Top 10 Updates in Infectious Diseases

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Disclosure

I have no financial interests or relationships to disclose.

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Learning Objectives

1. To discuss emerging or re-emerging infectious diseases, including mpox, polio, fungal infections, influenza (H5N1)
2. To review new treatment or vaccine strategies for infectious diseases including for STDs (DoxyPEP), TB (short courses), RSV (vaccine), malaria
3. To provide an overview of the degree of trust in public health in 2024 and pandemic preparedness

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Top 10 Infectious Diseases (Non-HIV, Non-COVID) Updates

- MPOX
- DoxyPEP
- Polio
- Influenza, including H5N1
- Shorter courses of therapy for TB
- RSV vaccine
- Emerging or re-emerging fungal infections
- Antimicrobial resistance
- Malaria
- Pandemic preparedness and trust in public health

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What Country Currently Has the Highest Numbers of Cases and Deaths from the Mpox Outbreak?

A. United States
B. Kenya
C. Burundi
D. Uganda
E. Democratic Republic of Congo

Viruses Are All Different and Classified by the Genetic Material They Contain

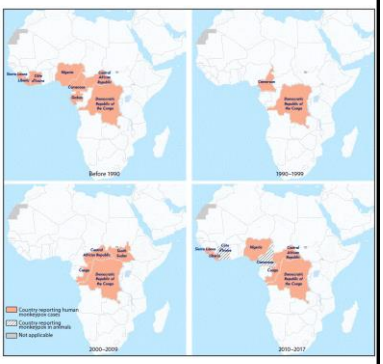
MPOX is member of the Poxviridae family of viruses called Orthopoxvirus and is a double-stranded DNA virus. Subset includes the smallpox (variola, now eradicated), vaccinia, cowpox virus, and Borealpox virus

Monkeypox	→	DNA virus
HIV	→	Retrovirus (RNA virus but makes RNA into DNA in host)
SARS-CoV-2, poliovirus, measles virus	→	RNA virus

Mandel. Principles of ID 2022

Emergence of Monkeypox — West and Central Africa, 1970–2017

- MPOX first described in 1958 where two outbreaks occurred in monkeys used for research
- Monkeys not major carriers of disease
- Closely related to smallpox, mass smallpox vaccine programs protected humans against MPOX
- Smallpox eradicated in 1980 worldwide (1970 in US) so smallpox vaccine programs gradually ceased in 1970s
- Countries in Central & West Africa became susceptible to "endemic" outbreaks increasing in the past decade
- Monkeypox name changed to MPOX on Nov 28, 2022 during global outbreak; Variants renamed from regional names to "Clades" I and II



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"Endemic" Outbreaks

- Thought in past that MPOX was usually transmitted to humans from bite or touching infected animal (mainly rodents- rats, mice, squirrels)
- In US, MPOX was usually seen in returning travelers (e.g. two cases in 2021 Nigeria)
- In 2003, outbreak in US in Midwest (71 people) from interacting with pet prairie dogs –interacted with infected animals Ghana
- **HOWEVER,** Nigeria reports that sexual transmission may have been occurring there since 2019, likely among men-who-have-sex-with-men, new light

CDC MMWR 2003; CDC MMWR 2021; Ogoina PLOS One 2019

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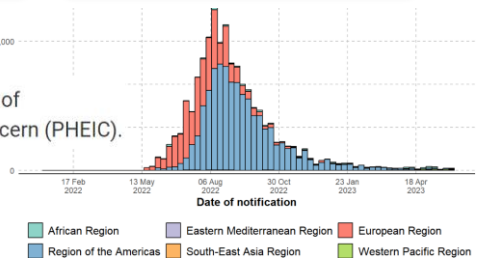
Major Global Outbreak Of MPOX 2022-23

- ~97,208 cases in 121 countries as of August 24, 2024; first case reported to WHO on May 2, 2022 – declared public health emergency of international concern 22 July 2022
- Early cases in UK, then rest of Europe, Canada/Australia then US, Latin America

Total cases	Total deaths	Countries reporting cases
102 997	223	121

On 23 July 2022, the WHO Director-General declared the multi-country outbreak of mpox (monkeypox), constitutes a Public Health Emergency of International Concern (PHEIC).



World Health Organization MPOX Outbreak Global Trends. https://www.who.int/emergencies/situations/monkeypox-oubreak-2024

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PAHO Pan American Health Organization World Health Organization Americas Region

Home / News / WHO declares end of mpox emergency, calls for sustained efforts for long-term management of the disease

WHO declares end of mpox emergency, calls for sustained efforts for long-term management of the disease

11 May 2023

On May 11, 2023, first public health emergency declared over (despite no vaccines to Africa…)

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What Were Symptoms in the 2022 Global Outbreak?

- First large case report (n=528), 16 countries, median age 38, 98% gay/bisexual men, 75% White, 41% had HIV
- Skin lesions 95% -most common anatomical sites anus and genital regions (73%)
- Can be singular or multiple – uncomfortable
- Ranging from flat to blisters to crusted lesions- most have fewer than 10 lesions
- Mouth lesions in 5%
- Common systemic features included fever (in 62%), lethargy (41%), muscle aches (31%), headache (27%), and big lymph nodes (56%), symptoms that frequently preceded the rash.
- Same symptoms if HIV negative or positive

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Monkeypox Virus Infection in Humans across 16 Countries — April–June 2022

J.P. Thornhill, S. Barkati, S. Walmsley, J. Rockstroh, A. Antinori, L.B. Harrison, R. Palich, A. Nori, I. Reeves, M.S. Habibi, V. Apea, C. Boesecke, J. Vandekerckhove, M. Yakubovsky, E. Sendagorta, J.I. Blanco, E. Florence

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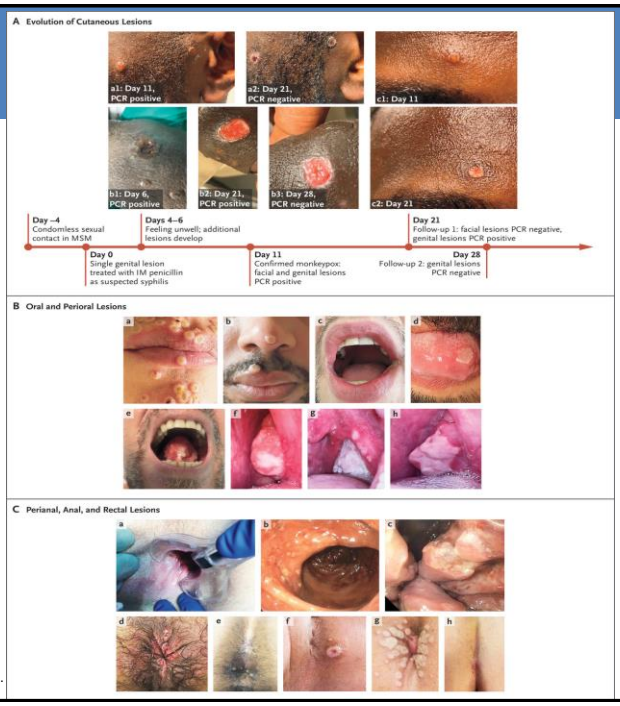

JP Thornhill et al. N Engl J Med 2022;387:679-691.

