Emerging Infections

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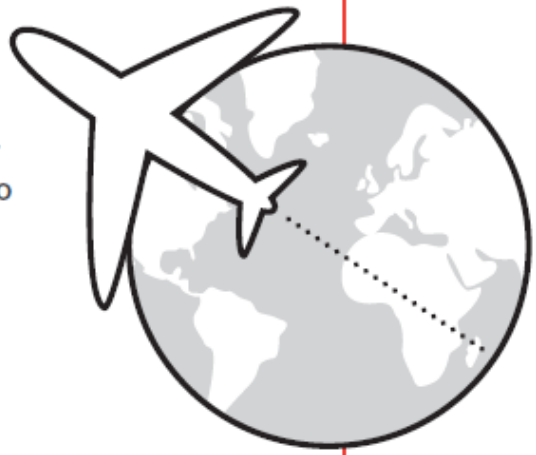
Emerging Infections

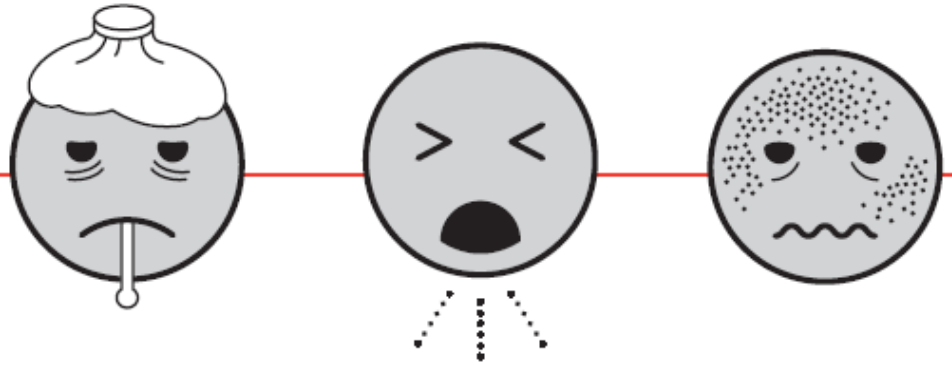
- Discussed today
  - Antimicrobial resistance
  - Zika update
- Not discussed today
  - Measles, pertussis, novel influenza, Ebola, MERS, Lyme, cholera, and many more…

IF YOU

recently **traveled internationally** or had close contact with someone who recently traveled internationally and was ill,



AND YOU HAVE



fever, cough, trouble breathing, rash, vomiting or diarrhea,

PLEASE TELL STAFF IMMEDIATELY!

Contributing Factors

- International travel and commerce (movement of goods and people)
- Ecological changes (economic development, land use; agriculture; dams; deforestation and reforestation; climate change)
- Human demographic factors (population growth, migration, war and conflict; sexual behavior, IV drug use)

Institute of Medicine Report, 1992; Stephen Morse, EID Vol. 1, No. 1, Jan-March 1995

Contributing Factors

- Technology and industry (mass food production, globalization of food supply, organ transplants)
- Microbial adaptation, evolution, e.g., genetic drift and genetic shift in influenza A, selective (antimicrobial) pressure
- Breakdown in public health measures (conflict, bankruptcy, premature program cuts, inadequate sanitation / inadequate sterile environment)

Institute of Medicine Report, 1992; Stephen Morse, EID Vol. 1, No. 1, Jan-March 1995

Antimicrobial Resistance

Forward to the Past

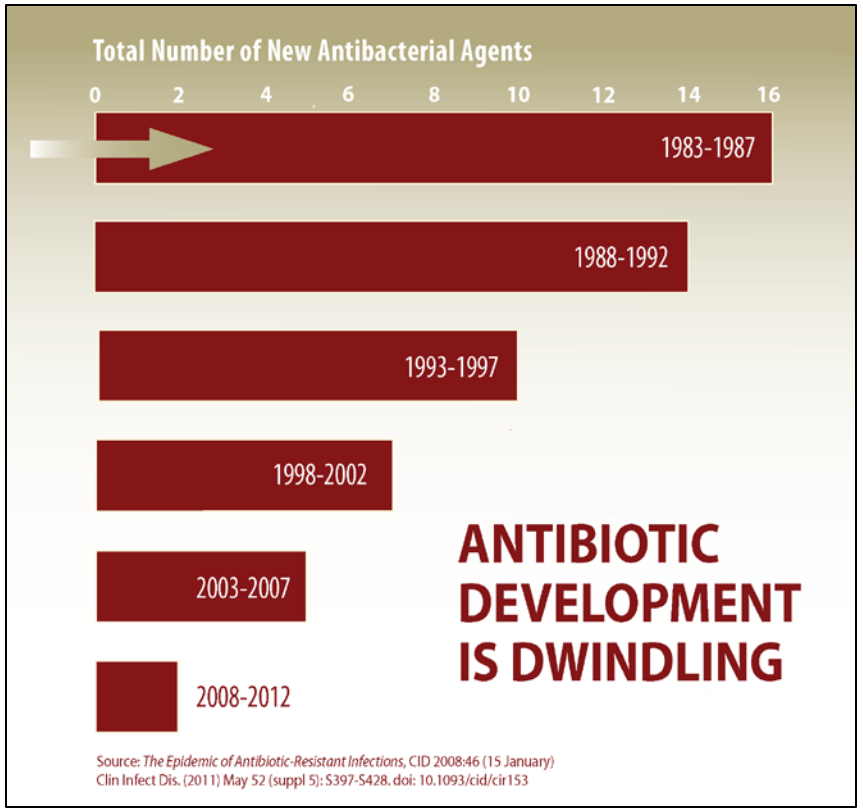
The Life-Saving Benefits of Antibiotic Use

- Once deadly infectious diseases treatable, substantially reducing deaths compared to the pre-antibiotic era
- Important adjunct to modern medical advances
  - Surgeries
  - Transplants
  - Cancer therapies

Lauri Hicks, CDC: "Call to Action: Improving Antibiotic Use"

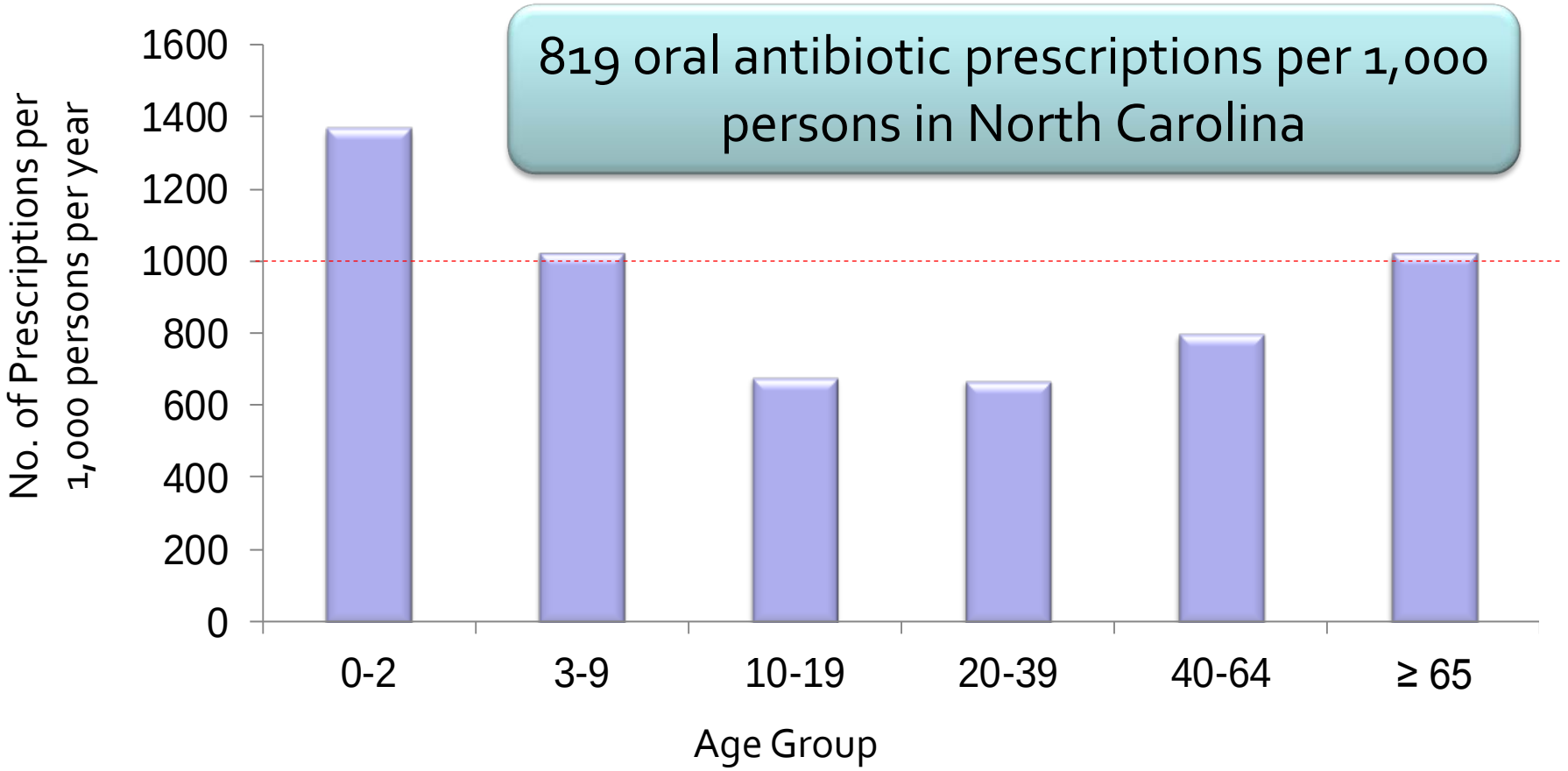
The End of the Antibiotic Era?

