The Emerging Threat of Zika Virus and the Public Health Response

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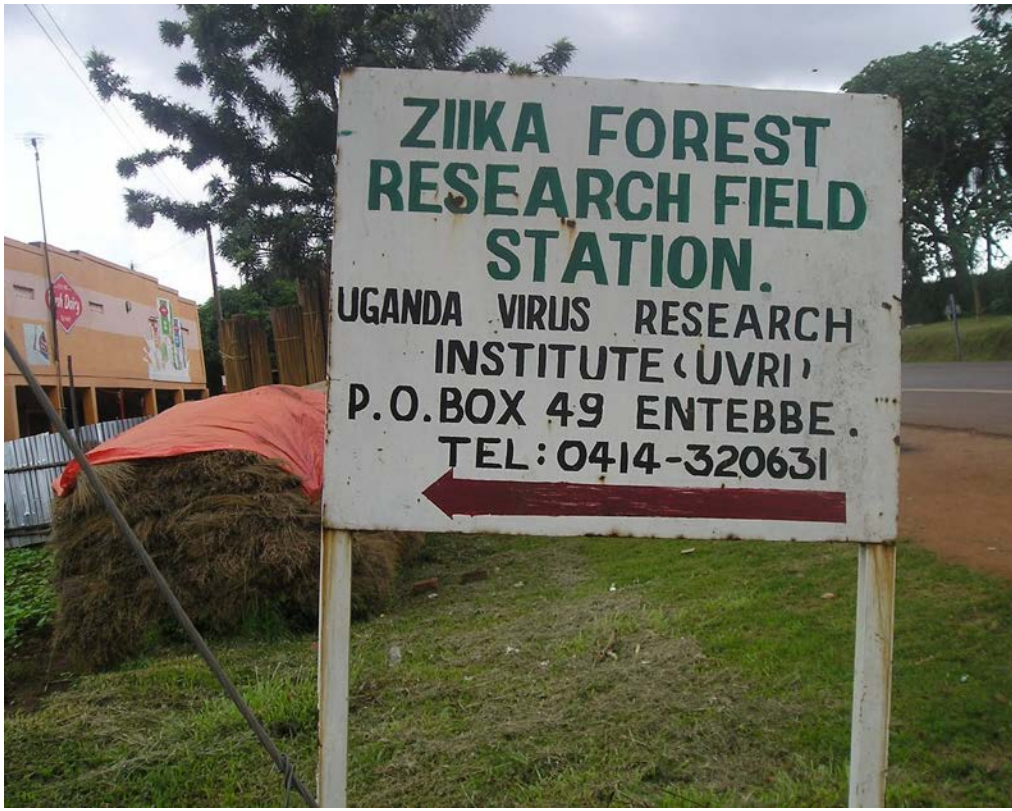
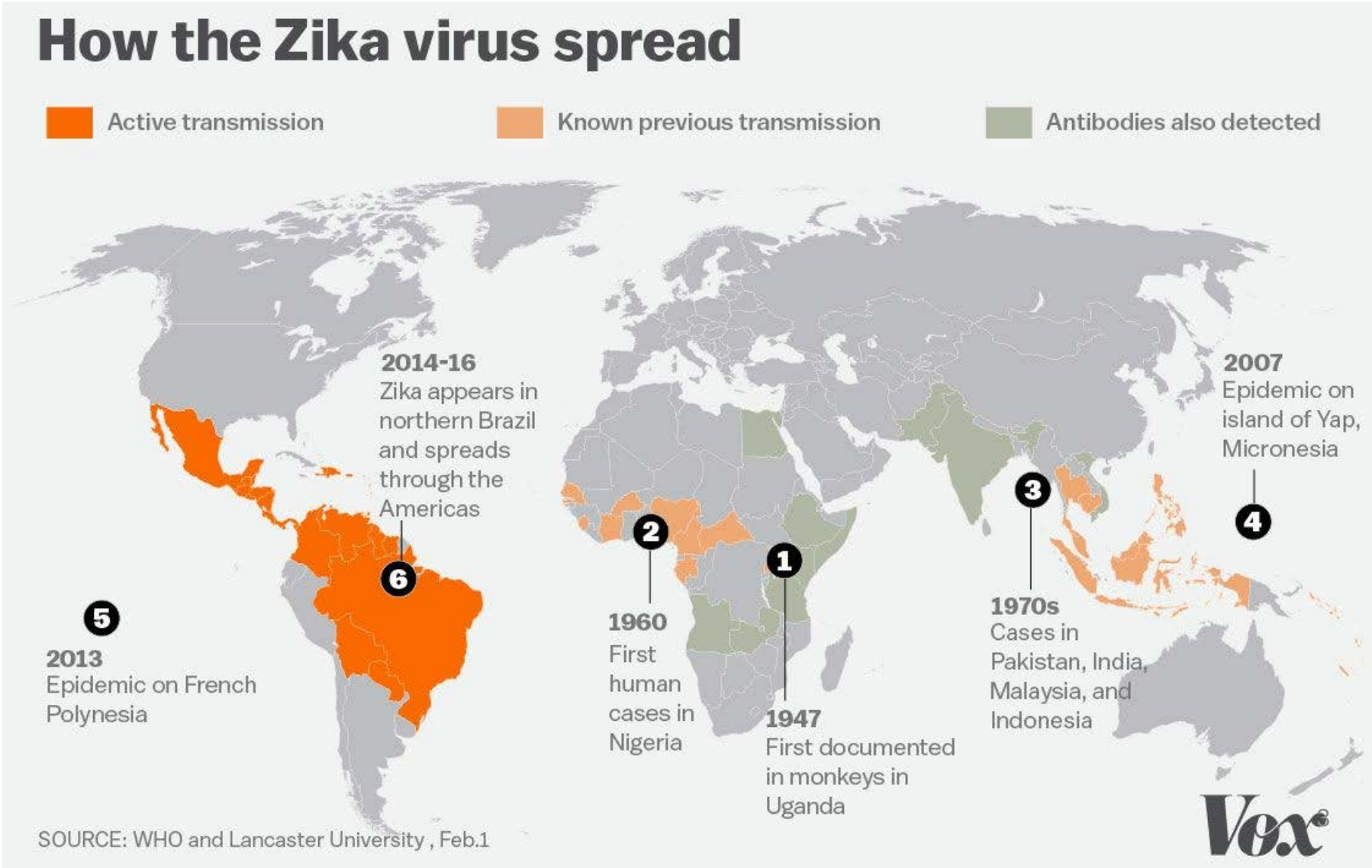
Emergence of Zika Virus

