

Infectious Diseases 2016

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Outline

- Overview
- Antibiotic resistance
- Zika
- Hepatitis C
- HIV



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

2016	mcr-1 gene for colistin resistance
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



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.



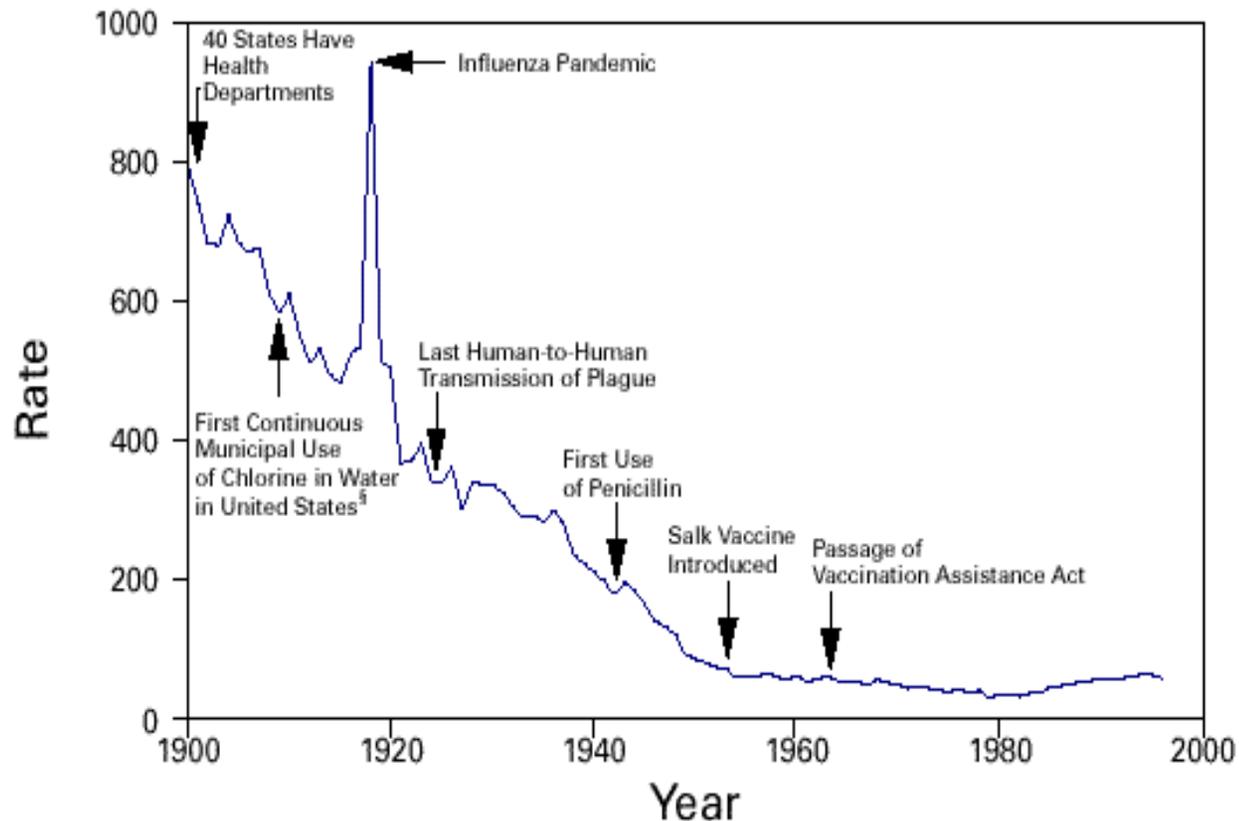
A Historical Perspective

- 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†

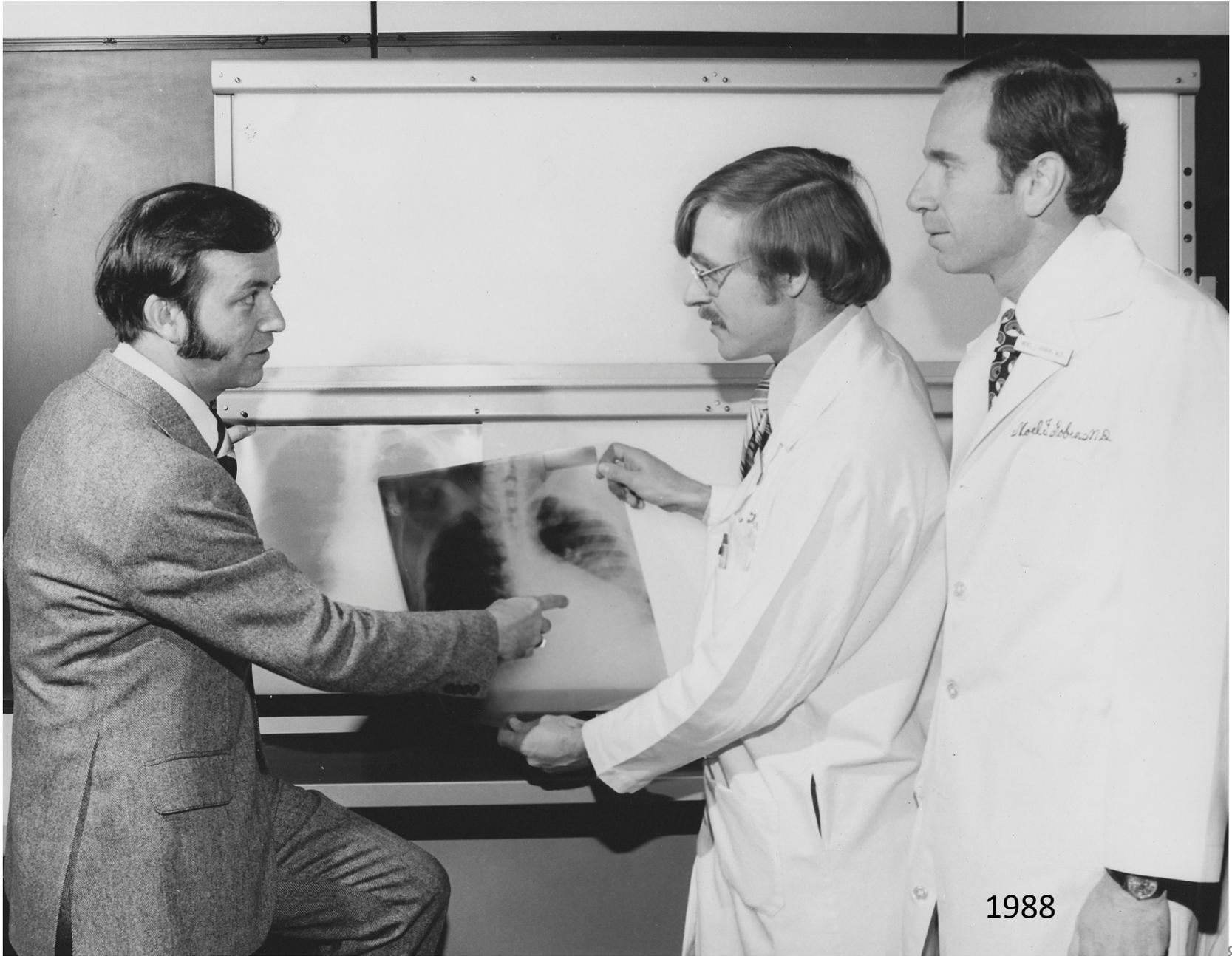


*Per 100,000 population per year.

†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.





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

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



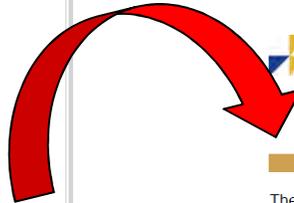
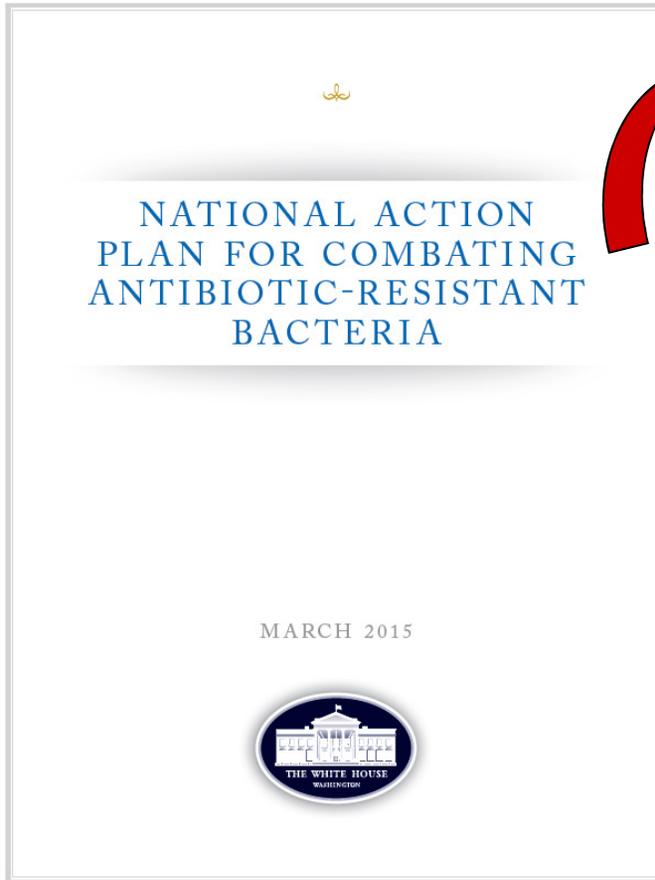
Research scientist Rosslyn Mayback was part of the team that identified a strain of E. coli bacteria with a gene that could spread antibiotic resistance. (Walter Reed Army Institute of Research)

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.





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.jcinc.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

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

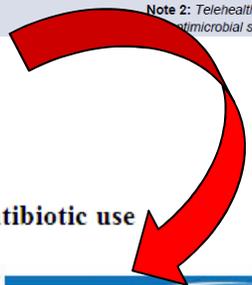
Note: Examples of leadership commitment to an antimicrobial stewardship program are as follows:

- 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>.

- 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 antimicrobial stewardship multidisciplinary team.



Proposed CMS rule on infection control and inappropriate antibiotic use

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 2016:

ESCAPE pathogens

- *Enterococcus* (VRE)
- *Staphylococcus aureus* (MRSA and VISA)
- *Carbapenem resistant Enterobacteriaceae* (CRE) *E coli*, *Klebsiella*, *Enterobacter* (and others: NDM-1, etc)
- *Acinetobacter* (multi-drug resistant)
- *Pseudomonas* (FQ resistant)
- *Extended spectrum beta-lactamase producing GNR* (ESBL positive *E. coli*, *Klebsiella*, *Enterobacter*)
plus
- *Clostridium difficile* (NAP-1 strains, and others)



Multi-drug resistant organisms

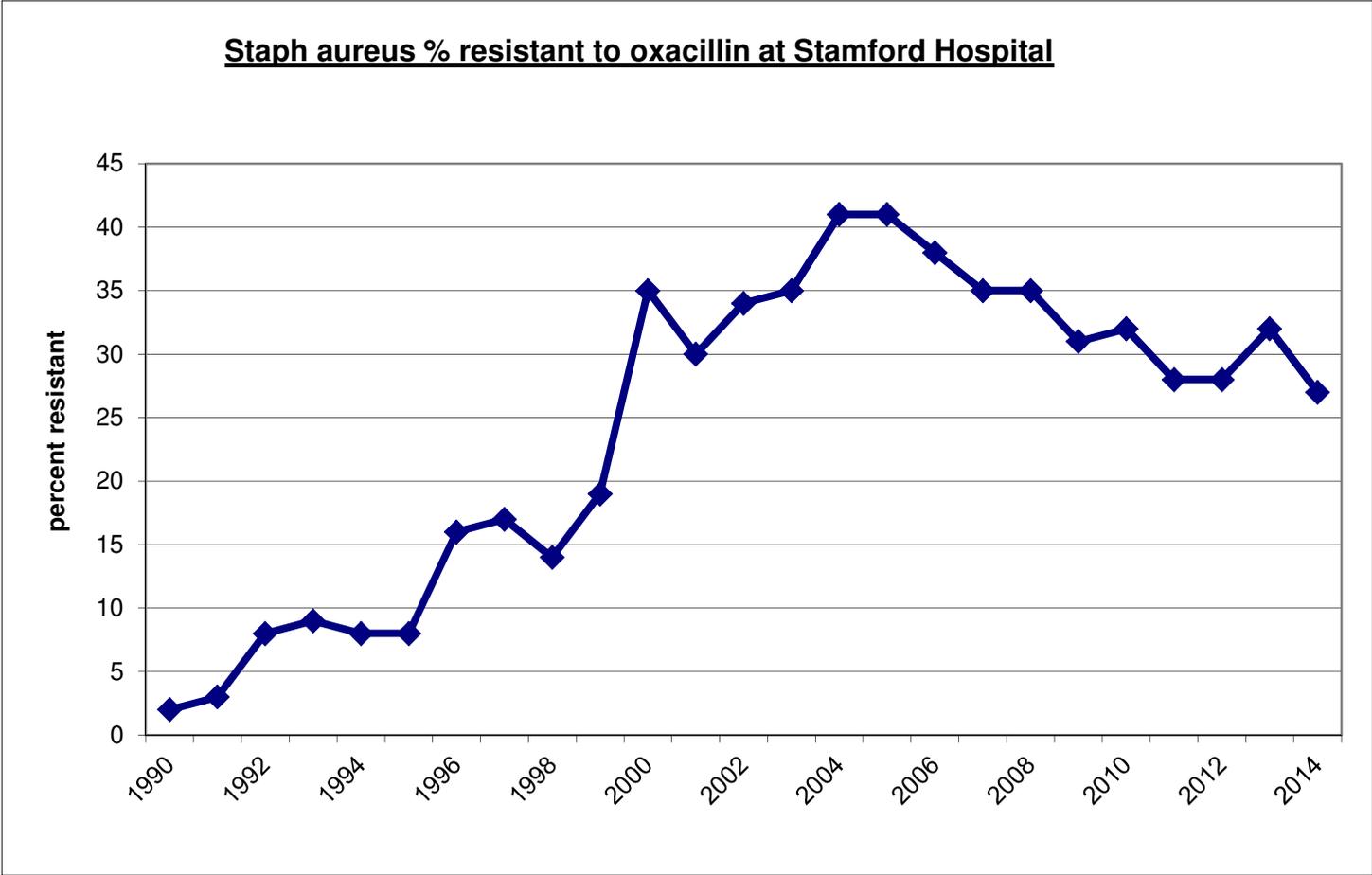
MDRO Infections



Emergence of MRSA over 20 years in Stamford

Hospital Microbiology Lab data

(community and hospital strains)



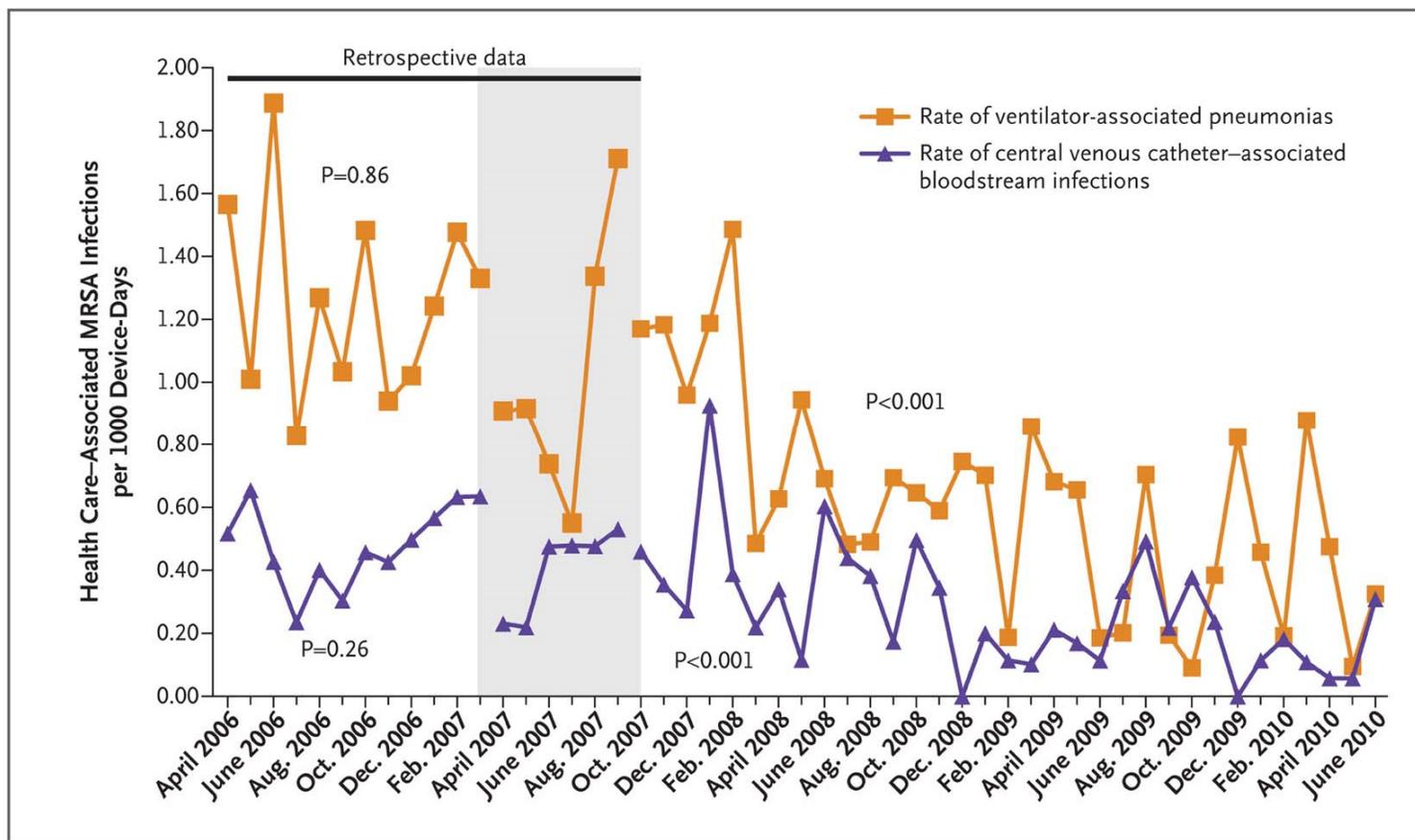
MRSA Treatment Options

- Oral
 - Bactrim, Doxy/Minocycline, Linezolid >90%
 - Clindamycin 60%
- Parenteral
 - Vancomycin
 - Bactrim / Doxy / Mino, Linezolid
 - Daptomycin
 - Ceftaroline
 - Synercid
 - Telavancin / Dalbavancin / Oritavancin
(lipoglycopeptides)



Impact of an “MRSA Bundle” on MRSA rates: Veterans Affairs (VA) Intensive Care Units.