- No new types of antibiotics developed in over 10 years
- More toxic antibiotics being used to treat common infections
- Must treat antibiotics as precious and finite resource



Lauri Hicks, CDC: "Call to Action: Improving Antibiotic Use"

Volume of Antibiotic Prescriptions, 2010



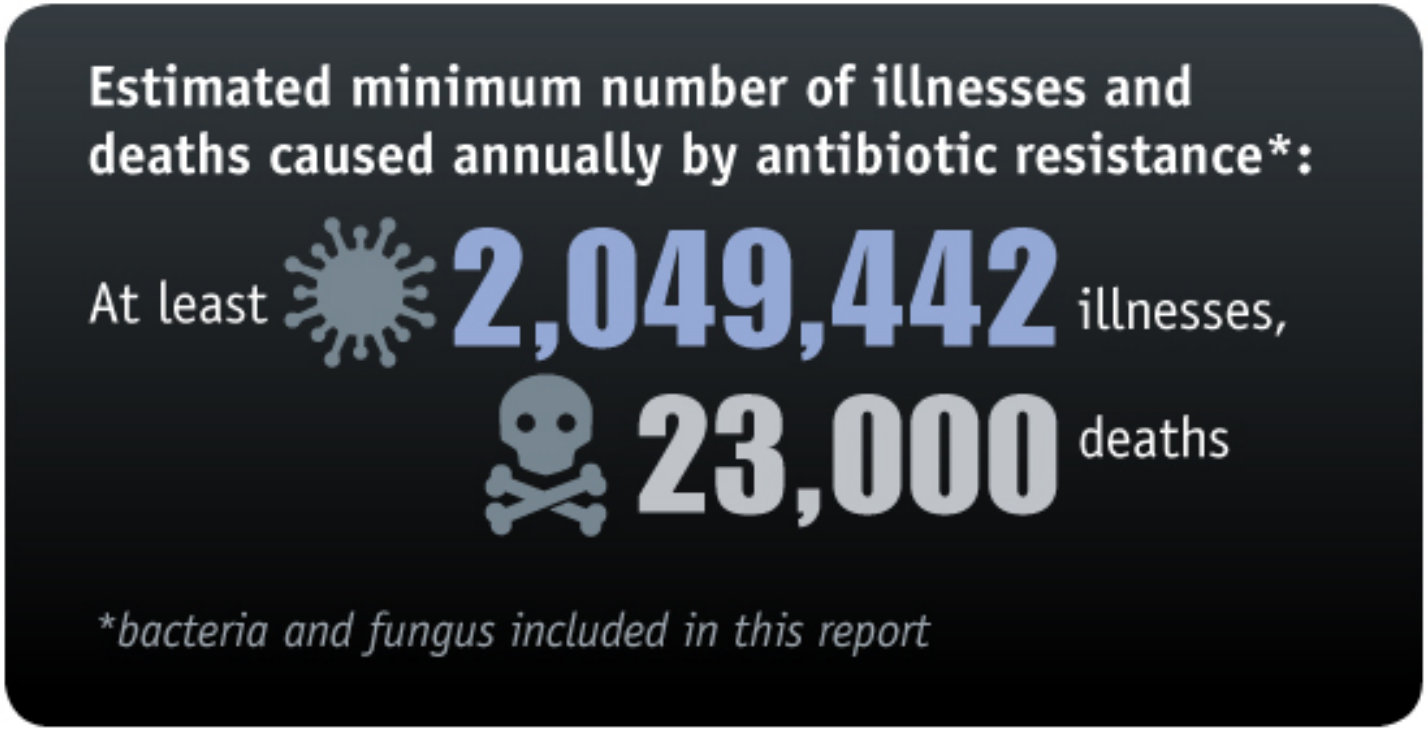
Hicks LA et al. N Engl J Med 2013;368:1461-1462 and
http://www.cddep.org/resistancemap/use

Unintended Consequences of Antibiotic Use

- Antibiotic resistance
- Increased health-care costs
- Adverse drug events
  - Hypersensitivity/allergy
  - Antibiotic associated diarrhea/colitis
  - Other side effects
  - *Clostridium difficile* infection

Ohl CA, Luther VP. J. Hosp. Med. 2011;6:S4

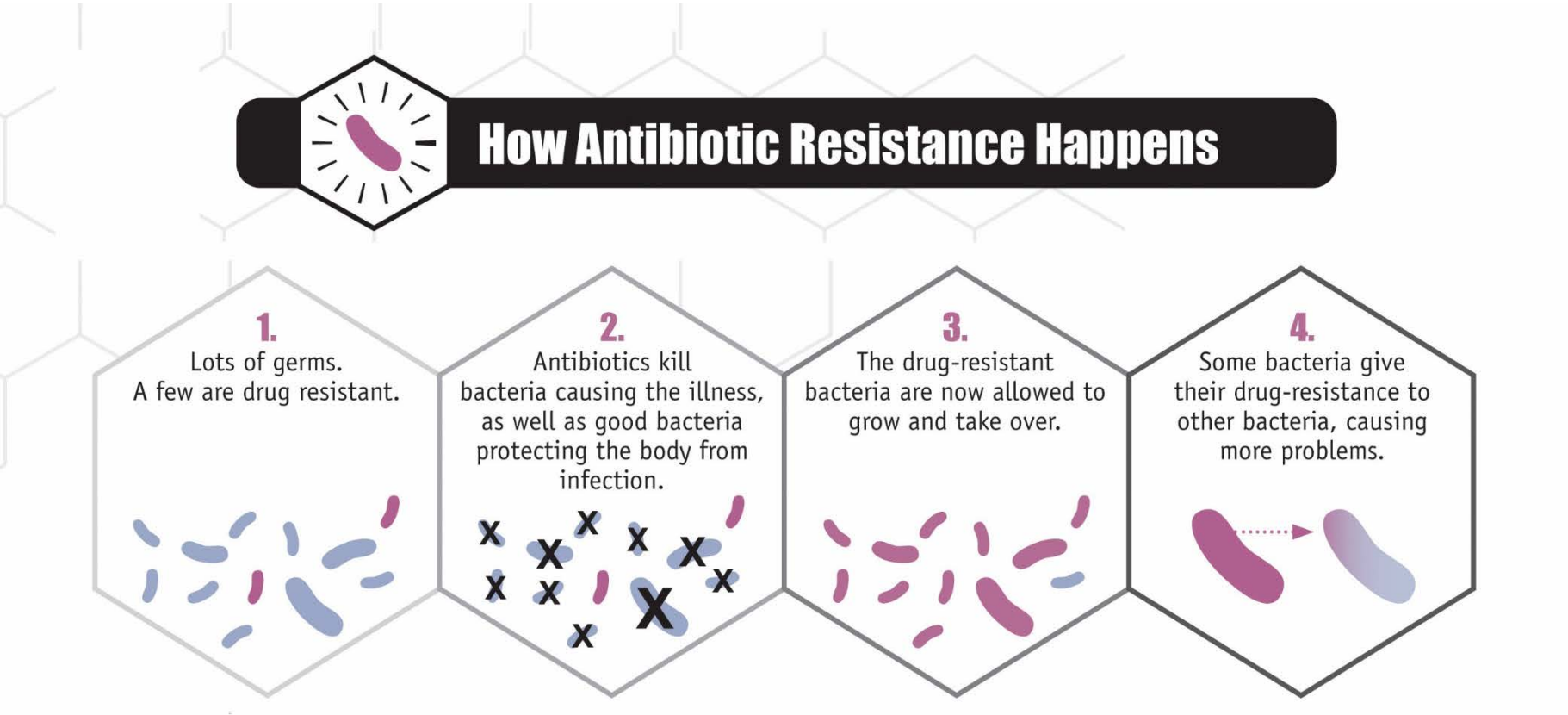
Unintended Consequences of Antibiotic Use: Antibiotic Resistance