The NEW ENGLAND JOURNAL of MEDICINE

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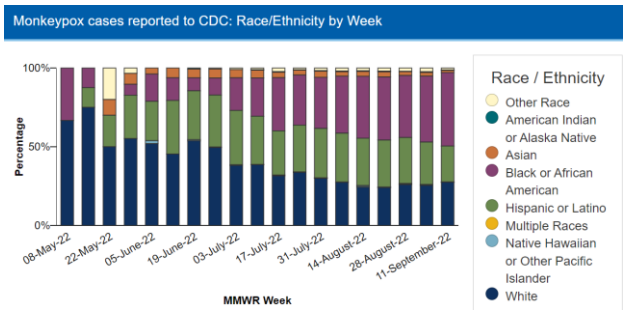
CDC Centers for Disease Control and Prevention
CDC 24/7: Saving Lives, Protecting People™

Weekly / August 12, 2022 / 71(32);1018-1022

Epidemiologic and Clinical Characteristics of Monkeypox Cases — United States, May 17–July 22, 2022

- May 17–July 22, 2022
- 2,891 U.S. monkeypox cases reported by 43 states, Puerto Rico DC
- 99% men; (available data)
- 94% same sex activity
- 41% White; 28% Latino; 26% Black (changing)
- 41% HIV
- 42% without prodrome
- 46% genital lesions



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Centers for Disease Control and Prevention
MMWR
Morbidity and Mortality Weekly Report
Weekly / Vol. 71 / No. 36
September 9, 2022

HIV and Sexually Transmitted Infections Among Persons with Monkeypox — Eight U.S. Jurisdictions, May 17–July 22, 2022

Kathryn G. Curran, PhD[1]; Kristen Eberly, MPH[1]; Olivia O. Russell, MPH[2]; Robert E. Snyder, PhD[3]; Elisabeth K. Phillips, MPH[3]; Eric C. Tang, MD[3]; Philip J. Peters, MD[1,3]; Melissa A. Sanchez, PhD[4]; Ling Hsu, MPH[4]; Stephanie E. Cohen, MD[4]; Ekow K. Sey, PhD[5]; Sherry Yin, MPH[5];

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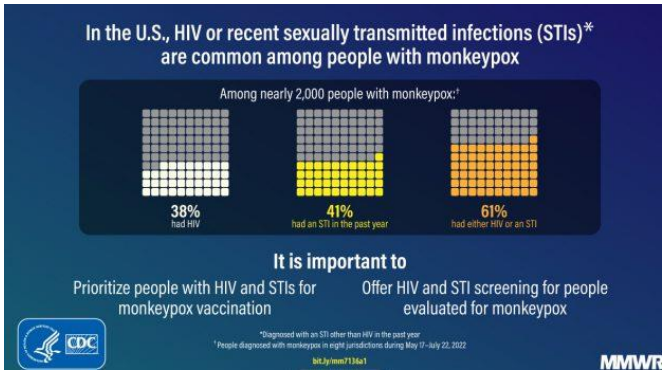
MPOX Cases: High Rates of Other STDs and HIV

- Never have an orthopoxvirus & HIV temporally overlapped before
- High rates of other STDs and HIV in this large (>1900 cases in US) evaluation
- HIV with CD4 <200 risk factor for severe disease so mpox now classified as an OI in HIV



CDC. MMWR 71(36). Sept 2022; Mitja Lancet 2024

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Clinical Infectious Diseases
VIEWPOINTS
IDSA Infectious Diseases Society of America
hivma hiv medicine association
OXFORD

A Position Statement on Mpox as a Sexually Transmitted Disease

Lao-Tzu Allan-Blitz,[1] Monica Gandhi,[2,3] Paul Adamson,[4] Ina Park,[5] Gail Bolan,[6] and Jeffrey D. Klausner[7]

[1]Division of Global Health Equity, Department of Medicine, Brigham and Women's Hospital, USA; [2]Division of HIV, Infectious Diseases, and Global Medicine, Department of Medicine, University of California, USA; [3]Ward 86 HIV Clinic, San Francisco General Hospital, USA; [4]Division of Infectious Diseases, Department of Medicine, University of California, USA; [5]Department of Family and Community Medicine and Department of Obstetrics, Gynecology, and Reproductive Sciences, School of Medicine, University of California, San Francisco, USA; [6]Berkeley, California; and [7]Department of Population and Public Health Sciences, Keck School of Medicine, University of Southern California, USA

NEWS QUEEN ELIZABETH II LIVE UPDATES POLITICS PLAN YOUR VOTE U.S. NEWS BUSINESS COVID OPINION WATCH NOW

Herpes, syphilis, molluscum contagiosum all STDs that can spread by other means as well (close contact)

OUT HEALTH AND WELLNESS

Sex between men, not skin contact, is fueling monkeypox, new research suggests

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Prior to Universal Gloving, Some STDs Could Spread By Skin-to-skin

Herpetic whitlow

1952 Aug; 77(2): 149–150.

Extragenital Syphilis in Physicians

ERVIN EPSTEIN, M.D., *Oakland*

In reply to a questionnaire, 51 cases of extragenital chancres in physicians were reported by 32 contributors. Thirty-five of these lesions occurred on the fingers, six inside the nose, one on an eyelid and one on an arm.

CDC Centers for Disease Control and Prevention
CDC 24/7: Saving Lives, Protecting People™

- In the current mpox outbreak, reported cases of mpox in children and adolescents are infrequent (<0.3% of total cases) and disease is generally not severe. Exposure to a household contact with mpox is the predominant route of exposure for children, while sexual contact is the predominant route of exposure for adolescents.

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ACOG
The American College of Obstetricians and Gynecologists

A Primer on Monkeypox Virus for Obstetrician–Gynecologists

Diagnosis, Prevention, and Treatment

Meaney-Delman, Dana M. MD, MPH; Galang, Romeo R. MD, MPH; Petersen, Brett W. MD, MPH

Last updated December 8, 2022

There are limited data on mpox infection during pregnancy. It is unknown whether pregnant people are more susceptible to mpox virus or whether infection is more severe in pregnancy. Monkeypox virus can be transmitted to the fetus during pregnancy or to the newborn by close contact during and after birth (CDC). Adverse pregnancy outcomes, including spontaneous pregnancy loss and stillbirth, have been reported in cases of confirmed mpox infection during pregnancy (Meaney-Delman, 2022). Preterm delivery and neonatal mpox infection have also been reported. The risk factors associated with severe infection and adverse pregnancy outcomes are not known (CDC Pregnancy).

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What Do We Know About the Vaccine?

CDC

Major increase in human monkeypox incidence 30 years after smallpox vaccination campaigns cease in the Democratic Republic of Congo

Anne W. Rimoin[a,b,1], Prime M. Mulembakani[c], Sara C. Johnston[d], James O. Lloyd Smith[b,e], Neville K. Kisalu[f], Timothee L. Kinkela[c], Seth Blumberg[b,e], Henri A. Thomassen[g], Brian L. Pike[h], Joseph N. Fair[h], Nathan D. Wol Robert L. Shongo[i], Barney S. Graham[j], Pierre Formenty[k], Emile Okitolonda[c], Lisa E. Hensley[d], Hermann Meye Linda L. Wright[m], and Jean-Jacques Muyembe[n]

Most convincing evidence that smallpox vaccine protects against mpox is rise in latter 30 years (1 generation) after mass smallpox vaccination campaigns ceased

- ACAM2000- smallpox vaccine
- Jynneos- smallpox and mpox vaccine

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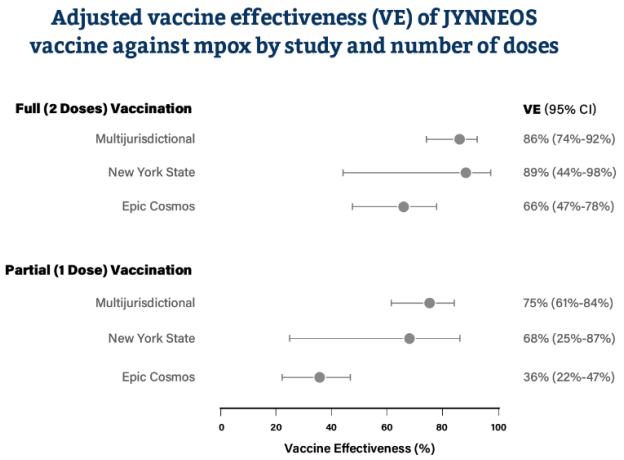
Estimated Effectiveness of JYNNEOS Vaccine in Preventing Mpox: A Multijurisdictional Case-Control Study — United States, August 19, 2022–March 31, 2023



Two doses important (given 4 weeks apart); provided greater protection

CDC MMWR May 19, 2023; 72(20): 553

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Mpox Outbreak in Africa 2023-2024

- Two clades of mpox – I (formerly Congo) and II (formerly West African), each with two subclades (Clades 1a, 1b; Clades IIa, IIb)
- Most cases in 2022 outbreak were clade IIb among MSM
- While global outbreak was being controlled with widespread vaccine availability and administration in high-resource settings 2022-2023, **no attention STILL being paid to African endemicity & global vaccines**
- In August 2024, WHO needed to declare new public health emergency from clade 1b in Africa

August 14, 2024

WHO Director-General declares mpox outbreak a public health emergency of international concern

14 August 2024 | News release | Reading time: 3 min (789 words)

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Characteristics of the MPOXV Clades

- Two clades of mpox – I (formerly Congo) and II (formerly West African), each with two subclades (Clades 1a, 1b; Clades IIa, IIb)
- Clade I causes more severe illness and death- can have fatality rates of up to 10%, endemic to Central Africa
  - Clade Ia: Mostly affects mainly children (<15 years) in DRC, multiple transmission modes.
  - Clade Ib: Eastern DRC, sexually spread, likely also close contact , recently identified as contributing to DRC/Africa outbreak
- Clade II endemic to West Africa-– lower mortality rate (99.9% survival)
  - Clade IIa: Original Clade II variant which was in West Africa over decades
  - Clade IIb: Named in August 2022 by the WHO as the subclade that caused the 2022 global outbreak, predominantly sexually transmissible, mainly men-who-have-sex-with-men

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World Health Organization

WHO declares mpox outbreaks in Africa a global health emergency as a new form of the virus spreads

The WHO Director-General determined that the mpox upsurge was a public health emergency of international concern on 14 August 2024, given the detection and rapid spread of a new clade of mpox in eastern Democratic Republic of the Congo, its detection in neighbouring countries that had not previously reported mpox, and the potential for further spread within Africa and beyond.

