

The background features a gradient from orange on the left to blue on the right. In the center, there is a detailed, textured illustration of a virus particle with numerous spikes. Scattered throughout the background are various circular shapes, some resembling cells or bacteria, and small white symbols: a plus sign, a solid dot, and an open circle.

# Emerging Infectious Diseases

Hannah Nam MD MSc

Assistant Professor of Clinical Medicine

Director, Transplant and Immunocompromised Host Infectious Diseases

Department of Infectious Diseases

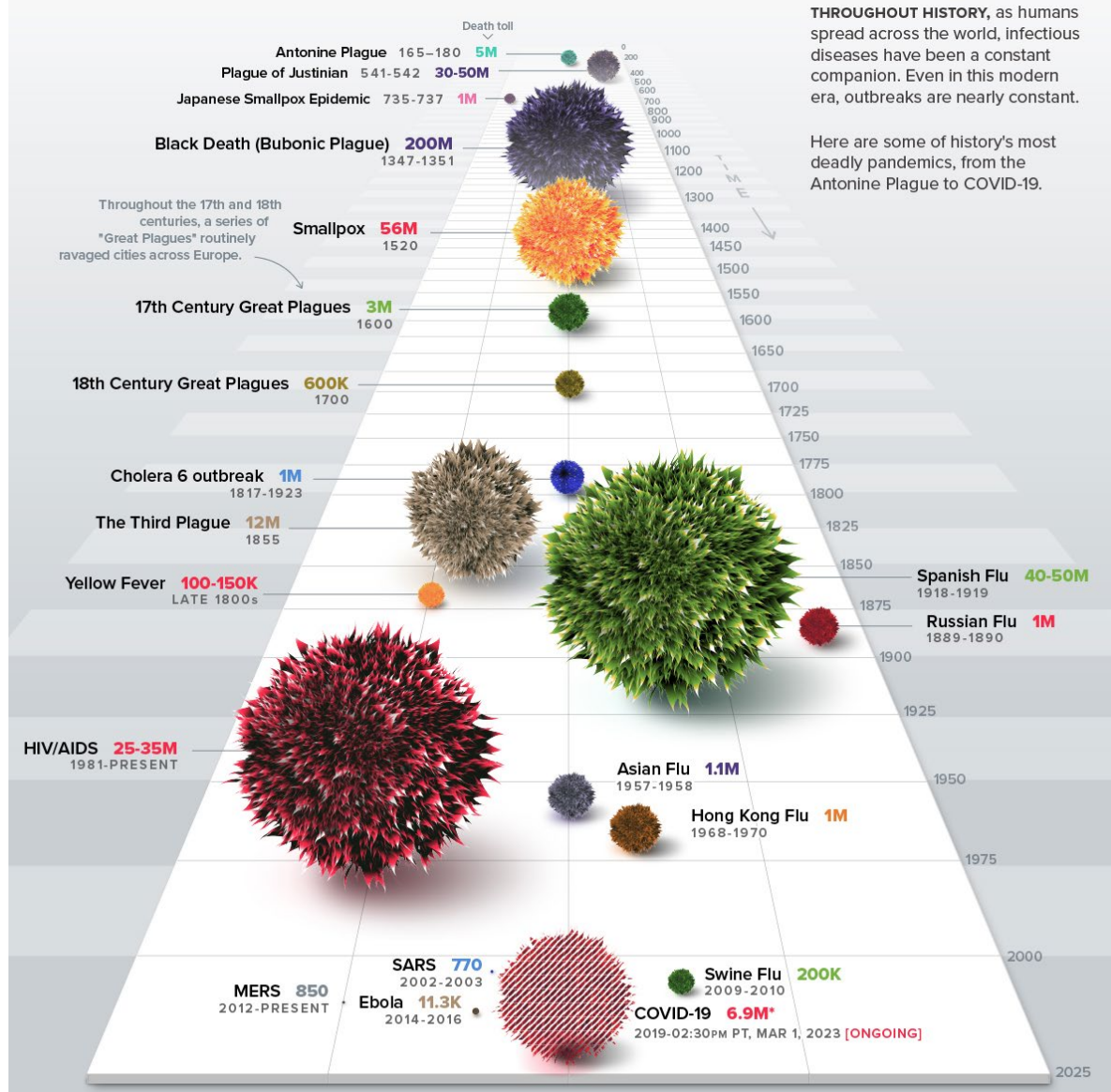
University of California – Irvine

# Financial Disclosure

- None

# HISTORY OF PANDEMICS

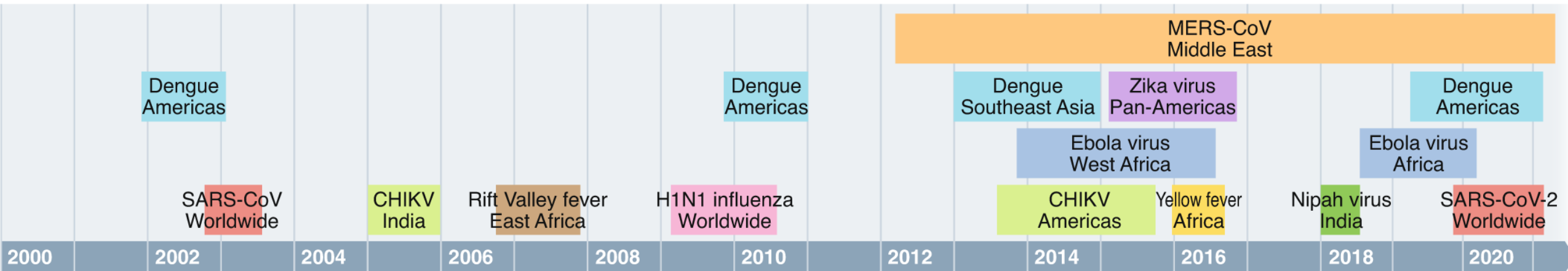
PAN-DEM-IC (of a disease) prevalent over a whole country or the world.



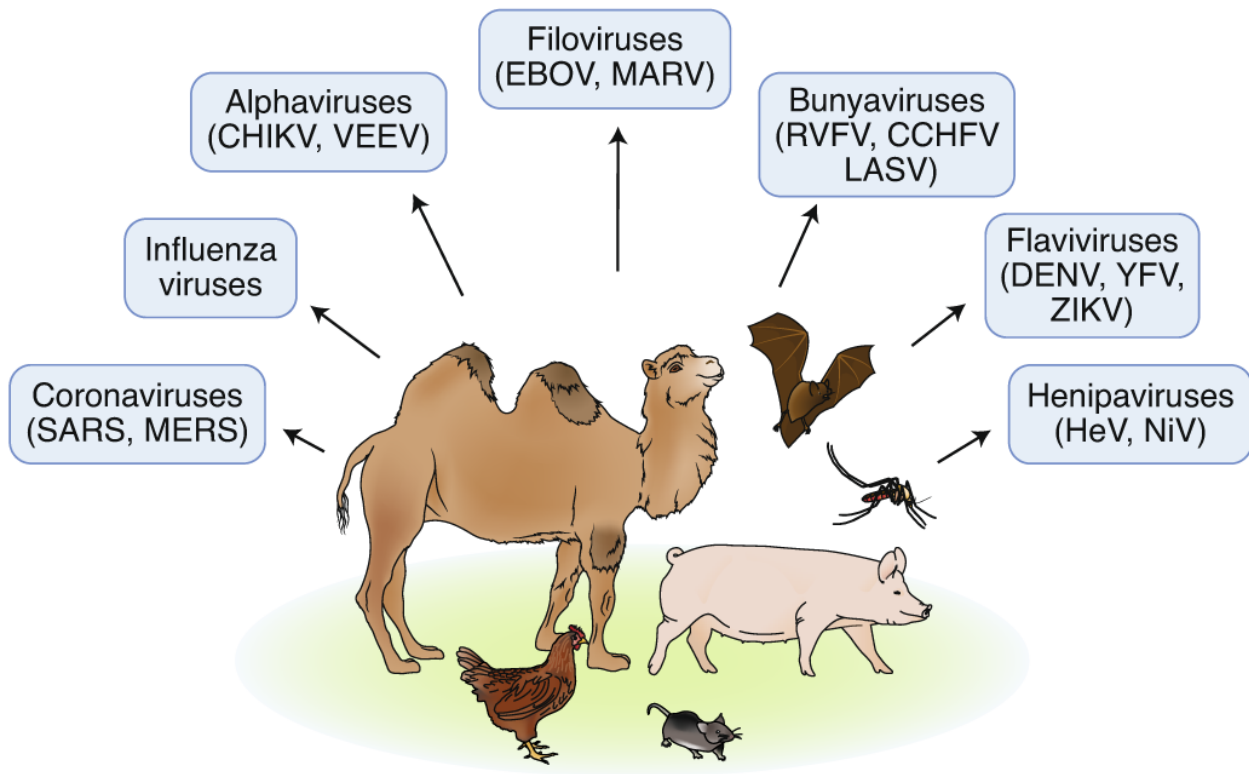
THROUGHOUT HISTORY, as humans spread across the world, infectious diseases have been a constant companion. Even in this modern era, outbreaks are nearly constant.

Here are some of history's most deadly pandemics, from the Antonine Plague to COVID-19.

**a** 21st century viral disease outbreaks



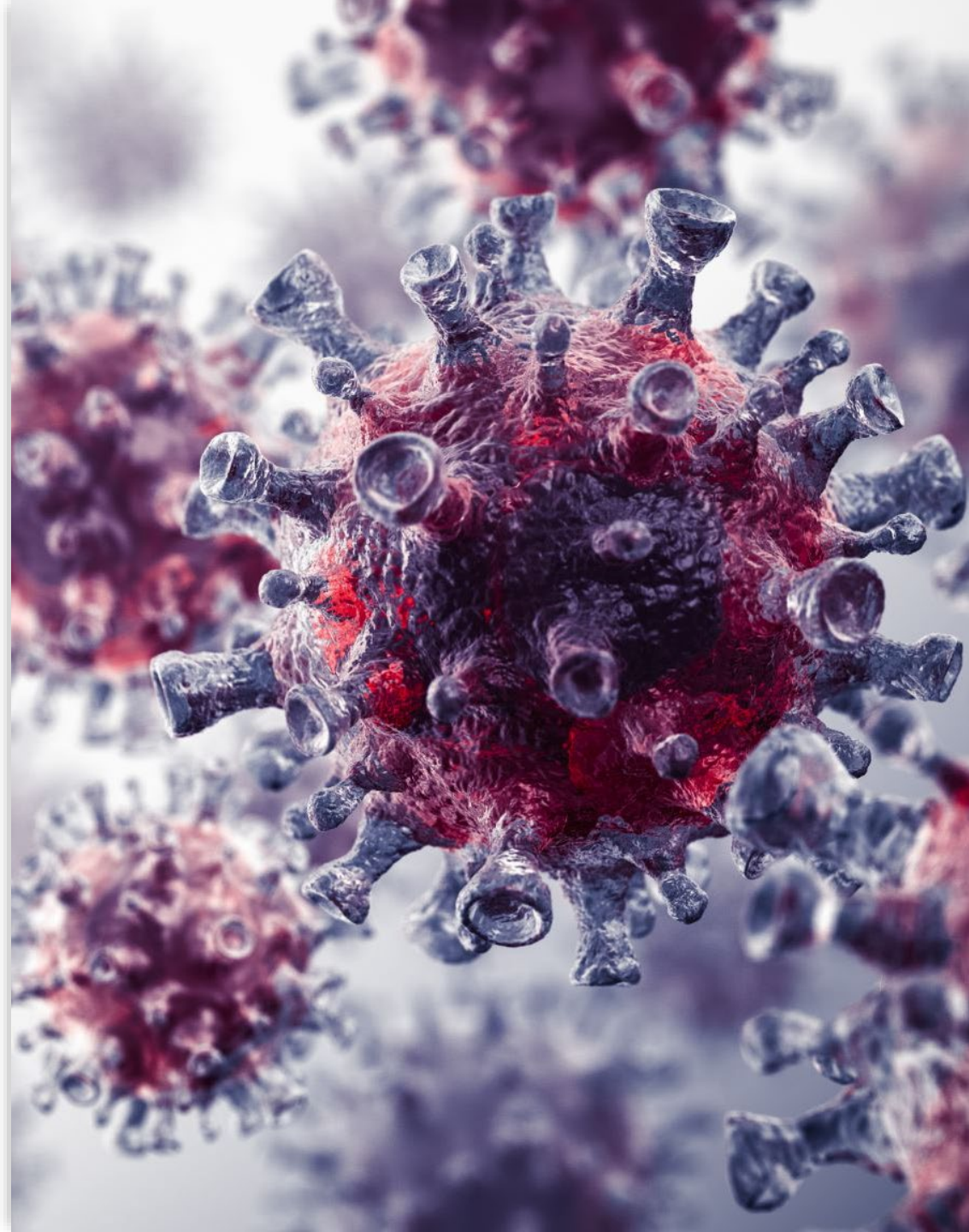
**b** Zoonotic reservoirs and vectors



# Emerging Infectious Diseases: Why now?

The threat posed by emerging infectious diseases will continue to **increase**.

The longer we wait, the harder it becomes to build on lessons learned from COVID-19.

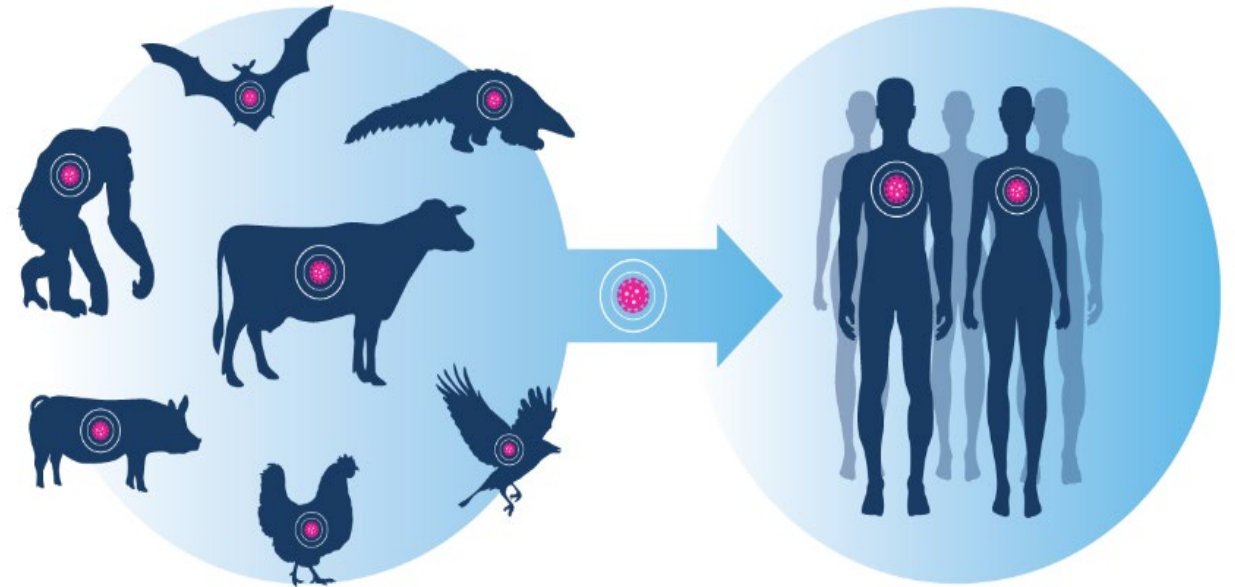


# Emerging Infectious Diseases: Why now?

## Urbanization and the expanding animal-human interface

- 60% of human infectious diseases are zoonotic in origin.
- However, 75% of **emerging** infectious diseases have a zoonotic origin.