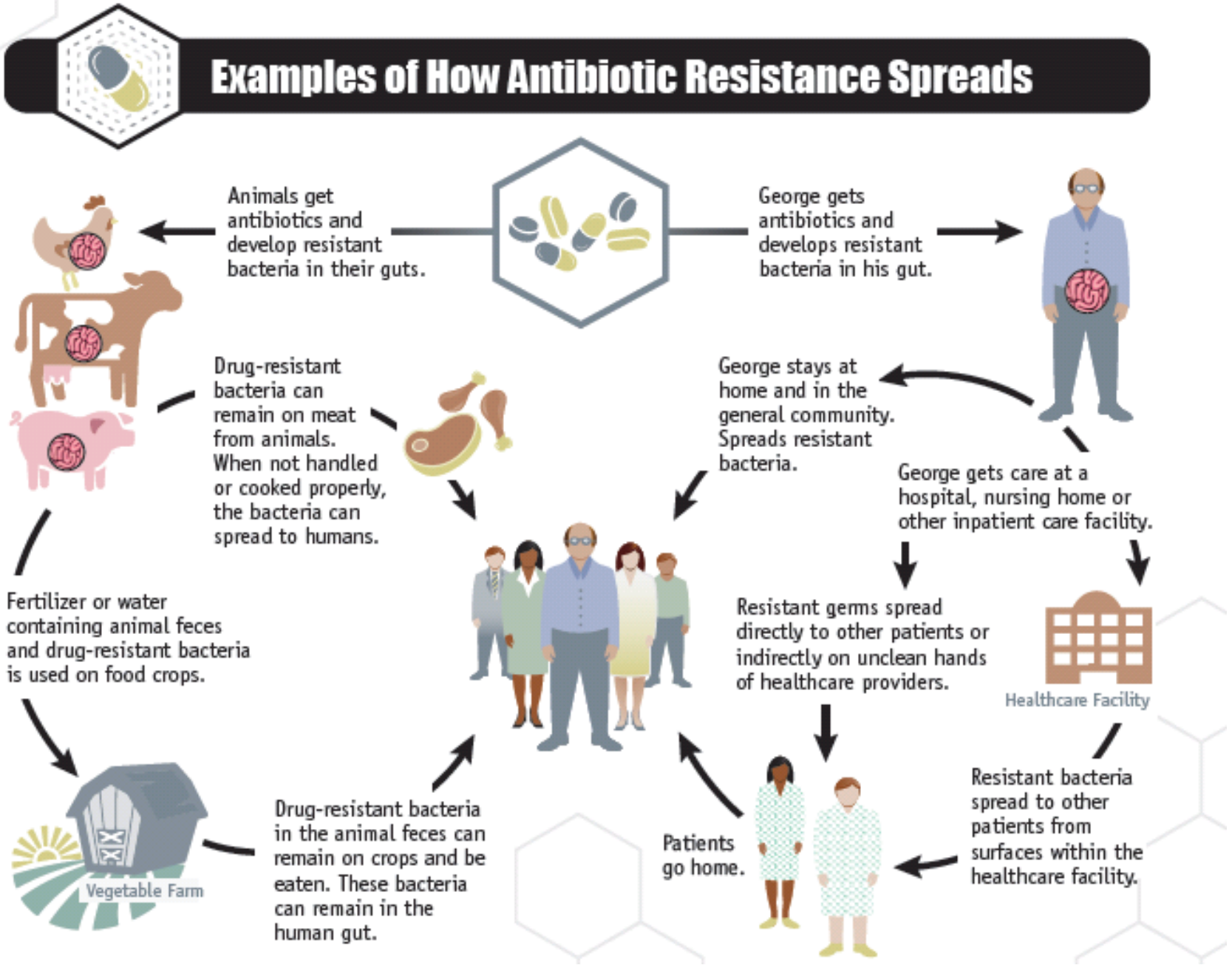
Estimated cost of $30 billion annually
(range $20-$35 billion, 2008 dollars)

Lauri Hicks, CDC: "Call to Action: Improving Antibiotic Use"

Unintended Consequences of Antibiotic Use: Antibiotic Resistance

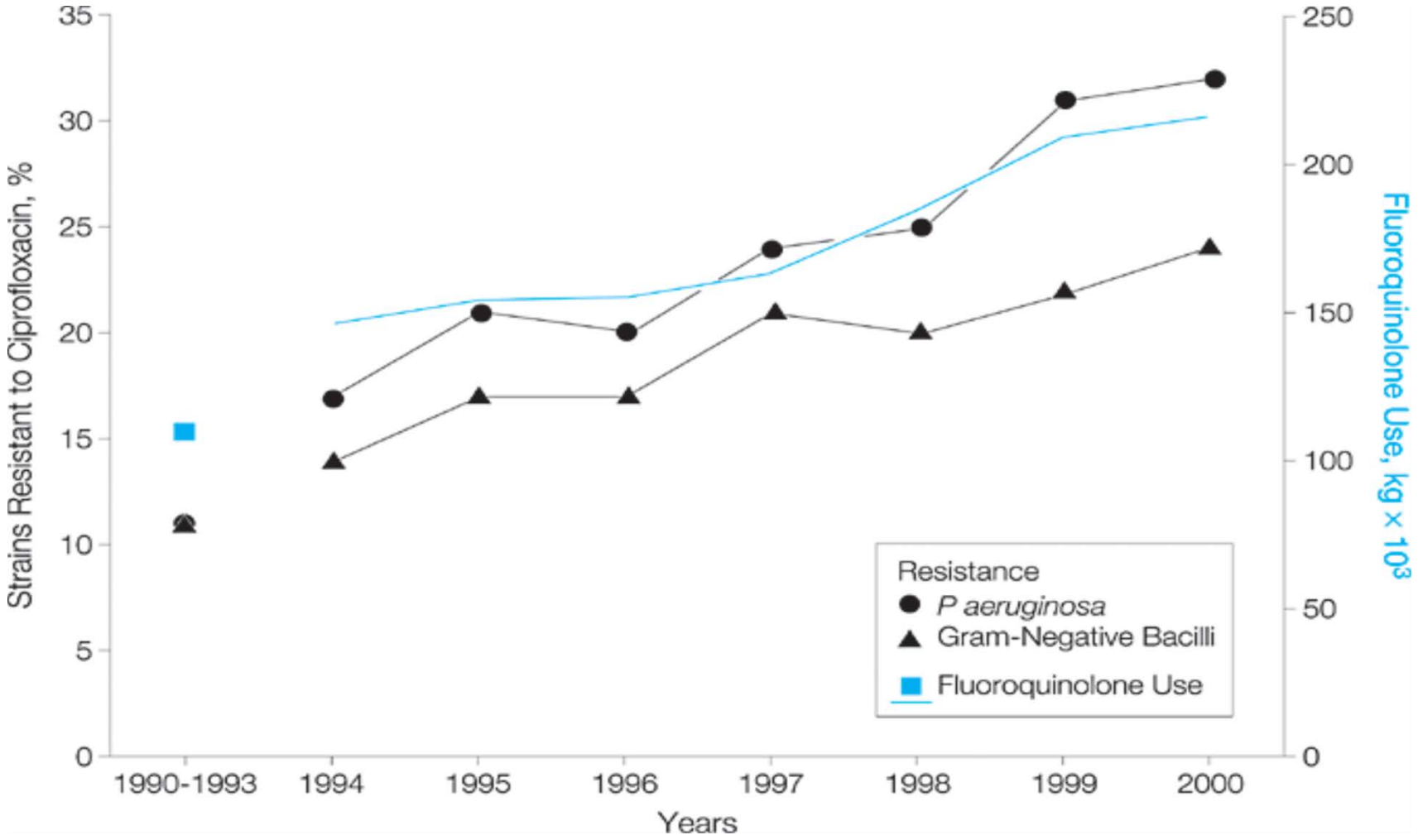


CDC. Antibiotic resistance threats in the United States, 2013.
www.cdc.gov/drugresistance/threat-report-2013/



http://www.cdc.gov/drugresistance/threat-report-2013/

Fluoroquinolone Use and Resistance in ICUs, 1993–2000



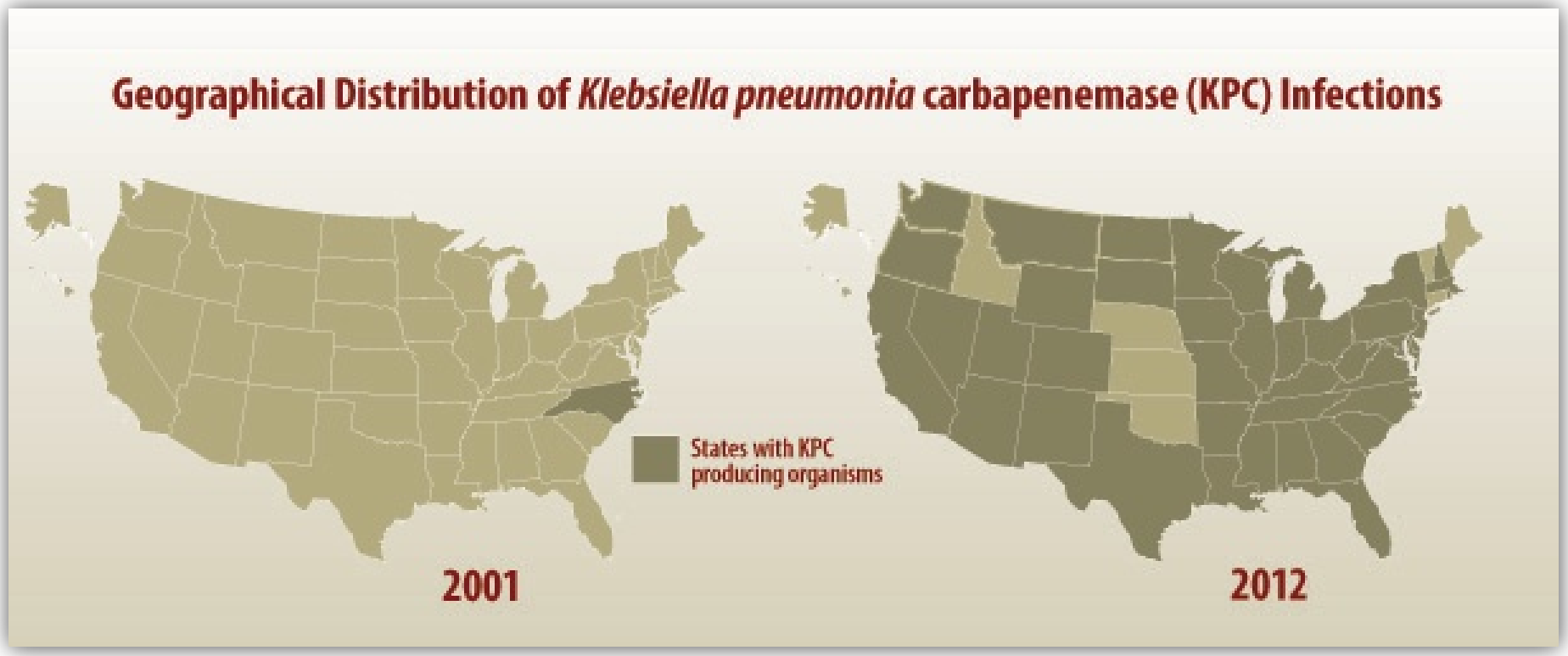
Neuhauser et al. JAMA. 2003;289(7):885-888