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CDC Mpox

Clade I Mpox Outbreak Originating in Central Africa

Print

Since January 2023, the Democratic Republic of the Congo (DRC) has reported more than 27,000 suspect mpox cases and more than 1,300 deaths.

There are two types of mpox, clade I and clade II. Clade I usually causes a higher percentage of people with mpox to get severely sick or die compared to clade II.

On This Page

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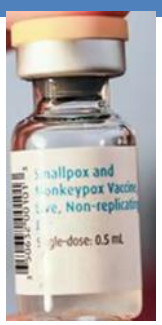
On 14 August, the World Health Organisation declared the mpox outbreak in Africa a "public health emergency of international concern", a day after Africa CDC declared it a "public health emergency of continental security" in Africa.

"Prior to this, we were really struggling to get access to vaccines," Helen Rees, the chairperson of the South African Health Products Regulatory Authority, tells *The Africa Report*.



The Guardian US

Fri 6 Sep 2024

DRC receives first donation of 100,000 mpox vaccines to contain outbreak

Jab not yet approved for children, who make up most cases, while officials warn millions more doses will be required

Two cases of Clade 1b now in Thailand and Sweden (both from travelers to Africa) – Vaccine equity for Africa!

"The world has said this should not happen again. This is not equitable, nor does it make public health sense or global health sense

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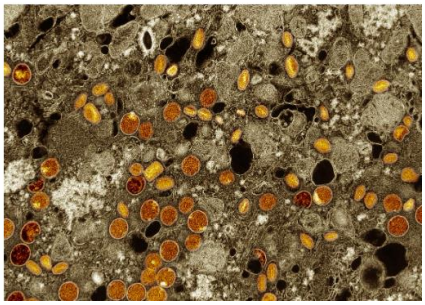
Thursday, August 15, 2024

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.

Study in the US (clade II) of tecovirimat ongoing (STOMP or A5418)

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-



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- Shorter courses of therapy for TB
- RSV vaccine
- Emerging or re-emerging fungal infections
- Antimicrobial resistance
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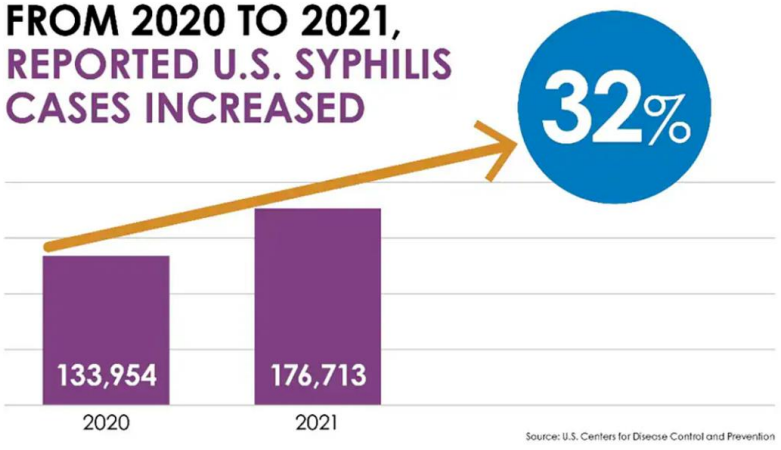
Why Was DoxyPEP Not Effective for Women in Kenya in a Large Trial in Preventing STDs?

A. More gonorrhea there and doesn't work for gonorrhea
B. Tetracycline resistance is increasing among sexually transmitted infections
C. Doxycycline tissue concentrations in vagina lower than in anal tissue
D. Inadequate adherence to the doxycycline

Sexually Transmitted Infections



The NEW ENGLAND JOURNAL of MEDICINE

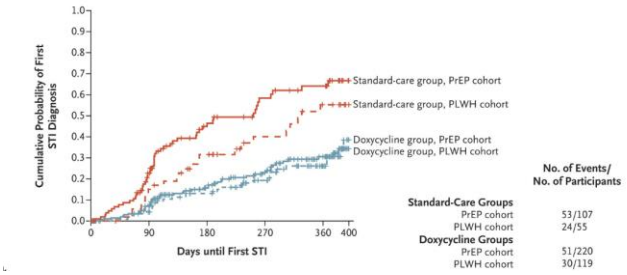
April 6, 2023

ORIGINAL ARTICLE

DoxyPEP Study

Postexposure Doxycycline to Prevent Bacterial Sexually Transmitted Infections

Anne F. Luetkemeyer, M.D., Deborah Donnell, Ph.D., Julia C. Dombrowski, M.D., M.P.H., Stephanie Cohen, M.D., M.P.H.,



- DoxyPEP participants (MSM and transgender women)
- -200 mg of doxycycline within 72 hours after condomless sex as post-exposure prophylaxis
- DoxyPEP reduced gonorrhea by 55%, chlamydia by 83%, syphilis by 87%
- Preliminary data showed antimicrobial resistance didn't increase in Staph aureus
- However, increasing resistance in gonorrhea to tetracycline

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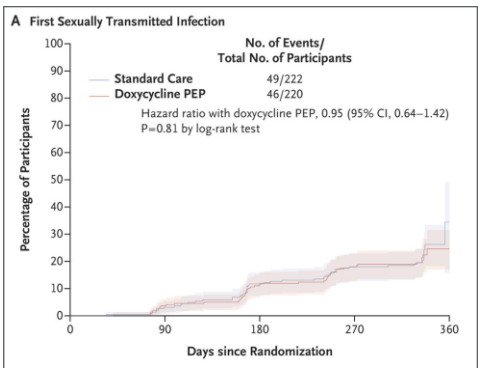
December 20, 2023

ORIGINAL ARTICLE

DPEP Study of DoxyPEP in Women in Kenya

Doxycycline Prophylaxis to Prevent Sexually Transmitted Infections in Women

Jenell Stewart, D.O., M.P.H., Kevin Oware, M.A., Deborah Donnell, Ph.D., Lauren R. Violette, M.P.H., Josephine Odoyo, R.N., M.P.H., Olusegun O. Soge, Ph.D., Caitlin W. Scoville, M.P.H.,



- dPEP participants (cisgender women in Kenya-
- -200 mg of doxycycline within 72 hours after condomless sex as post-exposure prophylaxis
- DoxyPEP did not reduce STDs in this study
- Hair samples taken for doxycycline as a metric of adherence found that pill taking was low (29%) explaining null efficacy (no differences in vaginal/anal doxy levels)

