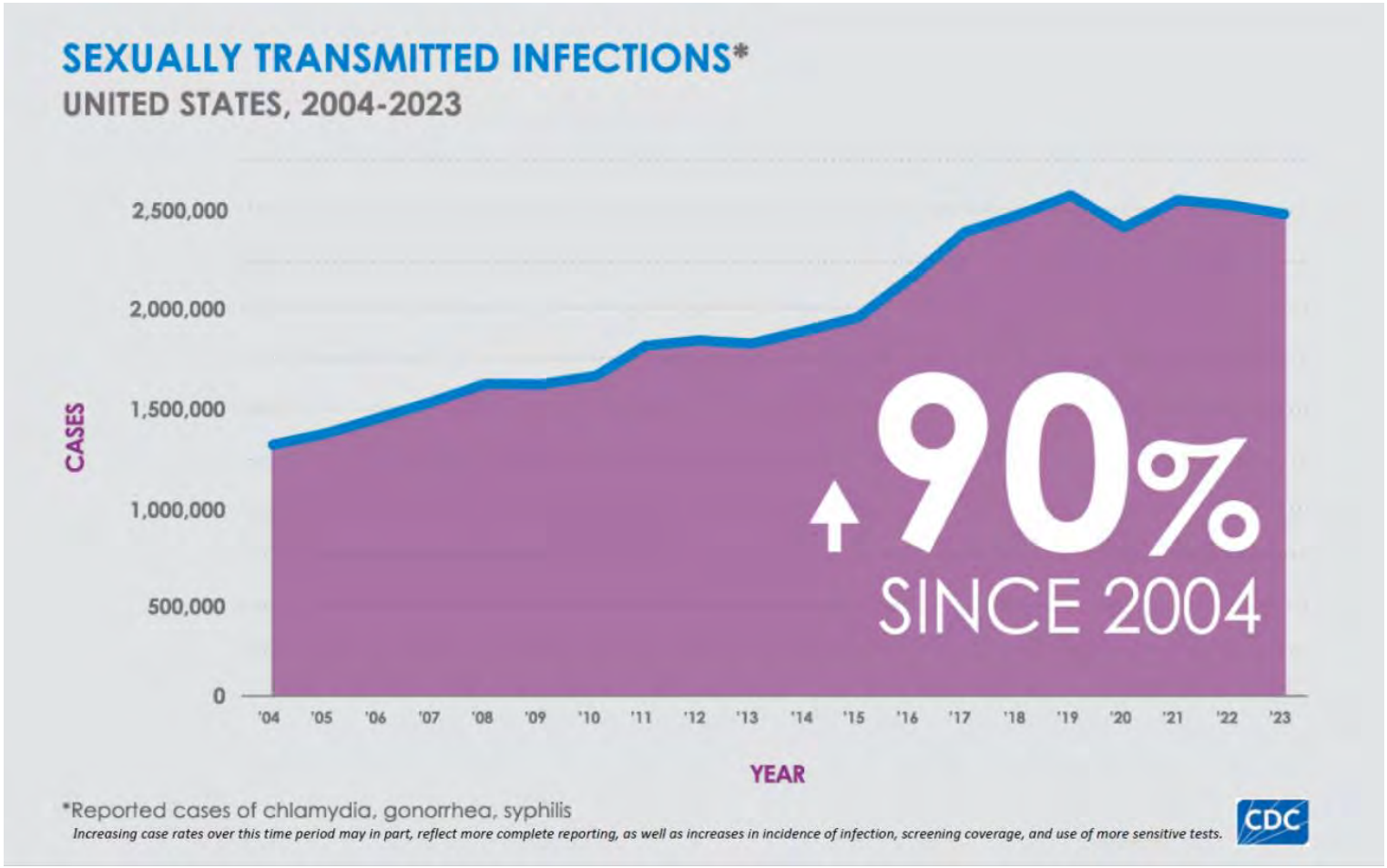
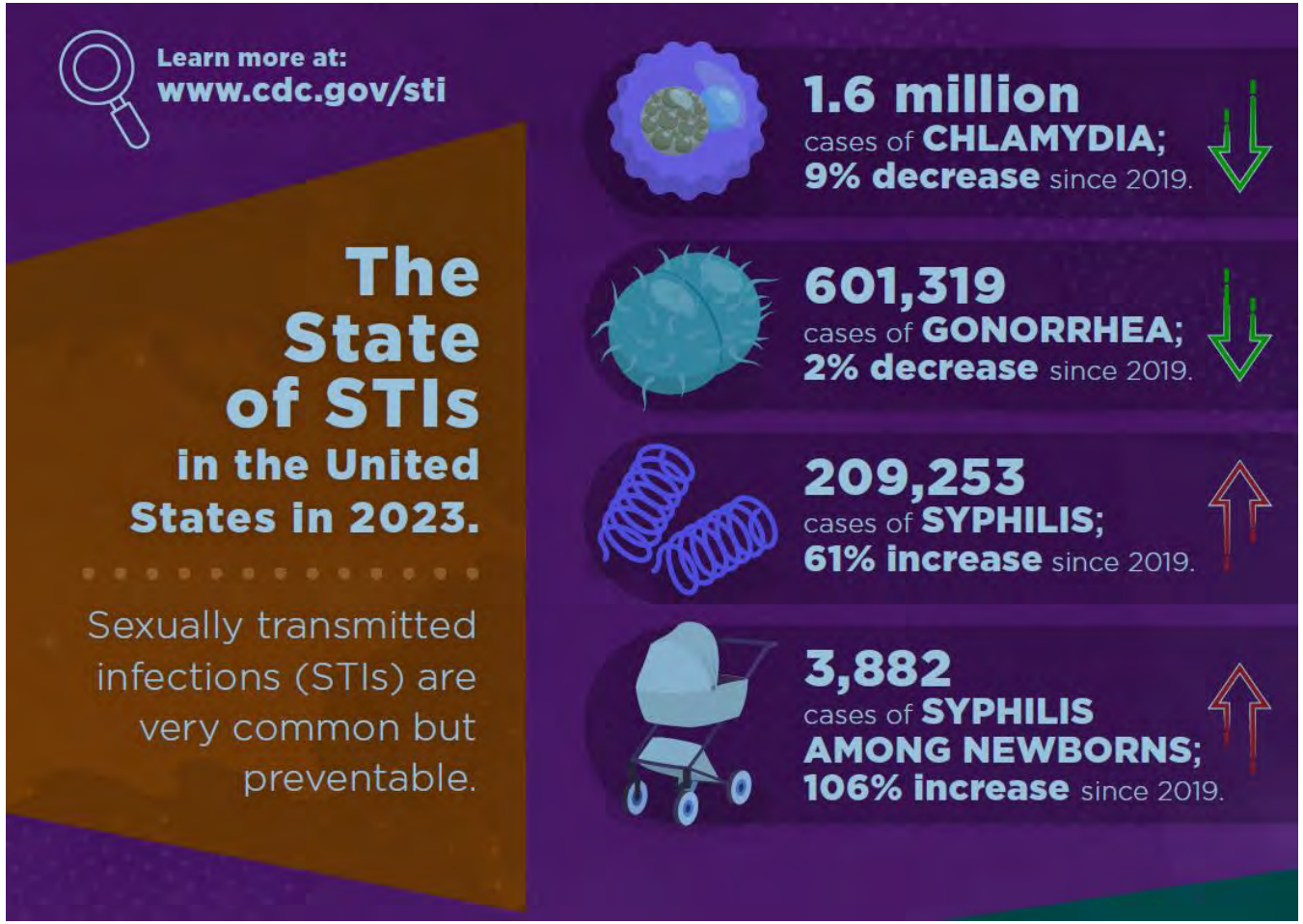
New and Emergent STIs

Natalie Neu, MD, MPH
Jason Zucker, MD

Possible slowing of the epidemic of STIs…



Highlights

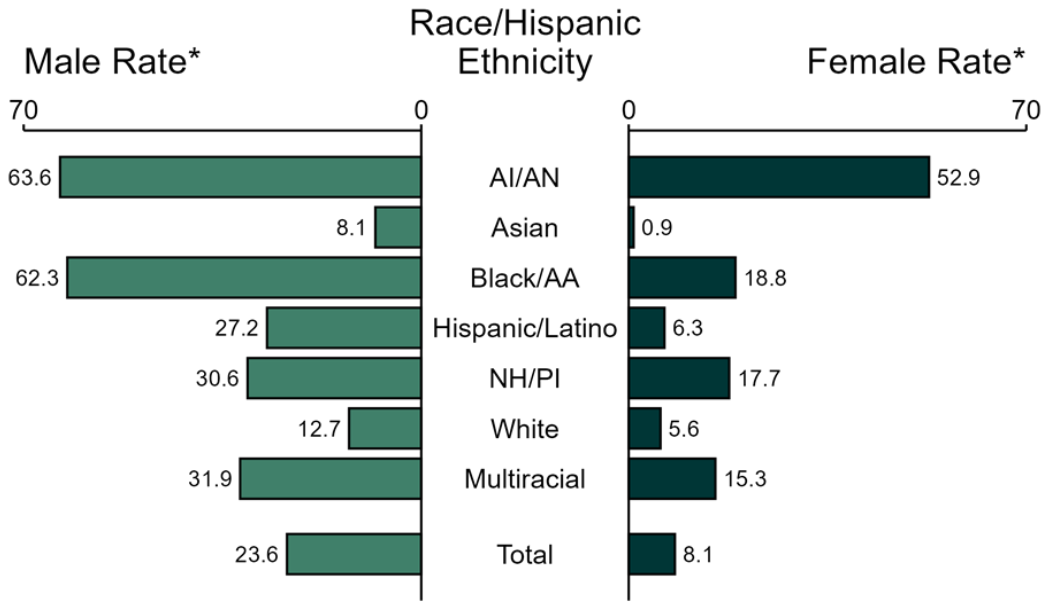


- 2.4 million cases of STI reported in 2023
- Gonorrhea dropped by 7% which is a first since 2019
- Syphilis still increasing but only by 1%
  - Primary and secondary syphilis cases decreased (10%)
- Slowing of cases of congenital syphilis
  - Only 3% increase since 2022 compared to 30% prior years

Federal, Commercial and Local Initiatives to Combat STI Increases

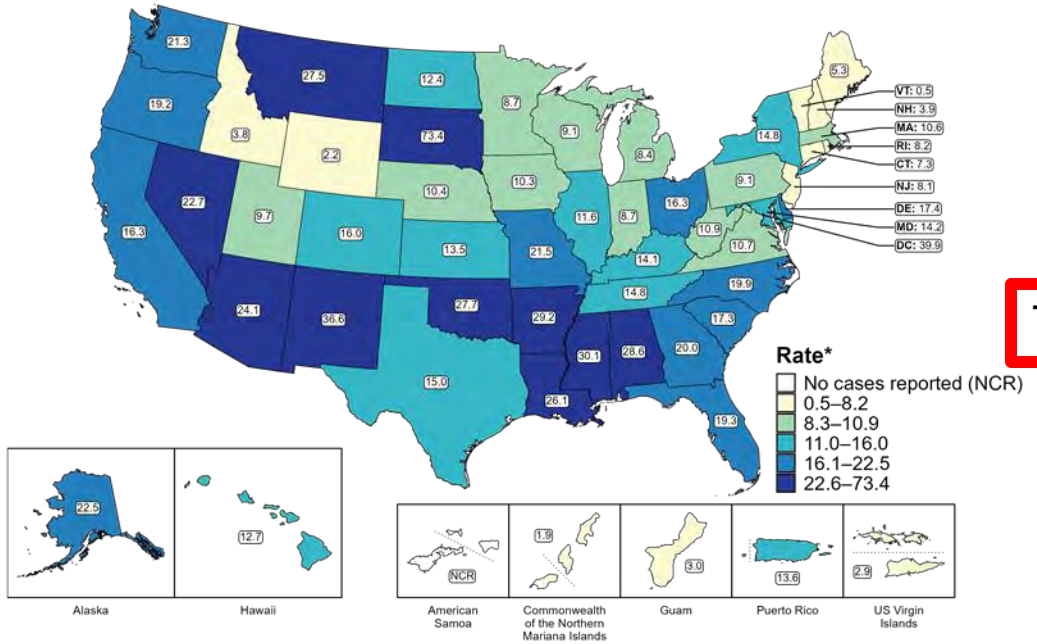
- Prioritizing STI work, federally, locally
  - News spot lights
  - Funding
  - FDA authorization of self-tests and/or at home tests (syphilis, GC/CT)
- Prevention improvements
  - Doxy PEP, PrEP
  - Vaccinations
- Enhanced training and education
  - NNPTCs
  - DOH
- Workforce and TaskForces
  - Disease Intervention Specialists (DIS) – supplemental award from CDC for workers
  - Federally qualified health centers
  - National Syphilis and Congenital Syphilis Syndemic (NSCSS) Federal Task Force (Jan 30, 2024)

Health Inequities for STIs by Race: Primary and Secondary Syphilis



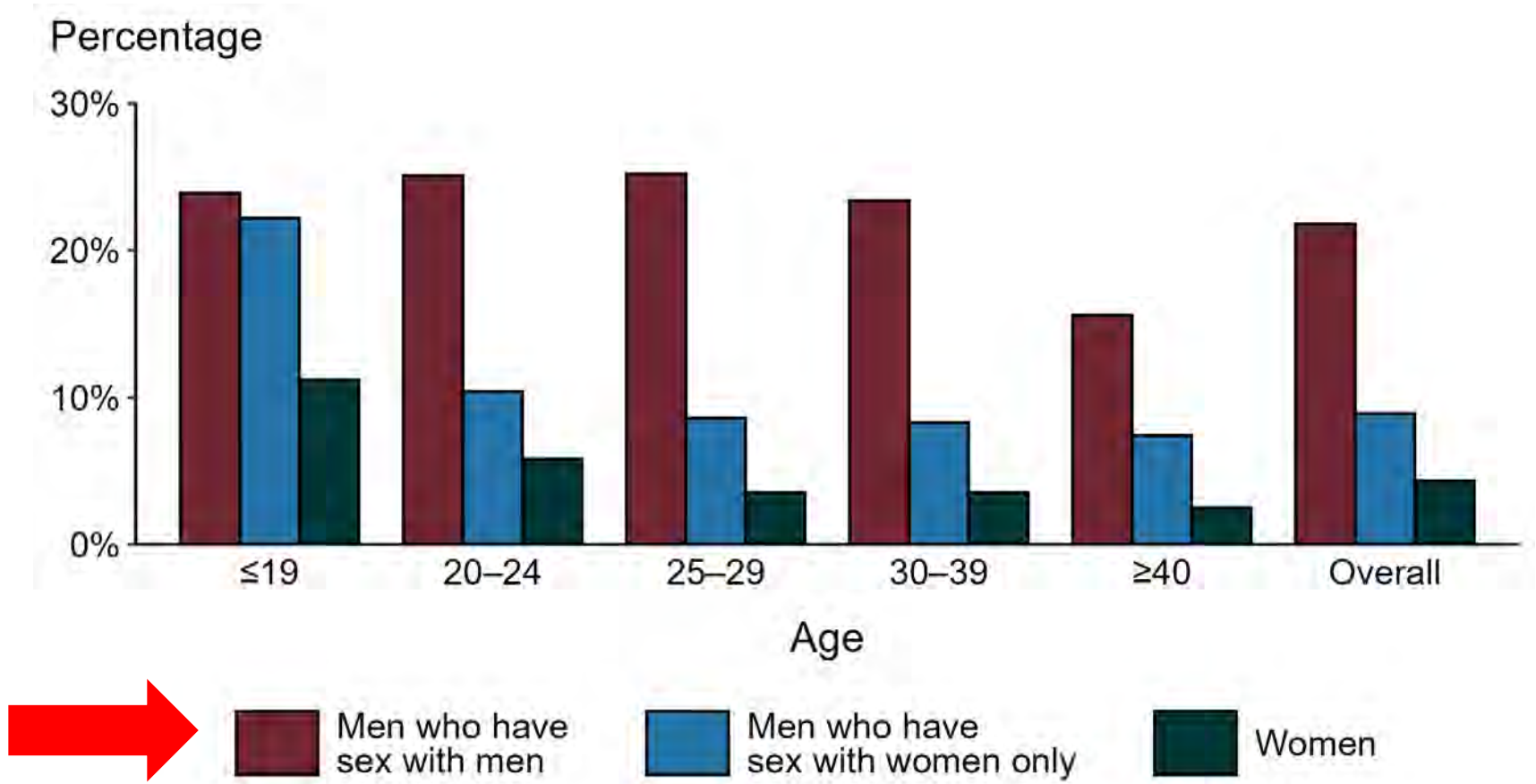
Highest among non-Hispanic American Indian or Alaska native men followed by Black or African American males especially when compared to the proportion of the population they represent