Carbapenem-Resistant Enterobacteriaceae (CRE)

- Resistant to all or nearly all antibiotics
- *Klebsiella pneumoniae* carbapenemase (KPC) reported in 2001 from NC isolate
  - Plasmid-mediated
  - Confers resistance to all β-lactams/carbapenems
  - Easily transferred to nonresistant bacteria

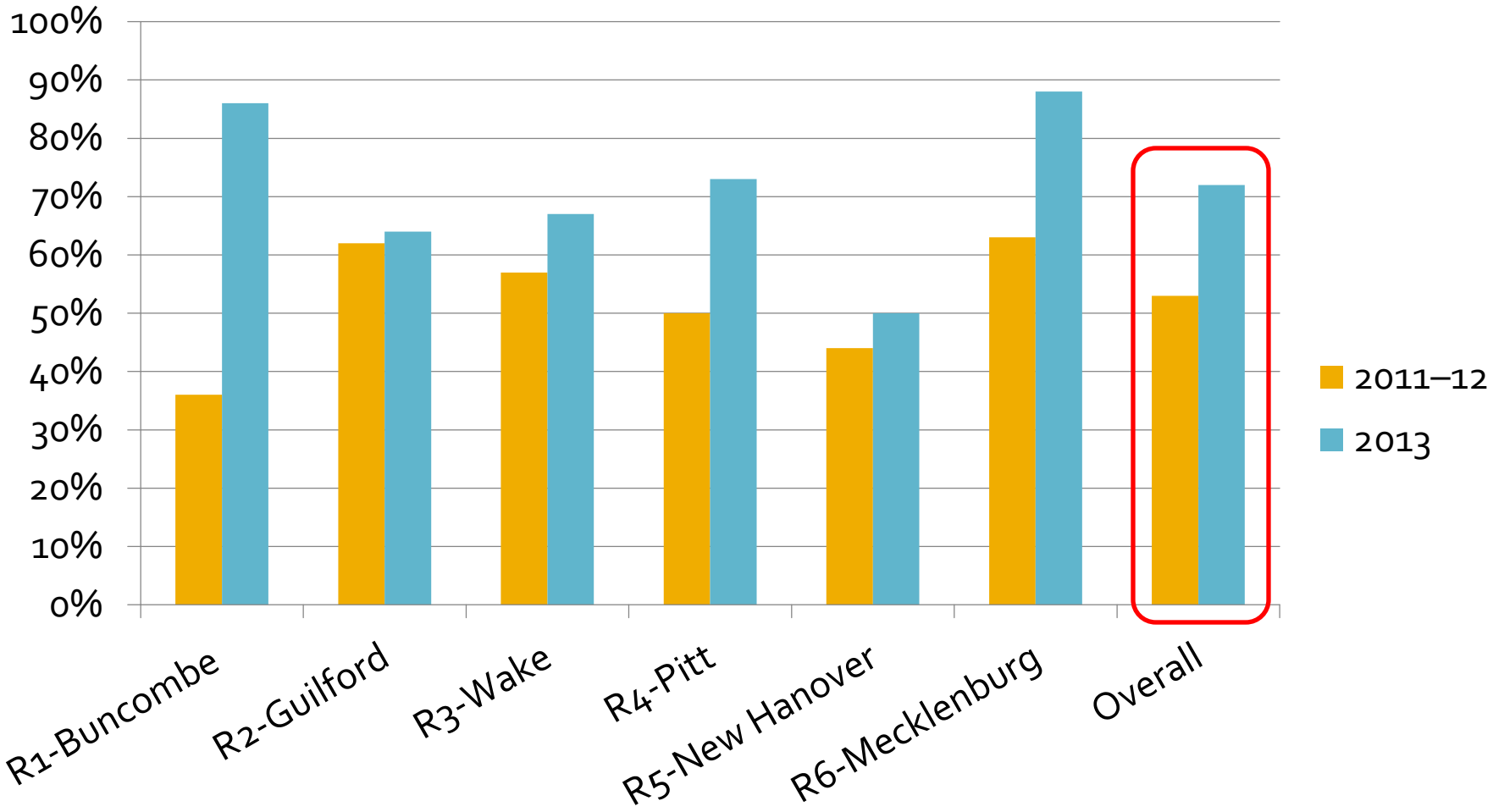
Yigit et al. Antimicrob Agents Chemother 2001; 45:1151-61

CRE in the United States



http://www.cdc.gov/getsmart/campaign-materials/week/images/kpc-states.png

Proportion of NC Hospitals Identifying CRE at Least Once per Year



N.C. Division of Public Health, unpublished data

Colistin Resistance in China

- Older, toxic antibiotic brought back as last resort for treatment of CRE
- Resistance rarely reported before 2015
- Plasmid-mediated resistance first reported November 2015 from China, found in
  - 15% of raw meat samples
  - 21% pigs
  - Clinical samples from inpatient infections

Colistin Resistance in China

- "Progression… to pan-drug resistance is inevitable and will ultimately become global"

GERMINATION *A Blog by Maryn McKenna*

Apocalypse Pig: The Last Antibiotic Begins to Fail

POSTED SAT, 11/21/2015

A pig being home-raised for a festival in China. PHOTOGRAPH BY CLEMSON, FLICKR (CC)

Liu et al. Lancet Infectious Diseases. Published online November 18, 2015

Inappropriate Antibiotic Use: Adults

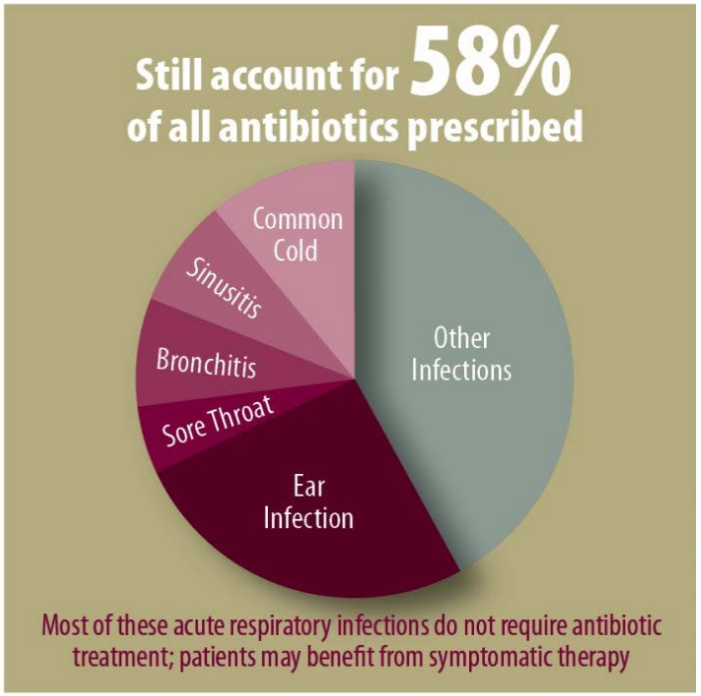
- Acute respiratory infection is most common reason adults receive an antibiotic
- >25% prescriptions for adult outpatients are for conditions for which antibiotics are not needed
  - Even when antibiotics are indicated, the wrong drug is frequently prescribed
- Providers in the South more likely to prescribe for conditions that do not warrant antibiotic use

Shapiro et al. J Antimicrob Chemother 2013 Jul 25

Antibiotic Prescriptions: Children

- Good news

- Bad news



Lauri Hicks, CDC: "Call to Action: Improving Antibiotic Use"
CDC. MMWR. 2011;60:1153-6

Drivers of Inappropriate Antibiotic Use

Patient perspective

- Want symptoms resolved quickly
- Want clear explanations, even when there is no "cure"
- May harbor misconceptions about when antibiotics work
- Cycle of expectations – previous experiences influence current behaviors

Clinician perspective

- Perceived patient expectations
- Concern for misdiagnoses and potential negative consequences
- Time pressure
- Cycle of broad-spectrum prescribing – concern for resistance leads to broad-spectrum use

Both increasingly concerned with antibiotic overuse and resistance

Barden at al. Clin Pediatr 1998 Nov;37(11):665-71
Finkelstein et al. Clin Pediatr 2013 Oct 17.
Sanchez et al. Emerg Infect Dis. 2014. In Press.

Insight from In-Depth Interviews with Primary Care Providers

- The perception that **broad-spectrum antibiotics** are easier to prescribe drives **injudicious antibiotic selection**:

> **"[Broad-spectrum antibiotics] take the thinking out of it for me so that I am not trying to figure out what the organism is and [which] particular antibiotic treats the organism."**

Sanchez et al. Emerg Infect Dis. 2014.