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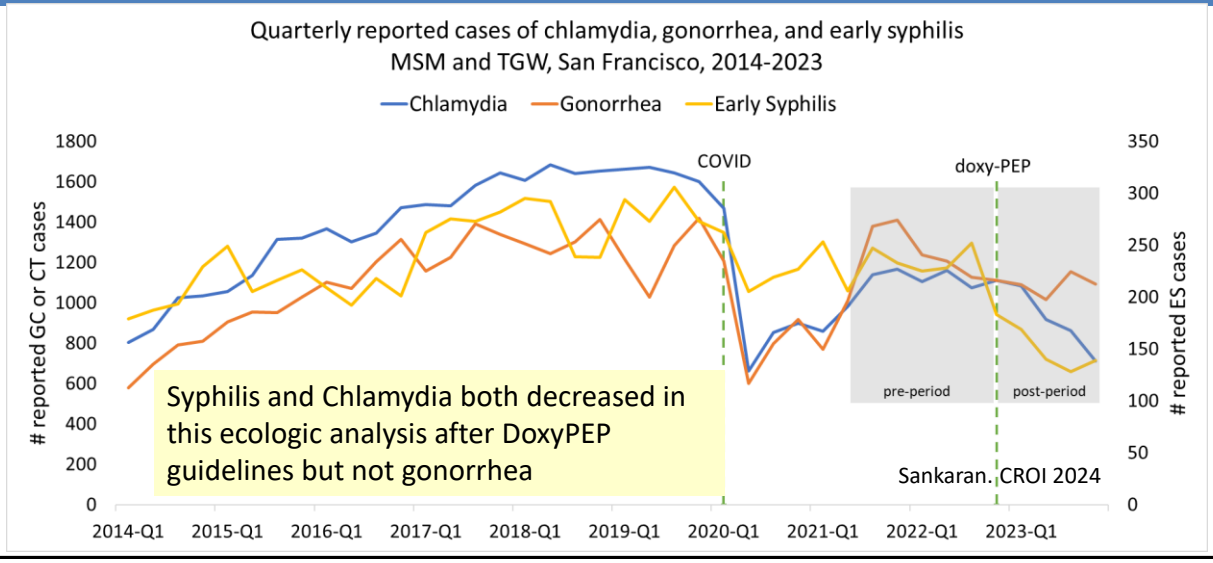
STI Trends in San Francisco with DoxyPEP



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Morbidity and Mortality Weekly Report (*MMWR*)

Search

CDC Clinical Guidelines on the Use of Doxycycline Postexposure Prophylaxis for Bacterial Sexually Transmitted Infection Prevention, United States, 2024

Recommendations and Reports / June 6, 2024 / 73(2):1–8

BOX 1. CDC recommendations for use of doxycycline as postexposure prophylaxis for bacterial sexually transmitted infections prevention

Recommendation*	Strength of recommendation and quality of evidence†
• Providers should counsel all gay, bisexual, and other men who have sex with men (MSM) and transgender women (TGW) with a history of at least one bacterial sexually transmitted infection (STI) (specifically, syphilis, chlamydia or gonorrhea) during the past 12 months about the benefits and harms of using doxycycline (any formulation) 200 mg once within 72 hours (not to exceed 200 mg per 24 hours) of oral, vaginal, or anal sex and should offer doxycycline postexposure prophylaxis (doxy PEP) through shared decision-making. Ongoing need for doxy PEP should be assessed every 3–6 months.	AI High-quality evidence supports this strong recommendation to counsel MSM and TGW and offer doxy PEP.
• No recommendation can be given at this time on the use of doxy PEP for cisgender women, cisgender heterosexual men, transgender men, and other queer and nonbinary persons.	Evidence is insufficient to assess the balance of benefits and harms of the use of doxy PEP

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Which Polio Vaccine Should Be Used in the Context of an Outbreak in a Low-income Country?

A. Oral polio vaccine
B. Inactivated polio vaccine
C. Oral vaccine for children; inactivated for adults
D. Oral vaccine x 2 doses, followed by inactivated vaccine one shot

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July 21, 2022

First polio case since 2013 in U.S. reported in New York state

POLIO in NYC Wastewater 2022; Wastewater & Child in Palestine (Paralysis) 2024

Polio vaccination rate for 2-year-olds is as low as 37% in parts of N.Y. county where paralysis case was found

WORLD NEWS

Aid groups in Gaza aim to avert a polio outbreak with a surge of vaccinations

August 18, 2024

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Some Facts About Polio

- Enterovirus – fecal oral route
- Host range limited to primates (hopes for eradication)
- Syndromes: 1) asymptomatic (90-95%); many called, few chosen); 2) abortive poliomyelitis (mild febrile illness characterized by headache, sore throat, N/V) ; 3) nonparalytic polio (aseptic meningitis); 4) paralytic polio (descending, asymmetric descending flaccid paralysis; painful muscle spasms).
- Post-polio syndrome can cause marked deterioration of muscles years later
- Vaccine (3 antigenic types so covers all 3 although type 2 wildtype virus now eradicated)
- Killed vaccine (Salk) or live attenuated vaccine(Sabin, oral vaccine)
  - Oral should not be given to immunodeficient individuals and adults
  - Advantage to the oral vaccine – provides local mucosal immunity & in gut- used in low-income countries, outbreaks
  - Live vaccine associated with paralysis in 1 in 2.4 million doses (case in Rockland – revertant OPV- had just traveled to Europe)
- IPV (killed vaccine) schedule in US

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How Many of the Human H5N1 Influenza Cases in the US in 2024 Been Linked to Dairy Cow Exposure?

A. 14 out of 14
B. 13 out of 14
C. 12 out of 14
D. 11 out of 14
E. 10 out of 14

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Influenza

- Influenza virus is classified into 3 types; A, B and C.
- Type A
  - Avian, human, mammalian
  - Pandemics
- Type B
  - Human, causes epidemics disease similar to type A
- Type C
  - Humans, swine
  - 7 segments
  - Lacks NA but contains esterase
  - Mild infections

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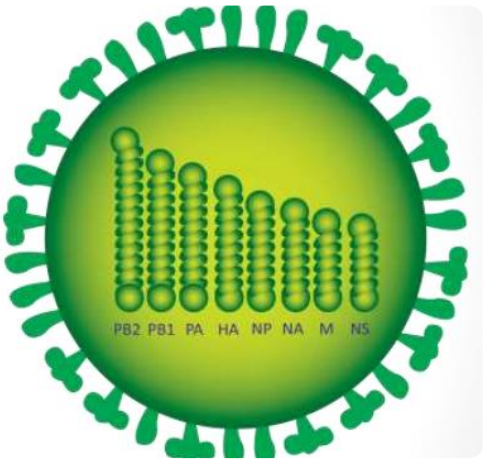
Avian Influenza



- Two spike proteins
  - HA has 16 subtypes (H1–H16) and contains neutralizing epitopes
  - Antibodies against the NA are not neutralizing, and there are 9 neuraminidase or "N" subtypes
- "H" and N subtypes seem to be able to be assorted into any combination, and many of the 144 possible combinations have been found in natural reservoir species (some more common than others)
- All 16 HA subtypes have been found in ducks, gulls, or shorebirds, the natural reservoir host species of the virus
- 2022-2024 avian influenza is H5N1

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H5N1 Avian Influenza

- H5N1 influenza widespread in birds and high fatality rates in birds
- Has spread to mammals and in US, dairy cows
- 14 human cases in US from March 24, 2024 to now, all but one from dairy cow exposure; viral fragments (not infectious) in pasteurized milk
- Conjunctivitis and respiratory symptoms
- Spreading to other mammals (cows, dogs, mice) from birds
- Have vaccine candidates (2) with others in works including mRNA
- Concern about vaccine hesitancy

May 7, 2024 ·

healthline **Bird Flu: U.S. Could Produce and Ship 100 Million Vaccine Doses Within Months**

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CDC Confirms Human H5 Bird Flu Case in Missouri

First case in US of the 14 without exposure to dairy cows; "one of" but still investigating

Case Information

Missouri DHSS reports that the patient, who was hospitalized, had underlying medical conditions, was treated with influenza antiviral medications, subsequently discharged, and has recovered. There is no immediate known animal exposure. No ongoing transmission among close contacts or otherwise has been identified.

This is the 14th human case of H5 reported in the United States during 2024 and the first case of H5 without a known occupational exposure to sick or infected animals. H5 outbreaks in cattle have not been reported in Missouri, but outbreaks of H5 have been reported in commercial and backyard poultry flocks in 2024. H5N1 bird flu has been detected in wild birds in that state in the past.

