La Crosse Encephalitis: North Carolina's Most Important Mosquito-borne Disease

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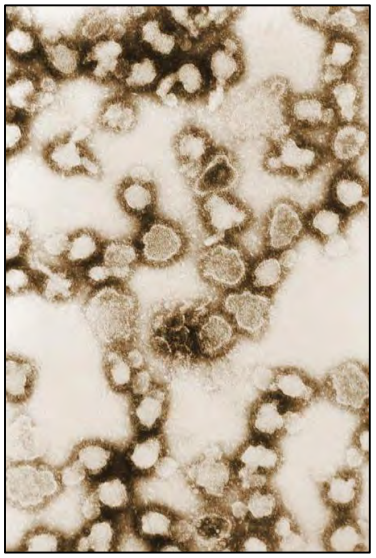
Western Carolina University | Environmental Health

NC Mosquito-borne Pathogens

- **Zoonotic**
  - (Animal-Mosquito-Human)

    La Crosse virus*
    West Nile virus
    Eastern Equine Encephalitis virus
    Saint Louis Encephalitis virus

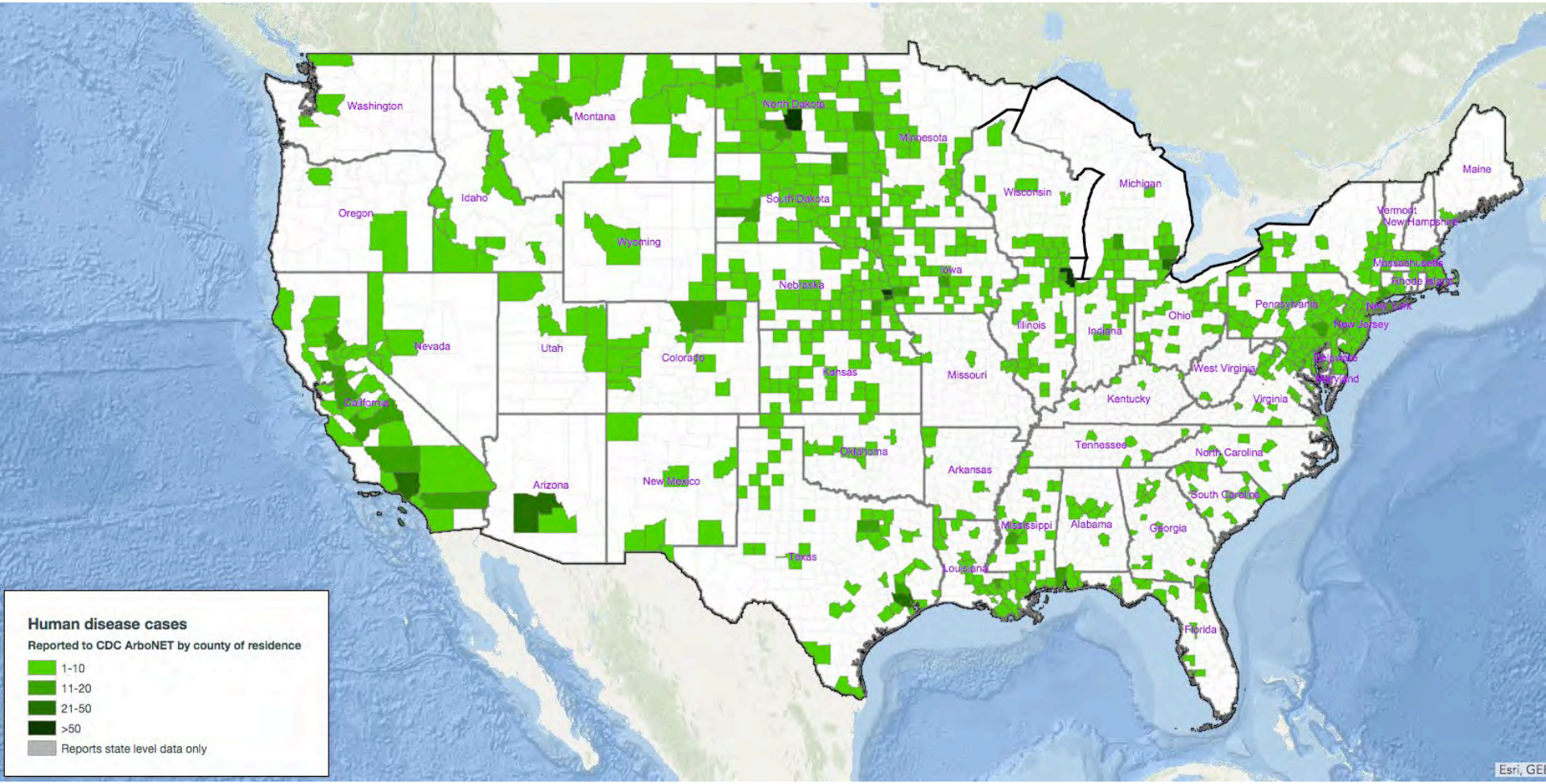


- **“Anthroponotic”**
  - (Human-Mosquito-Human)

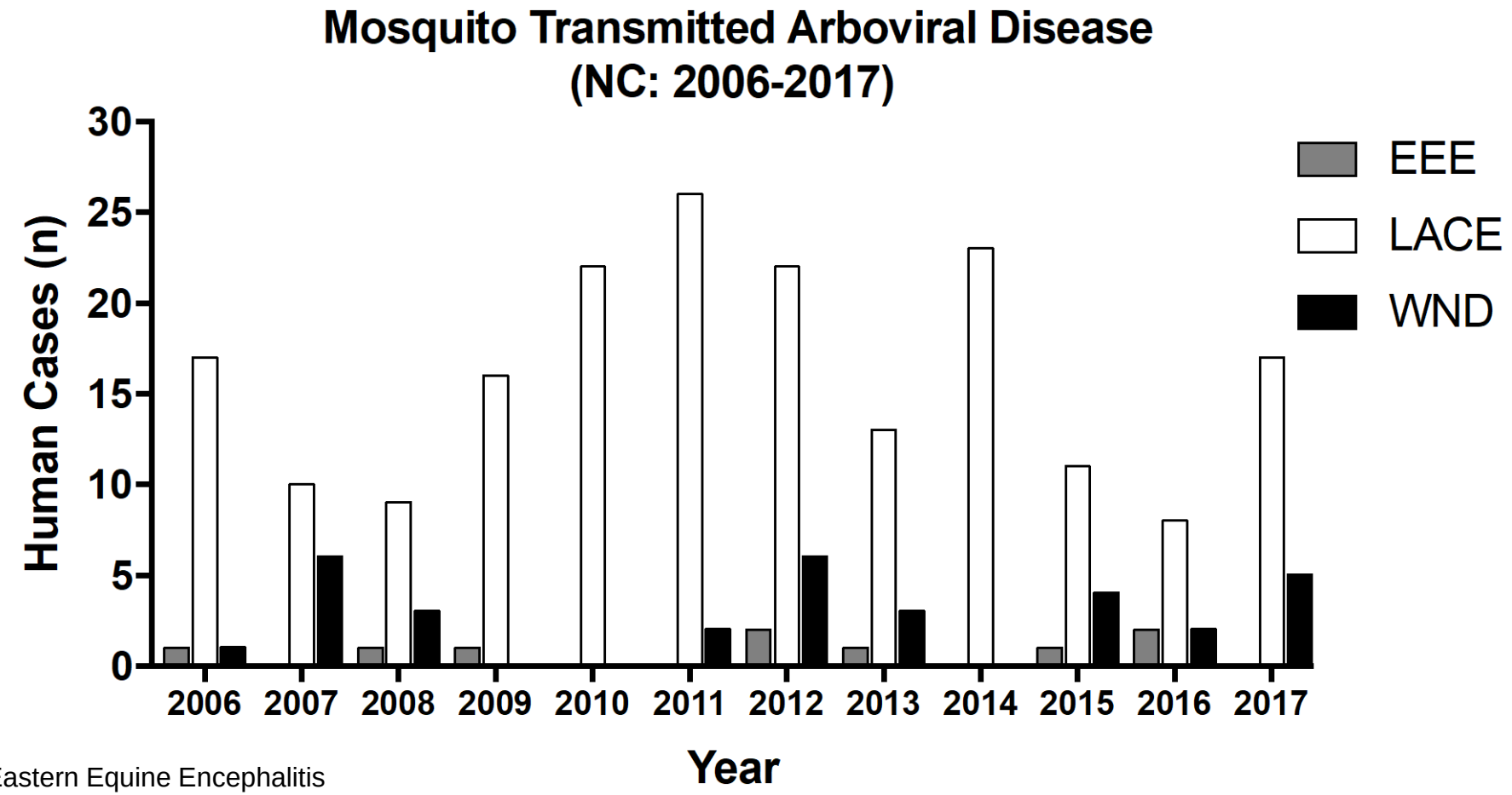
    Chikungunya*
    Dengue*
    Malaria
    Zika*