**Zoonotic diseases** are responsible for 2.5 billion cases of illness and 2.7 million deaths worldwide, each year.



**75%**

of newly emerging infectious diseases are zoonoses

**60%**

of infectious diseases in humans are spread from animals

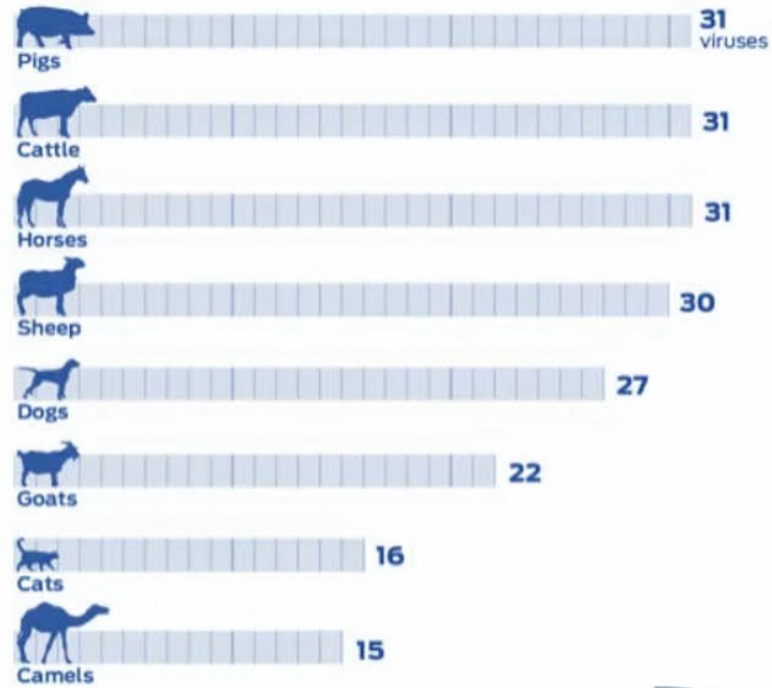
# Species sharing the most zoonotic viruses with humans to date

Global shifts in mammalian population trends reveal key predictors of virus spillover risk

Christine K. Johnson<sup>1</sup>, Peta L. Hitchens<sup>2</sup>, Pranav S. Pandit<sup>1</sup>, Julie Rushmore<sup>1</sup>, Tierra Smiley Evans<sup>1</sup>, Cristin C. W. Young<sup>1</sup> and Megan M. Doyle<sup>1</sup>

<sup>1</sup>EpiCenter for Disease Dynamics, One Health Institute, School of Veterinary Medicine, University of California, Davis, CA 95616, USA

## DOMESTICATED MAMMALS



Linked to agricultural production

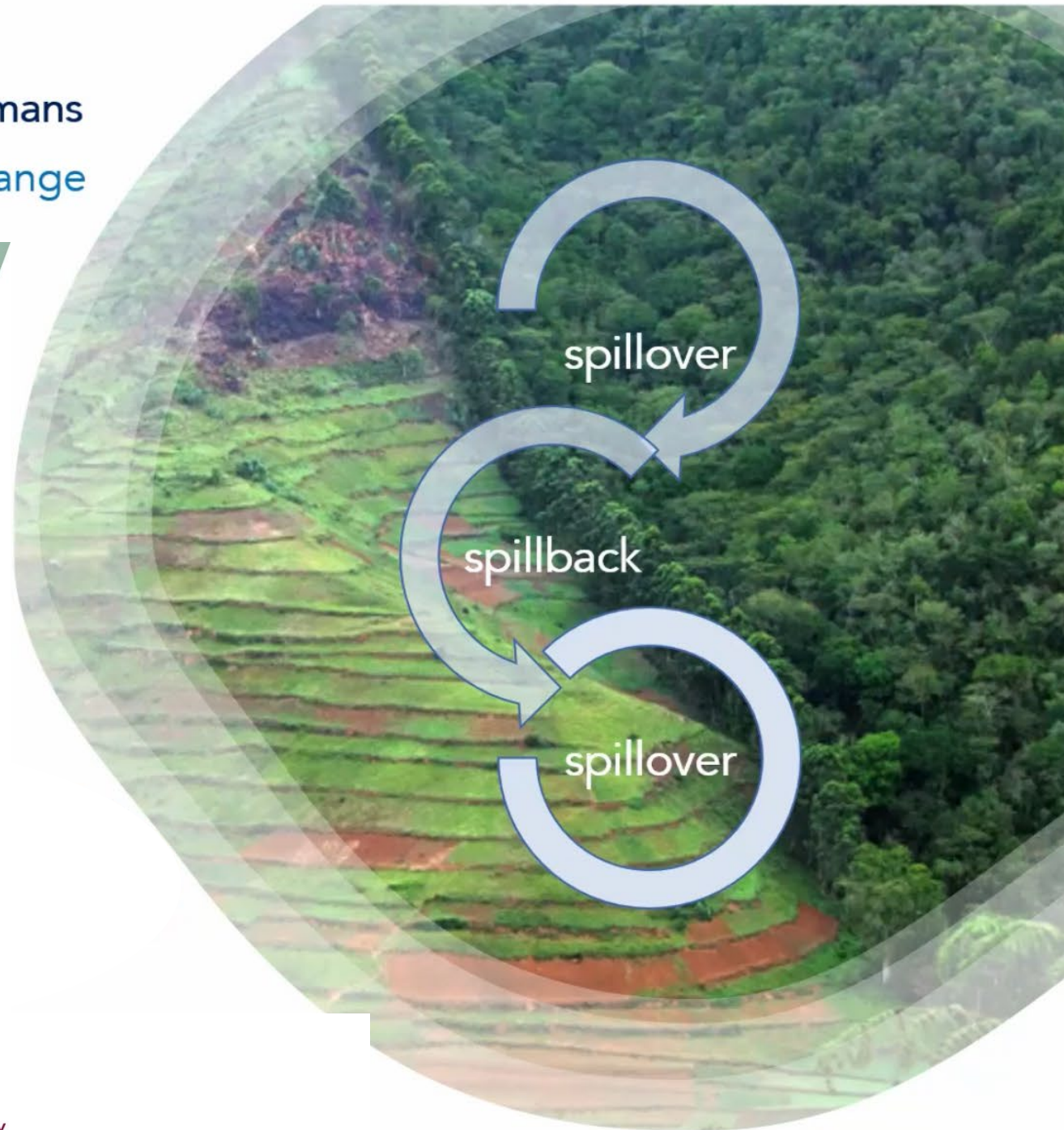
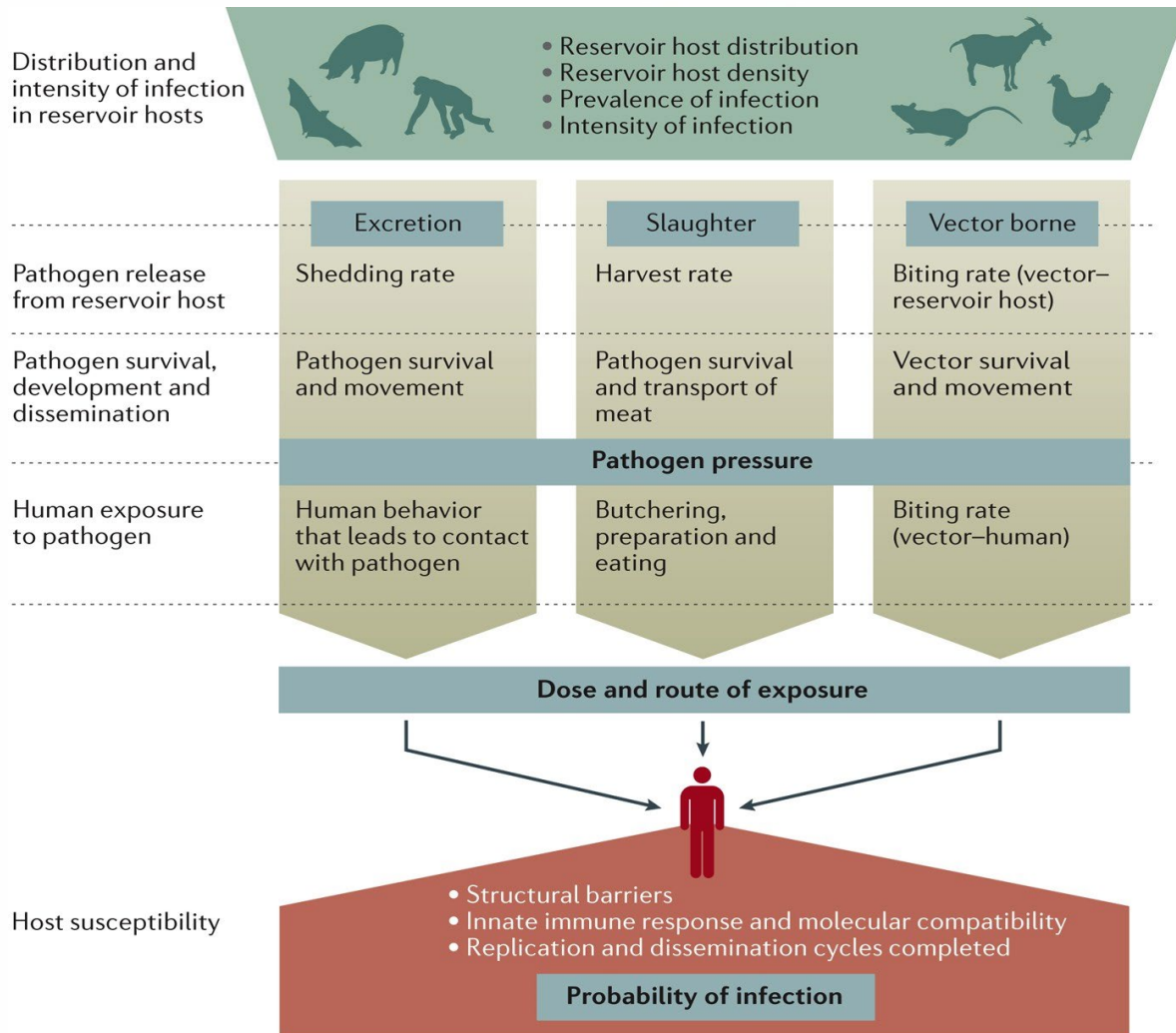
## WILD MAMMALS



Linked to urbanization

# Spillover of infectious disease from animals to humans

## an irreversible consequence of ecosystem change





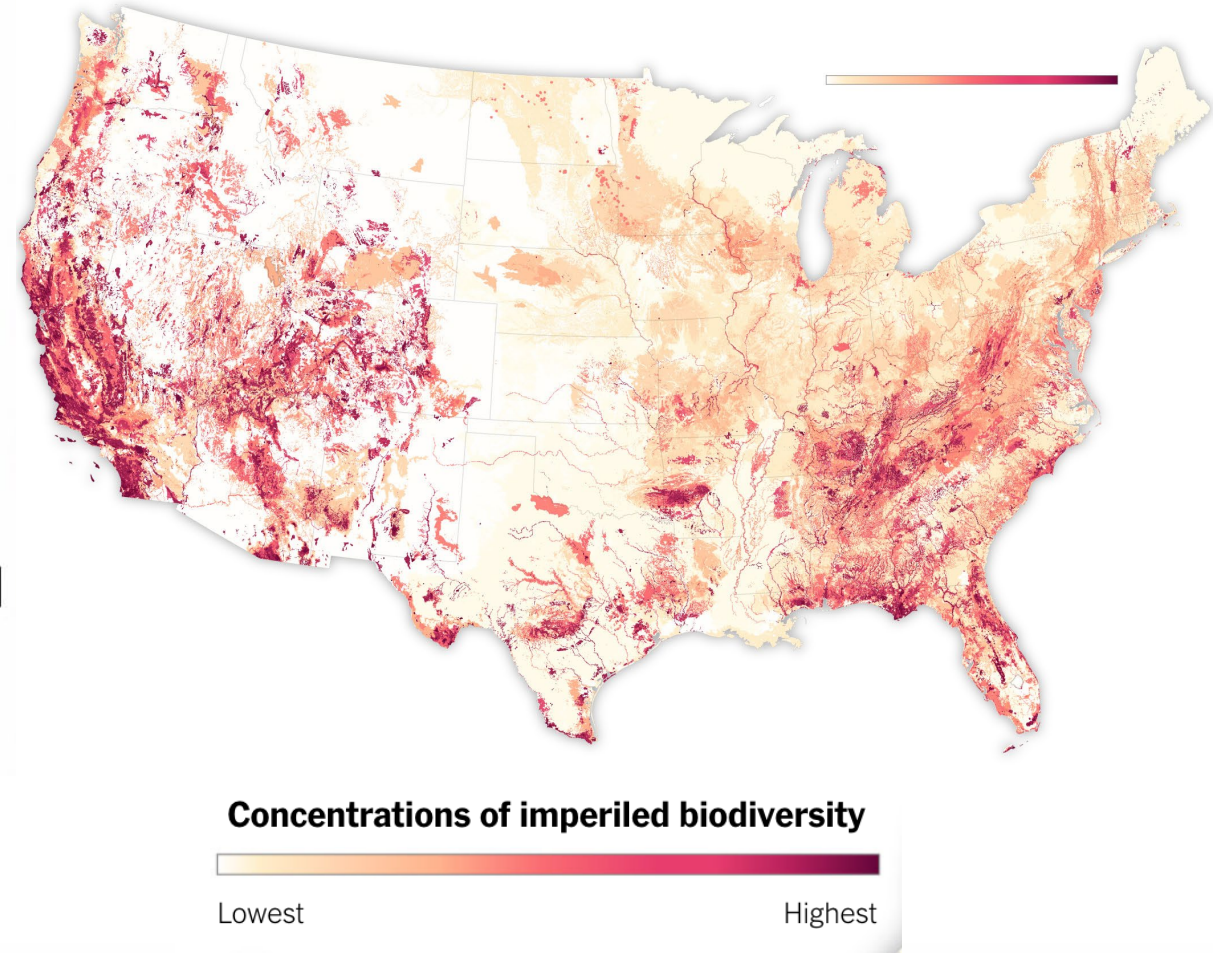
# Activities driving spillover of viruses from wildlife

- Species in global decline because of exploitation and habitat loss shared more viruses with people
- Degradation of habitat, due to deforestation, development, and conversion to cropland – increases animal-human interactions
- Exploitation of wildlife through hunting and the live wild animal trade – facilitate contact and virus transmission

Global shifts in mammalian population trends reveal key predictors of virus spillover risk

Christine K. Johnson<sup>1</sup>, Peta L. Hitchens<sup>2</sup>, Pranav S. Pandit<sup>1</sup>, Julie Rushmore<sup>1</sup>, Tierra Smiley Evans<sup>1</sup>, Cristin C. W. Young<sup>1</sup> and Megan M. Doyle<sup>1</sup>

<sup>1</sup>EpiCenter for Disease Dynamics, One Health Institute, School of Veterinary Medicine, University of California, Davis, CA 95616, USA



# Emerging Infectious Diseases: Why now?

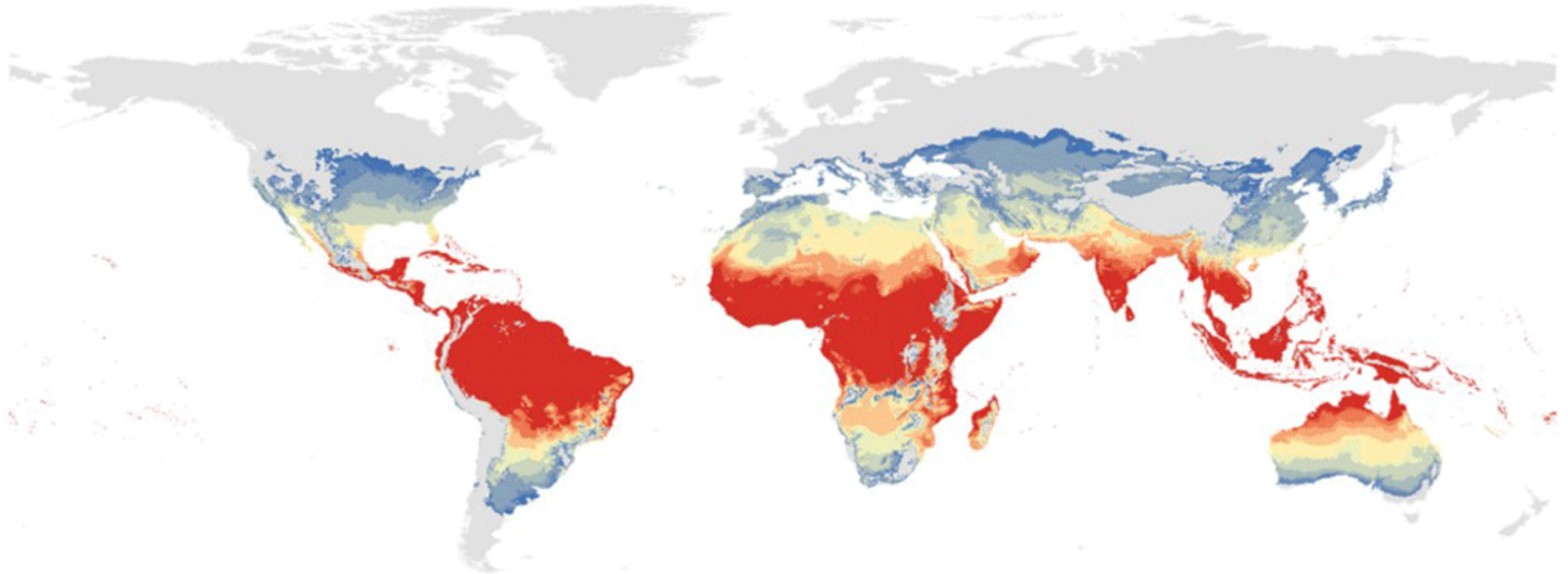
- **Climate change:** expansion of mosquito and tick-borne illnesses, changing habitats for animals and fungi, and alterations to water habitats.



