

Top 10 Updates in Infectious Diseases

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1

Disclosure

I have no financial interests or relationships to disclose.

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2

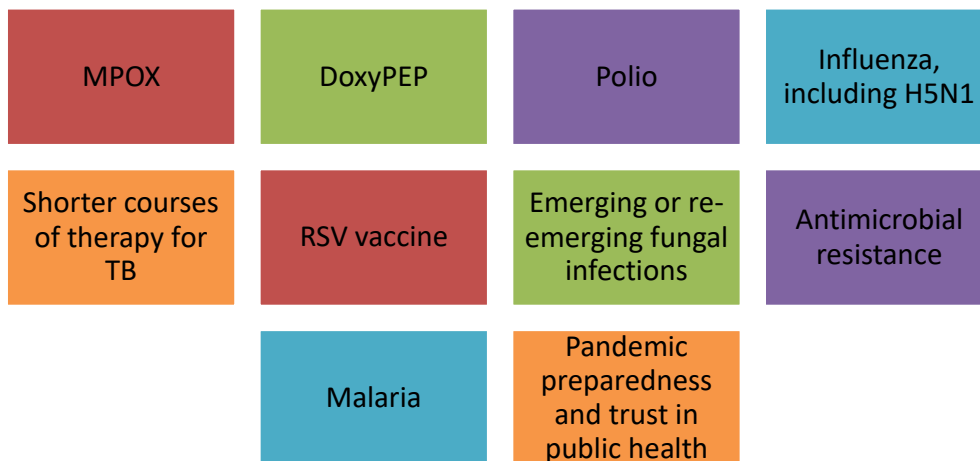
Learning Objectives

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



3

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



4

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

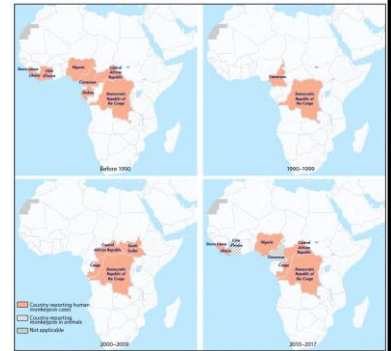


RNA virus

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



7

“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



8



9

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

102 997

Total deaths

223

Countries reporting cases

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>

The chart shows a sharp increase in cases starting in May 2022, peaking in late July 2022 at approximately 6,000 cases per day, and then gradually declining through October 2022 and January 2023. The regions contributing to the outbreak are: African Region (light blue), Eastern Mediterranean Region (purple), European Region (red), Region of the Americas (dark blue), South-East Asia Region (orange), and Western Pacific Region (green).

10



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

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

11 May 2023



11

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, I. Vandekerckhove, M. Yakubovskiy, F. Sendaonorta, I.I. Blanco, F. Florence

12

A Evolution of Cutaneous Lesions

Day -4 Condomless sexual contact in MSM

Day 0 Single genital lesion treated with 1M penicillin as suspected syphilis

Days 4-6 Feeling unwell; additional lesions develop

Day 11 Confirmed monkeypox; facial and genital lesions PCR positive

Day 21 Follow-up 1: facial lesions PCR negative, genital lesions PCR positive

Day 28 Follow-up 2: genital lesions PCR negative

B Oral and Perioral Lesions

C Perianal, Anal, and Rectal Lesions

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

The NEW ENGLAND JOURNAL of MEDICINE

13

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

Monkeypox cases reported to CDC: Race/Ethnicity by Week

Race / Ethnicity

- Other Race
- American Indian or Alaska Native
- Asian
- Black or African American
- Hispanic or Latino
- Multiple Races
- Native Hawaiian or Other Pacific Islander
- White

14

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, PhD¹; Kristen Eberly, MPH¹; Olivia O. Russell, MPH²; Robert E. Snyder, PhD³; Elisabeth K. Phillips, MPH³; Eric C. Tang, MD³; Phillip T. Porco, MD^{1,3}; Malena A. Sanchez, PhD⁴; Ling-Hui, MPH⁴; Stephanie E. Cohen, MD⁴; Elzou K. Sarr, PhD⁵; Sherry Yin, MPH⁵