*Transmission is primarily by container-inhabiting *Aedes*

Human West Nile Disease: 2018



Arboviral Disease: Zoonotic



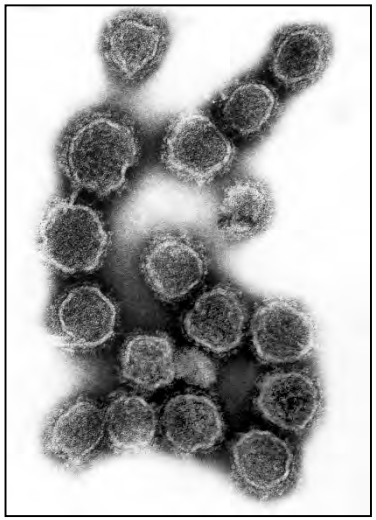
EEE: Eastern Equine Encephalitis
LACE: La Crosse Encephalitis
WND: West Nile Neuroinvasive Disease

Not shown: 3 SLE Cases (2009)

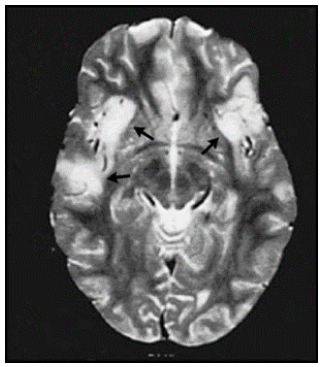
Data: CDC/ArboNet

La Crosse Virus

- **Isolated in 1960's in La Crosse, Wisconsin**
  - Bunyavirus (California serogroup virus)
- **Acquired through the bite of a mosquito**
  - Eastern-tree hole mosquito (principle vector; daytime active)
- **LACv is the most common arboviral cause of pediatric encephalitis in the US**



LACv Disease



- **Symptoms**
  - Incubation Period: 5-15 days
  - Fever, Headache, Vomiting, Fatigue, Lethargy
  - Severe neuroinvasive disease occurs mostly in children under 16 years
  - Seizures during acute illness are common; fatal cases are rare (~1%)
- **Neurologic Sequelae**
  - Vary in duration and severity
  - Recurrent seizures, hemiparesis, and cognitive and neurobehavioral abnormalities

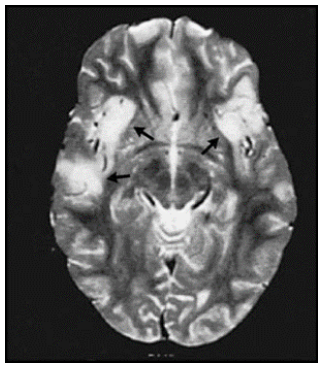
LACE (Acute)

http://wlos.com/news/local/burnsville-boy-almost-dies-all-because-of-a-mosquito
http://www.wsoctv.com/news/local/nc-boy-fighting-for-life-after-contracting-la-cross-virus-from-mosquito-bite/421409113

LACE (Recovery)

LACv Disease

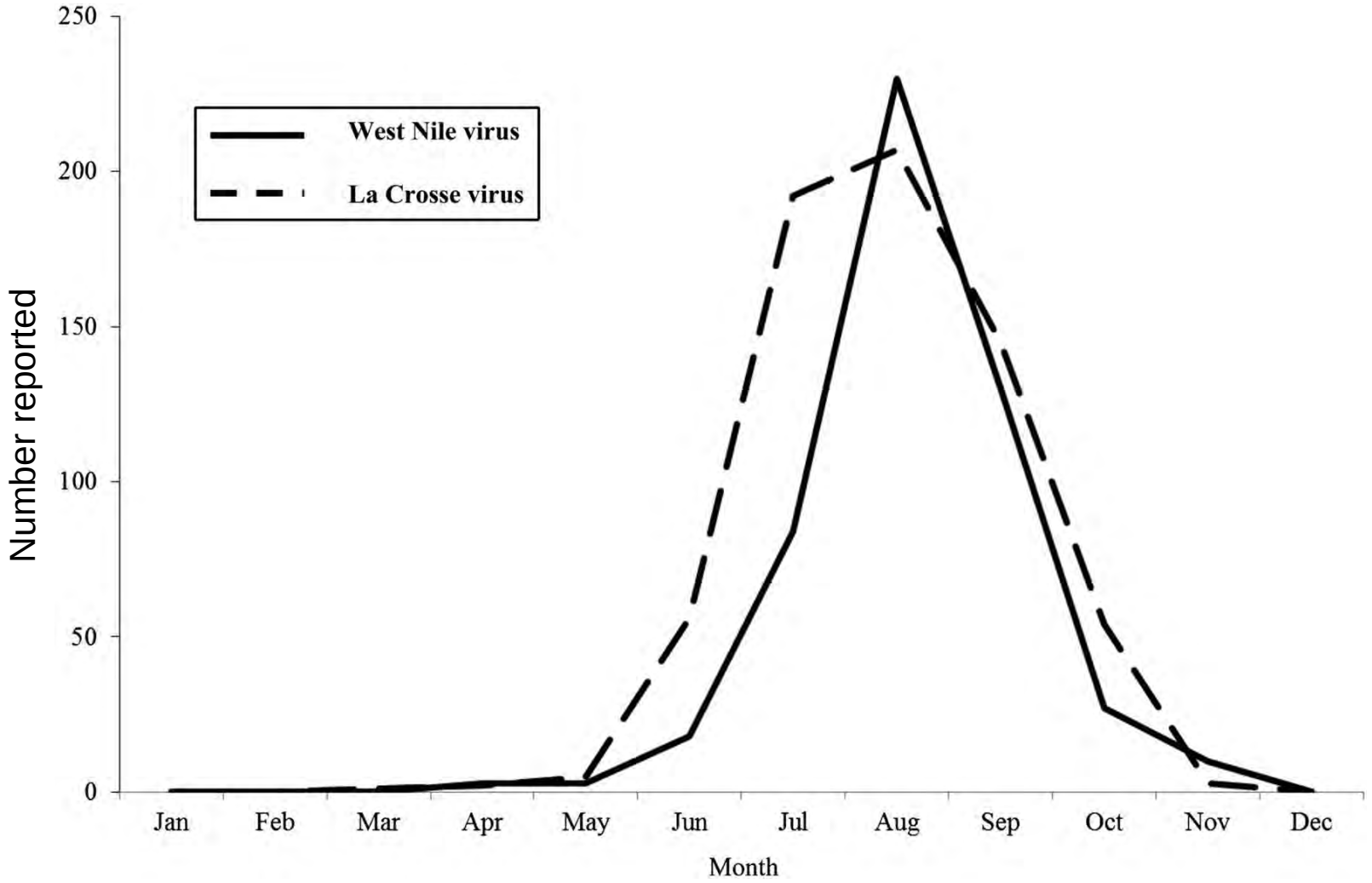
- **Treatment**
  - No vaccine
  - No specific antiviral treatment
  - Supportive treatment only
  - "Prevention is the Cure"
- **Economic and Social Impacts: High**
  - Direct and Indirect Medical Costs
    - $7,521-$175,586 (mean= $32,974)*
  - Lifelong Neurologic Sequelae
    - $48,775-$3,098,798*



*2003 USD Value

Utz et al. Economic and Social Impacts of La Crosse Encephalitis in Western North Carolina *American Journal of Tropical Medicine and Hygiene*. 69 (5) 2003.

Number of reported pediatric neuroinvasive arboviral disease cases due to La Crosse and West Nile viruses, by month of illness onset: United States, 2003–2012.