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Influenza Vaccine – Recommended Once Yearly

Three different kinds of influenza vaccines

INACTIVATED(IIV4)
(Multiple brands, don't give to those with history of egg allergy)

RECOMBINANT(RIV4)
(Only Flublok Quadrivalent® available; for those with egg allergy)

LIVE ATTENUATED (LAIV4)
(FluMist quadrivalent®; not recommended for people with HIV, even with high CD4 counts by CDC)

If >65 years, use high-dose quadrivalent vaccine (recombinant, allV4, HD-IIV4 in inactivated)

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Top 10 Infectious Diseases (Non-HIV, Non-COVID) Updates

- MPOX
- DoxyPEP
- Polio
- Influenza, including H5N1
- Shorter courses of therapy for TB
- RSV vaccine
- Emerging or re-emerging fungal infections
- Antimicrobial resistance
- Malaria
- Pandemic preparedness and trust in public health

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What Did a Recent Study Show in Terms of the Duration of Therapy for Rifampicin-sensitive TB

A. Can give 8 weeks of therapy with 4 drugs
B. Can give 8 weeks of therapy with 5 drugs
C. Can give 12 weeks of therapy with 4 drugs
D. Can give 12 weeks of therapy with 5 drugs

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The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 MARCH 9, 2023 VOL. 388 NO. 10

Treatment Strategy for Rifampin-Susceptible Tuberculosis

Nicholas I. Paton, M.D., Christopher Cousins, M.B., Ch.B., Celina Suresh, B.Sc., Erlina Burhan, M.D., Ka Lip Chew, F.R.C.P.A., Victoria B. Dalay, M.D., Qingshu Lu, Ph.D., Tutik Kusmiati, M.D., Vincent M. Balanag, M.D., Shu Ling Lee, B.Sc., Rovina Ruslami, Ph.D., Yogesh Pokharkar, M.Sc., Irawaty Djaharuddin, M.D., Jani J.R. Sugiri, M.D., Rholine S. Veto, M.D., Christine Sekaggya-Wiltshire, Ph.D., Anchalee Avihingsanon, M.D., Rohit Sarin, M.D., Padmasayee Papineni, F.R.C.P., Andrew J. Nunn, M.Sc., and Angela M. Crook, Ph.D., for the TRUNCATE-TB Trial Team*

ABSTRACT

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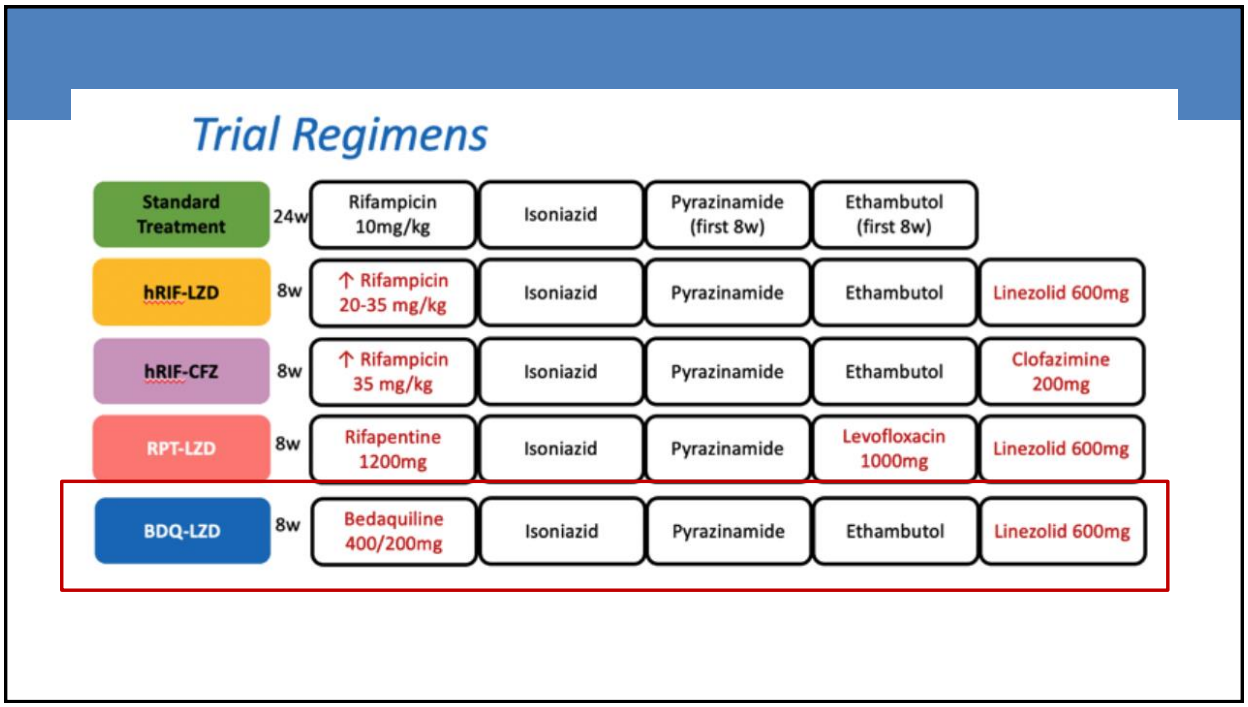

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Table 2. Primary Efficacy Outcome.*

Outcome	Standard Treatment (N=181)	Strategy with Rifampin–Linezolid (N=184)	Strategy with Rifampin–Linezolid vs. Standard Treatment Adjusted Difference (97.5% CI)†	Strategy with Bedaquiline–Linezolid (N=189)	Strategy with Bedaquiline–Linezolid vs. Standard Treatment Adjusted Difference (97.5% CI)†
Intention-to-treat population‡					
Primary outcome: composite of death, ongoing treatment, or active disease at wk 96 — no. (%)§	7 (3.9)	21 (11.4)	7.4 (1.7 to 13.2)	11 (5.8)	0.8 (−3.4 to 5.1)
Death before wk 96	2 (1.1)	5 (2.7)	—	1 (0.5)	—
Ongoing treatment at wk 96	2 (1.1)	8 (4.3)	—	5 (2.6)	—
Active disease at wk 96¶	1 (0.6)	4 (2.2)	—	3 (1.6)	—
Evaluation by telephone at wk 96 with no evidence of active disease but insufficient evidence of disease clearance when last seen	2 (1.1)	3 (1.6)	—	1 (0.5)	—
No evaluation at wk 96 and insufficient evidence of disease clearance when last seen	0	1 (0.5)	—	1 (0.5)	—
Outcomes classified as unassessable — no. (%)	1 (0.6)	1 (0.5)	—	2 (1.1)	—
Single positive culture at wk 96 but no other evidence of active disease‖	0	1 (0.5)	—	0	—
Death from a cause that was definitively unrelated to tuberculosis**	1 (0.6)	0	—	0	—
No evaluation at wk 96 and sufficient evidence of disease clearance when last seen	0	0	—	2 (1.1)	—
No primary outcome or outcome classified as unassessable — no. (%)	173 (95.6)	162 (88.0)	—	176 (93.1)	—
Assessable population††					
Primary outcome — no./total no. (%)	7/180 (3.9)	21/183 (11.5)	7.5 (1.7 to 13.2)	11/187 (5.9)	0.8 (−3.4 to 5.1)
Per-protocol population‡‡					

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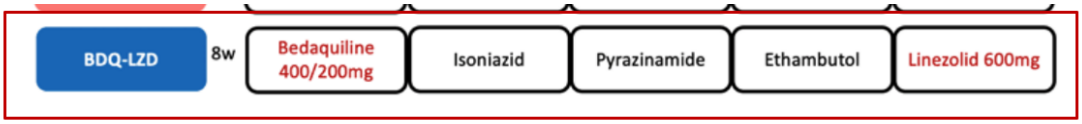
CONCLUSIONS

A strategy involving initial treatment with an 8-week bedaquiline–linezolid regimen was noninferior to standard treatment for tuberculosis with respect to clinical outcomes. The strategy was associated with a shorter total duration of treatment and with no evident safety concerns. (Funded by the Singapore National Medical Research Council and others; TRUNCATE-TB ClinicalTrials.gov number, NCT03474198.)

Important caveat: Those with more severe disease on initial chest radiograph or cavitations more likely to relapse on shorter course



51

Top 10 Infectious Diseases (Non-HIV, Non-COVID) Updates

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- Malaria
- Pandemic preparedness and trust in public health

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Respiratory Syncytial Virus (RSV)

- Common RNA respiratory virus
- Most common viral pathogen after influenza A and B pre-COVID
- Classified into 2 major subtypes—A and B—based on antigenic and genetic analysis
- One subtype predominates during one season
- Spreads through air via respiratory droplets
- Contagious for 3 to 8 days but immunosuppressed might shed longer
- RSV infection does not confer long-term immunity recurrent infections common
- Most severe disease in neonates and older individuals >65
- Two new RSV vaccines for those >60 developed & administered 2023 fall/winter

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CDC

For this season, due to rare Guillian-Barre with this vaccine, CDC changed recommendation from >60 to 75 and older

RSV Vaccine Guidance for Older Adults

WHAT TO KNOW

- CDC recommends a single dose of any FDA-licensed RSV vaccine for all adults ages 75 and older and adults ages 60–74 at increased risk of severe RSV.
- Three RSV vaccines are currently available for adults ages 60 and older: GSK's Arexvy, Moderna's mResvia, and Pfizer's Abrysvo. Eligible older adults may receive any of the licensed RSV vaccines.
- Eligible adults can get an RSV vaccine at any time, but the best time to vaccinate patients is in late summer and early fall before RSV usually starts to spread in the community.

