Public Health and Clinical Malaria in the U.S.

Seymour Williams, MD, MPH

Malaria Branch

Division of Parasitic Diseases and Malaria

BLOOD PRODUCTS ADVISORY COMMITTEE meeting

May 9, 2024

Public Health and Clinical Malaria in the U.S.: Outline

- Brief on Biology/Burden/History
- Surveillance & Epidemiology
- Prevention and Clinical Care
- Local malaria outbreak, U.S., 2023

Malaria: a parasitic disease transmitted by *Anopheles* mosquitos

- 5 species of *Plasmodium* cause human disease
  - *P. falciparum*
  - *P. vivax* (relapsing)
  - *P. ovale (*relapsing*)*
  - *P. malariae*
  - *P. knowlesi* (zoonotic)

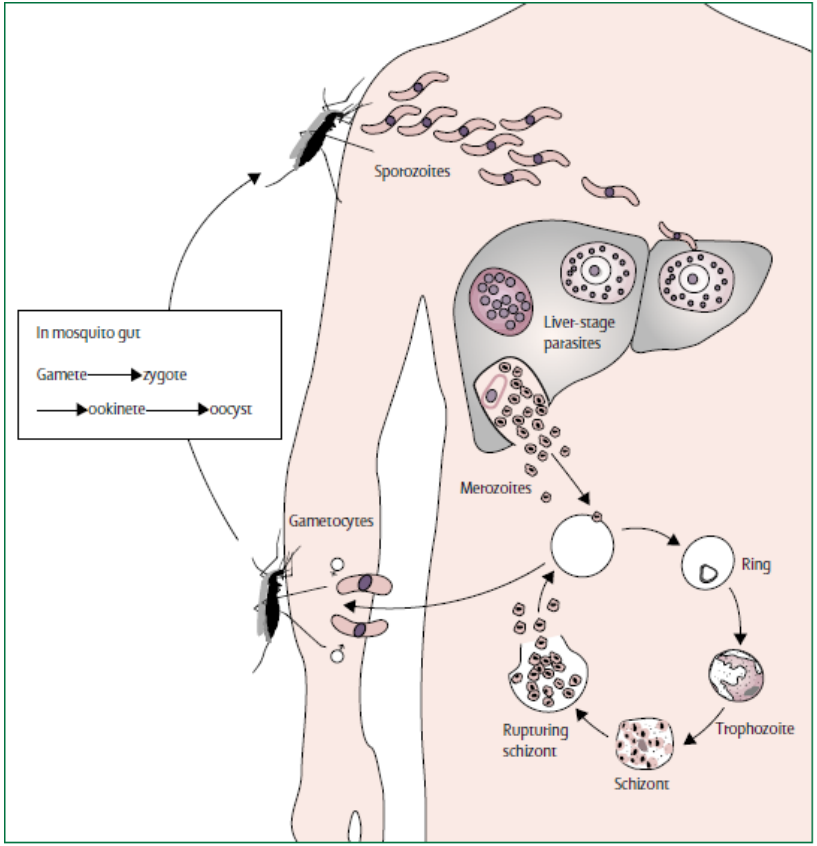


Figure 1: **Life cycle of the malaria parasite**
Adapted from Good MF. Vaccine-induced immunity to malaria parasites and the need for novel strategies. *Trends Parasitol* 2005; **21:** 29–34.