2019

# Mosquito Habitat: Current & Projected

THIS PROJECTION IS BASED ON A WORST-CASE SCENARIO  
WITH THE IMPACT OF CLIMATE CHANGE UNMITIGATED.



Number of months per year when disease  
transmission by *Aedes aegypti* mosquito is possible



<https://www.npr.org/sections/goatsandsoda/2019/03/28/707604928/chart-where-disease-carrying-mosquitoes-will-go-in-the-future>

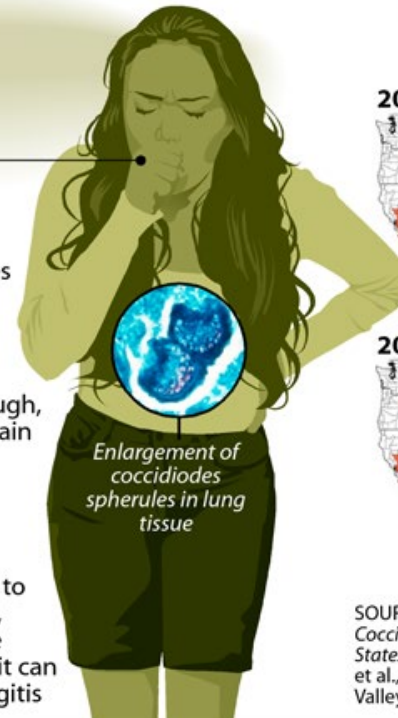
# Projected changes to coccidiomycoses distribution

## VALLEY FEVER AT A GLANCE

**1** Coccidioidomycosis fungus spores grow in soil and become airborne when dirt and dust are stirred up by wind or from digging



**2** If the dust is inhaled, the fungus spores can cause a variety of respiratory symptoms including cough, fever, chest pain and lethargy



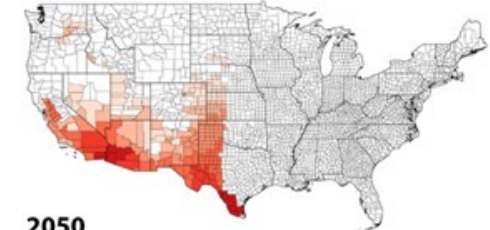
**3** The infection can spread through the bloodstream to other organs, including the brain, where it can cause meningitis

## ESTIMATED VALLEY FEVER INCIDENCE

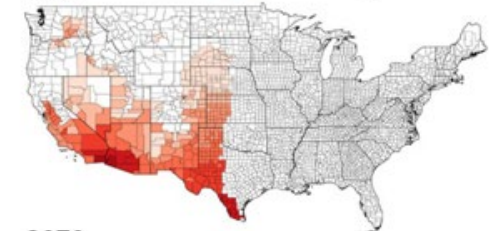
Cases per 100,000 population per year



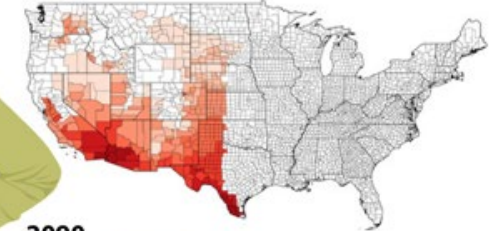
2030



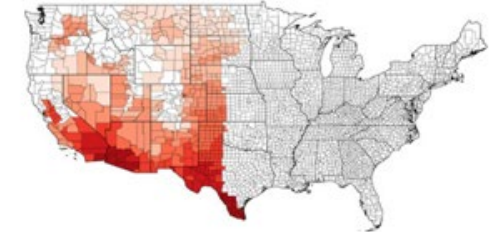
2050



2070



2090



SOURCES: Calif. Dept. of Health; *Economic Valuation of Coccidioidomycosis (Valley Fever) Projections in the United States in Response to Climate Change* by Morgan E. Gorris et al., 2020; Dr. Steven L. Oscherwitz, University of Arizona Valley Fever Center for Excellence

# Emerging Infectious Diseases: Why now?



- **Increasing international travel:** International travel anticipated to reach pre-pandemic levels by 2024 and double by 2040.
  - Animals are also globally transported in wildlife trade supply chains.

# The Global Spread of COVID-19

As of Jan. 20: **4**



# Major Infectious Disease Outbreaks in 2023

Antimicrobial resistance

Arboviruses

Avian influenza

Botulism

Candida auris

Candida auris

COVID-19

Diphtheria

Fungal meningitis

mpox

Nipah Virus

Plague

Polio

STI's

Viral Hemorrhagic Fevers



# COVID-19 and Influenza

The Continued Pandemic



# CDC Fall/Winter 2023-2024 Vaccine Recommendations

- **Updated COVID-19 Vaccine** - Recommended for all persons 6 months and older
- **Influenza Vaccine** - Recommended for persons 6 months and older; People 65 and older should get a higher dose or adjuvanted flu vaccine
- **RSV Vaccine**
  - **Adults 60+** should talk to their medical provider to see if the vaccine is right for them
  - **Infants during RSV season:** We have two ways to protect infants from RSV. Most infants will not need both.
    1. **Maternal RSV vaccination** at 32-36 weeks of gestation
    2. **Nirsevimab:** Infants younger than 8 months entering RSV season and some older children between 8-19 months with increased risk for severe RSV

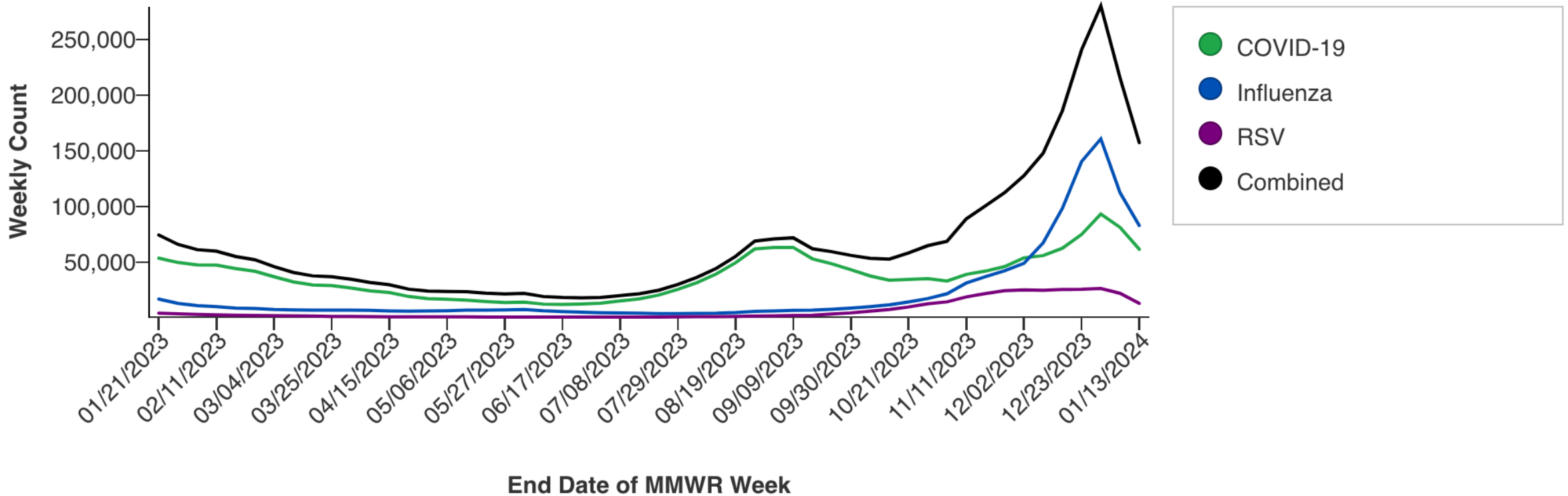


# Weekly Emergency Department Visits

Make a selection from the filters to change the visualization information.

## Age Group

All Ages

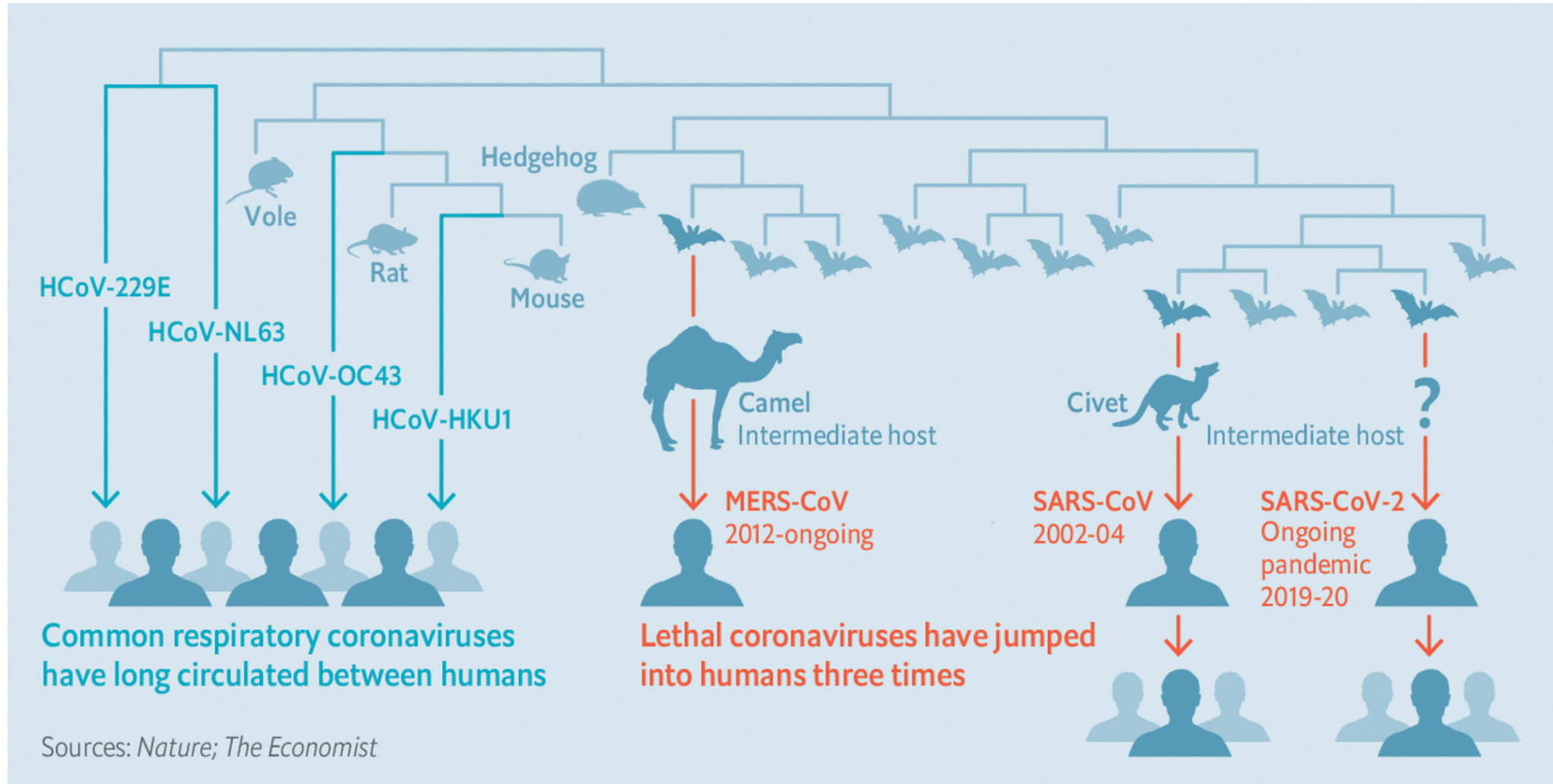


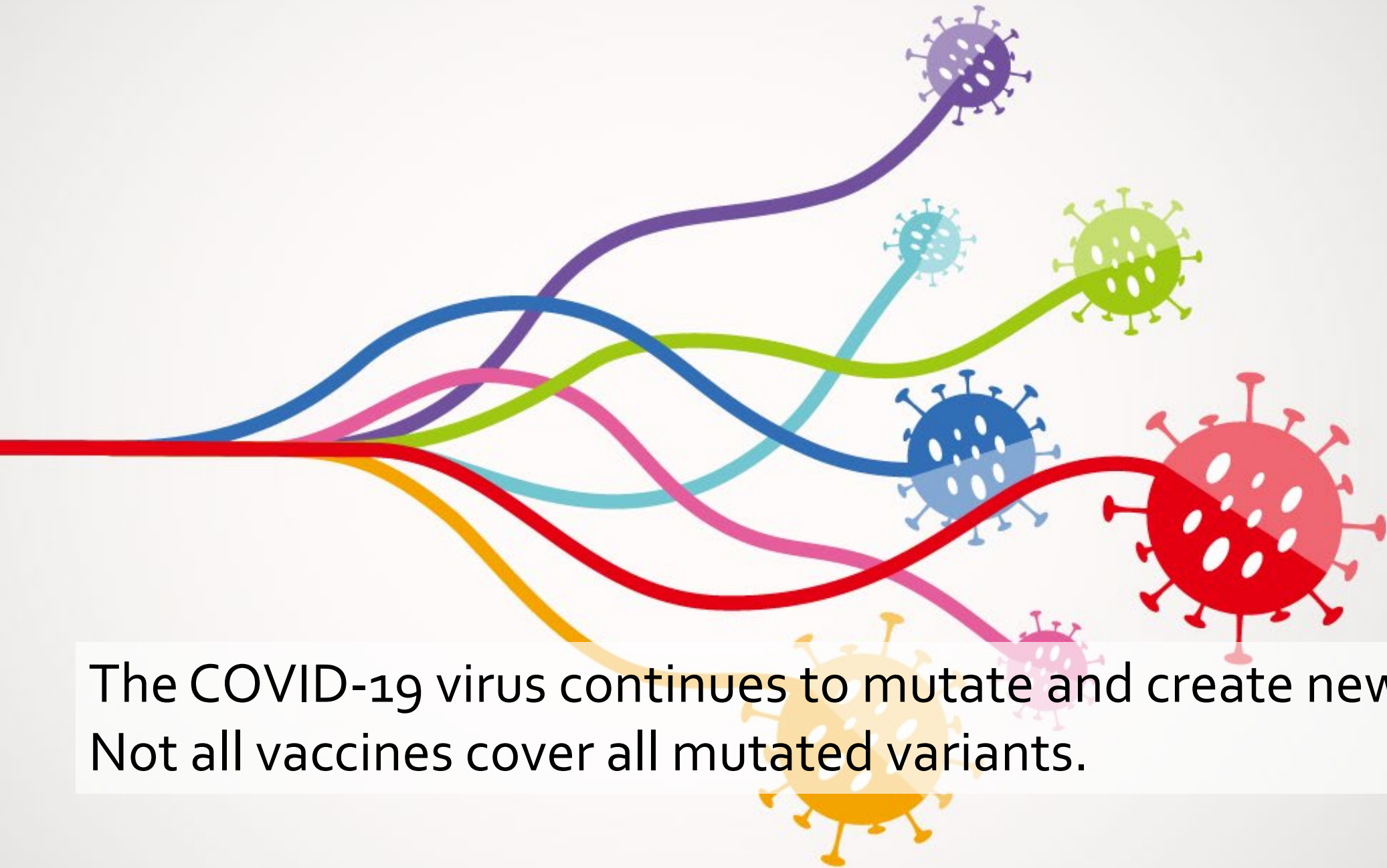
A close-up photograph of a woman with dark hair wearing a light blue surgical face mask. A hand in a white lab coat sleeve holds a white non-contact forehead thermometer against her forehead. The thermometer's digital display shows the number '98.7'. In the background, other people wearing face masks are visible but out of focus. The overall image has a muted, blue-tinted color palette.