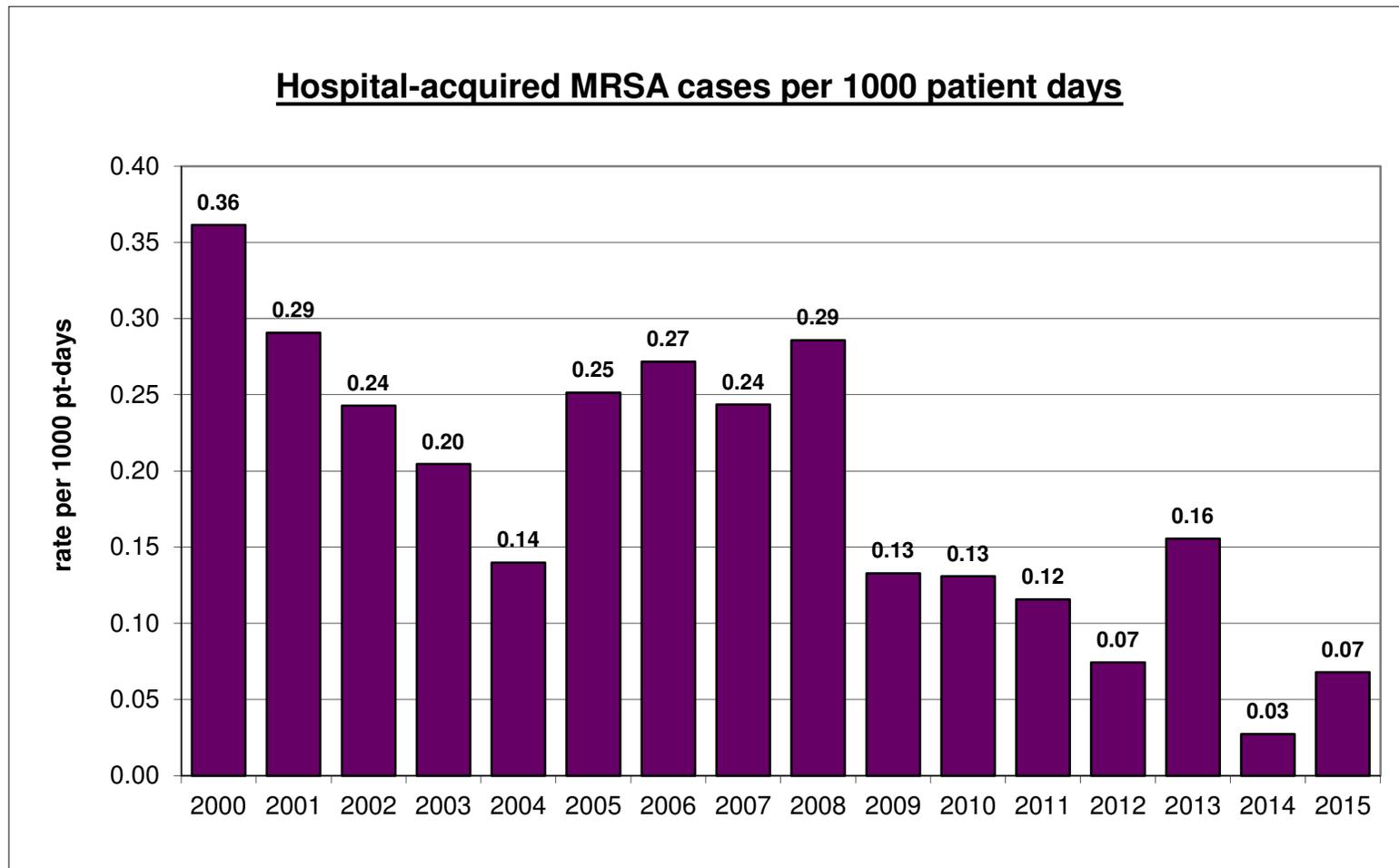
Hand hygiene, Active Surveillance testing, Contact Precautions



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



Stamford – Hospital-acquired MRSA cases



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

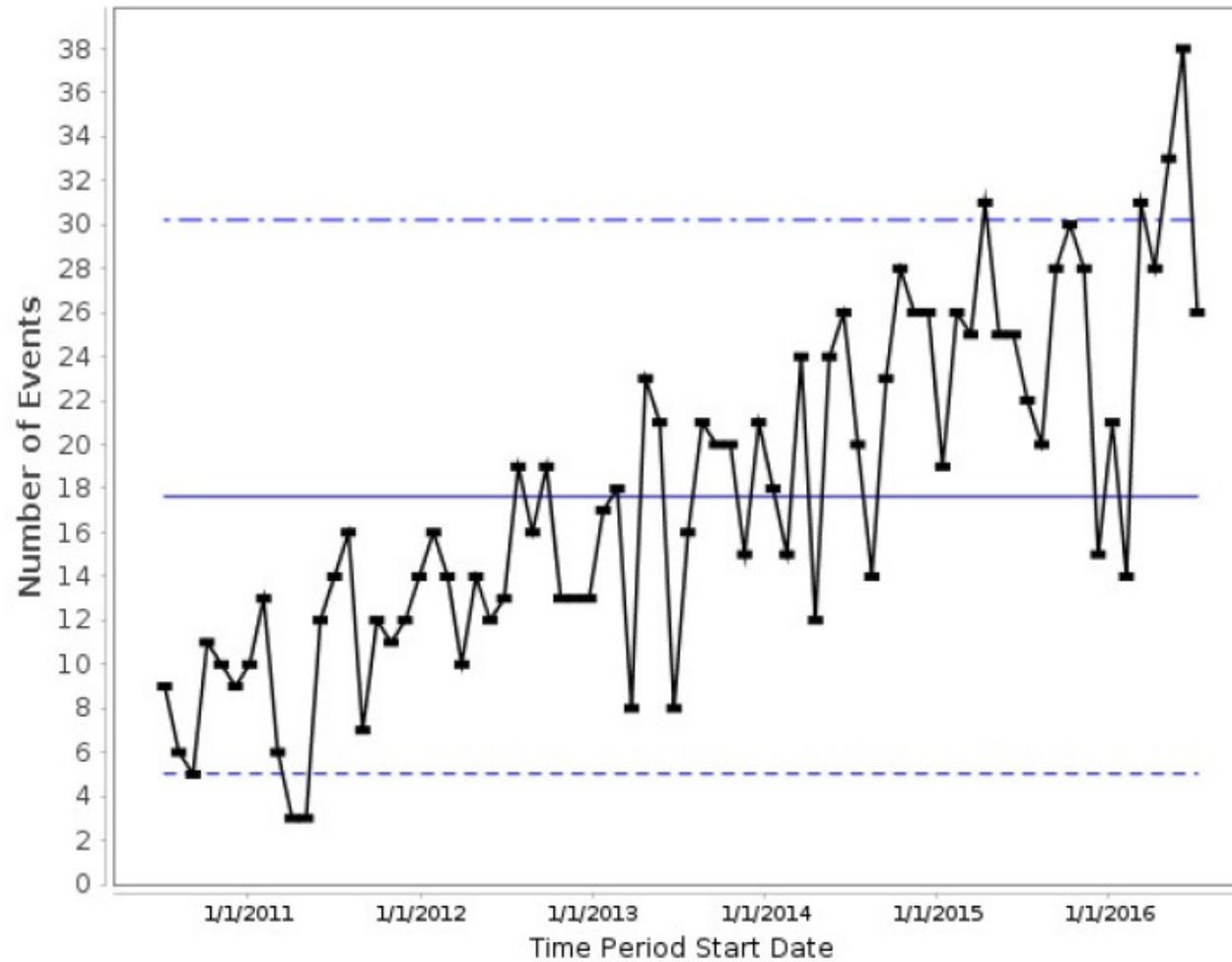


Risk factors for Hospital ESBL acquisition

- Length of hospital stay
- Length of ICU stay
- Presence of central venous or arterial catheters
- Emergency abdominal surgery
- Presence of a gastrostomy or jejunostomy tube
- Prior administration of any antibiotic
- Prior residence in a SNF or LTAC
- Severity of illness
- Presence of a urinary catheter
- Ventilator assistance
- Hemodialysis



ESBL-positive isolates at Stamford



Outpatient urine culture

Procedure	Result	Verified																								
URINE CULTURE Final Source: URINE CLEAN CATCH MIDSTREAM		Verified 07/27/15-0835																								
<p>This organism exhibits extended spectrum beta lactamase (**ESBL**) activity. In vitro susceptibility testing may be unreliable. Consider Infectious Diseases consultation.</p>																										
Organism 1 Colony Count:	ESCHERICHIA COLI **ESBL** >100,000 COL./CC.																									
	<table border="1"> <thead> <tr> <th>E.COLI **</th> <th>MIC</th> <th>RX</th> </tr> </thead> <tbody> <tr> <td>TRIMET/SULFA</td> <td>>2/38</td> <td>R</td> </tr> <tr> <td>AMPICILLIN</td> <td>>16</td> <td>R*</td> </tr> <tr> <td>CEFAZOLIN</td> <td>>16</td> <td>R*</td> </tr> <tr> <td>CIPROFLOXACIN</td> <td>>2</td> <td>R</td> </tr> <tr> <td>GENTAMICIN</td> <td>>8</td> <td>R</td> </tr> <tr> <td>NITROFURANTOIN</td> <td><=32</td> <td>S</td> </tr> <tr> <td>TETRACYCLINE</td> <td>>8</td> <td>R</td> </tr> </tbody> </table>	E.COLI **	MIC	RX	TRIMET/SULFA	>2/38	R	AMPICILLIN	>16	R*	CEFAZOLIN	>16	R*	CIPROFLOXACIN	>2	R	GENTAMICIN	>8	R	NITROFURANTOIN	<=32	S	TETRACYCLINE	>8	R	
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ESBL Treatment Options

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



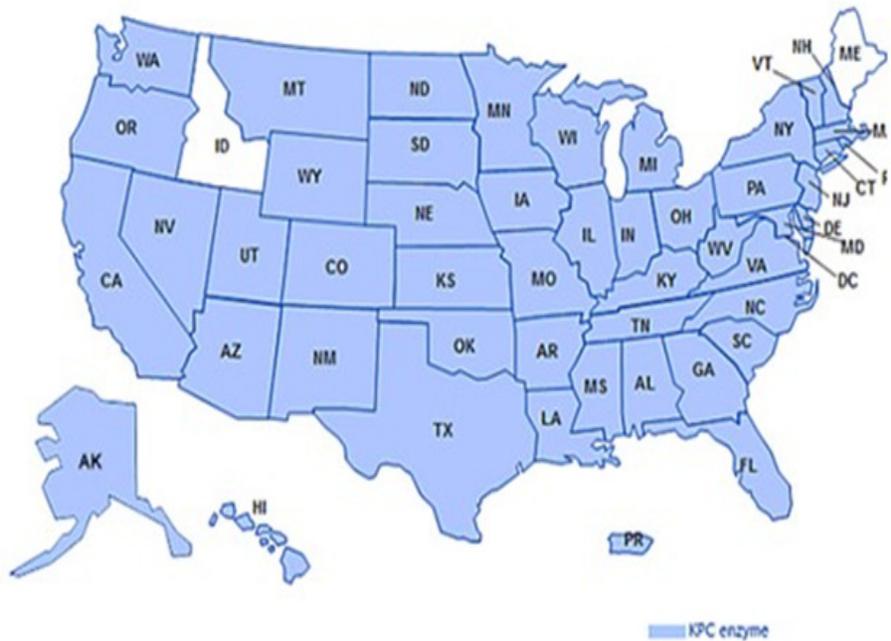
Emergence of Carbapenem-resistant *Enterobacteriaceae* (CRE)

- 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**

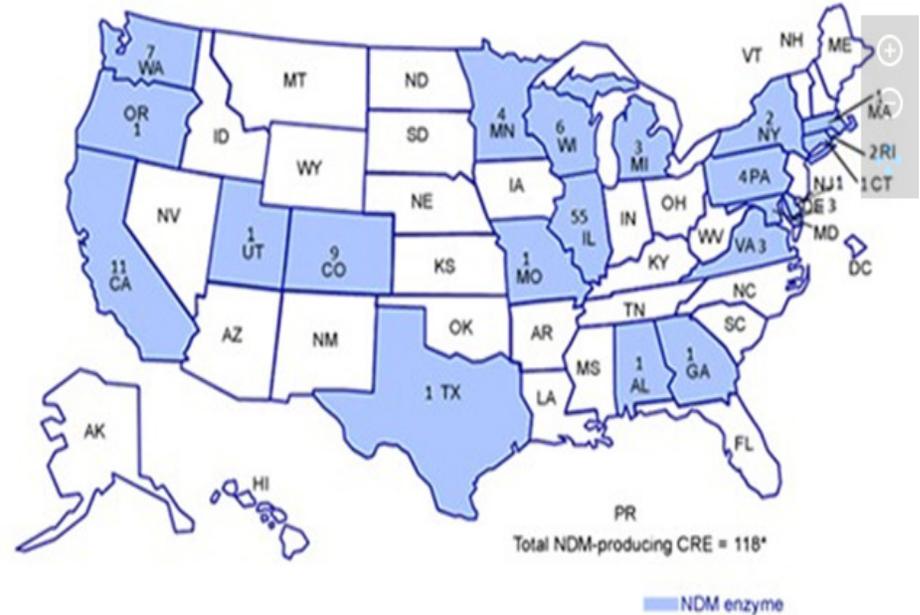


Evolution of CRE in the United States

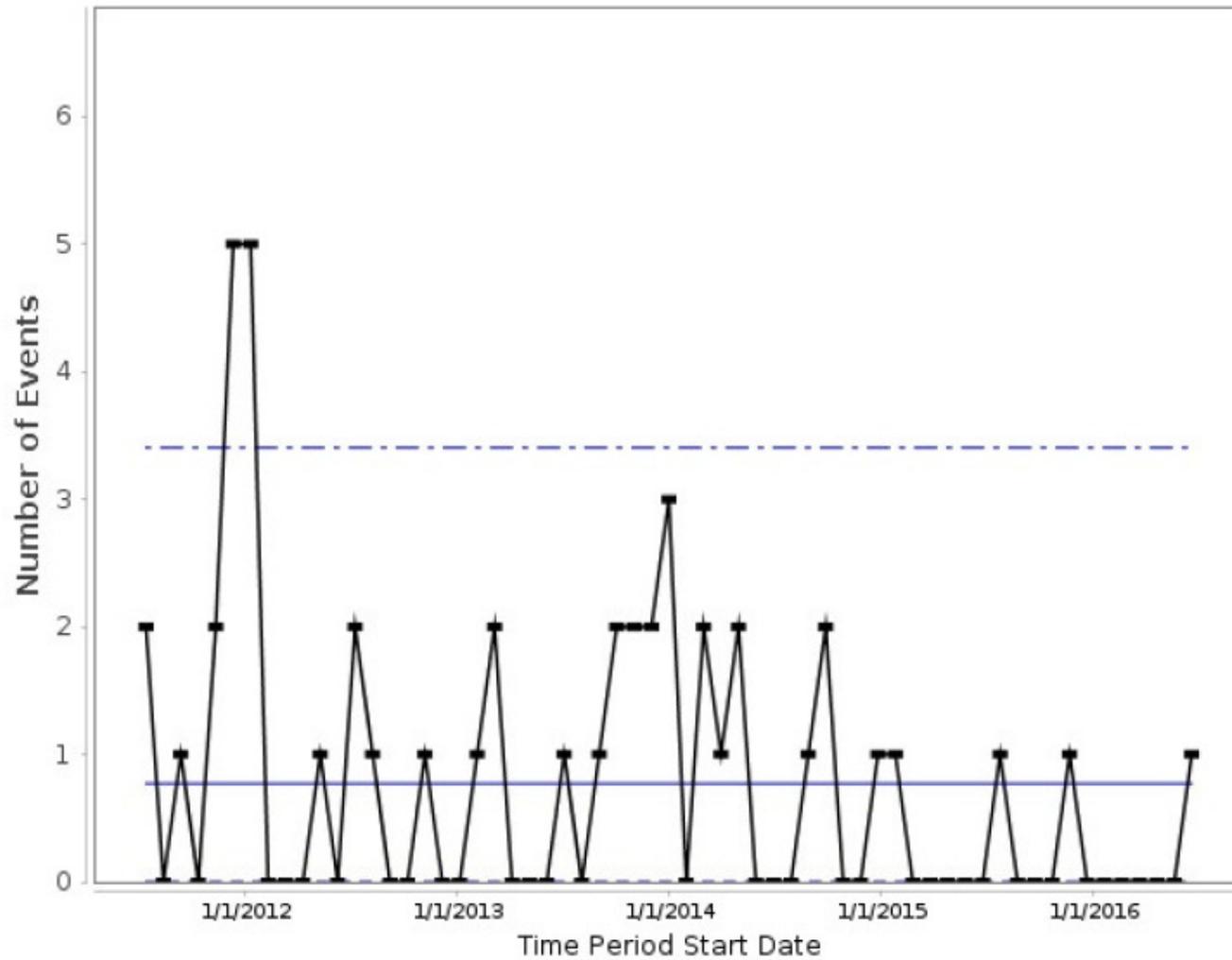
KPC-producing CRE



NDM-producing CRE



CRE isolates at Stamford



Mic Specimen Internal Inquiry - MEDITECH Document Preview

File Help

SPEC : 16:M0031627R PATIENT: HAUSCHILD, JACQUELINE ACCT : V00041433715

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.	IO	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		