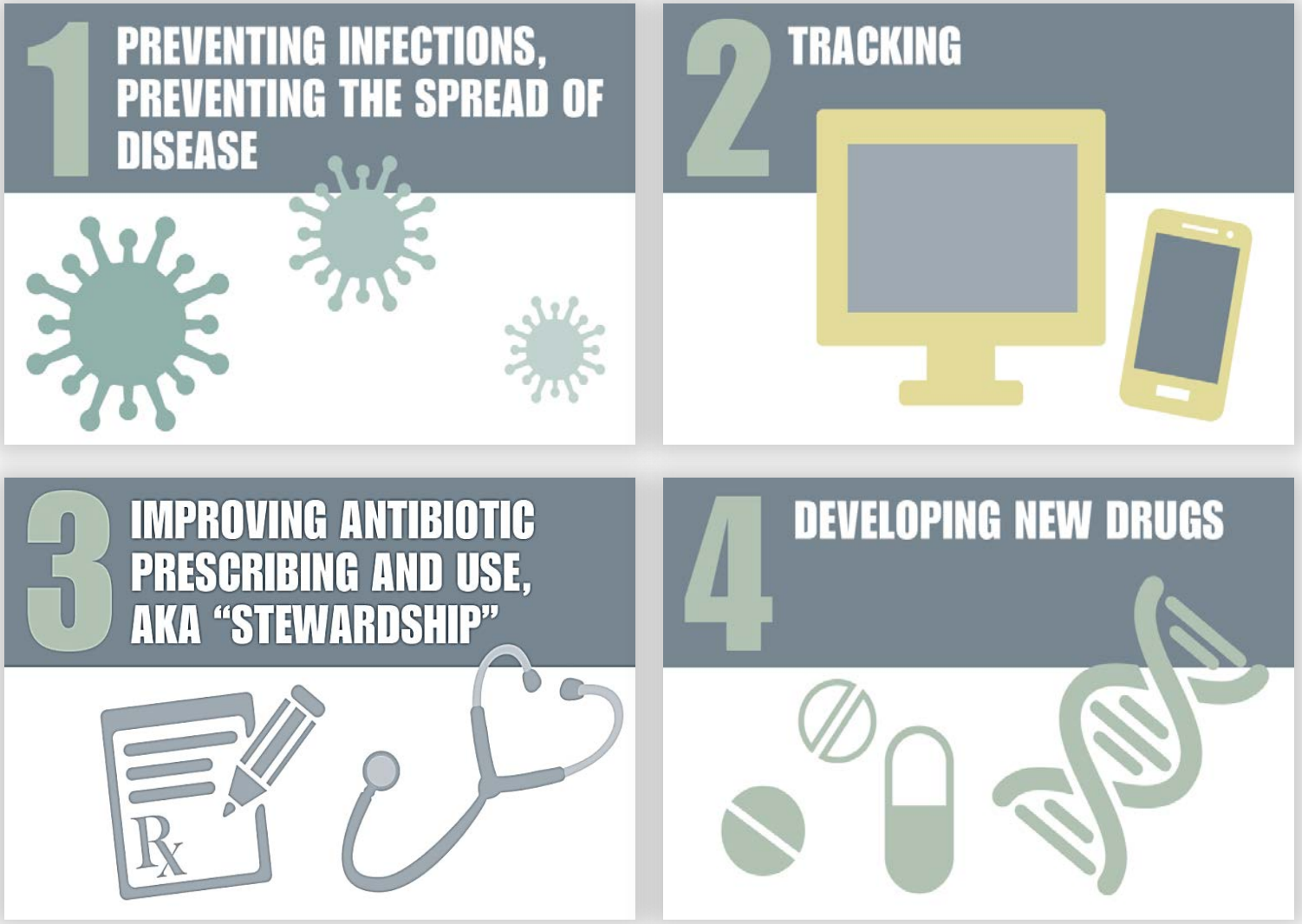
Insight From In-Depth Interviews with Primary Care Providers

- **Patient satisfaction drives antibiotic overuse:**

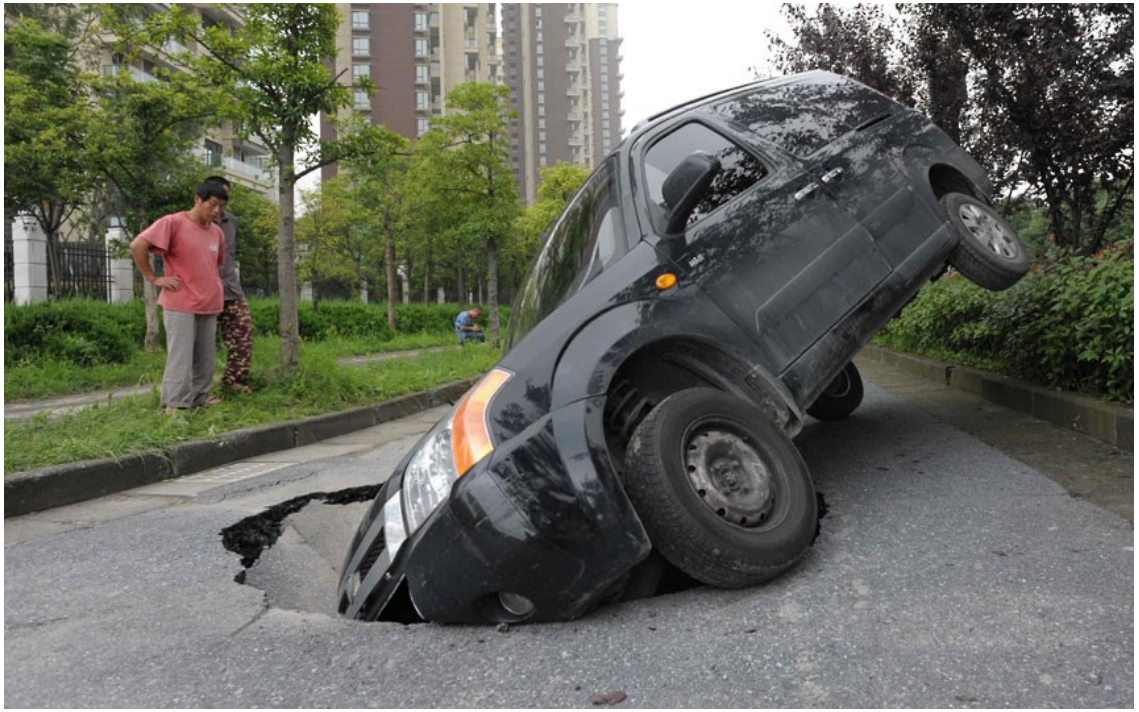
> **"We as doctors are business people. We're no different than running a shoe store. If somebody comes in and wants black shoes, you don't sell them white shoes. And if you do, they get upset."**
>
> **"…patients in general don't understand that concept of not taking [an antibiotic] if you don't need it… [and] if you don't give it to them, they don't come back to you."**

Sanchez et al. Emerg Infect Dis. 2014.

Four Core Actions to Prevent Antibiotic Resistance



"Bringing new antibiotics into our current environment is akin to buying a new car because you hit a pot hole, but doing nothing to fix the road"



CDC. "Get Smart for Healthcare: Know When Antibiotics Work"

Antimicrobial Stewardship

- Processes designed to measure and optimize the appropriate use of antimicrobials
- Achieved by selecting the appropriate agent, dose, duration of therapy and route of administration

Fishman N. Am J Med 2006;119:S53

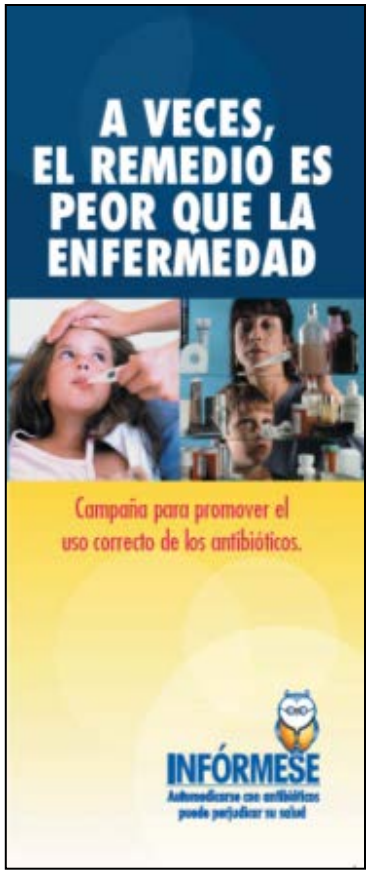
Get Smart Campaign

Know When Antibiotics Work

Get Smart Campaign: Goals

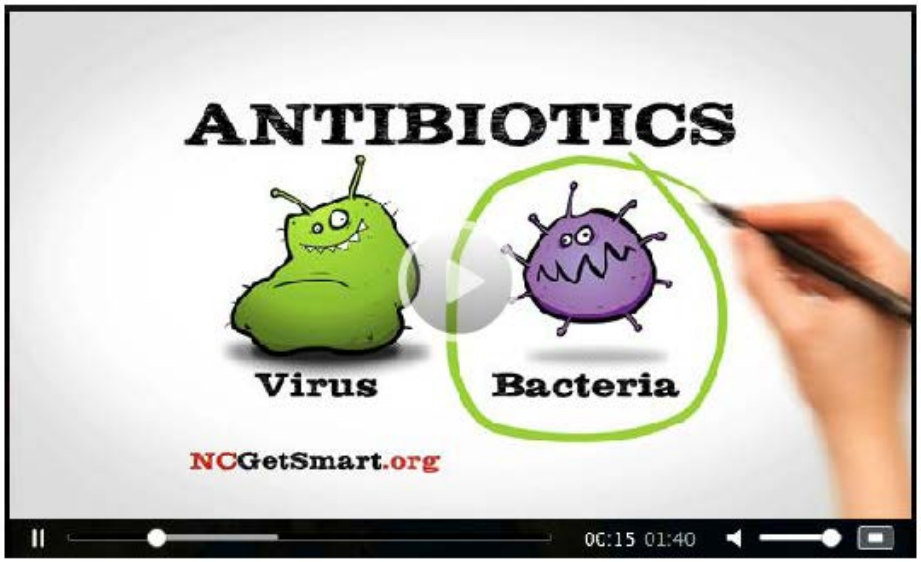
1. Improve patient safety through better treatment of infections.
2. Reduce the emergence of antimicrobial resistant pathogens and *Clostridium difficile*.
3. Heighten awareness of the challenges posed by antimicrobial resistance in healthcare and encourage better use of antimicrobials as one solution.