# COVID-19

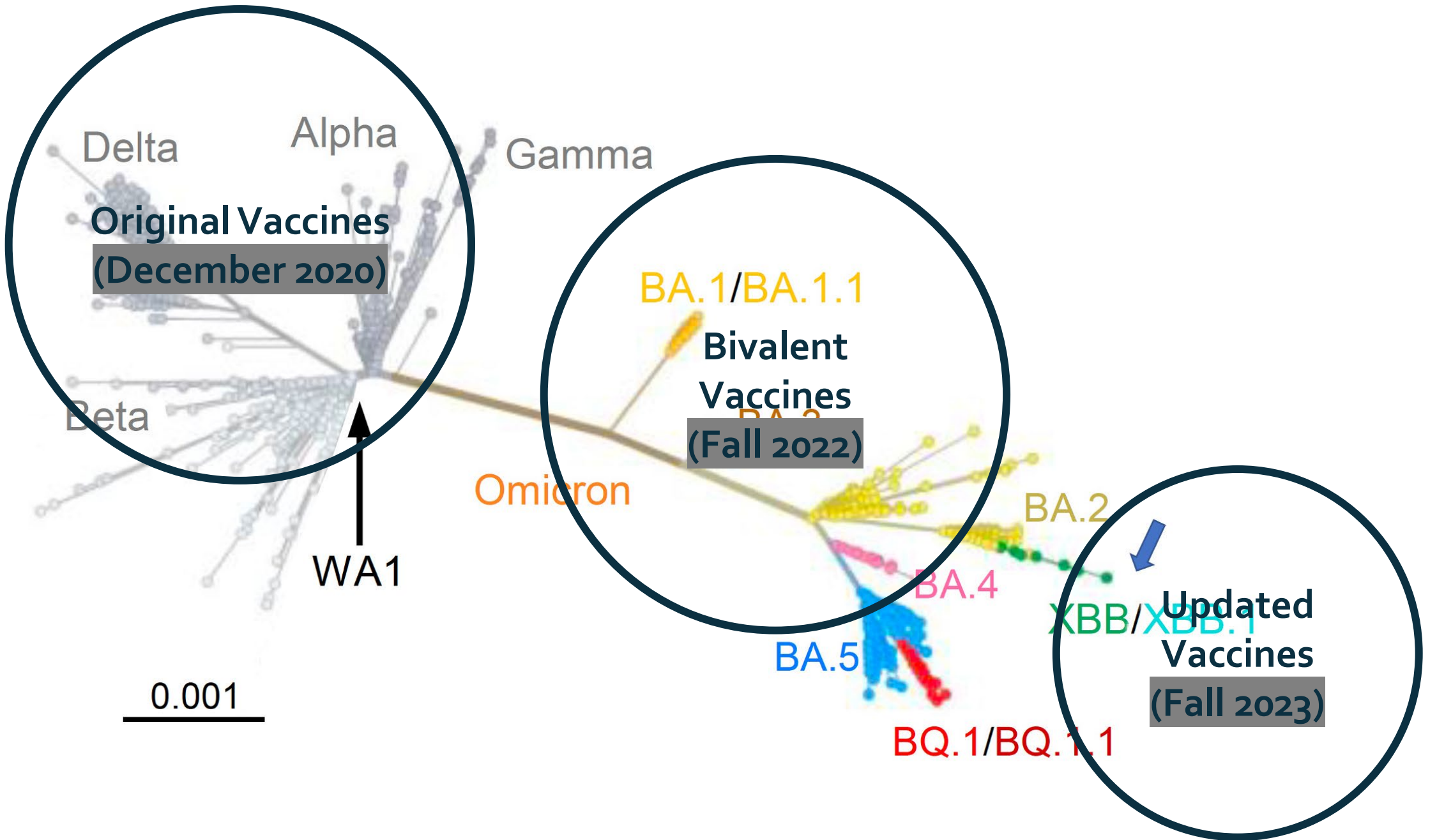
The Current State

# Coronavirus Outbreaks and Zoonotic Origins





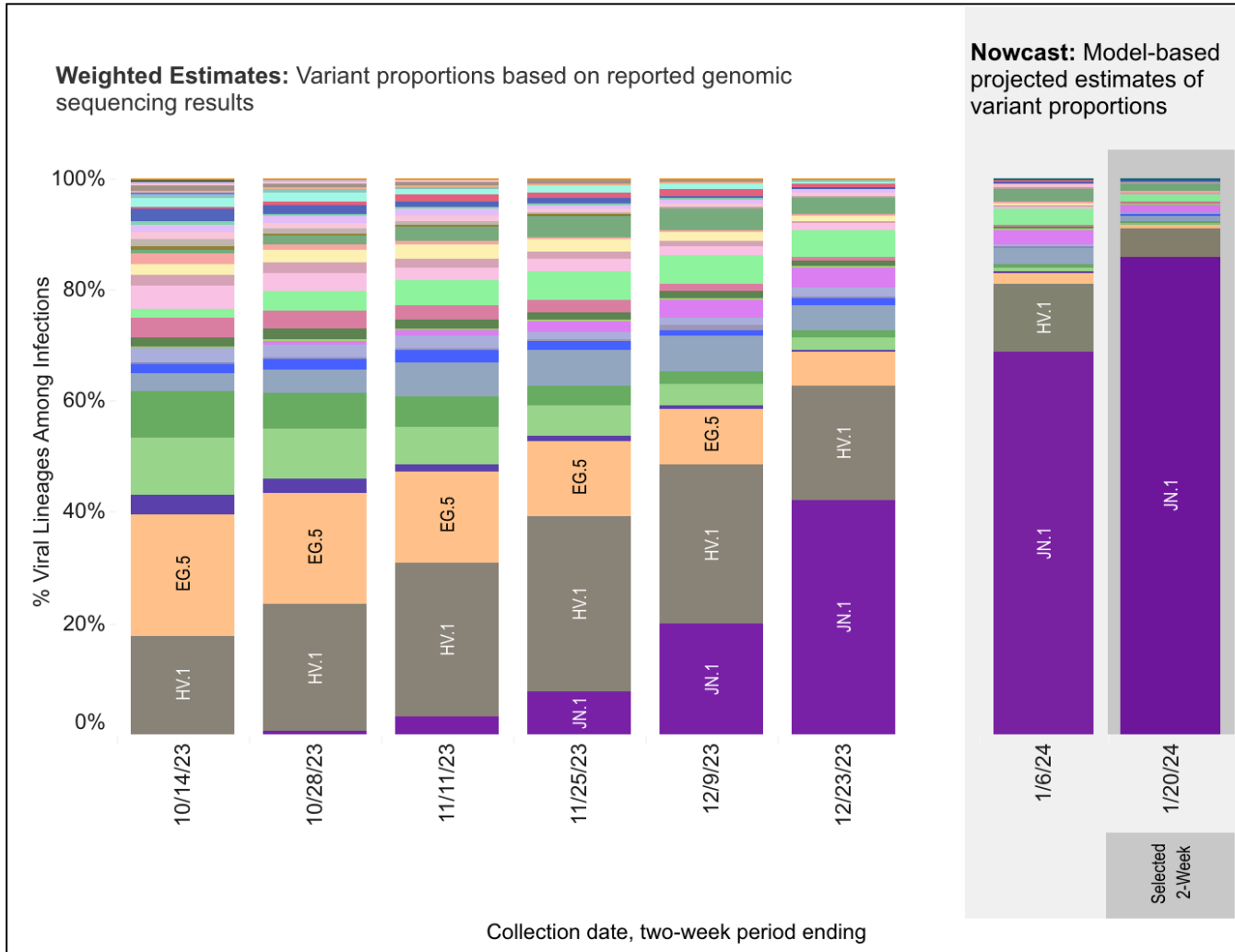
The COVID-19 virus continues to mutate and create new variants. Not all vaccines cover all mutated variants.






































# Weighted and Nowcast Estimates in United States for 2-Week Periods in 10/1/2023 – 1/20/2024

# Nowcast Estimates in United States for 1/7/2024 – 1/20/2024

 Hover over (or tap in mobile) any lineage of interest to see the amount of uncertainty in that lineage's estimate.

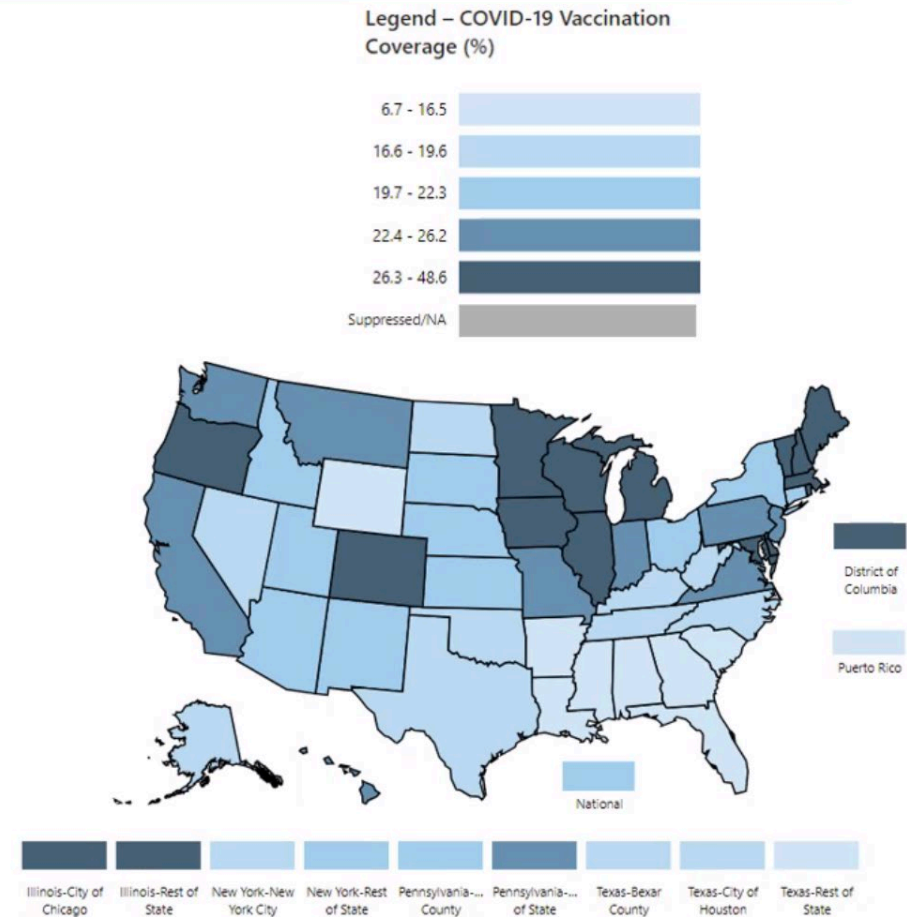


USA				
WHO label	Lineage #	%Total	95%PI	
Omicron	JN.1	85.7%	82.9-88.2%	
	HV.1	5.3%	4.4-6.4%	
	JD.1.1	1.6%	1.4-2.0%	
	BA.2.86	1.5%	1.1-2.1%	
	JG.3	1.5%	1.2-1.9%	
	HK.3	1.5%	1.2-1.8%	
	EG.5	0.6%	0.5-0.8%	
	GE.1	0.4%	0.1-1.5%	
	JF.1	0.2%	0.2-0.3%	
	FL.1.5.1	0.2%	0.2-0.3%	
	EG.5.1.8	0.2%	0.2-0.3%	
	BA.2	0.1%	0.0-0.6%	
	XBB.1.16.6	0.1%	0.1-0.2%	
	XBB.1.16.17	0.1%	0.1-0.3%	
	XBB.1.5.70	0.1%	0.1-0.2%	
	XBB.1.16.11	0.1%	0.1-0.1%	
	GK.1.1	0.1%	0.1-0.1%	
	XBB	0.1%	0.0-0.1%	
	XBB.1.9.1	0.1%	0.0-0.1%	
	HF.1	0.1%	0.0-0.1%	
	XBB.1.16.15	0.1%	0.0-0.1%	
	XBB.2.3	0.0%	0.0-0.1%	
	XBB.1.16	0.0%	0.0-0.0%	
GK.2	0.0%	0.0-0.0%		
CH.1.1	0.0%	0.0-0.0%		
XBB.1.5	0.0%	0.0-0.0%		
EG.6.1	0.0%	0.0-0.0%		
XBB.1.16.1	0.0%	0.0-0.0%		
XBB.1.5.68	0.0%	0.0-0.0%		
XBB.1.9.2	0.0%	0.0-0.0%		
XBB.2.3.8	0.0%	0.0-0.0%		
XBB.1.42.2	0.0%	0.0-0.0%		
XBB.1.5.72	0.0%	0.0-0.0%		
XBB.1.5.59	0.0%	0.0-0.0%		
Other	Other*	0.0%	0.0-0.0%	

\* Enumerated lineages are US VOC and lineages circulating above 1% nationally in at least one 2-week period. "Other" represents the aggregation of lineages which are circulating <1% nationally during all 2-week periods displayed.  
 # While all lineages are tracked by CDC, those named lineages not enumerated in this graphic are aggregated with their parent lineages, based on Pango lineage definitions, described in more detail here:  
<https://www.pango.network/the-pango-nomenclature-system/statement-of-nomenclature-rules/>.