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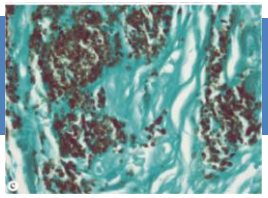
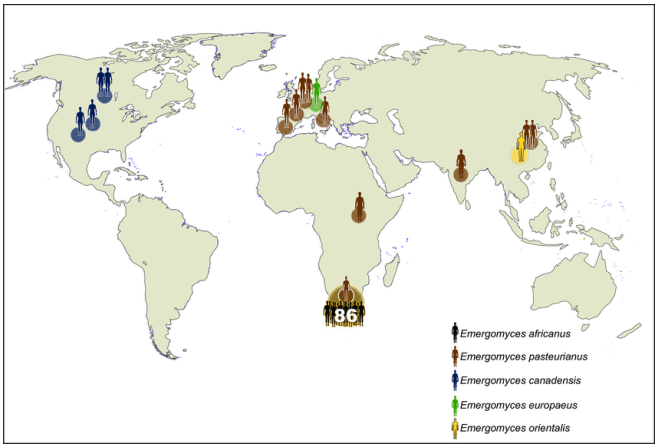
Emergomycosis



- Have to mention here as the name is literally emergomycosis
- fDimorphic endemic fungi classified in 2017
- Found in soil and distributed in Africa (*Es. pasteurianus, Es. Africanus, 74%)*, North America (*Es. Canadensis, 9.1%)*, Europe (*Es. pasteurianus, Es. Europaeus, 6.5%)* and Asia (*Es. pasteurianus, Es. Orientalis, 9.1%)*



Reddy. J of Medical Mycology 2023

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Emergomycosis

- Most common clinical manifestation is cutaneous lesions
- Hyperpigmented plaques with surface scaling or nodules
- Respiratory disease possible
- Most prevalent as an opportunistic infection in HIV
- Treatment is AmphoB followed by itraconazole usually

Reddy. J of Medical Mycology 2023

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Drug-Resistant Superbugs: 4th Leading Cause of Death in U.S.

October 22, 2019 David Wallinga, MD

Over the summer, the Centers for Disease Control and Prevention (CDC) updated its National Vital Statistics System to reflect the leading causes of deaths in the U.S., as of 2017. The top three listed are as follows:

1. Heart disease: 647,457
2. Cancer: 599,108
3. Accidents (unintentional injuries): 169,936.

CDC Newsroom

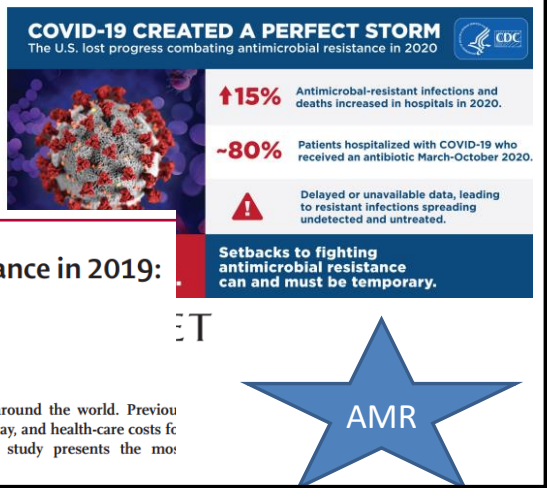
CDC Newsroom Home

COVID-19 Reverses Progress in Fight Against Antimicrobial Resistance in U.S.

Hospitalization related infections grew 15% from 2019 to 2020

Media Statement

For Immediate Release: Tuesday, July 12, 2022
Contact: Media Relations
(404) 639-3286



Global burden of bacterial antimicrobial resistance in 2019: a systematic analysis

*Antimicrobial Resistance Collaborators**

Summary

Background Antimicrobial resistance (AMR) poses a major threat to human health around the world. Previou publications have estimated the effect of AMR on incidence, deaths, hospital length of stay, and health-care costs fc specific pathogen–drug combinations in select locations. To our knowledge, this study presents the mos comprehensive estimates of AMR burden to date.

AMR

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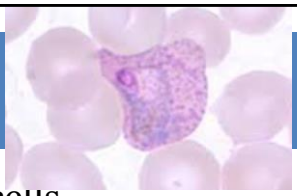
Malaria



- Mosquito-borne parasite that infects red blood cells.
- Four Plasmodium parasites; P. falciparum, P. vivax, P. ovale, and P. malariae (P. knowlesi usually infects primates)
- Malaria can cause flu-like symptoms, fever, chills, sweats, headaches, nausea and vomiting, body aches, and malaise.
- Severe cases of malaria (children more at risk) can cause deadly complications such as organ failure, hemoglobinuria, acute respiratory distress syndrome, hyperparasitemia (more than 5% of red blood cells are infected), etc.

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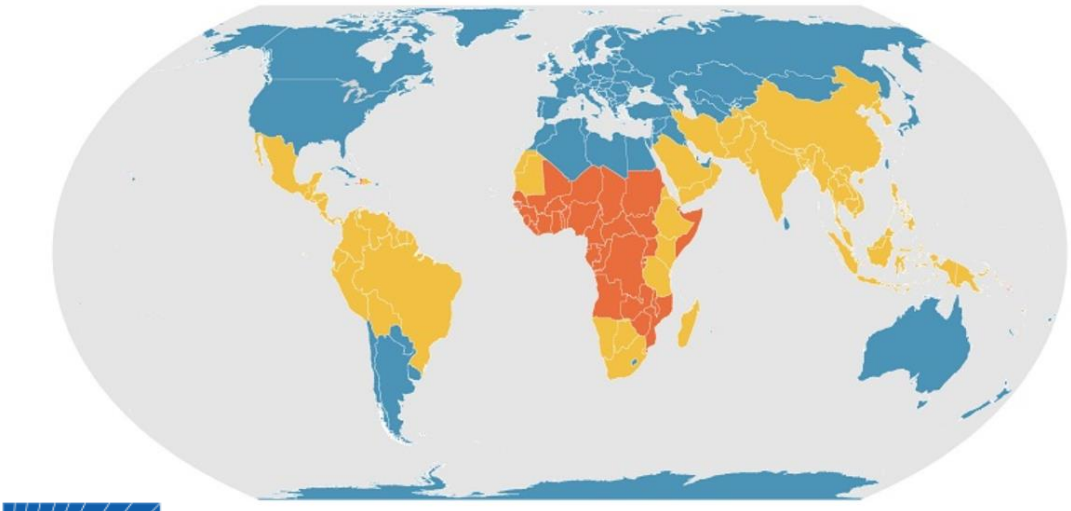

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Malaria

- Nearly half the world's population lives in areas at risk of malaria transmission in 87 countries and territories.
- In 2022, 249 million malaria cases and 608,000 deaths worldwide. An estimated 95% of deaths in 2022 were in the WHO African Region
- Sporadic local transmission in U.S. – first time in over 40 years

August 19, 2023

Maryland reports first locally acquired malaria case in 40 years

The latest case was reported in the Washington, D.C., area by a patient who had not traveled outside the U.S.

CDC

Outbreak of Locally Acquired Mosquito-Transmitted (Autochthonous) Malaria — Florida and Texas, May–July 2023 ...

This report describes eight cases of autochthonous malaria reported to CDC by health

60

Pandemic Preparedness

61

In the "Era of Pandemics" – Critical to Have Trust in Public Health

"I Fear We Are at the Beginning of an Era of Pandemics"

Activity	Consequence
 **Global Warming**	• Pathogens can go to new niches, have access to new hosts
 **Interaction with animals (hunting, eating, pets)**	• Zoonoses is when a microbe jumps from nonhuman to human hosts 
 **Changes in agriculture**	• New crops attract new pests
 **Encroachment on animal habitats**	• Other animals crowded, microbes can mutate, mix • Destruction of rain forests bring humans into contact with unfamiliar microbes
 **Urbanization**	• People more crowded together, contagious diseases
 **Other**	• Jet travel spreads diseases even when asymptomatic • Ships can carry "unintended passengers" • Breakdown of public health measures, poverty, war, famine, intent to harm

Information provided by Dr. Gandhi for educational purposes.

