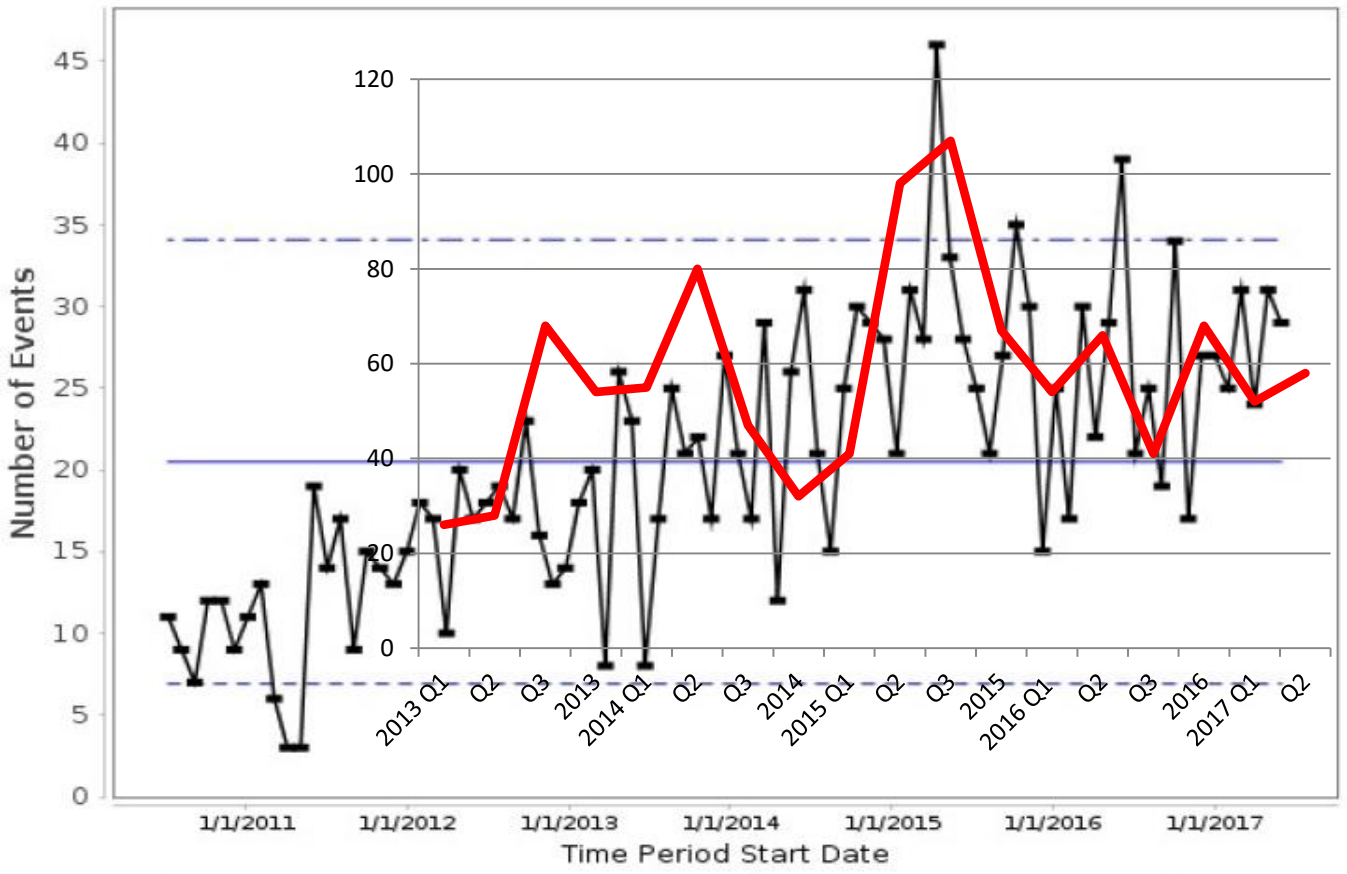
ESBL-positive isolates at Stamford



ESBL Treatment Options

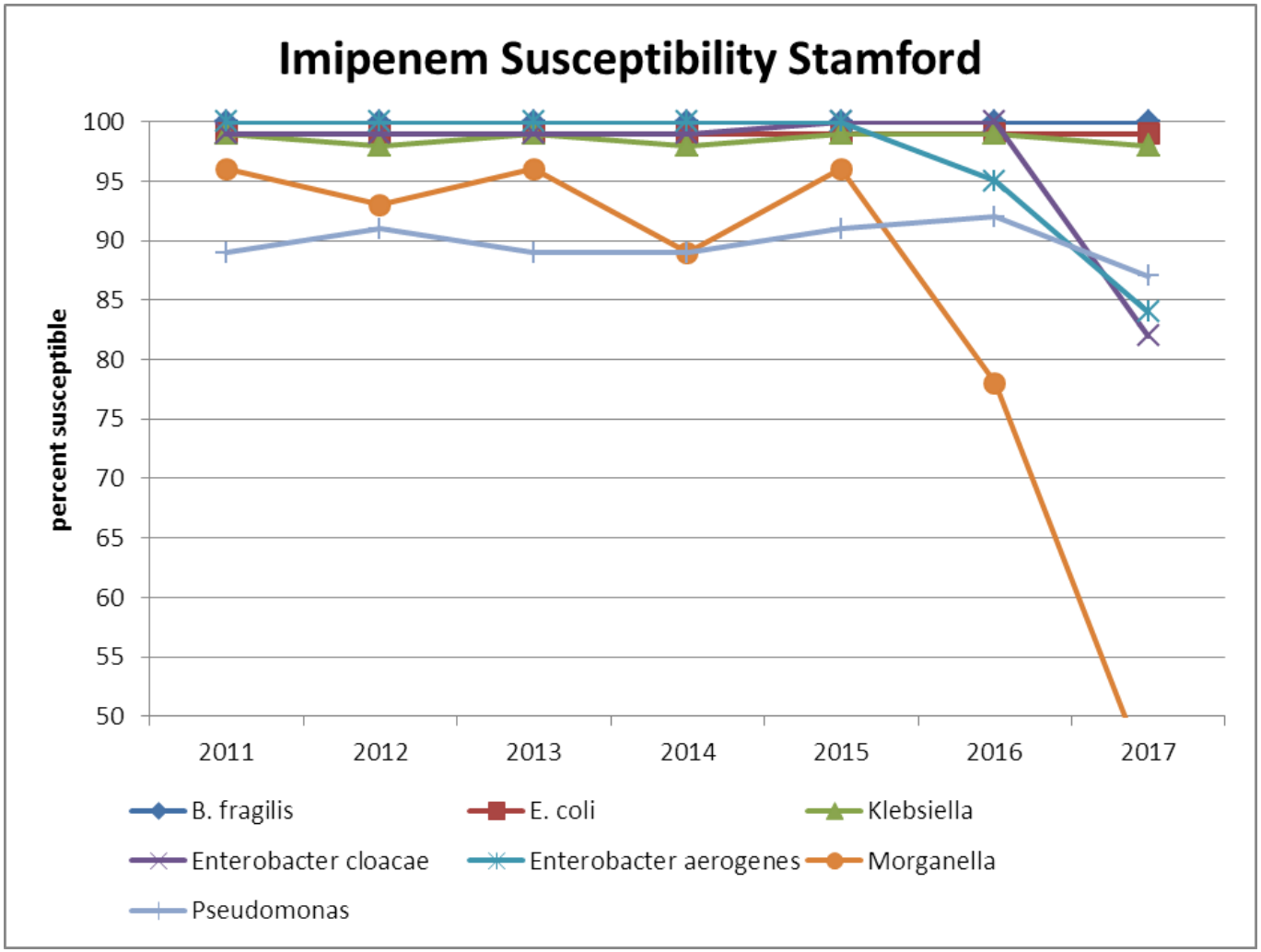
- Oral
  - Nitrofurantoin
  - Fosfomycin
- Parenteral
  - Carbapenems
    - Ertapenem, imipenem, meropenem, doripenem
  - Tigecycline
  - Avycaz and Zerbaxa (new cephs+BLI)
  - Gentamicin (some)
  - Ciprofloxacin (some)
  - Cefamycins: cefoxitin and cefotetan (some)

Carbapenem Orders / ESBL isolates



Carbapenem orders

Carbapenem Susceptibility



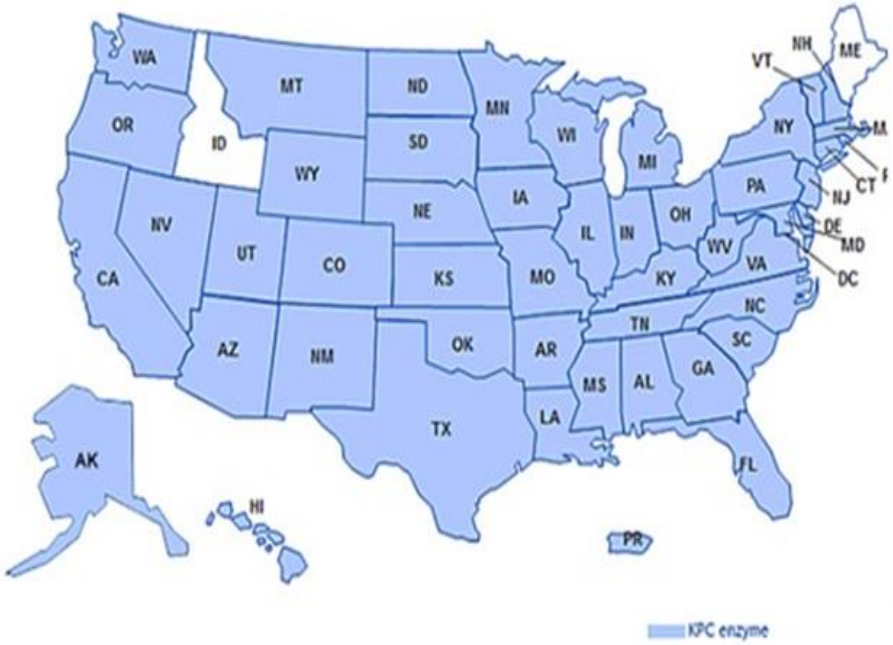
Emergence of Carbapenem-resistant *Enterobacteriaceae* (**CRE**)

- Carbapenems have remained effective against most of the *Enterobacteriaceae,* including ESBL producing strains.
  - imipenem, meropenem, ertapenem
- CRE (KPC most common)
  - Appeared 1996; 2690 cases in NYS, 50% hospital acquired in 2014
  - Klebsiella, E. coli, Enterobacter and others
  - Confer resistance to all β-lactams including extended-spectrum cephalosporins and carbapenems
  - Usually co-resistant to multiple other agents
  - Multiple enzyme profiles (KPC, NDM, VIM, OXA, others)
  - High mortality due to co-morbidities and lack of effective treatment
  - **Plasmid mediated**

PCR technology will allow rapid patient screening for CRE enzymes in the laboratory

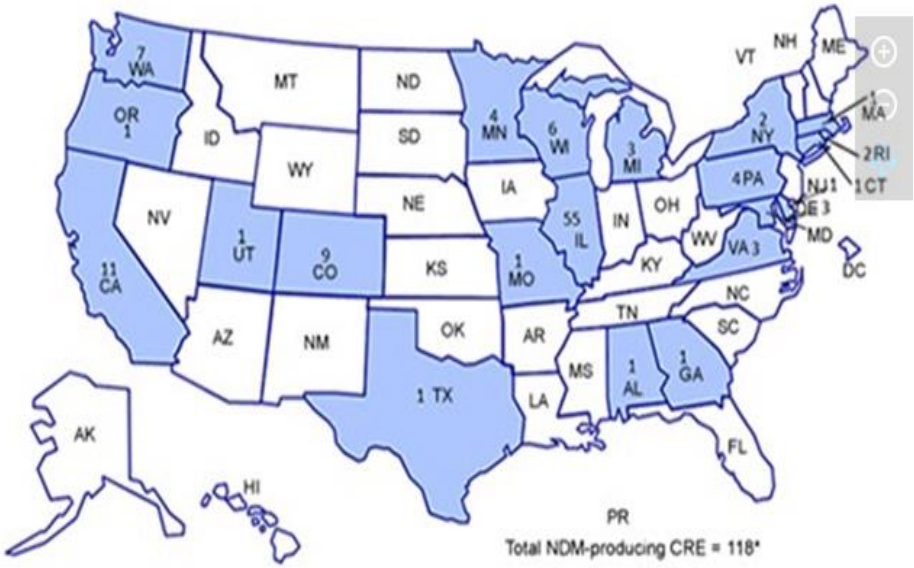
Evolution of CRE in the United States

KPC-producing CRE

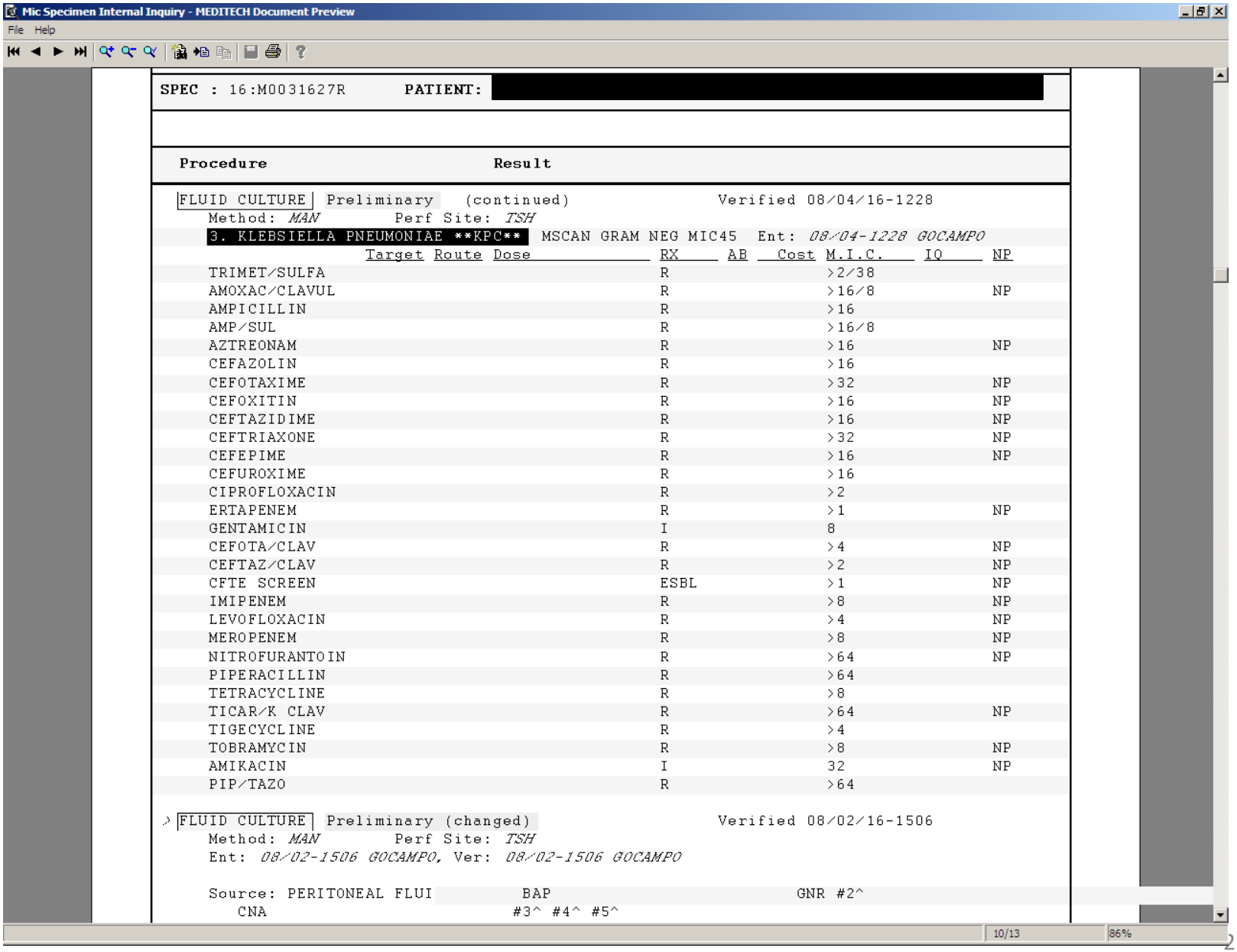


This map was last updated on February 2015

NDM-producing CRE



This map was last updated on January, 2015


Mic Specimen Internal Inquiry - MEDITECH Document Preview
File Help
SPEC : 16:M0031627R PATIENT: [redacted]
Procedure Result
FLUID CULTURE Preliminary (continued) Verified 08/04/16-1228
Method: MAN Perf Site: TSH
3. KLEBSIELLA PNEUMONIAE **KPC** MSCAN GRAM NEG MIC45 Ent: 08/04-1228 GOCAMPO
Target Route Dose RX AB Cost M.I.C. IQ NP
TRIMET/SULFA R >2/38
AMOXAC/CLAVUL R >16/8 NP
AMPICILLIN R >16
AMP/SUL R >16/8
AZTREONAM R >16 NP
CEFAZOLIN R >16
CEFOTAXIME R >32 NP
CEFOXITIN R >16 NP
CEFTAZIDIME R >16 NP
CEFTRIAXONE R >32 NP
CEFEPIME R >16 NP
CEFUROXIME R >16
CIPROFLOXACIN R >2
ERTAPENEM R >1 NP
GENTAMICIN I 8
CEFOTA/CLAV R >4 NP
CEFTAZ/CLAV R >2 NP
CFTE SCREEN ESBL >1 NP
IMIPENEM R >8 NP
LEVOFLOXACIN R >4 NP
MEROPENEM R >8 NP
NITROFURANTOIN R >64 NP
PIPERACILLIN R >64
TETRACYCLINE R >8
TICAR/K CLAV R >64 NP
TIGECYCLINE R >4
TOBRAMYCIN R >8 NP
AMIKACIN I 32 NP
PIP/TAZO R >64
FLUID CULTURE Preliminary (changed) Verified 08/02/16-1506
Method: MAN Perf Site: TSH
Ent: 08/02-1506 GOCAMPO, Ver: 08/02-1506 GOCAMPO
Source: PERITONEAL FLUI BAP GNR #2^
CNA #3^ #4^ #5^
10/13
86%

Which of the following agents is an appropriate choice for systemic infection due to CRE-producing *E. coli*?