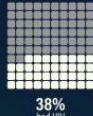
15

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

In the U.S., HIV or recent sexually transmitted infections (STIs)* are common among people with monkeypox


Among nearly 2,000 people with monkeypox[†]



38%
had HIV



41%
had an STI in the past year




61%
had either HIV or an STI


It is important to

Prioritize people with HIV and STIs for monkeypox vaccination

Offer HIV and STI screening for people evaluated for monkeypox



*Diagnosed with an STI other than HIV in the past year
†People diagnosed with monkeypox in eight jurisdictions during May 17–July 22, 2022
MMWR/71/36/1



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

16

Clinical Infectious Diseases

VIEWPOINTS





A Position Statement on Mpox as a Sexually Transmitted Disease

Lao-Tzu Allan-Blitz,^{1,6} Monica Gandhi,^{2,3} Paul Adamson,⁴ Ina Park,⁵ Gail Bolan,⁶ and Jeffrey D. Klausner⁷

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

 **NEWS**
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U.S. NEWS
BUSINESS
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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

17

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.



Centers for Disease Control and Prevention
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- 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.

18



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).

19

What Do We Know About the Vaccine?

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^g, Seth Blumberg^{b,g}, Henri A. Thomassen^h, Brian L. Pike^h, Joseph N. Fai^h, Nathan D. Wol Robert L. Shongoⁱ, Barney S. Graham^j, Pierre Formenty^k, Emile Okitolonda^l, Lisa E. Hensley^d, Hermann Meye Linda L. Wright^m, and Jean-Jacques Muyembeⁿ



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

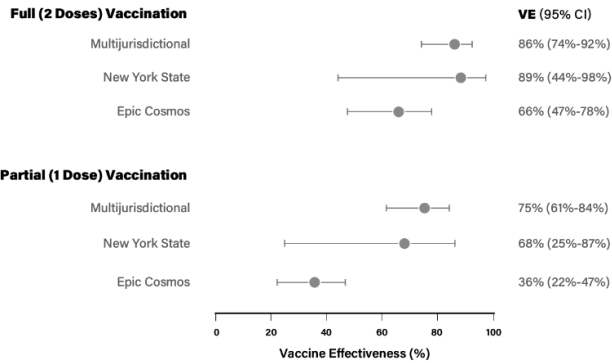
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Estimated Effectiveness of JYNNEOS Vaccine in Preventing Mpox: A Multijurisdictional Case-Control Study — United States, August 19, 2022–March 31, 2023

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



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



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

21

Mpox Outbreak in Africa 2023-2024

August 14, 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

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

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



22

Characteristics of the MPOXV Clades

- Two clades of mpox – I (formerly Congo) and II (formerly West African), each with two subclasses (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 subclass that caused the 2022 global outbreak, predominantly sexually transmissible, mainly men-who-have-sex-with-men



23



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.

24



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

[Situation in the United States](#)

[Situation in DRC](#)



25

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*.