Mechanisms of Malaria Transmission, US

- **Mosquito**

- Congenital

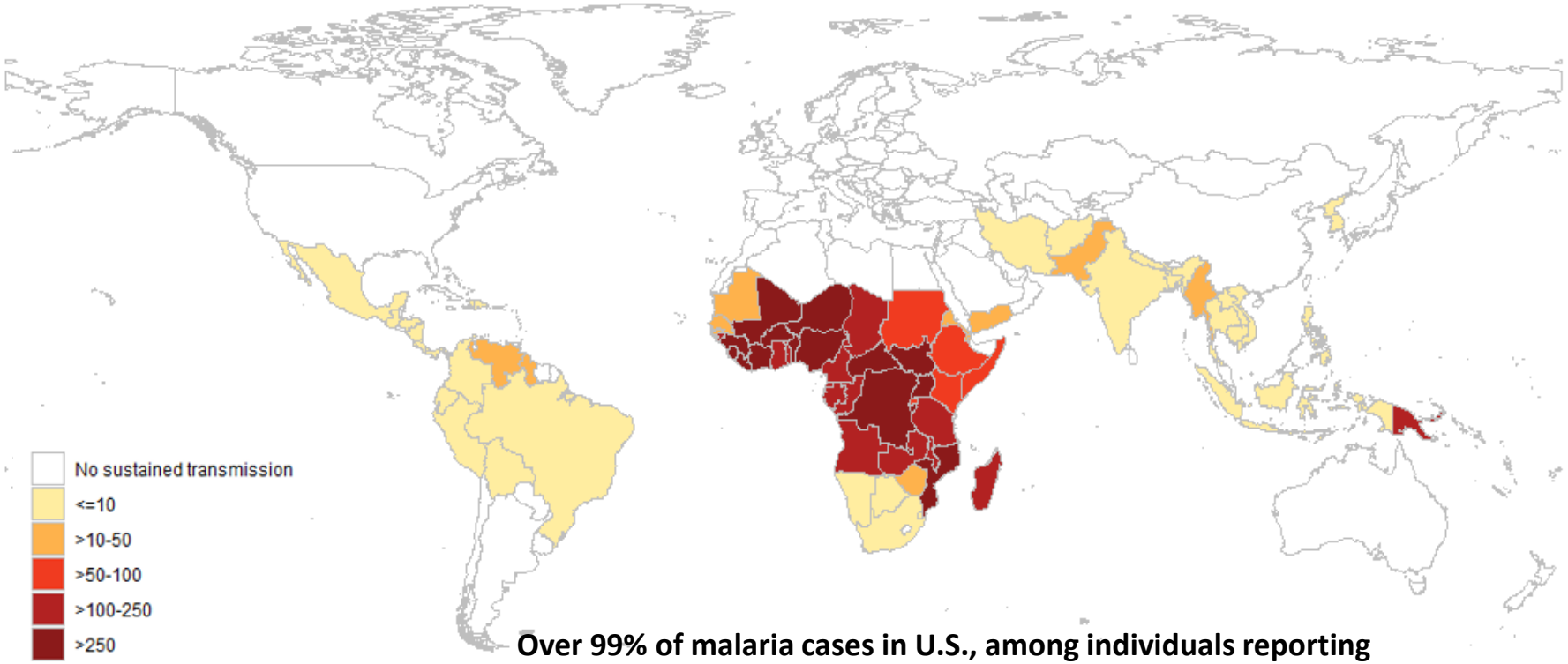
- Blood transfusions

- Organ transplant

- Sharing needles or syringes

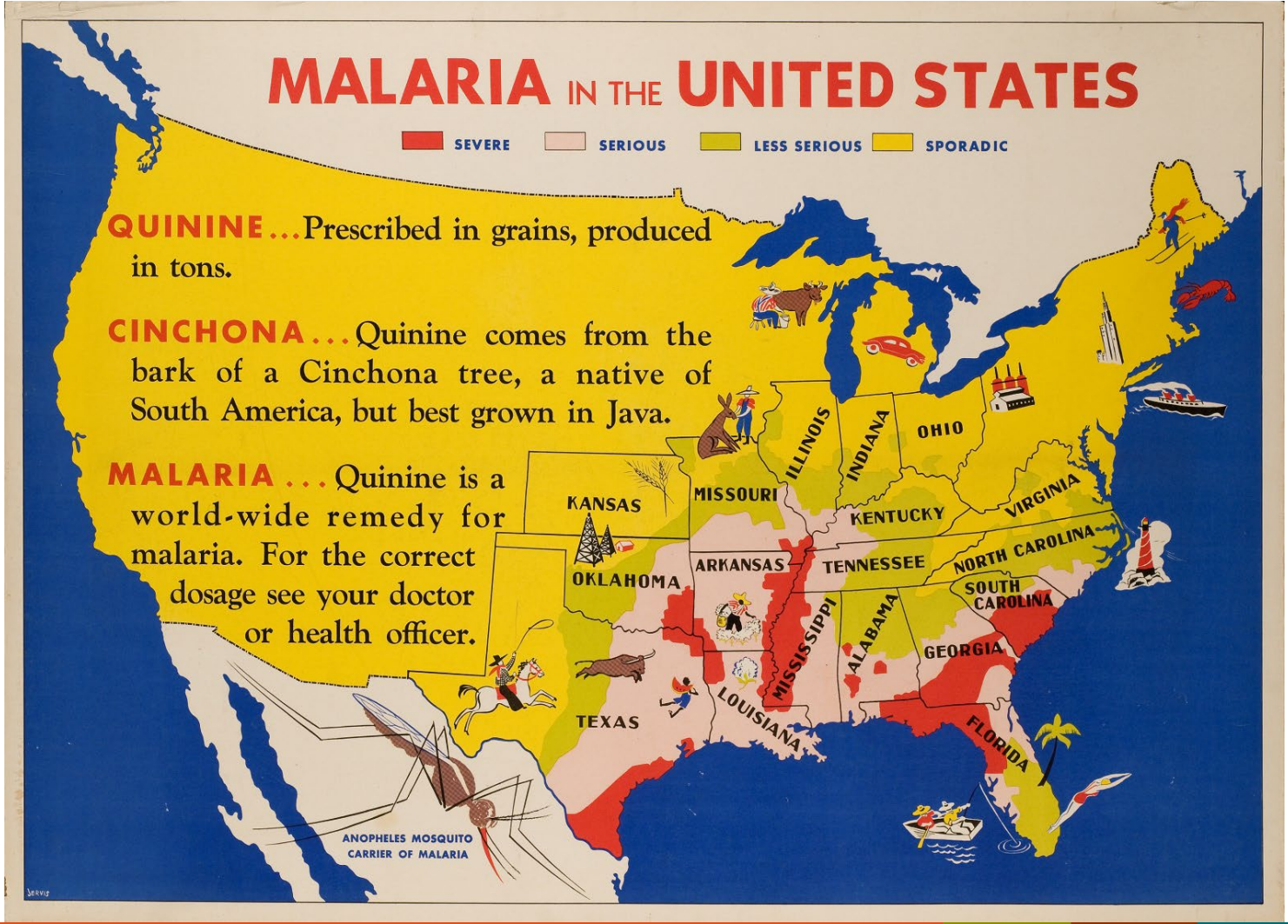
Credits
Blood in bag : https://pixels.com/featured/blood-transfusion-antonia-reevescience-photo-library.html
Organ box- https://www.news-medical.net/health/How-has-COVID-19-affected-Organ-Transplantation.aspx
Sharing needles- https://www.northridgeaddiction.com/recovery-blog/intravenous-drug-use/dangers-of-drug-injection-use-and-sharing-needles/
Baby in utero: Magic nine/Shutterstock.com in https://www.news-medical.net/health/What-is-Vertical-Transmission.aspx

Global Malaria cases, 2023



Over 99% of malaria cases in U.S., among individuals reporting travel to or from malaria-endemic region ≤1 year of presentation

WHO, 2023



Malaria in the United States, early 1940s

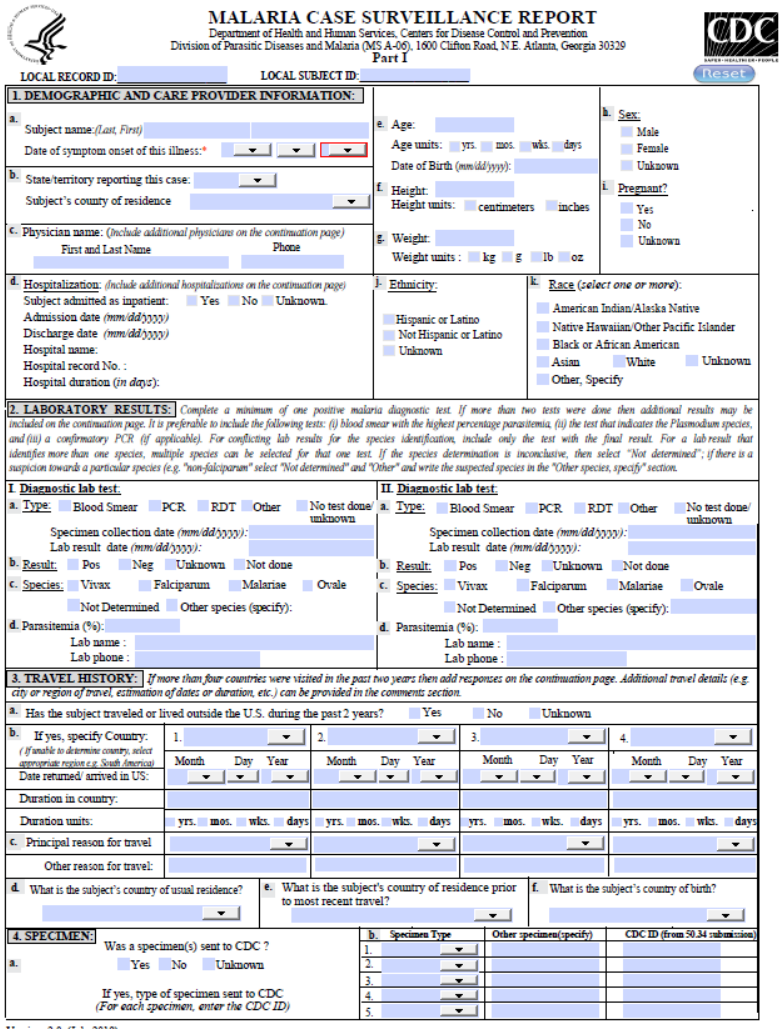
~65,000 cases/yr

Source: NLM/NIH
Cinchona Inc. NYC

Malaria Surveillance

Malaria case investigation

- **Laboratory tests**
- **Travel history:** dates, reason for travel
- **Clinical:** Illness onset, hospitalization, complications, chemoprophylaxis, treatments, outcome
- **History:** prior malaria, transfusion



MALARIA CASE SURVEILLANCE REPORT

Department of Health and Human Services, Centers for Disease Control and Prevention
Division of Parasitic Diseases and Malaria (MS A-06), 1600 Clifton Road, N.E. Atlanta, Georgia 30329

Part I

CDC

Reset

LOCAL RECORD ID: LOCAL SUBJECT ID:

1. DEMOGRAPHIC AND CARE PROVIDER INFORMATION:

a. Subject name:*(Last, First)*
Date of symptom onset of this illness:*

b. State/territory reporting this case:
Subject's county of residence

c. Physician name: *(Include additional physicians on the continuation page)*
First and Last Name Phone

e. Age:
Age units: yrs. mos. wks. days
Date of Birth *(mm/dd/yyyy)*:

f. Height:
Height units: centimeters inches

g. Weight:
Weight units : kg g lb oz

h. Sex:
Male
Female
Unknown

i. Pregnant?
Yes
No
Unknown

d. Hospitalization: *(Include additional hospitalizations on the continuation page)*
Subject admitted as inpatient: Yes No Unknown
Admission date *(mm/dd/yyyy)*
Discharge date *(mm/dd/yyyy)*
Hospital name:
Hospital record No. :
Hospital duration (*in days*):

j. Ethnicity:
Hispanic or Latino
Not Hispanic or Latino
Unknown

k. Race (*select one or more*):
American Indian/Alaska Native
Native Hawaiian/Other Pacific Islander
Black or African American
Asian White Unknown
Other, Specify