Get Smart:
Patient Communication Tools



Get Smart NC – Public Outreach

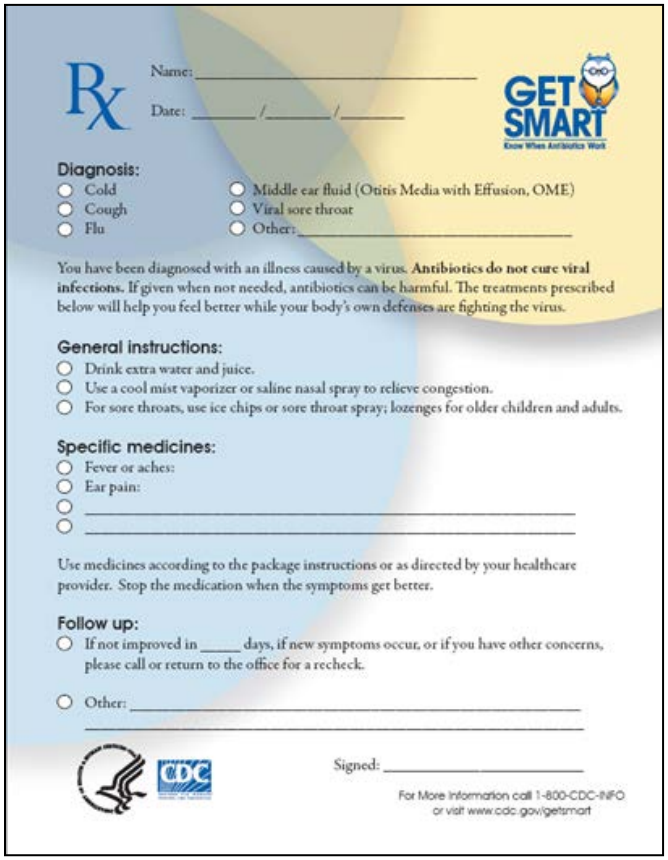
- Media campaign (November – March)



www.ncgetsmart.org

Get Smart: Provider Tools

- Guide for symptomatic treatment
- Symptomatic prescribing pad
- Continuing education opportunities
- Patient education handouts
- Medical school curriculum
- Clinical practice guidelines



Rx

Name: _____

Date: ____/____/____

GET SMART
Know When Antibiotics Work

Diagnosis:

- ○ Cold
- ○ Cough
- ○ Flu
- ○ Middle ear fluid (Otitis Media with Effusion, OME)
- ○ Viral sore throat
- ○ Other: _____

You have been diagnosed with an illness caused by a virus. **Antibiotics do not cure viral infections.** If given when not needed, antibiotics can be harmful. The treatments prescribed below will help you feel better while your body's own defenses are fighting the virus.

General instructions:

- ○ Drink extra water and juice.
- ○ Use a cool mist vaporizer or saline nasal spray to relieve congestion.
- ○ For sore throats, use ice chips or sore throat spray; lozenges for older children and adults.

Specific medicines:

- ○ Fever or aches:
- ○ Ear pain:
- ○ _____
- ○ _____

Use medicines according to the package instructions or as directed by your healthcare provider. Stop the medication when the symptoms get better.

Follow up:

- ○ If not improved in ____ days, if new symptoms occur, or if you have other concerns, please call or return to the office for a recheck.
- ○ Other: _____
  _____

Signed: _____

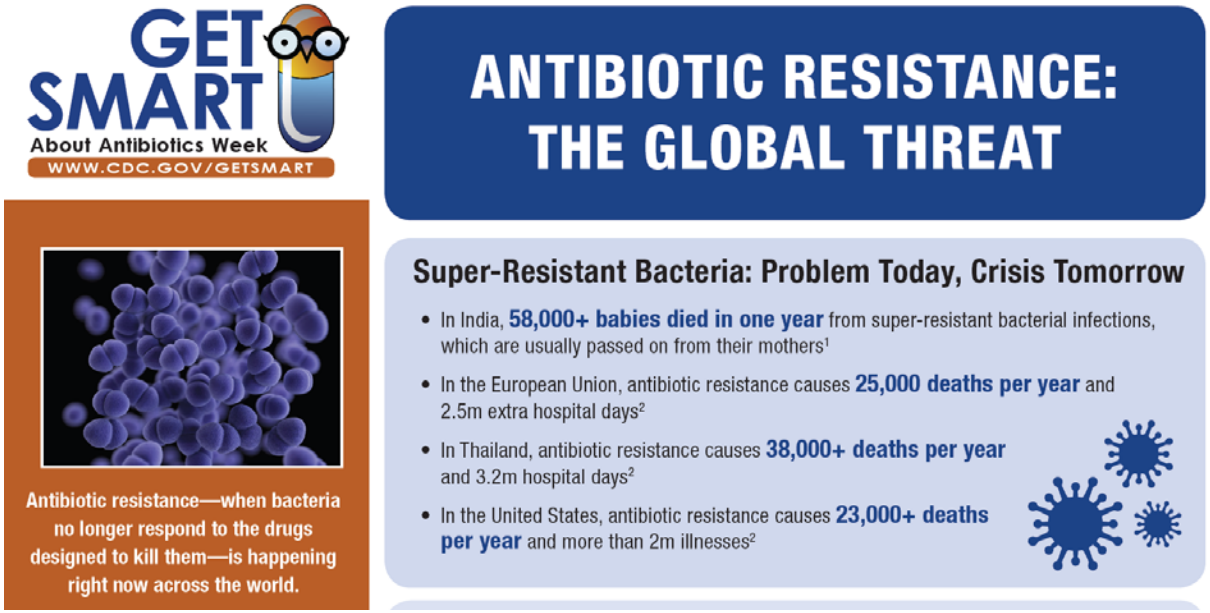
For More Information call 1-800-CDC-INFO or visit www.cdc.gov/getsmart

Conclusions

- Investigate occurrences of highly-resistant or unusual pathogens
  - VISA/VRSA
  - Potentially CRE, other multidrug-resistant organisms
- Promote antimicrobial stewardship and infection prevention efforts in communities

Get Smart Campaign Resources

- http://epi.publichealth.nc.gov/cd/diseases/antibiotics.html
- http://www.cdc.gov/getsmart/healthcare/



Arboviral disease update

- Last year we talked about chikungunya and dengue, what's next?
- Zika virus
- Is it any reason for concern?
- 1st a quick orientation to mosquito borne viral infections

Neuroinvasive Arboviral Infections

	Reportable	Vector	Geography	Genus	Reservoir
LaCrosse	Y	*Aedes spp*	Western NC	Bunyavirus	Small rodents
EEE	Y	*Aedes*, *Coquillettidia*, *Culex spp*	Piedmont and Coastal NC	Alphavirus	Birds
WNv	Y	*Culex*, *Culiseta spp*	Statewide	Flavivirus	Birds
Powassan	Y (as other)	*Ixodes spp*	Upper Midwest & New England	Flavivirus	Small rodents
St. Louis	Y (as other)	*Culex spp*	Ohio-Mississippi River Basin	Flavivirus	Songbirds; blue jay, robin
JE	Y (as other)	*Culex* spp	Eastern Asia	Flavivirus	Pigs, wading birds

Other Arboviral Infections

	Reportable	Vector	Geography	Genus	Reservoir
Dengue	Y	*Aedes aegypti* & *albopictus*	Worldwide	Flavivirus	People
Chikungunya	Y	*Aedes aegypti* & *albopictus*	Worldwide	Alphavirus	People
Yellow Fever	Y	*Aedes aegypti* & *albopictus*	Tropical Africa, S. America	Flavivirus	People and NHPs
Zika	N	*Aedes aegypti* & *albopictus*	Worldwide	Flavivirus	People and NHPs

Zika Virus Concern

Pan American Health Organization

World Health Organization

REGIONAL OFFICE FOR THE Americas

Epidemiological Update

Zika virus infection

16 October 2015

Given the increased transmission of Zika virus in the Region of the Americas, the Pan American Health Organization/World Health Organization (PAHO/WHO) recommends that its Member States establish and maintain the capacity to detect and confirm cases of Zika virus infection, prepare their health services for a potential additional burden at all levels of health care, and implement an effective public communications strategy to reduce the mosquitoes that transmit this disease, particularly in areas where this vector is present.