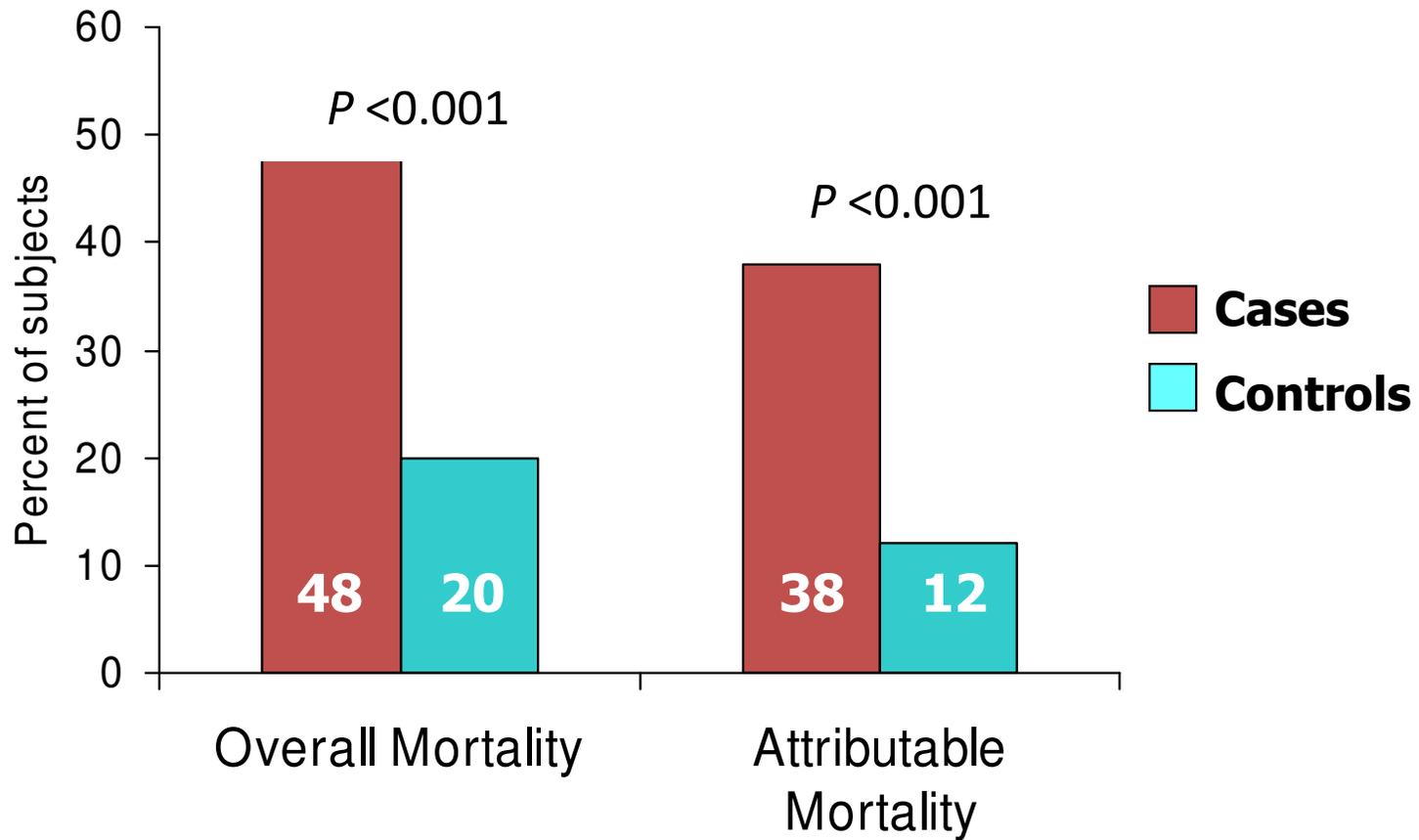
> FLUID CULTURE Preliminary (changed) Verified 08/02/16-1506
 Method: MAN Perf Site: TSH
 Ent: 08/02-1506 GOCAMPO, Ver: 08/02-1506 GOCAMPO

Source: PERITONEAL FLUI BAP GNR #2^
 CNA #3^ #4^ #5^

10/13 86%



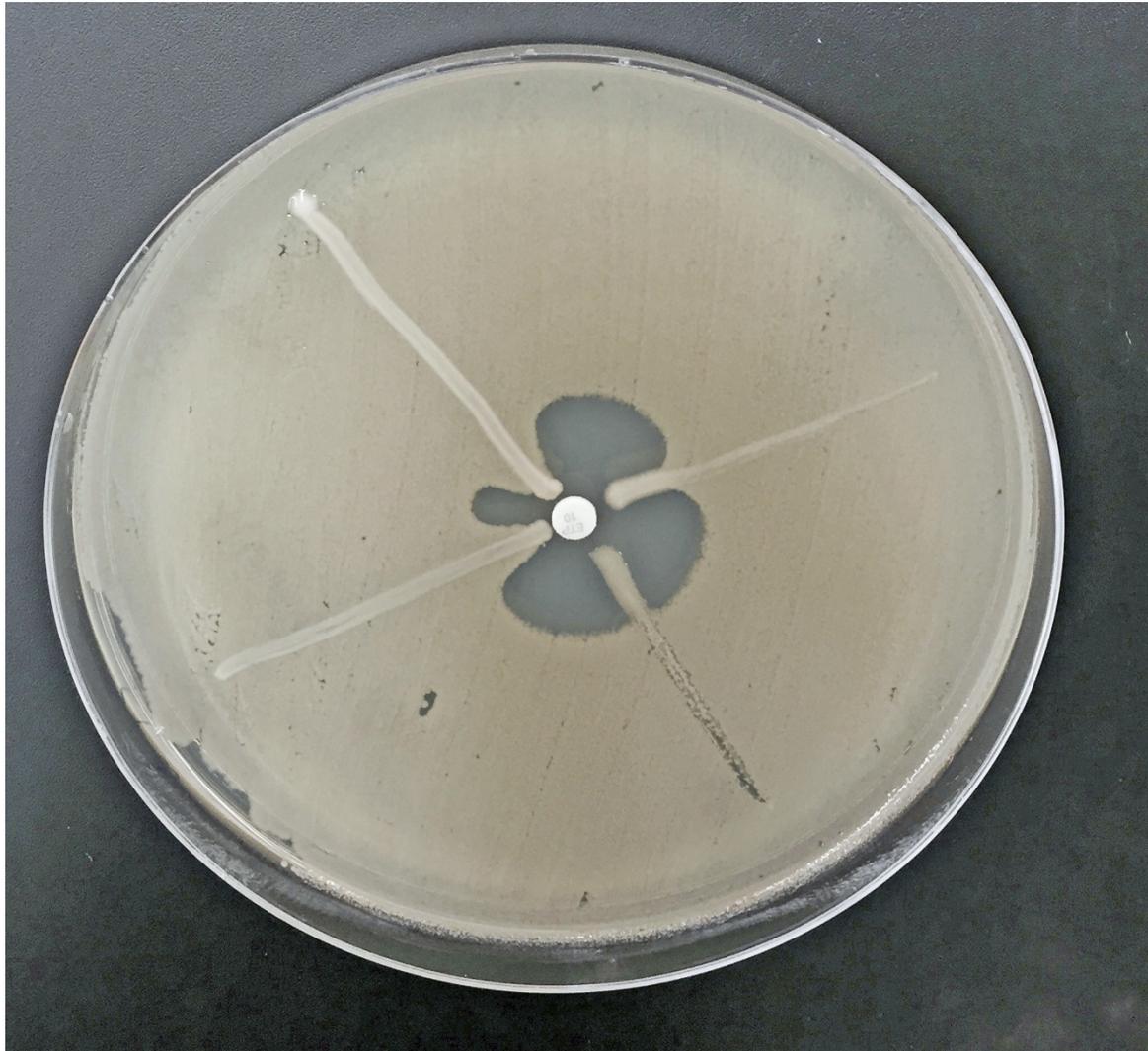
CRE Infections-- Outcome data from NYC



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



Positive 'Hodge' Test



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



Rapid Diagnostics: Stopping Unnecessary Use of Antibiotics
The Review on Antimicrobial Resistance, Chaired by Jim O'Neill. October 2015

↓
THE NEED

- Carbapenem resistance results in increased mortality in hospitalized patients and is associated with higher total hospital costs.¹

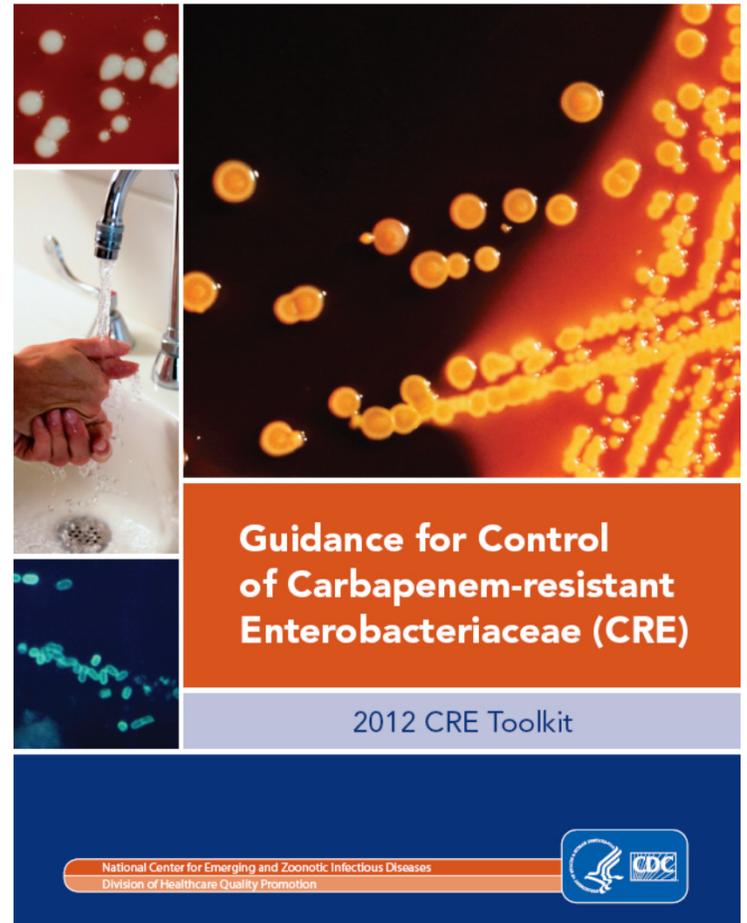
↓
THE SOLUTION

Xpert® Carba-R can detect and differentiate the most prevalent carbapenemase gene families in just 48 minutes.



CDC Action Plan for CRE Control

- Surveillance
- HCW education
- Laboratory detection
 - lab education
- Mandatory Reporting
- Strict isolation / contact tracing / screening
- Antibiotic stewardship
- Limited options for treatment
 - colistin, ceftazidime + avibactam (Avycaz), fosfomycin



Highly resistant MCR-1 'superbug' found in US for first time

Filed Under: [MCR-1](#); [Antimicrobial Resistance](#)

[Jim Wappes](#) | Editorial Director | [CIDRAP News](#) | May 26, 2016

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Bacteria carrying the very worrisome MCR-1 resistance gene—which makes the last-line antibiotic colistin useless against them—have been found in human and animal samples for the first time in the United States, according to a report today in *Antimicrobial Agents and Chemotherapy* and a statement by federal health officials.

A Chinese team first described the MCR-1 gene last November, after finding it in pigs, pork, and humans. Since then scientists in several countries have found the gene, sometimes alongside other resistance genes, after examining their sample collections. The gene can be transferred to other organisms, compounding the concern.

Today's findings involve a 49-year-old woman whose urine contained *Escherichia coli* harboring the MCR-1 gene and an *E coli* isolate from a pig intestine that also contained the colistin-resistance gene.

MCR-1 in urine sample

The woman sought care at a Pennsylvania clinic for symptoms of a urinary tract infection 1 month ago



FDA, Michael J. Ermarth / Flickr cc



Investigation of *Escherichia coli* Harboring the *mcr-1* Resistance Gene – Connecticut, 2016

Early Release / September 9, 2016 / 65



Format:

Amber M. Vasquez, MD^{1,2}; Noelia Montero, MPH^{3,4}; Mark Laughlin, DVM^{1,5}; Ehren Dancy⁵; Russell Melmed, MPH³; Lynn Sosa, MD³; Louise Francois Watkins, MD⁵; Jason P. Folster, PhD⁵; Nancy Strockbine, PhD⁵; Heather Moulton-Meissner, PhD²; Uzma Ansari, MS²; Matthew L. Cartter, MD³; Maroya Spalding Walters, PhD² ([View author affiliations](#))



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The *mcr-1* gene confers resistance to the polymyxins, including the antibiotic colistin, a medication of last resort for multidrug-resistant infections. The *mcr-1* gene was first reported in 2015 in food, animal, and patient isolates from China (1) and is notable for being the first plasmid-mediated colistin resistance mechanism to be identified. Plasmids can be transferred between bacteria, potentially spreading the resistance gene to other bacterial species. Since its discovery, the *mcr-1* gene has been reported from Africa, Asia, Europe, South America, and North America (2,3), including the United States, where it has been identified in *Escherichia coli* isolated from three patients and from two intestinal samples from pigs (2,4-6). In July 2016, the Pathogen Detection System at the National Center for Biotechnology Information (Bethesda, Maryland) identified *mcr-1* in the whole genome sequence of an *E. coli* isolate from a Connecticut patient (7); this is the fourth isolate from a U.S. patient to contain the *mcr-1* gene.

The isolate was non-Shiga toxin-producing *E. coli* O157 from stool collected on June 16, 2016 from a pediatric patient with diarrhea. The patient traveled to the Caribbean for approximately 2 weeks to visit friends and relatives and developed fever and bloody diarrhea on June 12, 2 days before returning to the United States. The patient took paromomycin, an aminoglycoside antibiotic, from symptom onset until a pediatric outpatient visit on June 16, at which time a stool specimen was collected. The patient was not hospitalized and, in addition to the primary care visit, had one brief emergency department visit during the illness.

E. coli O157 harboring *mcr-1* was isolated from three stool cultures from the patient: the June 16 culture and follow-up cultures on June 18 and 23. Reference susceptibility testing by broth microdilution showed that the isolates had a colistin (also known as polymyxin E) minimum inhibitory concentration (MIC) of 2 µg/ml, and polymyxin B MIC of 4 µg/ml. The isolates also carried a plasmid *bla*_{cmv-2} gene, which encodes AmpC, an enzyme that confers resistance to third generation cephalosporins; the isolates were susceptible to carbapenems. Stool cultures on June 24 and July 1 were negative for *E. coli* O157.

The patient's parent and health care provider were interviewed to assess patient risk factors and close contacts who might be at risk for acquiring bacteria carrying *mcr-1*. The patient was typically healthy with no prior surgeries or hospitalizations. The patient's usual diet included fruit, dairy products, and meat (pork, chicken, and beef). While traveling, the patient ate chicken and goat meat from a live animal market that the patient did not visit. The patient stayed in a home with a pet cat and dog in the Caribbean but did not have any animal contact in the United States.