# 2023 US COVID Vaccine Uptake

- **National** (as of Jan 6)
  - 21% of adults vaccinated
    - 43% among  $\geq 75$  yo
  - Of the remaining 79%
    - Definitely will: 18%
    - Probably will: 35%
    - Probably or definitely will not: 47%
- **California** (as of Jan 2)
  - 12% of adults vaccinated





# Vaccination Reduces Risk of Long COVID

- **Prevents Long COVID**
  - Reduces viral load during infection
  - Large staggered cohort study of patients in UK, Spain, and Estonia [Catala et al. Lancet Respir Med 2024]
    - Vaccine reduces long COVID by 29-52% across 3 cohorts
  - Meta analysis of 24 studies [Marra et al. Antimicrob Stewardship Healthcare Epi Oct 2023]
    - 2 doses reduce long COVID by 37%, 3 doses by 69%



# COVID-19 Global Challenges Ahead



Reduced testing and surveillance



Decline in submission and delay in availability of genomic sequences



Emergence and re-emergence of variants



Difficulty assessing changes in disease severity



Waning immunity and low booster coverage in at-risk populations



Access and affordability of life-saving medical countermeasures



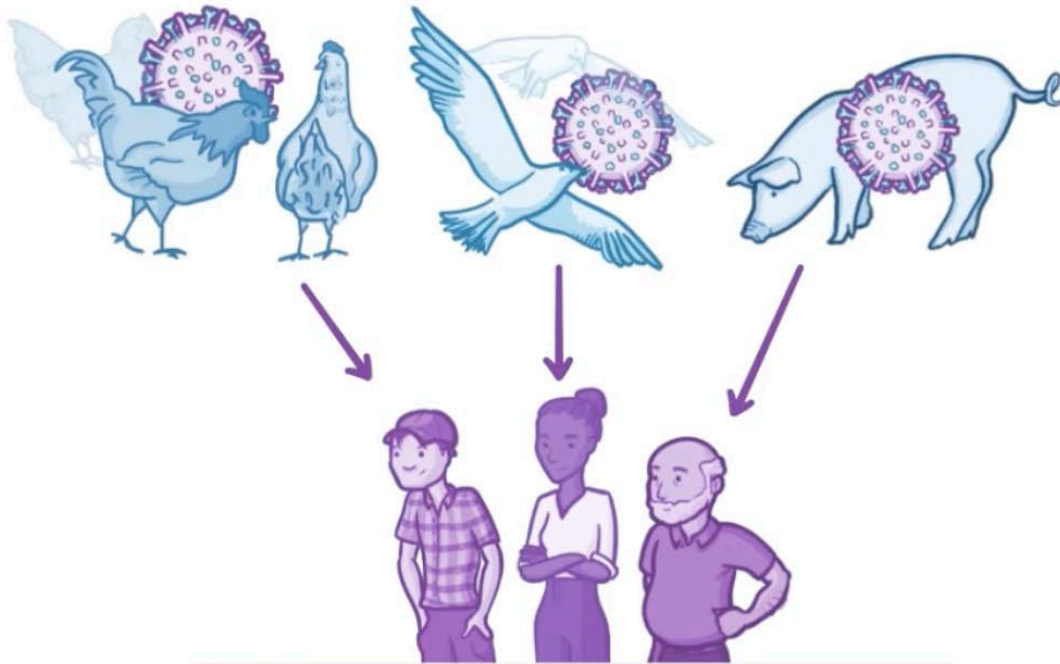
Reduced funding to WHO



# Influenza

Update and Surveillance

# ZOONOTIC INFLUENZAS

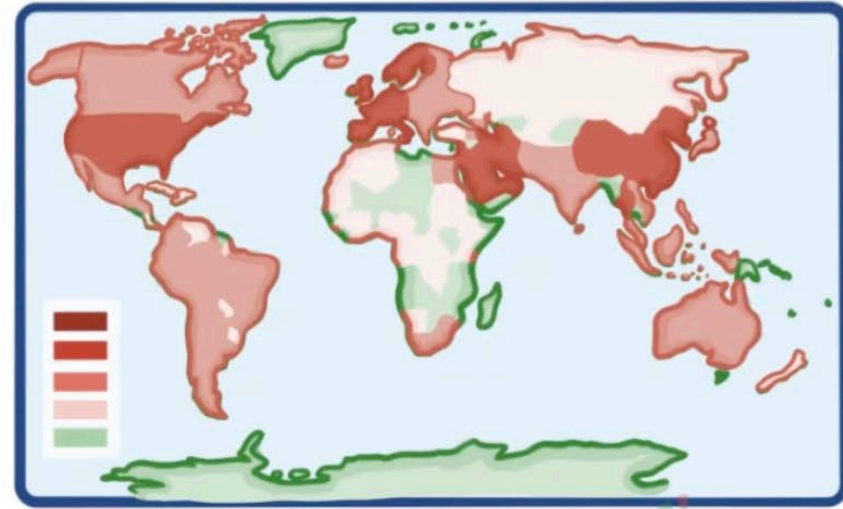


yearly

~ 3-5 MILLION cases of SEVERE ILLNESS

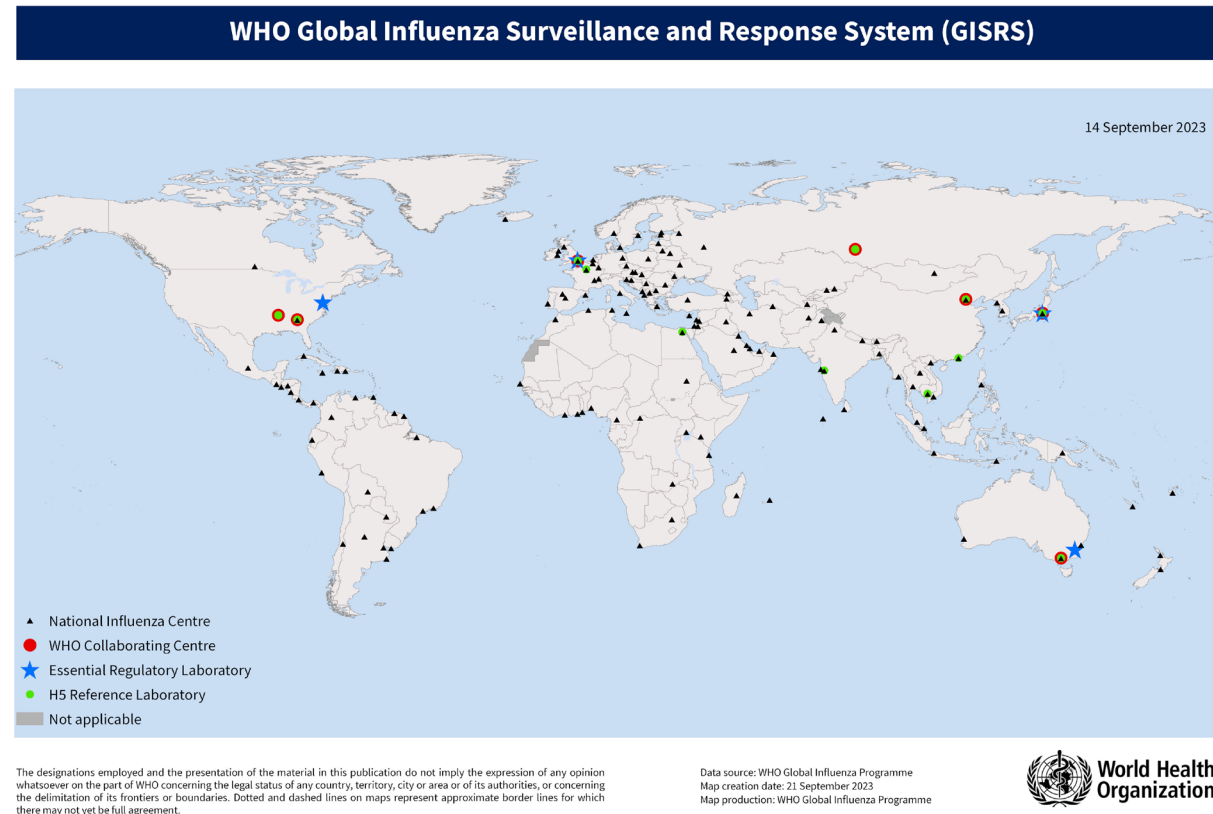
~ 500,000 DEATHS

- \* RESPIRATORY SYMPTOMS
- \* FEVER
- \* EPIDEMICS or PANDEMICS



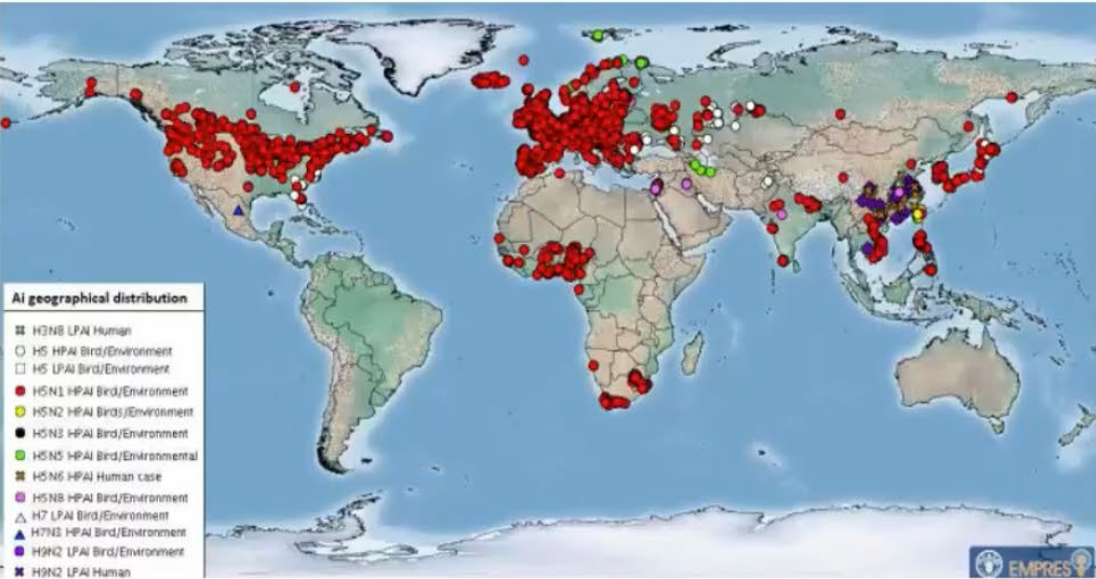
# Predicting Seasonal Influenza

- 144 Influenza Centers in 114 countries conduct ongoing surveillance for circulating flu viruses
- Epidemiological, Genetic, Antigenic data, Evolutionary Analysis, and Vaccine Effectiveness studies are analyzed
- Twice-yearly meetings from WHO to determine the composition of flu vaccines
- Production of vaccines take 6 months

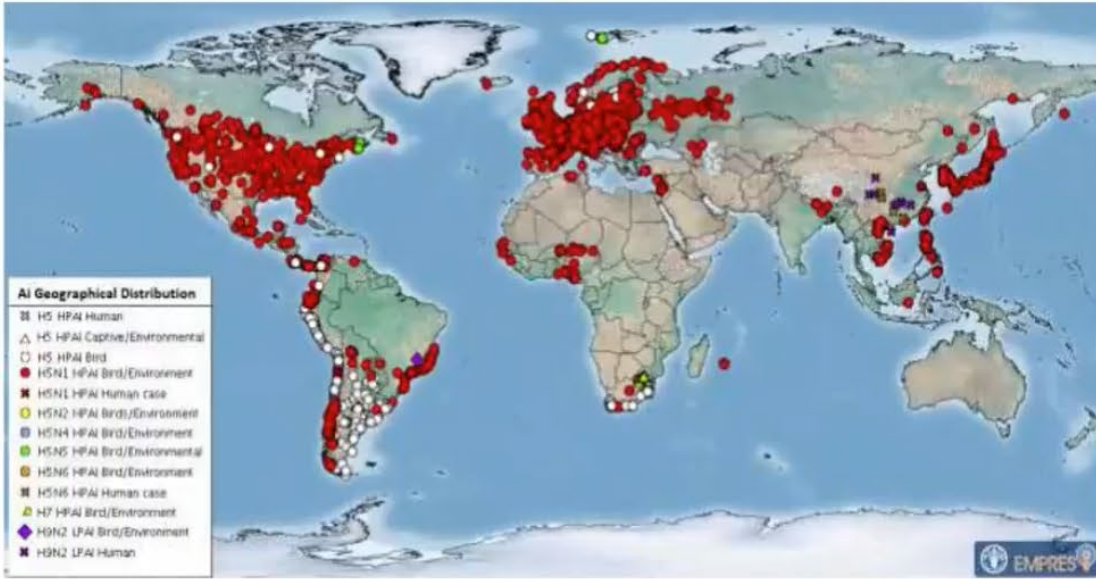


# Global Avian Influenza with Zoonotic Potential H5N1

October 2021 - October 2022



October 2022 - October 2023



# H5N1 in Mammals vs Humans



Since 2020, H5 has spread predominantly via migratory birds



Increased detections in non-avian species likely through contact with live or dead birds



Outbreaks in farmed mink (Spain), seals (USA), sea lions (Peru and Chile), foxes and mink (Finland)

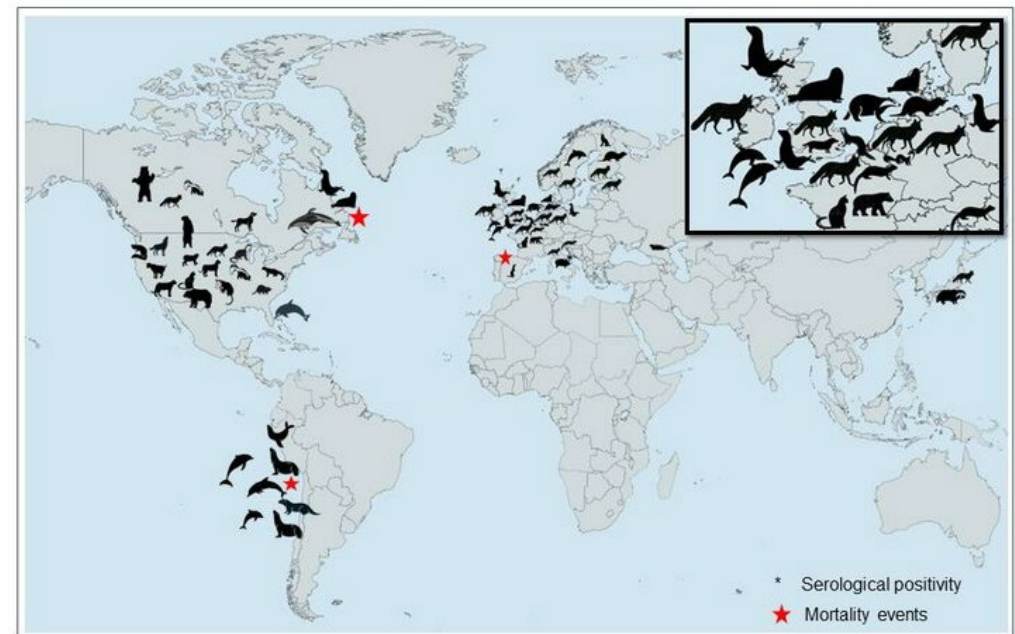


Detected in domesticated animals such as cats in Poland and South Korea

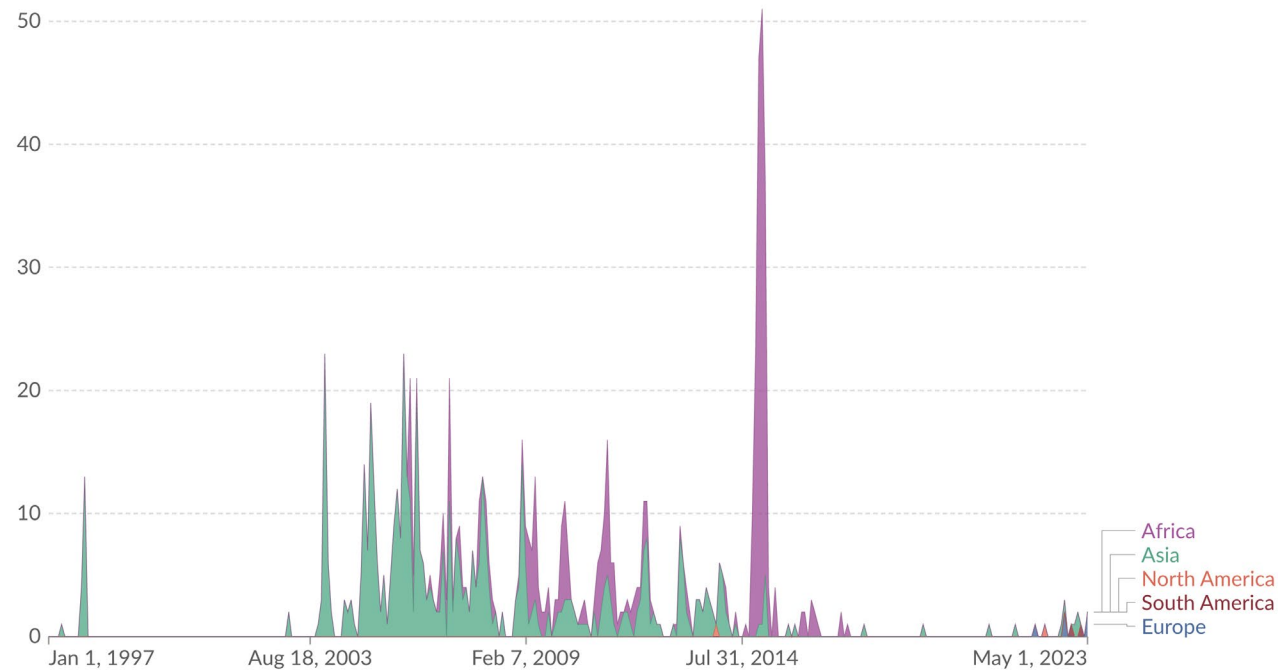


Limited number of human infections despite poultry outbreaks, detection in mammals

Geographic distribution of A(H5) virus in non-human mammals since 2016



# Monthly Incidence of Influenza A (H5N1) in humans



Data source: WHO, Global Influenza Programme (2023)

[OurWorldInData.org/influenza](https://ourworldindata.org/influenza) | CC BY

1. **Highly-pathogenic avian influenza (HPAI):** Highly-pathogenic avian influenza (HPAI) is a severe form of bird flu that can quickly spread and cause deadly disease in poultry. Some cases have also been recorded in humans, particularly from H5N1 and H7N9 flu strains, and have had a high case fatality rate.