PEDIATRICS

James T. Gaensbauer et al. *Pediatrics* 2014;134:e642-e650

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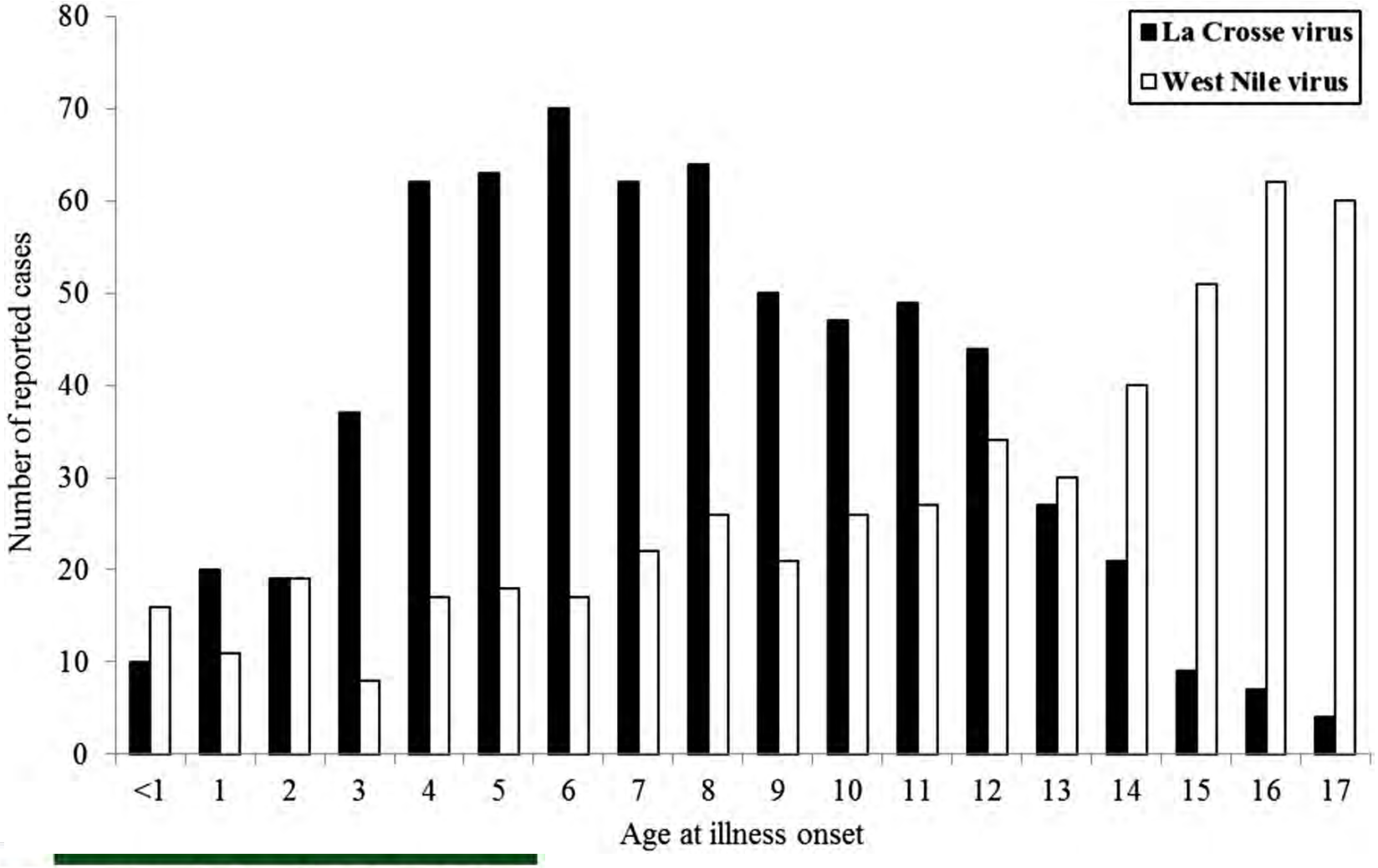

PEDIATRICS®

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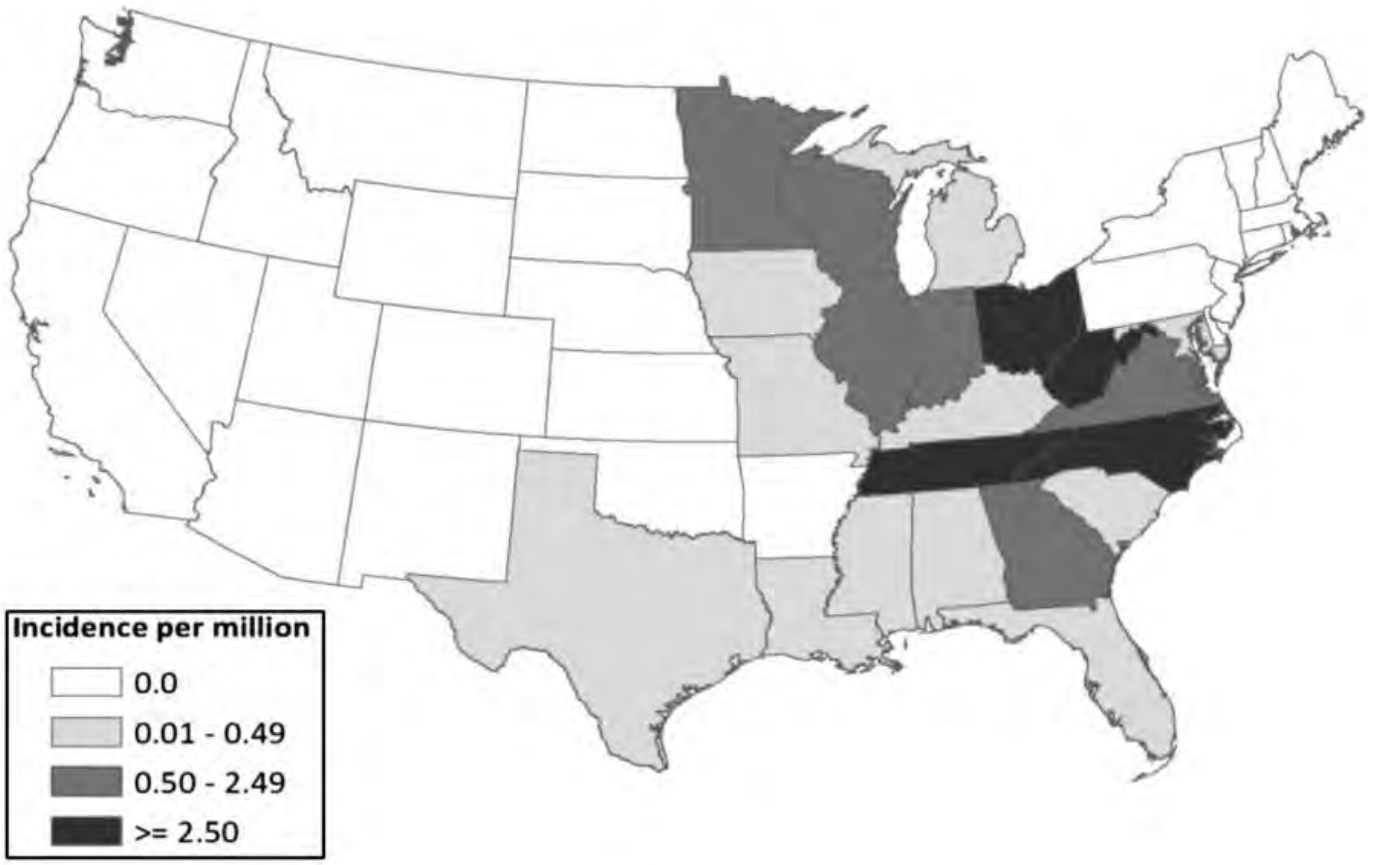
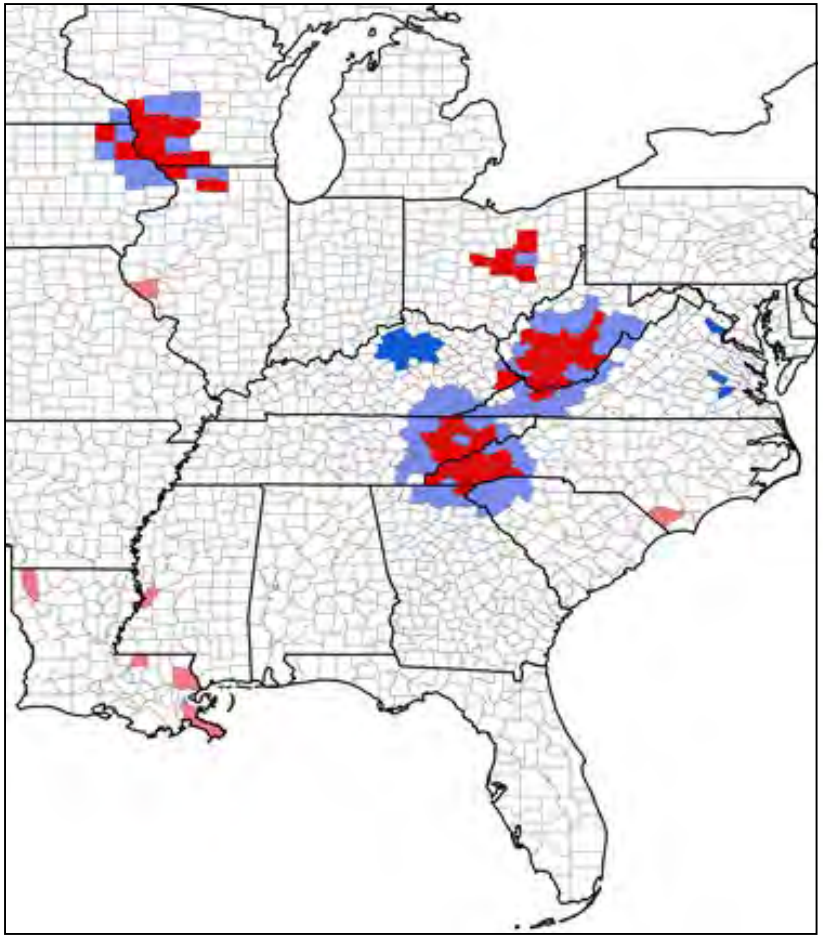
LACE (2003-2012)