- 1947 – Rhesus 766 develops a fever
- 1956 – First cluster of cases in Nigeria
- 1970-80s – Sporadic reports of infections
- 2007 – Outbreak on Yap Island, Micronesia

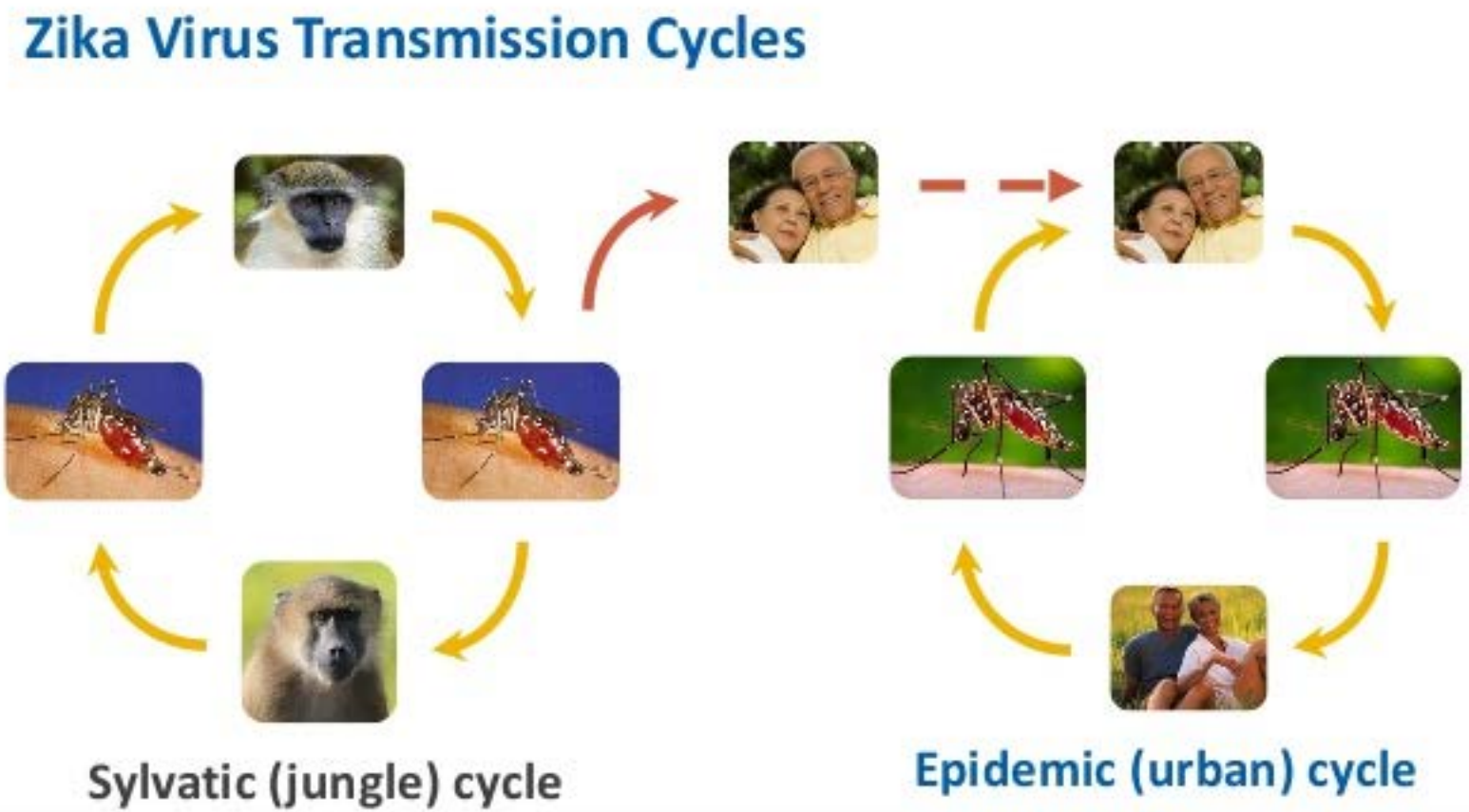


- 2013 – Outbreak in French Polynesia
- 2014 – Outbreaks in Brazil and Latin America

Global Spread of Zika



Zika Virus Transmission Cycle



Zika Virus Clinical Illness

- About 80% of infections asymptomatic
- Symptoms 3-12 d post exposure
- Symptomatic illness mild, lasting <1 week
- Rare hospitalization & death
- Symptoms/signs from 683 cases from Puerto Rico shown in the Table
  - 9 with thrombocytopenia and 5 with Guillain-Barre Syndrome

Symptom	Percent
Rash	74%
Myalgia	68%
Arthralgia	63%
Fever	63%
Headache	63%
Eye pain	51%
Chills	50%
Sore throat	34%
Petichiae	31%
Conjunctivitis	20%

CDC MMWR, April 29, 2016

Zika Conjunctivitis and Rash

Zika Virus Congenital Infection

- Series of 72 Zika pos. pregnant women from Rio de Janeiro
- All women with symptomatic infection
- Of 42 women with ultrasound, 12 (29%) were abnormal
  - Fetal death (36 and 38 wks gestation)
  - *In utero* growth restriction
  - Microcephaly
  - Cerebral calcification
  - Other abnormalities (ocular defect, CNS lesions, reduced cerebral or umbilical artery flow, abnormal amniotic fluid volume)
- Of 8 births, only 2 were normal

Brasil, N Engl J Med 2016