Zika Virus Concern

Pan American Health Organization

World Health Organization

REGIONAL OFFICE FOR THE Americas

Epidemiological Alert

Increase of microcephaly in the northeast of Brazil

17 November 2015

Given the unusual increase in cases of microcephaly in some northeast states of Brazil, the Pan American Health Organization (PAHO) / World Health Organization (WHO) calls upon Member States to remain alert to the occurrence of similar events in their territories and to notify its occurrence through the channels established under the International Health Regulations (IHR).

Zika Virus Concern

Pan American Health Organization
World Health Organization
REGIONAL OFFICE FOR THE Americas

Epidemiological Alert

Neurological syndrome, congenital malformations, and Zika virus infection. Implications for public health in the Americas

1 December 2015

Given the increase of congenital anomalies, Guillain-Barré syndrome, and other neurological and autoimmune syndromes in areas where Zika virus is circulating and their possible relation to the virus, the Pan American Health Organization / World Health Organization (PAHO/WHO) recommends its Member States establish and maintain the capacity to detect and confirm Zika virus cases, prepare healthcare facilities for the possible increase in demand at all healthcare levels and specialized care for neurological syndromes, and to strengthen antenatal care. In addition, Member States should continue efforts to reduce the presence of mosquito vectors through an effective vector control strategy and public communication.

What is Zika virus?

- ZIKV is an emerging arbovirus that was first isolated from a Rhesus monkey in Uganda, in 1947
- It is related to DENV and has a similar epidemiology and transmission cycle in urban environments
- Patients develop a mild dengue-like syndrome, including fever, headache, rash, arthralgia and conjunctivitis.
- This clinical similarity with other, more commonly diagnosed arboviral infections such as chikungunya and dengue might delay the diagnosis and/or lead to underestimation of ZIKV infections.

Where did Zika come from?

OPEN ACCESS Freely available online

PLOS | NEGLECTED TROPICAL DISEASES

Zika Virus in Gabon (Central Africa) – 2007: A New Threat from *Aedes albopictus*?

Background: Chikungunya and dengue viruses emerged in Gabon in 2007, with large outbreaks primarily affecting the capital Libreville and several northern towns. Both viruses subsequently spread to the south-east of the country, with new outbreaks occurring in 2010. The mosquito species *Aedes albopictus*, that was known as a secondary vector for both viruses, recently invaded the country and was the primary vector involved in the Gabonese outbreaks. We conducted a retrospective study of human sera and mosquitoes collected in Gabon from 2007 to 2010, in order to identify other circulating arboviruses.

Conclusions/Significance: We provide the first direct evidence of human ZIKV infections in Gabon, and its first occurrence in the Asian tiger mosquito, *Aedes albopictus*. These data reveal an unusual natural life cycle for this virus, occurring in an urban environment, and potentially representing a new emerging threat due to this novel association with a highly invasive vector whose geographic range is still expanding across the globe.

Where did Zika come from?

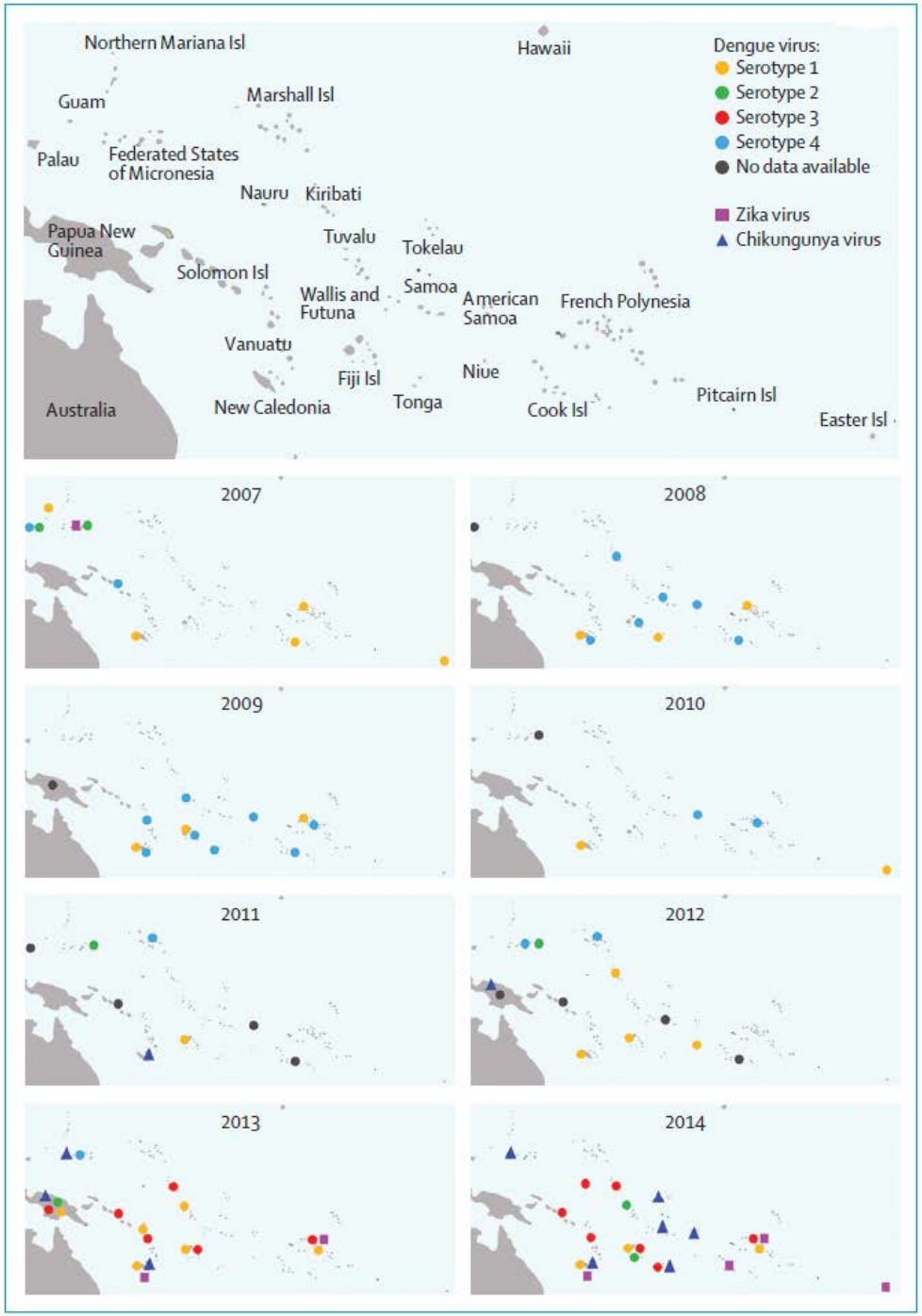
Duffy, et. al. Zika Virus Outbreak on Yap Island, Federated States of Micronesia NEJM 360;24 nejm.org june 11, 2009

BACKGROUND

In 2007, physicians on Yap Island reported an outbreak of illness characterized by rash, conjunctivitis, and arthralgia. Although serum from some patients had IgM antibody against dengue virus, the illness seemed clinically distinct from previously detected dengue. Subsequent testing with the use of consensus primers detected Zika virus RNA in the serum of the patients but no dengue virus or other arboviral RNA. No previous outbreaks and only 14 cases of Zika virus disease have been previously documented.

CONCLUSIONS

This outbreak of Zika virus illness in Micronesia represents transmission of Zika virus outside Africa and Asia. Although most patients had mild illness, clinicians and public health officials should be aware of the risk of further expansion of Zika virus transmission.



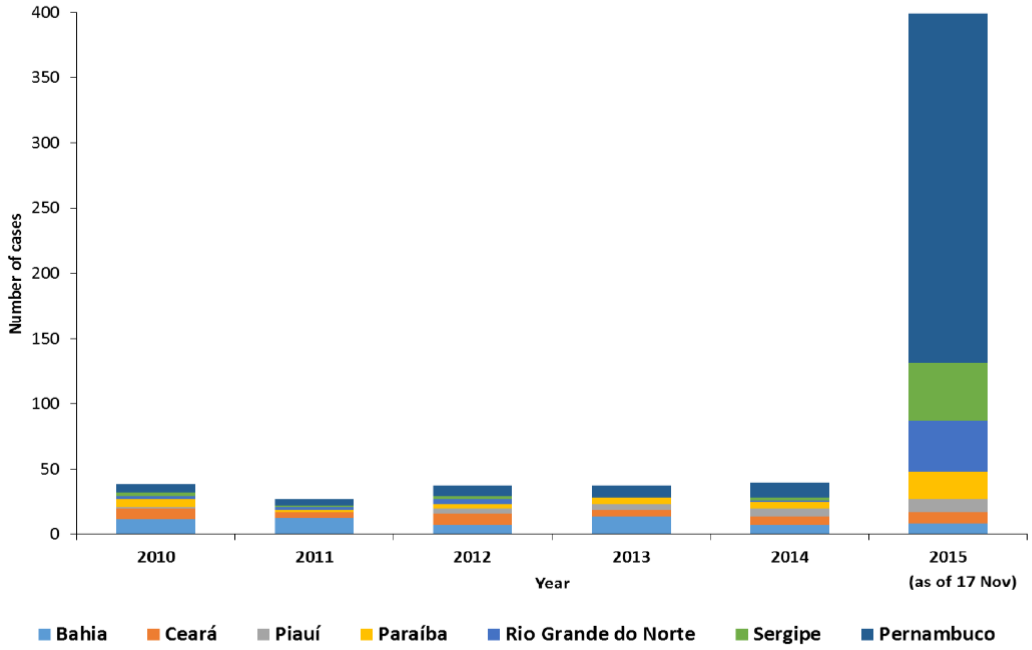
Van-Mai Cao-Lormeau, Didier Musso.