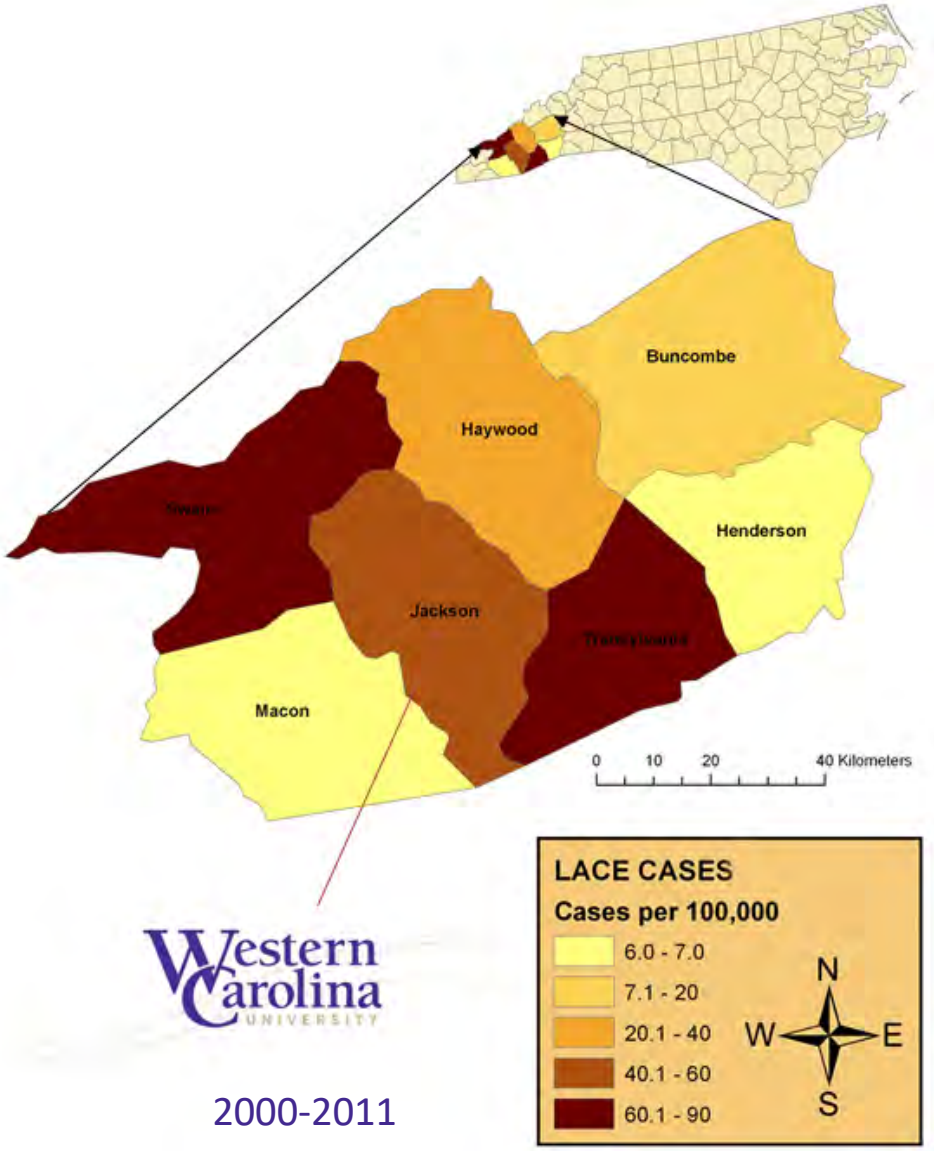


Although LACE was historically found throughout the Midwest, burden has shifted to Appalachian region: 81% reported from Ohio, West Virginia, North Carolina, and Tennessee

(Gaensbauer et al., 2014)



Haddow AD and Odoi A, The incidence risk, clustering, and clinical presentation of La Crosse virus infections in the eastern United States, 2003-2007. *PLoS One*. 2009 Jul 3;4(7):e6145.



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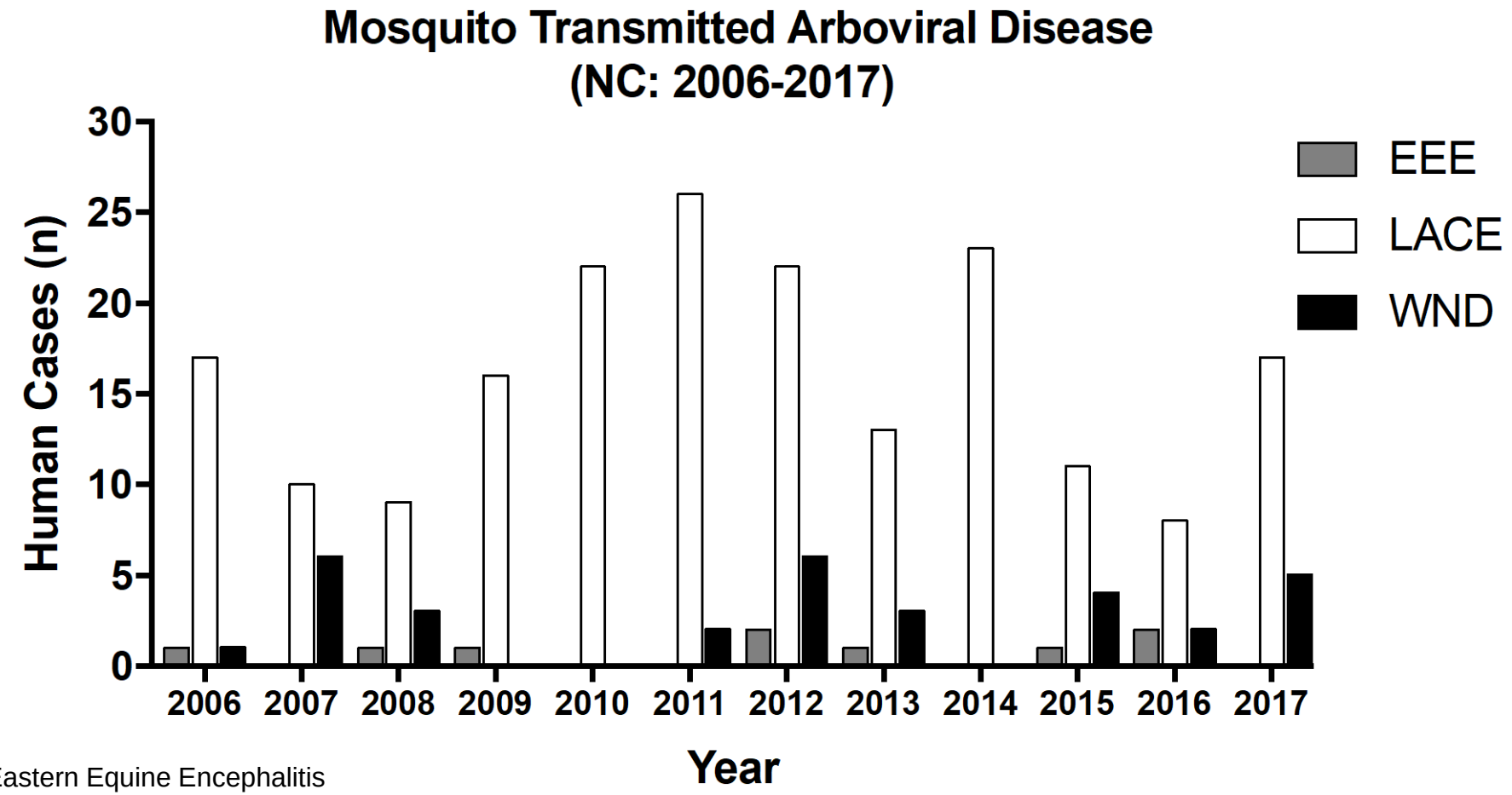
2000-2011

LACE (NC: 1997-2016)

NC DHHS (2017)

Arboviral Disease: Zoonotic



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Tip of the Iceberg: 1 recognized LACE case

Iceberg: est.100-300 individuals exposed to LACV

Prevalence of La Crosse virus antibody in blood serum or Nobuto strip samples collected in western North Carolina*

Location	n	% positive per location	Overall % positive
Cherokee Indian Reservation	311	20.6	6.8
Macon County	36	8.3	0.3
Swain County	175	8.0	1.5
Jackson County	225	4.9	1.2
Haywood County	162	2.5	0.4
Eight additional counties	32	3.0	0.1

* The county of origin for 66 samples collected off the reservation was missing.