Persons with close contact with the patient, particularly those involved in bathing or diapering, were considered to be at risk for *mcr-1* acquisition. On July 19–20, perirectal swabs were obtained from all six identified household contacts; a perirectal swab and swab of a soiled diaper from the patient were collected approximately 24 hours apart. Bacteria with the *mcr-1* gene were not

Infection Prevention Escalation

MRSA, VRE, ESBL

Basic

Infection Control

- Hand Hygiene
- Contact precautions

CRE

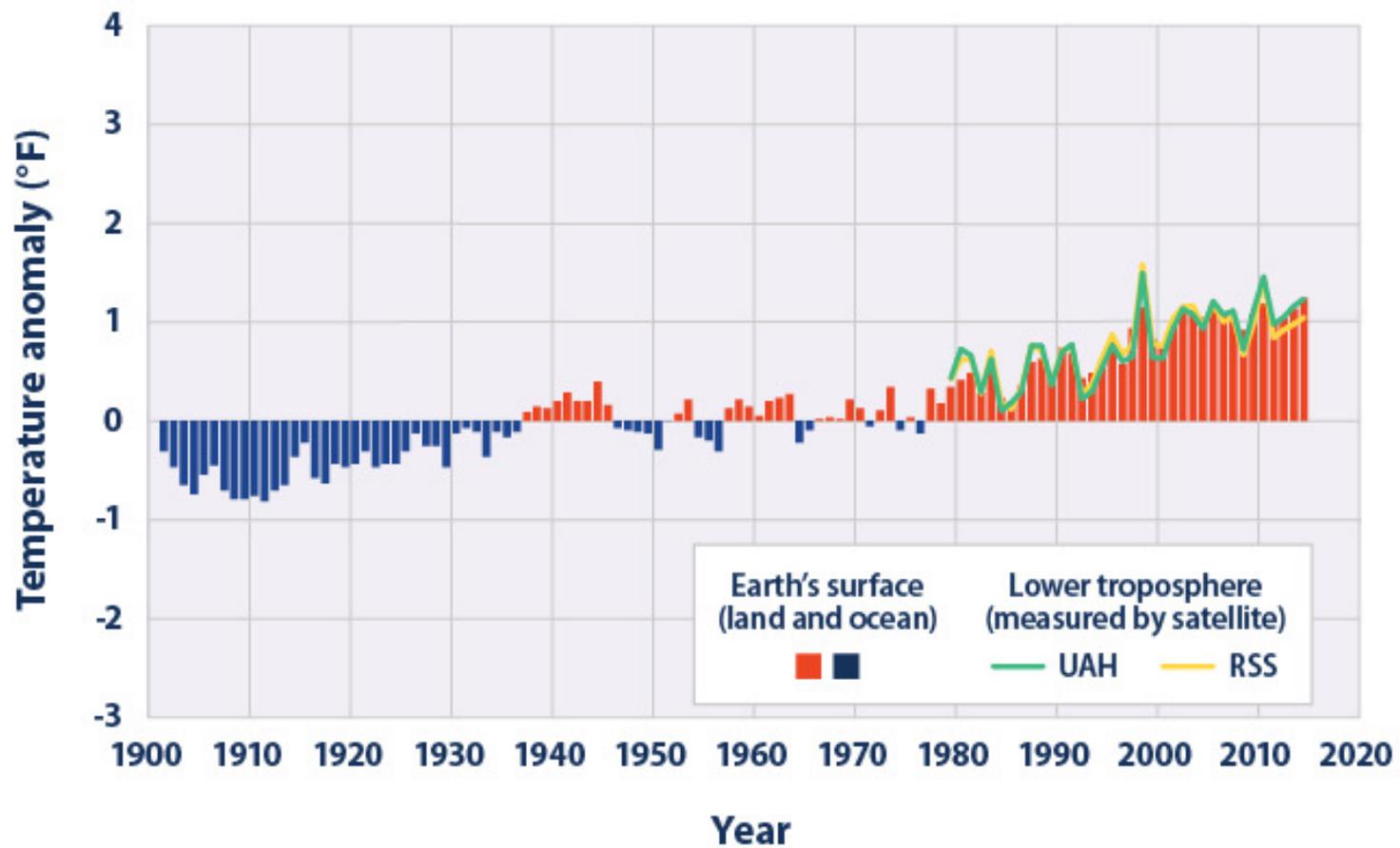
Intensive

Infection Control

- Hand Hygiene
- Contact precautions
- Cohort patients and staff
- Screening cultures of patient contacts
- Report to DPH



Temperatures Worldwide, 1901–2014

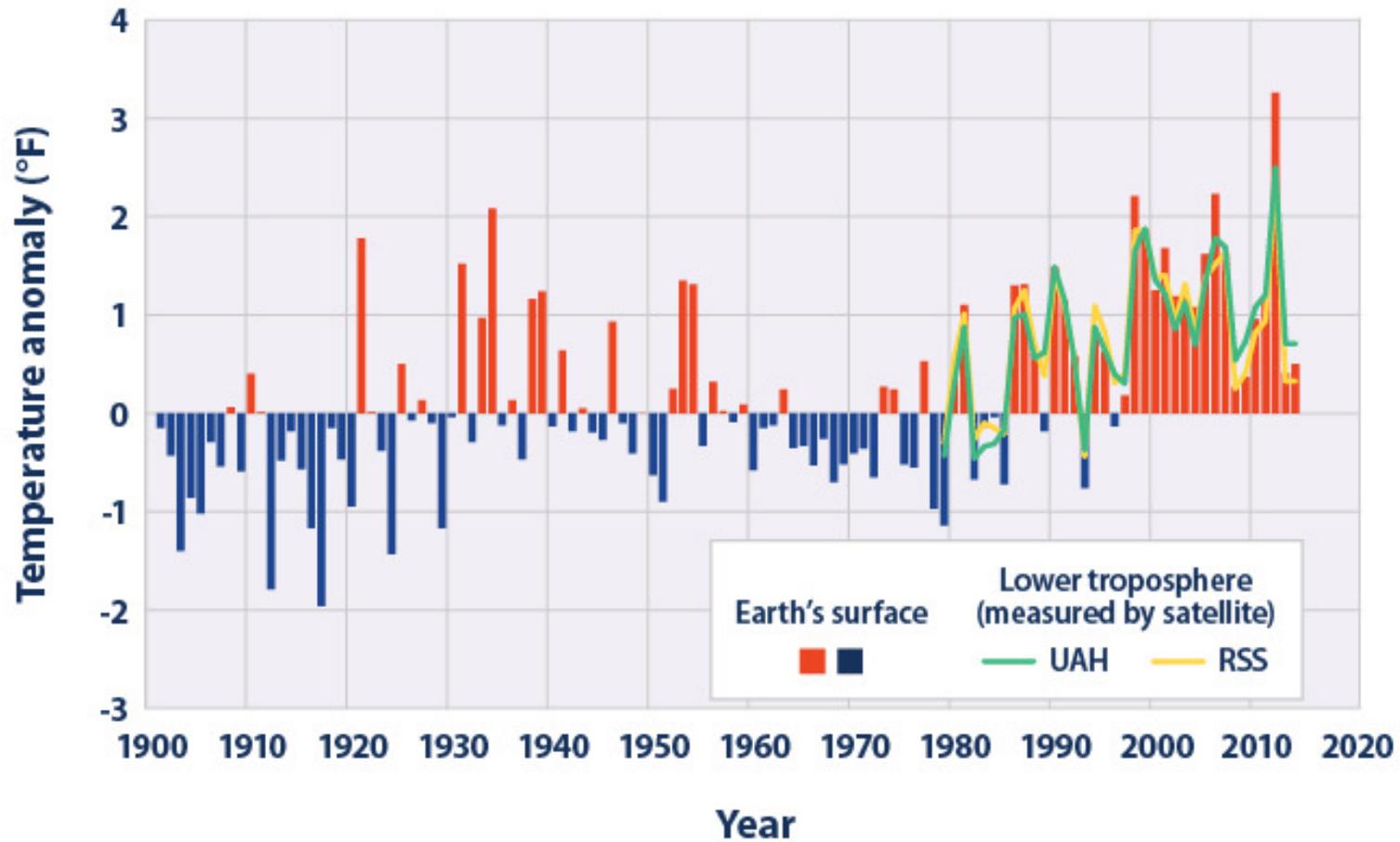


Data source: NOAA (National Oceanic and Atmospheric Administration). 2015. National Centers for Environmental Information. Accessed April 2015. www.ncei.noaa.gov.

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

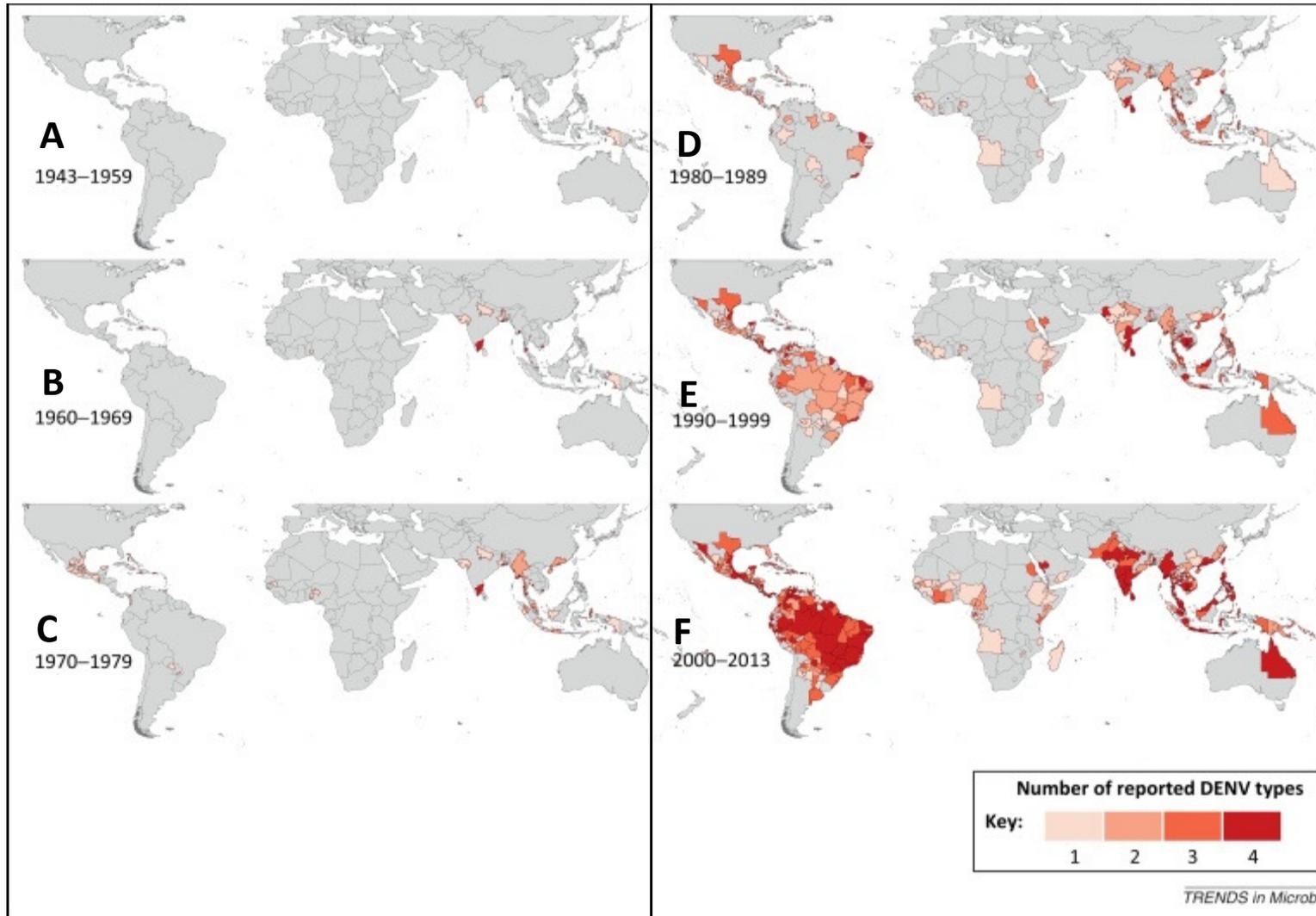


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For more information, visit U.S. EPA's "Climate Change Indicators in the United States" at www.epa.gov/climatechange/indicators.



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



Aedes species transmit:



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

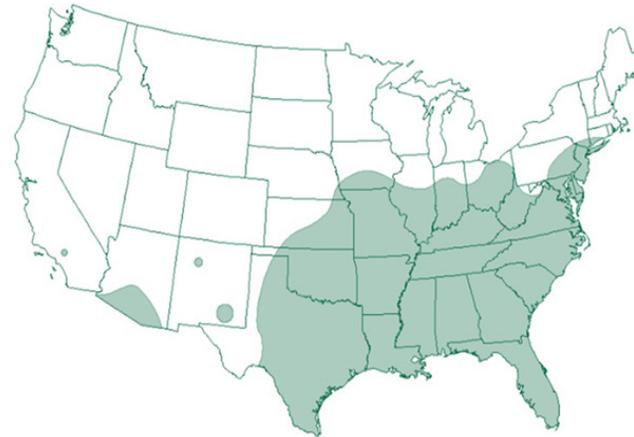


Aedes Distribution in United States

Aedes aegypti and *Aedes albopictus* Mosquitoes: Geographic Distribution in the United States



Aedes aegypti



Aedes albopictus



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



Where has Zika virus been found?

- Before 2015, Zika outbreaks occurred in Africa, Southeast Asia, and the Pacific Islands.
- As of June 20, 2016, outbreaks are occurring in over 50 countries
- Recent focus in South America, Central America and the Caribbean
- Mainland US cases are most related to travel (over 3500 cases so far; pregnant cases)
- Local cases in Florida
 - Other gulf coast states to follow



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



Example Zika virus incidence and attack rates, Yap 2007

- Infection rate: 73% (95% CI 68–77)
- Symptomatic attack rate among infected: 18% (95% CI 10–27)
- All age groups affected
- Adults more likely to present for medical care
- No severe disease, hospitalizations, or deaths

Note: Rates based on serosurvey on Yap Island, 2007
(population 7,391)



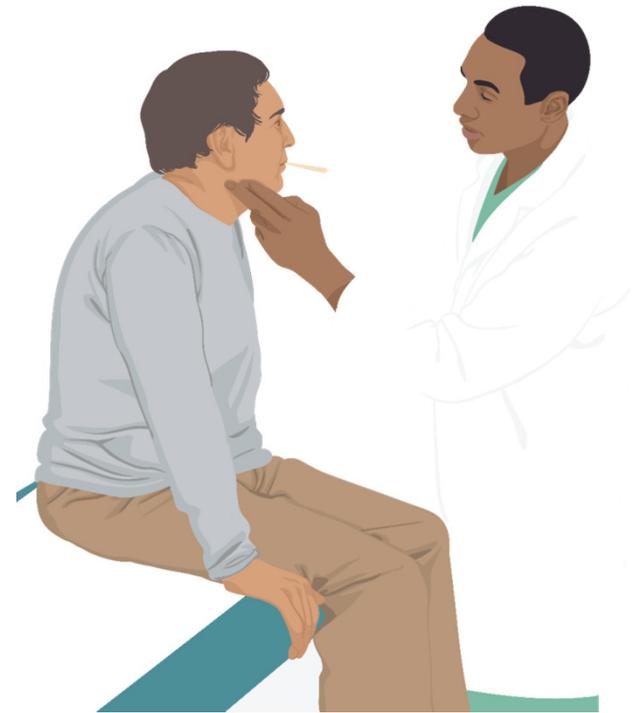
Incubation and viremia

- 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 – up to 2 months.
- Duration of virus in vaginal secretions, saliva, etc uncertain
- 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



Zika virus clinical disease course and outcomes

Barcellos C, Xavier DR, Pavao A, Boccolini C, Pina F, Pedroso M, et al. Increased hospitalizations for neuropathies in Brazil as indicators of Zika virus infection, according to health information system data, Brazil. *CDC release 9/8/16*

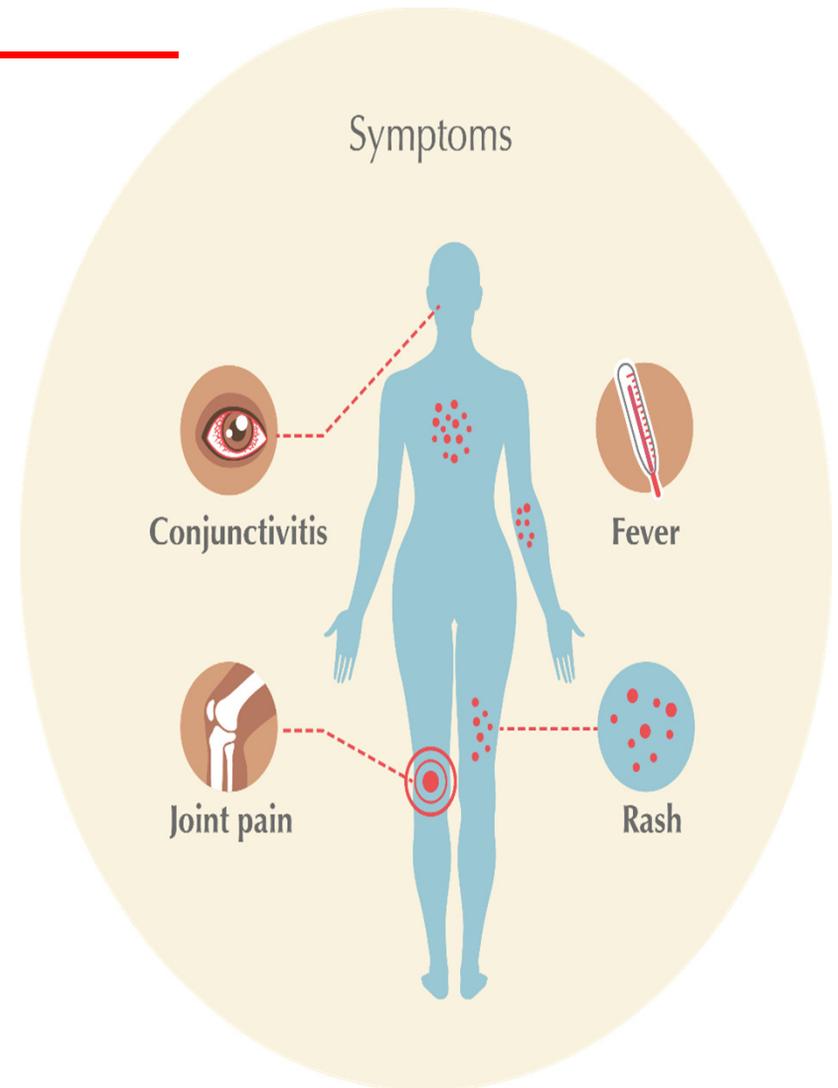
Abstract

Evidence is increasing that Zika virus can cause extensive damage to the central nervous system, affecting both fetuses and adults. We sought to identify traces of possible clinical manifestations of nervous system diseases among the registers of hospital admissions recorded in the Brazilian Unified Health System. Time series of several diagnoses from the International Classification of Diseases, 10th Revision, were analyzed by using control diagrams, during January 2008-February 2016. Beginning in mid-2014, we observed an unprecedented and significant rise in the hospitalization rate for congenital malformations of the nervous system, Guillain-Barré syndrome, encephalitis, myelitis, and encephalomyelitis. These conditions are compatible with viral infection and inflammation-associated manifestations and may have been due to the entrance of Zika virus into Brazil. These findings show the necessity of adequately diagnosing and treating suspected cases of Zika virus infection and also that health surveillance systems can be improved by using routine data.