- Amikacin
- Levofloxacin
- Colistin
- Fosfomycin
- Zosyn
- Minocycline
- Avycaz / Vabomere

Action Plan for CRE Control

- Active surveillance
- HCW education
- Laboratory enhanced detection
  - lab education
- Strict isolation / contact tracing / screening
- Antibiotic stewardship
- Mandatory Reporting to DOH
- Preserve the limited antibiotic options for treatment

INFECTIOUS DISEASE

A Nasty Bug Breaks Out

Drug-resistant staph bacteria now stalk even students

By Lindsay Lyon

The trouble started in May, wit
fever and what felt like a l
Within days, 12-year-o'
Spence had a temperature of
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MEDICAL DEVICES

Defibrillators'

PATRIK GIARDINO—GETTY IMAGES

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

The first sign
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The New York Times

Opinion

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OP-ED CONTRIBUTOR

To Catch a Deadly Germ

By BETSY McCAUGHEY
Published: November 14, 2006

WHAT kills more than fi
Hospital infection
every year

The New York Times

N.Y. / Region

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THE CITY | IN THE REGION | N.Y./REGION OPINIONS

Dead Student Had Infection, Officials Say

By WINNIE HU and SARAH KERSHAW
Published: October 26, 2007

New York City health officials said yesterday that a Brooklyn middle
dent who died on Oct. 14 had become infected with a
resistant strain of bacteria that is primarily spread in
in recent years has surfaced increasingly in schools,
pital settings.

The health officials, who said they were
tigating the circumstances of the
unable to confirm whether
tracted the infection at the school,
l 211 in Canarsie. The school
officials said that schoo
ision to close it.

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The New York Times

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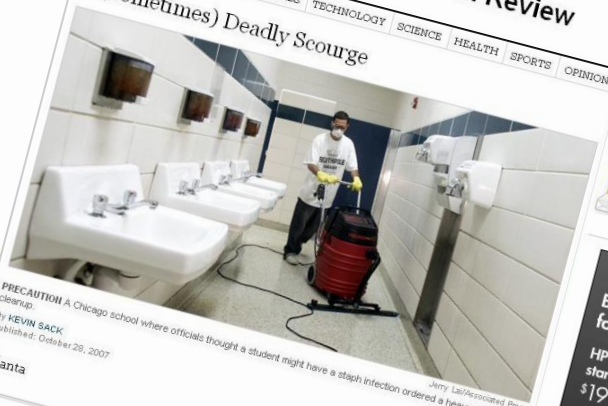
Week in Review

A (Sometimes) Deadly Scourge



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

Atlanta

TWO weeks ago, the

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The ADVOCATE

STAMFORD

Community Almanac/A12
Obituaries/A13
Police Blotter/A16

Stamford student has staph infection

Officials: Northeast school disinfected

By Natasha Lee
Staff Writer

STAMFORD — Health and school officials confirmed yesterday that a student at Northeast Elementary School was being treated for drug-resistant staph infection.

The school was disinfected Monday evening after officials learned of the case, schools spokeswoman Sarah Arnold said.

Students attended class yesterday.

"The surfaces were washed down thoroughly overnight to prepare for a safe opening," Arnold said.

Principal Ethan Margolis could not be reached for comment.

Stamford Hospital notified health and school officials Monday after the student's culture tested positive, said Anne Fountain, a spokeswoman for the Stamford Health Department.

The student was taken to the hospital over the weekend after exhibiting symptoms, Fountain said.

Methicillin-resistant staphylococcus aureus, MRSA, is a form of bacteria that looks like a boil or pimple and causes open wounds. It is resistant to penicillin-based antibiotics but is treatable with other drugs.

LogOn

To read the letter that was sent by Stamford Public Schools to alert students, visit www.stamfordadvocate.com.

The staph infection is common and spread through skin contact or an infected open wound. The state Department of Public Health reported 880 MRSA cases in Connecticut last year, up from 114 in 2001.

The child is being treated with antibiotics and will return to school once a doctor approves, Fountain said.

Letters and e-mails explaining the infection and prevention measures were sent to parents and school employees throughout the district and to Board of Education members, Arnold said.

The Stamford case follows one confirmed at Weston High School on Oct. 17.

Awareness of MRSA intensified after a 12-year-old Brooklyn, N.Y., boy and a 17-year-old Virginia high school student died this month.

Several nonlethal cases have been reported recently on Long Island, N.Y.

According to newspaper reports, the mother of the Brooklyn boy, who died Oct. 14, filed a $25 million lawsuit yesterday against the New York City Health and Hospital Corp.

Fountain said it's hard to track the number of cases in Stamford because doctors are not required to report them.

"We do see a lot of MRSA cases over the years, but there have been some very serious cases in the media lately that have really put it on the forefront," she said.

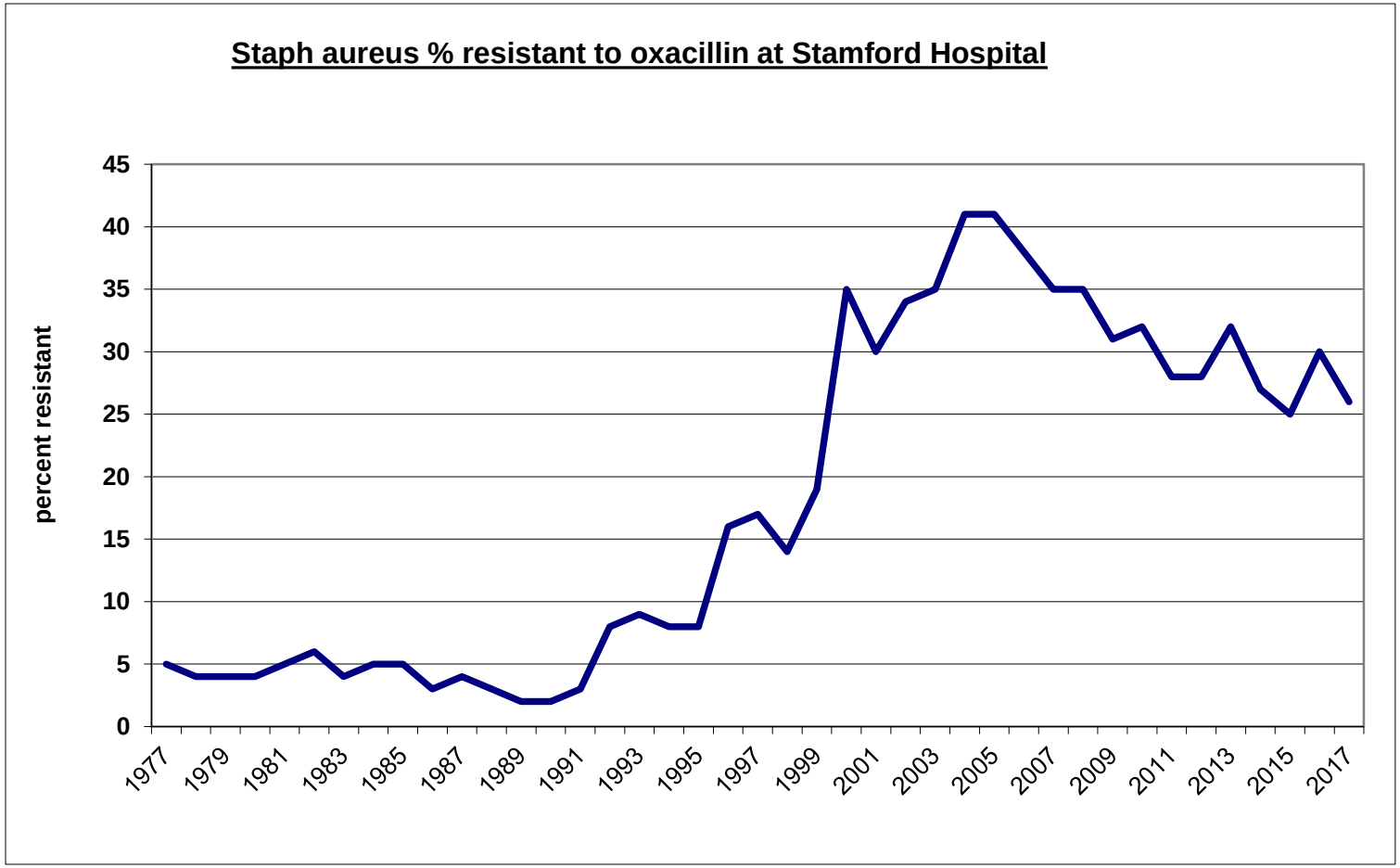
Residents should not panic, she said.

Experts' advice

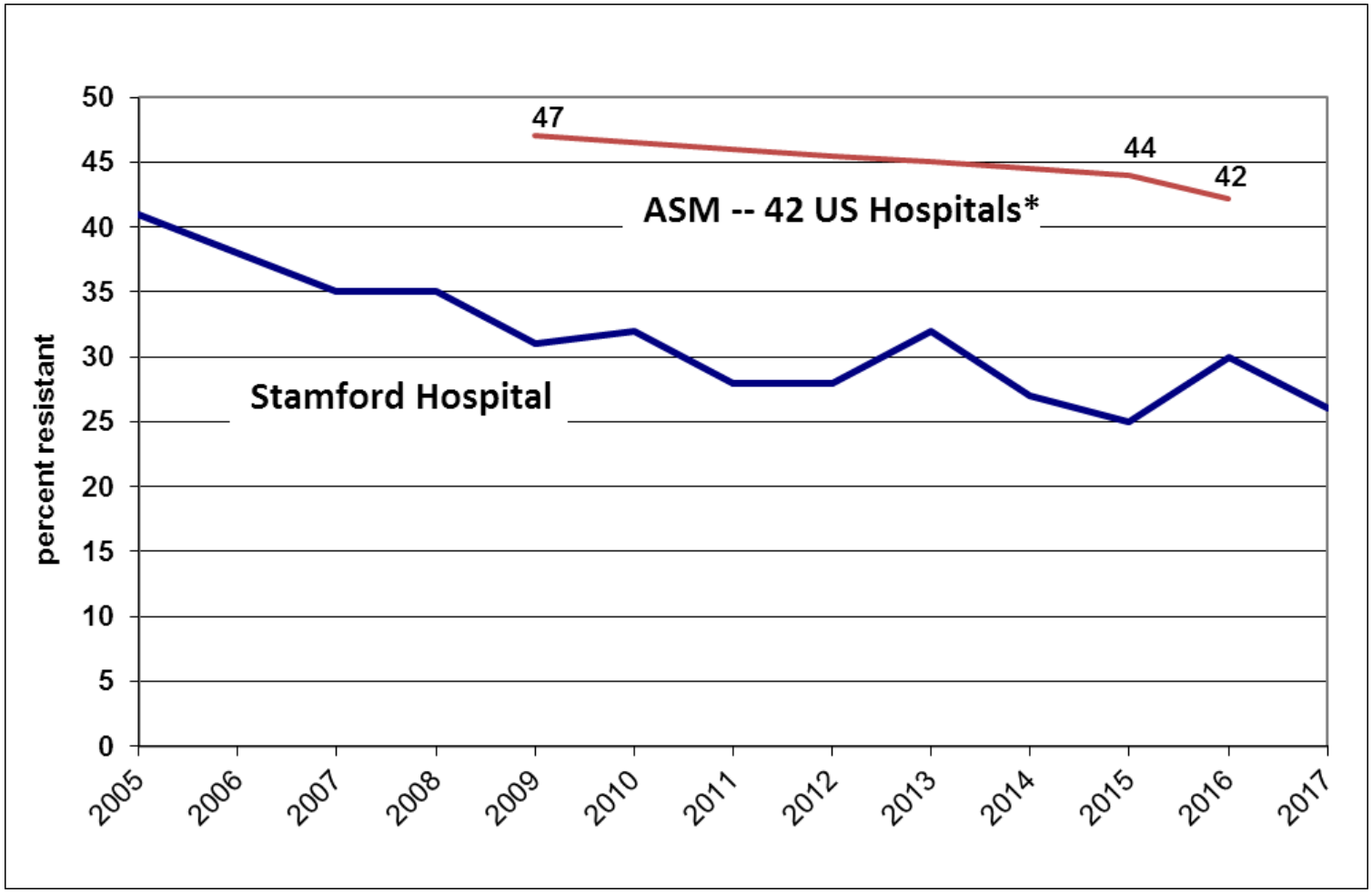
- Stamford health officials said the best way to prevent staph infections is to:
  - Wash hands frequently
  - Cover open sores with bandages
  - Avoid sharing personal items such as towels, soap and clothes
- For more information on staph infections, contact Dr. Tsung-Wen Kuo, epidemiologist at the Stamford Health Department, at 977-4390; your child's school nurse; or the state Health Department information line at (800) 830-9426.