Risk of Microcephaly with Zika

- French Polynesia (2013-14)
  - First trimester risk of microcephaly estimated at 0.95% (95% CI 0.34 – 1.91)
- Bahia, Brazil (2015-16)
  - Based on various estimates of infection rate, over-reporting, and baseline microcephaly risk, estimate first trimester microcephaly rate from 0.88% to 13.2%
  - Microcephaly in 2nd and 3rd trimesters – "negligible association"

Johansson, NEJM 2016

Polling Question: Perception of Zika

Given the 1% to 13% risk of microcephaly, what's your perception of the level of concern Zika has engendered in the U.S.?

A. The concern is exaggerated as so few infants will get this defect

B. The concern is appropriate and about the right level

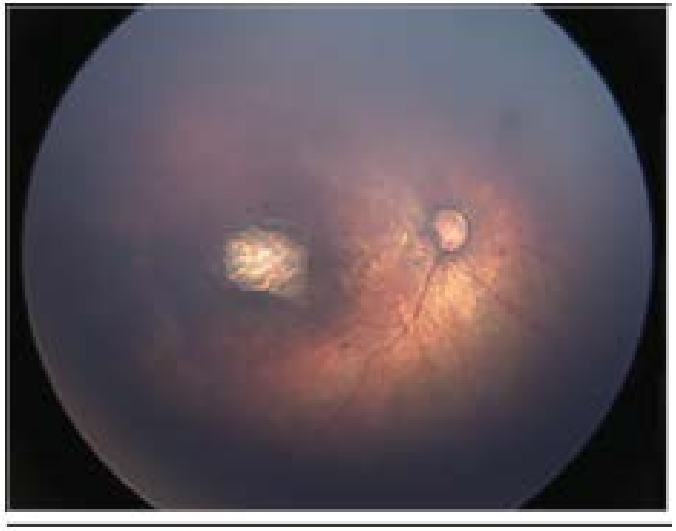
C. We should be more concerned since Zika is likely to spread and even 1% would be a lot of infants

Congenital Zika Syndrome

- Severe microcephaly (<3 SD below mean) – consistent with fetal brain disruption sequence (overlapping cranial sutures, redundant scalp skin, severe neurological impairment)
- Subcortical calcifications, cortical thinning, decreased myelination, consistent with neural cell injury & death
- Ocular abnormalities – optic nerve atrophy, chorioretinal mottling and atrophy
- Congenital contractures – arthrogryposis, clubfoot, hip dislocation associated with motor neuron involvement