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The New York Times

Countries Fail to Agree on Treaty to Prepare the World for the Next Pandemic

May 24, 2024

Negotiators plan to ask for more time. Among the sticking points are equitable access to vaccines and financing to set up surveillance systems.

Project Syndicate | THE WORLD'S OPINION PAGE

May 29, 2024 | **WINNIE BYANYIMA** and **JOSEPH E. STIGLITZ**

How to Protect the World from the Next Pandemic

The pillars of effective pandemic prevention, preparedness, and response are well-known: relevant knowledge and technology must be shared openly, and vaccines, tests, and treatments must be produced widely. A global pandemic accord can ensure that these conditions are met next time – but only if it has teeth.

World Health Organization

Pandemic prevention, preparedness and response accord

10 June 2024 | Q&A

Member States of the World Health Organization have agreed to a global process to draft and negotiate a convention, agreement or other international instrument under the Constitution of the World Health Organization to strengthen pandemic prevention, preparedness and response.

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PUBLIC HEALTH

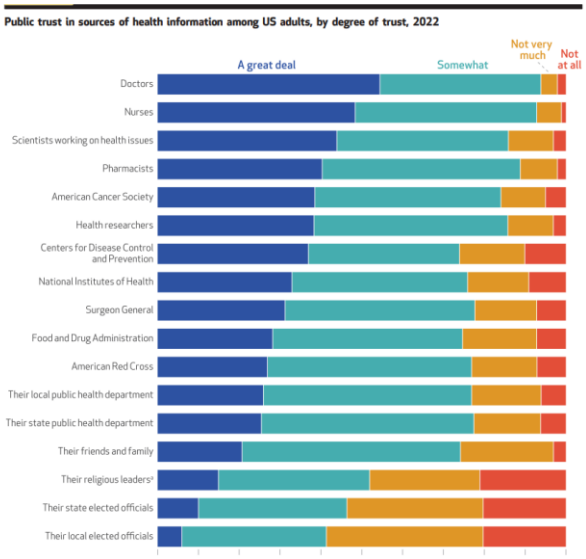
By Gillian K. SteelFisher, Mary G. Findling, Hannah L. Caporello, Keri M. Lubell, Kathleen G. Vidoloff Melville, Lindsay Lane, Alyssa A. Boyea, Thomas J. Schafer, and Eran N. Ben-Porath

Trust In US Federal, State, And Local Public Health Agencies During COVID-19: Responses And Policy Implications

HealthAffairs

March 2023 (reflecting data to February 2022- Harvard survey)
Trust in CDC 37%
Trust in NIH 33%
Trust in FDA, state-local health departments 30%
Trust in state elected officials 15%

TRUST IN DOCTORS/NURSES HIGH 54%/48%



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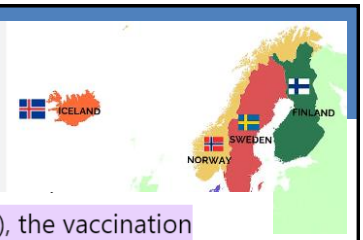
10 things you should know about Nordic trust, governance and openness

nature



In the Nordic countries (Denmark, Finland, Iceland, Norway and Sweden), the vaccination uptake has been notably high. In Iceland 91.2% of the population had received one dose and

1 **Trust – the Nordic gold**: The Nordic region has the highest levels of trust in the world. One important aspect stimulating social trust in the Nordic region has been the relationship between the state and the associations.

10 **Fighting fakes**: 'Fake News' – understood as propaganda, lies, disinformation and fake factory stories – are serious threats to our democracies. Nordic experts are working to counter the fake news trend by promoting quality journalism, media and information literacy, ethical standards and self-regulation.

Sigridur Islind Nature October 2022

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Vaccine 40 (2022) 7262–7269

Contents lists available at ScienceDirect

Vaccine

journal homepage: www.elsevier.com/locate/vaccine

Is vaccine confidence an unexpected victim of the COVID-19 pandemic?

Alessandro Siani *, Amy Tranter

School of Biological Sciences, University of Portsmouth, Portsmouth, UK

We measured vaccine confidence pre-pandemic and in 2022 – it's declined considerably

November 4, 2022 10.05am EDT

Lower Public Confidence in Vaccines

Confidence in vaccines is declining despite overwhelming evidence they are safe and effective, according to a new survey from the University of Pennsylvania's Annenberg Public Policy Center. A total of 71% of those surveyed in October agreed with the statement "Vaccines approved for use in the U.S. are safe," down from 77% in April 2021.

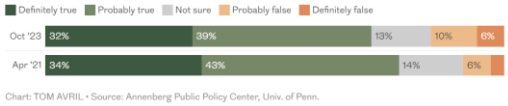

Chart: TOM AVRIL • Source: Annenberg Public Policy Center, Univ. of Penn.

Exemptions for required vaccines for US kindergartners reach record high

CNN Health

November 9, 2023

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After 'historic backslide' during pandemic, global childhood immunization rates stall, new data shows

By Maya Davis, CNN
6 minute read · Published 8:01 PM EDT, Sun July 14, 2024

July 15, 2024

CNN Health

The data revealed that previous progress in reaching pre-pandemic immunization levels has stalled. Worldwide DTP coverage was 84% in 2023, the same as in 2022 but below 86% recorded in 2019. The report's authors say this is a derailment on the trajectory toward the Immunization Agenda 2030 goal of 90% coverage for essential childhood and adolescent vaccines.

This stagnation reflects ongoing challenges with disruptions in health-care services, logistical challenges, vaccine hesitancy and inequities in access to services, the organizations said in a news release.

World Health Organization

WHO/UNICEF Immunization Coverage Estimates - 2023 revision

15 July 2024 | Technical document

67

Zimbabwe Says Measles Outbreak Has Killed 700 Children

CONFIRMATION OF MUMPS OUTBREAK, SOUTH AFRICA (11 MAY 2023)

11 May , 2023

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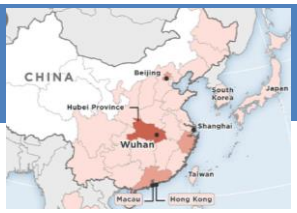
SARS-CoV-2 History[1-3]



- Illness with fever, cough, pneumonia reported from Wuhan, China on New Years' Eve to WHO (December 31, 2019)
- January 7, 2020: Identified etiology a new coronavirus and called SARS-CoV-2
- January 30, 2020: WHO declared global health emergency
- February 11, 2020: Disease of SARS-CoV-2 named COVID-19
- March 11, 2020: WHO—COVID-19 declared a pandemic
- December 11, 2020: First EUA from FDA for COVID-19 vaccine in US (Pfizer), others to follow
- 6.99 million deaths total to date (~12 million collateral deaths likely)
- May 5, 2023: WHO declares global health emergency over, endemic state will continue to need work (May 11, US public health emergency ends)

1. WHO [internet]. Cited 5 December 2023. Available from: https://covid19.who.int/
2. Centers for Disease Control [internet]. Cited 5 December 2023. Available from: https://www.cdc.gov/museum/timeline/covid19.html
3. WHO [internet]. Cited 5 December 2023. Available from: https://www.who.int/news/item/05-05-2023-statement-on-the-fifteenth-meeting-of-the-international-health-regulations-(2005)-emergency-committee-regarding-the-coronavirus-disease-(covid-19)-pandemic

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Company or name	Type of vaccine	Reference
Moderna	mRNA vaccine (US)	Baden NEJM, Feb 4, 2021
Pfizer	mRNA vaccine (US)	Polack NEJM, December 31, 2020
Johnson & Johnson	Adenovirus + DNA vaccine (US)	J&J NEJM 2021; FDA document Feb 24
AstraZeneca	Adenovirus + DNA vaccine	Voysey Lancet December 8, 2020; Preprint Feb 1, 2021
NovaVax	Spike protein + an adjuvant (US)	Novavax press release June 14; Novavax NEJM June 30, 2021
Sputnik V	Adenovirus + DNA vaccine	Logunov Lancet, February 2, 2021
Sinopharm	Whole inactivated virion	Sinopharm, JAMA, May 28, 2021
Sinovac	Whole inactivated virion	Sinovac, JAMA May 28, 2021
Covaxin	Whole inactivated virion	Bharat Covaxin, Lancet 2021

There are actually 8 unique vaccines approved by WHO for COVID-19 (Sputnik V pending), three authorized in U.S.