2. LABORATORY RESULTS: *Complete a minimum of one positive malaria diagnostic test. If more than two tests were done then additional results may be included on the continuation page. It is preferable to include the following tests: (i) blood smear with the highest percentage parasitemia, (ii) the test that indicates the Plasmodium species, and (iii) a confirmatory PCR (if applicable). For conflicting lab results for the species identification, include only the test with the final result. For a lab result that identifies more than one species, multiple species can be selected for that one test. If the species determination is inconclusive, then select "Not determined"; if there is a suspicion towards a particular species (e.g. "non-falciparum" select "Not determined" and "Other" and write the suspected species in the "Other species, specify" section.*

I. Diagnostic lab test.	II. Diagnostic lab test.
a. Type: Blood Smear PCR RDT Other No test done/ unknown	a. Type: Blood Smear PCR RDT Other No test done/ unknown
Specimen collection date *(mm/dd/yyyy)*:	Specimen collection date *(mm/dd/yyyy)*:
Lab result date *(mm/dd/yyyy)*:	Lab result date *(mm/dd/yyyy)*:
b. Result: Pos Neg Unknown Not done	b. Result: Pos Neg Unknown Not done
c. Species: Vivax Falciparum Malariae Ovale	c. Species: Vivax Falciparum Malariae Ovale
Not Determined Other species (specify):	Not Determined Other species (specify):
d. Parasitemia (%):	d. Parasitemia (%):
Lab name :	Lab name :
Lab phone :	Lab phone :

3. TRAVEL HISTORY: *If more than four countries were visited in the past two years then add responses on the continuation page. Additional travel details (e.g. city or region of travel, estimation of dates or duration, etc.) can be provided in the comments section.*

a. Has the subject traveled or lived outside the U.S. during the past 2 years? Yes No Unknown

b. If yes, specify Country: *(If unable to determine country, select appropriate region e.g. South America)*	1.	2.	3.	4.
Date returned/ arrived in US:	Month Day Year	Month Day Year	Month Day Year	Month Day Year
Duration in country:				
Duration units:	yrs. mos. wks. days	yrs. mos. wks. days	yrs. mos. wks. days	yrs. mos. wks. days
c. Principal reason for travel				
Other reason for travel:				

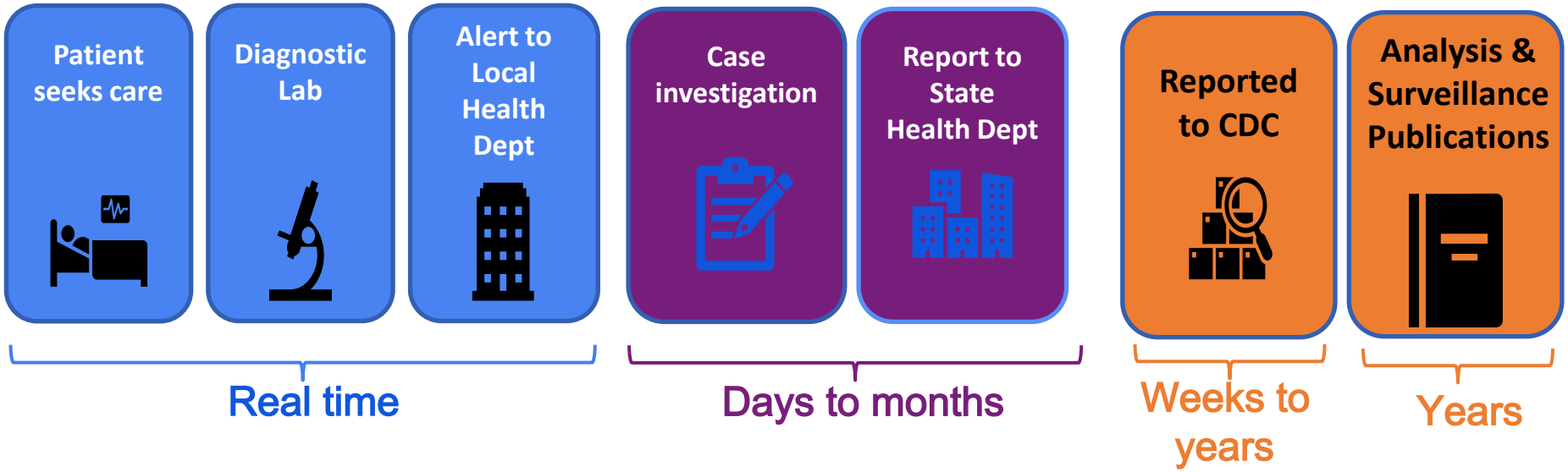
d. What is the subject's country of usual residence?
e. What is the subject's country of residence prior to most recent travel?
f. What is the subject's country of birth?

4. SPECIMEN:
a. Was a specimen(s) sent to CDC ? Yes No Unknown
If yes, type of specimen sent to CDC *(For each specimen, enter the CDC ID)*

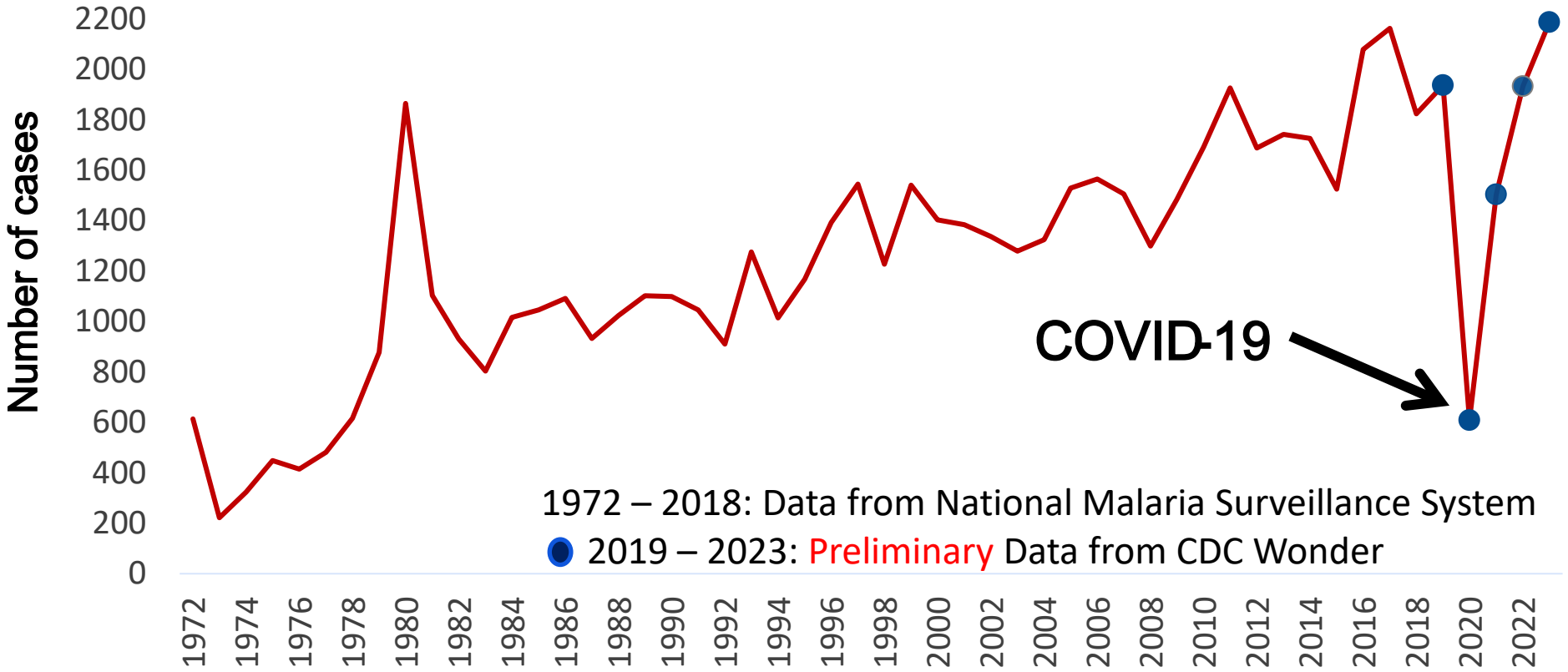
b. Specimen Type	Other specimen(specify)	CDC ID (from 50.34 submission)
1.		
2.		
3.		
4.		
5.		