Congenital Zika Syndrome

Microcephaly from fetal brain disruption



Optic nerve hypoplasia and chorioretinal scar

Congenital contractures

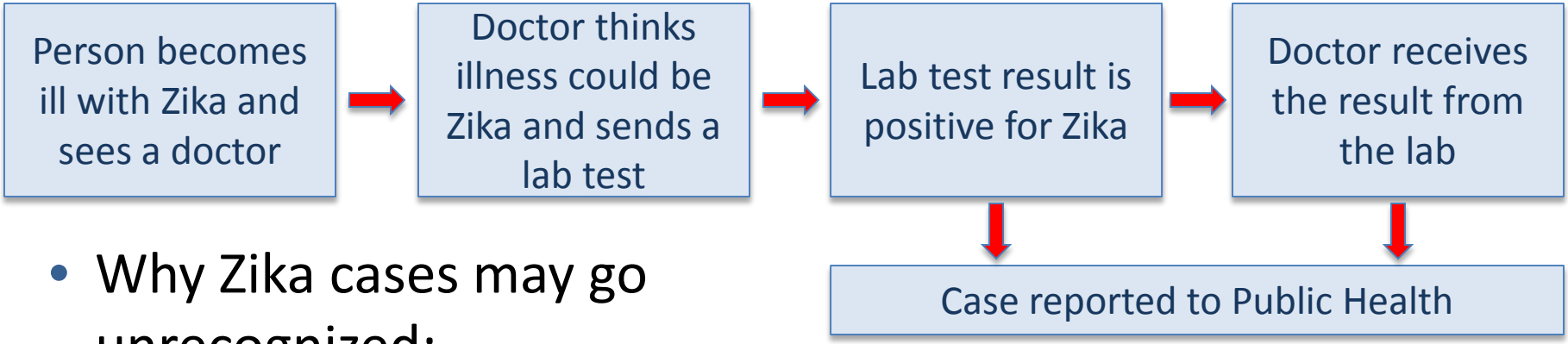
Moore, JAMA Pediatr. doi:10.1001/jamapediatrics.2016.3982

Other Neurological Findings of Zika Infection

- In series of infants with microcephaly, ocular findings in 35% and hearing loss in 10%
  - Unclear how often these occur in infants without microcephaly
- Guillain-Barre syndrome
- Case reports of encephalitis and encephalomyelitis in adults
- Currently no evidence of abnormal post-natal neurological development associated with congenital infection

Zika Surveillance

- Clinical suspicion, laboratory diagnosis



- Why Zika cases may go unrecognized:
  - Infection often asymptomatic (80%)
  - Ill person may not seek medical care
  - Doctor may not think of Zika or send a test

Zika Testing and Reporting

- Testing recommended **1**) for all pregnant women exposed through travel to an affected area or by sexual contact; **2**) others with Zika consistent symptoms and an exposure history; **3**) all infants of Zika infected moms
- Lab testing available at the Public Health Lab and commercially

County of Los Angeles Public Health

Public Health Laboratories
12750 Erickson Avenue
Downey, CA 90242
Phone: 562-658-1330/1300
Fax: 562-401-5999

CA Certified PHL #335637
CLIA #05D1066369

ZIKA TEST REQUEST FORM

FAILURE TO COMPLETE ALL FIELDS WILL RESULT IN SPECIMEN REJECTION OR DELAYED TESTING

For Zika virus testing eligibility:
www.publichealth.lacounty.gov/acd/Diseases/EpiForms/ZikaEligibility.pdf
For Zika virus testing and notification information:
www.publichealth.lacounty.gov/acd/ZikaTesting.htm

PUBLIC HEALTH LAB USE ONLY

SUBMITTER INFORMATION
Date Submitted
Requesting Physician Name (Last, First)
Requesting Physician Phone
Requesting Physician Email
Facility Name
Facility Address (Street)
City
State
Zip
Facility Phone Number
Secure Fax Number For Results Reporting
Contact Person For Specimen and Phone Number

PATIENT INFORMATION
Patient Name (Last, First, Middle Initial)
Date of Birth (mm/dd/yyyy)
Sex
Male Female
Patient Address (Street)
City
State
Zip
Patient Primary Telephone Number
Patient Alternate Phone Number
MRN/Patient ID

LAB INFORMATION
Specimen Source
Serum Cord Blood Amniotic Fluid
Urine Placenta Other:
Specimen Collection Date/Time (hh:mm AM/PM)
Specimen Storage Condition
Refrigerated
Frozen (-20°C)

TEST(S) REQUESTED – Current Lab Testing Algorithms Available at http://www.cdc.gov/zika/laboratories/lab-guidance.html
Arbovirus serology panel (with reflex to confirmatory PRNT or rRT-PCR if required) for Zika, Chikungunya, Dengue, and West Nile Viruses
Arbovirus rRT-PCR (with reflex to serology, PRNT, or rRT-PCR if required) for Zika, Chikungunya, and Dengue Viruses
Immunohistochemistry (fixed tissue or paraffin block)
Histopathology (fixed tissue or paraffin block)
PRNT for Zika/Chikungunya/Dengue/West Nile Virus Confirmation