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COVID-19 Can Be Controlled Not Eradicated – So, Frequency of Boosters Will Depend on Variants

- **Control:** Reduction of disease incidence to acceptable levels
- **Elimination**: Reduction to zero incidence in a defined geographical area
- **Eradication**: Permanent reduction to zero worldwide
- **Extinction:** Infectious agent no longer exists in nature or laboratories.

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COVID-19 Does Not Have Features of an Eradicable Infectious Disease, Can Still Be Controlled

Smallpox- eradicated

- No animal reservoir
- Clear pathogenic features
- Short period of infectiousness
- Immune for life, highly effective vaccine

COVID-19 – will get under control

- COVID-19 looks like other respiratory illnesses
- Can spread when presymptomatic
- Found in animals
- Highly effective vaccine for severe disease; increasingly non-sterilizing with variants

We won't eradicate covid. The pandemic will still end.

By Monica Gandhi

September 21, 2021

The Washington Post

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Vaccine Confidence Slipped During COVID-19

1. Vaccine fastest approval in history
2. Multiple reports that strongest predictor of mortality from COVID - rates of vaccination especially over 60
3. Harm reduction approach needed for any pandemic
4. School closures did harm to the young & increased non-COVID related deaths in this population (overdoses, homicide, road-related injuries, alcohol)
5. Yes, there is misinformation on vaccines, but what can we in public health do to increase trust?

March 10, 2022

Estimating excess mortality due to the COVID-19 pandemic: a systematic analysis of COVID-19-related mortality, 2020–21

COVID-19 Excess Mortality Collaborators † • Show footnotes

Open Access • Published: March 10, 2022 • DOI: https://doi.org/10.1016/S0140-6736(21)02796-3 •

THE LANCET

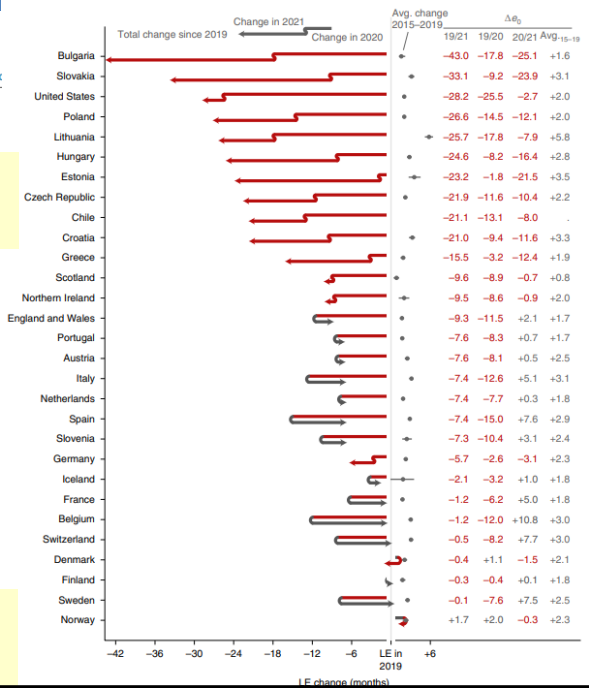
73

nature human behaviour

Article https://doi.org/10.1038/s41562-(

Life expectancy changes since COVID-19

October 2022: Life expectancy deficits across Europe, US, Chile negatively correlated with vaccination uptake



JAMA Network

COVID-19 and Excess All-Cause Mortality in the US and 20 Comparison Countries, June 2021-March 2022

Research Letter

November 18, 2022

Excess COVID mortality in US driven by states with lower vaccination uptake (10 highest vaccinated states like Europe)

74

National Institute for Health and Care Excellence

Final

Vaccine uptake in the general population

[B] Evidence review for the barriers to, and facilitators for, vaccine uptake

NICE guideline NG218

Evidence review underpinning research recommendations in the NICE guideline

May 2022

Greatest Facilitator?
Perception of Risk

75

Vaccines Are Mainstay for Pandemics, Along with Global Surveillance

JAMA Network Open. February 3, 2023

Original Investigation | Public Health

Estimation of Vaccine Effectiveness of CoronaVac and BNT162b2 Against Severe Outcomes Over Time Among Patients With SARS-CoV-2 Omicron

Yuchen Wei, PhD; Katherine Min Jia, MSc; Shi Zhao, PhD; Chi Tim Hung, MBBS; Chris Ka Pun Mok, PhD; Paul Kwok Ming Poon, MBChB; Eman Yee Man Leung, PhD;

REVIEW ARTICLE

https://doi.org/10.1038/s41590-017-0007-9

nature immunology

2018

Emerging viral diseases from a vaccinology perspective: preparing for the next pandemic

Barney S. Graham* and Nancy J. Sullivan*

Emerging infectious diseases will continue to threaten public health and are sustained by global commerce, travel and disruption of ecological systems. Most pandemic threats are caused by viruses from either zoonotic sources or vector-borne sources.

Ocugen Announces Positive Top-Line Data for COVID-19 Vaccine Candidate COVAXIN™ (BBV152) in Phase 2/3 Immuno-bridging and Broadening Study: Both Co-primary Endpoints Met

January 09, 2023 06:00 ET | Source: Ocugen

- Vaccines mainstay for any pathogen
- Those at risk want vaccines
- Targeted messaging campaign towards those at risk, safety, health

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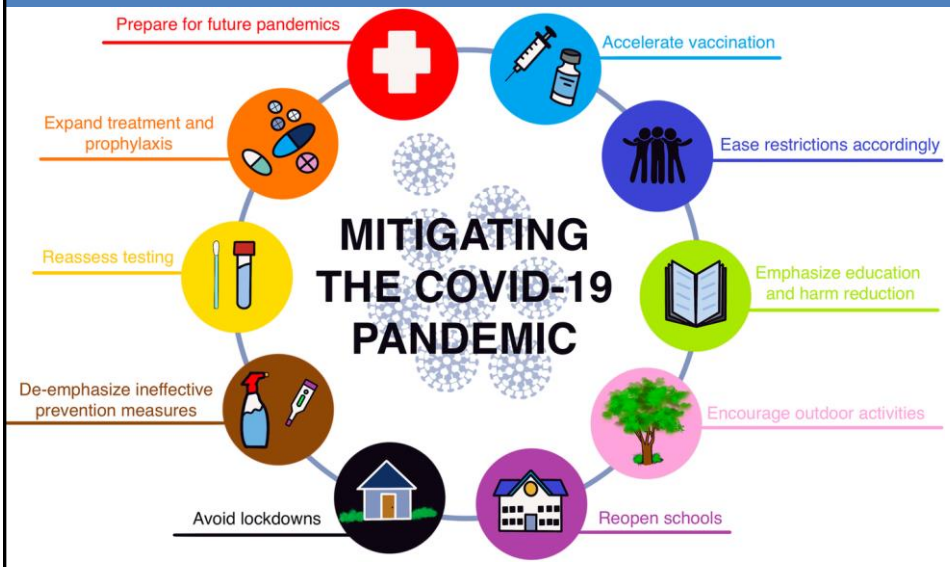
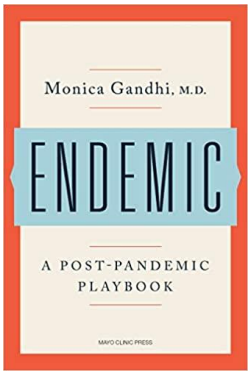
Revisiting COVID-19 policies: 10 evidence-based recommendations for where to go from here

BMC Public Health

Halperin D....Gandhi M





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Take Home Points

- MPOX declared a new global health emergency of international concern on August 14, 2024 after failing to provide vaccines to Africa with the global outbreak 2022-2024
- DoxyPEP recommended now for STD post-exposure prophylaxis for MSM by the CDC
- Old diseases (e.g. polio, measles, mumps) re-emerging in the face of war and vaccine hesitancy
- Watching H5N1 avian influenza carefully as all influenza viruses have pandemic potential
- Need strong global systems of cooperation (e.g. WHO pandemic treaty) in this new era of pandemic preparedness
- Trust in public health has decreased- how do we increase it and prepare?

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