https://www.cdc.gov/malaria/report.html

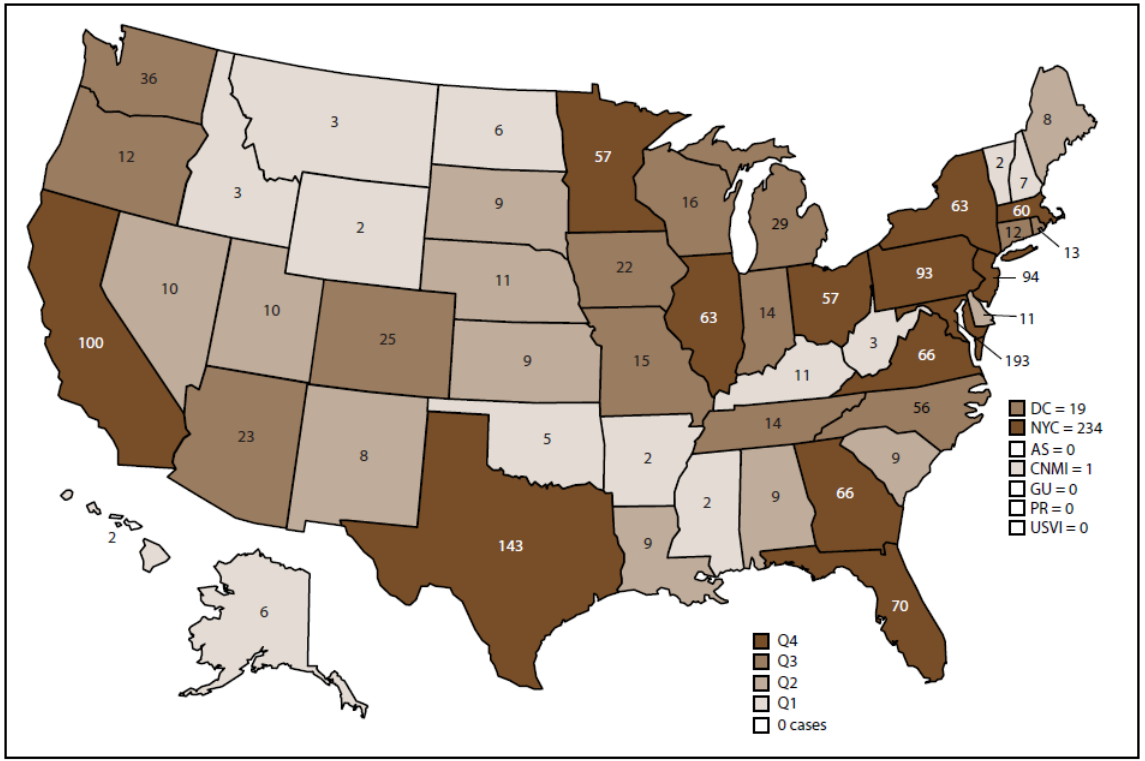
Malaria surveillance in the U.S.



The number of malaria cases in the U.S. has been increasing.



Most years, every state reports at least 1 person diagnosed with malaria

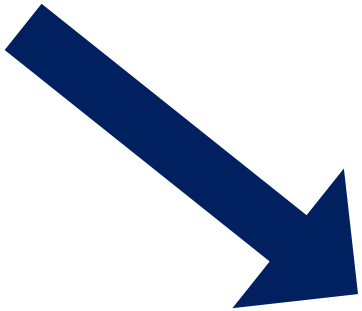


SOURCE: Malaria Surveillance— United States, 2018 | MMWR (cdc.gov)