CLINICAL INFORMATION
PREGNANCY STATUS
Yes: # Weeks Pregnant OR Estimated Due Date: Ultrasound Evidence of Microcephaly/Calcification
Not Pregnant Not Applicable
SYMPTOMS (CHECK ALL APPLICABLE)
Symptomatic: Fever Arthralgia Rash Conjunctivitis AND Symptom Onset Date:
Asymptomatic
Guillain-Barré Syndrome: Onset Date:
Other, Specify:
FLAVIVIRUS HISTORY (CHECK ALL PREVIOUS KNOWN VACCINATIONS AND ILLNESS) Flavivirus History Unknown
Tick-borne Encephalitis Yellow Fever Japanese Equine Encephalitis West Nile Virus Saint Louis Encephalitis Dengue
TRAVEL AND EXPOSURE HISTORY See current areas with Zika transmission at http://www.cdc.gov/zika/geo/active-countries.html
Did patient travel to an area with Zika transmission (including U.S location with ongoing local Zika spread) within 14 days of symptom onset?
Yes No Unknown
List all cities/countries/areas of travel: Last Date of Travel:
Did patient's sexual partner travel to area with Zika transmission (including U.S. location with ongoing local Zika spread)? Yes No Unknown
List all cities/countries/areas of travel: Last Date of Travel:
Last Date of Unprotected Sexual Intercourse: OR Unknown

Zika Cases by Jurisdiction

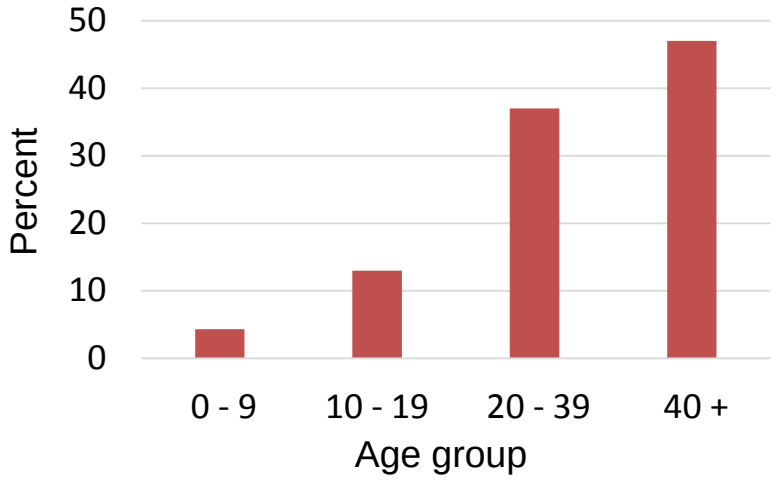
LAC – 2016; other through end of January February 2017

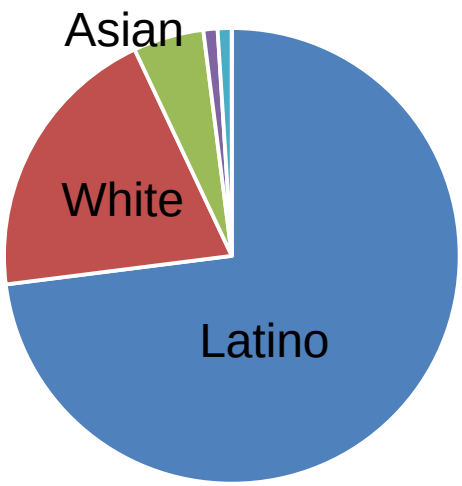
	Total cases	Pregnant women	Local transmission	Sexually acquired
LA County	96	14	0	0
California	486	81	0	0
US States/DC	4,973	1,394*	220	41
US Territories	36,414	3,071	36,274	NA

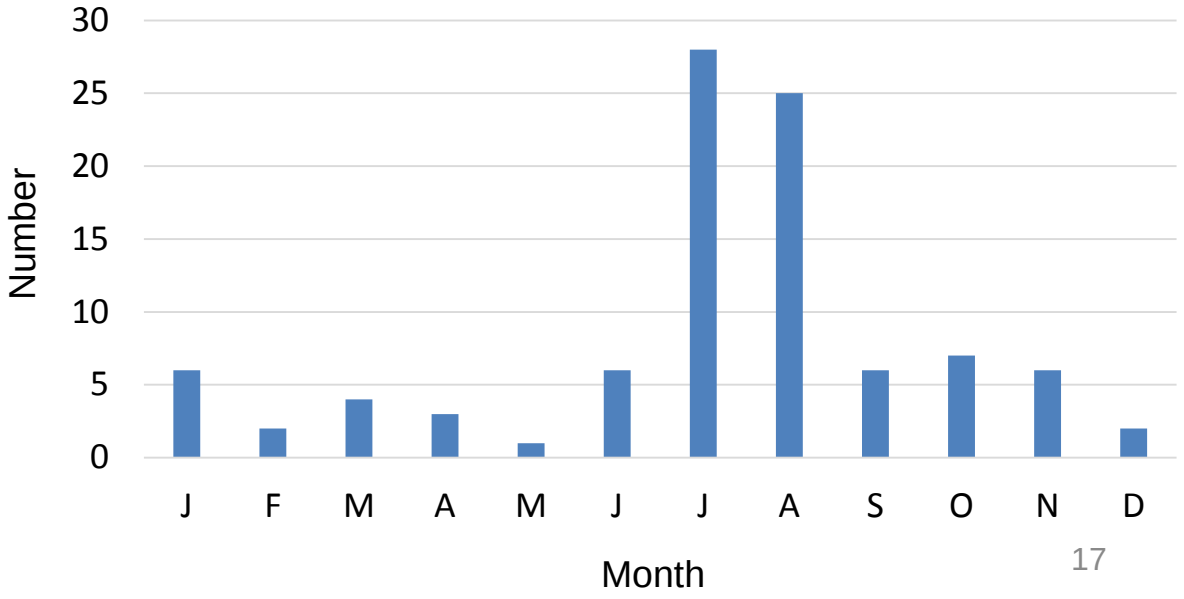
*999 completed pregnancies, 43 known with birth defects