Szumlas et al. 1996

Environmental Risk Factors

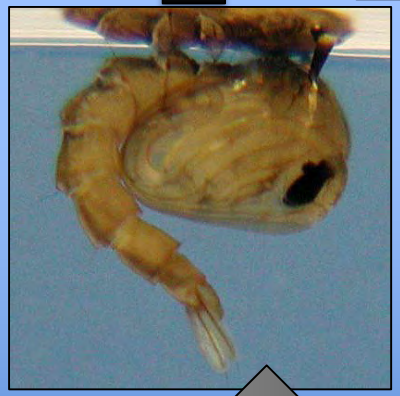
- **Time spent outdoors**
- **Residence near one or more tree holes**
- **Abundance of the Asian Tiger mosquito**

Erwin PC, Jones TF, Gerhardt RR, Halford SK, Smith AB, Patterson LE, Gottfried KL, Burkhalter KL, Nasci RS, Schaffner W. La Crosse encephalitis in Eastern Tennessee: clinical, environmental, and entomological characteristics from a blinded cohort study. *Am J Epidemiol.* 2002 Jun 1;155(11):1060-5.

Mosquito Life Cycle

Western Carolina University

Adult



Pupa

Larva

Tree holes and *Ae. triseriatus* larvae

Tree holes

Treehole Communities

Aedes triseriatus
Aedes albopictus
Aedes japonicus
Orthopodomyia signifera
Toxorhynchites sp.
Anopheles barberi

Transylvania County, NC 2005

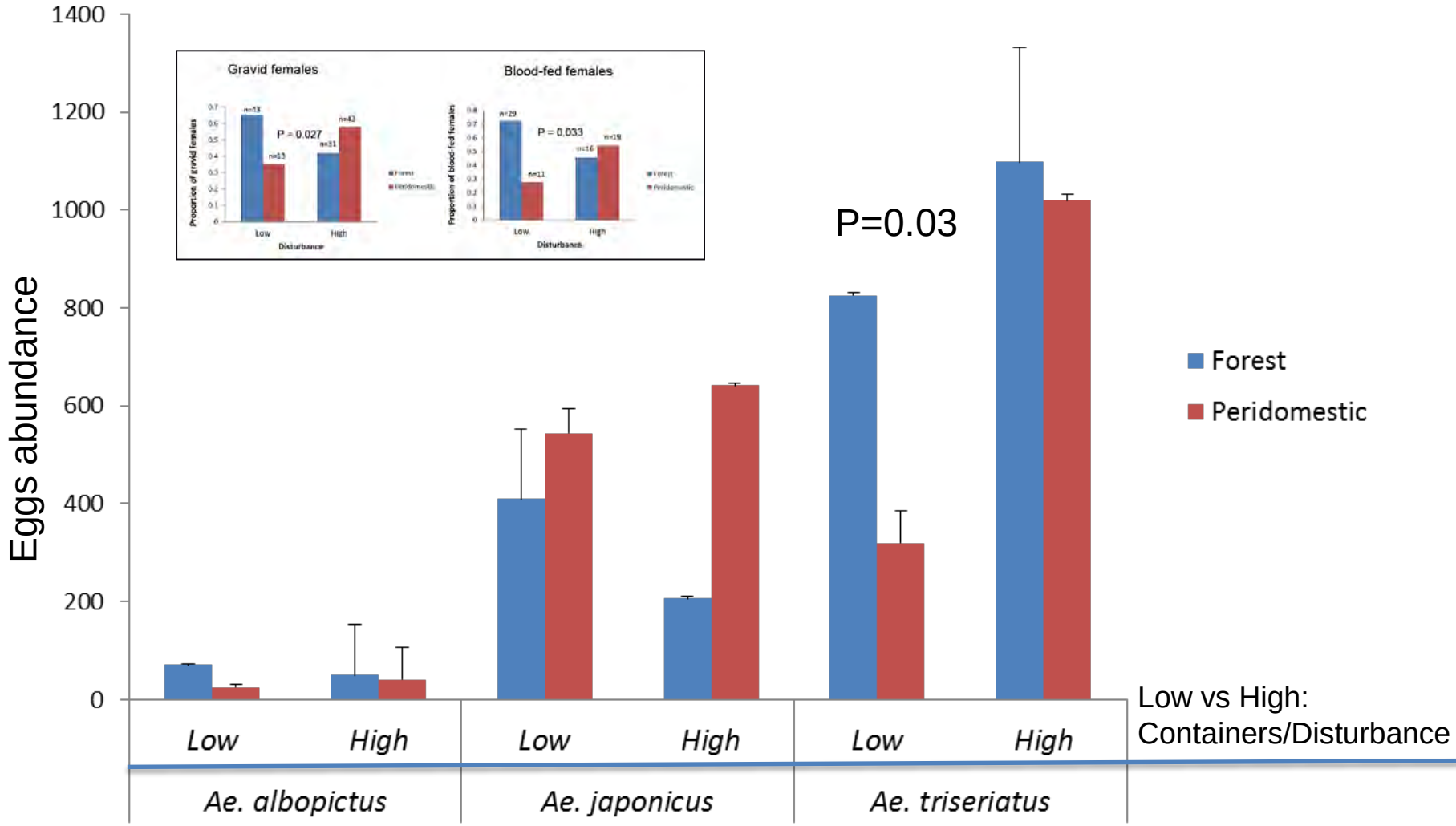
Artificial Containers

LACE Case Residence

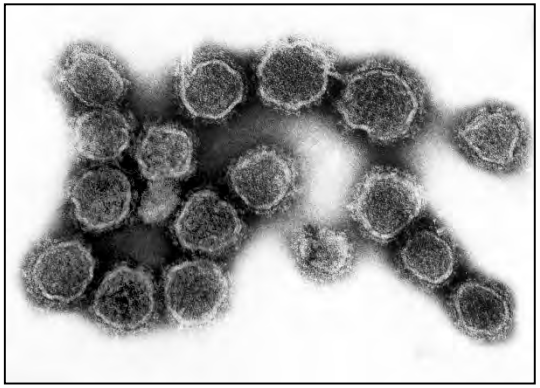
LACE Case Residence

Mosquito Larvae
n=62 Ae. albopictus

Peridomestic Artificial Containers Increase the abundance of *Aedes triseriatus*



Tamini T, Byrd B, Wasserberg G, et al, *In Prep*



Small Mammals
Tamias striatus
Sciurus carolinensis

Human Host
("Dead End")

Mosquito Vector
(*Ae. triseriatus*)

Mosquito Vector
(*Ae. triseriatus*)

Small Mammals
Tamias striatus
Sciurus carolinensis

Transovarial Transmission

(Virus dissemination/Transovarial transmission)

Female Mosquito
(*Ae. triseriatus*)

Infected Progeny
(Male and Female)

Female Mosquito
(*Ae. triseriatus*)

Male Mosquito
(*Ae. triseriatus*)

Venereal Transmission
(male to uninfected female)

Adapted from Beaty and Marquardt (1996)

Invasive Vectors

Aedes albopictus: "Asian Tiger Mosquito"