Emergence of MRSA over 45 years in Fairfield County (Stamford Hospital Microbiology Lab data)

(community and hospital strains)



National Trends in MRSA

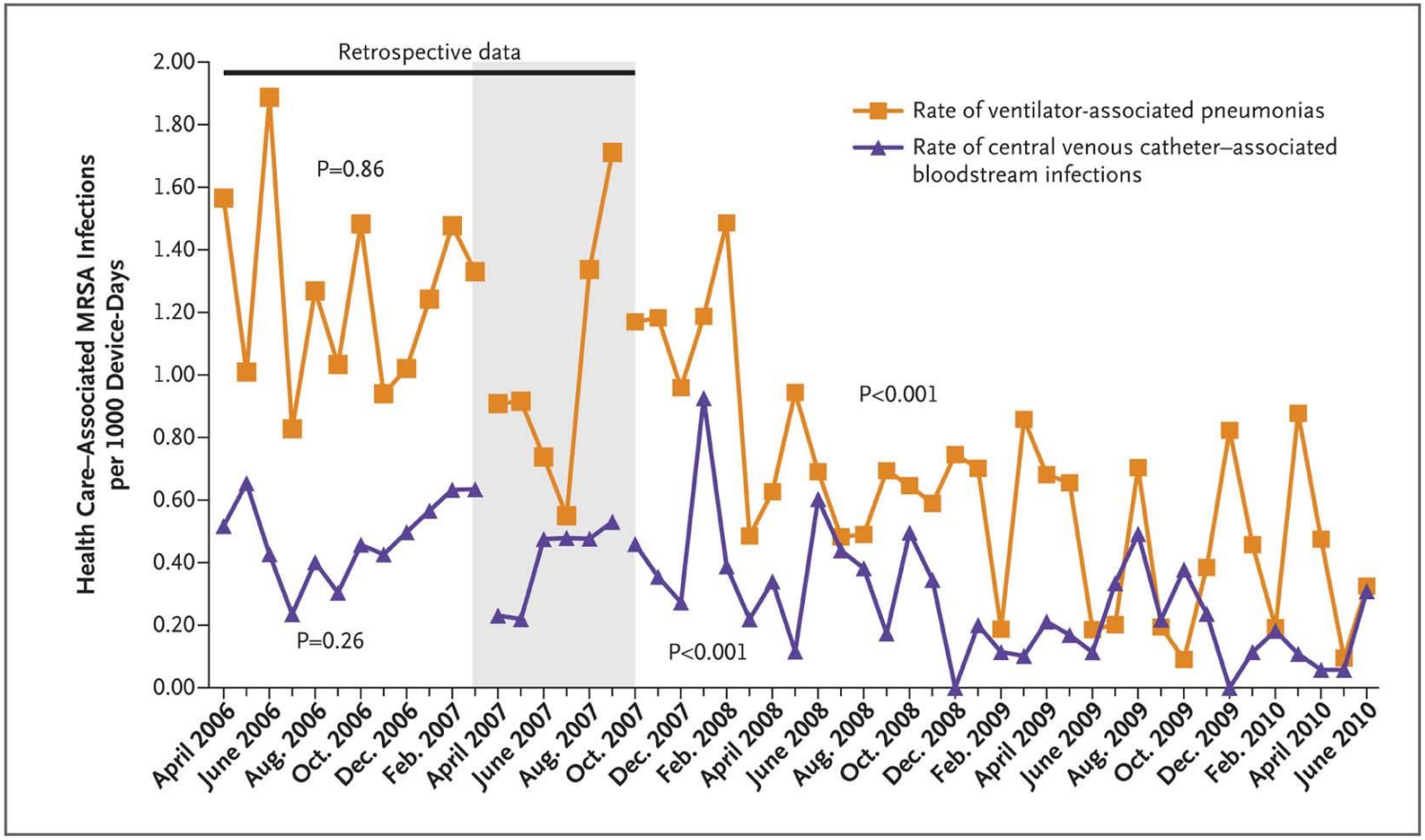


*American Society for Microbiology annual meeting 6/4/17

Impact of an “MRSA Bundle” on MRSA rates:

Veterans Affairs (VA) Intensive Care Units.

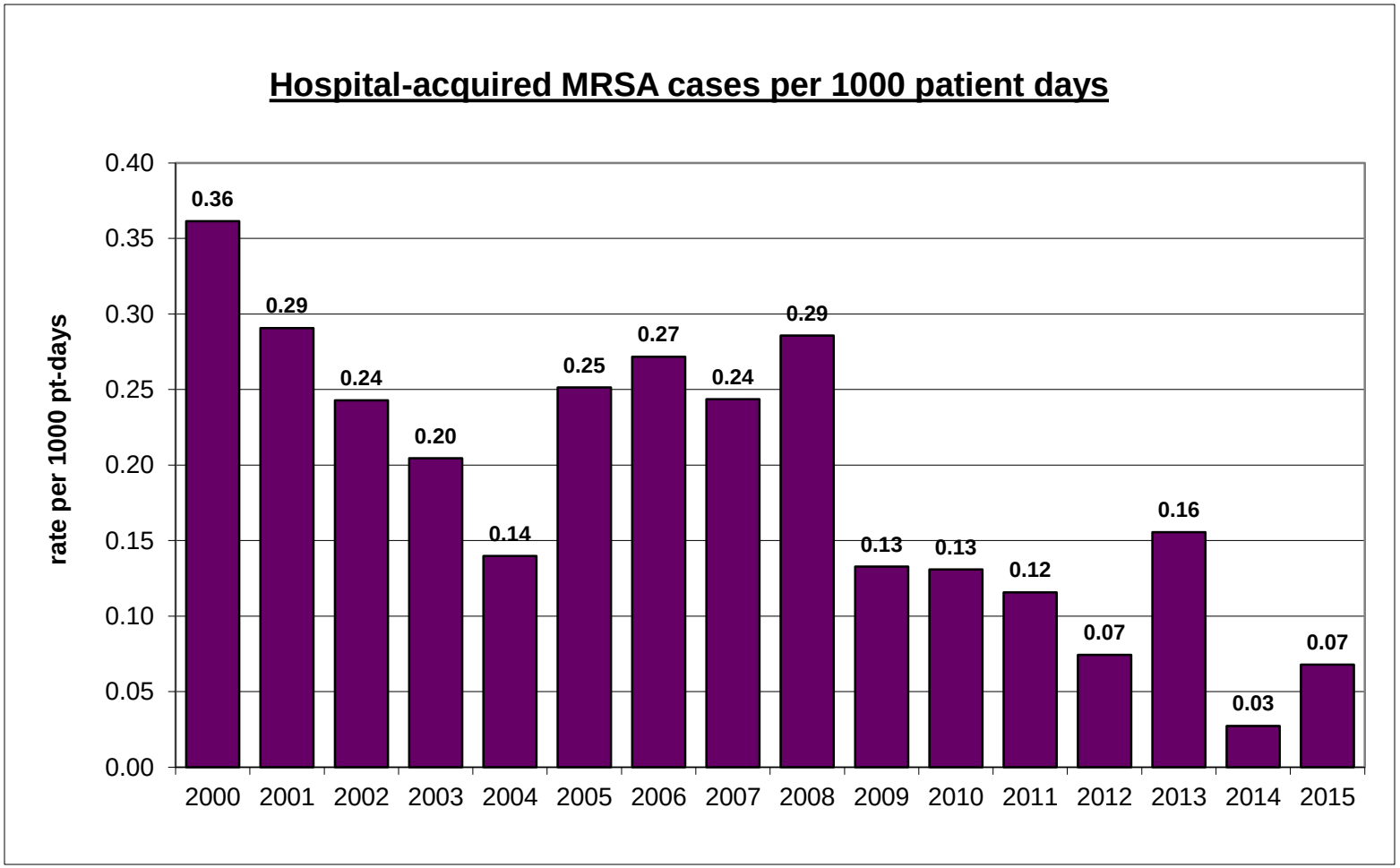
Hand hygiene, Active Surveillance testing, Contact Precautions



Jain R et al. N Engl J Med 2011;364:1419-1430 (VA Cooperative study)

The NEW ENGLAND JOURNAL of MEDICINE

Stamford – Hospital-acquired MRSA cases



Hospital-acquired infection = Medical Mistake

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The Sunday ADVOCATE

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Tax hike blocking budget

Battle waged over effects of increase

By Ken Dixon
STAFF WRITER

HARTFORD — For a solution to the state budget impasse, lawmakers — and the voters who elect them — are arguing whether a couple earning $600,000 a year should pay another $20 a week in income taxes for the benefits of living in Connecticut.

In a nutshell, it's the obstacle that's on the verge of giving Connect-

Top rates

- Connecticut: 5 percent
- New Jersey: 10.75 percent, a temporary one-year raise over the current top rate of 8.97 percent
- Rhode Island: 9.9 percent
- Vermont: 9.5 percent
- New York: 8.97 percent
- North Carolina: 7.75 percent
- California: 10.55 percent

A SPECIAL REPORT ON PATIENT SAFETY

Dead by mistake

CONTRIBUTED PHOTOS

An estimated 98,000 people die each year in the U.S. of preventable medical errors. Each photo represents a

One-bin program takes off

Recycling up 47 percent in system's first month

By Magdalene Perez
STAFF WRITER

STAMFORD — The city saved $15,000 on waste-hauling costs in the first month of a new recycling program that allows residents to recycle more materials with less effort, city officials said.

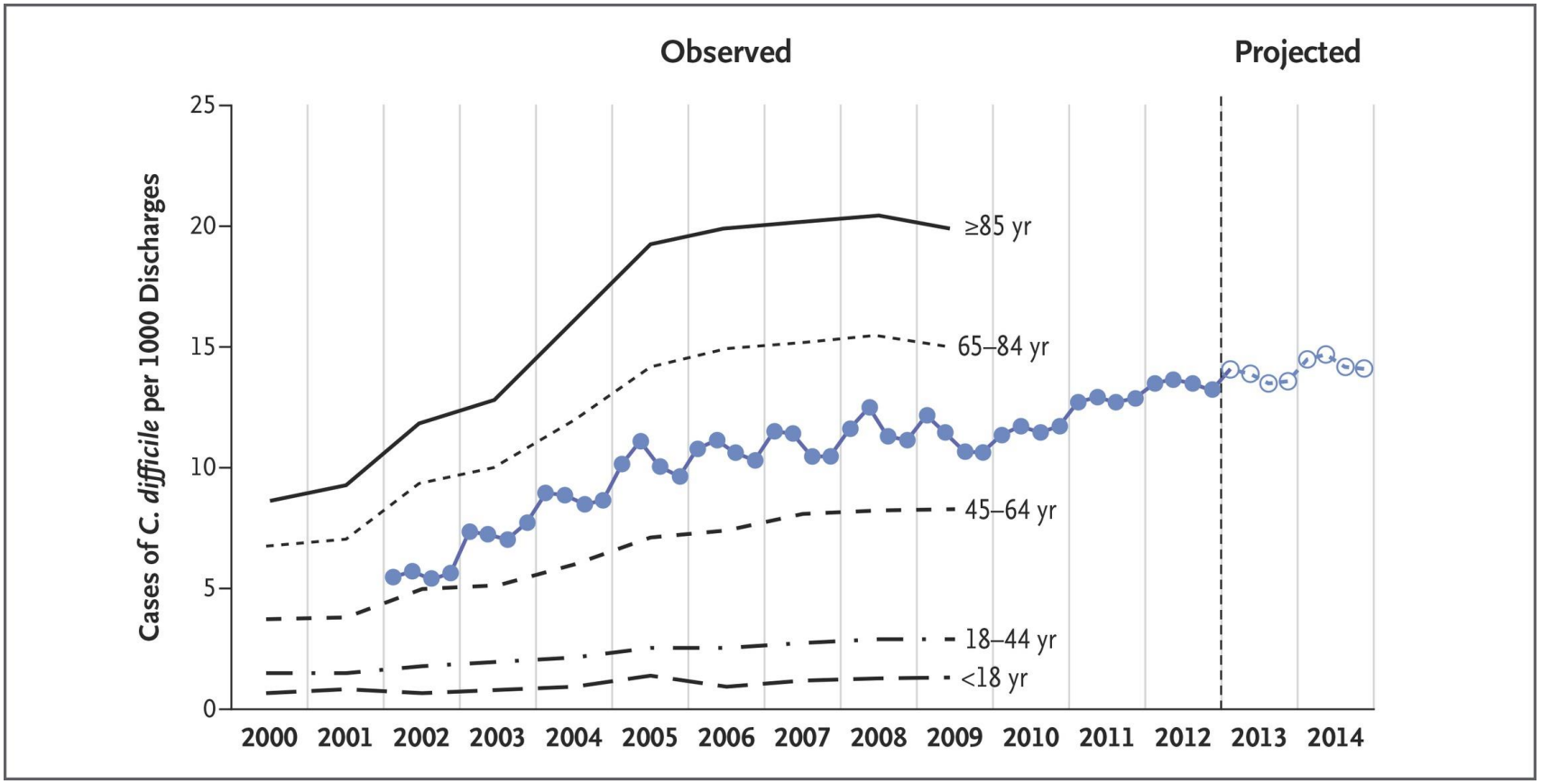
Under the new single-stream program, which took effect July 1, residents who use city recycling no longer have to separate paper from other recyclable materials. They also can recycle a much wider range of materials, including paperboard, such as egg cartons and cereal or tissue boxes; milk cartons and juice boxes; plastics coded 1 through 7; plastic bags, waxed paper or cardboard; and pa-

The city picked up 623.5 tons of recycling in July 2009 compared with 423.5 tons in July 2008, said Alex Tergis, chief

MRSA Treatment Options

- Oral
  - Bactrim, Doxy/Minocycline, Linezolid >90%
  - Clindamycin 60%
- Parenteral
  - Vancomycin
  - Bactrim, Doxy/Mino, Linezolid
  - Daptomycin
  - Ceftaroline
  - Telavancin / Dalbavancin / Oritavancin
- Decolonization
  - CHG bathing or cloth wipes
  - nasal / wound rx (mupirocin / povidone iodine / alcohol)
  - oral agent

Rising Incidence of Hospital-acquired *Clostridium difficile* Infection.



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

Difficulties in controlling the spread of *C. difficile*

- High community prevalence
- Prolonged fecal and skin carriage
- Frequent recurrence
- Persistence of spores in the environment
- “Incident density” pressure – carriers + symptomatic
- Antibiotic use and overuse

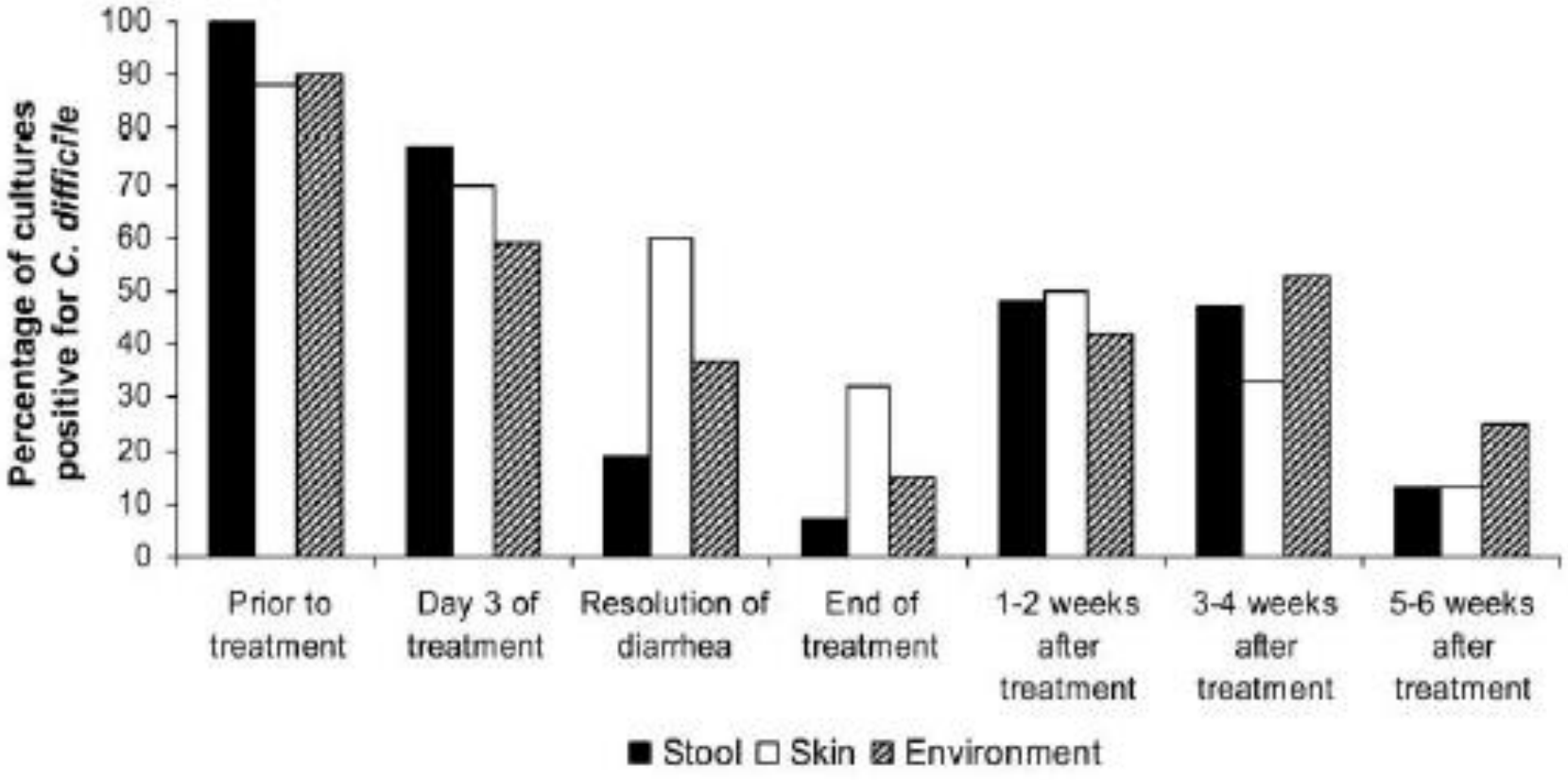
Risk of C. difficile with Perioperative Antibiotic Prophylaxis

Carignan, Sherbrooke Hospital, Quebec. SHEA, 2007

- 7256 class 1 and 2 surgeries
- CDAD rate 9.2/1000 cases
  - 5.1 / 1000 cases after only prophylactic antibiotics
  - 21.8 / 1000 cases after treatment
- Risk related to number of antibiotic doses received