Demographics of LAC Zika Patients (n=96)

Gender	N (%)
Male	**25 (26%)**
Female	**71 (74%)**
Pregnant	14 (15%)
Non-pregnant	57 (59%)







LAC Zika Cases' Country of Exposure

Country	Number (%)
Mexico	25 (26%)
Nicaragua	15 (16%)
Guatemala	13 (14%)
Honduras	9 (9%)
El Salvador	7 (7%)
Dominican Republic	7 (7%)
Puerto Rico	4 (4%)
Jamaica	3 (3%)
Costa Rica	3 (3%)
Virgin Islands	2 (2%)
Brazil	2 (2%)
Bahamas	1 (1%)
Florida	**1 (1%)**
Fiji	1 (1%)
St. Maarten	1 (1%)
Peru	1 (1%)

72 (75%) cases from Mexico and Central America

Polling Question: Travel Plans

How would the threat of Zika affect your plans to travel to Latin America or the Caribbean?

A. It makes me much less likely to go

B. It makes me somewhat less likely to go

C. It wouldn't affect my plans because I can use mosquito protection and take other precautions

D. I don't want to go to Latin America or the Caribbean anyway

Profile of LAC Pregnant Women with Zika (n=16)

- 85% are Latina
  - 60% report Spanish as their first language
  - 90% were born outside of the U.S.
- All traveled to Mexico or Central America
- 40% traveled to a rural area
- 50% had a residence in the country where they traveled and 25% were visiting family

- Most traveled for >30 days, spent >8 hours per day outside, and used mosquito repellent

Additional Surveillance Activities

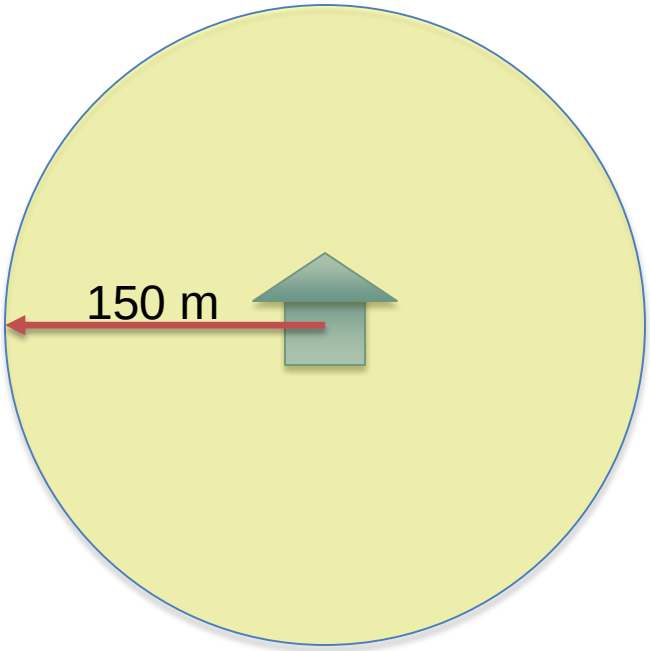
- National Zika Pregnancy Registry – Pregnant women with Zika are included in the registry and information on the baby collected at birth, 2, 6, and 12 months to determine outcome
- Birth defects surveillance – Information for newborns with specific deficits will be collected and testing may be done to determine if the defect was related to Zika
- Vector surveillance – Mosquito and vector control agencies identify locations of mosquitos that can spread Zika

Prevention of Zika Infection

- Pregnant women should not travel to Zika affected countries
- All persons traveling to an affected country should take measures to reduce mosquito exposure
  - Insect repellent with an EPA registered ingredient (DEET, Picaridin, IR3535, Oil of Lemon Eucalyptus)
    - Repellents safe for use by pregnant women
    - Most can be used on children aged >2 months
  - Wear long sleeves and pants
  - Stay in places with air conditioning or screens