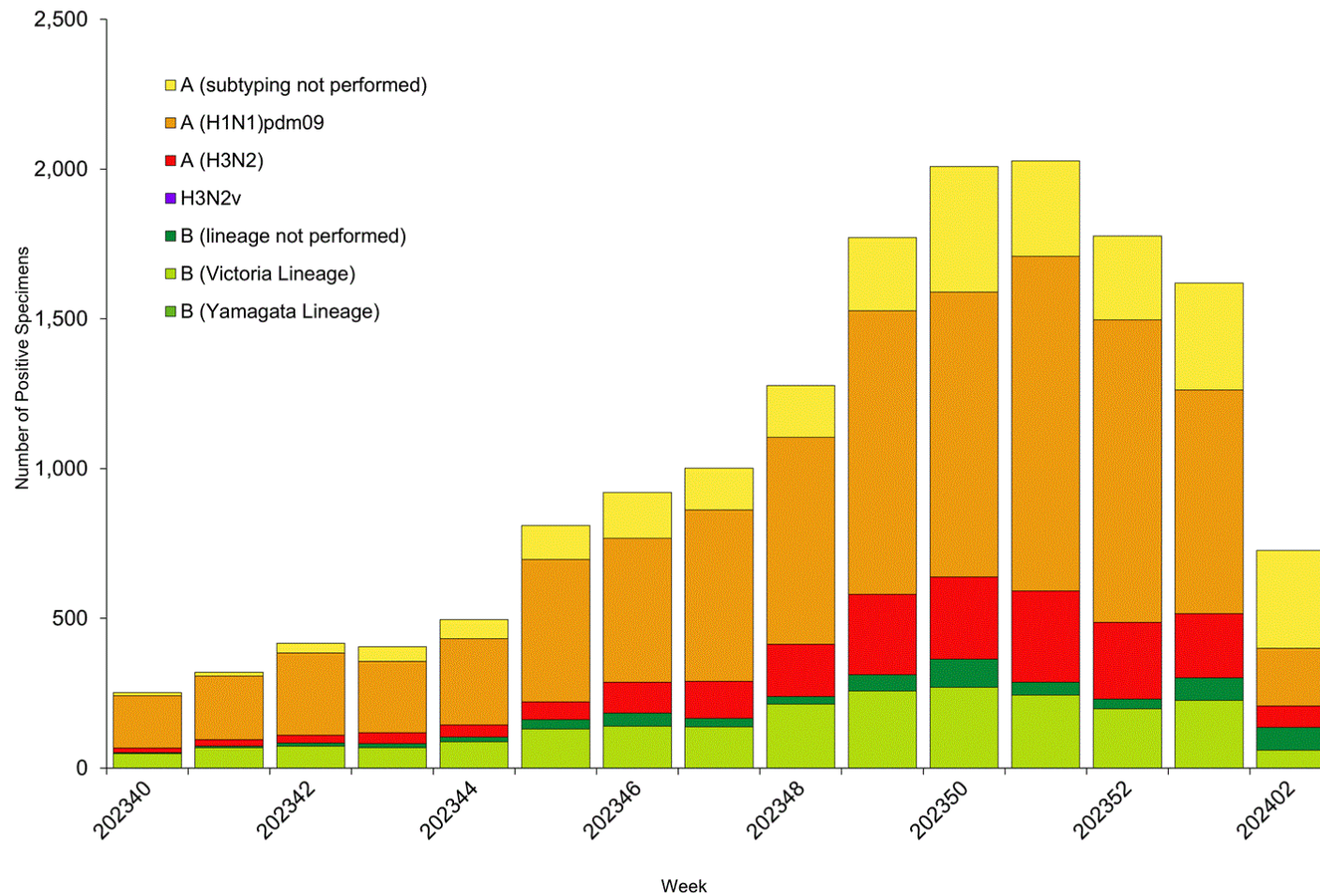
# Avian Influenza: Continued Challenges

- Diversity of viruses and continued evolution
- Introduction in new geographic areas
- Little to no population immunity
- May cause severe disease in humans
- Affects food security
- Politically sensitive
- Pandemic fatigue



# Current Influenza Subtypes in the US

Influenza Positive Tests Reported to CDC by U.S. Public Health Laboratories, National Summary, 2023-2024 Season



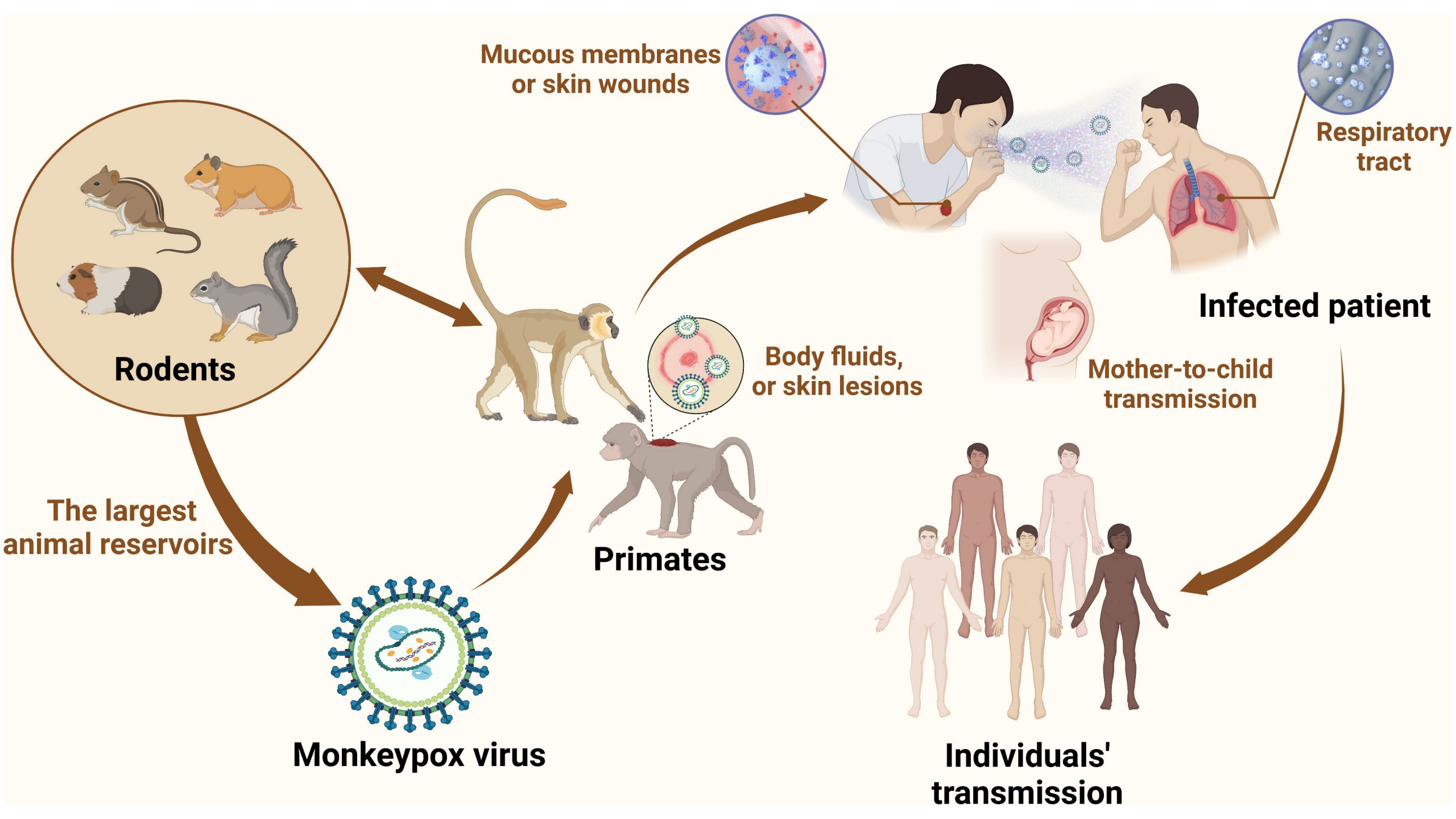
# PSA: Flu Vaccine

- Efficacy
  - Vaccination decreased likelihood of hospitalization in those age 18-64 by 23%, and  $\geq 65$  by 41%
  - Decreased ED/UC Visits in those age 18-64 by 45%, and  $\geq 65$  by 41%
- Vaccine Uptake
  - Continued overall decline since 2020
  - Age 18-29 at 32% vs Age  $\geq 75$  at 80%
  - All adults 47% (vs 50% in 2020-2021)



mpox

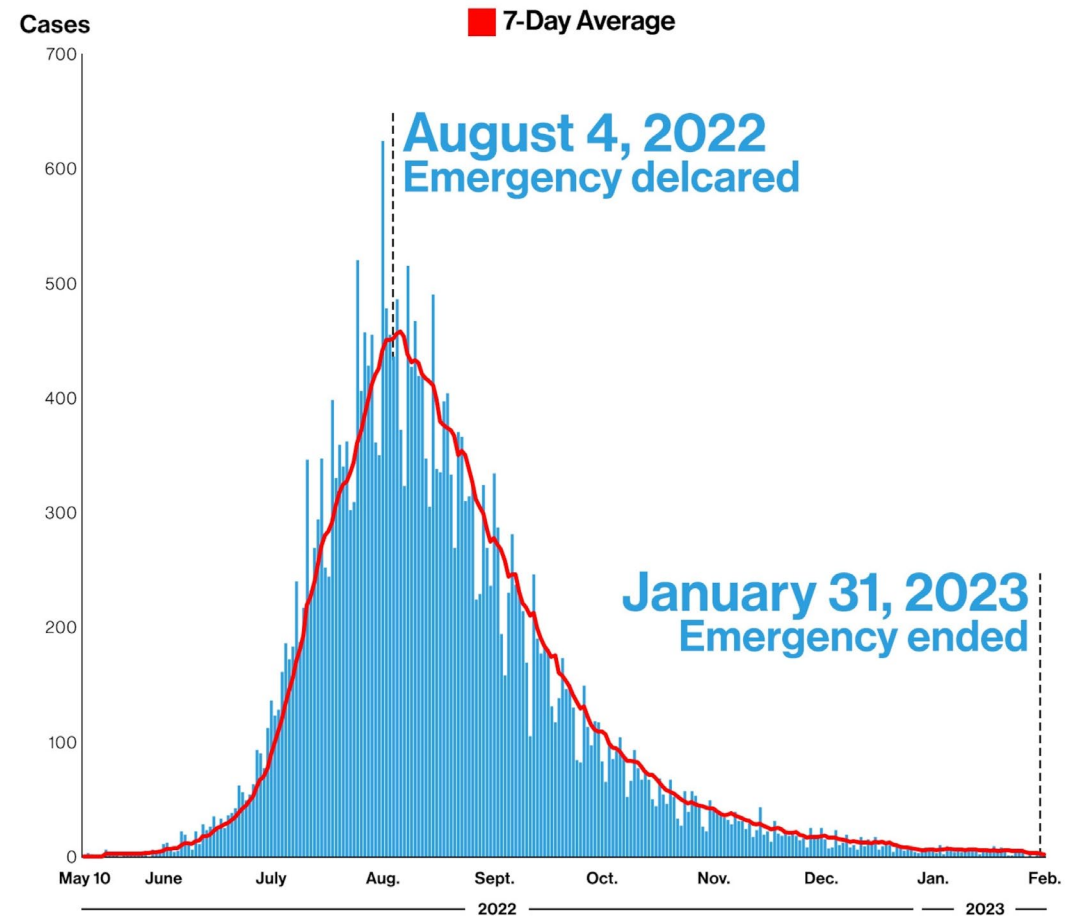
Isn't gone



## Rapid mpox control in the US (2023)

- Aggressive, highly coordinated public health response
- Strong, unified response from leaders in the LGBTQ community
- Evidence-based public outreach and education
- Rapid deployment of existing vaccines and treatments that had been stockpiled for smallpox

## Daily Mpox Cases

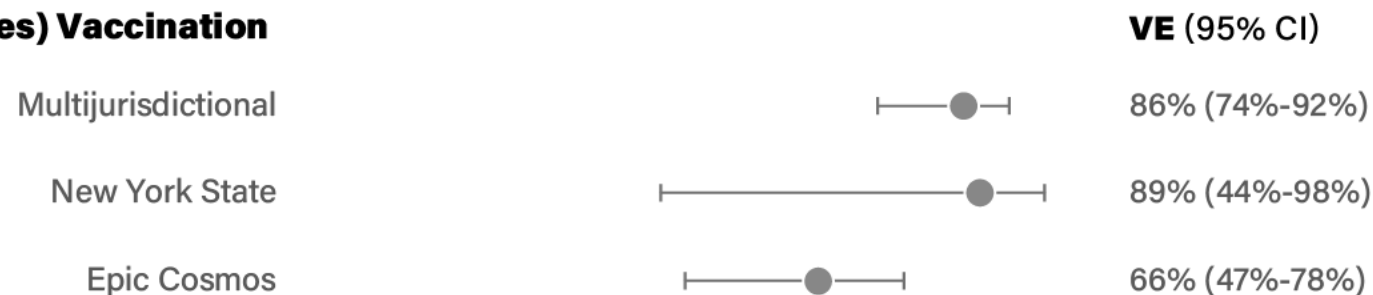


SOURCE: CDC

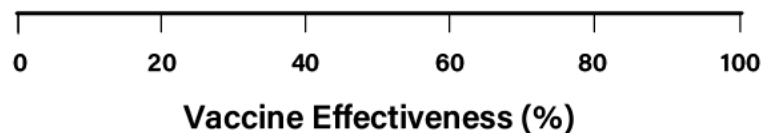
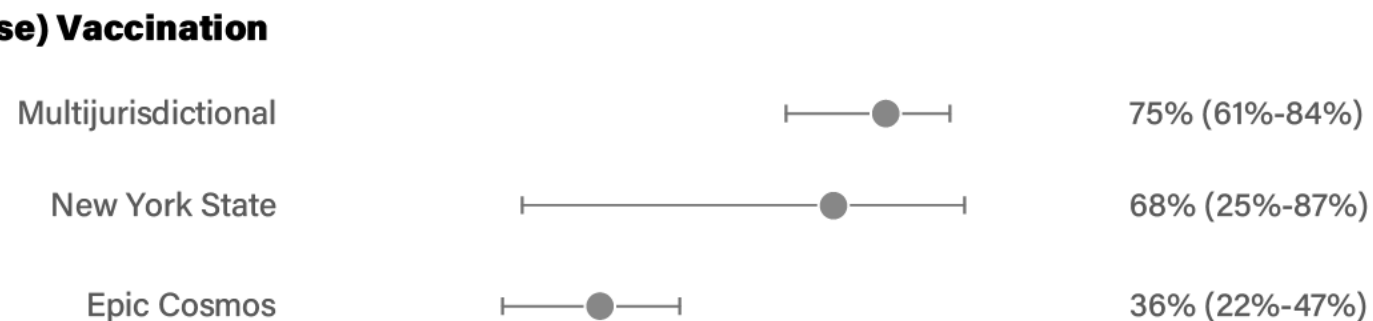
abc NEWS