Health Inequities by State/Location: Syphilis and the South



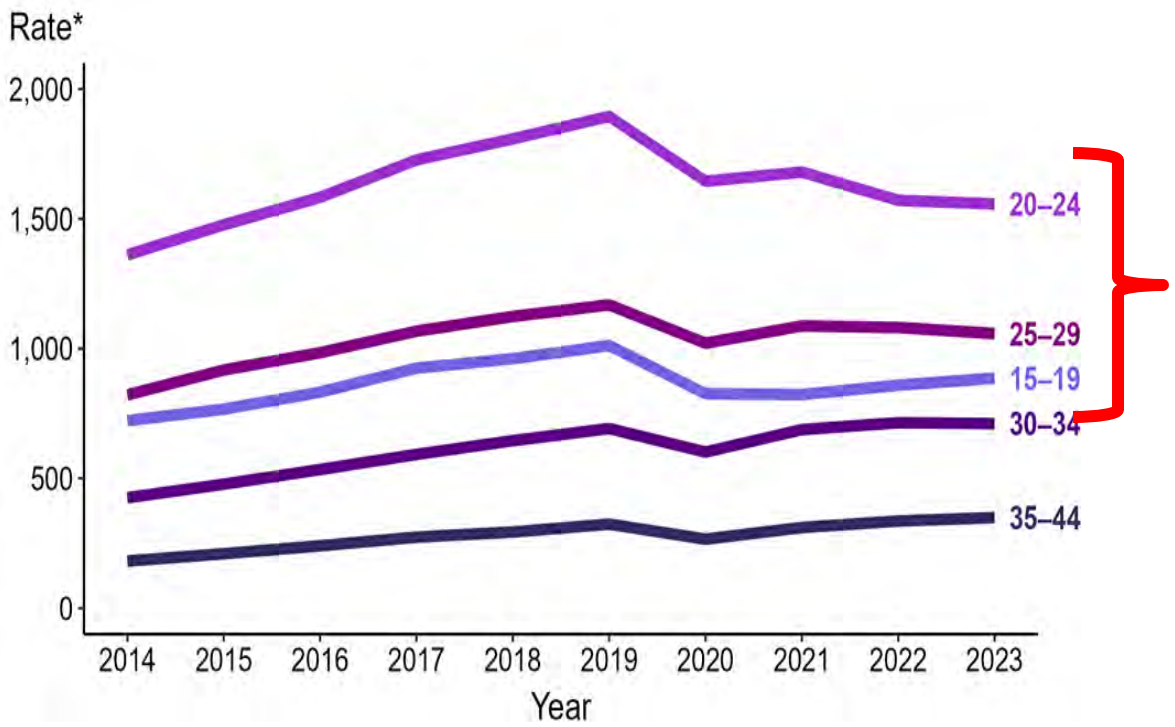
The South!

Inequities by Sex and Sex partners (SSuN), 2023 data, Gonorrhea

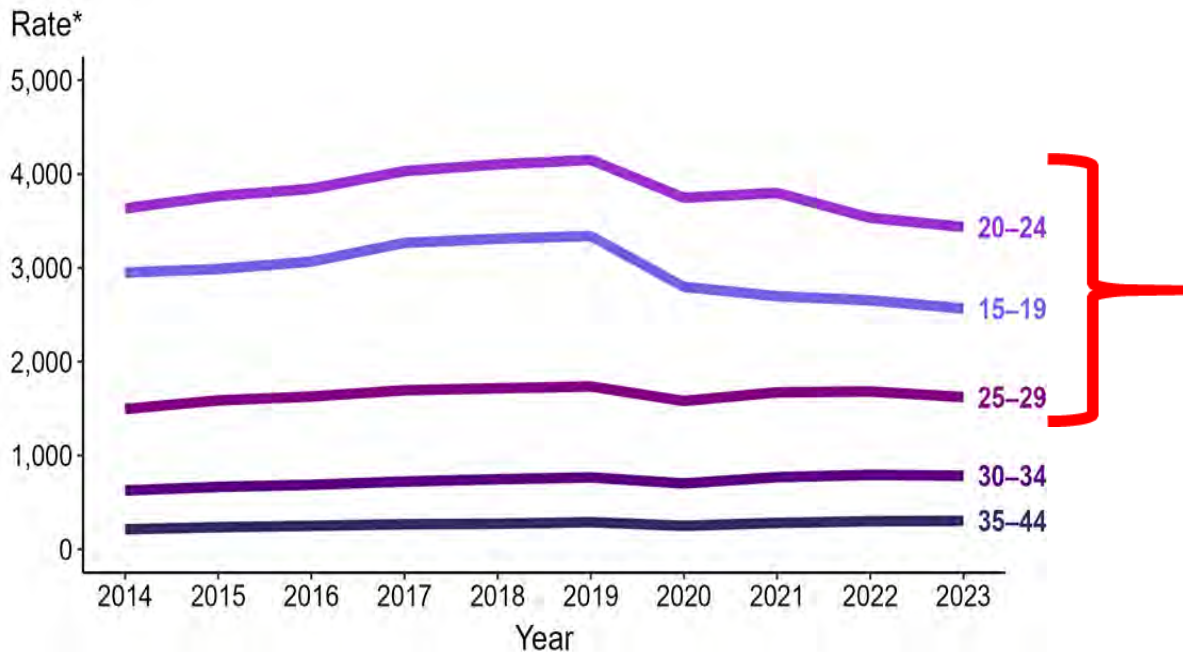


Inequities by Age and Sex: Impact on our Youth!

- Chlamydia rates (per 100,000)
- Men, 15-44 years, 2014-2023

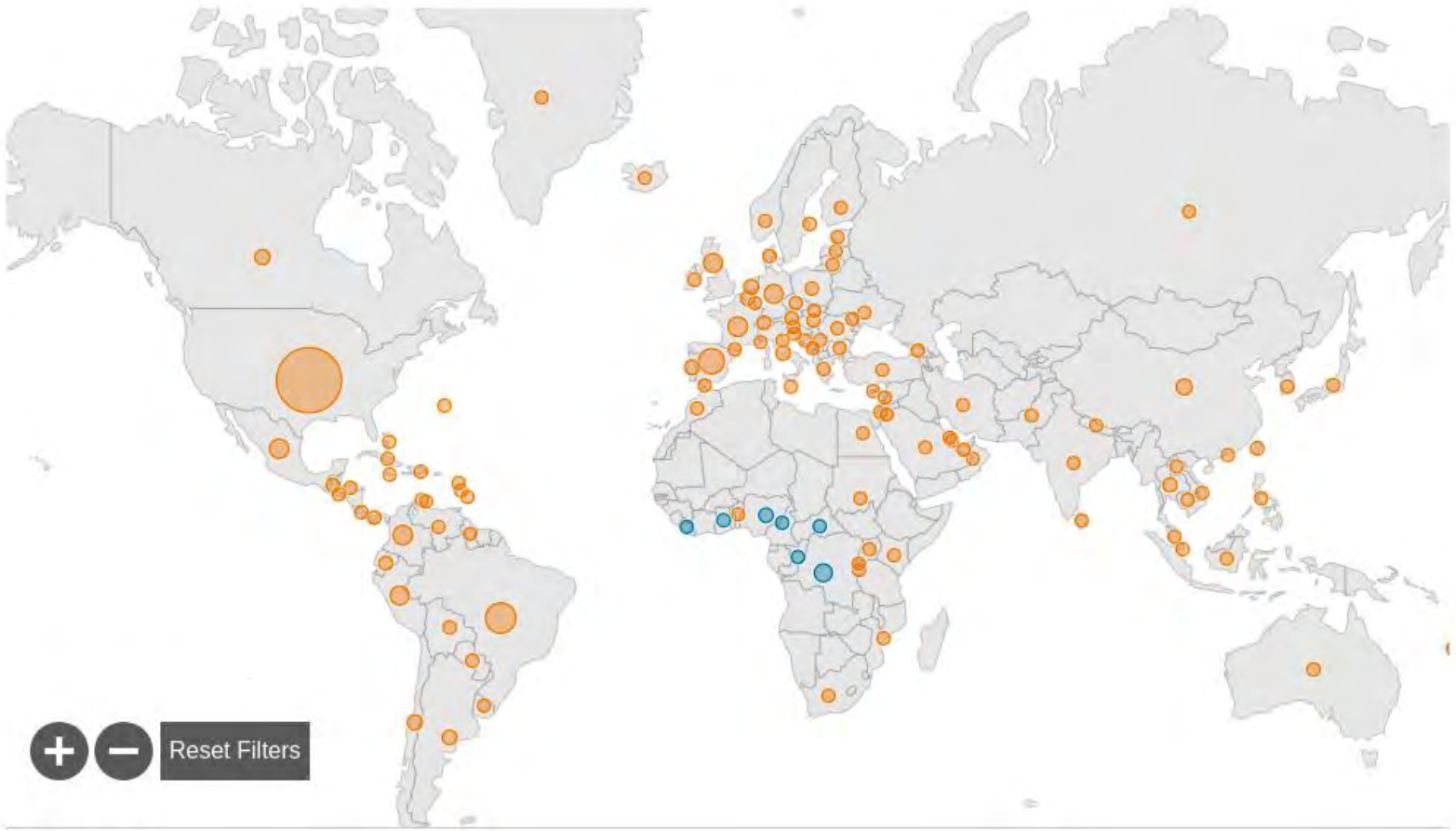


- Chlamydia rates (per 100,000)
- Women, 15-44 years , 2014-23



- Chlamydia rates (per 100,000)
- Women, 15-44 years , 2014-23

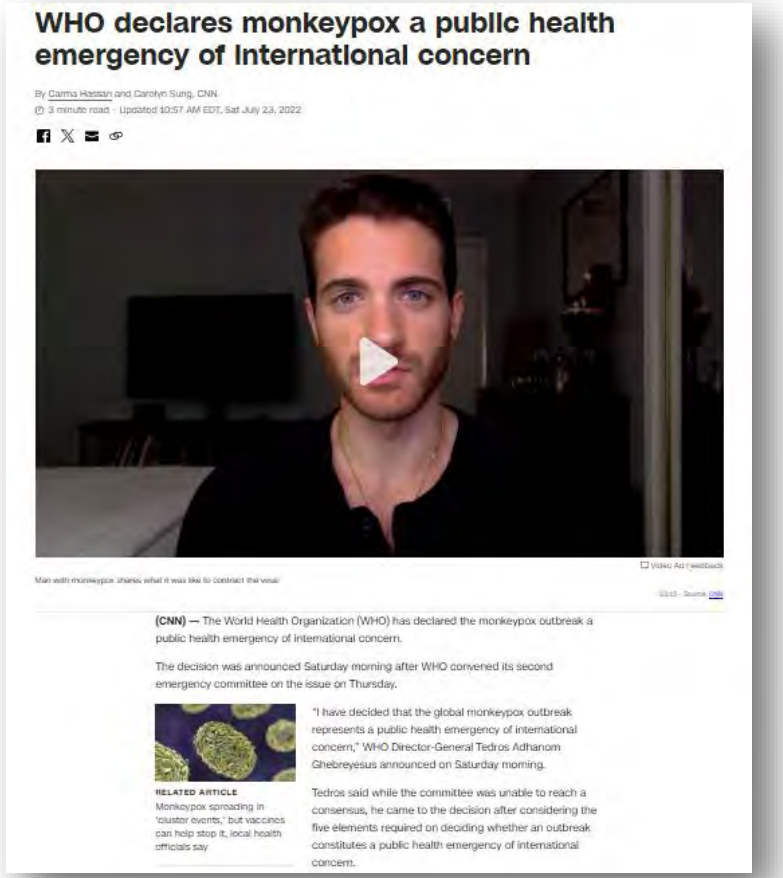
(2022) Multinational Mpox Clade II Outbreak



Clade II

- >100,000 cases
- 122 countries
- 115 non-endemic

Start of PHEIC - July 23, 2022



WHO declares monkeypox a public health emergency of international concern

By Carma Hassan and Carolyn Sung, CNN

3 minute read · Updated 10:57 AM EDT, Sat July 23, 2022

(CNN) — The World Health Organization (WHO) has declared the monkeypox outbreak a public health emergency of international concern.