Expansion of dengue, chikungunya, and Zika viruses in Pacific Island countries and territories between 2007 and 2014.

Lancet, Vol 384 November 1, 2014 , 1571-1572

Zika in the Americas / Microcephaly

Figure 2. Number of cases of microcephaly reported annually in the seven Brazilian states reporting an unusual increase of microcephaly, 2010–2015

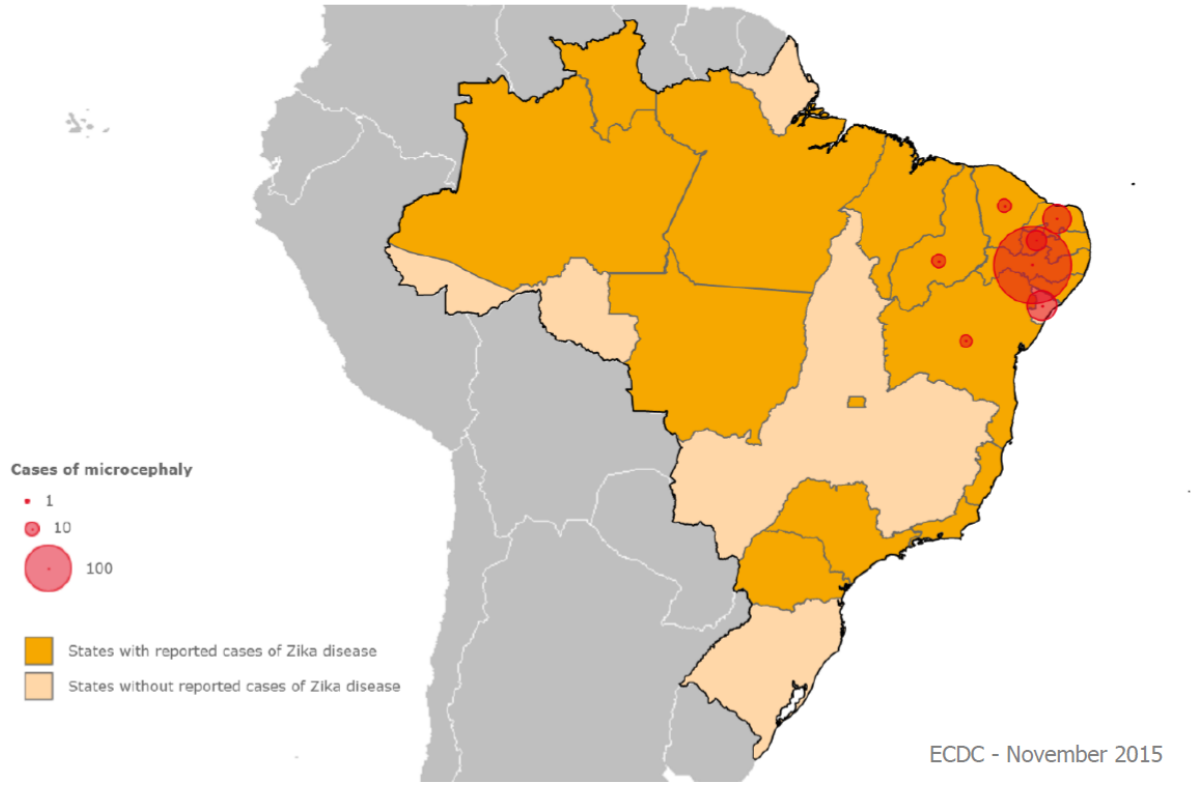


Jose Wesley, a Brazilian baby shown here on Dec. 23, 2015, was born with microcephaly. His mother was diagnosed with the Zika virus that researchers think may cause the birth defect. (AP Photo/Felipe Dana)

ECDC Rapid Risk Assessment. Microcephaly in Brazil potentially linked to the Zika virus epidemic. 24 November 2015

Zika in the Americas / Microcephaly

Figure 3. States of Brazil with reported confirmed autochthonous cases of ZIKV virus infection 2014–2015, and reported cases of microcephaly in 2015, as of 17 November 2015.



ECDC Rapid Risk Assessment. Microcephaly in Brazil potentially linked to the Zika virus epidemic. 24 November 2015

Similarities to CHIK and DENGUE

- The adaptation of ZIKV to an urban or peri-urban cycle, involving *Aedes aegypti* and other mosquitoes as vectors and humans as amplification hosts, should be of great concern to public health officials.
- With more than half of the world's human population living in areas infested with these mosquitoes, the potential for major urban epidemics of ZIKV, DENV, CHIKV, yellow fever, epidemic polyarthritis, and other as yet unknown mosquito borne viruses that might emerge, is overwhelming, and **underscores the desperate need to develop more effective mosquito control** as well as vaccines and drugs.

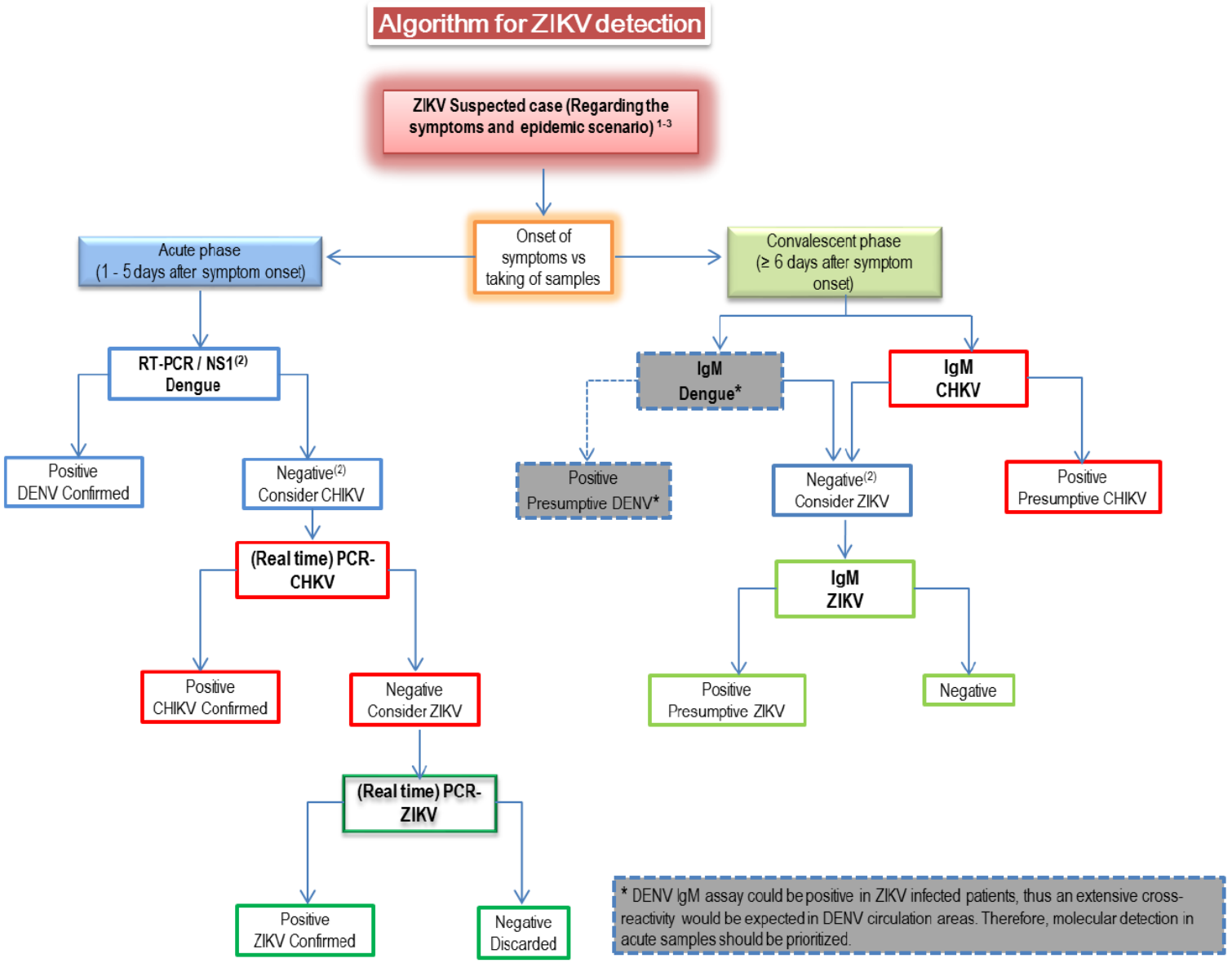
Musso, et. al. Zika virus: following the path of dengue and chikungunya? Lancet, Vol 386 July 18, 2015, p. 243-244

What should NC public health do?

- Alert clinicians to the possibility of travel associated cases of Zika (and CHIK, DENV, Malaria, etc.)
- Inform diagnostic steps
- Develop mosquito surveillance and control

The Wall Street Journal, 1/12/16

- Texas Woman Diagnosed With Mosquito-Borne Zika Virus: Development raises concern that health crisis in Brazil is spreading
- http://www.wsj.com/articles/houston-area-woman-diagnosed-with-mosquito-borne-zika-virus-1452628952



PAHO/WHO: Zika virus (ZIKV) Surveillance in the Americas: Interim guidance for laboratory detection and diagnosis. 29 June 2015

Vector Surveillance/Control

Questions, Comments?