## Adjusted vaccine effectiveness (VE) of JYNNEOS vaccine against mpox by study and number of doses

### Full (2 Doses) Vaccination



### Partial (1 Dose) Vaccination

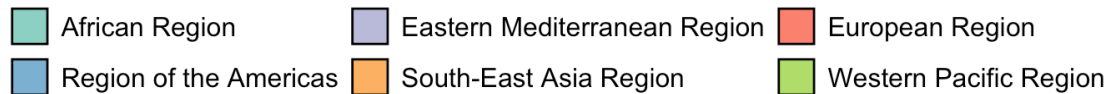
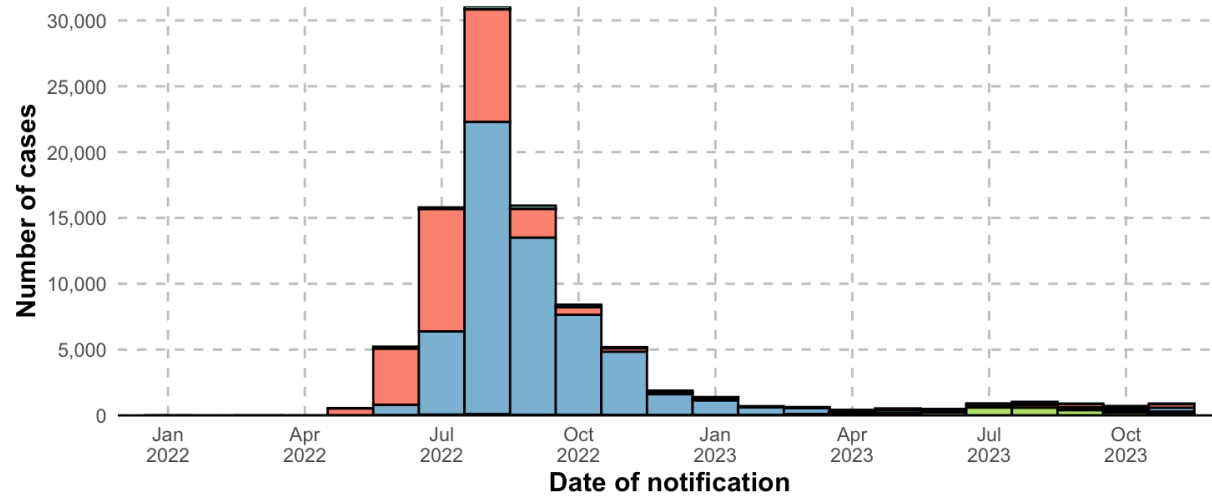
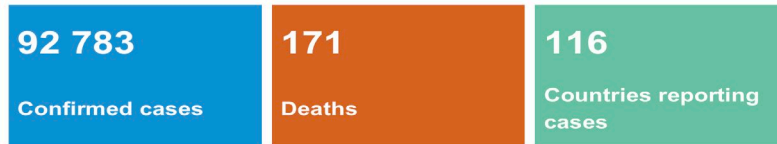


# Global Mpox Cases (through November 2023)

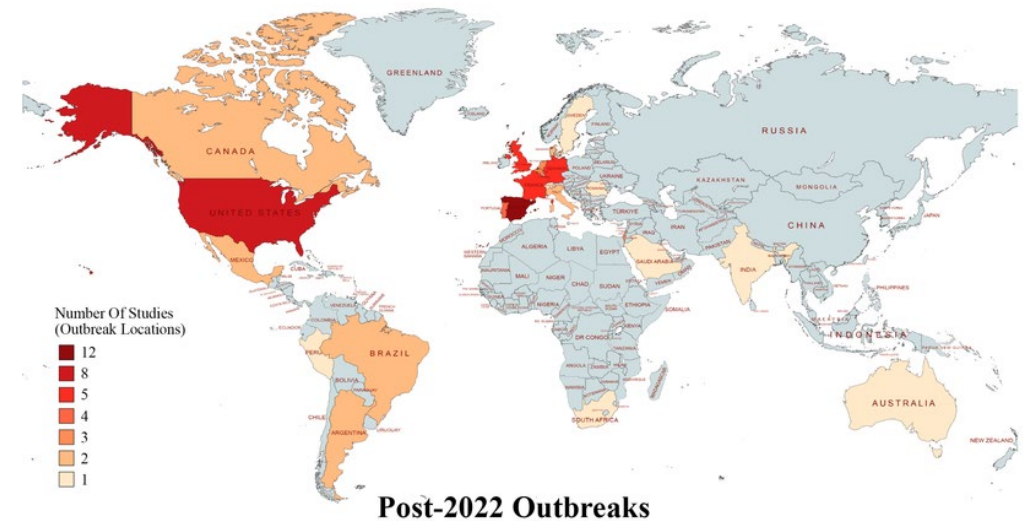
November 2023



Overall



Source: WHO





# Mpox kills 600 in largest ever DRC outbreak

Experts warn the strain of the disease behind the new outbreak has the potential to spread worldwide

Maeve Cullinan, GLOBAL HEALTH REPORTER  
24 November 2023 · 3:13pm



Experts warn the outbreak is being driven by a strain of the virus that previously spread exclusively between humans. | CREDIT: HOGP/National Institute of Allergy and Infectious Diseases/AP

Morbidity and Mortality Weekly Report (MMWR)

## Mpox Outbreak — Los Angeles County, California, May 4–August 17, 2023

Weekly / January 18, 2024 / 73(2);44–48

[Print](#)

Colleen M. Leonard, MPH<sup>1</sup>; Kathleen Poortinga, MPH<sup>1</sup>; Erin Nguyen, MPH<sup>1</sup>; Abraar Karan, MD<sup>2</sup>; Sonali Kulkarni, MD<sup>1</sup>; Rebecca Cohen, MD<sup>1</sup>; Jacob M. Garrigues, PhD<sup>1</sup>; Amy N. Marutani, MPH<sup>1</sup>; Nicole M. Green, PhD<sup>1</sup>; Andrea A. Kim, PhD<sup>1</sup>; Kwa Sey, PhD<sup>1</sup>; Mario J. Pérez, MPH<sup>1</sup> [VIEW AUTHOR AFFILIATIONS](#)

[View suggested citation](#)

China | Viral slurs

## Many of the world's new mpox cases are in China

Conservatism and nationalism are blocking efforts to curb the disease's spread



IMAGE: CHLOE CUSHMAN

Oct 5th 2023 | BEIJING

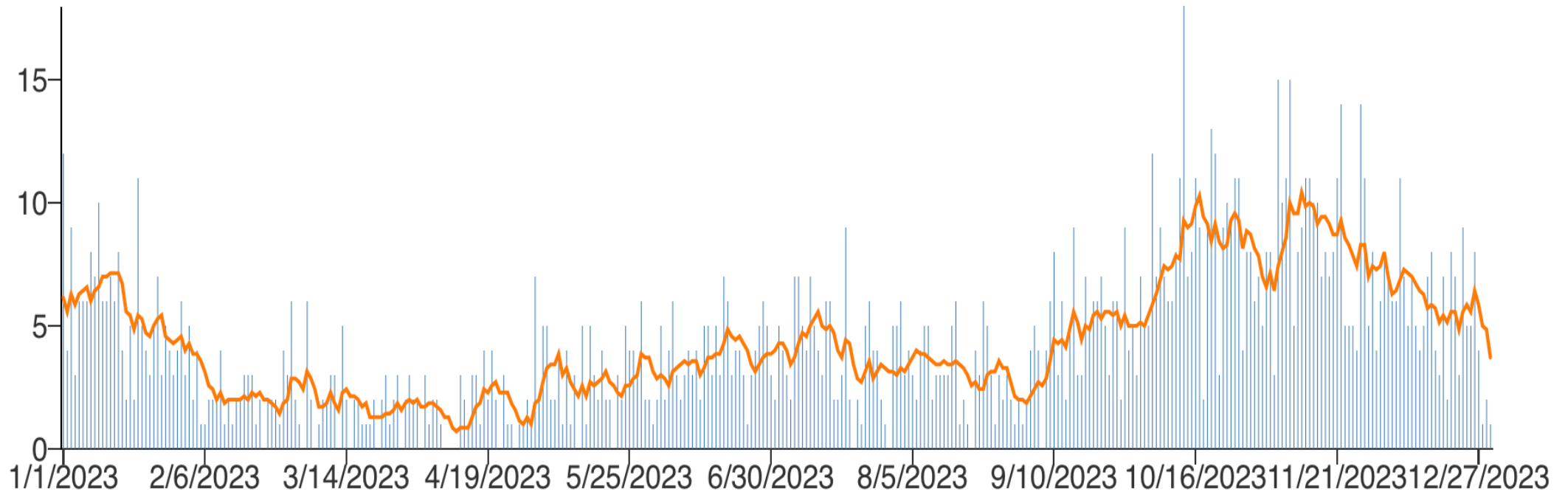
[Share](#)

# US Cases: After ending the Public Health Emergency (1/2023 – 12/2023)

2023 ▾

Apply Filters

[Reset All](#)



# Global situation: mpox

- Outside of Africa: mostly gay, bisexual, and other men who have sex with men
- In Africa: men, women and children
- 30~50% of persons living with HIV
- Immunosuppressed at a greater risk of severe disease
- Clade I and II sexually transmissible



---

# WHO Strategic Framework for mpox (2023 – 2027)

- Maintain global surveillance, make mpox nationally notifiable to share information with WHO
- Integrate mpox surveillance, detection, prevention, care, and research with HIV and STI programs
- Strengthen capacity in resource-limited settings including Risk Communication and Community Engagement (RCCE) and One Health/Animal Health
- Implement a strategic research agenda for evidence generation
- Enhance access to diagnostics, vaccines, and therapeutics to enhance global health equity
- Each country to develop elimination or control plans according to the context



# Mpox: Challenges

- Fear and stigma
- Decreased surveillance and reporting
- Gaps in testing capacity and genomic surveillance
- Equity to countermeasures
- Understanding mpox virus ecology and dynamics of spillover events
- Elimination of human-to-human transmission depends on local action



A microscopic image of Candida auris, showing numerous spherical yeast cells and branching filamentous structures (hyphae) in shades of blue and brown. The cells have a textured, porous appearance. The text is overlaid on the central part of the image.

# Candida auris

A Global Threat

# *Candida auris*

- *Candida* species resistant to multiple classes of antifungals
  - Invasive infections associated with 30-72% mortality
  - Can lead to clusters of infections with pan-resistance
- Very difficult to limit spread and eliminate from the patient environment
  - Bed and handrails can remain contaminated for weeks if not cleaned properly
- Isolation is “lifelong,” as patients can remain colonized for many months



# *C. auris* Background



- First discovered 2009 in Japan
- However genomic data reveals emergence from all around the globe (Asia, Americas, Africa, etc)

ORIGINAL ARTICLE

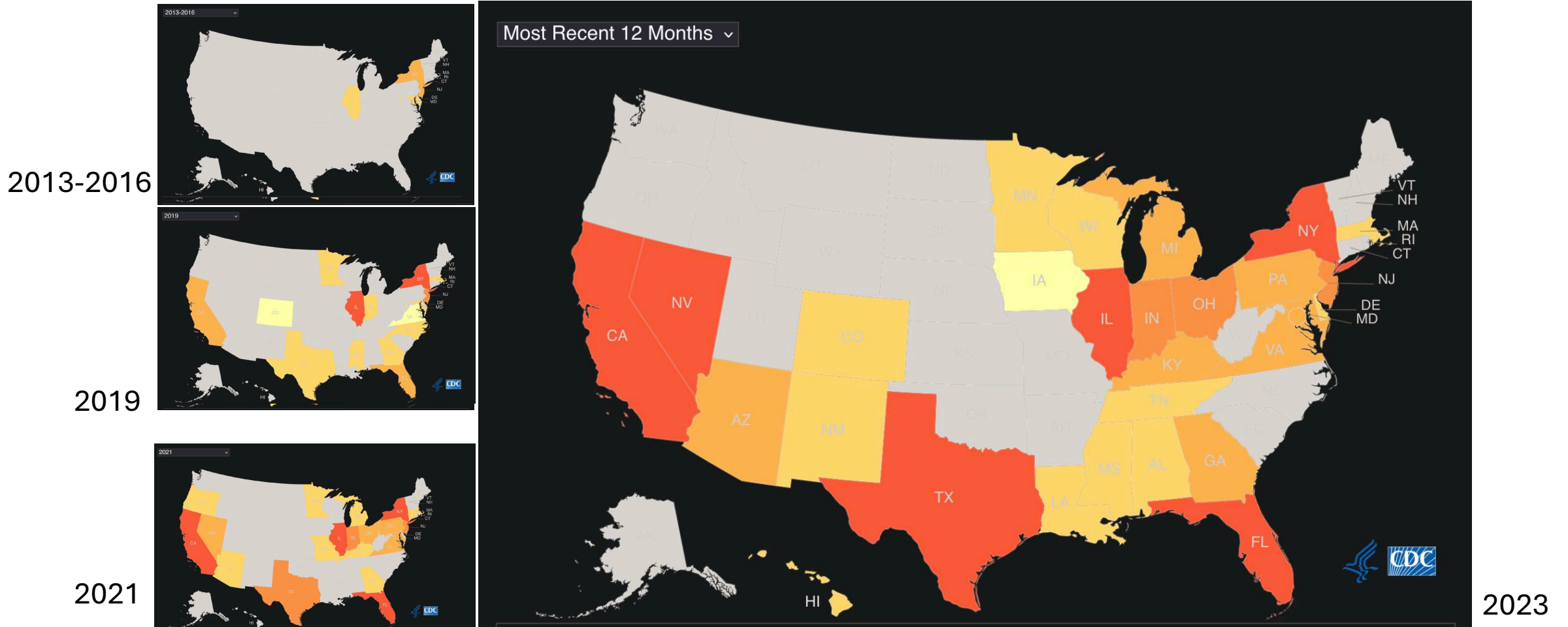
## ***Candida auris* sp. nov., a novel ascomycetous yeast isolated from the external ear canal of an inpatient in a Japanese hospital**

Kazuo Satoh<sup>1,2</sup>, Koichi Makimura<sup>1,3</sup>, Yayoi Hasumi<sup>1</sup>, Yayoi Nishiyama<sup>1</sup>, Katsuhisa Uchida<sup>1</sup> and Hideyo Yamaguchi<sup>1</sup>

<sup>1</sup>Teikyo University Institute of Medical Mycology, 359 Otsuka, Hachioji, Tokyo 192-0395, <sup>2</sup>Japan Health Sciences Foundation, 13-4 Nihonbashi-Kodenmacho, Chuo-ku, Tokyo 103-0001 and <sup>3</sup>Genome Research Center, Graduate School of Medicine and Faculty of Medicine, Teikyo University, Otsuka 359, Hachioji, Tokyo 192-0395, Japan