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

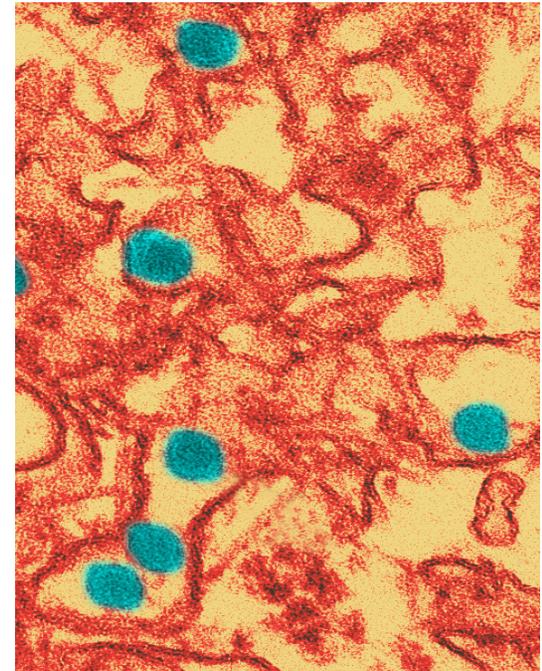
Skin rashes seen in Zika infections



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

Diagnostic testing for Zika virus

- PCR for viral RNA in clinical specimens collected ≤ 7 days (serum) or ≤ 14 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.



Testing availability

- State DOH
 - Requires preapproval
 - Phone -- **860-509-7994**
 - Fax -- **860-509-7910**
 - PCR
 - IgM antibody
 - PRNT (plaque reduction neutralization test)
- LabCorp
 - IgM antibody
 - PCR
- Quest
 - PCR



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
- Fetal and newborn outcomes
 - Microcephaly
 - Stillbirth
 - Poorly developed brain structures
 - Defects of the eye
 - Hearing deficits
 - Impaired intrauterine growth
 - Neurodevelopmental delay
 - Cognitive impairment



Zika virus in Pregnancy Brazil

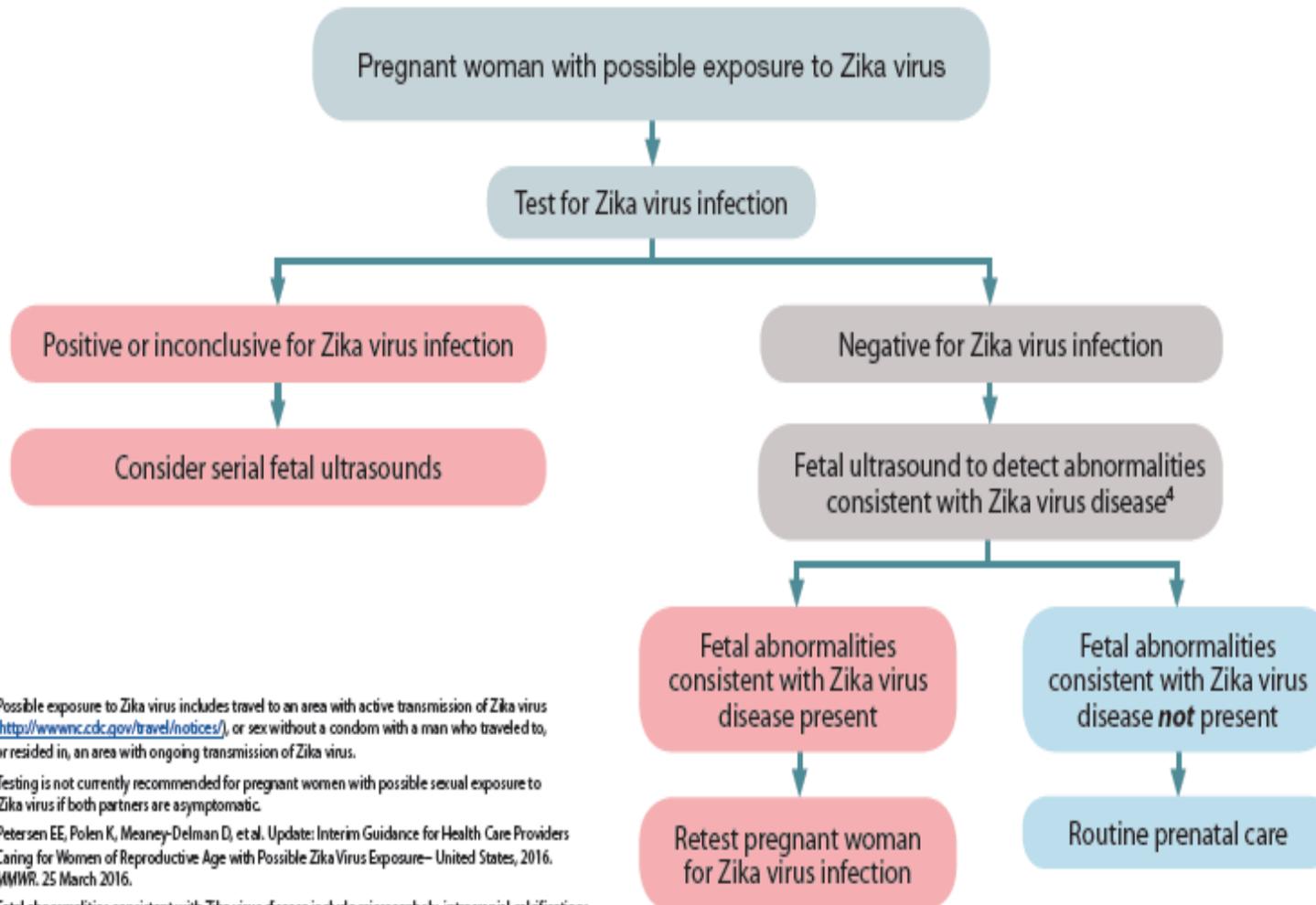
- 2016 Brazil study: 42 women with laboratory-confirmed Zika virus infection with prenatal ultrasound in 1st trimester
 - 12 (29%) abnormalities detected, including 2 intrauterine fetal deaths
 - 7 (17%) structural brain anomalies (microcephaly, calcifications, cerebellar atrophy)
- 2013-14 outbreak in French Polynesia
 - 8 cases of microcephaly identified
 - Modeling estimated infection with Zika during 1st trimester of pregnancy resulted in microcephaly risk of = 1%



CDC's Response to Zika

Updated Interim Guidance:

Testing Algorithm for a Pregnant Woman with Possible Exposure to Zika Virus^{1,2}, Not Residing in an Area with Active Zika Virus Transmission³



¹Possible exposure to Zika virus includes travel to an area with active transmission of Zika virus (<http://wwwnc.cdc.gov/travel/notices/>), or sex without a condom with a man who traveled to, or resided in, an area with ongoing transmission of Zika virus.

²Testing is not currently recommended for pregnant women with possible sexual exposure to Zika virus if both partners are asymptomatic.

³Petersen EE, Polen K, Meaney-Delman D, et al. Update: Interim Guidance for Health Care Providers Caring for Women of Reproductive Age with Possible Zika Virus Exposure— United States, 2016. *MMWR*. 25 March 2016.

⁴Fetal abnormalities consistent with Zika virus disease include microcephaly, intracranial calcifications, and brain and eye abnormalities. Fetal ultrasounds might not detect abnormalities until late second or early third trimester of pregnancy.



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

- Additional hearing screen at 6 months of age and audiology follow up of abnormal newborn hearing screening
- 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



Recommendations for Testing

- CDC recommends Zika virus testing for symptomatic people living in an active Zika transmission area, or who have recently traveled to an area with Zika, or who have had unprotected sex with a person confirmed to have Zika virus infection.
- CDC recommends for testing all pregnant women, regardless of symptoms, who have lived in or traveled to a Zika endemic area, or had sex with anyone who has recently traveled to a Zika endemic area
- CDC recommends testing newborns of mothers with positive or equivocal testing for Zika using PCR and IgM antibody at birth (not cord blood)



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 male partner who traveled

- If the male partner has been diagnosed with Zika or has (or had) symptoms, the couple should consider using condoms or not having sex for **at least 6 months** after symptoms begin.
- If the male partner does not develop symptoms, the couple should consider using condoms or not having sex for **at least 8 weeks (WHO 6 months)** after the man returns.



Prevention:

Non-pregnant couples with female partner who traveled

- Discuss signs and symptoms and potential adverse outcomes associated with Zika
- If Zika virus disease diagnosed, wait at least **8 weeks** after symptom onset to have sex and attempt conception.
- If **NO** symptoms develop, wait at least **8 weeks** after last date of exposure before having sex and attempting conception.



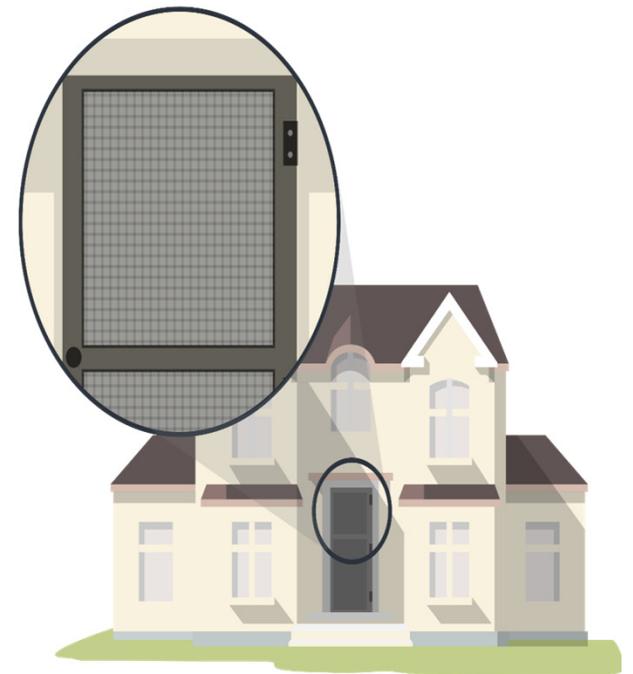
Patients returning from Zika Endemic area

- The virus can be passed from an infected person to a mosquito through bites.
- An infected mosquito can spread the virus to other people.
- If asymptomatic, use protection from mosquito bites for 3 weeks after returning from Zika endemic area
- If ill, protect from mosquito bites during the first week of illness, when Zika virus can be found in blood



Mosquito bite protection

- Wear long-sleeved shirts and long pants.
- Stay and sleep in places with air conditioning and window and door screens to keep mosquitoes outside.
- Take steps to control mosquitoes inside and outside your home
- Sleep under a mosquito bed net if you are overseas or outside and are not able to protect yourself from mosquito bites.
- Use EPA-registered insect repellents with one of the following active ingredients:
 - DEET, Picaridin, Oil of lemon eucalyptus
- If you are also using sunscreen, apply sunscreen before applying insect repellent.
- Use Permethrin to treat clothing
- Do not use insect repellent for children >2mo



Mosquito Bite Prevention (United States)



Not all mosquitoes are the same. Different mosquitoes spread different viruses and bite at different times of the day.

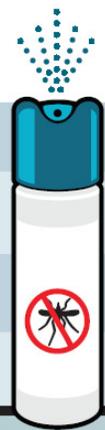
Type of Mosquito	Viruses spread	Biting habits
 <i>Aedes aegypti</i>, <i>Aedes albopictus</i>	Chikungunya, Dengue, Zika	Primarily daytime, but can also bite at night
 Culex species	West Nile	Evening to morning

Protect yourself and your family from mosquito bites

Use insect repellent

Use an Environmental Protection Agency (EPA)-registered insect repellent with one of the following active ingredients. When used as directed, EPA-registered insect repellents are proven safe and effective, even for pregnant and breastfeeding women.

Active ingredient	Some brand name examples*
Higher percentages of active ingredient provide longer protection	
DEET	Off!, Cutter, Sawyer, Ultrathon
Picaridin , also known as KBR 3023 , Bayrepel , and icaridin	Cutter Advanced, Skin So Soft Bug Guard Plus, Autan (outside the United States)
Oil of lemon eucalyptus (OLE) or para-menthane-diol (PMD)	Repel
IR3535	Skin So Soft Bug Guard Plus Expedition, SkinSmart



* Insect repellent brand names are provided for your information only. The Centers for Disease Control and Prevention and the U.S. Department of Health and Human Services cannot recommend or endorse any name brand products.



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.

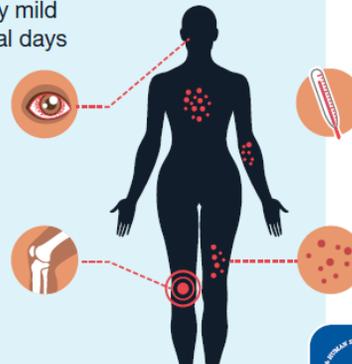
- For a current list of places with Zika outbreaks, see CDC's Travel Health Notices: <http://wwwnc.cdc.gov/travel/page/zika-travel-information>
- This notice follows reports in Brazil of microcephaly in babies of mothers who were infected with Zika virus while pregnant.

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



Hepatitis C



Identifying Patients with Hepatitis C

- 4-5 million people in the US have hepatitis C virus (HCV) infection
- Most were infected in 1960's through 1980's
 - Up to 250,000 cases per year in 1980's
 - About 50% infected via IDU, rest from blood transfusions, sex, tattoos, medical procedures, and other factors
- Up to 75% of people have not been diagnosed
- Risk-based screening misses many people
 - Stigma associated with IDU, even if decades ago

Smith BD et al. MMWR. August 17, 2012/61(RR04);1-18. Armstrong GL et al. Ann Intern Med. 2006 May 16;144(10):705-14.

<http://www.iom.edu/Reports/2010/Hepatitis-and-Liver-Cancer-A-National-Strategy-for-Prevention-and-Control-of-Hepatitis-B-and-C.aspx>



Who Should Be Tested for HCV?

CDC Recommendations

- Everyone born from 1945 through 1965 (one-time)
- Persons who ever injected illegal drugs
- Persons who received clotting factor concentrates produced before 1987
- Chronic (long-term) hemodialysis
- Persons with persistently abnormal ALT levels.
- Recipients of transfusions or organ transplants prior to 1992
- Persons with recognized occupational exposures
- Children born to HCV-positive women
- HIV positive persons

AHRQ Recommendations

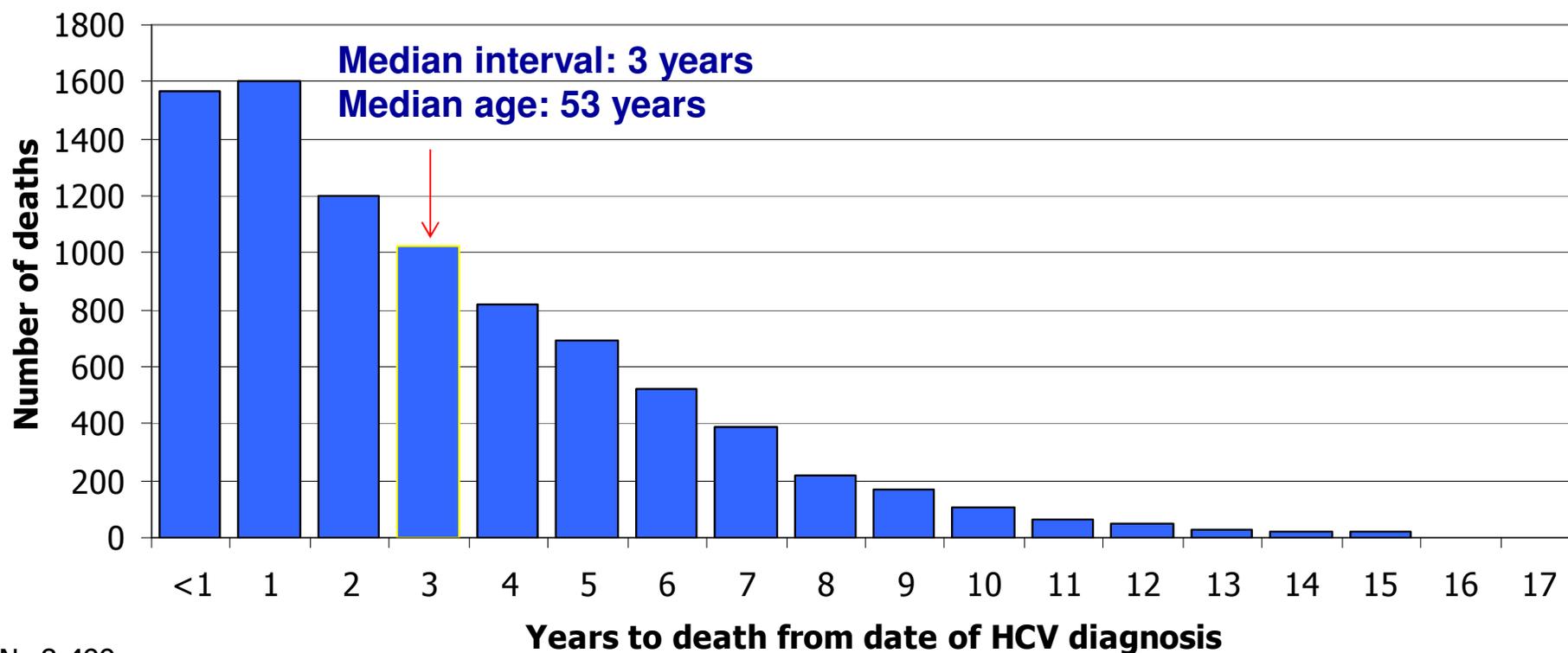
- Everyone born from 1945 through 1965 (one-time)
- Past or present injection drug use
- Sex with an IDU; other high-risk sex
- Blood transfusion prior to 1992
- Persons with hemophilia
- Long-term hemodialysis
- Born to an HCV-infected mother
- Incarceration
- Intranasal drug use
- Receiving an unregulated tattoo
- Occupational percutaneous exposure
- Surgery before implementation of universal precautions