A preview of the 2019 – 2020 surveillance data

More than 2050 cases

2019

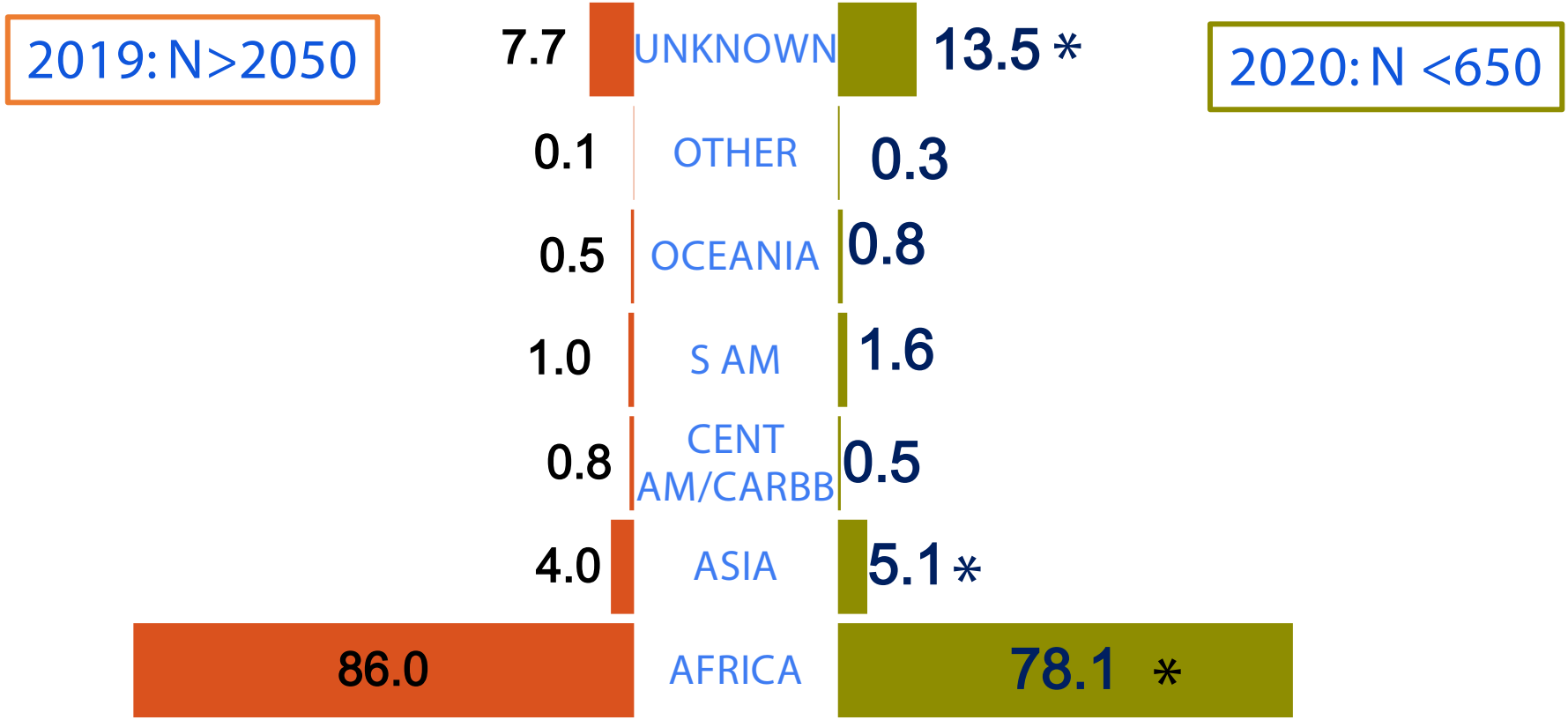


2020

Approx 600 cases

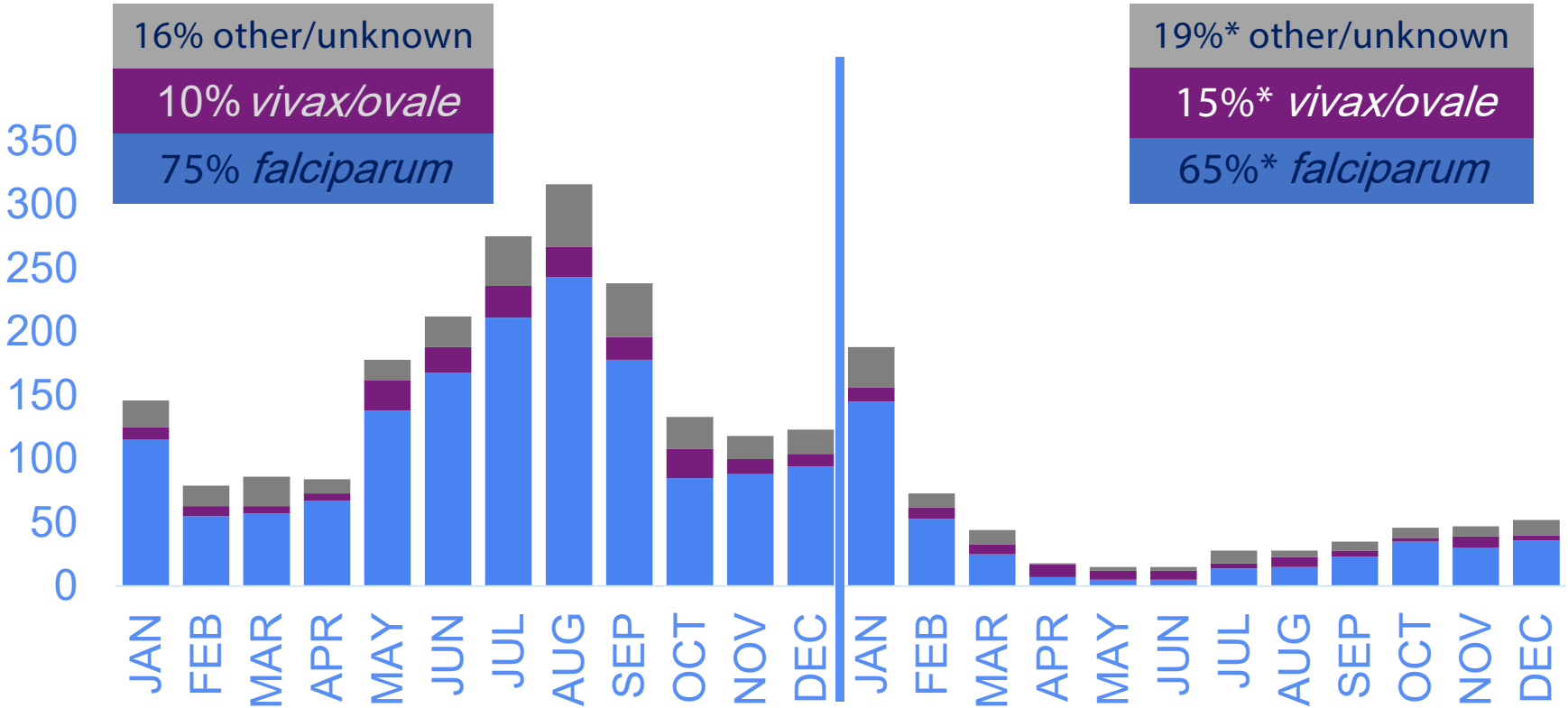
2019–2020 National Malaria Surveillance data are unpublished and preliminar

Global Region of Malaria acquisition, 2019 – 2020



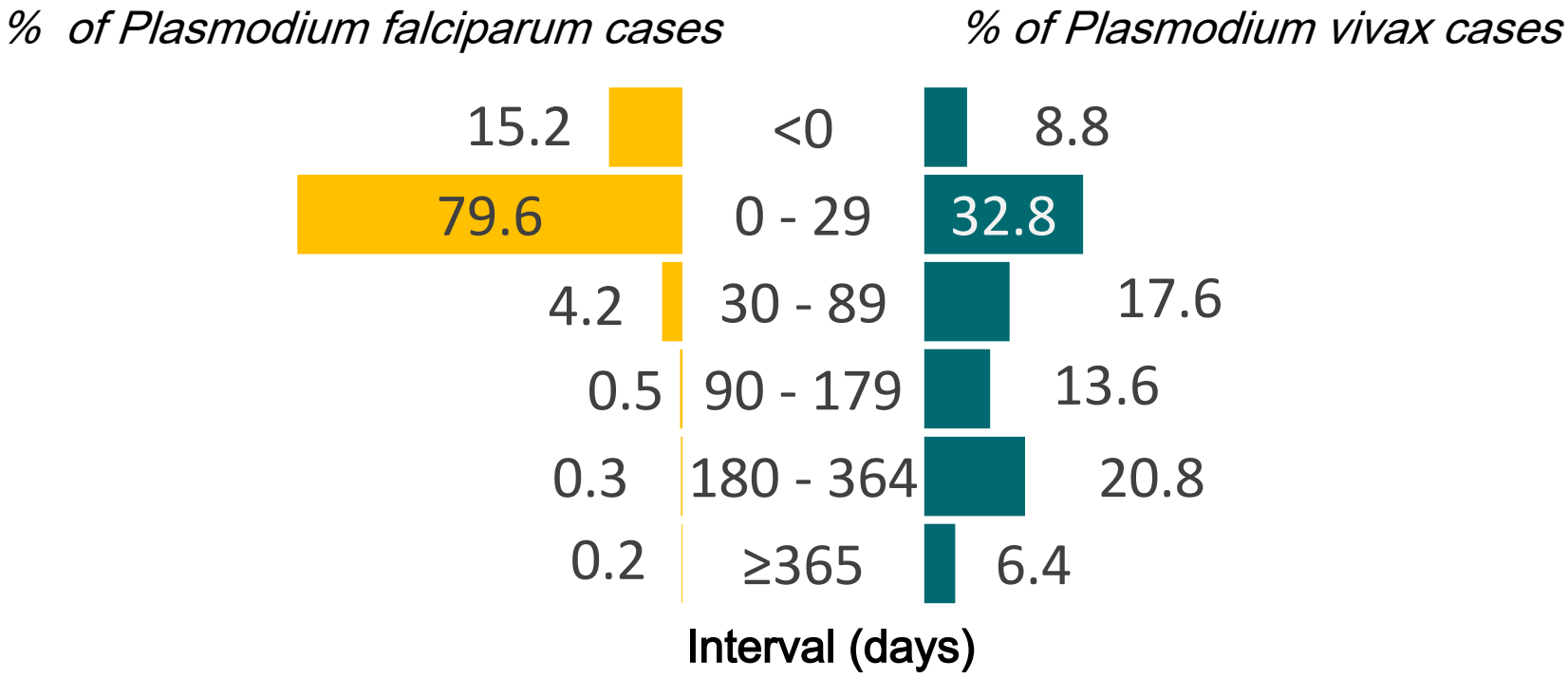
2019 – 2020 National Malaria Surveillance data are unpublished and preliminary

US Malaria cases 2019 – 2020, onset month & species



2019 – 2020 National Malaria Surveillance data are unpublished and preliminary

Time interval between date of arrival in the U.S. and date of illness onset, by *Plasmodium* species, 2018