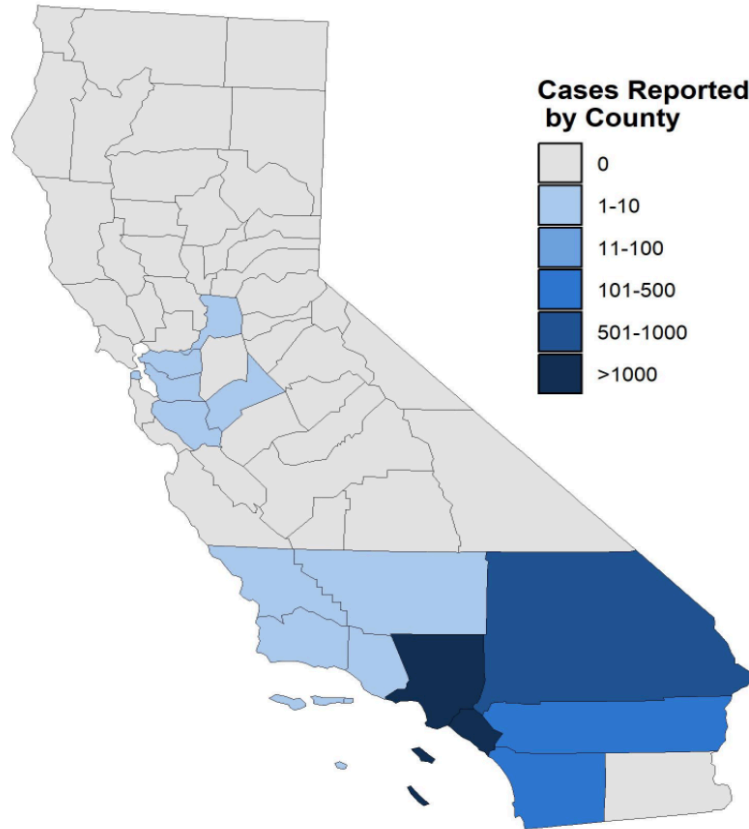
# The spread of *Candida auris* (US)



Data Source: CDC <https://www.cdc.gov/fungal/candida-auris/tracking-c-auris.html>

# *C. auris* in California (2023)

***Candida auris* Cases by County through October 2023, N= 6,401**



Counties with $\geq 1$ Reported Case	Cases through October 2023
Alameda	<11
Contra Costa	<11
Kern	<11
Los Angeles	3,173
Orange	2,116
Riverside	345
Sacramento	<11
San Bernardino	619
San Diego	124
San Francisco	<11
San Luis Obispo	<11
Santa Barbara	<11
Santa Clara	<11
Stanislaus	<11
Ventura	<11
<b>Total</b>	<b>6,401</b>

**1** Global warming is responsible for raising the ambient climate temperatures, which selects fungal clades that can reproduce at avian and mammalian basal temperatures.



## Rural environment



**3** Thermotolerant *C. auris* may have been transplanted by birds across the globe to rural areas where human and birds are in constant contact.



**4** Rural environment activities (e.g., farming) provide the opportunity for interspecies transmission of virulent pathogens such as *C. auris*

## Wetlands

**2** *Candida auris* previously existed as a plant saprophyte that gained thermotolerance and salinity tolerance as a result of the effects of climate change on the wetland ecosystem.



## Urban environment

**5** Human migration towards urban areas eventually led *C. auris* into health care environments.

## Hospital

# Summary

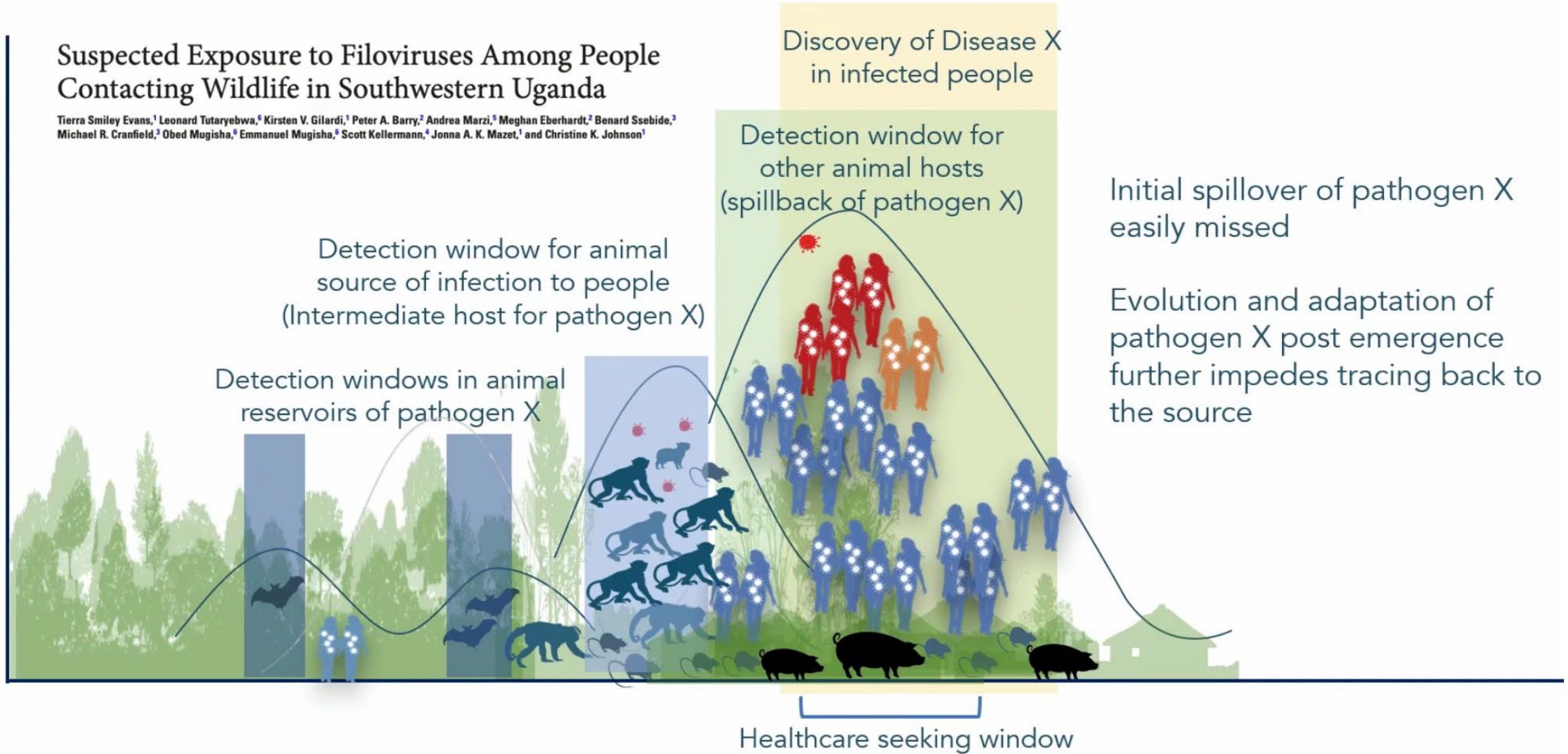
- Emerging infections will continue to increase, likely due to multiple factors:
  - **Urbanization** and the expanding animal-human interface
  - Climate change
  - **Increasing international travel and global trade**
- Up to 75% of emerging infectious agents are zoonotic in origin
  - Coronavirus
  - Zoonotic influenza
  - Mpox
- Climate change can potentially lead to multidrug pathogens such as *Candida auris*

# Challenges to Tracing Emerging Infectious Disease Events to their Source

## Suspected Exposure to Filoviruses Among People Contacting Wildlife in Southwestern Uganda

Tierra Smiley Evans,<sup>1</sup> Leonard Tutaryebwa,<sup>6</sup> Kirsten V. Gilardi,<sup>1</sup> Peter A. Barry,<sup>2</sup> Andrea Marzi,<sup>5</sup> Meghan Eberhardt,<sup>2</sup> Benard Ssebide,<sup>3</sup> Michael R. Cranfield,<sup>3</sup> Obed Mugisha,<sup>5</sup> Emmanuel Mugisha,<sup>5</sup> Scott Kellermann,<sup>4</sup> Jonna A. K. Mazot,<sup>1</sup> and Christine K. Johnson<sup>1</sup>

Detection Probability



**POLICY FORUM**

ECOLOGY AND ECONOMICS: COVID-19

# Ecology and economics for pandemic prevention

Investments to prevent tropical deforestation and to limit wildlife trade will protect against future zoonosis outbreaks

*Science* 24 Jul 2020

DOI: 10.1126/science.abc3189

US\$22-  
31bn/yr  
Prevention costs

>US\$10tn

Economic losses from COVID-19

The economic cost of COVID-19 was over 10 trillion dollars, while less than 31 billion per year are spent on prevention of future zoonosis outbreaks

Where do we go  
from here?

Emerging  
Infectious  
Disease  
Preparedness



Transdisciplinary collaboration between animal, human, and environmental health professionals strengthened by routine data and information sharing



Internationally collaborative research in between outbreaks



Community engagement in all stages of research and outbreak control



Next generation tools and techniques should be developed for pathogen X surveillance

*I'm an  
#OrganDonor,  
are you?*

1 organ donor can save up to 8 lives. Register today.

organ  
donor  
+

Thank you!

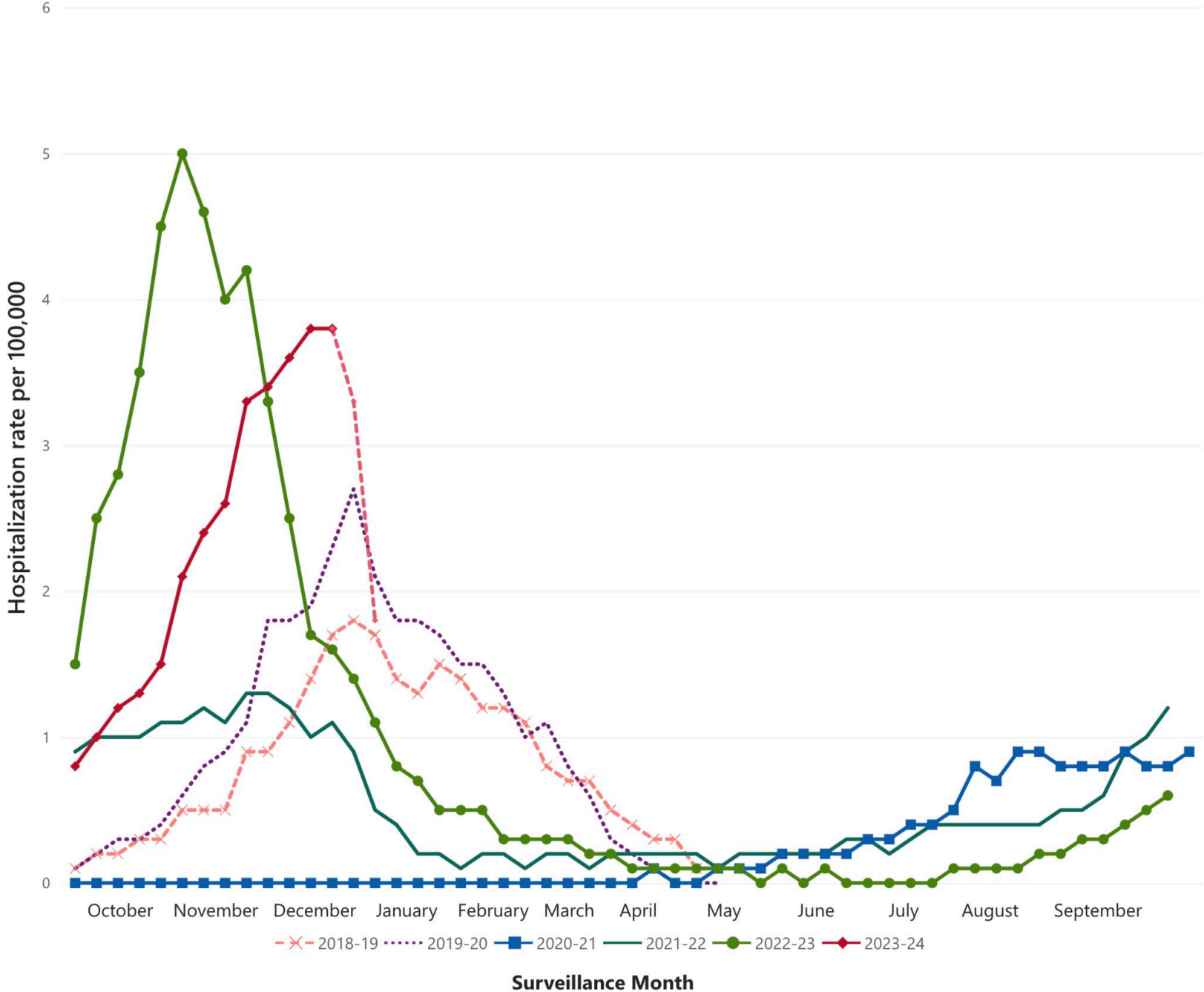




RSV

Just FYI

Weekly Rates of RSV Associated Hospitalizations, by Season



**TABLE 2. In-hospital outcomes among adults aged ≥60 years hospitalized with respiratory syncytial virus, COVID-19, or influenza — Investigating Respiratory Viruses in the Acutely Ill Network, 25 hospitals,\* 20 U.S. states, February 1, 2022–May 31, 2023**

In-hospital outcomes	No./Total no. (%)			RSV vs. COVID-19		RSV vs. influenza	
	RSV patients n = 304	COVID-19 patients n = 4734	Influenza patients n = 746	aOR <sup>†</sup> (95% CI)	p-value	aOR <sup>†</sup> (95% CI)	p-value
Standard flow oxygen therapy <sup>§</sup>	157/197 (79.7)	2,169/3,726 (58.2)	390/593 (65.8)	2.97 (2.07–4.27)	<0.001	2.07 (1.37–3.11)	<0.001
HFNC or NIV <sup>¶</sup>	59/256 (23.0)	495/4,223 (11.7)	94/687 (13.7)	2.25 (1.65–3.07)	<0.001	1.99 (1.36–2.90)	<0.001
ICU admission	74/304 (24.3)	819/4,734 (17.3)	125/746 (16.8)	1.49 (1.13–1.97)	0.005	1.55 (1.11–2.19)	0.01
IMV or death	41/304 (13.5)	481/4,734 (10.2)	52/746 (7.0)	1.39 (0.98–1.96)	0.07	2.08 (1.33–3.26)	0.001

**Abbreviations:** aOR = adjusted odds ratio; HFNC = high-flow nasal cannula; ICU = intensive care unit; IMV = invasive mechanical ventilation; NIV = noninvasive ventilation; RSV = respiratory syncytial virus.

\* <https://www.cdc.gov/flu/vaccines-work/ivy.htm>

<sup>†</sup> Multivariable logistic regression models were adjusted for age, sex, race and ethnicity, number of organ systems with chronic medical conditions, and U.S. Department of Health and Human Services region.

<sup>§</sup> Standard flow oxygen therapy was defined as receipt of supplemental oxygen therapy at a flow rate <30 L/minute as the highest level of oxygen support received during hospitalization.

<sup>¶</sup> HFNC or NIV was defined as patients who received either HFNC (oxygen therapy at a flow rate ≥30 L/minute) or NIV as the highest level of oxygen support received during hospitalization.

- RSV outstripped both COVID-19 vs influenza in terms of in-hospital mortality and morbidity with higher need for O<sub>2</sub> (OR 2.97 vs 2.07), HFNC (OR 2.25 vs 1.99), ICU admission (OR 1.49 vs 1.55), IMV, or death (OR 1.39 vs 2.08)
- IMV or death: RSV 13.5% ≥ COVID-19 10.2% ≥ influenza 7.0%