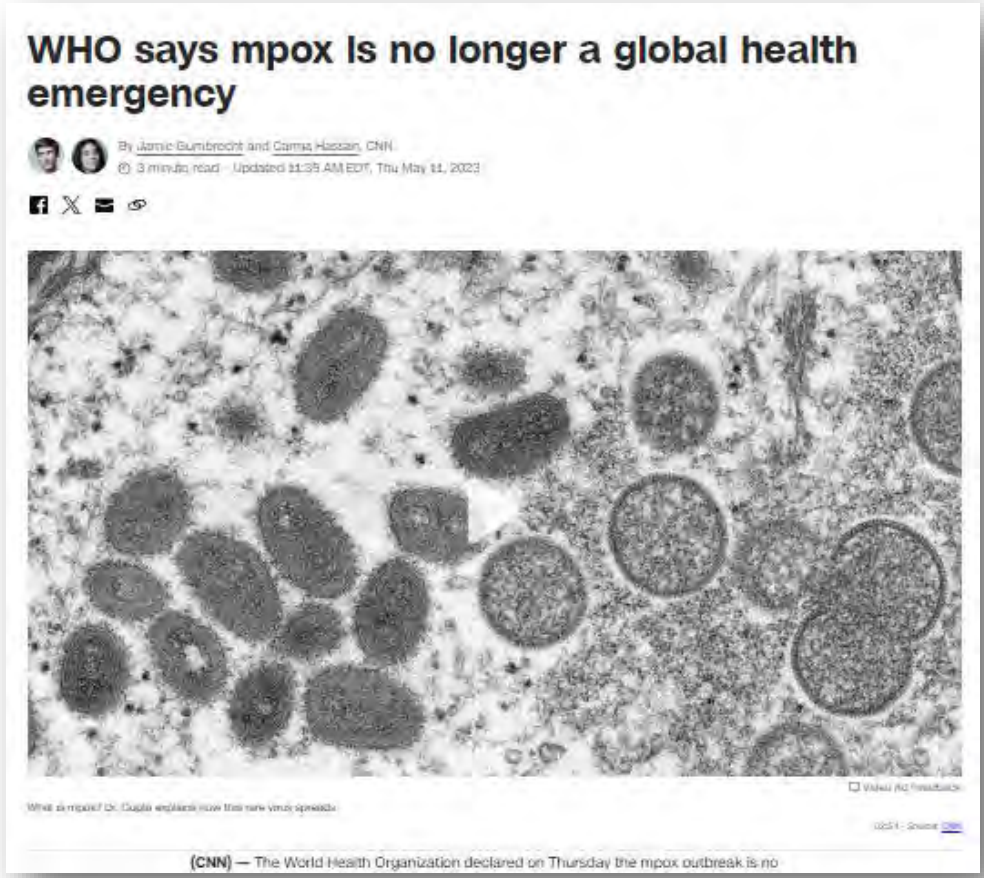
The decision was announced Saturday morning after WHO convened its second emergency committee on the issue on Thursday.

"I have decided that the global monkeypox outbreak represents a public health emergency of international concern," WHO Director-General Tedros Adhanom Ghebreyesus announced on Saturday morning.

RELATED ARTICLE
Monkeypox spreading in 'cluster events,' but vaccines can help stop it, local health officials say

Tedros said while the committee was unable to reach a consensus, he came to the decision after considering the five elements required on deciding whether an outbreak constitutes a public health emergency of international concern.

End of PHEIC – May 11, 2023



WHO says mpox is no longer a global health emergency

By Jamie Gumbrecht and Carma Hassan, CNN

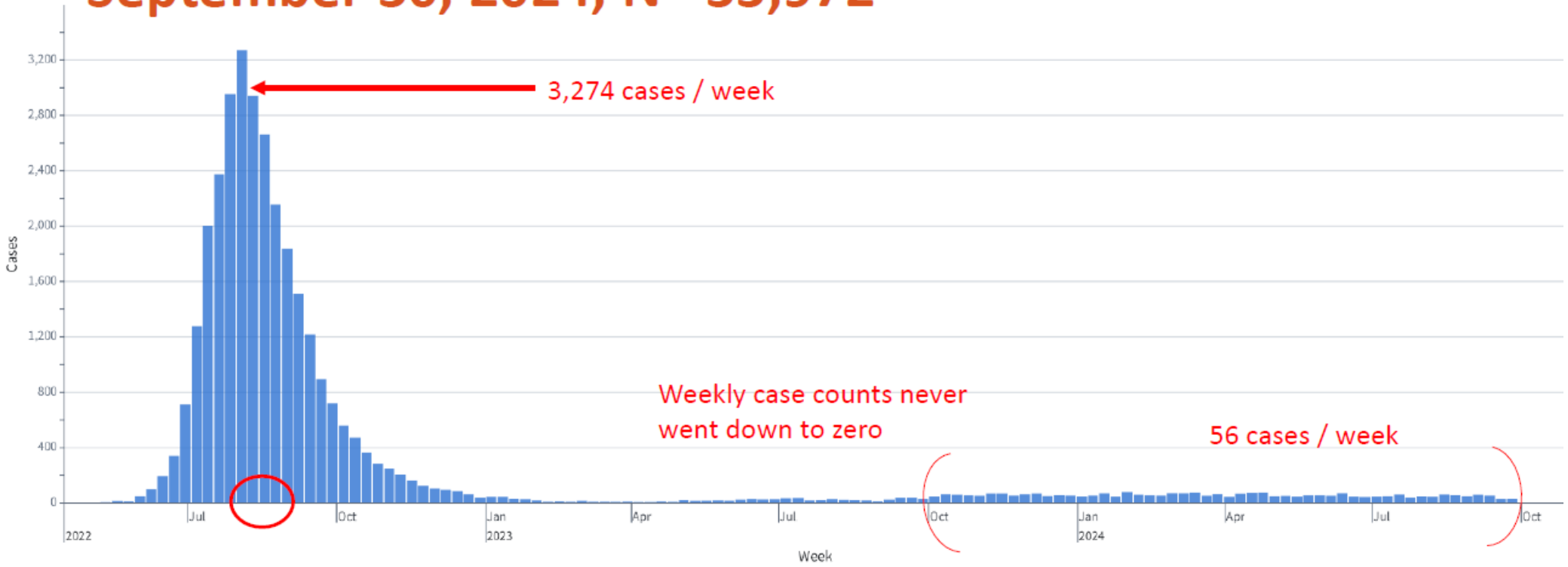
3 minute read · Updated 11:39 AM EDT, Thu May 11, 2023

(CNN) — The World Health Organization declared on Thursday the mpox outbreak is no

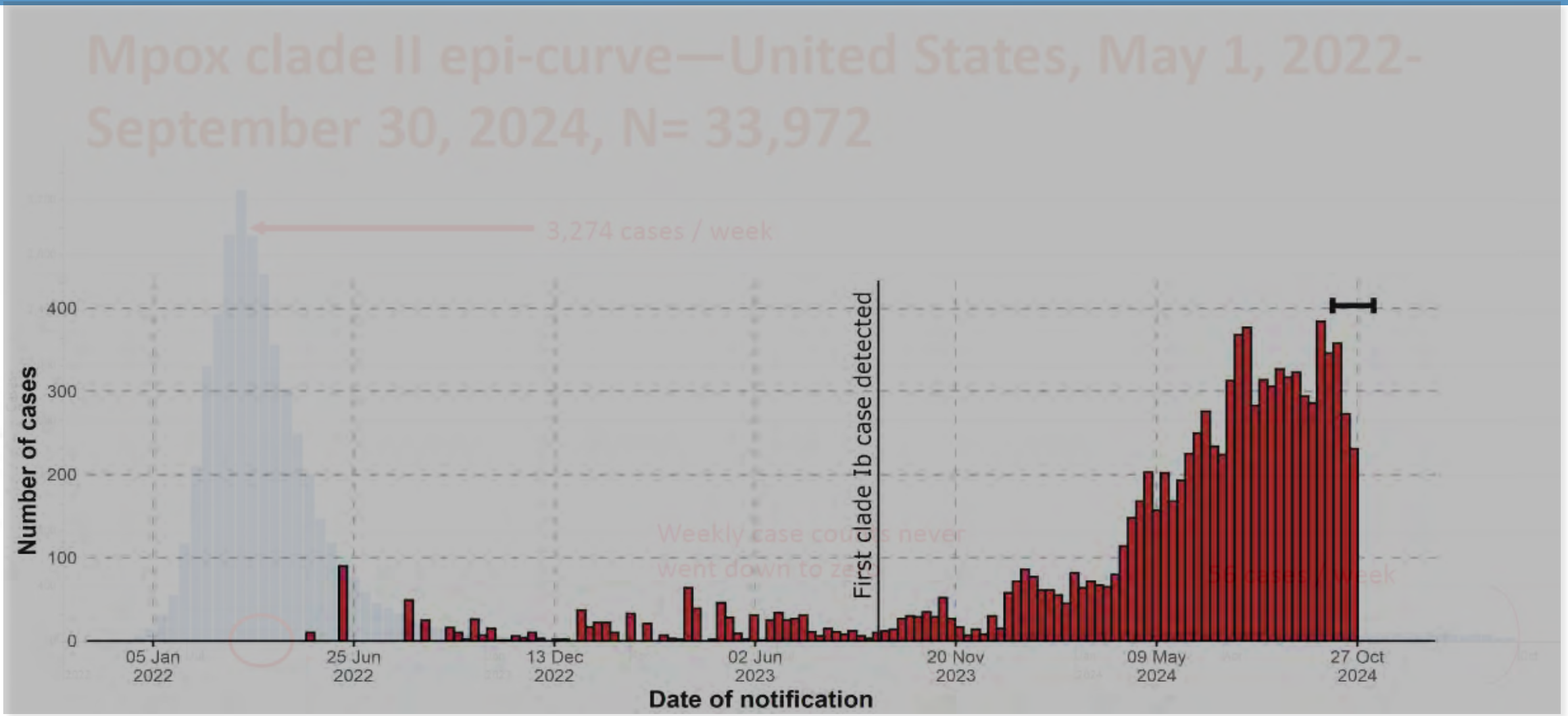
- News articles available at: https://www.cnn.com/2022/07/23/health/monkeypox-who-intl/index.html and https://www.cnn.com/2023/05/11/health/mpox-global-health-emergency-who/index.html

2022 United States Mpox Clade II Outbreak

Mpox clade II epi-curve—United States, May 1, 2022-September 30, 2024, N= 33,972



Democratic Republic of the Congo Epi Curve

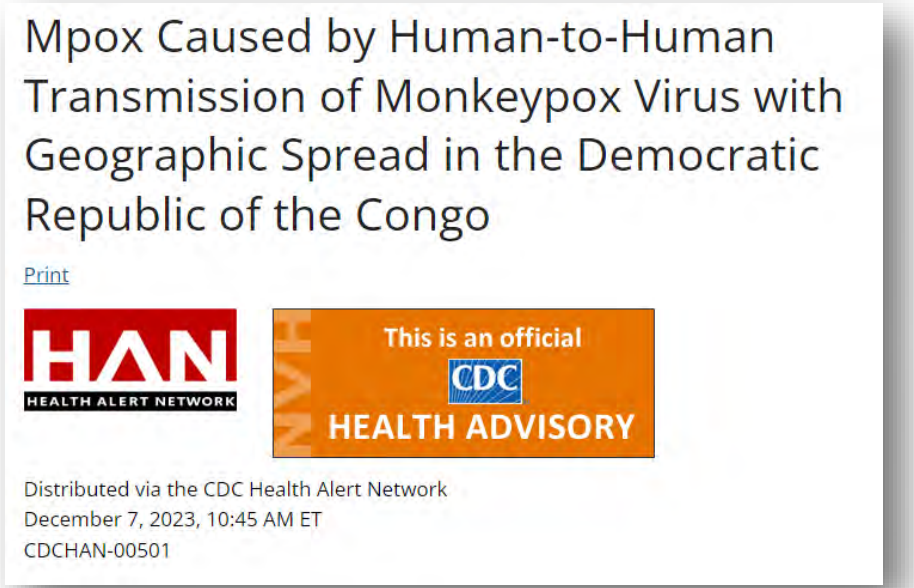


- https://worldhealthorg.shinyapps.io/

Clade I Outbreak in the DRC

- **Since January 1, 2024**
  - 39,501 suspected cases
    - 1,073 deaths (2.7%)
  - 8,662 lab-confirmed
    - 42 deaths (0.48%)

- **Clade I Divergence**
  - High % of pediatric patients (Ia)
  - Human to human transmission (Ib)
    - Suspected sexual transmission


Mpox Caused by Human-to-Human Transmission of Monkeypox Virus with Geographic Spread in the Democratic Republic of the Congo

Print

HAN HEALTH ALERT NETWORK

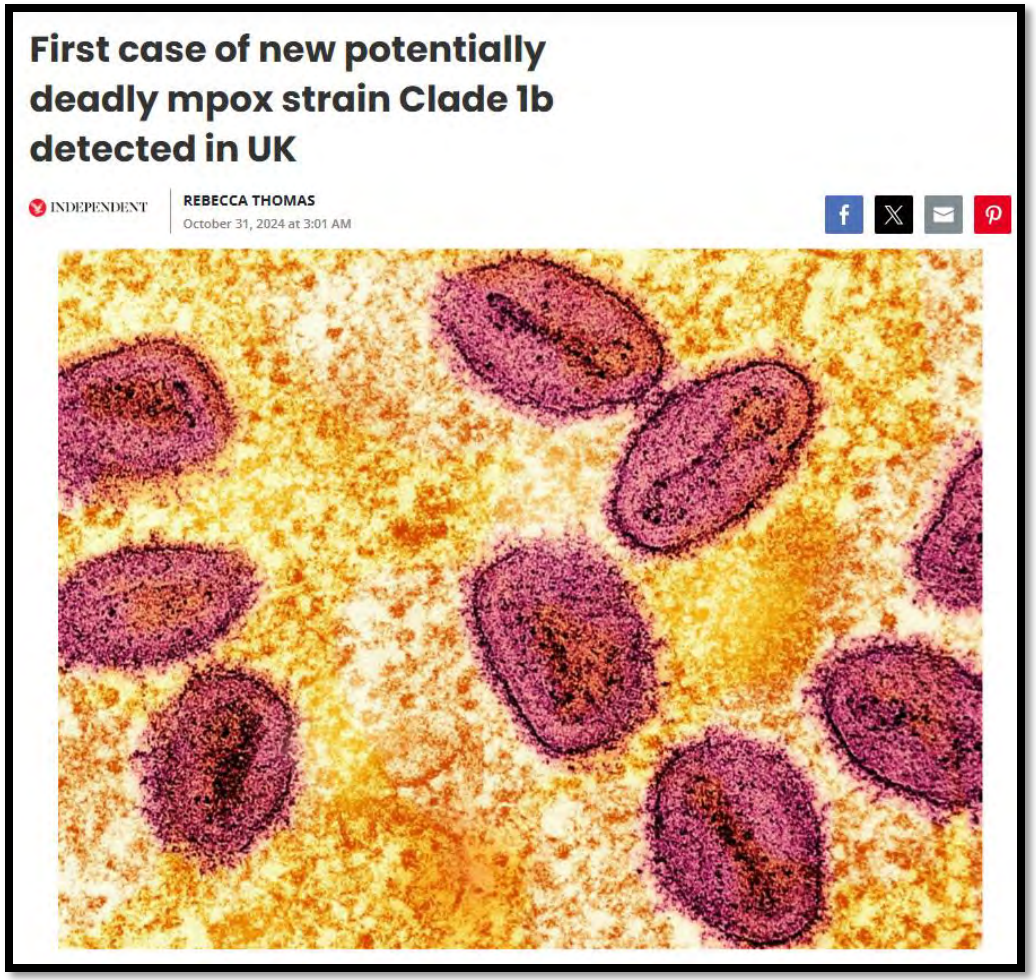
This is an official CDC HEALTH ADVISORY

Distributed via the CDC Health Alert Network
December 7, 2023, 10:45 AM ET
CDCHAN-00501