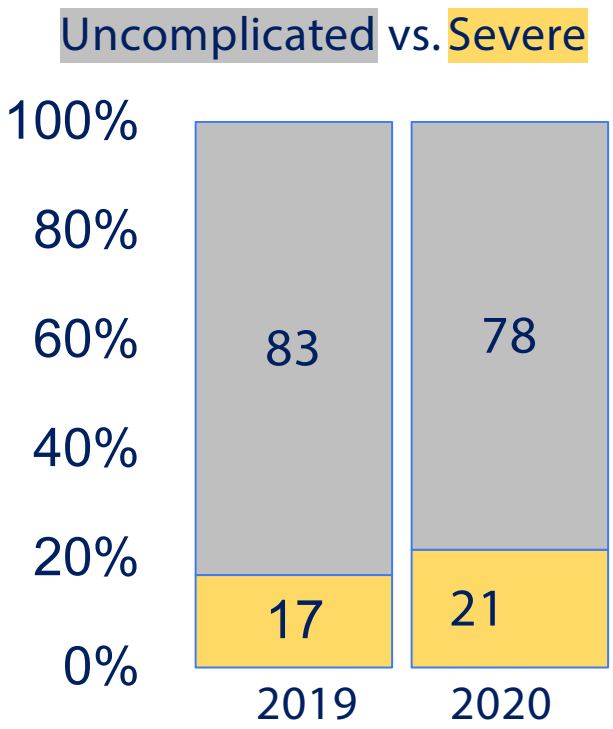
Malaria Surveillance— United States, 2018 | MMWR (cdc.gov

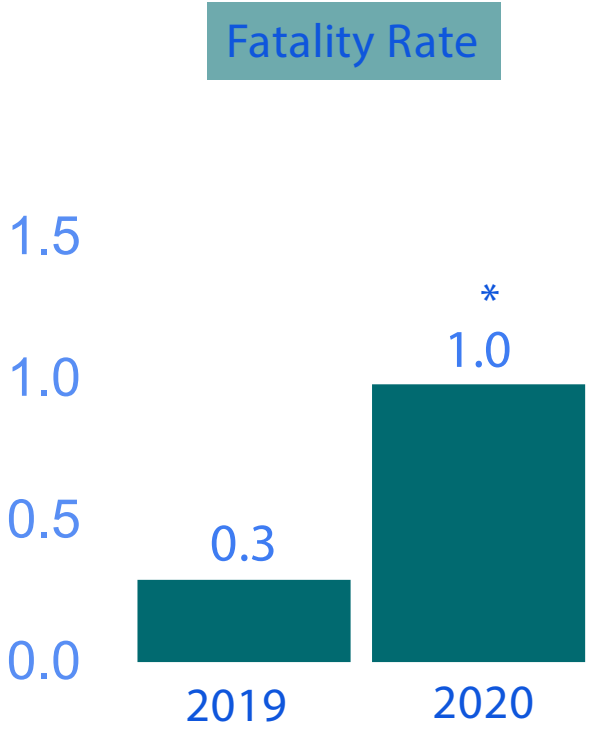
Defining Severity of malaria cases in the US

Surveillance criteria

- Neurologic symptoms
- Acute kidney injury
- Severe anemia
- Acute respiratory distress syndrome
- 5% or higher parasitemia
- Documented IV antimalarial
- Fatal cases with malaria as cause of death

Severity of malaria cases in the US, 2019 – 2020



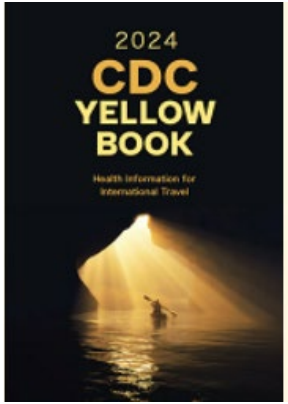


2019 – 2020 National Malaria Surveillance data are unpublished and preliminary

Malaria Prevention

CDC Malaria Chemoprophylaxis Recommendations

- **Reviewed every two years; may be updated more frequently**
- **Information sources**
  - WHO “Country List,” World Malaria Report, and other reports
  - Country ministries of health and malaria control programs
  - CDC Country Offices (in 62 countries)
  - U.S. President’s Malaria Initiative (in 30 countries)
  - U.S. domestic surveillance
  - Literature review
- **Low-risk, conservative prevention approach for chemoprophylaxis**



https://wwwnc.cdc.gov/travel/yellowbook/2024/infections-diseases/malaria#prevent

Actions for Travelers to Prevent Malaria

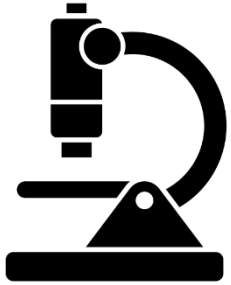
- Medication Prophylaxis for travel to endemic area
  - Prescribed medication based on parasite drug sensitivities
  - Take before, during and after travel
- Mosquito Avoidance
  - Insect repellants – topical and impregnated
  - Bed nets
  - Avoid being outdoors when mosquito active

https://wwwnc.cdc.gov/travel/yellowbook/2024/infections_-diseases/malaria#prevent

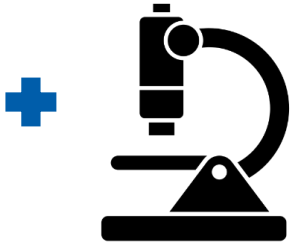
Malaria Diagnosis & Treatment

Malaria Diagnostic Test Results Should be Available STAT!

- **Thick and thin blood smears (gold standard)**
  - Thick smears: most sensitive for presence of parasites
  - Thin smears: species and parasite density



- **Rapid Diagnostic Test (RDT)**
  - Can decrease time to treatment
  - Smear still required to confirm RDT result



Other Tests Not Recommended for Initial Diagnosis

- **PCR**
  - Used to identify or confirm species
  - Lengthy turnaround time

- **Serology**
  - Cannot distinguish between acute and prior infection
  - Lengthy turnaround time

Key Considerations for Malaria Treatment in the U.S.

- Management in the United States differs from endemic areas due to low malaria immunity status and available drug regimens
- Hospitalization decision
- Treatment regimen is dictated by:
  - Severity
  - Species and resistance patterns
  - Drug availability
  - Age and pregnancy status

Drugs Available in the U.S. to Treat Acute Infection of Uncomplicated Malaria

***P. falciparum* / Species unidentified** (appropriate for all species)	***P. vivax*, *P. ovale*, *P. malariae***
Treatment of **acute** infection	Treatment of **acute** infection (chloroquine-susceptible)
Artemether-lumefantrine (Coartem®) Atovaquone-proguanil (Malarone®) Quinine PLUS [doxycycline, clindamycin, or tetracycline] Mefloquine	Chloroquine (Aralen®) Hydroxychloroquine (Plaquenil®)