*Only pertains to persons with normal liver enzymes; if elevated liver enzymes need HBV and HCV testing

Smith et al. Ann Intern Med 2012; 157:817-822. Moyer et al. Ann Intern Med epub 25 June 2013



Timing of Mortality Among Known HCV Cases in Massachusetts, 1992-2009



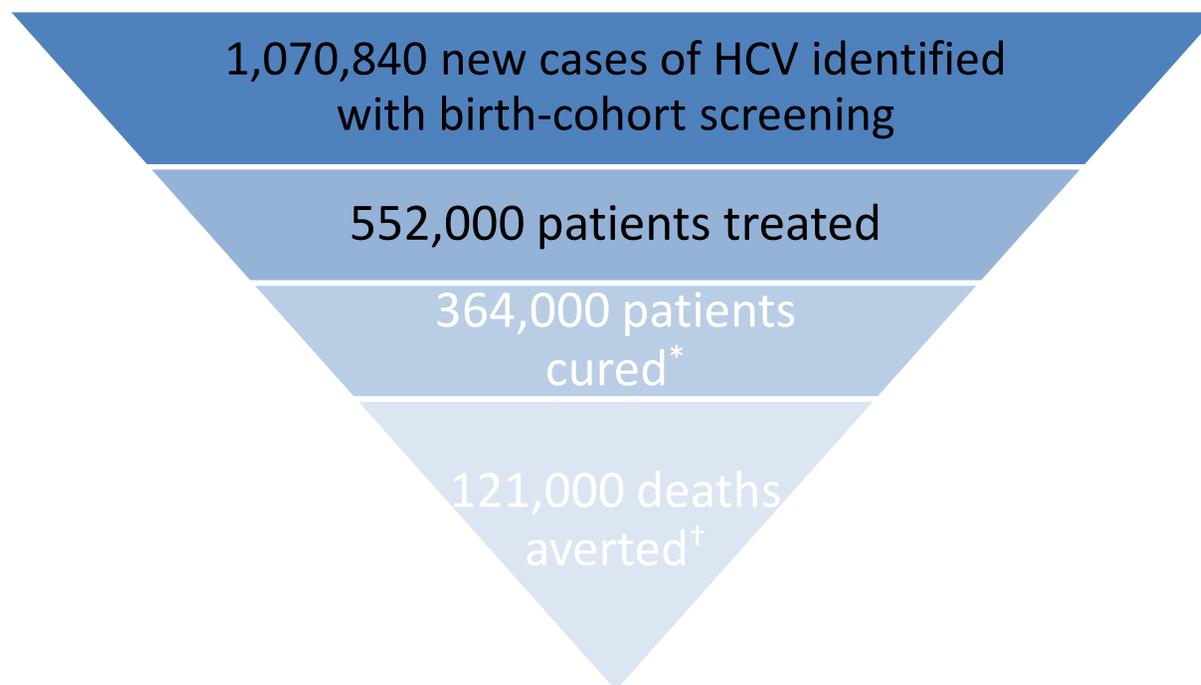
N=8,499

76,122 HCV diagnoses were reported to the MDPH between 1992 and 2009, 8,499 of these reported HCV cases died and are represented in the figure. Data as of 1/11/2011.



Lijewski, et al, 2012

Screening of Baby Boomers May Prevent >120,000 Deaths Due to HCV Infection



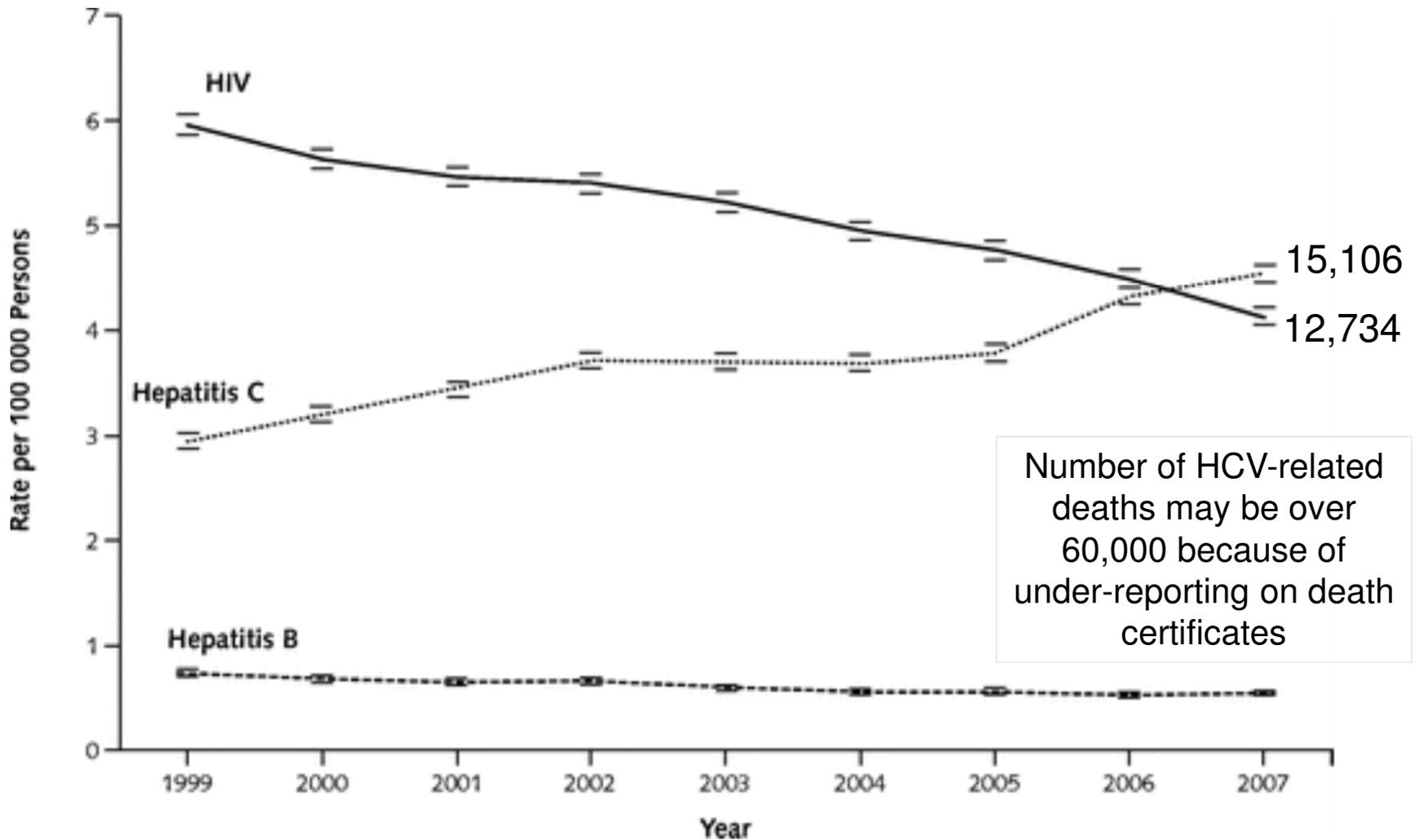
- › Birth-cohort screening in primary care would identify 86% of all undiagnosed cases in the birth cohort, compared with 21% under risk based screening¹
- › Cost effectiveness of HCV screening is comparable to cervical cancer or cholesterol screening (cost/QALY gained with protease inhibitor+IFN+RBV = \$35,700)

Markov chain Monte Carol simulation model of prevalence of hepatitis C antibody stratified by age, sex, race/ethnicity, history of injection drug use, and natural history of chronic hepatitis C.

*With pegylated interferon and ribavirin plus DAA treatment.

†Deaths due to decompensated cirrhosis or hepatocellular carcinoma within 1945-1965 birth cohort. 470,000 deaths under birth cohort screening vs 592,000 deaths under risk-based screening
1. Reir D et al. *Ann Intern Med.* 2012;156(4):263-270; 2. McGarry LJ et al. *Hepatology.* 2012;55(5):1344-1355.

Deaths Due to HCV Infections Now Exceed Those Due to HIV Infection



Goal of Hep C Treatment

- The goal of therapy is to cure HCV infection to prevent hepatic cirrhosis, decompensation of cirrhosis, HCC, severe extra-hepatic manifestations and death (
- The endpoint of therapy is undetectable HCV RNA in a sensitive assay (\leq 15 IU/ml) 12 weeks (SVR12) and 24 weeks (SVR24) after the end of treatment
- In patients with advanced fibrosis and cirrhosis, HCV eradication reduces the rate of decompensation and will reduce, albeit not abolish, the risk of HCC. In these patients surveillance for HCC should be continued
- In patients with decompensated cirrhosis, HCV eradication reduces the need for liver transplantation. Whether HCV eradication impacts mid- to long-term survival in these patients is unknown



Treatment Recommendations

- All treatment-naïve and treatment-experienced patients with compensated or decompensated chronic liver disease due to HCV should be considered for therapy
- Treatment should be prioritized for patients with significant fibrosis or cirrhosis (METAVIR score F3 to F4)
- Patients with decompensated cirrhosis (Child-Pugh B and C) should be urgently treated
- Treatment should be prioritized regardless of the fibrosis stage in patients with HIV or HBV coinfection, patients in the re- or post-liver transplant setting, patients with clinically significant extra-hepatic manifestations (e.g. symptomatic vasculitis associated with HCV-related mixed cryoglobulinaemia, HCV immune complex-related nephropathy and non-Hodgkin B cell lymphoma), and patients with debilitating fatigue



SVR-12 in Genotype 1 Patients Treated with Sofosbuvir+Ledipasvir (Harvoni)

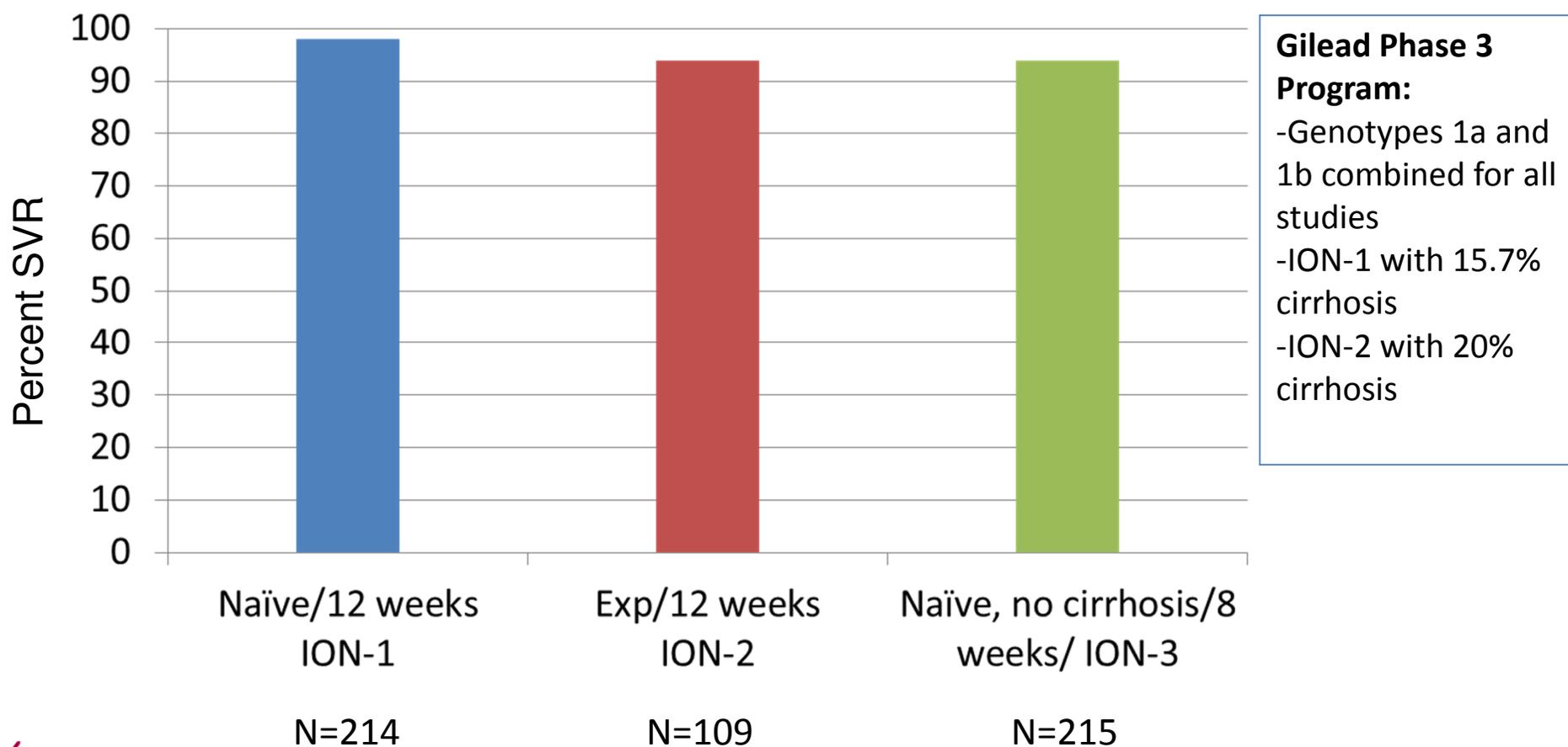


Table 1. Sofosbuvir/Velpatasvir Clinical Trials

Study Design	Duration	SVR12 Rate
Treatment-Naive and -Experienced Patients with or without Compensated Cirrhosis		
ASTRAL-1: genotypes 1, 2, 4, 5, 6 ¹ ; double-blind ²		
Sofosbuvir/velpatasvir (n=624)	12 weeks	99% ³
Placebo (n=116)	12 weeks	0%
ASTRAL-2: genotype 2; open-label ⁴		
Sofosbuvir/velpatasvir (n=134)	12 weeks	99% ⁵
Sofosbuvir + ribavirin (n=132)	12 weeks	94%
ASTRAL-3: genotype 3; open-label ⁴		
Sofosbuvir/velpatasvir (n=277)	12 weeks	95% ⁵
Sofosbuvir + ribavirin (n=275)	24 weeks	80%
Treatment-Naive and -Experienced Patients with Decompensated (Child-Pugh B) Cirrhosis		
ASTRAL-4: genotypes 1, 2, 3, 4, 5, 6 ⁶ ; open-label ⁷		
Sofosbuvir/velpatasvir (n=90)	12 weeks	83%
Sofosbuvir/velpatasvir + ribavirin (n=87)	12 weeks	94%
Sofosbuvir/velpatasvir (n=90)	24 weeks	86%

SVR12 = sustained virologic response (HCV RNA <15 IU/mL) at 12 weeks after the end of treatment

1. Because of the small number of patients with HCV genotype 5 (n=35), all received the active treatment.
2. JJ Feld et al. N Engl J Med 2015; 373:2599.
3. SVR12 rates by genotype: 1a - 98%, 1b - 99%, 2 - 100%, 4 - 100%, 5 - 97%, and 6 - 100%.
4. GR Foster et al. N Engl J Med 2015; 373:2608.
5. Statistically significant difference versus sofosbuvir + ribavirin for ASTRAL-2 (p = 0.02) and ASTRAL-3 (p<0.001).
6. No subjects with genotype 5 and only 1 with genotype 6 were enrolled.
7. MP Curry et al. N Engl J Med 2015; 373:2618.



Treatment Follow-up

- Non-cirrhotic patients with SVR should be retested for ALT and HCV RNA at 48 weeks post-treatment, then discharged if ALT is normal and HCV RNA is negative
- Cirrhotic patients, and probably also patients with advanced fibrosis (F3), with SVR should undergo surveillance for HCC every 6 months by means of ultrasound
- Guidelines for management of portal hypertension and varices should be implemented, though index variceal bleed is seldom seen in low-risk patients after the achievement of SVR (unless additional causes for ongoing liver damage are present and persist)
- The risk of reinfection should be explained to individuals with on-going risk behaviour, to positively modify risk behavior. Most relapses after successful SVR are new infections.
- Following SVR, monitoring for HCV reinfection through annual HCV RNA assessment should be undertaken in people who inject drugs or men who have sex with men with on-going risk behaviour



Table 4C. Drug-drug interactions between HCV DAAs and lipid lowering drugs.