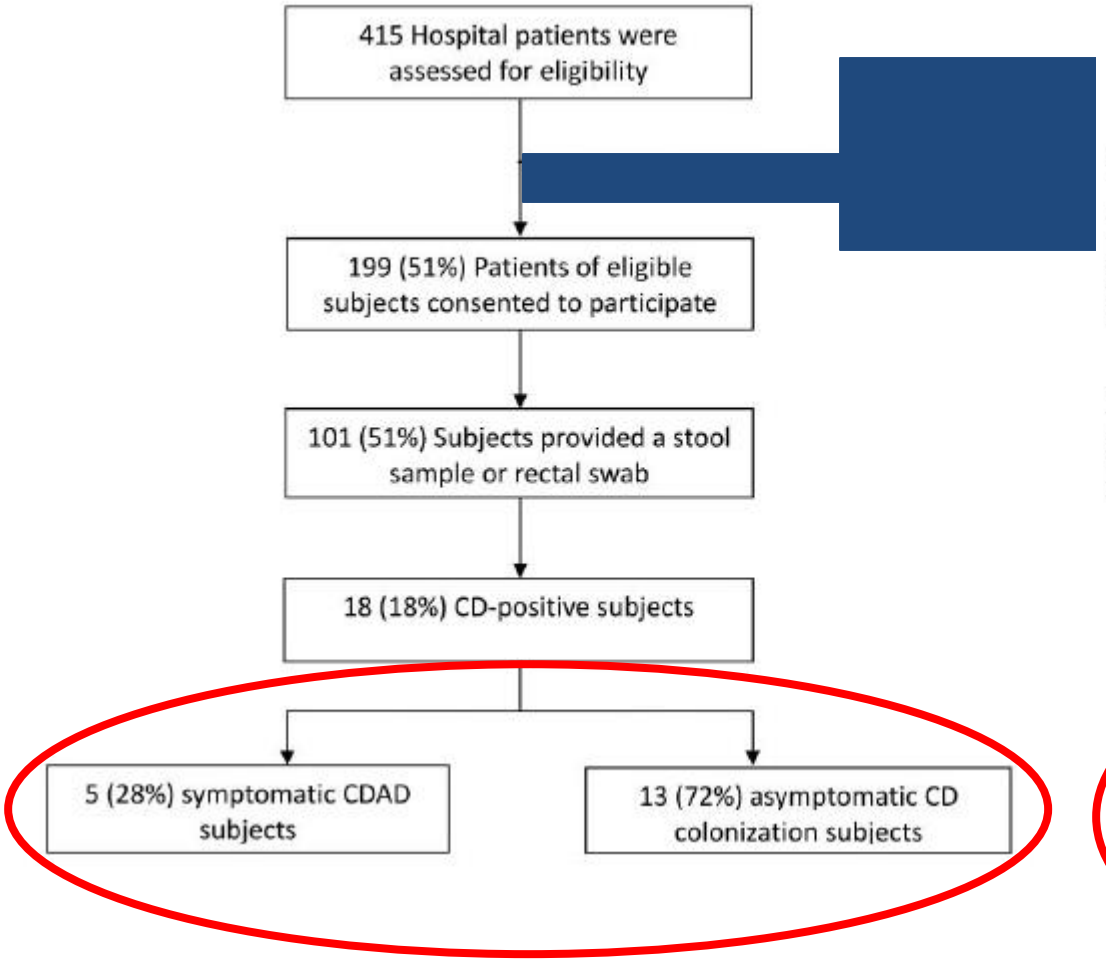
0 doses	0 cases
1 dose	1.6 / 1000
2 to <48hrs	3.4 / 1000
≥48 hrs	13 / 1000

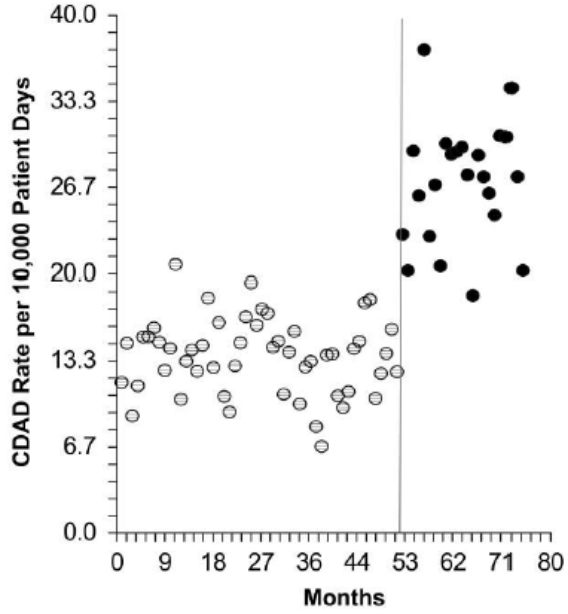
Persistence of *C. difficile* During and After Treatment



Sethi, Al-Nassir, Donskey, et al ICHE 2010; 31:22

PCR Detection of Asymptomatic *C difficile* Colonization and Rising *C diff* Rates



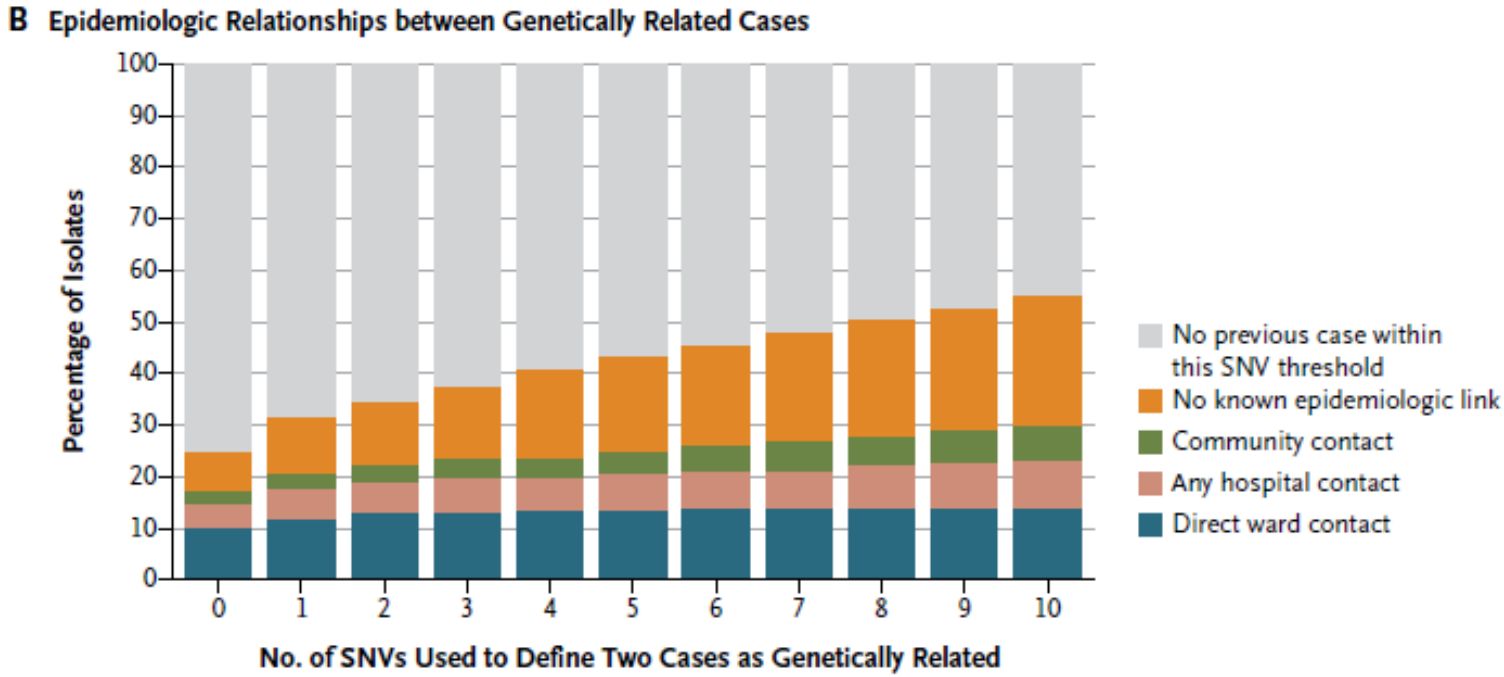


Rate doubled from 13.4 to 27.0 with change from toxin assay to PCR

Koo, Van, DuPont, et al. Infect Control Hosp Epidemiol 2014;35(6):667-673

The NEW ENGLAND JOURNAL of MEDICINE
ESTABLISHED IN 1812 SEPTEMBER 26, 2013 VOL. 369 NO. 13

Diverse Sources of *C. difficile* Infection Identified on Whole-Genome Sequencing



Only 35% of cases were genetically related to at least one previous case (i.e., ≤2 SNVs). These data show that in the majority of cases, *C. difficile* infection is not transmitted from another symptomatic patient. We observed diverse subtypes in patients with *C. difficile* infection, each representing a separate transmission event from a reservoir or asymptomatic carrier.

CDC / JC / CMS Mandate for Stewardship

Core element		NHSN Description		
1	Leadership Commitment	23	Written Antibiotic Stewardship support?	Yes to both
		26	Salary for Antibiotic Stewardship Activities?	
2	Accountability: Leader	24	Physician Steward?	Yes
3	Drug Expertise: Pharmacist	25	Pharmacist Responsible for Improving Antibiotic Use?	Yes
4	Action: at least one	29	Procedure for Antibiotic Treatment Review?	Yes to either
		30	Antibiotic Approval?	
5	Tracking: prescribing, resistance	27, 27.1	Policy to Require Prescribers to Document Antibiotic Use in Medical Record? -> Policy Monitored? Document indications for antibiotic order?	Yes to one
		28, 28.1	Antibiotic Treatment Recommendations -> Monitored?	
		31*	Antibiotic Audit with Feedback?	
		32**	Monitor Antibiotic Use?	
6	Reporting: antibiotic use, resistance: doctors, nurses, staff	31*	Antibiotic Audit with Feedback?	Yes to one
		32,** 32.1	Monitor Antibiotic Use? -> Antibiotic Use Shared with Prescribers?	
		33	Stewardship Program Feedback?	
7	Education: to clinicians on resistance, prescribing	34	Stewardship Program Education?	Yes

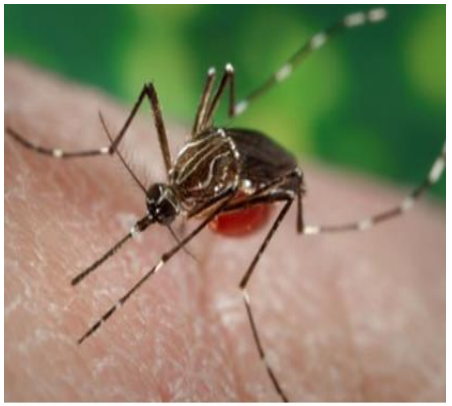
* NHSN survey question 31 applies to two Core Elements (5, 6); ** 32 to Core Element 5 and 32.1 to Core Element 6

Aedes species transmit:

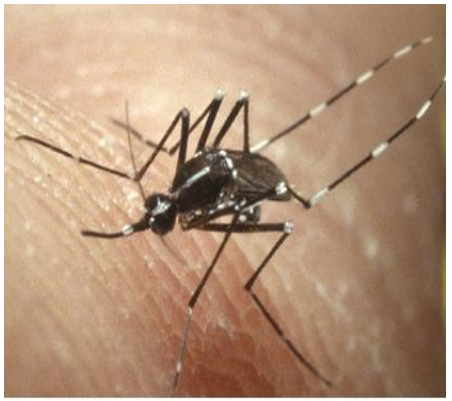
- Dengue
- Yellow fever
- West Nile
- Eastern Equine Encephalitis
- Zika virus
- Chikungunya

Zika virus

- Single stranded RNA virus
- Genus *Flavivirus*, family *Flaviviridae*
- Closely related to Dengue, Yellow Fever, Japanese encephalitis, and West Nile viruses
- Primarily transmitted through the bite of an infected *Aedes* species mosquito *(Ae. aegypti >> Ae. albopictus).*
- Aggressive biter, indoors and outdoors, rural and urban, day-time > night-time