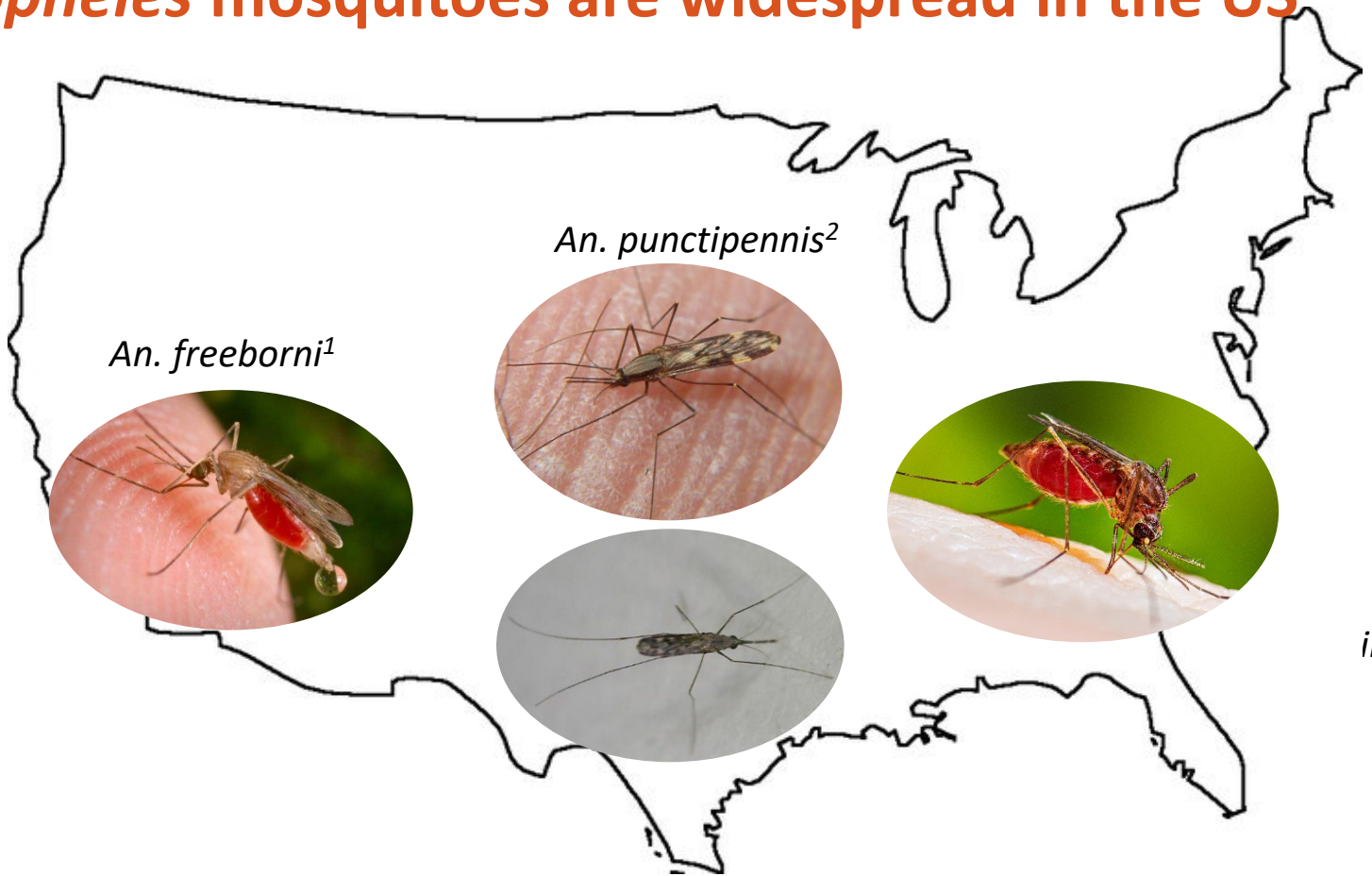
Drugs Available to Treat Severe Malaria in the U.S.

P. falciparum, *P. vivax*, *P. ovale*, *P. malariae*, species unidentified
(appropriate for all species)

IV artesunate (severe disease)

2023 Locally Acquired Malaria Cases

Anopheles mosquitoes are widespread in the US



An. freeborni[1]

An. punctipennis[2]

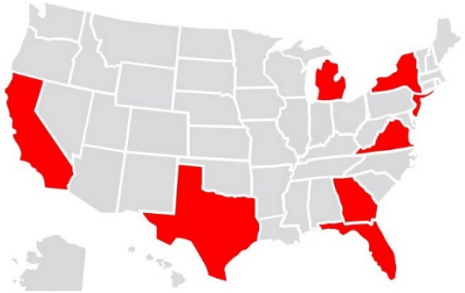
imaculatus[1]

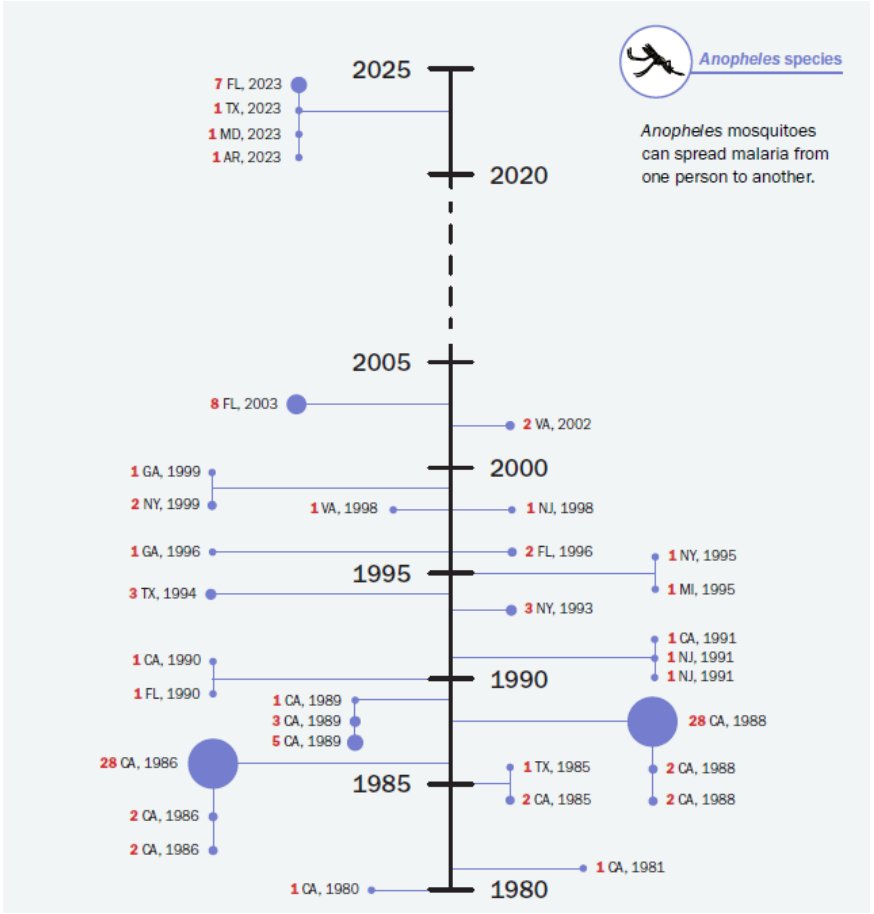
Photo credits:
1. CDC
2. U of Fla
3. BugGuide

History of Locally Acquired Malaria in U.S., 1980-2023

- Between 1980 – 2003, 30 outbreaks of malaria occurred in 8 states

Affected states, 1980–2003 (n=8)

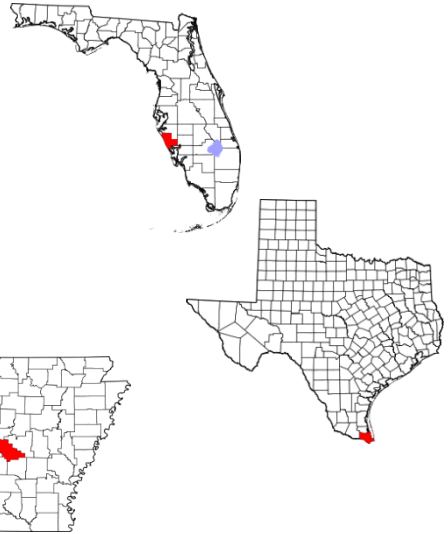


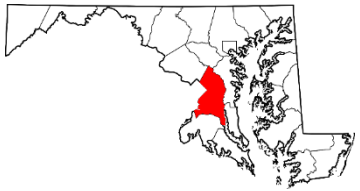


https://www.cdc.gov/ncezid/dvbd/framework.html

US Locally Acquired Malaria Cases – Florida, Texas, Maryland, Arkansas, 2023 (n=10)

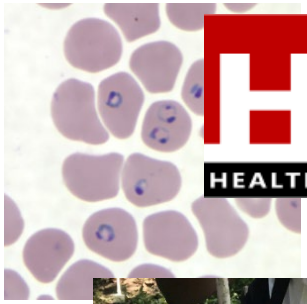
Species	State	County	Cases	Reported
P. vivax				
	Florida	Sarasota	7	May-Jul
	Texas	Cameron	1	Jun
	Arkansas	Saline	1	Oct
P. falciparum				
	Maryland	National Capital Region	1	Aug





Locally Acquired Malaria 2023: Investigation Components

- Laboratory
  - Case confirmation & species identification
  - Genotyping
- Epidemiological
  - In-depth interviews to assess risk factors
  - Active case finding
  - Community engagement
- Environmental
  - Household visits
  - Entomologic surveillance & analysis
  - Vector control actions
- Public Health communications