	SIM	DCV	SOF	SOF/ LDV	3D
Atorvastatin	•	•	•	•	•
Bezafibrate	•	•	•	•	•
Ezetimibe	•	•	•	•	•
Fenofibrate	•	•	•	•	•
Fluvastatin	•	•	•	•	•
Gemfibrozil	•	•	•	•	•
Lovastatin	•	•	•	•	•
Pitavastatin	•	•	•	•	•
Pravastatin	•	•	•	•	•
Rosuvastatin	•	•	•	•	•
Simvastatin	•	•	•	•	•

SIM, simeprevir; DCV, daclatasvir; SOF, sofosbuvir; SOF/LDV, sofosbuvir plus ledipasvir; 3D, ritonavir-boosted paritaprevir, plus ombitasvir and dasabuvir.
Colour legend. Green: No clinically significant interaction expected. Amber: Potential interaction which may require a dosage adjustment, altered timing of administration or additional monitoring. Red: These drugs should not be co-administered.

- Some drugs may require dose modifications dependent on hepatic function. Please refer to the product label for individual drugs for dosing advice.
- The symbol (green, amber, red) used to rank the clinical significance of the drug interaction is based on www.hep-druginteractions.org (University of Liverpool). For additional drug-drug interactions and for a more extensive range of drugs, detailed pharmacokinetic interaction data and dosage adjustments, refer to the above-mentioned website.

****Particularly important for HIV antiretroviral, cardiovascular, psychotherapeutic , and lipid lower agents**



Cost of Treatment

The Medical Letter®

Vol. 58 (1501)

August 15, 2016

Table 2. Some Oral Regimens for HCV Infection

Brand Name	Formulation	Usual Dosage	Approved Genotypes	Number of Tabs/Day	Cost ¹
<i>Epclusa</i> (Gilead)	400/100 mg sofosbuvir/ velpatasvir tabs	1 tab once/d x 12 wks ^{2,3}	1-6	1 ⁴	\$74,760
<i>Harvoni</i> (Gilead)	90/400 mg ledipasvir/ sofosbuvir tabs	1 tab once/d x 12 wks ^{3,5}	1, 4, 5, 6	1 ⁴	94,500
<i>Sovaldi</i> (Gilead) + <i>Daklinza</i> (BMS)	400 mg sofosbuvir tabs + 60 mg daclatasvir tabs	1 sofosbuvir ³ tab and 1 daclatasvir tab once/d x 12 wks ⁶	1, 3	2 ⁴	147,000
<i>Sovaldi</i> (Gilead) + <i>Olysio</i> (Janssen)	400 mg sofosbuvir tabs + 150 mg simeprevir caps	1 sofosbuvir ³ tab and 1 simeprevir ⁷ cap once/d x 12 wks ⁸	1	2	150,360
<i>Technivie</i> (Abbvie)	12.5/75/50 mg ombitasvir/ paritaprevir/ritonavir tabs	2 tabs qAM x 12 wks ^{9,10}	4	2 ⁴	76,653
<i>Viekira Pak</i> (Abbvie)	12.5/75/50 mg ombitasvir/ paritaprevir/ritonavir tabs + 250 mg dasabuvir tabs	2 ombitasvir/paritaprevir/ritonavir tabs qAM and 1 dasabuvir tab bid x 12 wks ^{10,11}	1	4 ⁴	83,319
<i>Viekira XR</i> (Abbvie)	200/8.33/50/33.33 mg dasabuvir/ ombitasvir/paritaprevir/ritonavir extended-release tabs	3 tabs once/d x 12 wks ^{10,11}	1	3 ⁴	83,319 ¹²
<i>Zepatier</i> (Merck)	50/100 mg elbasvir/ grazoprevir tabs	1 tab once/d x 12 wks ^{10,13}	1, 4	1 ⁴	54,600



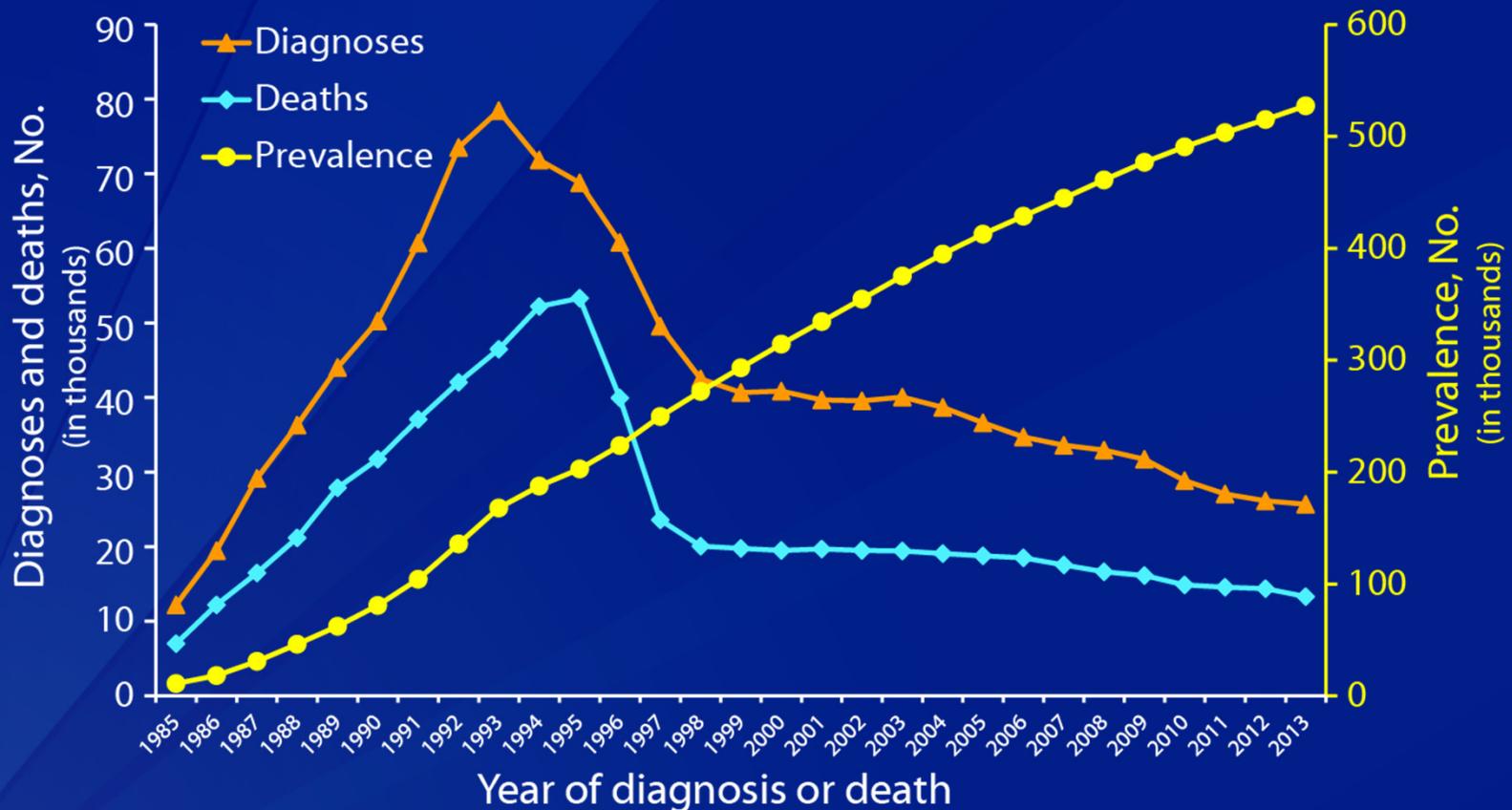
New Concepts in HIV

PreP – Pre-exposure Prophylaxis

TasP – Treatment as Prevention



Stage 3 (AIDS) Classifications, Deaths, and Persons Living with HIV Infection Ever Classified as Stage 3 (AIDS) 1985–2013—United States and 6 Dependent Areas



Note: All displayed data have been statistically adjusted to account for reporting delays, but not for incomplete reporting. Deaths of persons with HIV infection, stage 3 (AIDS) may be due to any cause.

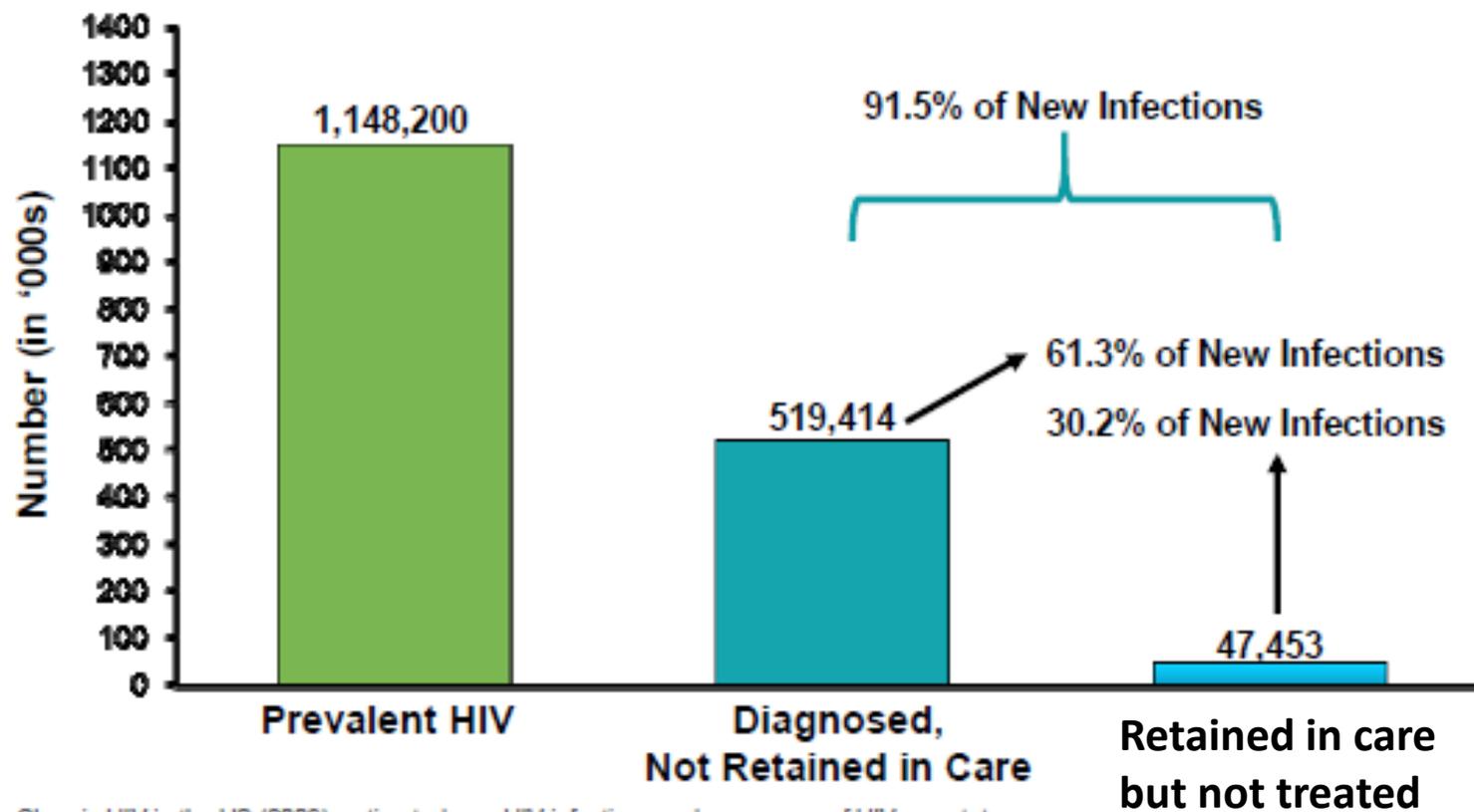


In the United States...

- More than 1.1 million people living with HIV infection
 - 1 in 6 are unaware that they are HIV positive
- Currently 50,000 new infections occur each year
- Highest transmission risk behaviors:
 - Men who have sex with men (MSM)
 - Particularly young, black/African men – incidence almost 8 times as high as whites
 - High risk heterosexual sex



Why PrEP? Almost 50,000 US HIV infections last year

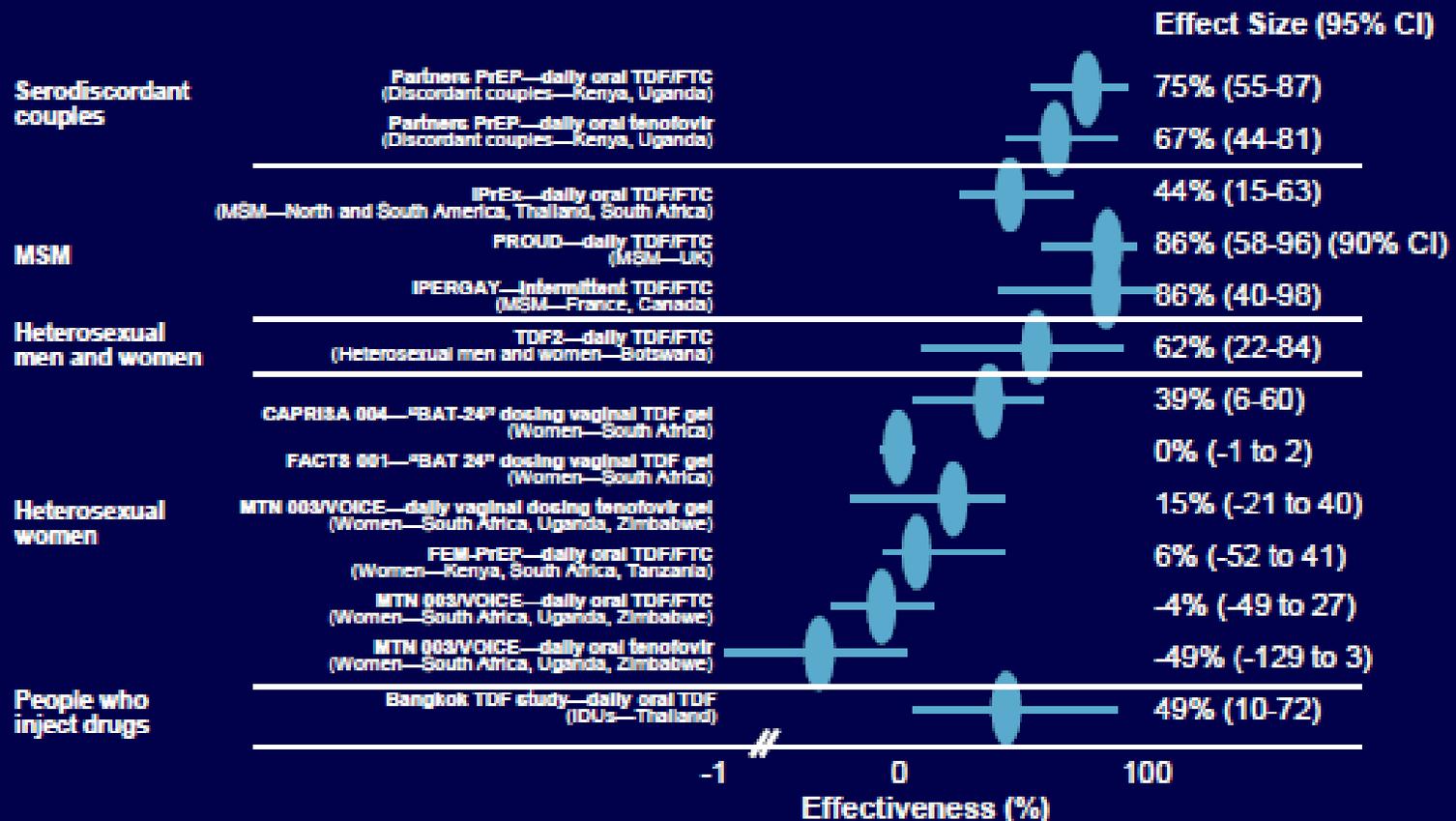


Chronic HIV in the US (2009): estimated new HIV infections and awareness of HIV serostatus.

Skarbinski J, et al. *JAMA Intern Med.* 2015;175:588-596.