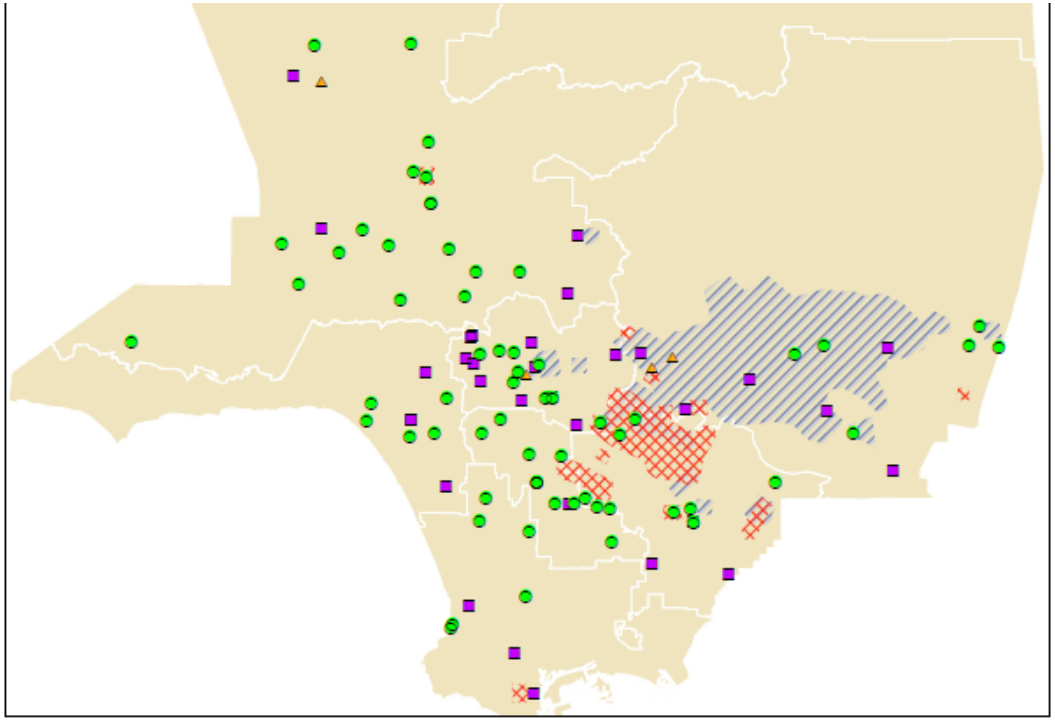
Vector Control Investigation for Zika Cases

- Conduct surveillance for *Aedes* mosquitos within 150 m radius of case residences in Vector Control districts where *Aedes* previously identified
- If *Aedes* are found, implement control (adulticiding, larvaciding) and prevention
- Provide education on reducing mosquito breeding



Zika Cases and *Aedes* Mosquito Locations

- 9/38 (24%) investigations positive for *Aedes* mosquitoes, some in areas not previously known to be infested



Will Investigation & Abatement Prevent Local Spread of Zika?

- By the time a patient seeks healthcare and Zika is identified, the period of viremia already would have occurred
  - Mean time from onset of symptoms to case referral to Vector control = 9.3 days

- Most Zika cases are not detected so no abatement occurs
- Thus, the incremental benefit is likely to be low

Detecting Locally Acquired Zika

- Astute clinician testing someone with Zika symptoms
- Positive screen on an asymptomatic blood donor
- Detection from sentinel surveillance (pending)

Los Angeles County is designated by CDC as one of the seven highest risk jurisdictions for local transmission in the U.S.

Invasive *Aedes* Mosquitos in LA County

- *Aedes albopictus*
  El Monte, 2011
- *Aedes aegypti*
  Los Angeles, 2014

Aedes aegypti

Zika Virus Vectors

Aedes albopictus

- *Aedes aegypti* (Yellow Fever mosquito) is the primary vector
- *Aedes albopictus* (Tiger mosquito) also may transmit
- Peak feeding during day; aggressive!
- Container breeders - lay eggs in small amounts of water around houses
- Eggs resistant to desiccation

Aedes Response: Eliminate Breeding Sites

Inspection of a Yard near a Zika Case

Polling Question: Plant Saucers

What will you do with the saucers you have under flower pots after hearing this presentation?

A. I'll get rid of them immediately

B. I might get rid of them if the mosquitos are bad this summer

C. I will keep using them since I don't want to get water all over my porch

D. I don't have flower pots around my residence

Local Pesticide Application

- Larviciding at the breeding source
- Hand-held adulticiding
- ULV truck-mounted fogging

Aerial Spraying

- Aerial strategy may be used to control a local outbreak
- Very small amount of active ingredient
- Degrades with exposure to sunlight
- No adverse effects