- Health Alert Network (HAN) - 00501 | Mpox Caused by Human-to-Human Transmission of Monkeypox Virus with Geographic Spread in the Democratic Republic of the Congo (cdc.gov)
- Data up to date as of Nov 3, 2024 available at https://worldhealthorg.shinyapps.io/

A Second PHEIC

Clade I Panic



First case of new potentially deadly mpox strain Clade 1b detected in UK

INDEPENDENT | REBECCA THOMAS
October 31, 2024 at 3:01 AM

Warnings over lethal and contagious strain of mpox as children in DRC die

Alarm over high mortality and miscarriage rates as mutated virus spreads in eastern Democratic Republic of the Congo

A child with mpox in the Democratic Republic of the Congo in 2022. Unlike that outbreak, the new strain is far more virulent and no vaccines are so far available in the DRC. Photograph: Reuters

A dangerous strain of mpox that is killing children and causing miscarriages

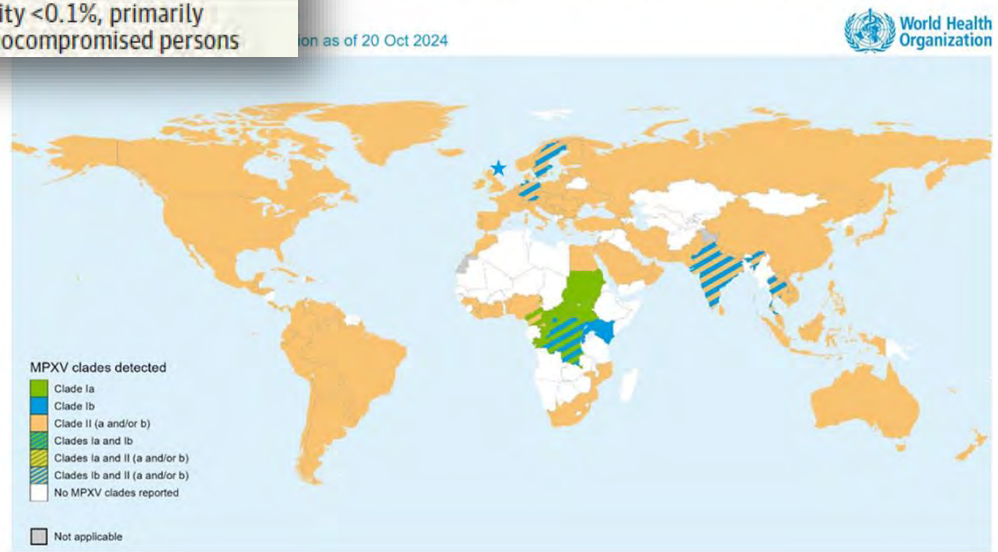
- https://www.theguardian.com/global-development/article/2024/jun/26/democratic-republic-congo-drc-virulent-strain-mpox-monkeypox-virus-killing-children-miscarriages
- https://www.aol.com/first-case-potentially-deadly-mpox-153951005.html

Four Clades with Ongoing Transmission

Table 1. Major Epidemiologic and Burden of Disease Facts

Mpox features	Clade I	Emerging clade Ib	Clade IIa	Clade IIb
Primary geographical distribution	Central Africa	Democratic Republic of Congo	West Africa	Global outbreak involving at least 118 countries
Spread	Introduction into the human population typically through zoonotic transmission event. Mainly children and close household contacts of infected persons	The spread was described in heterosexual networks and case clusters in the Democratic Republic of Congo, with 30% of the population being adult females Accumulation of APOBEC3 variations, which signify recent sustained human to human transmission	Households with families and children are frequently affected	Primarily close physical contact between gay, bisexual, and other men who have sex with men
Severity of disease	Mortality, 5%-10% (outbreaks prior to 2022)	Mortality, 1.7%-3.6%	Mortality, 1%	Mortality <0.1%, primarily immunocompromised persons

MPXV clades reported to WHO, by country, as of 20 October 2024.



- Titanji BK, et al, JAMA. Published online October 14, 2024. doi:10.1001/jama.2024.21091
- https://www.who.int/publications/m/item/multi-country-outbreak-of-mpox--external-situation-report--41--26-october-2024

How Can I Treat Mpox?

- Supportive care
  - Most patients fully recover
  - Symptomatic treatment
- Antibody therapy
  - Vaccinia Immunoglobulin (VIGIV)
- Antiviral medications
  - Tecovirimat
  - Cidofovir
  - Brincidofovir
  - Trifluridine (eye disease)

Supportive Care

- **Supportive care**
  - Most patients fully recover
  - **Symptomatic treatment**
- Antibody therapy
  - VIGIV
- Antiviral medications
  - Tecovirimat
  - Cidofovir
  - Brincidofovir
  - Trifluridine (eye disease)

Table 2. Supportive Care Recommendations for Mpox

	Skin (including genital) lesions	Proctitis	Pharyngitis
Supportive care recommendations	Lidocaine gel Nonsteroidal anti-inflammatory medications Opioids (if indicated) Keep lesions clean and dry If infected: Debridement with wet-to-dry dressings Antibiotics	Lidocaine gel Nonsteroidal anti-inflammatory medications Opioids (if indicated) Stool softeners Sitz baths Gabapentin	Viscous lidocaine Nonsteroidal anti-inflammatory medications Opioids (if indicated) Saltwater gargles Oral antiseptics

- https://www.cdc.gov/poxvirus/mpox/clinicians/pain-management.html
- Titanji Bket al, JAMA. Published online October 14, 2024. doi:10.1001/jama.2024.21091

Medical Countermeasures (MCM) Against Mpox

- Supportive care
  - Most patients fully recover
  - Symptomatic treatment
- **Antibody therapy**
  - Vaccinia Immunoglobulin (VIGIV)
- **Antiviral medications**
  - Tecovirimat
  - Cidofovir
  - Brincidofovir
  - Trifluridine (eye disease)

Medical Countermeasures (MCM)

- Severe disease
- At risk of severe disease
  - Immunocompromised
  - Serious underlying skin conditions
  - Pregnant persons
  - Pediatric persons (Age <8 or <1)
- Participation in clinical trials


Interim Clinical Treatment Considerations for Severe Manifestations of Mpox — United States, February 2023

Agam K. Rao, MD[1]; Caroline A. Schrodt, MD[1]; Faisal S. Minhaj, PharmD[1,2]; Michelle A. Waltenburg, DVM[3]; Shama Cash-Goldwasser, MD[2]; Yon Yu, PharmD[4]; Brett W. Petersen, MD[1]; Christina Hutson, PhD[1]; Inger K. Damon, MD, PhD[3]

Rao et al, MMWR, PMID:36862595

Medical Countermeasures (MCM) Against Mpox

- Supportive care
  - Most patients fully recover
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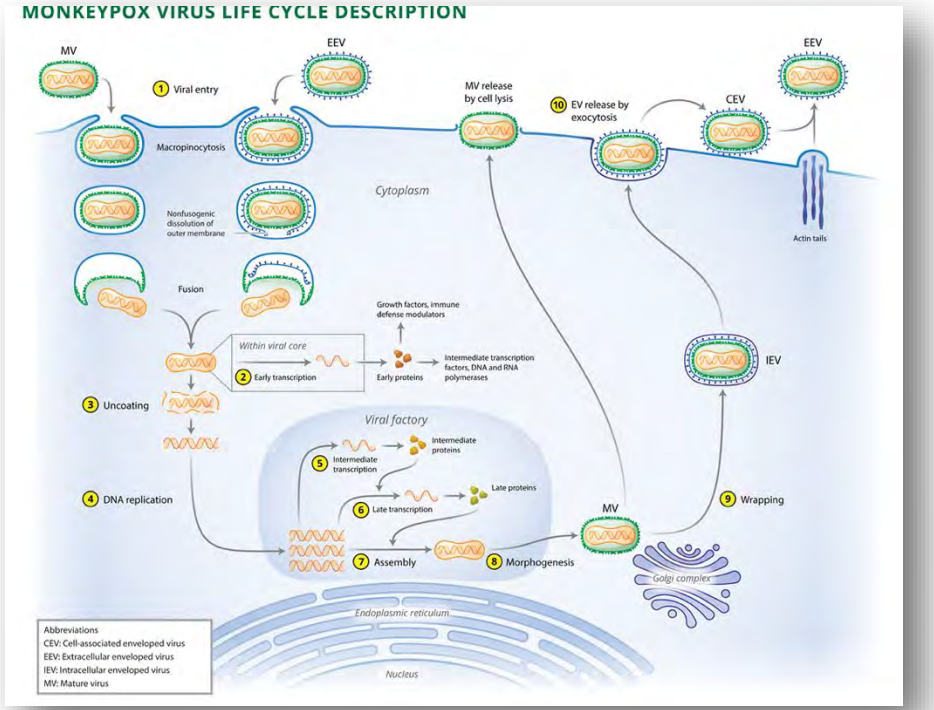
- **Antibody therapy**
  - Vaccinia Immunoglobulin (VIGIV)
- **Antiviral medications**
  - Tecovirimat
  - Cidofovir
  - Brincidofovir
  - Trifluridine (eye disease)

Given Similarities In the Viral Lifecycle No <u>Expected</u> Treatment Difference Clade I vs II



Tecovirimat Use In the United States – 5/29/2022 – 7/10/202

- **Supportive care**
  - Most patients fully recover
  - Symptomatic treatment
- Antibody therapy
  - VIGIV
- Antiviral medications
  - **Tecovirimat**
  - Cidofovir
  - Brincidofovir
  - Trifluridine (eye disease)

- 7,181 patients treated
  - 1,626 outcome forms (22.6%)
- Most common reasons for treatment
  - Sensitive anatomical areas (83.5%)
  - Pain (52.5%)
- 223 severe adverse events (132 patients) (1.8%)
  - 40 deaths
  - 12 headache
  - 10 nausea
  - 10 vomiting
  - 8 elevated liver function tests
  - 8 urticaria

Does Tecovirimat Work? – PALM007

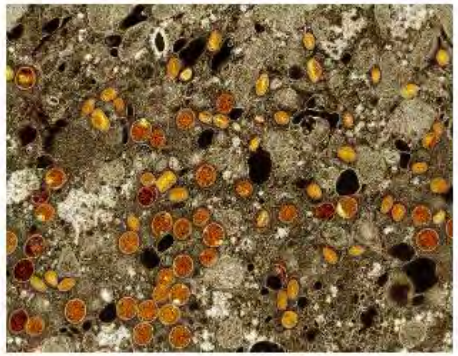
NEWS RELEASES

Thursday, August 15, 2024

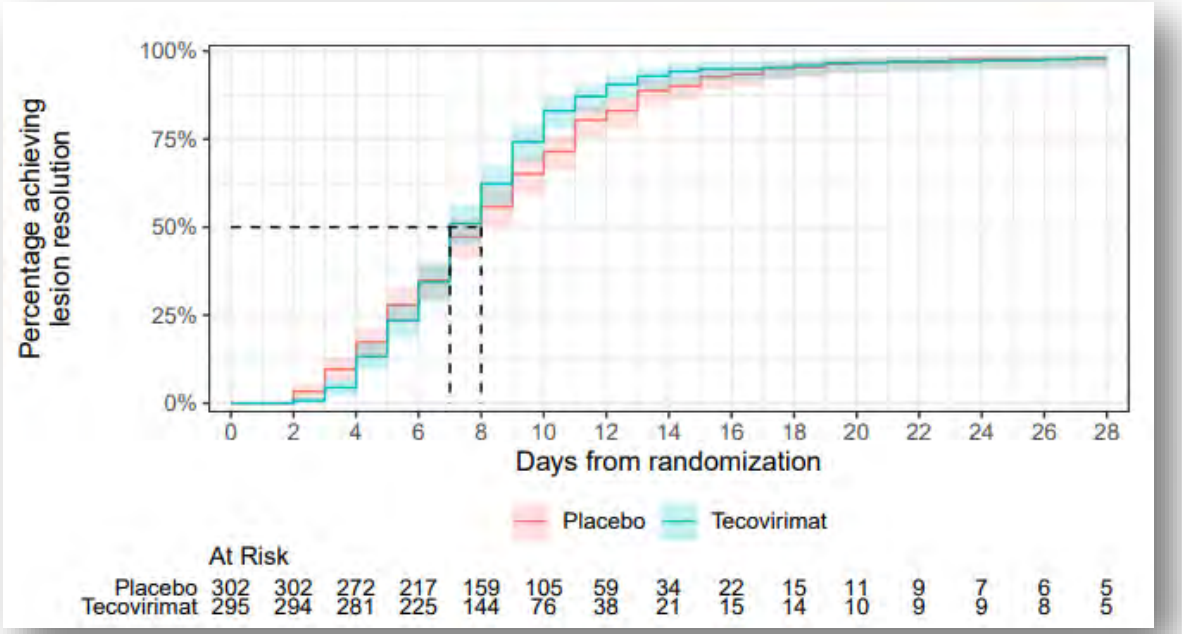
The antiviral tecovirimat is safe but did not improve clade I mpox resolution in Democratic Republic of the Congo

NIH-cosponsored study examined tecovirimat in mpox-endemic country.