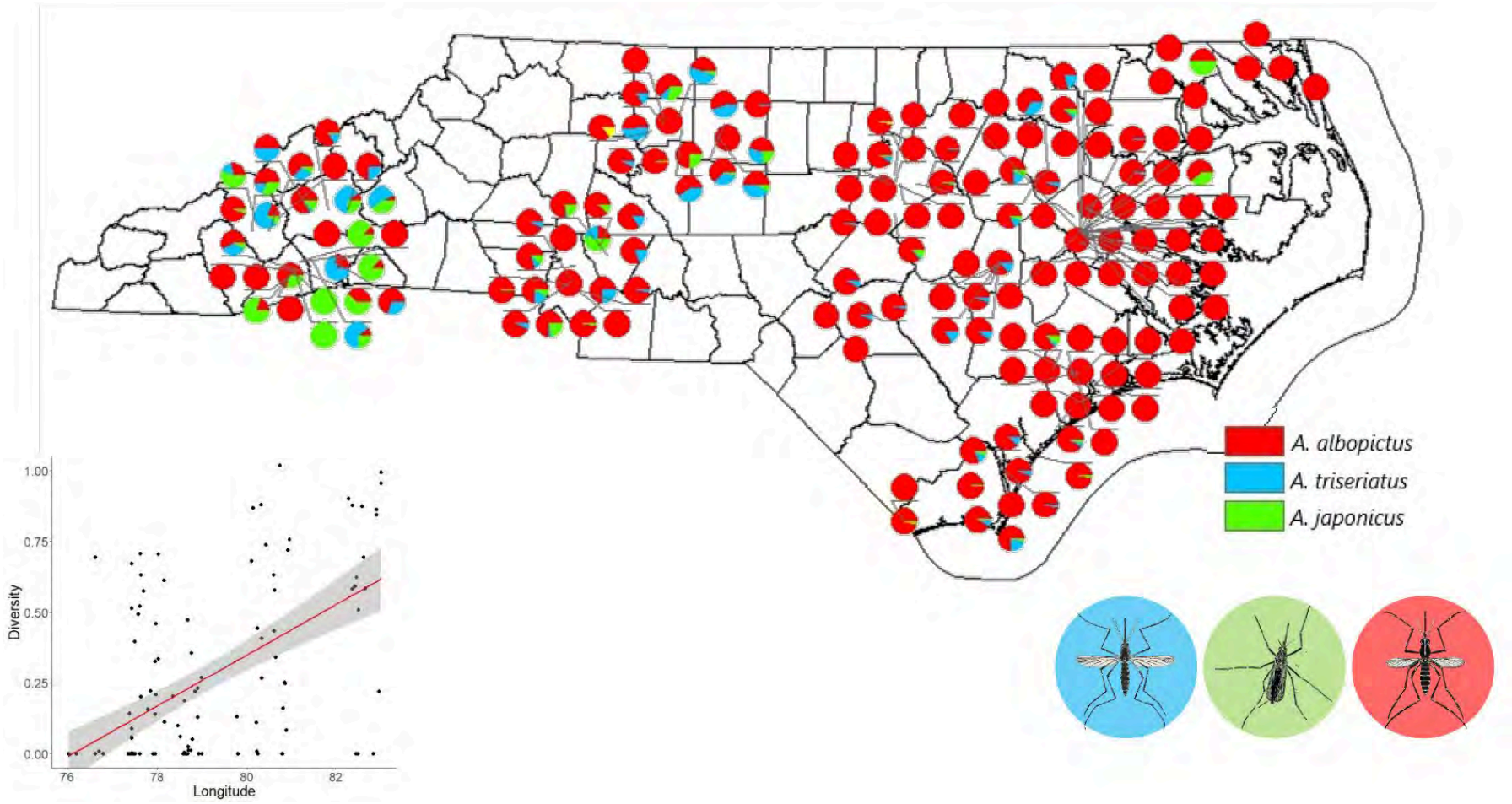
- Can transmit La Crosse virus
- Readily feeds on Humans
- Aggressive, Daytime Feeder

Aedes japonicus: "Asian Bush Mosquito"

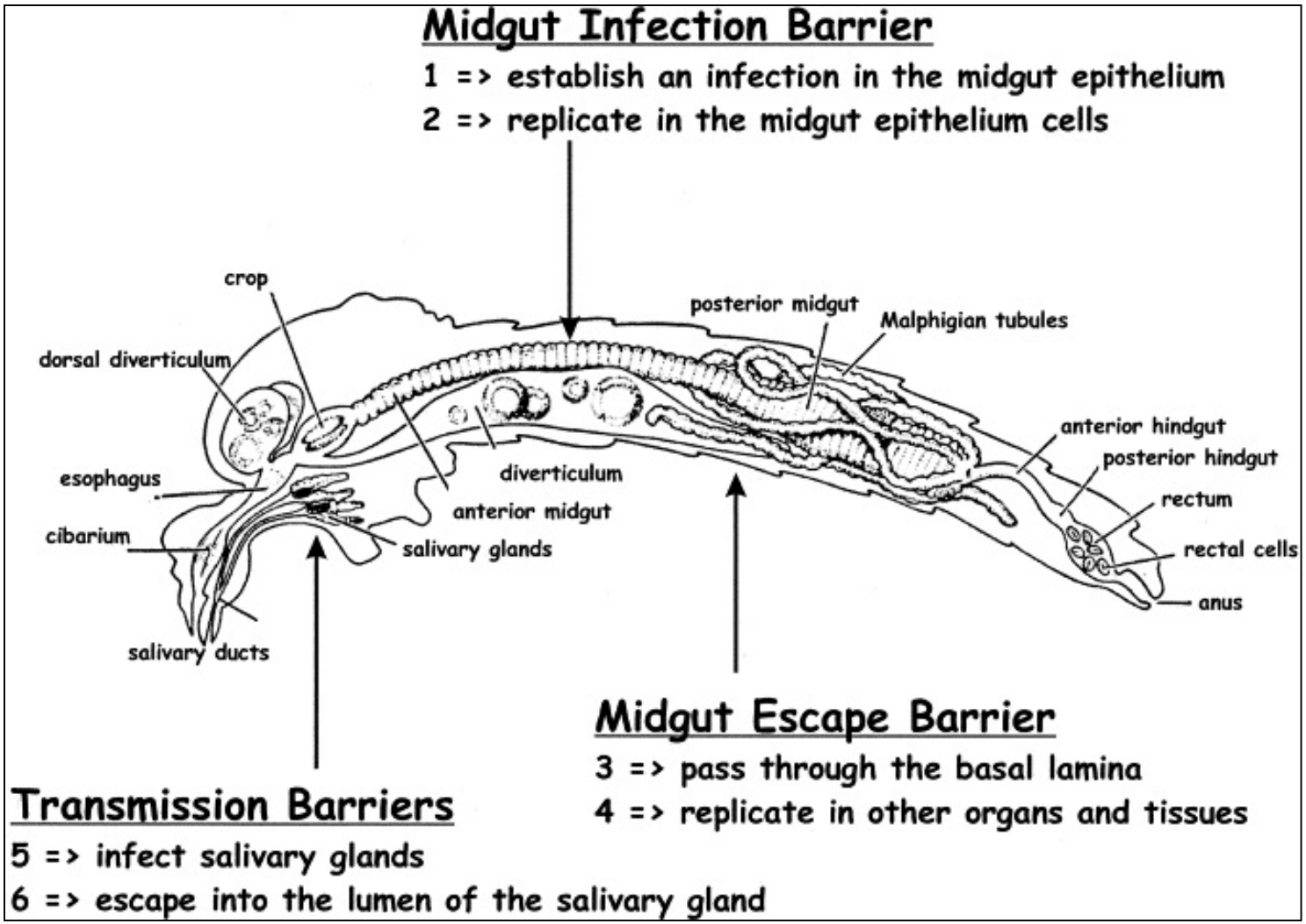
- Can transmit La Crosse virus
- Feeds on Humans
- Less Aggressive, Daytime/Evening Feeder

East TN: LACv IRs for *Ae. japonicus* (0.63) were lower than *Ae. triseriatus* (2.72) and *Ae. albopictus* (3.01) (Westby et al., 2015)