Clinical Trial Evidence for Oral and Topical TDF-Based Prevention

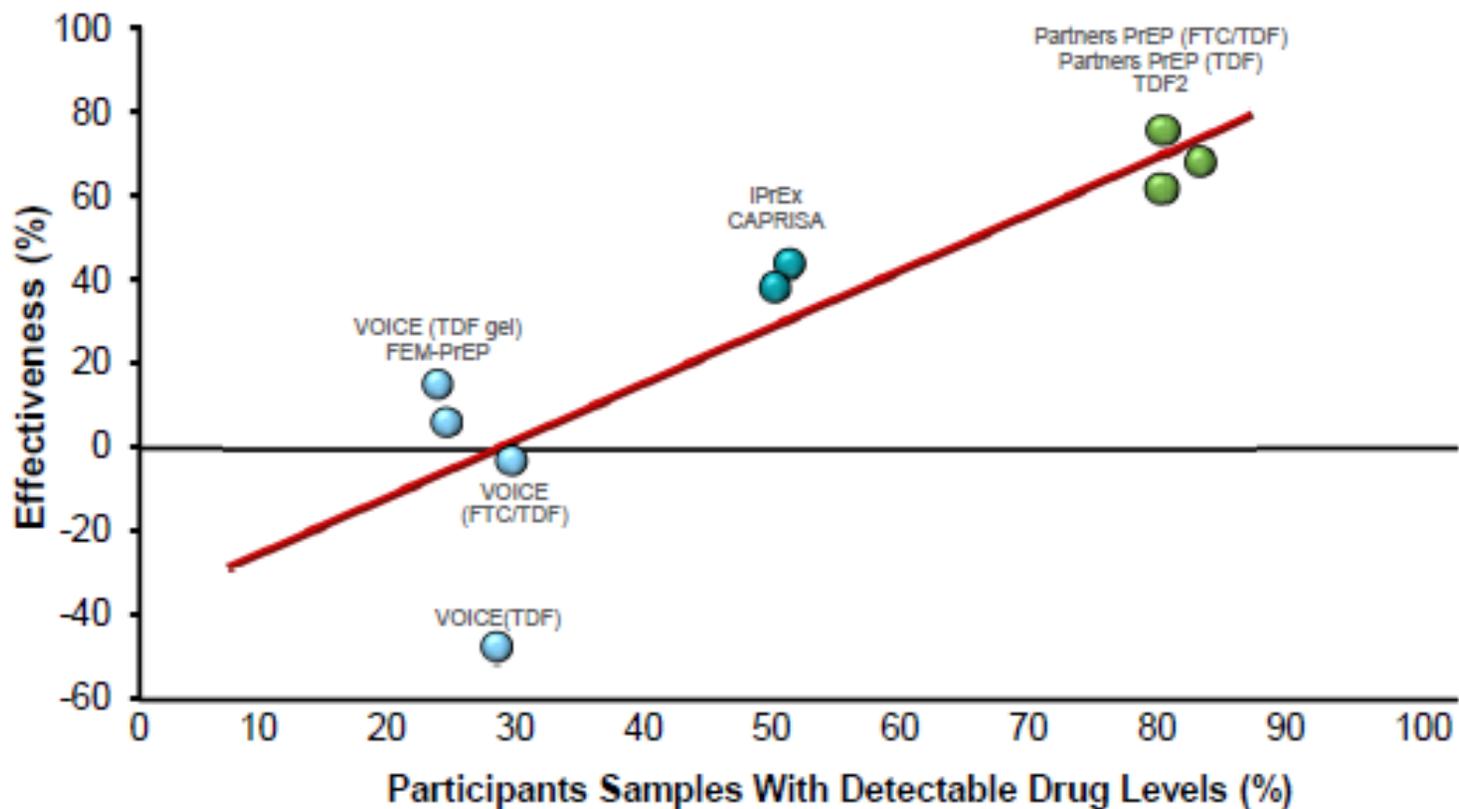


Mayer, KH, et al. *Curr Opin HIV AIDS*. 2015;10:226-232.

Modified from AVAC Report. 2013.



PrEP Is Effective: Adherence Is Critical

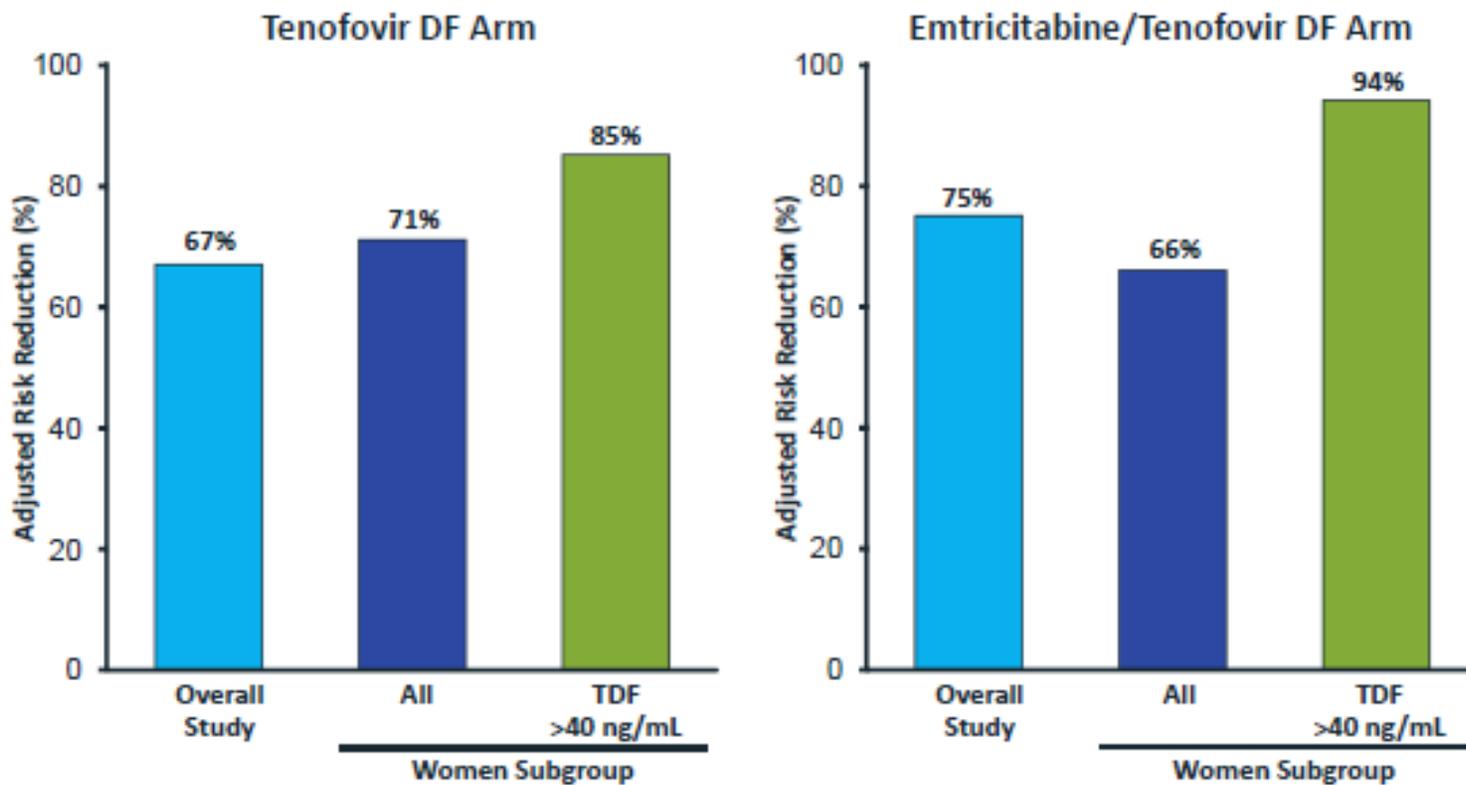


Pearson correlation: 0.86 ($P=0.003$).

AVAC Report 2013. http://www.avac.org/sites/default/files/resource-files/AVAC%20Report%202013_0.pdf.



Partners PrEP Study: Risk Reduction in HIV Acquisition Based on Tenofovir Levels

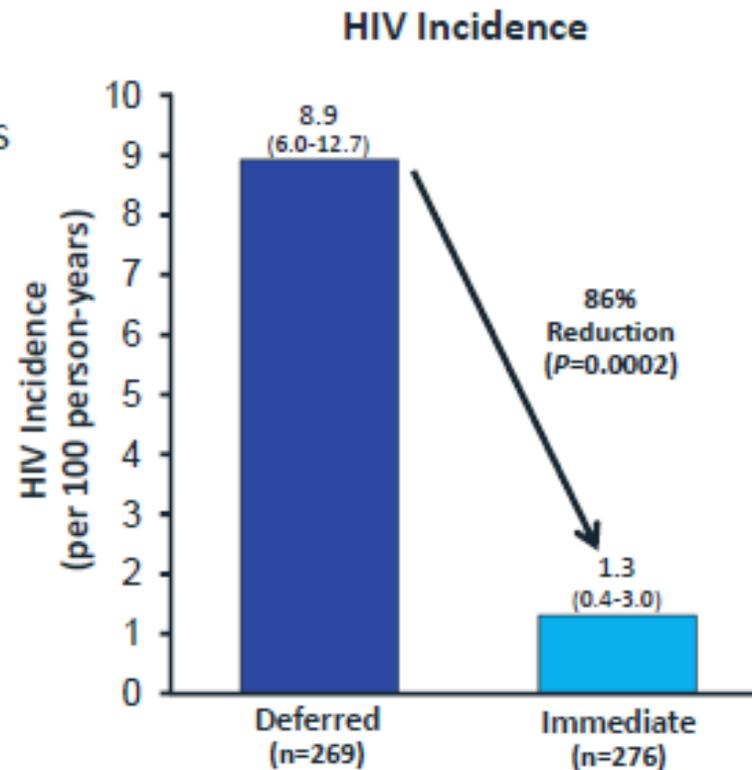


Thomson KA, et al. *Curr Opin HIV AIDS*. 2016;11:18-26.



PROUD Study: Results

- Significantly fewer new HIV infections with immediate versus deferred PrEP (3 versus 20 cases)
 - 86% reduction ($P=0.0002$)
- Incident HIV infection in the immediate group
 - HIV infection predated start of ART ($n=1$)
 - No drug/not adherent ($n=2$)
- Number needed to treat to prevent 1 HIV infection: 13



McCormack S, et al. *Lancet*. 2016;387:53-60.



PrEP Use and HIV/STI Incidence in a Clinical Practice Setting

- Analysis of PrEP use and HIV/STI incidence in PrEP users in large healthcare system (Kaiser Permanente San Francisco) from 2012 to 2015
- 1045 referrals for PrEP; 801 individuals with ≥ 1 intake visit
- 657 initiated PrEP (82%*); mean duration of use 7.2 mos
- Key results (PrEP initiators):
 - After 12 months, 50% diagnosed with any STI
 - 33% rectal STI; 33% chlamydia; 28% gonorrhea
 - No HIV diagnoses (388 PY follow-up)
 - After 6 mos PrEP, self-reported condom use was decreased in 41% of individuals

*Of persons with ≥ 1 intake visit.

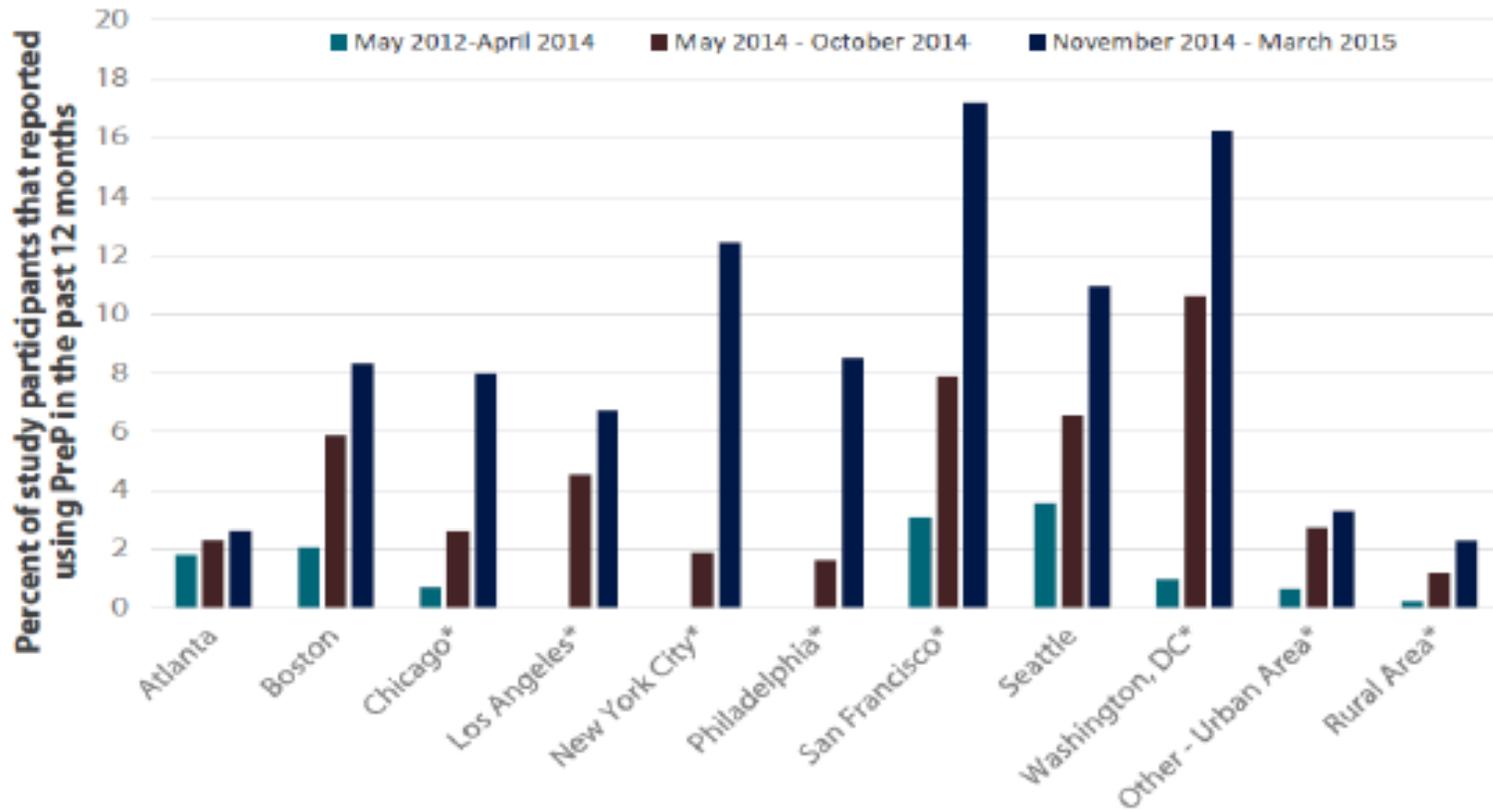
Volk JE, et al. Clin Infect Dis. 2015;61:1601-1603.



Changes in PrEP Use Among U.S. MSM

(3 web surveys, N=10,097)

Delaney et al, CROI, 2016



Treatment as Prevention (TasP)

Two major studies have underlined the considerable power of HIV treatment to prevent the spread of the virus, adding greater scientific heft to the notion that it may in fact be impossible to transmit HIV with a fully suppressed viral load.

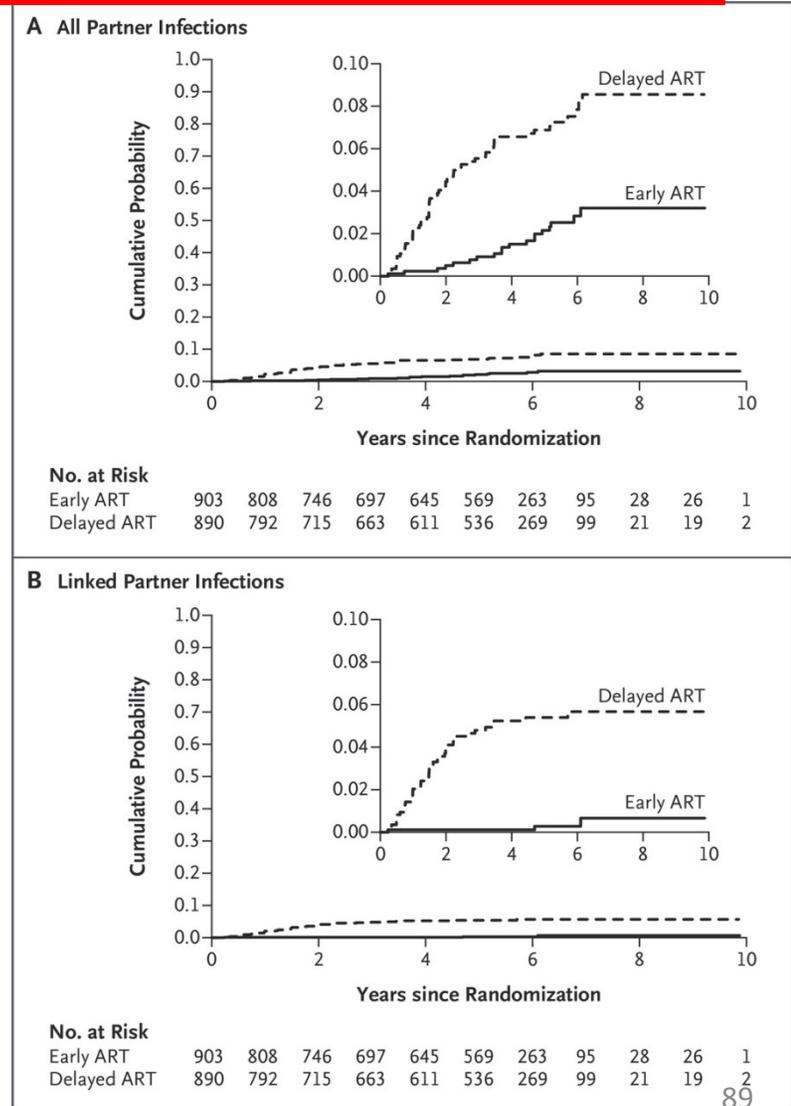
- In 2011, interim results from the HPTN 052 trial found that starting HIV treatment early rather than delaying was associated with a 96 percent reduced risk of transmission among mixed-HIV-status heterosexual couples
- Interim results from the PARTNER study in 2014, which included both heterosexual and male-male mixed-HIV-status couples, also found no transmissions between partners when the virus was fully suppressed.



Antiretroviral Therapy for the Prevention of HIV-1 Transmission (052)

- Over the course of the study involving HIV-1 serodiscordant couples, there was a 93% lower risk of genetically linked HIV-1 infection among partners in the early-ART group than in the delayed-ART group in the intention-to-treat analysis.
- Between May 2011 and May 2015, there were only two cases of linked HIV-1 infection per 2573 person-years of follow-up.

Cohen MS et al. N Engl J Med 2016;375:830-839.



Thank You!



Questions?