The antiviral drug tecovirimat did not reduce the duration of mpox lesions among children and adults with clade I mpox in the Democratic Republic of the Congo (DRC), based on an initial analysis of data from a randomized, placebo-controlled trial. However, the study's 1.7% overall mortality among enrollees, regardless of whether they received the drug or not, was much lower than the mpox mortality of 3.6% or higher reported among all cases in the DRC. This shows that better outcomes among people with mpox can be achieved when they are hospitalized and provided high-quality supportive care. The trial is sponsored by the National Institutes of Health's (NIH) National Institute of Allergy and Infectious Diseases (NIAID) and co-led through a government-to-government



Colorized transmission electron micrograph of mpox virus particles (red/yellow) found within infected

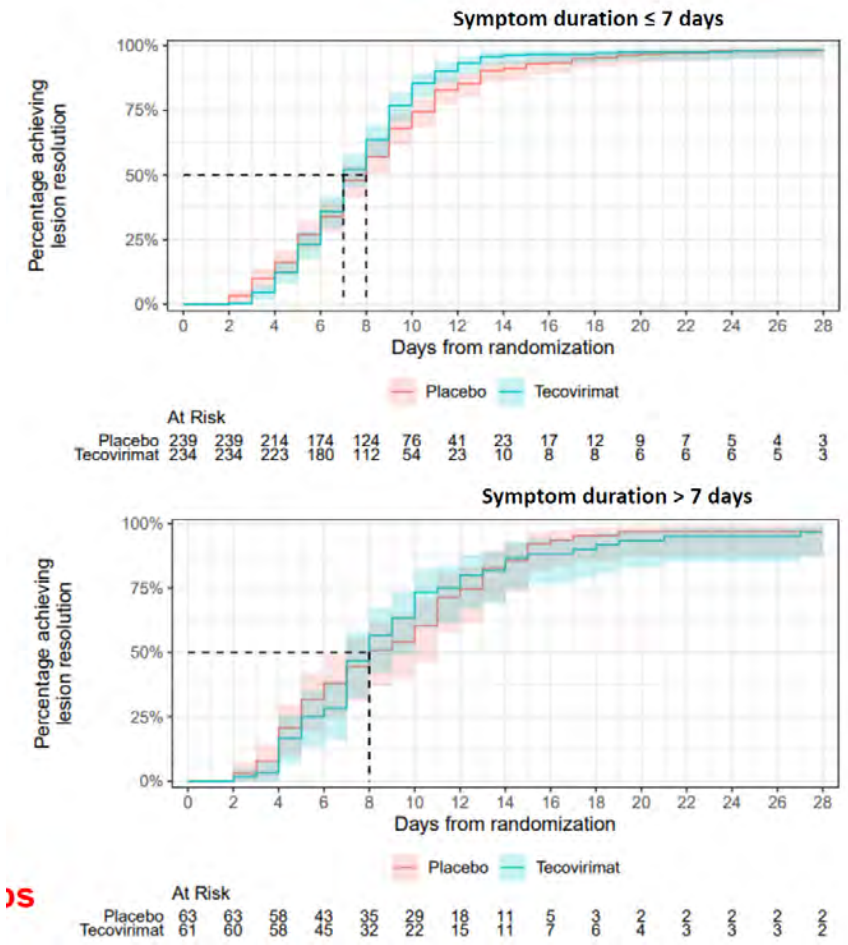


- **"No statistically significant difference in time to lesion resolution…"**

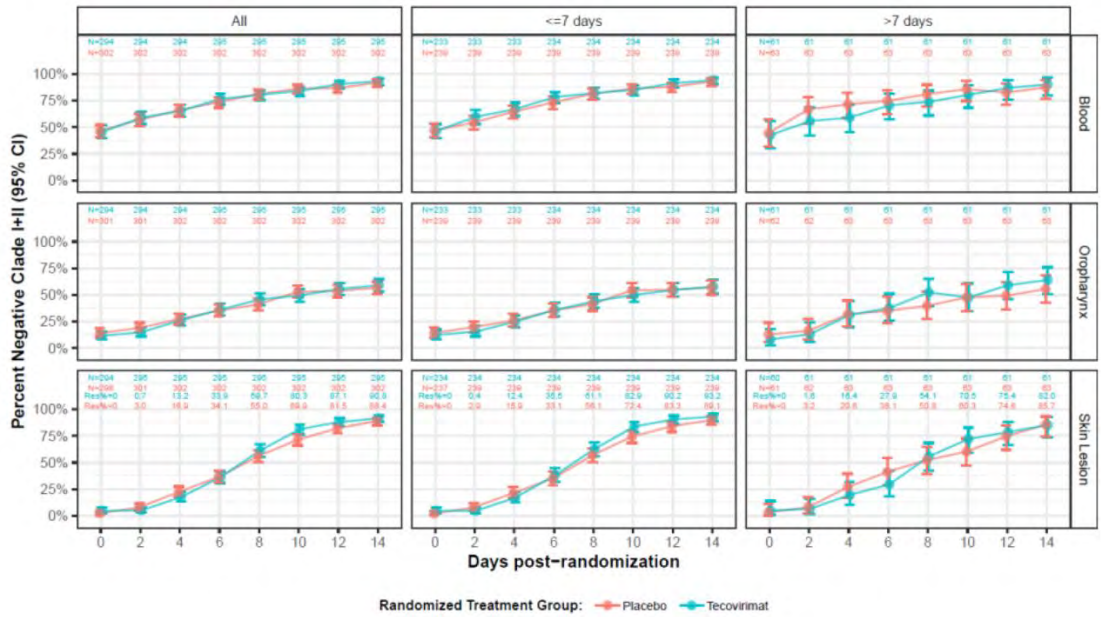
- Slides Presented by Dr. Tshianai at IDWeek 2024

Tecovirimat Did Not Work in PALM007

< or > 7 Days from Symptom Onset



Virologic Outcomes at Day 14



Tecovirimat Did Not Work in STOMP

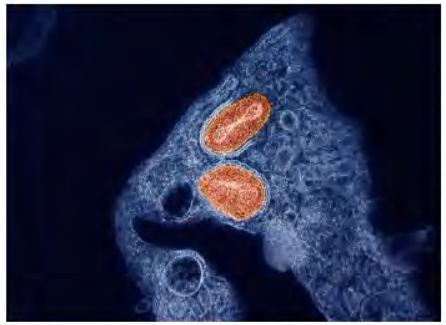
NEWS RELEASES

Tuesday, December 10, 2024

NIH Study Finds Tecovirimat Was Safe but Did Not Improve Mpox Resolution or Pain

Study Examined Tecovirimat in Countries Affected by Global Clade II Mpox Outbreak.

The antiviral drug tecovirimat did not reduce the time to lesion resolution or have an effect on pain among adults with mild to moderate clade II mpox and a low risk of developing severe disease, according to an interim data analysis from the international clinical trial called the Study of Tecovirimat for Mpox (STOMP). There were no safety concerns associated with tecovirimat.



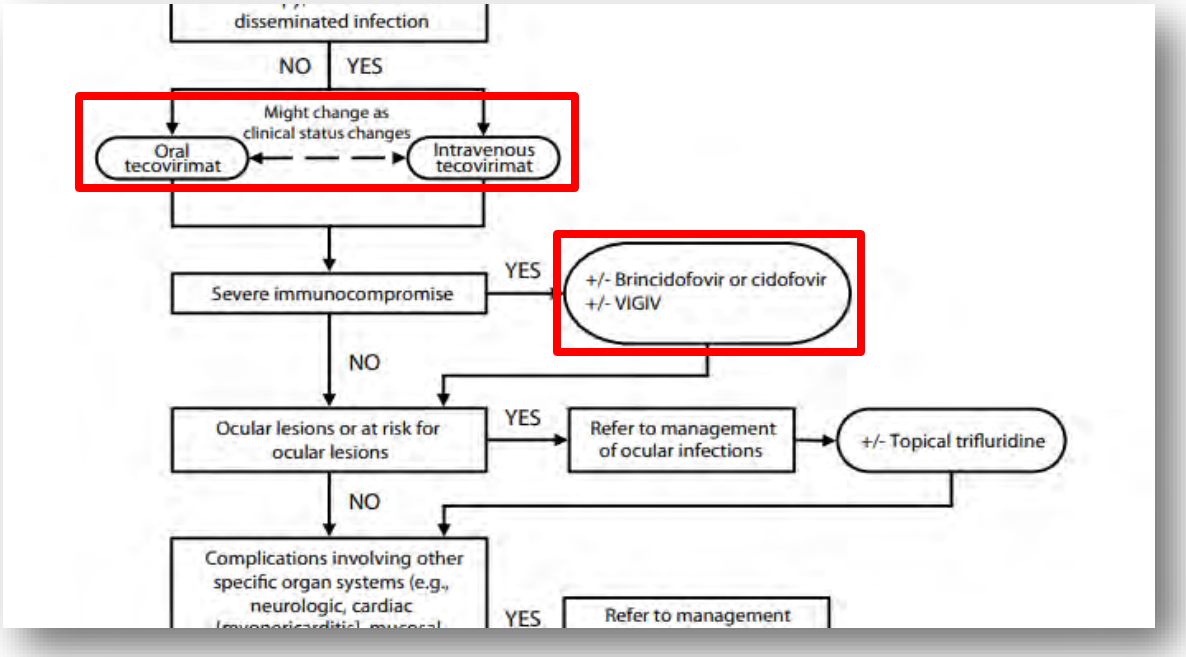
Colorized transmission electron micrograph of two particles of the virus that causes mpox, cultivated and purified from cell culture. *NIAID*

Considering these definitive findings, the study's Data Safety and Monitoring Board (DSMB) recommended stopping further enrollment of participants who were being randomized to tecovirimat or placebo. As the study sponsor, the National Institutes of Health's (NIH) National Institute of Allergy and Infectious Diseases (NIAID) accepted the DSMB's recommendation. Given the lack of an efficacy signal, NIAID also closed enrollment into an open-label study arm for participants with or at elevated risk of severe disease that was not designed to estimate the drug's efficacy.

"The initial STOMP findings provide valuable insight to inform clade II mpox medical countermeasures and underscore the critical importance of conducting well-designed randomized clinical trials during infectious disease outbreaks," said NIAID Director Jeanne Marrazzo, M.D., M.P.H. "Before 2022, no treatment candidate had been studied in people with mpox, and this trial is a critical step in our systematic evaluation of existing antivirals like tecovirimat while pursuing novel antivirals and antibody-based mpox therapeutics."

What else can do we do?

- Supportive care
  - Most patients fully recover
  - Symptomatic treatment
- Antibody therapy
  - **Vaccinia Immunoglobulin (VIGIV)**
- Antiviral medications
  - Tecovirimat
  - **Cidofovir**
  - **Brincidofovir**
  - Trifluridine (eye disease)



What else can do we do?

- Supportive care
  - Most patients fully recover
  - Symptomatic treatment
- Antibody therapy
  - Vaccinia Immunoglobulin (VIGIV)
  - **Monoclonal Antibodies**
- Antiviral medications
  - Tecovirimat
  - Cidofovir
  - Brincidofovir
  - Trifluridine (eye disease)

Identification of mpox M1R and B6R monoclonal and bispecific antibodies that efficiently neutralize authentic mpox virus

Zuning Ren[a,b,†], Mengjun Li[b,†], Jiayin Chen[b,†], Xiaohua Gong[c,†], Shuo Song[c,†], Delin Li[d,†], Minghui Yang[e,†], Jianhai Yu[b], Sadia Asghar[f], Yanxin Cui[c], Shiyu Niu[c], Zhonghui Liao[c], Yushan Jiang[b], Jiahui Liu[b], Yuqing Li[b], Bao Zhang[b], Wei Zhao[b], Jie Peng[a], Yang Yang[c], and Chenguang Shen[b,g]

Vaccination to Prevent Mpox?

Post-Exposure Prophylaxis

- Should be given ASAP after exposure:
  - Within 4 days to prevent disease
  - 4 to 14 days to reduce symptoms

Pre-Exposure Prophylaxis

- Clinical and research lab workers
- Public health response team members
- Epidemiological Risk Groups

Table 4. Observational Vaccine Efficacy Studies

Source	Vaccine	% (95% CI)[a] 1-Dose efficacy	2-Dose efficacy	Evaluation period
Fine et al,[86] 1988	Dryvax	85		1980 to 1984
Rimoin et al,[87] 2010	Dryvax	80.7 (68.2 to 88.4)		Nov 2005 to Nov 2007
Titanji et al,[88] 2023	Dryvax	72 (32 to 87)		Jul 1, 2022, to Oct 31, 2022
	ACAM2000	75 (68 to 85)		
Back et al,[89] 2024	MVA-BN	70 (44 to 84)	89 (12 to 99)	Aug 1, 2022, to Sep 30, 2022
Bertran et al,[90] 2023	MVA-BN	78 (54 to 89)		Jul 4, 2022, to Oct 9, 2022
Brousseau et al,[91] 2024	MVA-BN	35 (−2 to 59) 65 (1 to 87)[b]		Jun 19, 2022, to Jun 2, 2022
Charles et al,[92] 2024	MVA-BN		80	Jan 1, 2023, to Dec 31, 2023
Dalton et al,[93] 2023	MVA-BN	75 (61.2 to 84.2)	86 (73.8 to 92.4)	Aug 19, 2022, to Mar 31, 2023
Deputy et al,[94] 2023	MVA-BN	35.8 (22.1 to 47.1)	66 (47.4 to 78.1)	Aug 15, 2022, to Nov 19, 2022
Fontán-Vela et al[95] 2024	MVA-BN	79 (33.3 to 100)		Jul 12, 2022, to Dec 12, 2022
Navarro et al,[96] 2024	MVA-BN	58 (31 to 75)		Jun 2022 to Nov 2022
Ramchandani et al,[97] 2023	MVA-BN	81 (64 to 90)	83 (28 to 96)	Jan 1, 2020, to Dec 31, 2022
Rosenberg et al,[98] 2023	MVA-BN	68.1 (24.9 to 86.5)	75.7 (48.5 to 88.5)	Jul 24, 2022, to Oct 31, 2022
Wolff Sagy et al,[99] 2023	MVA-BN	86 (59 to 95)		Jul 31, 2022, to Dec 25, 2022
Yeganeh et al,[100] 2024	MVA-BN	69 (59 to 77)	85 (80 to 87)	May 19, 2022, to Jan 1, 2023

Abbreviation: MVA-BN, Modified Vaccinia Ankara Vaccine-Bavarian Nordic.

[a] All results are adjusted results for disease acquisition at ≥14 days after vaccination unless otherwise specified.

[b] Includes adjustment for self-reported risk.