2016 State-wide *Aedes* survey



Reed et al 2019

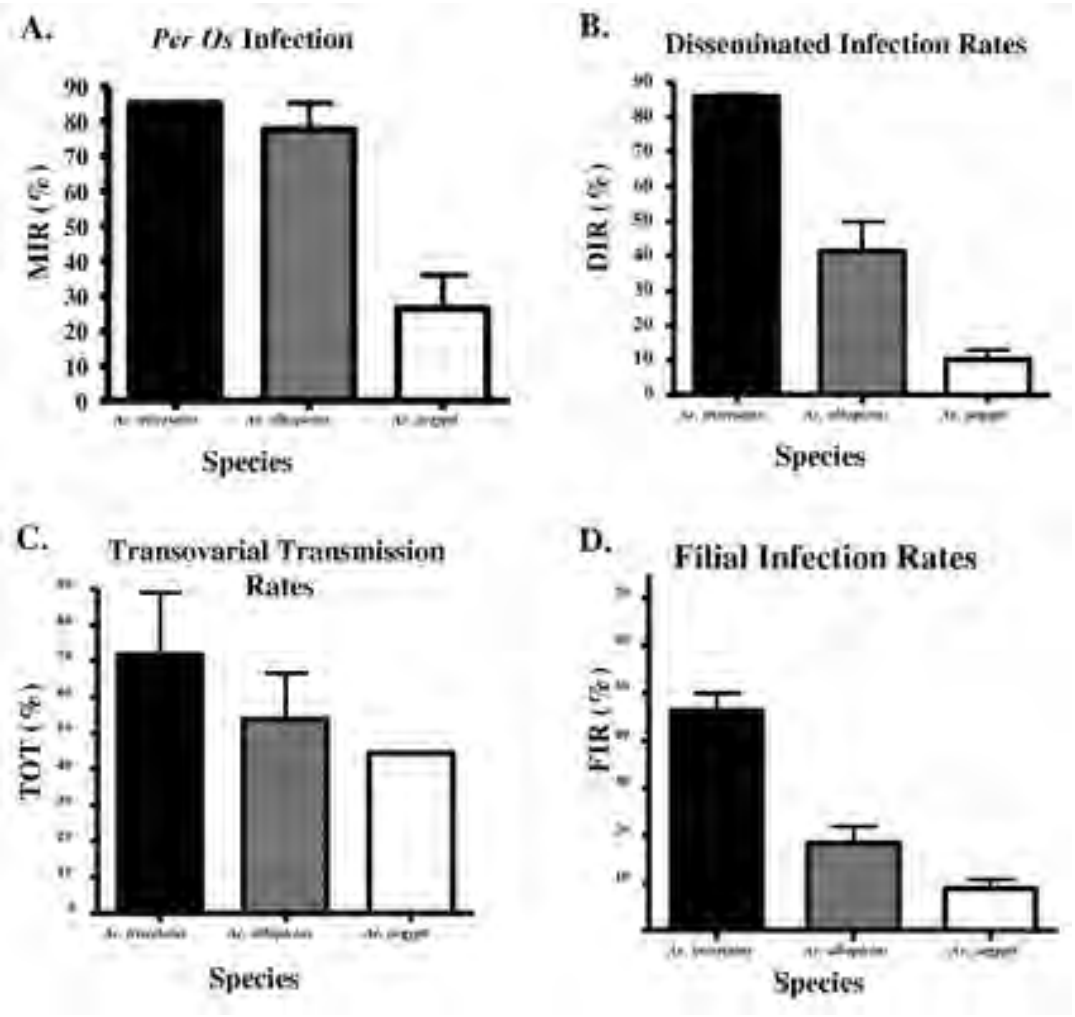


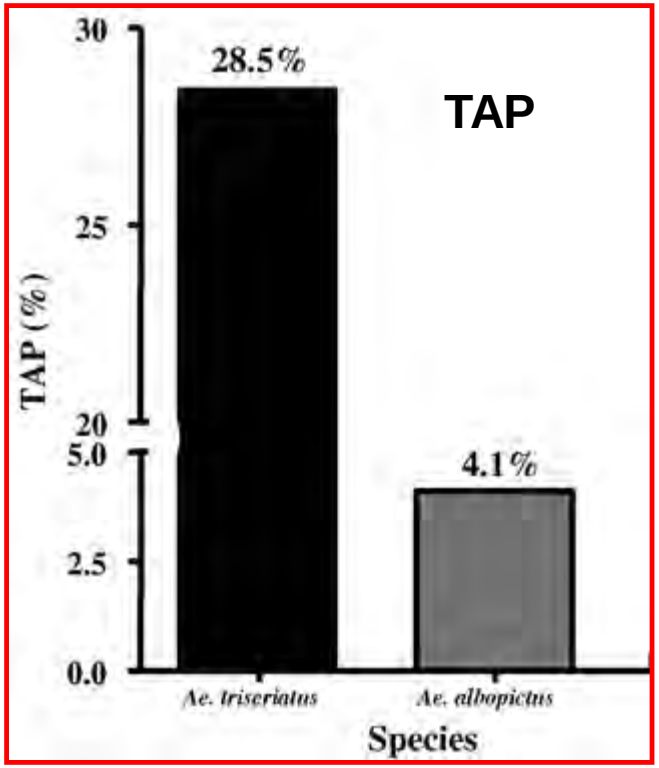
The proportion of infected mosquitoes that are orally exposed (infected) and then become infectious (virus in saliva) is called the vector competence.

The time period from exposure to infectious is called the extrinsic incubation period.

W. Black (Biology of Disease Vectors)

Transmission Amplification Potential





Hughes MT et al. Comparative potential of *Aedes triseriatus*, *Aedes albopictus*, and *Aedes aegypti* (Diptera: Culicidae) to transovarially transmit La Crosse virus. J Med Entomol. 2006 Jul;43(4):757-61.

Vectorial Capacity

$$C = \frac{ma^2\,(P^n)V}{(-\ln P)}$$

ma = bites per human per day (biting rate)
P = probability of daily survival
n = extrinsic incubation period
V = vector competence (innate transmission efficiency)

What to do about LACE?

“Once the kid is sick, the cat is out of the bag”

-WNC Clinician

“We just have to live with the La Crosse problem”

-Unnamed source

“Good Luck”

-Bad guy (speaking to Liam Neeson)

-Mosquito control working group

Fall 2017 Case Investigation

- In August 2017, the NC Division of Public Health was notified of probable LACE in a sibling pair (2 and 11-year-old boys) with exposure likely at the same residence.
- In response to the sibling cases, an interagency team conducted an environmental assessment of the residence.

Adult resting mosquitoes were collected by a large-bore aspirator and 10 ovitraps were placed at the residence for 1 week (70 trap-days). Mosquitoes were identified as adults and assessed for LACV infection by Vero cell isolation (adult collections) or reverse transcriptase qPCR (ovitrap collections).

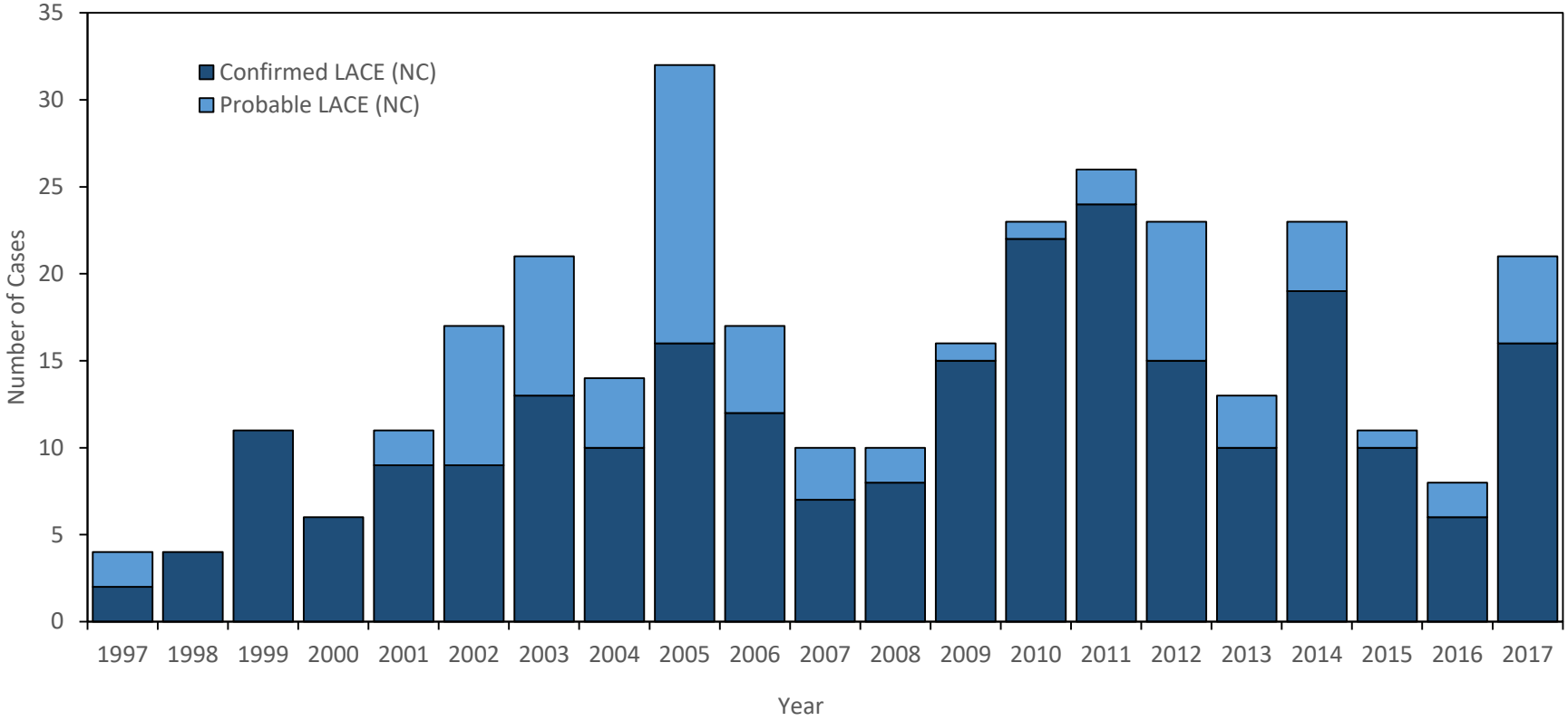
Fall 2017 Case Investigation

- The team identified multiple risk factors associated with the increased risk of LACV transmission:
  - Adult host-seeking and immature *Aedes* mosquitoes
    - *Ae. triseriatus*, *Ae. albopictus*, *Ae. japonicus*
  - Close proximity to mixed hardwood forest
  - Domicile with multiple windows lacking effective screens

- No LACV was detected in any of the mosquito samples obtained from the residence (WCU and CDC Labs).