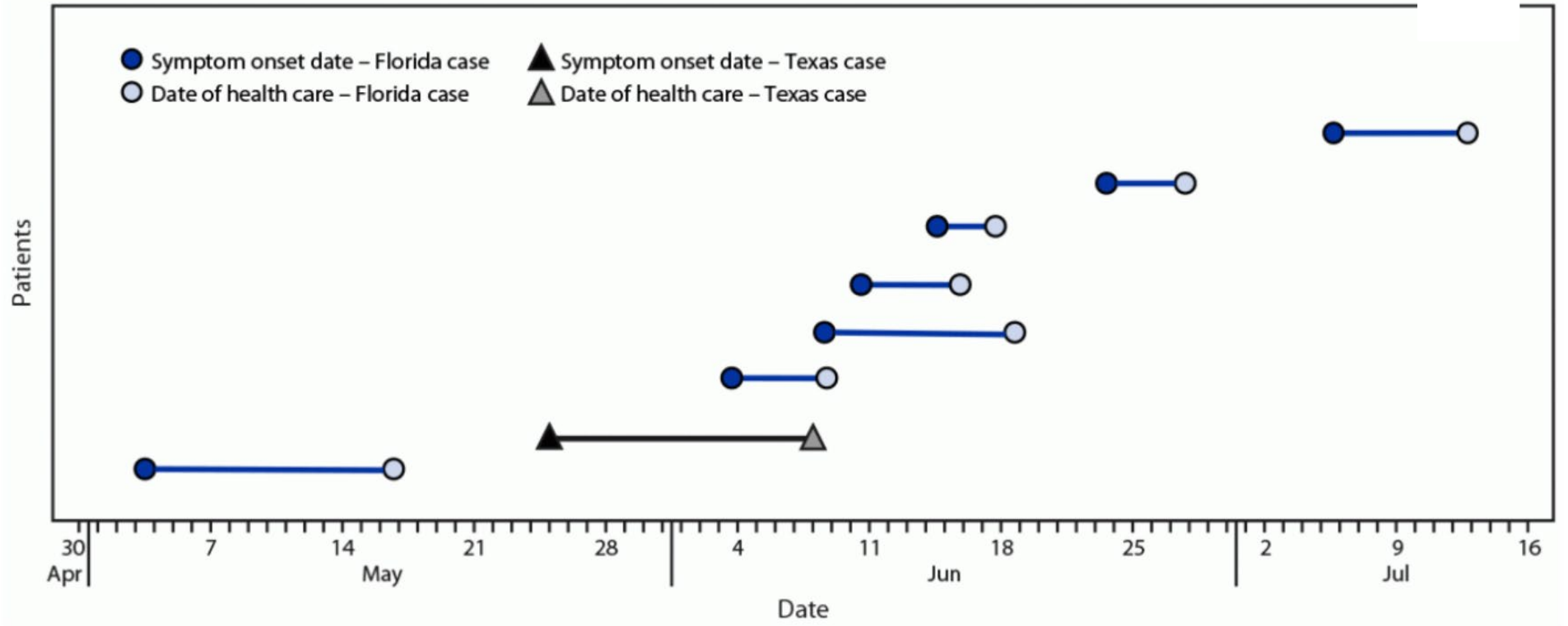


Health Department's Malaria Investigations Revealed

- None of the local cases reported
  - Recent (< 3 years) international travel to an area with malaria
  - Blood transfusion or organ transplantation

- 3 FL cases reported experiencing homelessness

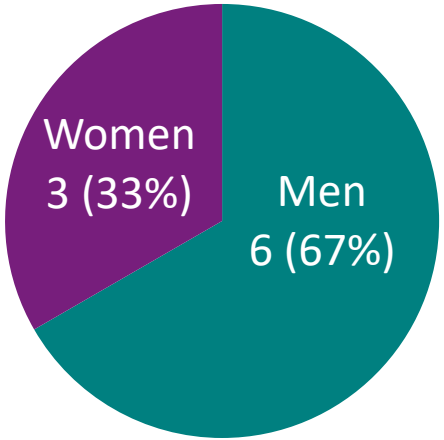
FIGURE 2. Intervals between symptom onset and health care date resulting in malaria diagnosis among patients with autochthonous malaria (N = 8) — Florida and Texas, May–July 2023



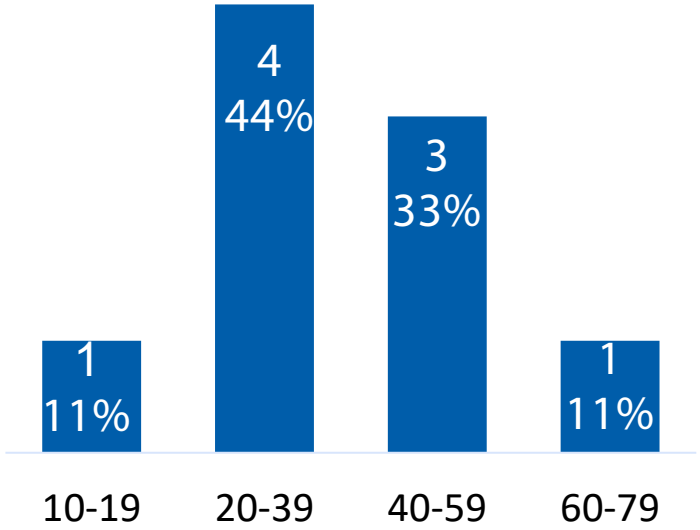
http://dx.doi.org/10.15585/mmwr.mm7236a1

Sex and Age of Malaria cases (N = 9, P. vivax, US 2023)

Sex



Age (years)



Clinical Features of Malaria cases (N = 9 , *P. vivax,* US 2023)

	N (%)
Fever	9 (100)
Vomiting	6 (67)
Abdominal Pain	5 (56)
Diarrhea	3 (33)

Clinical Testing (N = 9 , *P. vivax*)

	N (%)
Thrombocytopenia	9 (100)
Anemia	7 (78)

Malaria Diagnostic Testing (N = 9 , *P. vivax*)

	N (%)
Rapid Diagnostic Test	6/6 (100)
Blood Smear (*P. vivax*)	9 (100)
PCR (*P. vivax*)	9 (100)

Treatment (N = 9 , *P. vivax*)

	N (%)
Artemether-lumefantrine	6 (67)
Atovaquone-proguanil	3 (33)
Primaquine* (antirelapse therapy)	9 (100)

*All patients had normal G6PD activity on quantitative testing

Clinical Course and Outcome

- 8/9 (89%) Hospitalized
- None developed severe malaria
- No deaths reported
- All were reported rapidly to the local/state health department or CDC Malaria Hotline

Entomological investigation and response

- *Anopheles* trapping, testing and mosquito control
- Traps placed in locations where the patients likely had mosquito exposures and where patients spent time in the evenings
- Traps and control approaches were tailored to each site

Photo credit: Sarasota Herald Tribune; Sarasota County Mosquito Management Services

Photo credit: PacMOSSI; City of Brownsville

Domestic Malaria Outbreak Lessons, 2023 U.S.

- US remains at risk for sporadic mosquito outbreaks
- Essential Support/partnership with local jurisdictions
  - Surveillance
  - Laboratory
  - Entomology

Summary

The US, although endemic malaria is eliminated

- Has ~ 2000 case/yr, mainly among returning travelers visiting friends and relatives and not taking prophylaxis
- Risk of sporadic local mosquito transmission
  - Low, given small number of cases and geographically restricted
  - Competent vector
  - Delays in presentation and diagnosis
- Effective medications available to prevent and treat malaria however challenges to adherence and prompt access

Thank you

For more information, contact CDC
1-800-CDC-INFO (232-4636)
TTY: 1-888-232-6348 www.cdc.gov