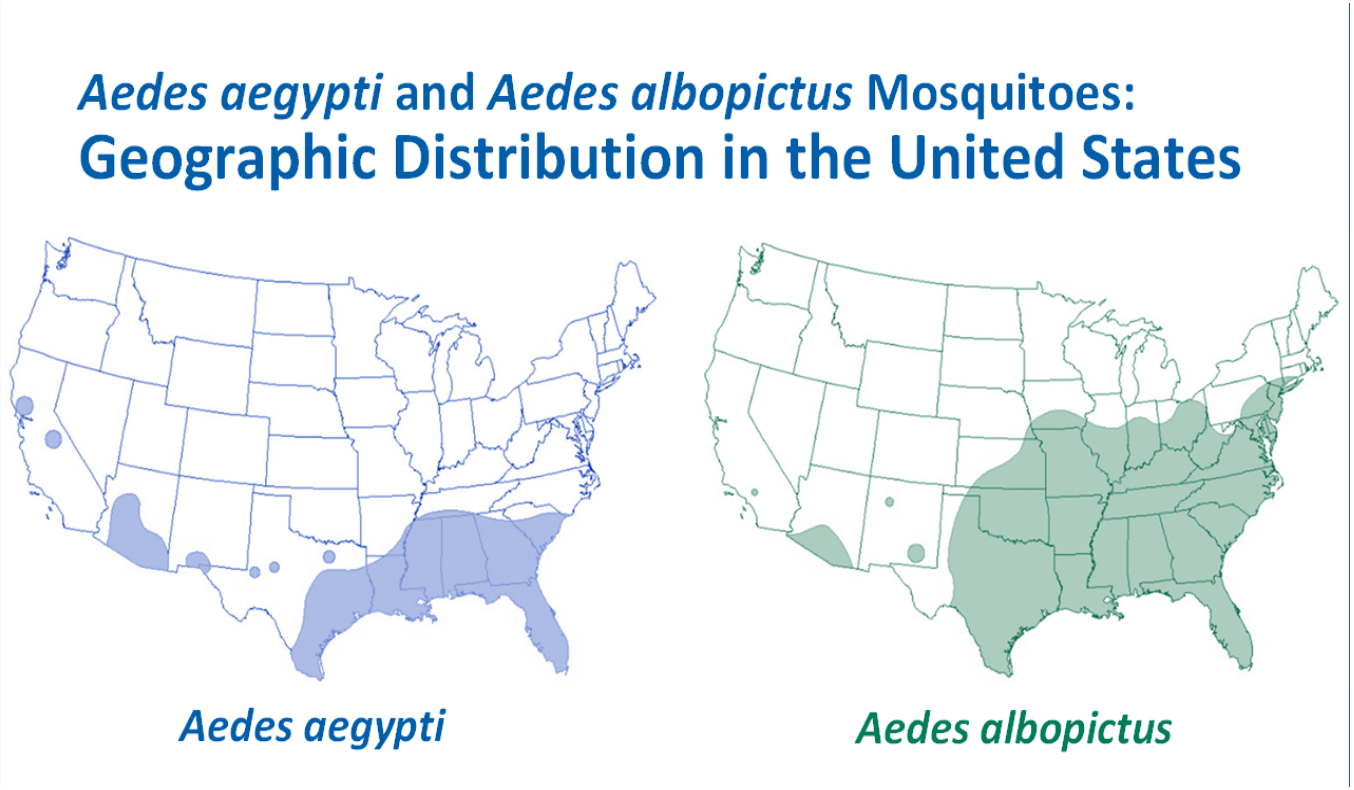


Aedes aegypti



Aedes albopictus

Aedes Distribution in United States

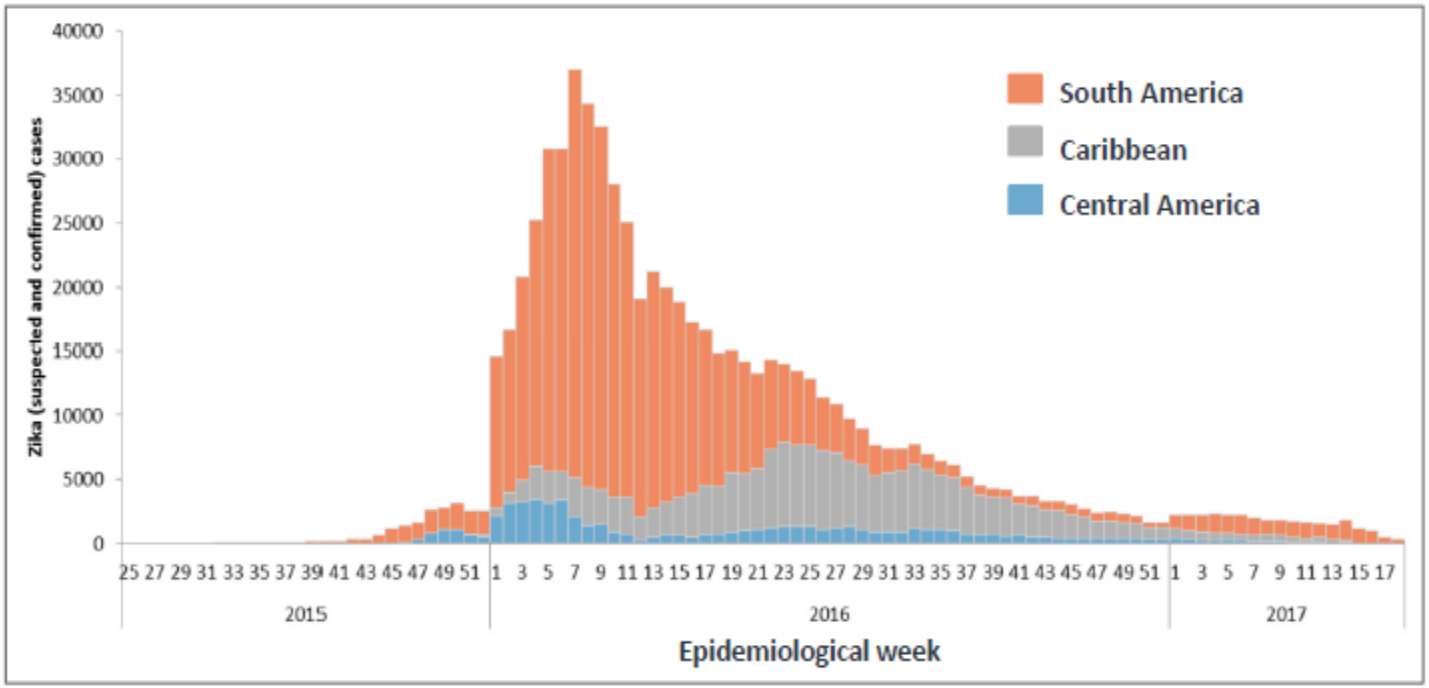


Where has Zika virus been found?

- Before 2015, Zika outbreaks occurred in Africa, Southeast Asia, and the Pacific Islands.
- Outbreaks are occurring in over 50 countries past 2 years
- Recent focus in South America, Central America and the Caribbean
- Mainland US cases are most related to travel (over 5000 cases)
- Local cases in Florida
  - Other gulf coast states to follow

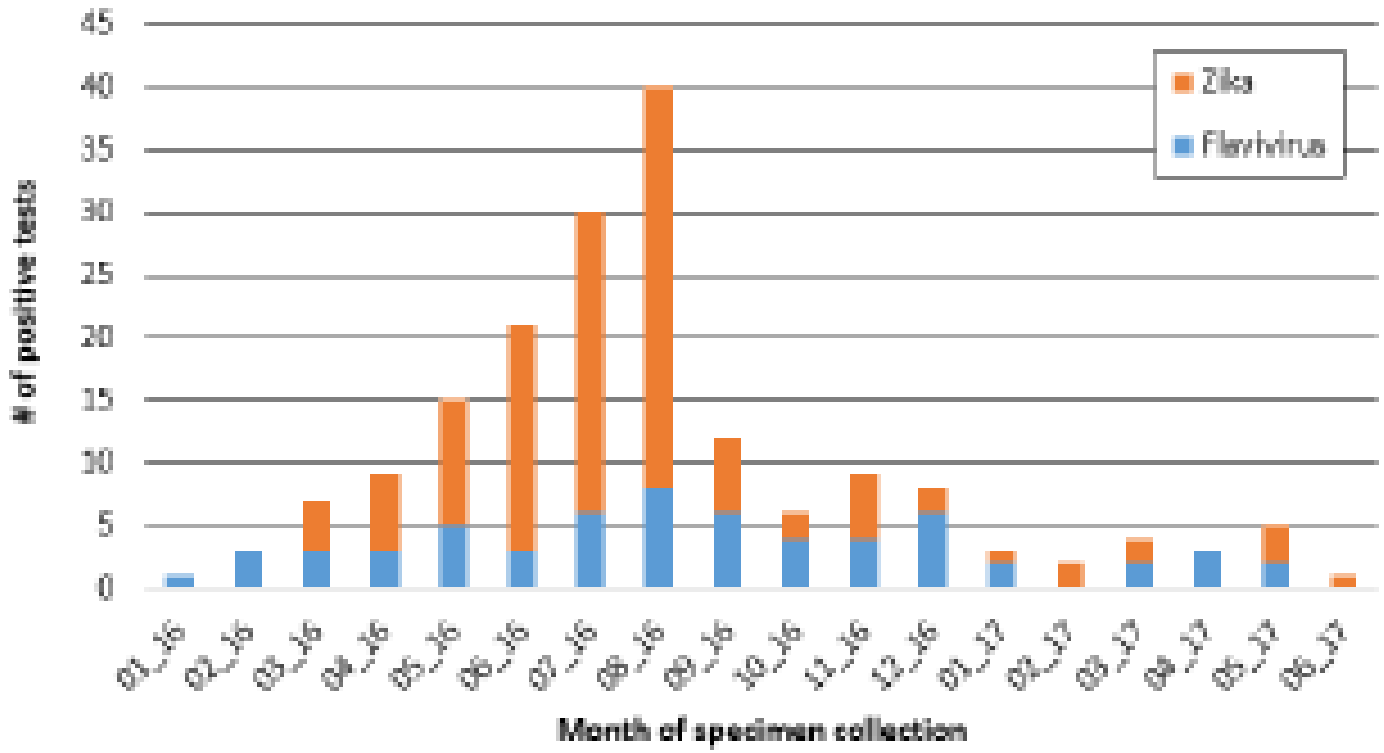
Declining Trends in Reported Zika Cases in the Americas

Confirmed and suspected Zika virus in the Americas, 2015–2017 (as of May 25, 2017)



PAHO Regional Zika Epidemiological Update (May 25, 2017):
http://www.paho.org/hq/index.php?option=com_content&view=article&id=11599&Itemid=41691&lang=en

Figure 2. Number of potential Zika-related infections by month (n=179)-Connecticut, February 1, 2016-June 30, 2017



Connecticut Epidemiologist 37:4, 2017

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Modes of transmission

- Bite from an infected mosquito
- Sexual transmission
  - Primarily from infected male partners
  - Mainly from symptomatic partners
- Maternal-fetal-Intrauterine or perinatal
- Laboratory exposure
- Likely (with screening recommendations)
  - blood transfusion, organ and tissue transplant
  - fertility treatment
  - breast feeding
  - other blood and body fluid exposure

Incubation and viremia

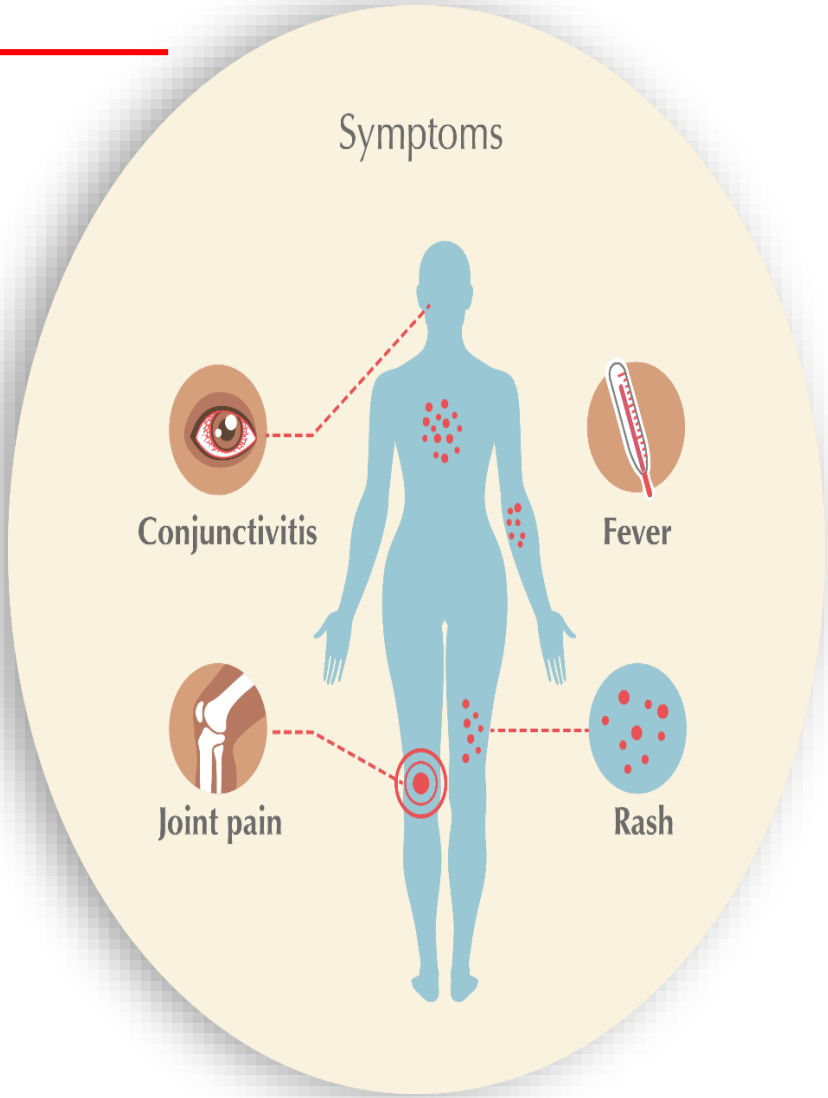
- Incubation period for Zika virus disease is 3–14 days.
- Zika viremia ranges from a few days to 1 week.
- Virus remains in urine longer than in blood – up to 3 weeks.
- Virus remains in semen even longer – infectious virus up 3-6 months by PCR.
- Duration of virus in vaginal secretions, saliva also prolonged
- Virus may be secreted by infected newborns for several weeks

Zika virus clinical disease course and outcomes

- Clinical illness is usually mild.
- Symptoms last several days to a week.
- Severe disease requiring hospitalization is uncommon.
- Fatalities are rare.
- Guillain-Barré syndrome (GBS) reported in patients following suspected Zika virus infection.
- Intrauterine infections problematic

Symptoms

- Many infections asymptomatic
  - 80%
- Most common symptoms
  - Fever
  - Maculopapular rash
  - Joint pain
  - Conjunctivitis
- Other symptoms include muscle pain and headache.

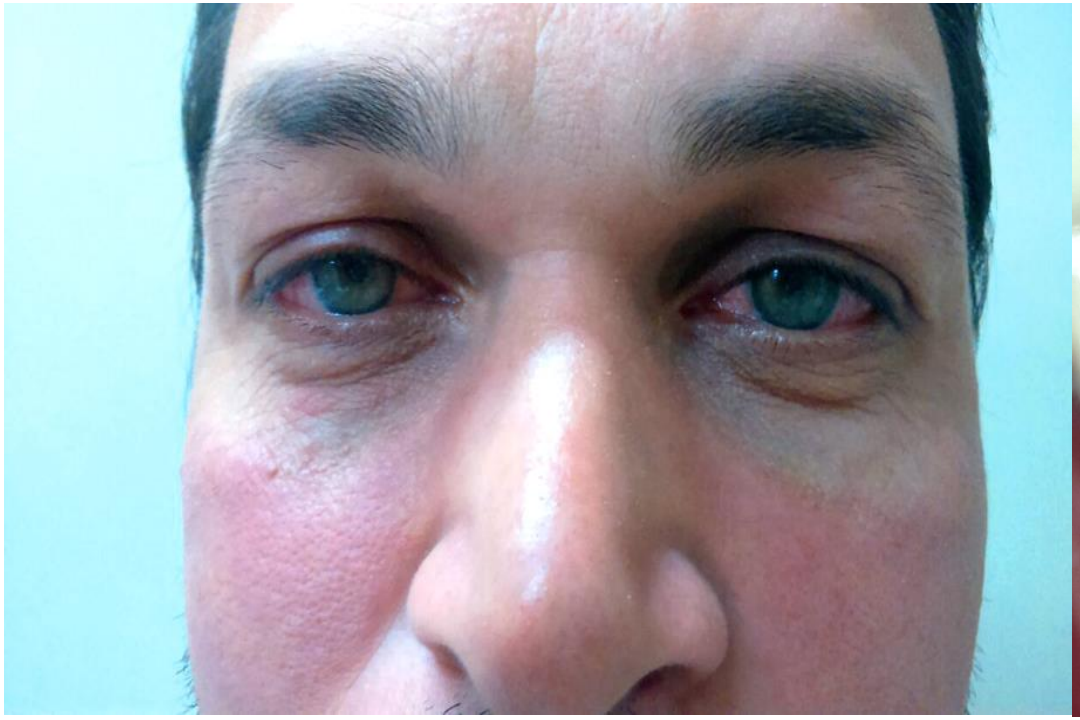


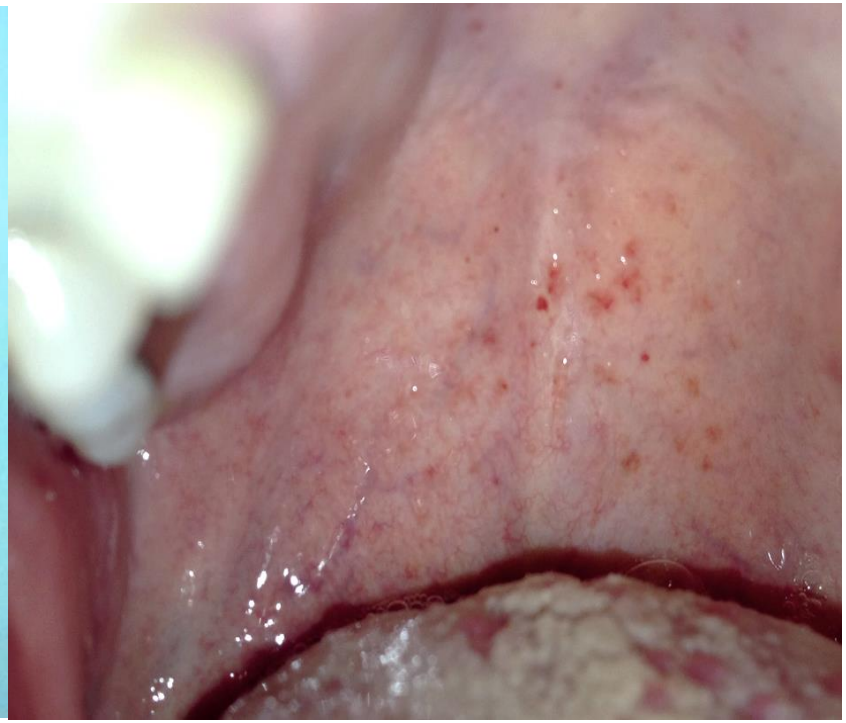
Clinical features: Zika virus compared to dengue and chikungunya

Features	Zika	Dengue	Chikungunya
Fever	++	+++	+++
Rash	+++	+	++
Conjunctivitis	++	-	-
Arthralgia	++	+	+++
Myalgia	+	++	+
Headache	+	++	++
Hemorrhage	-	++	-
Shock	-	+	-

Rabe, Ingrid MBChB, MMed "Zika Virus- What Clinicians Need to Know?" (presentation, Clinician Outreach and Communication Activity (COCA) Call, Atlanta, GA, January 26 2016)