Co-incident LACE

- Coincident disease may be a factor of shared: 1) residential risk, 2) behavioral risk, 3) familial/genetic predisposition, or other factors.
- Coincident LACE cases are expected to be rare. A review of surveillance records (1997-2017) was performed.



Coincident LACE

Coincident or Spatially Associated La Crosse Virus Disease Cases — North Carolina

---Coincident Cases---

Year (Onset Week)	Age (Sex)	Association	Laboratory evidence*	Outcome
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---Spatially Linked Asynchronous Cases---

Years	Age (Sex)	Association	Laboratory evidence*	Outcome
2015 (29)	8 (F)	Sibling pair residing at same residence	LACV IgM ELISA and PRNT positive (serum)	Survived
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2012 (27)	4 (M)	No familial relationship, linked by residence (Homeownership changed)	LACV IgM ELISA positive (CSF and serum)	Survived
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Coincident LACE

- These data suggest
  - Disease risk is focal and may be residentially-linked
  - Disease can occur coincidently or asynchronously at the same physical residence
  - LHD outreach and environmental modifications at LACE residences may reduce further disease
    - Personal protection measures
    - Installing and repairing window or door screens
    - Removing containers of standing water
    - Filling tree holes

Coincident LACE

- Evidence-based control interventions should be evaluated
  - Physical modifications (tree hole management)
  - Barrier insecticide treatments
  - Autodissemination approaches (e.g., In2Care)
  - Passive “sink” traps (e.g., AGO, GAT)
- Methods that reduce entomologic risk should be recommended as a coordinated response to LACE cases

Case Report Summary

- We describe residentially-linked cases that occurred coincidently and asynchronously.
- Case Series: MMWR (Oct. 5th, 2018; Byrd et al.)
- Public health agencies should recommend risk reduction measures to all persons living at the residence of a LACE case.
- Evidence-based mosquito control interventions that target LACV vectors should be evaluated in LACE endemic areas.

Final Thoughts…

- **Mosquito-borne diseases in NC:**
  - None are vaccine preventable in humans
  - None have a therapeutic “silver bullet”
  - Reduce disease risk by decreasing mosquito bites
- **“Prevention is the cure”**
- **Some mosquito-borne diseases may require municipal assistance to reduce risk**

Prevention Messaging

- **Source Reduction (DRAIN)**
  - "Tip and Toss" containers holding water
  - Solid Waste Management
  - Remember "cryptic" habitats
    - Check Rain Gutters
  - Tree-hole Management

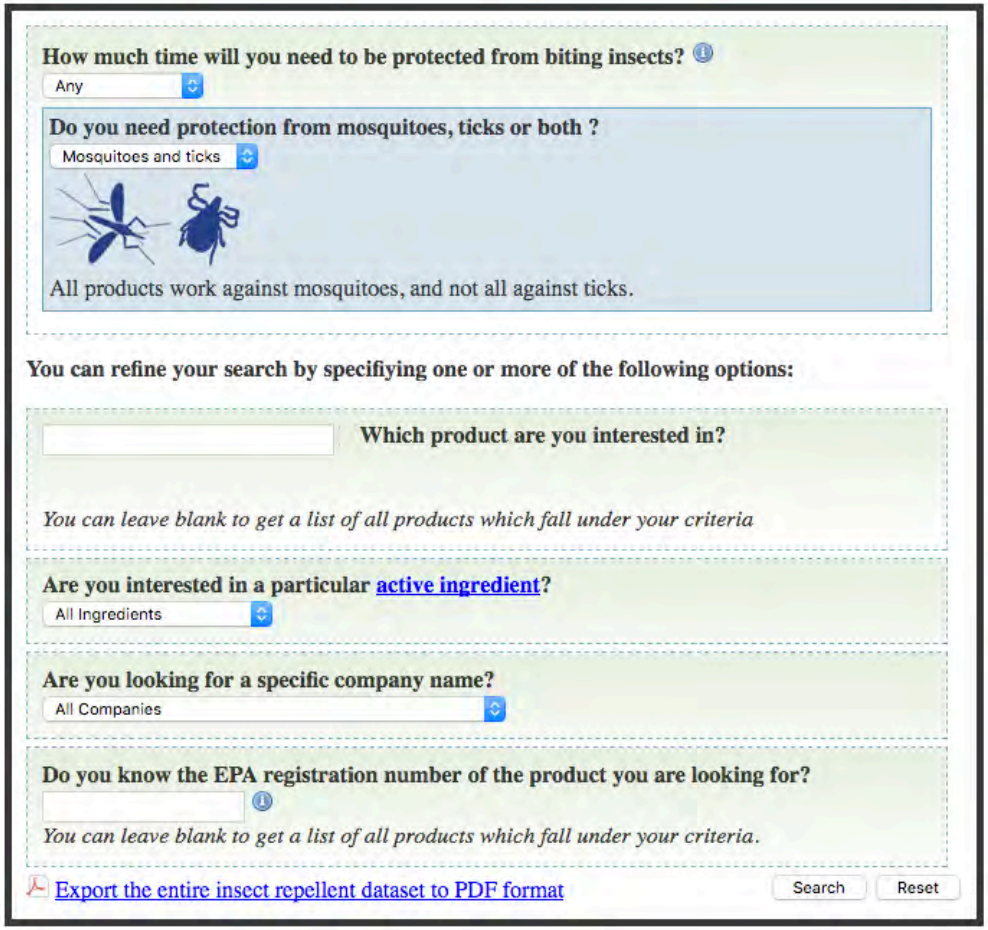


Prevention: Personal

- **Long Sleeves and Pants (DRESS)**
- **Apply Repellents According to the Label (DEFEND)**
  - CDC Recommends EPA Registered Repellents*
  - DEET, picaridin, IR3535, and some oil of lemon eucalyptus products
- **Avoid contact at "peak" hours (afternoon/evening)**

*EPA registration means that EPA does not expect the product to cause adverse effects to human health or the environment when used according to the label.`

EPA Repellent Tool



https://www.epa.gov/insect-repellents/find-repellent-right-you

CDC VCEHP

Vector Control for Environmental Health Professionals (VCEHP)

Environmental health professionals are on the frontline of helping individuals, institutions, and communities reduce threats from mosquitoes, ticks, and other vectors. This training—Vector Control for Environmental Health Professionals—emphasizes the use of integrated pest management to address public health pests and vectors that spread pathogens, including Zika virus and others.

VCEHP includes a subset of courses particularly helpful for understanding and addressing Zika virus and other mosquito-borne diseases.

Get Started Today

1. **Visit the Website:** http://lms.southcentralpartnership.org/vcehp.php
2. **Create a New Account**
3. **Enroll in VCEHP Courses**

What Are the Benefits of This Training?

- **It's free and flexible:** Take the courses you want, when you want in this online learning program.
- **It's credible:** Learn the latest science and evidence from vector control experts to improve your awareness and understanding of vector control and pest management.
- **It's practical:** Access concrete principles, practices, and resources to address vector control issues affecting your community.
- **You can earn continuing education units (CEUs):** Obtain CEUs from the National Environmental Health Association upon completing the courses and final evaluation (optional).

Consider the CDC's VCEHP Online Training

CDC VCEHP

Western Carolina University

11 Courses: Take all or pick and choose (first 3 required)

- Vector-Borne Diseases of Public Health Importance*
- Integrated Pest Management Basics*
- Performance Assessment and Improvement of Vector Control Services*
- Tick Biology and Control
- Mosquito Biology and Control
- Toxicology of Pesticides
- Rodent Management
- Pests and Vectors in Food and Housing Environments
- Special Pest Management Considerations for Schools
- Risk Communication Basics
- Bed Bug Biology and Control

Obtain CEUs from NEHA upon completing the course!

Questions?

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