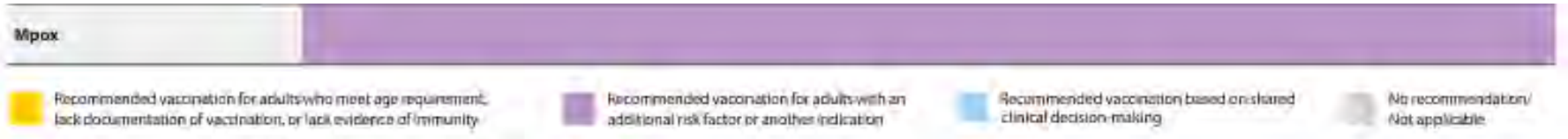
https://www.cdc.gov/vaccines/acip/recommendations.html

Titanji BK, et al, JAMA. Published online October 14, 2024. doi:10.1001/jama.2024.21091

ACIP Recommendations

ACIP recommends vaccination with the 2-dose MVA vaccine series for persons aged 18 years and older at risk for mpox as defined by:

- Gay, bisexual, and other men who have sex with men, transgender or nonbinary people who in the past 6 months have had one of the following:
  - A new diagnosis of ≥1 sexually transmitted disease
  - More than one sex partner
  - Sex at a commercial sex venue
  - Sex in association with a large public event in a geographic area where mpox transmission is occurring
- Sexual partners of persons with the risks described above
- Persons who anticipate experiencing any of the above



Summary

- The 2022 mpox outbreak was different and changed a lot about **what we had previously known** about the epidemiology, transmission, and presentation of mpox
- **Epidemiology**
  - The clade IIb mpox outbreak spread rapidly, can be serious, and **cases are still occurring**
  - The clade I PHEIC is ongoing
- **Treatment**
  - Most patients will get better with supportive care
  - Tecovirimat was not effective in its first and second RCTs
  - Consider combination therapy for those at risk of severe disease
- **Vaccination**
  - MVA is effective for preventing or attenuating disease

Emerging Dermatophytes

- **Common Ringworm (Tinea/Dermatophytosis)**
  - Traditionally mild and treatable with standard antifungals
  - Increasing global reports of severe (inflammatory), hard-to-treat cases
  - Emergence of antifungal-resistant strains complicating treatment

- **Three strains being reported in the US**
  - *Trichophyton indotineae*
  - ***Trichophyton mentagrophytes* genotype type VII**
  - Terbinafine-resistant *Trichophyton rubrum*
  -

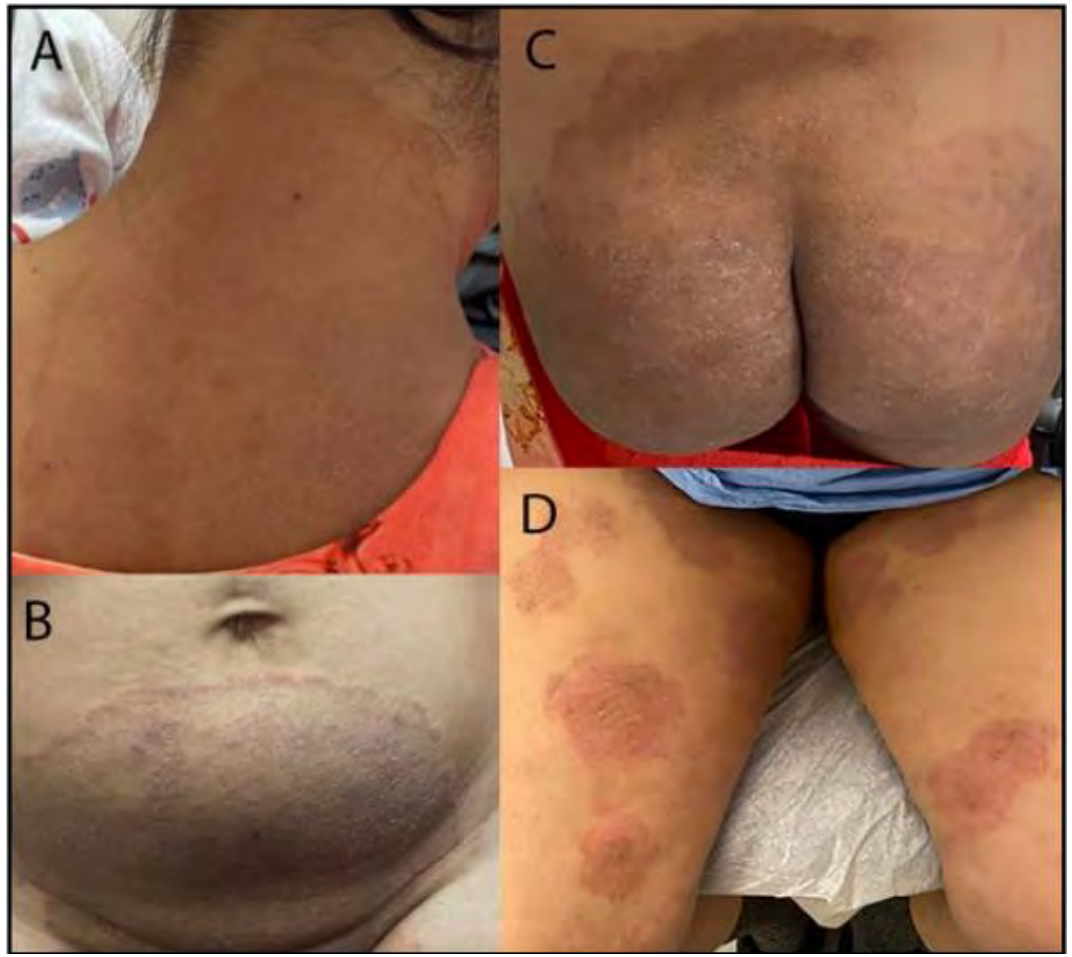
Trichophyton indotineae

Notes from the Field

First Reported U.S. Cases of Tinea Caused by *Trichophyton indotineae* — New York City, December 2021–March 2023

Avrom S. Caplan, MD[1]; Sudha Chaturvedi, PhD[2]; YanChun Zhu, MS[2]; Gabrielle C. Todd, PhD[2]; Lu Yin, MD[1]; Adriana Lopez, MD[1]; Lisa Travis, MD[1]; Dallas J. Smith, PharmD[3,4]; Tom Chiller, MD[3]; Shawn R. Lockhart, PhD[3]; Karen A. Alroy, DVM[5]; William G. Greendyke, MD[5]; Jeremy A. W. Gold, MD[3]

Tinea is a common, highly contagious, superficial infection of the skin, hair, or nails caused by dermatophyte molds.* During the past decade, an epidemic of severe, antifungal-resistant tinea has emerged in South Asia because of the rapid spread of *Trichophyton indotineae*,† a novel dermatophyte species; the epidemic has likely been driven by misuse and overuse of topical antifungals and corticosteroids§ (*1*,*2*). *T. indotineae* infections are highly transmissible and characterized by widespread, inflamed, pruritic plaques on the body (tinea corporis), the crural fold, pubic region, and adjacent thigh (tinea cruris), or the face (tinea faciei) (*1*). *T. indotineae* isolates are frequently resistant to terbinafine, a mainstay of tinea treatment (*1*,*3*). *T. indotineae* infections have been reported throughout Asia



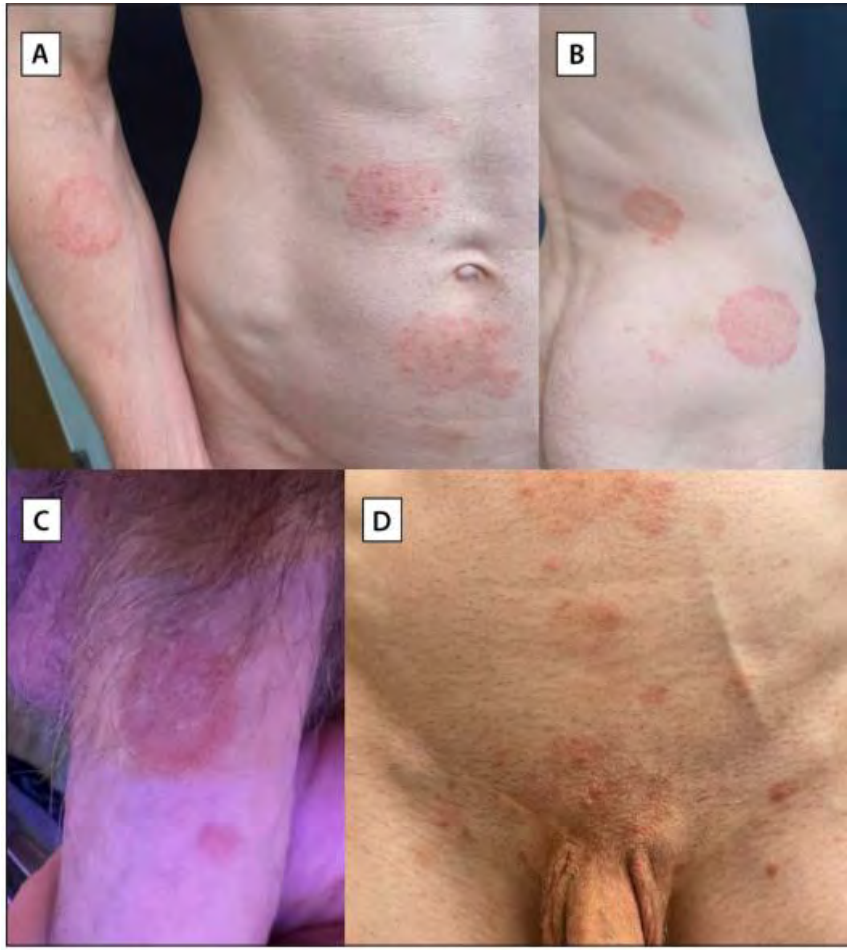
Trichophyton mentagrophytes genotype VII (TMVII)

Notes from the Field

Trichophyton mentagrophytes Genotype VII — New York City, April–July 2024

Jason Zucker, MD[1,*]; Avrom S. Caplan, MD[2,*]; Shauna H. Gunaratne, MD[1]; Stephanie M. Gallitano, MD[3]; John G. Zampella, MD[2]; Caitlin Otto, PhD[4]; Rachel Sally, MD[2]; Sudha Chaturvedi, PhD[5,6]; Brittany O'Brien, MS[5]; Gabrielle C. Todd, PhD[5]; Priyanka Anand, MD[7,8]; Laura A.S. Quilter, MD[7]; Dallas J. Smith, PharmD[9]; Tom Chiller, MD[9]; Shawn R. Lockhart, PhD[9]; Meghan Lyman, MD[9]; Preeti Pathela, DrPH[10]; Jeremy A.W. Gold, MD[9]

Trichophyton mentagrophytes genotype VII (TMVII) is an emerging dermatophyte fungus, causing tinea that can be spread through sexual contact (*1*). TMVII can cause pruritic, annular, scaly lesions on the trunk, groin, genitals, or face; might be mistaken for eczema, psoriasis, or other dermatologic conditions; and frequently requires oral antifungal therapy.[†] Some patients experience inflamed, painful, and persistent lesions that can lead to scarring or secondary bacterial infection. TMVII infections have been reported among men who have sex with men in France since March 2021 and previously in men who traveled to Southeast Asia for sex tourism (*1*,*2*). In June 2024, a TMVII case in the United States was reported in a man who developed genital lesions after traveling to several countries in Europe and to California and who had sexual contact with multiple men while traveling (*3*). Clinicians subsequently alerted public health officials of additional patients in the United States who had laboratory-confirmed TMVII infection.



Trichophyton mentagrophytes genotype VII (TMVII)

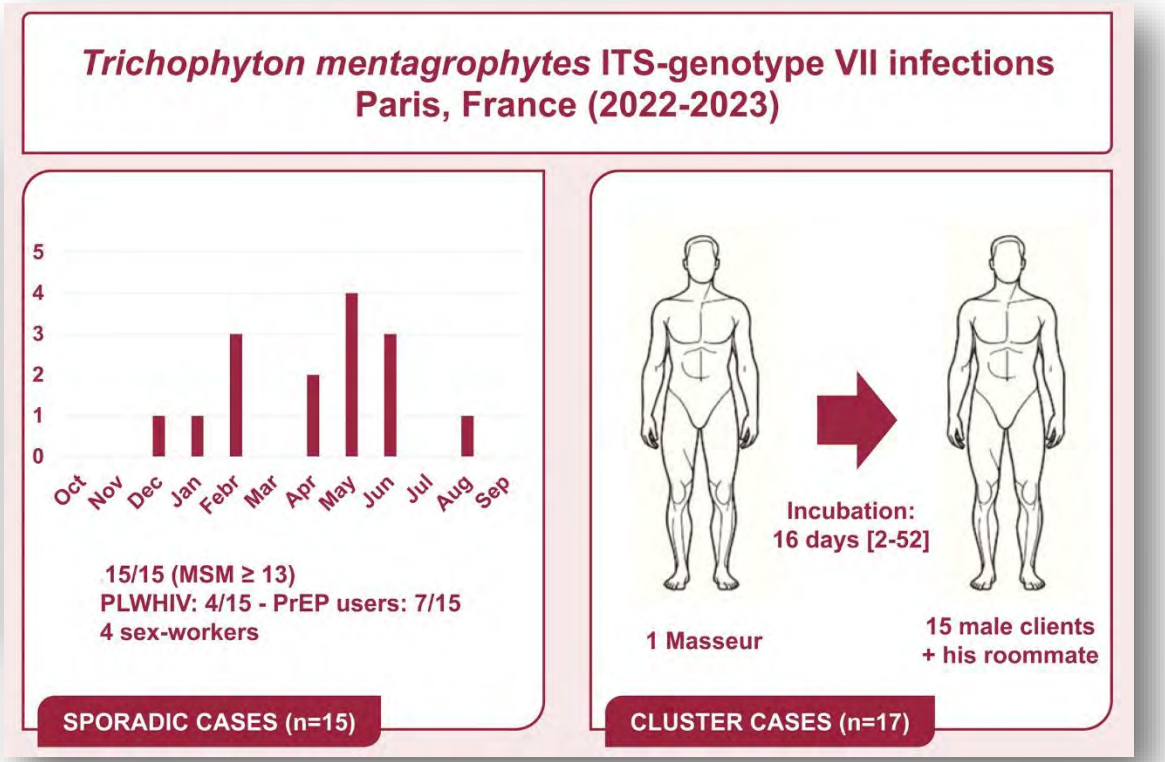
JEADV
JOURNAL OF THE EUROPEAN ACADEMY OF DERMATOLOGY & VENEREOLOGY

ORIGINAL ARTICLE | Open Access

Trichophyton mentagrophytes ITS genotype VII infections among men who have sex with men in France: An ongoing phenomenon

A. Jabet, V. Bérot, T. Chiarabini, S. Dellière, P. P. Bosshard, M. Siguier, R. Tubiana, M. Favier, A. Canestri, S. Makhloufi, A. Nouchi, T. de Risi-Pugliese, F. Boquel, G. Crémer, R. Khoury, O. Sidali ... See all authors

First published: 26 November 2024 | https://doi.org/10.1111/jdv.20439



Trichophyton mentagrophytes genotype VII (TMVII)

Sexually Transmitted *Trichophyton mentagrophytes* Genotype VII Infection among Men Who Have Sex with Men

Arnaud Jabet, Sarah Dellière, Sophie Seang, Aziza Chermak, Luminita Schneider, Thibault Chiarabini, Alexandre Teboul, Geoffroy Hickman, Alizée Bozonnat, Cécile Brin, Marion Favier, Yanis Tamzali, François Chasset, Stéphane Barete, Samia Hamane, Mazzouz Benderdouche, Alicia Moreno-Sabater, Eric Dannaoui, Christophe Hennequin, Arnaud Fekkar, Renaud Piarroux, Anne-Cécile Normand, and Gentiane Monsel

Author affiliations: Assistance Publique-Hôpitaux de Paris, Paris, France (A. Jabet, S. Dellière, S. Seang, A. Chermak, L. Schneider, T. Chiarabini, A. Teboul, G. Hickman, A. Bozonnat, C. Brin, M. Favier, Y. Tamzali, F. Chasset, S. Barete, S. Hamane, M. Benderdouche, A. Moreno-Sabater, E. Dannaoui, C. Hennequin, A. Fekkar, R. Piarroux, A.-C. Normand, G. Monsel); Université de Paris, Paris, France (S. Dellière, E. Dannaoui); Sorbonne Université, Paris, France (F. Chasset, A. Moreno-Sabater, C, Hennequin, A. Fekkar, R. Piarroux)