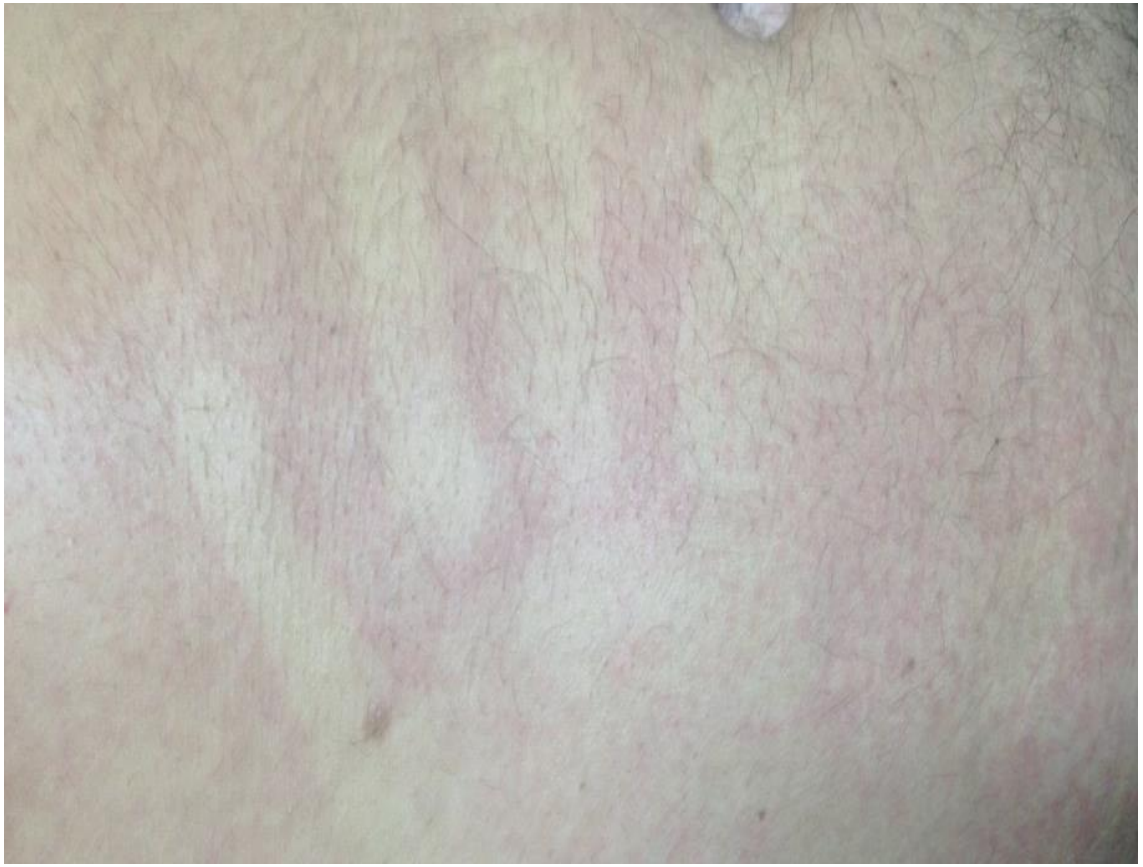
Skin rashes seen in Zika infections





Cruz, O:. www.thelancet.com/infection Vol 16 July 2016

Skin rashes seen in Zika infections



Cruz, O:. www.thelancet.com/infection Vol 16 July 2016

Connecticut Cases

Connecticut Epidemiologist 37:4, 2017

Table. Descriptive epidemiology among persons testing positive for Zika and unidentified Flavivirus infections—Connecticut, February 15, 2016-June 30, 2017

Characteristic	Total infections (n=179)	Zika positive (n=118)	Unidentified Flavivirus positive (n=61)
Female	134 (75%)	78 (66%)	56 (92%)
Median age (range)	32 yrs. (3-88)	34.5 yrs. (3-88)	30 yrs. (10-56)
≥1 primary symptom	127 (71%)	114 (97%)	13 (21%)
Rash	114 (90%)	103 (90%)	11 (85%)
Fever	71 (56%)	65 (57%)	6 (46%)
Arthralgia	82 (65%)	76 (67%)	6 (46%)
Conjunctivitis	47 (37%)	45 (39%)	2 (15%)
Pregnant Females	55 (31%)	8 (7%)	47 (77%)
1st trimester	14 (25%)	4 (50%)	10 (21%)
2nd trimester	12 (22%)	1 (13%)	11 (23%)
3rd trimester	29 (53%)	3 (38%)	26 (55%)
Travel to affected area outside CT	179 (100%)	118 (100%)	61 (100%)

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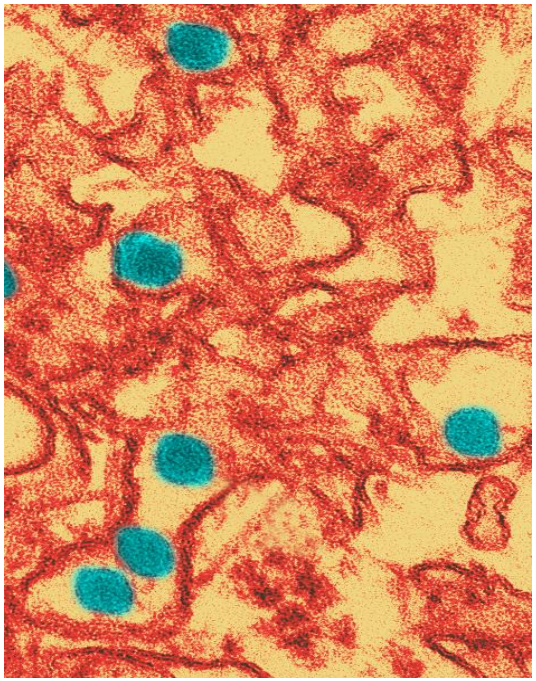
Diagnostic testing for Zika virus

- PCR for viral RNA in clinical specimens collected ≤ 7 days (serum) or ≤ 21 days (urine) after illness onset.
- Serology for IgM and neutralizing antibodies in serum collected 1 to 12 weeks after illness onset.
- Zika virus serology (IgM) can be positive due to antibodies against related *flaviviruses* (e.g., dengue and yellow fever viruses)
- Plaque reduction neutralization test (PRNT) for presence of flavivirus-specific neutralizing antibodies in paired serum samples.



Zika and pregnancy outcomes

- Zika virus can be transmitted from a pregnant woman to her fetus during pregnancy or around the time of birth.
- Greatest risk is in first trimester
- "Congenital Zika Syndrome" -- fetal brain atrophy – interference with neuronal migration during embryogenesis
  - Microcephaly and cerebral calcifications
  - Poorly developed brain structures
  - Defects of the eye
  - Hearing deficits
  - Impaired intrauterine growth
  - *Neurodevelopmental delay*
  - Cognitive impairment

Results from Zika Pregnancy and Infant Registries

Findings	US States and DC USZPR[1] % (95% CI)	US Territories USZPR/ZAPPS[2] % (95% CI)
Symptomatic vs. Asymptomatic		
% Symptomatic with birth defects	8 (4-13)	5 (4-6)
% Asymptomatic with birth defects	12 (7-19)	7 (4-11)
Birth Defects by Trimester of Infection at DX		
First trimester	15 (8-26)	8 (5-12)
Second trimester	--	5 (4-7)
Third trimester	--	4 (3-6)

1. Reynolds MR, Jones AM, Petersen EE, et al. Vital Signs: Update on Zika Virus–Associated Birth Defects and Evaluation of All U.S. Infants with Congenital Zika Virus Exposure — U.S. Zika Pregnancy Registry, 2016. MMWR Morb Mortal Wkly Rep 2017;66:366-373. DOI: http://dx.doi.org/10.15585/mmwr.mm6613e1.
2. Shapiro-Mendoza CK, Rice ME, Galang RR, et al. Pregnancy Outcomes After Maternal Zika Virus Infection During Pregnancy — U.S. Territories, January 1, 2016–April 25, 2017. MMWR Morb Mortal Wkly Rep 2017;66:615-621. DOI: http://dx.doi.org/10.15585/mmwr.mm6623e1

Zika Update: Findings from the U.S. Zika Pregnancy Registry and Updated Clinical Guidance
CDC May 4, 2017

Congenital Defects US data

Box. Birth Defects Potentially Related to Zika Virus Infection During Pregnancy and Monitored by the US Zika Pregnancy Registry for Enhanced Surveillance

Brain Abnormalities With and Without Microcephaly

Confirmed or possible congenital microcephaly[a]

Intracranial calcifications

Cerebral atrophy

Abnormal cortical formation (eg, polymicrogyria, lissencephaly, pachygyria, schizencephaly, gray matter heterotopia)

Corpus callosum abnormalities

Cerebellar abnormalities

Porencephaly

Hydranencephaly

Ventriculomegaly/hydrocephaly (excluding "mild" ventriculomegaly without other brain abnormalities)

Fetal brain disruption sequence (collapsed skull, overlapping sutures, prominent occipital bone, scalp rugae)

Other major brain abnormalities including intraventricular hemorrhage in utero (excluding postnatal intraventricular hemorrhage)

Neural Tube Defects and Other Early Brain Malformations

Neural tube defects including anencephaly, acrania, encephalocele, spina bifida

Holoprosencephaly (arhinencephaly)

Eye Abnormalities

Microphthalmia/anophthalmia

Coloboma

Cataract

Intraocular calcifications

Chorioretinal anomalies involving the macula (eg, chorioretinal atrophy and scarring, macular pallor, gross pigmentary mottling and retinal hemorrhage; excluding retinopathy of prematurity)

Optic nerve atrophy, pallor, and other optic nerve abnormalities

Consequences of Central Nervous System Dysfunction

Congenital contractures (eg, arthrogryposis, clubfoot, congenital hip dysplasia) with associated brain abnormalities

Congenital deafness documented by postnatal audiological testing

[a] Live births: measured head circumference (adjusted for gestational age and sex) less than the third percentile at birth or, if not measured at birth, within first 2 weeks of life. Pregnancy loss: prenatal head circumference more than 3 SDs below the mean based on ultrasound or postnatal head circumference less than the third percentile. Birth measurements are evaluated using the Intergrowth-21st standards (http://intergrowth21.ndog.ox.ac.uk/) based on measurements within 24 hours of birth.

Zika Update: Findings from the U.S. Zika Pregnancy Registry and Updated Clinical Guidance CDC May 4, 2017

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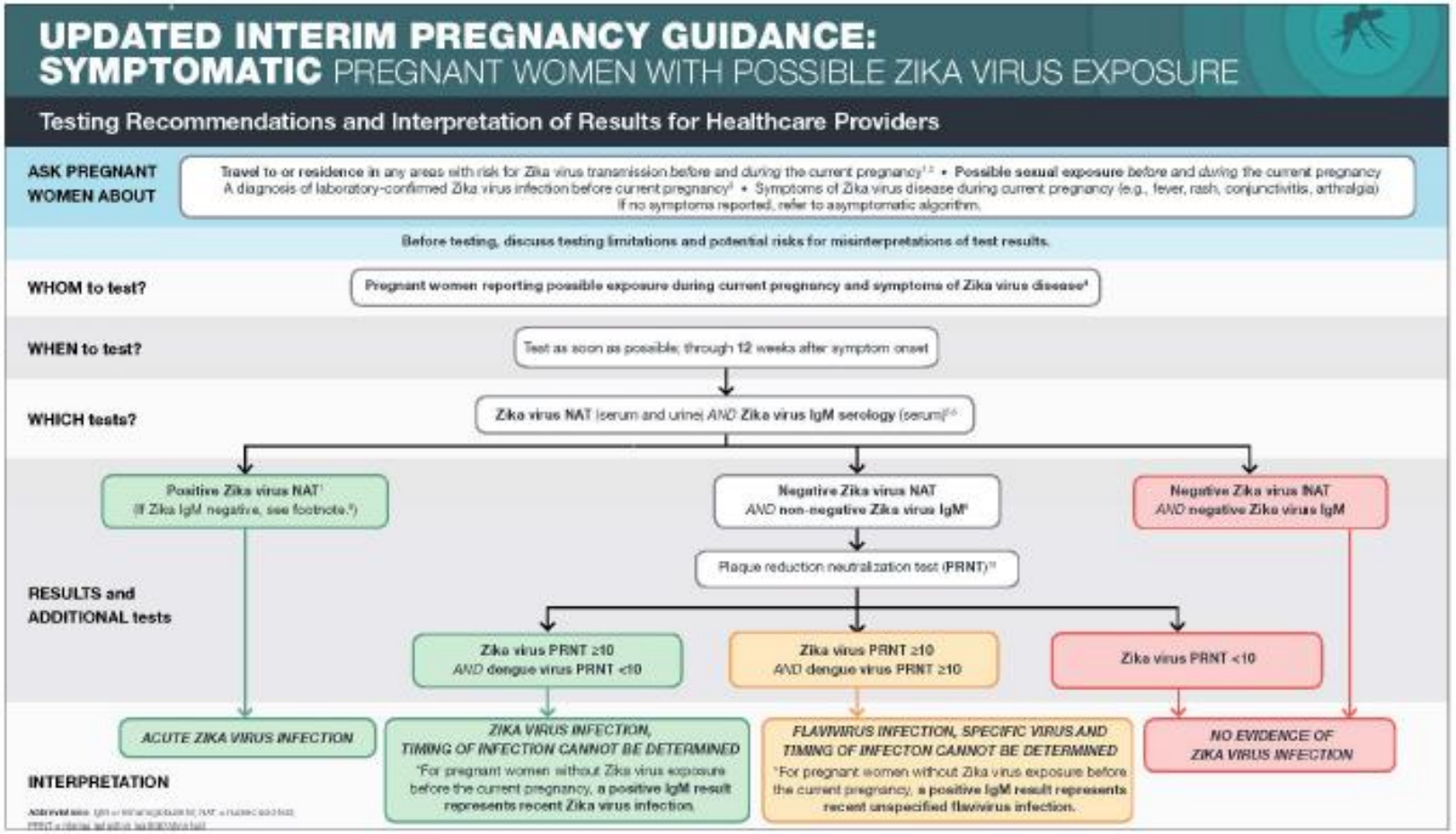
Eye Findings in Congenital Infections

	Zika	Toxoplasmosis	Rubella	CMV	Herpes Simplex	Syphilis
Conjunctivitis					+	
Keratitis					+	+
Macular Mottling	+ focal pigmentary clumping		+ granular (Salt-and-pepper retinopathy)			+ granular (Salt-and-pepper retinopathy)
Chorioretinal Atrophy	+	+				
Optic Nerve abnormalities	Hypoplasia, cupping, pallor		pallor	pallor		
Cataract	+		+	+	+	
Microphthalmia	+		+	+		
Iris Coloboma	+					
Active inflammation:		+	+	+	+	+

Zika Update: Findings from the U.S. Zika Pregnancy Registry and Updated Clinical Guidance
CDC May 4, 2017

Symptomatic Pregnant Women with Possible Zika virus Exposure



Long term follow up for infants with positive or inconclusive Zika virus test results

- Auditory and ophthalmological screen at 6 months intervals
- Continued evaluation of developmental characteristics and milestones, as well as head circumference, through 1st year of life
- Consultation with appropriate medical specialists (e.g., pediatric neurology, developmental and behavioral pediatrics, physical and speech therapy) if any abnormalities are noted and as concerns arise

Prevention: couples who are pregnant

- Do not travel to Zika area
- If patient must travel to Zika area, use mosquito bite protection and take steps to prevent sexual transmission during and after travel.
- Not having sex can eliminate the risk of getting Zika from sex.
- Condoms can reduce the chance of getting Zika from sex.
- Male partner who has traveled should use a condom correctly from start to finish every time they have vaginal, anal, or oral sex throughout the pregnancy.

Prevention: Non-pregnant couples with female partner who traveled

- Discuss signs and symptoms and potential adverse outcomes associated with Zika
- CDC says wait at least **8 weeks** after symptom onset or last date of exposure to have sex and attempt conception (CDC).
- WHO applies the **6 month wait** recommendation to both men and women returning from Zika transmission area.

CDC's Response to **Zika**

PREGNANT? READ THIS BEFORE YOU TRAVEL

What we know about Zika

- Zika can be passed from a pregnant woman to her fetus.
- Zika infection during pregnancy can cause certain birth defects.
- Zika is spread mostly by the bite of an infected *Aedes* species mosquito.
  - » These mosquitoes are aggressive daytime biters. They can also bite at night.
- There is no vaccine to prevent or medicine to treat Zika.
- Zika can be passed through sex from a person who has Zika to his or her sex partners.

What we don't know about Zika

- If there's a safe time during your pregnancy to travel to an area with Zika.
- If you do travel and are infected, how likely it is that the virus will infect your fetus and if your baby will have birth defects from the infection.

Travel Notice

CDC has issued a travel notice (Level 2-Practice Enhanced Precautions) for people traveling to areas where Zika virus is spreading.