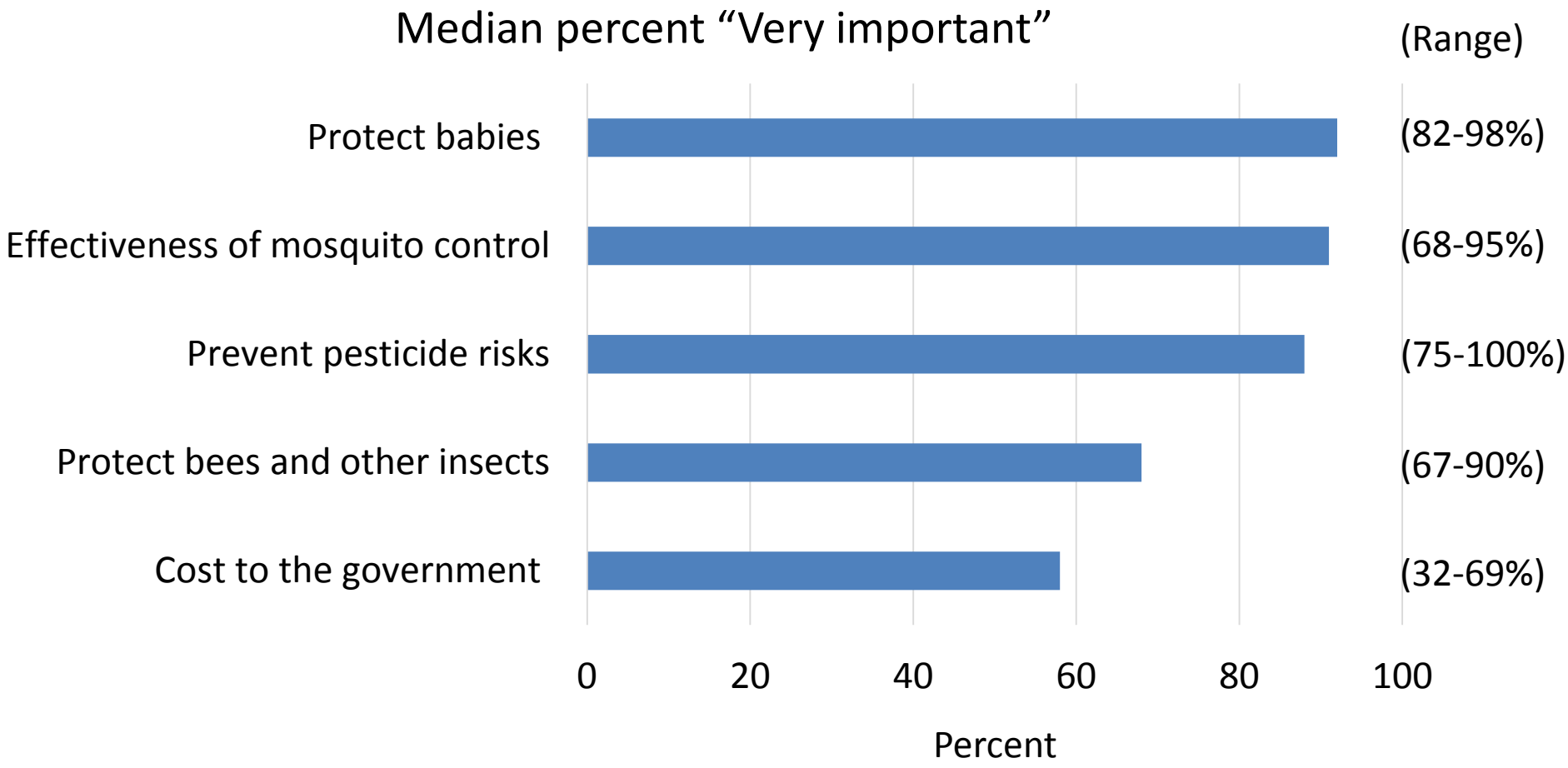
Challenges in Zika Prevention & Response

- Changing travel and personal protective behaviors
- Effective outreach to highest risk communities
- Improved physician diagnosis
- Reducing *Aedes* population
- Public opposition to use of pesticides for mosquito control if local spread occurs

Community Meetings: Zika & Vector Control

- Objective: Obtain information to support programs & policy on mosquito control for a local Zika outbreak
  - Learn community values, preferences and concerns associated with mosquito control techniques
  - Understand motivations, barriers and decision-making process that drive behavior changes related to mosquito control
- 3-hour community meetings
  - Locations: Van Nuys, San Gabriel, Silver Lake, East LA, South LA
  - Local recruitment – participants reflect communities
  - Pre-post surveys, brief presentations, Q & A, small group discussion, electronic polling

Values of Community Meeting Participants



Polling Question: Pesticides

If a local Zika outbreak occurred in Los Angeles County, which of the following would be more important to you…

A. Preventing birth defects from Zika?

B. Preventing the risks of pesticide exposure?

Balancing Risks: Birth Defects vs Pesticides

During a Zika outbreak, which of the following would be more important to you:

Preventing birth defects:

67% (range 40-81%)

Preventing risks of pesticide exposure:

33% (range 27-67%)

New *Aedes* Control Technologies

- Population control by release of *Wolbachia*-infected sterile male mosquitoes
- Spread of larvicide by release of chemical-dusted adult male mosquitoes
- Genetically-modified mosquitoes

Stay Up-to-Date

- **Los Angeles County, Department of Public Health**
  publichealth.lacounty.gov/acd/vectorZika.htm

- **Centers for Disease Control and Prevention**
  www.cdc.gov/zika/