Main Article

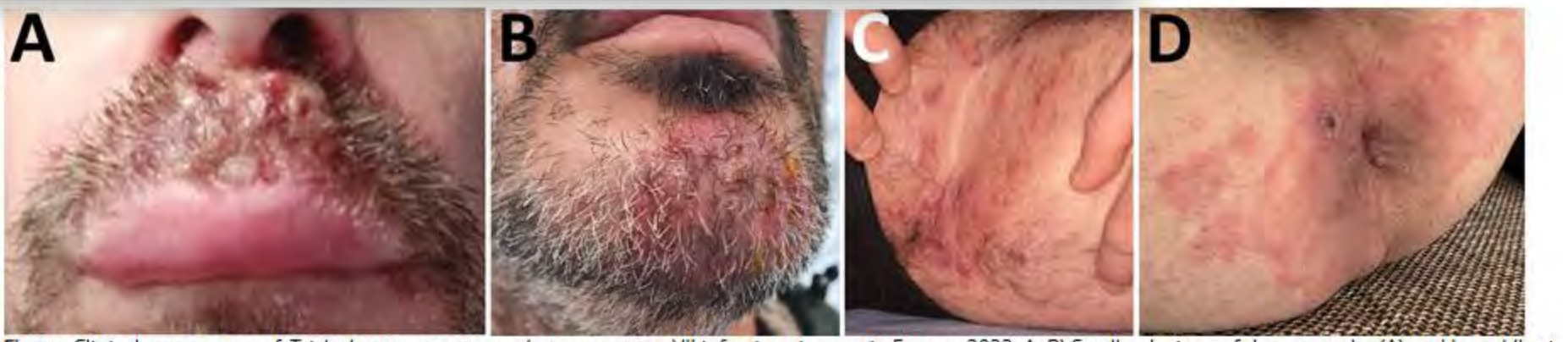


Figure. Clinical appearance of *Trichohpyton mentagrophytes* genotype VII infections in men in France, 2022. A, B) Swollen lesions of the mustache (A) and beard (keric with associated papules and pustules with central umbilication and a large lesion with a central necrotic crust, surrounded by extensive erythemato-squamous circina

- https://wwwnc.cdc.gov/eid/article/29/7/23-0025-f1

Trichophyton mentagrophytes genotype VII (TMVII)

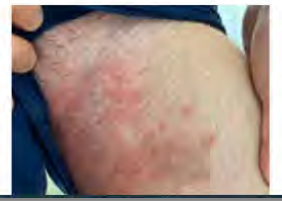
- https://www.cdc.gov/mmwr/volumes/73/wr/mm7343a5.htm

AAD Resources

TRICHOPHYTON INDOTINEAE INFECTIONS AND OTHER SEVERE OR ANTIFUNGAL-RESISTANT DERMATOPHYTOSES

Dermatophytosis (ringworm, tinea, jock itch, athlete's foot) is a very common and typically minor infection of the skin caused by dermatophyte fungi.[1] In the past decade, severe or antifungal-resistant dermatophytoses have become a global public health concern, including in the United States.

The AAD has assembled resources on *Trichophyton indotineae* and other severe or antimicrobial-resistant dermatophytes. These resources include information sheets on disease recognition, diagnosis, and treatment options, but do not constitute a clinical guideline. The AAD/ILDS emerging diseases registry helps to gather information on severe or antimicrobial-resistant dermatophytosis cases.[2] This content was developed by the Academy's Emerging Diseases Task Force and Avrom S. Caplan, MD, FAAD.



Clinically compatible with dermatophytosis*

+

- Widespread skin lesions, +/- severe pruritus, +/- topical steroid use,

OR

- International travel or migration (especially from endemic regions (e.g., South Asia)),

OR

- Contact with known or suspected case,

OR

- At least 2 weeks of oral terbinafine without improvement in confirmed dermatophytosis

Step 1: Confirm dermatophyte infection if not already done

- KOH preparation.
- Fungal culture from skin scraping or nail clipping for species identification. Consider genetic sequencing and antifungal susceptibility testing using culture specimen. [link].

Do not delay treatment while awaiting culture, sequencing, or susceptibility testing results.

Step 2: See review of treatment options and initiate antifungal therapy

(itraconazole is generally 1st line). [link]

Step 3: Treat to clear infection

- Ensure appropriate response, adherence to therapy, and monitor for recurrence.
- Avoid topical corticosteroids.
- For patients failing therapy**, consider consultation with specialists in fungal disease.

- https://www.aad.org/member/clinical-quality/clinical-care/emerging-diseases/dermatophytes

Summary

- Add TMVII to your **differential** when seeing sexual health patients with ringworm like rash
- Consider **dermatophyte cultures** when treating a ringworm like rash in the sexual health setting
- Consider **oral terbinafine** as first line treatment in compatible cases
  - Counsel patients that treatment may take **weeks to months**
- **Counsel** patients on ways to avoid transmission including from personal items and clothing

Gonorrhea Resistance

Rising Gonorrhea Resistance

First case of super-resistant gonorrhea reported

The Commonwealth of Massachusetts
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Department of Public Health
Bureau of Infectious Disease and Laboratory Sciences
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CLINICAL ALERT
January 19, 2023

MULTI-DRUG NON-SUSCEPTIBLE GONORRHEA IN MASSACHUSETTS

- A novel strain of multidrug-non-susceptible *Neisseria gonorrhoeae* with reduced susceptibility to ceftriaxone, cefixime, and azithromycin, and resistance to ciprofloxacin, penicillin, and tetracycline, has been identified in a Massachusetts resident. Although ceftriaxone 500 mg IM was effective at clearing infection for this case, this is the first isolate identified in the United States to demonstrate resistance or reduced susceptibility to all drugs that are recommended for treatment.
- Enhanced surveillance has identified a second isolate that, based on its genome, likely has similarly reduced susceptibility to ceftriaxone and cefixime.

V STUDY RAISING ALARMS ABOUT "SUPERBUGS"

Video Ad Feedback

How bugs become superbugs

00:58 · Source: CNN

Limited Antibiotics in the Pipeline

The Journal of Antibiotics (2023) 76:431–473
https://doi.org/10.1038/s41429-023-00629-8

Japan Antibiotics Research Association

The Society for Actinomycetes Japan

REVIEW ARTICLE

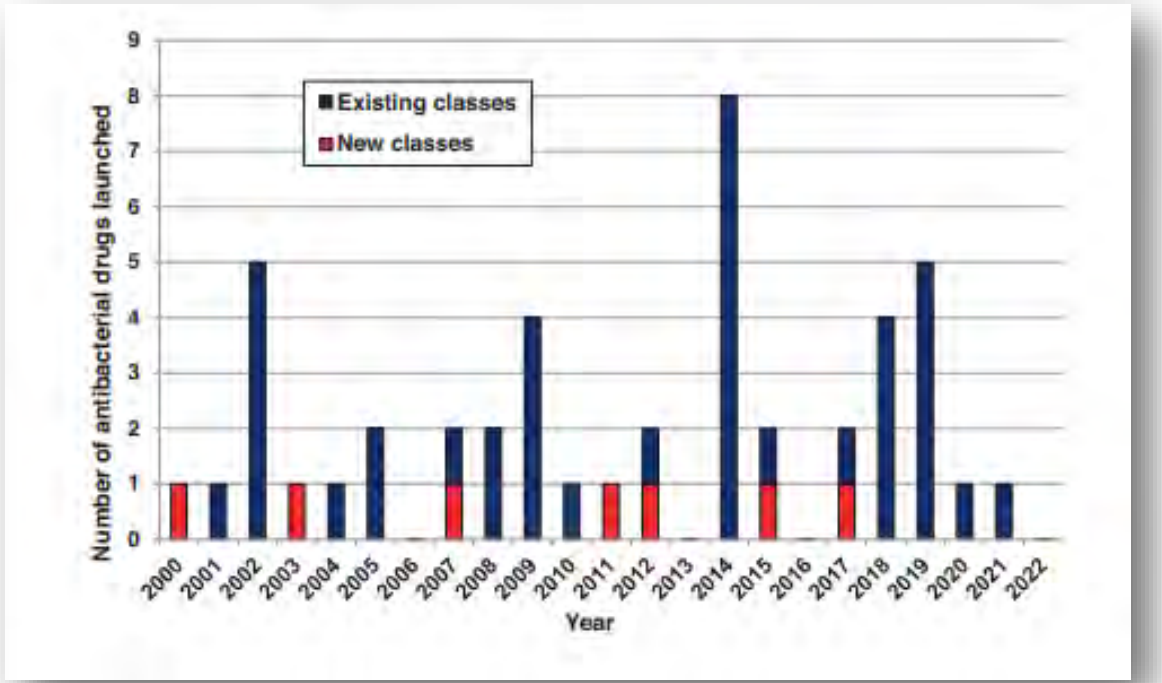
Antibiotics in the clinical pipeline as of December 2022

Mark S. Butler[1] · Ian R. Henderson[1] · Robert J. Capon[1] · Mark A. T. Blaskovich[1]

Received: 2 March 2023 / Revised: 20 April 2023 / Accepted: 25 April 2023 / Published online: 8 June 2023

Abstract

The need for new antibacterial drugs to treat the increasing global prevalence of drug-resistant bacterial infections has clearly attracted global attention, with a range of existing and upcoming funding, policy, and legislative initiatives designed to revive antibacterial R&D. It is essential to assess whether these programs are having any real-world impact and this review continues our systematic analyses that began in 2011. Direct-acting antibacterials (47), non-traditional small molecule antibacterials (5), and β-lactam/β-lactamase inhibitor combinations (10) under clinical development as of December 2022 are described, as are the three antibacterial drugs launched since 2020. Encouragingly, the increased number of early-stage clinical candidates observed in the 2019 review increased in 2022, although the number of first-time drug approvals from 2020 to 2022 was disappointingly low. It will be critical to monitor how many Phase-I and -II candidates move into Phase-III and beyond in the next few years. There was also an enhanced presence of novel antibacterial pharmacophores in early-stage trials, and at least 18 of the 26 phase-I candidates were targeted to treat Gram-negative bacteria infections. Despite the promising early-stage antibacterial pipeline, it is essential to maintain funding for antibacterial R&D and to ensure that plans to address late-stage pipeline issues succeed.



1. Butler MS, Henderson IR, Capon RJ, Blaskovich MAT. Antibiotics in the clinical pipeline as of December 2022. J Antibiot (Tokyo). 2023;76(8):431-473. doi:10.1038/s41429-023-00629-8

Growing Concern for Worldwide GC Resistance

High prevalence of ceftriaxone-resistant and XDR *Neisseria gonorrhoeae* in several cities of Cambodia, 2022–23: WHO Enhanced Gonococcal Antimicrobial Surveillance Programme (EGASP)

V. Ouk[1], L. Say Heng[1], M. Virak[2], S. Deng[3], M. M. Lahra[4], R. Frankson[5], K. Kreisel[5], R. McDonald[5], M. Escher[6], M. Unemo[7,8], T. Wi[9] and I. Maatouk [9]* on behalf of the EGASP Cambodia Working Group†

Table 3. Antimicrobial susceptibility profiles of *N. gonorrhoeae* isolates ($n = 306$) from Cambodia, January 2022–June 2023

Antimicrobials and susceptibility	*n* (%)
Ceftriaxone	
Resistant (MIC > 0.125 mg/L)[a]	47 (15.4)
Susceptible (MIC ≤ 0.125 mg/L)	259 (84.6)
Cefixime	
Resistant (MIC > 0.125 mg/L)[a]	132 (43.1)
Susceptible (MIC ≤ 0.125 mg/L)	174 (56.9)
Azithromycin	
Resistant (MIC > 1 mg/L)[b]	44 (14.4)
Susceptible (MIC ≤ 1 mg/L)	262 (85.6)
Ciprofloxacin	
Resistant (MIC > 0.06 mg/L)[a]	297 (97.1)
Susceptible (MIC ≤ 0.03 mg/L)	9 (2.9)
Gentamicin	
EGASP MIC alert value (MIC ≥ 32 mg/L)[c]	0 (0)
Susceptible (MIC < 32 mg/L)	306 (100)
Resistant to ceftriaxone, cefixime, azithromycin and ciprofloxacin (XDR NG isolates)	19 (6.2)

Morbidity and Mortality Weekly Report

Ceftriaxone-Resistant Gonorrhea — China, 2022

Xiaoyu Zhu[1,2,*]; Yue Xi[1,2,*]; Xiangdong Gong, MD[1,2]; Shaochun Chen, PhD[1,2,3]

Abstract

Gonorrhea is a widespread sexually transmitted infection; in 2022, China reported 96,313 cases of gonorrhea, making it the fourth most common notifiable infectious disease in the country after viral hepatitis, pulmonary tuberculosis, and syphilis. The rise in prevalence in antimicrobial-resistant strains, particularly the international spread of ceftriaxone-resistant clones, poses a formidable challenge to gonorrhea control. The China Gonococcal Resistance Surveillance Program

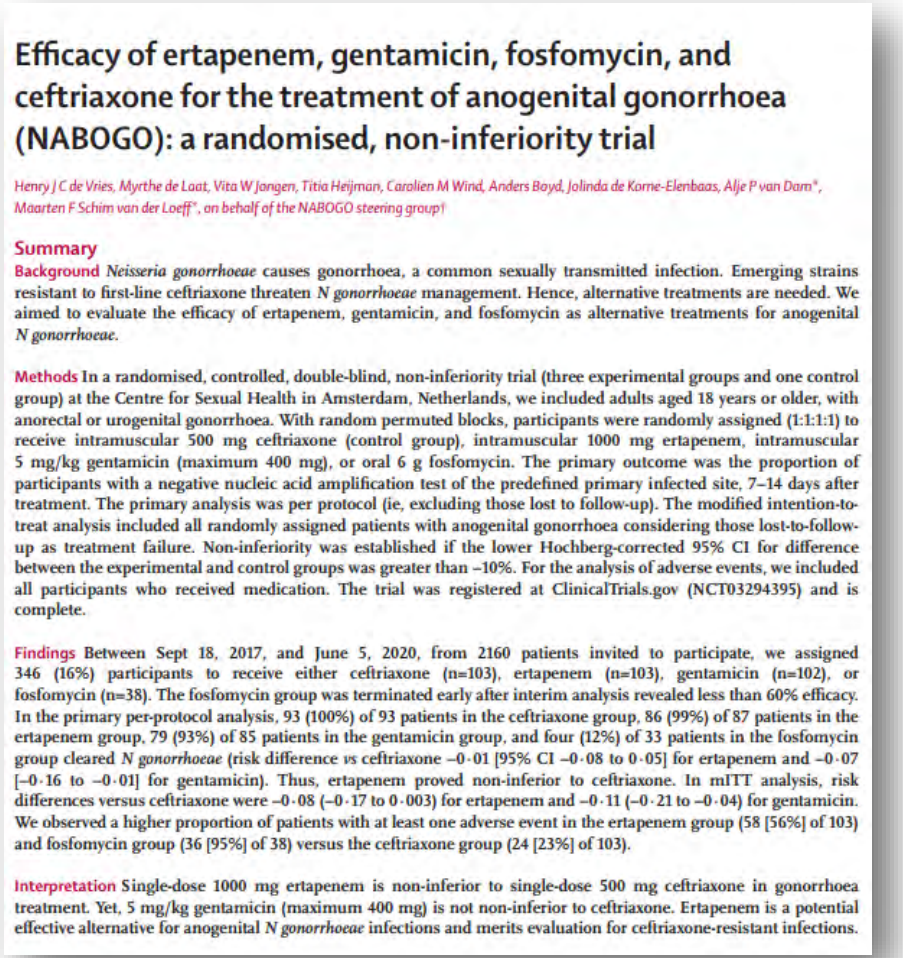
in the country,[¶] after viral hepatitis, pulmonary tuberculosis, and syphilis. In the United States, in 2022, a total of 648,056 cases of gonorrhea were reported.[**]