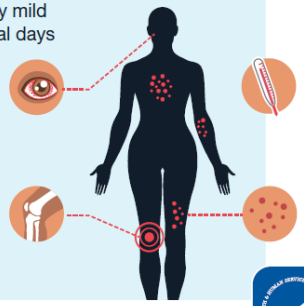
- For a current list of places with Zika outbreaks, see CDC's Travel Health Notices: http://wwwnc.cdc.gov/travel/page/zika-travel-information
- This notice follows reports in Brazil of microcephaly in babies of mothers who were infected with Zika virus while pregnant.

Symptoms of Zika

Most people with Zika won't even know they have it. The illness is usually mild with symptoms lasting for several days to a week.

The most common symptoms of Zika are

- Fever
- Rash
- Joint pain
- Red eyes



U.S. Department of Health and Human Services
Centers for Disease Control and Prevention

CDC's Response to **Zika**

TRAVELERS CAN PROTECT THEMSELVES **FROM ZIKA**

Zika Prevention Kit for Travelers

The products below can help protect you from Zika. Build your own Zika prevention kit and bring your kit with you on your trip.

Bed Net

- If your room is not well screened and air conditioned, use a bed net when sleeping or resting.
- Mosquitoes can live indoors and will bite at any time, day or night.

Insect Repellent

- Use EPA-registered insect repellent containing DEET, picaridin, OLE, PMD, or IR3535.
- Always use as directed.
- Do not apply repellent under clothing.
- If you are also using sunscreen, apply sunscreen first and insect repellent second.
- When used as directed, these insect repellents are proven safe and effective even for pregnant and breastfeeding women.
- Most repellents, including DEET, can be used on kids older than 2 months. Mosquito netting can be used to cover babies <2 months old in carriers, strollers, or cribs to protect them from mosquito bites.

Condoms

- Zika can be passed through sex. Bring male or female condoms with you when traveling. Use condoms during and after travel to protect yourself and your partner.
- If you are pregnant, use condoms for the rest of your pregnancy.
- Not having sex eliminates the risk of getting Zika through sex.

Permethrin Spray

- Spray your clothing and gear with permethrin to help protect you from mosquito bites or bring pre-treated items.
- Always follow the directions on the bottle. Reapply as directed.
- Do not spray permethrin on your skin.
- Long sleeves and long pants help protect against Zika.

www.cdc.gov/zika

U.S. Department of Health and Human Ser ı
Isease
Control and Prevention

National Center for Emerging and Zoonotic Infectious Diseases

Tackling an Invasive, Emerging, Multi-drug Resistant Yeast: *Candida auris*—What Healthcare Providers Need to Know

CDC August 15, 2017

What the public thinks

What the healthcare professionals think

Why Do We Care About an Obscure *Candida* Species called *C. auris*?

Candida auris Rapid Emergence since 2009

But This Really Got Our Attention…

- *C. auris* outbreak in a UK hospital
- 9 *C. auris* bloodstream infections
- >40 people colonized
- Clear patient-to-patient transmission

Hard to Control

- Contact precautions
- Screening for colonization
- Chlorhexidine bathing
- Cleaning room with bleach 3X/day
- Terminal cleaning with higher concentration bleach
- Eventually closed unit

C. auris cultured from many hospital surfaces

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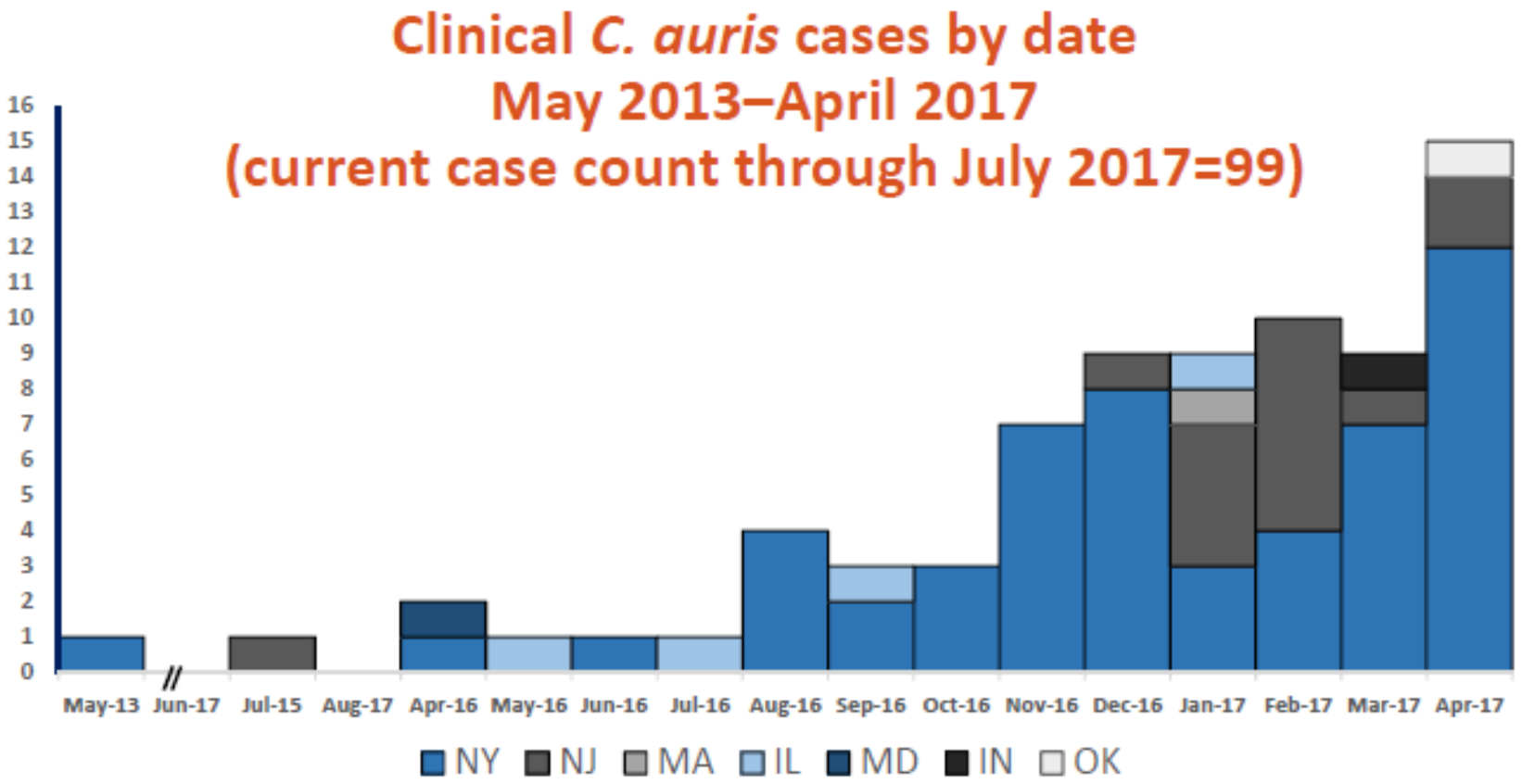
Tackling an Invasive, Emerging, Multidrug Resistant Yeast: Candida auris— CDC August 15, 2017

Candida auris in the US



Tackling an Invasive, Emerging, Multidrug Resistant Yeast: Candida auris—CDC August 15, 2017

C. auris clinical case features

Epidemiologic Characteristics of US Cases

- 75% of isolates from blood
- Median age: 70; one case in a neonate
- Multiple underlying medical conditions and indwelling devices
  - Tracheostomy tube, central venous catheter, gastrostomy tube
- Extensive healthcare exposure (acute care hospitals, LTACHs, vSNFs)
- Resistant: 80% to Fluconazole, 40% to Ampho B, ~3% to Echinocandins
- ~30% 30-day mortality

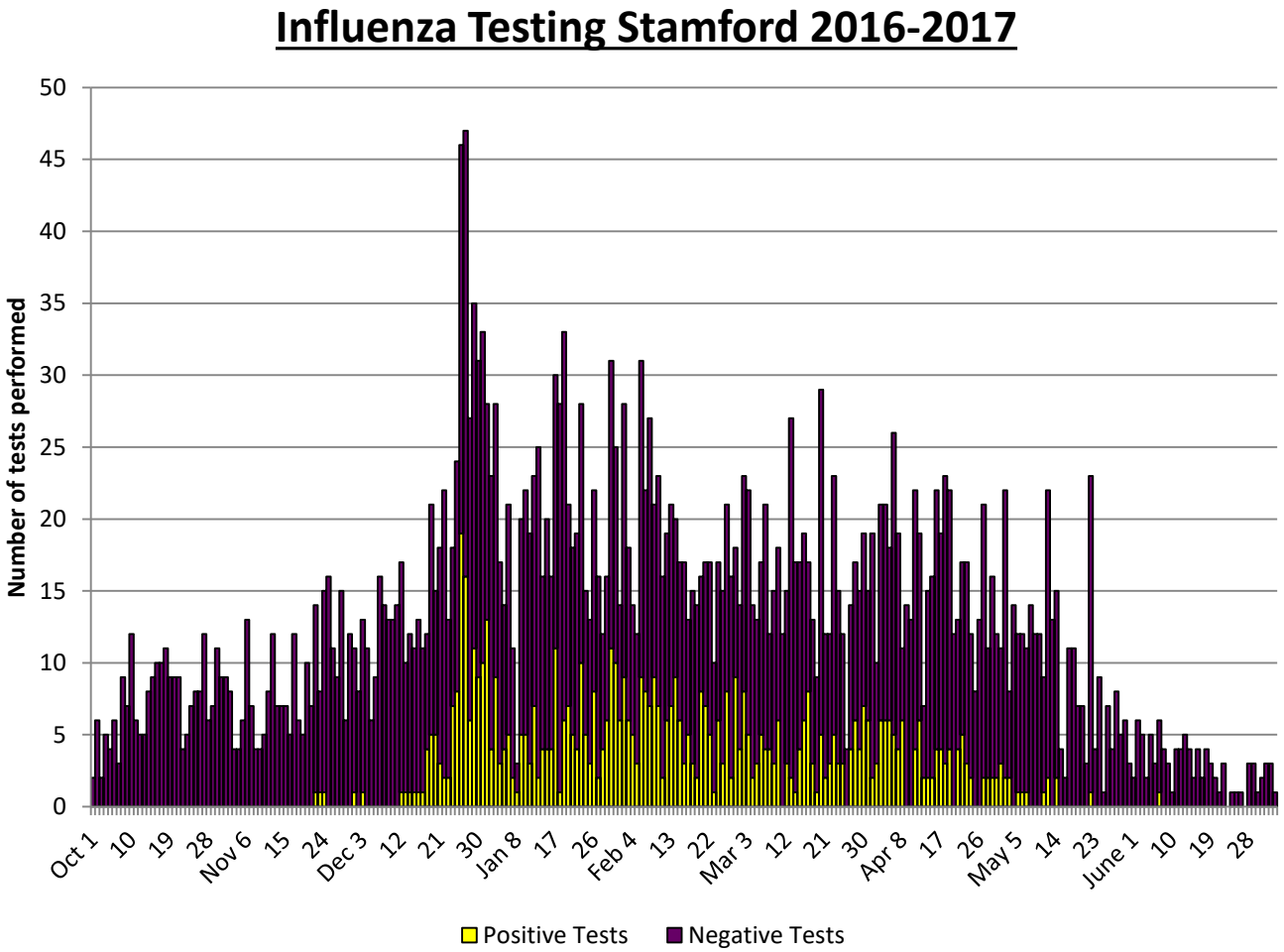
Tackling an Invasive, Emerging, Multidrug Resistant Yeast: Candida auris—CDC August 15, 2017

Global *C. auris* Situation

- Now common in some international hospitals
  - Up to 40% of *Candidas* in 1 Indian and 1 Kenyan hospital
  - 10% of *Candidas* in private South African hospitals
  - Probably well-established in Venezuela (limited dx capacity)
  - Cases now in Colombia and Panama
- UK continues to have introductions; seem to have controlled initial spread
- No further isolates in Japan; relatively few in South Korea
- Major unknowns in most of Africa and parts of Latin America

Tackling an Invasive, Emerging, Multidrug Resistant Yeast: Candida auris—CDC August 15, 2017

Influenza in Fairfield Country 2016-7



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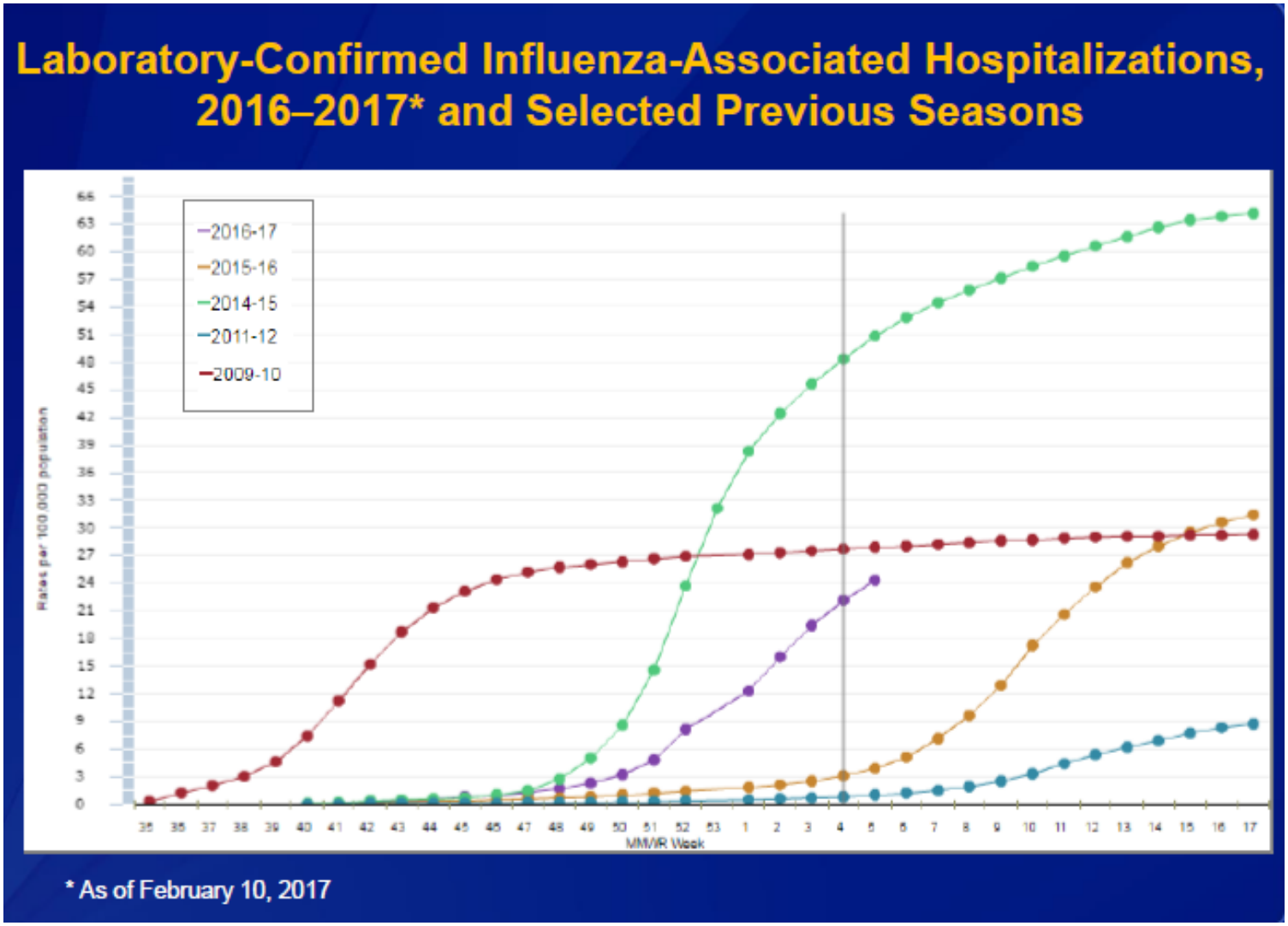
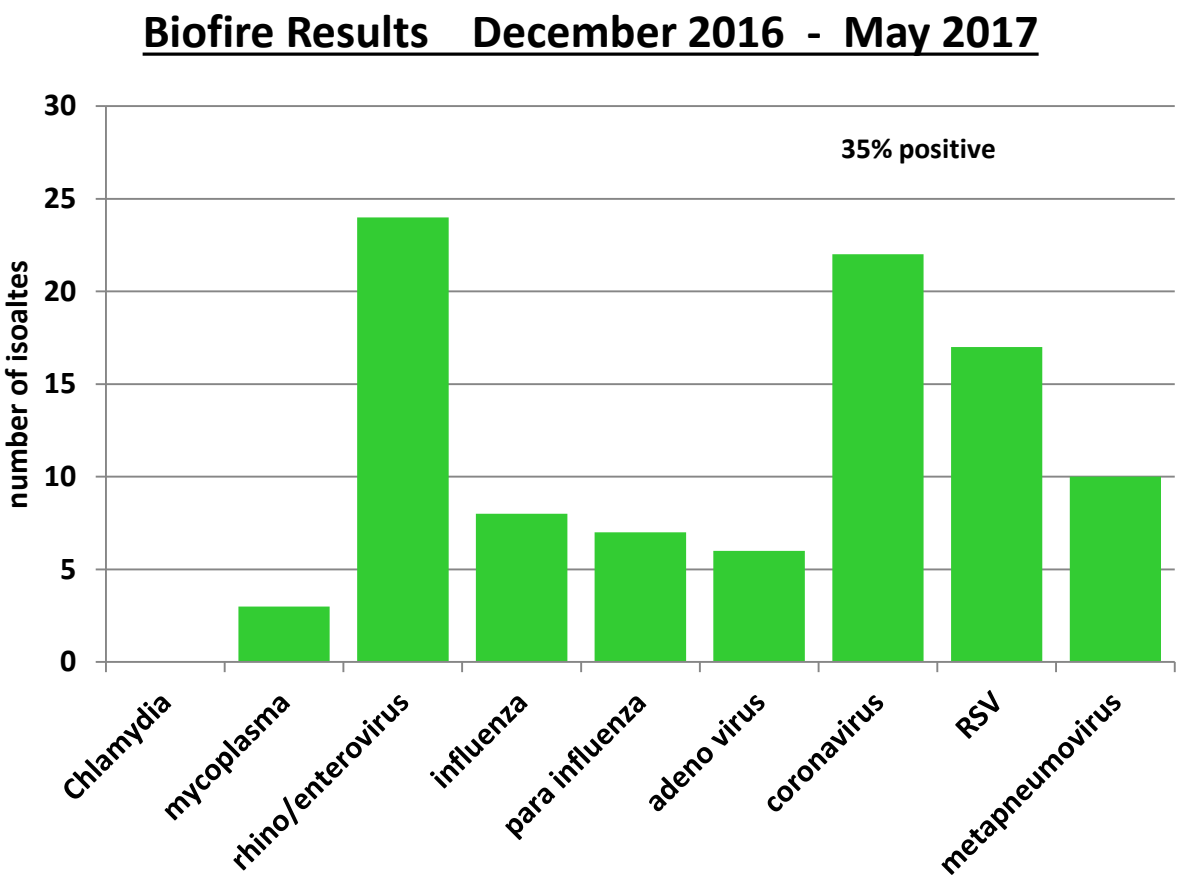
Annual Variation in Flu Seasons



Not all “ILI” is Influenza



STAMFORD HOSPITAL

Testing for Influenza

The overall pooled specificity was high for all influenza testing modalities (at least 98.3%). Sensitivity, however, varied.

	NAAT	DIA	RIDT
Influenza A	91.6%	80.0%	54.4%
Influenza B	95.4%	76.8%	53.2%

Centers for Disease Control and Prevention
MMWR
Morbidity and Mortality Weekly Report
Recommendations and Reports / Vol. 66 / No. 2
August 25, 2017

Prevention and Control of Seasonal Influenza with Vaccines: Recommendations of the Advisory Committee on Immunization Practices — United States, 2017–18 Influenza Season

2017–18 U.S. influenza vaccines will contain:

- A/Michigan/45/2015 (H1N1)pdm09–like virus
- A/Hong Kong/4801/2014 (H3N2)–like virus
- B/Brisbane/60/2008–like virus (Victoria lineage)
- B/Phuket/3073/2013–like virus (Yamagata lineage)*

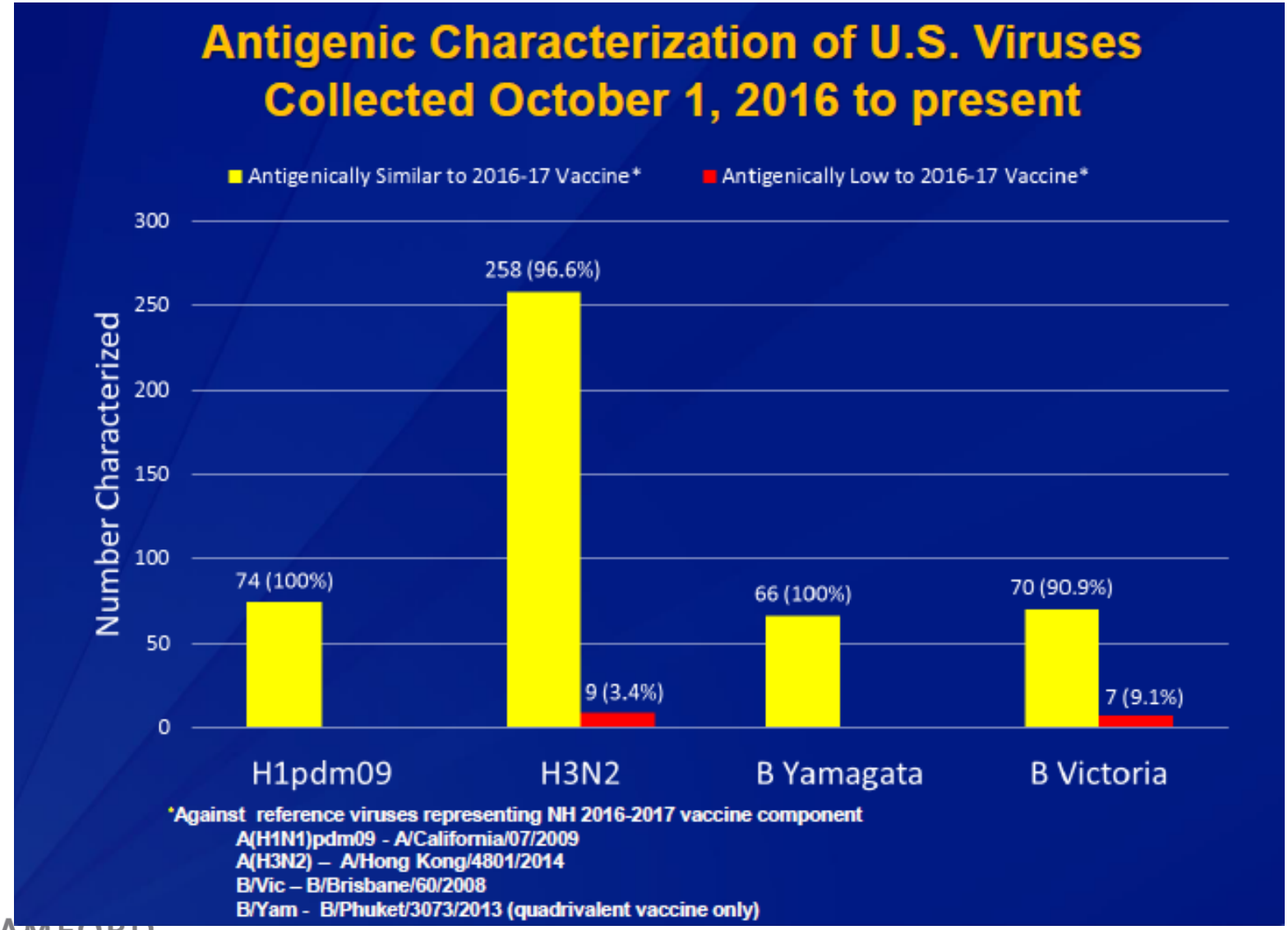
Guidance for Use in Specific Populations and Situations Populations at Higher Risk for Medical Complications Attributable to Severe Influenza

- All persons aged ≥6 months without contraindications should be vaccinated annually. However, vaccination to prevent influenza is particularly important for persons who are at increased risk for severe complications
- all children aged 6 through 59 months;
- all persons aged ≥50 years;
- adults and children who have chronic pulmonary (including asthma) or cardiovascular (except isolated hypertension), renal, hepatic, neurologic, hematologic, or metabolic disorders (including diabetes mellitus);
- persons who are immunocompromised due to any cause (including immunosuppression caused by medications or by HIV infection);
- women who are or will be pregnant during the influenza season;
- children and adolescents (aged 6 months through 18 years) who are receiving aspirin- or salicylate-containing medications
- residents of nursing homes and other long-term care facilities;
- American Indians/Alaska Natives; and
- persons who are extremely obese (BMI ≥40).
- ACIP recommends that LAIV4 not be used during the 2017–18 season

TABLE 1. Influenza vaccines — United States, 2017–18 influenza season*

Trade name	Manufacturer	Presentation	Age indication	Mercury (from thimerosal, μg/0.5 mL)	Latex	Route
Inactivated influenza vaccines, quadrivalent (IIV4s), standard-dose†						
Afluria Quadrivalent	Seqirus	0.5 mL prefilled syringe	≥18 years	NR	No	IM§
		5.0 mL multidose vial	≥18 years (by needle/syringe) 18 through 64 years (by jet injector)	24.5	No	IM
Fluarix Quadrivalent	GlaxoSmithKline	0.5 mL prefilled syringe	≥3 years	NR	No	IM
FluLaval Quadrivalent	ID Biomedical Corp. of Quebec (distributed by GlaxoSmithKline)	0.5 mL prefilled syringe	≥6 months	NR	No	IM
		5.0 mL multidose vial	≥6 months	<25	No	IM
Fluzone Quadrivalent	Sanofi Pasteur	0.25 mL prefilled syringe	6 through 35 months	NR	No	IM
		0.5 mL prefilled syringe	≥3 years	NR	No	IM
		0.5 mL single-dose vial	≥3 years	NR	No	IM
		5.0 mL multidose vial	≥6 months	25	No	IM
Inactivated influenza vaccine, quadrivalent (ccIIV4), standard-dose,† cell culture-based						
Flucelvax Quadrivalent	Seqirus	0.5 mL prefilled syringe	≥4 years	NR	No	IM
		5.0 mL multidose vial	≥4 years	25	No	IM
Inactivated influenza vaccine, quadrivalent (IIV4), standard-dose, intradermal¶						
Fluzone Intradermal Quadrivalent	Sanofi Pasteur	0.1 mL single-dose prefilled microinjection system	18 through 64 years	NR	No	ID**
Inactivated Influenza Vaccines, trivalent (IIV3s), standard-dose†						
Afluria	Seqirus	0.5 mL prefilled syringe	≥5 years	NR	No	IM
		5.0 mL multidose vial	≥5 years (by needle/syringe) 18 through 64 years (by jet injector)	24.5	No	IM
Fluvirin	Seqirus	0.5 mL prefilled syringe	≥4 years	≤1	Yes††	IM
		5.0 mL multidose vial	≥4 years	25	No	IM
Adjuvanted inactivated influenza vaccine, trivalent (aIIV3),† standard-dose						
Fluad	Seqirus	0.5 mL prefilled syringe	≥65 years	NR	Yes††	IM
Inactivated Influenza Vaccine, trivalent (IIV3), high-dose§§						
Fluzone High-Dose	Sanofi Pasteur	0.5 mL prefilled syringe	≥65 years	NR	No	IM
Recombinant Influenza Vaccine, quadrivalent (RIV4)¶¶						
Flublok Quadrivalent	Protein Sciences	0.5 mL prefilled syringe	≥18 years	NR	No	IM
Recombinant Influenza Vaccine, trivalent (RIV3)¶¶						
Flublok	Protein Sciences	0.5 mL single-dose vial	≥18 years	NR	No	IM
Live Attenuated Influenza Vaccine, quadrivalent (LAIV4)* (not recommended for use during the 2017–18 season)**						
FluMist Quadrivalent	MedImmune	0.2 mL single-dose prefilled intranasal sprayer	2 through 49 years	NR	No	NAS

2016-2017 Vaccine Match



Effectiveness of Flu Vaccine 2016-2017

Population = all patients admitted to Stamford Hospital with a flu test performed
Time period = two months December 2016 – January 2017
Vaccination history = abstracted from nurse charted flu vaccine assessment screen
Flu test by NP swab PCR (either Alere-i or Cepheid) abstracted from Meditech

	Vaccinated	Unvaccinated				
Flu negative	237	133	320	(64.1% vaccinated)	$X^2 = 3.278$	P = 0.07
Flu positive	17	18	35	(48.6% vaccinated)		
	254	151	405			

Vaccine effectiveness = (ARU – ARV)/ARU x 100 = 43.7%

Data collected [CDC] through the U.S. Influenza Vaccine Effectiveness Network during 11/28/16–4/14/17 indicate that influenza vaccination reduced the overall risk for influenza-associated medical visits by 42%

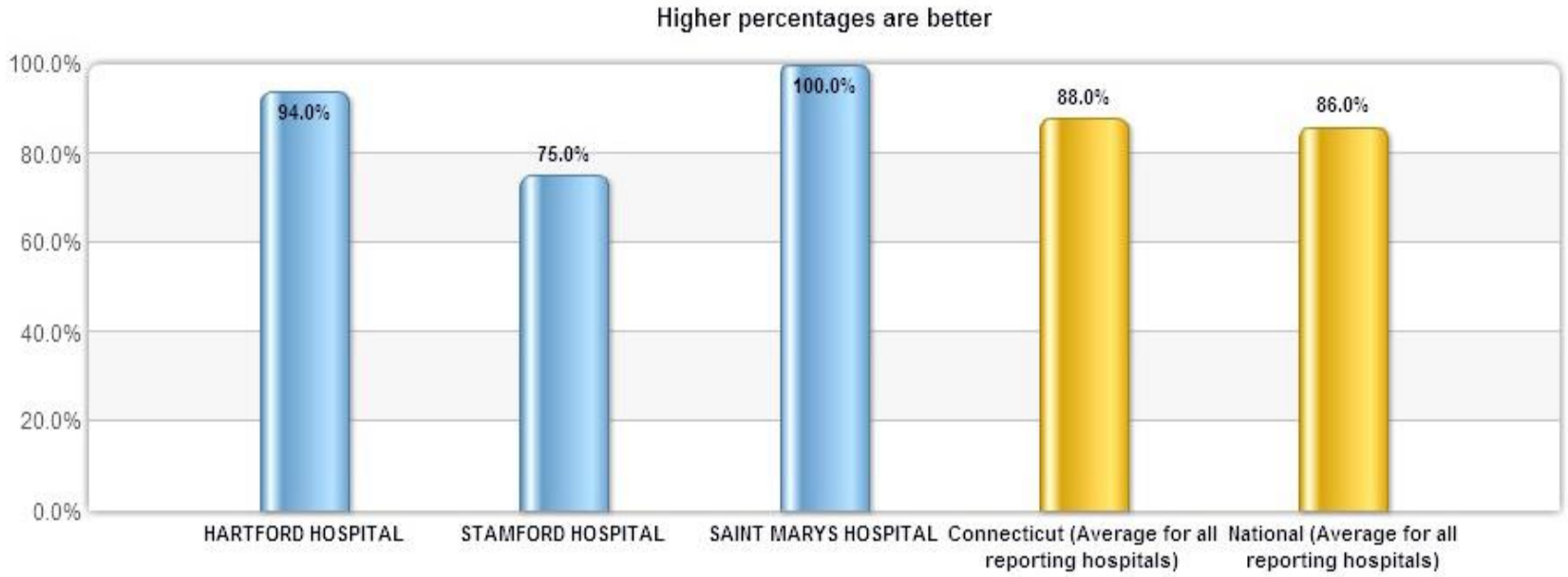
- Vaccine effectiveness against the predominant influenza A(H3N2) viruses was 34% (95% CI=24%–42%)
- Vaccine effectiveness against influenza B viruses was 56% (95% CI=47%–64%).

HCW Flu Vaccination
Hospital Compare Data for 2015-2016 season

Healthcare workers given influenza vaccination

Why is this important?

Hide Graph



For this measure, the rate for the top 10% of hospitals was Not Available.

Neuraminidase Treatment of Influenza

- FDA approved for patients with proven or highly suspect influenza infection within 48 hours of onset of symptoms
- Observational studies of hospitalized patients suggest that treatment might still be beneficial when initiated 4 or 5 days after symptom onset
- Observational data in pregnant women has shown antiviral treatment to provide benefit when started 3-4 days after onset
- A randomized placebo controlled study suggested clinical benefit when oseltamivir was initiated 72 hours after illness onset among febrile children with uncomplicated influenza

Muthuri, Lancet Resp Med 2014;2:395-404; Louie, CID 2012;55:1198-204; Yu, CID 2011;52:457-65;

Thank You!

Questions?