In recent years, gonococcal resistance to multiple antibiotics has emerged (*1*). Ceftriaxone is recommended as the first-line treatment option for gonorrhea in China (single dose of 1 g, administered intramuscularly)[††] as well as in the United States (single dose of 500 mg for persons weighing <150 kg, administered intramuscularly).[§§] However, the emergence

Antibiotic/MIC, no. of resistant isolates (%)						
Ciprofloxacin >0.06 mg/L	Penicillin >1 mg/L	Tetracycline >1 mg/L	Azithromycin >0.5 mg/L	Cefixime >0.125 mg/L	Ceftriaxone >0.125 mg/L	Spectinomycin >64 mg/L
2,737 (97.6)	**2,181 (77.8)**	**2,163 (77.1)**	**473 (16.9)**	**441 (16.0)**	**222 (8.1)**	**1 (<1)**

- Zhu X, Xi Y, Gong X, Chen S. Ceftriaxone-Resistant Gonorrhea - China, 2022. MMWR Morb Mortal Wkly Rep. 2024 Mar 28;73(12):255-259. doi: 10.15585/mmwr.mm7312a2. PMID: 38547027; PMCID: PMC10986818.
- Ouk V, Heng LS, Virak M, Deng S, Lahra MM, Frankson R, Kreisel K, McDonald R, Escher M, Unemo M, Wi T, Maatouk I; EGASP Cambodia Working Group. High prevalence of ceftriaxone-resistant and XDR Neisseria gonorrhoeae in several cities of Cambodia, 2022-23: WHO Enhanced Gonococcal Antimicrobial Surveillance Programme (EGASP). JAC Antimicrob Resist. 2024 Apr 4;6(2):dlae053. doi: 10.1093/jacamr/dlae053. PMID: 38577702; PMCID: PMC10993901.

What Could Be Our Next Option?



Efficacy of ertapenem, gentamicin, fosfomycin, and ceftriaxone for the treatment of anogenital gonorrhoea (NABOGO): a randomised, non-inferiority trial

Henry J C de Vries, Myrthe de Laat, Vita W Jongen, Titia Heijman, Carolien M Wind, Anders Boyd, Jolinda de Korne-Elenbaas, Alje P van Dam*, Maarten F Schim van der Loeff*, on behalf of the NABOGO steering group†

Summary

Background *Neisseria gonorrhoeae* causes gonorrhoea, a common sexually transmitted infection. Emerging strains resistant to first-line ceftriaxone threaten *N gonorrhoeae* management. Hence, alternative treatments are needed. We aimed to evaluate the efficacy of ertapenem, gentamicin, and fosfomycin as alternative treatments for anogenital *N gonorrhoeae*.

Methods In a randomised, controlled, double-blind, non-inferiority trial (three experimental groups and one control group) at the Centre for Sexual Health in Amsterdam, Netherlands, we included adults aged 18 years or older, with anorectal or urogenital gonorrhoea. With random permuted blocks, participants were randomly assigned (1:1:1:1) to receive intramuscular 500 mg ceftriaxone (control group), intramuscular 1000 mg ertapenem, intramuscular 5 mg/kg gentamicin (maximum 400 mg), or oral 6 g fosfomycin. The primary outcome was the proportion of participants with a negative nucleic acid amplification test of the predefined primary infected site, 7–14 days after treatment. The primary analysis was per protocol (ie, excluding those lost to follow-up). The modified intention-to-treat analysis included all randomly assigned patients with anogenital gonorrhoea considering those lost-to-follow-up as treatment failure. Non-inferiority was established if the lower Hochberg-corrected 95% CI for difference between the experimental and control groups was greater than –10%. For the analysis of adverse events, we included all participants who received medication. The trial was registered at ClinicalTrials.gov (NCT03294395) and is complete.

Findings Between Sept 18, 2017, and June 5, 2020, from 2160 patients invited to participate, we assigned 346 (16%) participants to receive either ceftriaxone (n=103), ertapenem (n=103), gentamicin (n=102), or fosfomycin (n=38). The fosfomycin group was terminated early after interim analysis revealed less than 60% efficacy. In the primary per-protocol analysis, 93 (100%) of 93 patients in the ceftriaxone group, 86 (99%) of 87 patients in the ertapenem group, 79 (93%) of 85 patients in the gentamicin group, and four (12%) of 33 patients in the fosfomycin group cleared *N gonorrhoeae* (risk difference *vs* ceftriaxone –0·01 [95% CI –0·08 to 0·05] for ertapenem and –0·07 [–0·16 to –0·01] for gentamicin). Thus, ertapenem proved non-inferior to ceftriaxone. In mITT analysis, risk differences versus ceftriaxone were –0·08 (–0·17 to 0·003) for ertapenem and –0·11 (–0·21 to –0·04) for gentamicin. We observed a higher proportion of patients with at least one adverse event in the ertapenem group (58 [56%] of 103) and fosfomycin group (36 [95%] of 38) versus the ceftriaxone group (24 [23%] of 103).

Interpretation Single-dose 1000 mg ertapenem is non-inferior to single-dose 500 mg ceftriaxone in gonorrhoea treatment. Yet, 5 mg/kg gentamicin (maximum 400 mg) is not non-inferior to ceftriaxone. Ertapenem is a potential effective alternative for anogenital *N gonorrhoeae* infections and merits evaluation for ceftriaxone-resistant infections.

- Randomized, controlled, double-blind, non-inferiority trial
- 346 randomly assigned
  - 103 – Ceftriaxone
  - 103 – Ertapenem
  - 102 – Gentamicin
  - 38 - Fosfomycin

Teker B, de Vries H, Heijman T, van Dam A, Schim van der Loeff M, Jongen VW. Spontaneous clearance of asymptomatic anogenital and pharyngeal *Neisseria gonorrhoeae*: a secondary analysis from the NABOGO trial. *Sex Transm Infect*. 2023;99(4):219-225. doi:10.1136/sextrans-2022-055488

What Could Be Our Next Option?

	Ceftriaxone group	Ertapenem group	Gentamicin group	Fosfomycin group	Ertapenem vs ceftriaxone		Gentamicin vs ceftriaxone		Fosfomycin vs ceftriaxone	
					Risk difference*	p†	Risk difference*	p†	Risk difference*	p†
Primary analysis per protocol*										
Clearance (7–14 days)	93/93 (100%; 96 to 100)	86/87 (99%; 94 to 100)	79/85 (93%; 85 to 97)	4/33 (12%; 3 to 28)	−0·01 (−0·08 to 0·05)	0·0089	−0·07 (−0·16 to −0·01)	0·37	−0·88 (−0·95 to −0·72)	1·000
Secondary analysis modified intention-to-treat‡										
Clearance (7–14 days)	93/93 (100%; 96 to 100)	86/93 (92%; 85 to 97)	79/89 (89%; 80 to 94)	4/35 (11%; 3 to 27)	−0·08 (−0·17 to 0·003)	0·64	−0·11 (−0·21 to −0·04)	1·000	−0·89 (−0·96 to −0·74)	1·000
Secondary analysis per protocol§										
Clearance (7–28 days)	93/93 (100%; 96 to 100)	87/88 (99%; 94 to 100)	82/88 (93%; 86 to 97)	4/33 (12%; 3 to 28)	−0·01 (−0·08 to 0·05)	0·0084	−0·07 (−0·16 to −0·003)	0·32	−0·88 (−0·95 to −0·72)	1·000
Secondary analysis strict per protocol¶										
Clearance (7–14 days)	81/81 (100%; 96 to 100)	78/79 (99%; 93 to 100)	75/81 (93%; 85 to 97)	3/28 (11%; 2 to 28)	−0·01 (−0·09 to 0·05)	0·015	−0·07 (−0·17 to −0·001)	0·44	−0·89 (−0·96 to −0·72)	1·000

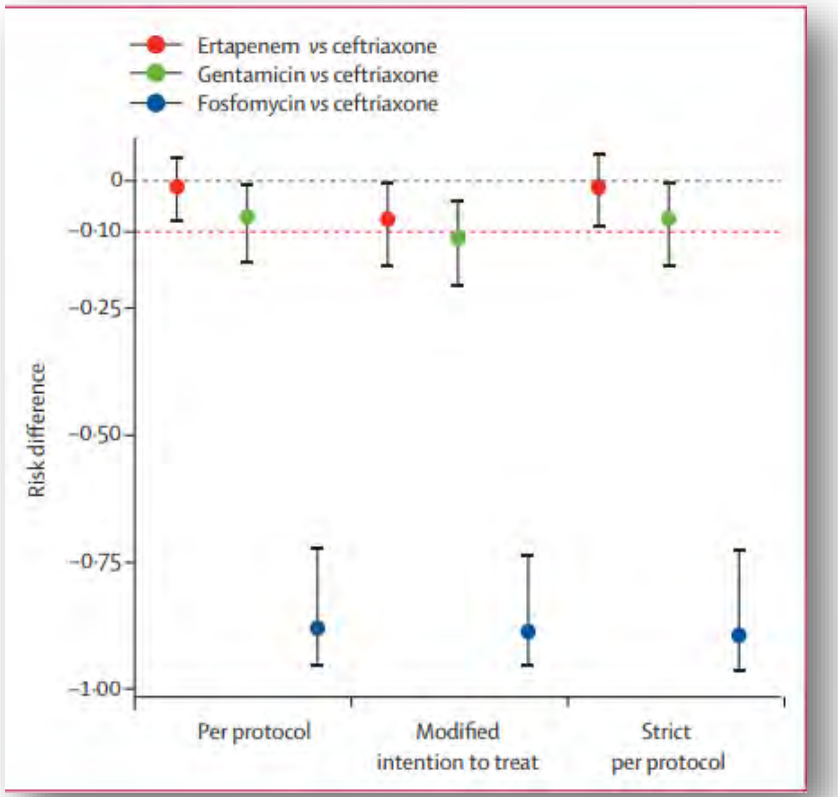
Efficacy

- Ceftriaxone 100%
- Ertapenem 99%
- Gentamicin 93%

- Teker B, de Vries H, Heijman T, van Dam A, Schim van der Loeff M, Jongen VW. Spontaneous clearance of asymptomatic anogenital and pharyngeal *Neisseria gonorrhoeae*: a secondary analysis from the NABOGO trial. *Sex Transm Infect*. 2023;99(4):219-225. doi:10.1136/sextrans-2022-055488

What Could Be Our Next Option?

- Single-dose ertapenem 1000 mg **is non-inferior** to single-dose ceftriaxone 500 mg for uncomplicated anogenital gonorrhea
- Single-dose 5 mg/kg gentamicin (max 400mg) is **not non-inferior** to ceftriaxone
- Single-dose oral fosfomycin was ineffective



- Teker B, de Vries H, Heijman T, van Dam A, Schim van der Loeff M, Jongen VW. Spontaneous clearance of asymptomatic anogenital and pharyngeal *Neisseria gonorrhoeae*: a secondary analysis from the NABOGO trial. *Sex Transm Infect*. 2023;99(4):219-225. doi:10.1136/sextrans-2022-055488

Upcoming Options

ORIGINAL ARTICLE

Single-Dose Zoliflodacin (ETX0914) for Treatment of Urogenital Gonorrhea

Authors: Stephanie N. Taylor, M.D., Jeanne Marrazzo, M.D., M.P.H., Byron E. Batteiger, M.D., Edward W. Hook, III, M.D., Arlene C. Seña, M.D., M.P.H., Jill Long, M.D., M.P.H., Michael R. Wierzbicki, Ph.D., Hannah Kwak, M.H.S., Shacondra M. Johnson, B.S.P.H., Kenneth Lawrence, Pharm.D., and John Mueller, Ph.D. Author Info & Affiliations

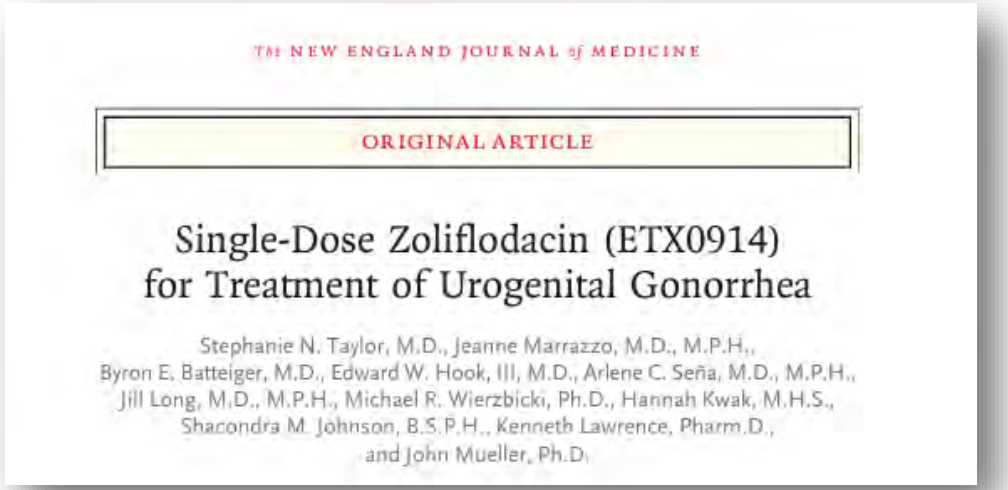
Published November 7, 2018 | N Engl J Med 2018;379:1835-1845 | DOI: 10.1056/NEJMoa1706988

VOL. 379 NO. 19 | Copyright © 2018

- The majority of uncomplicated urogenital and rectal gonococcal infections were successfully treated with oral zoliflodacin, but this agent **was less efficacious in the treatment of pharyngeal infections.**

- https://www.nejm.org/doi/full/10.1056/NEJMoa1706988

Future Options



THE NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Single-Dose Zoliflodacin (ETX0914) for Treatment of Urogenital Gonorrhea

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New gonorrhea antibiotic shows promise in pivotal phase 3 trial

Chris Dall, MA, November 2, 2023

Topics: Antimicrobial Stewardship , Gonorrhea

SHARE

A desperately needed new antibiotic for gonorrhea infections could soon be on the way.

In a phase 3 trial conducted in five countries, the investigational oral antibiotic zoliflodacin met its primary end point, demonstrating statistical non-inferiority in curing patients who had uncomplicated urogenital gonorrhea infections compared with the standard treatment of intramuscular ceftriaxone and oral azithromycin. Zoliflodacin was also found to be well tolerated by patients, with no serious adverse events or deaths recorded.

A first-in-class antibiotic with a novel mechanism of action,

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