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

26

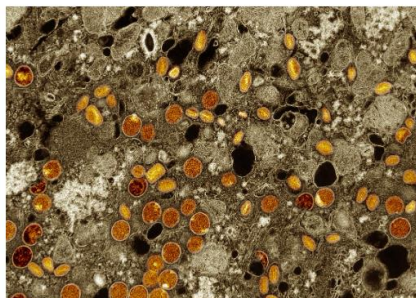
Thursday, August 15, 2024

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

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

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-



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

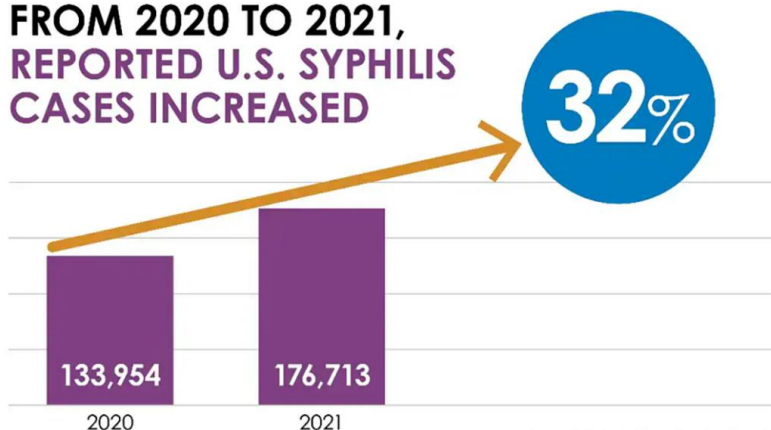
MPOX	DoxyPEP	Polio	Influenza, including H5N1
Shorter courses of therapy for TB	RSV vaccine	Emerging or re-emerging fungal infections	Antimicrobial resistance
	Malaria	Pandemic preparedness and trust in public health	

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

**FROM 2020 TO 2021,
REPORTED U.S. SYPHILIS
CASES INCREASED**



Source: U.S. Centers for Disease Control and Prevention

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ORIGINAL ARTICLE

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.,
Cole Crabb, M.D., Clara E. Brown, Ph.D., Chad Malinski, B.S.

DoxyPEP Study

April 6, 2023

Group	No. of Events / No. of Participants
Standard-Care Groups PrEP cohort	53/107
Standard-Care Groups PLWH cohort	24/55
Doxycycline Groups PrEP cohort	51/220
Doxycycline Groups PLWH cohort	30/119

- 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

31

December 20, 2023

ORIGINAL ARTICLE

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 Study of DoxyPEP in Women in Kenya

Group	No. of Events / Total No. of Participants
Standard Care	49/222
Doxycycline PEP	46/220

Hazard ratio with doxycycline PEP, 0.95 (95% CI, 0.64–1.42)
P=0.81 by log-rank test

- 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)

32

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

35

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

36

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

July 21, 2022

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

37

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

38

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Antimicrobial
resistance

Malaria

Pandemic
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39

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

- A. 14 out of 14 20%
- B. 13 out of 14 20%
- C. 12 out of 14 20%
- D. 11 out of 14 20%
- E. 10 out of 14 20%

40

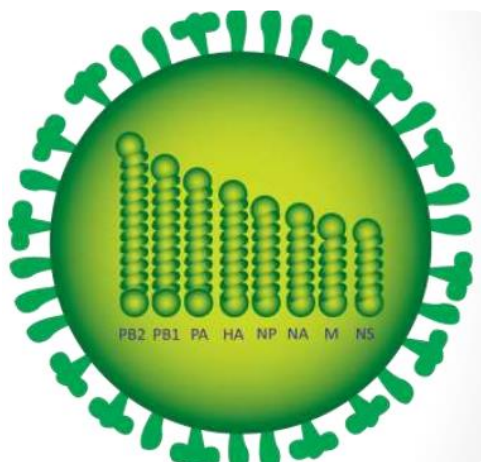
Influenza

- 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



41

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

42

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**

43



CDC Confirms Human H5 Bird Flu Case in Missouri

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.

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

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.

44

Influenza Vaccine – Recommended Once Yearly

Three different kinds of influenza vaccines

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graph TD
    A[Three different kinds of influenza vaccines] --> B[INACTIVATED(IIV4)  
(Multiple brands, don't give to those with history of egg allergy)]
    A --> C[RECOMBINANT(RIV4)  
(Only Flublok Quadrivalent® available; for those with egg allergy)]
    A --> D[LIVE ATTENUATED (LAIV4)  
(FluMist quadrivalent®; not recommended for people with HIV, even with high CD4 counts by CDC)]
            
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If >65 years, use high-dose quadrivalent vaccine (recombinant, allIV4, HD-IIV4 in inactivated)

45

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	Malaria	Pandemic preparedness and trust in public health	

46

How Long Can We Treat Rifampin-sensitive TB with a New Short-course Regimen?

- A. 2 months
- B. 4 months
- C. 6 months
- D. 12 months



47

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ORIGINAL ARTICLE

Four-Month Rifapentine Regimens with or without Moxifloxacin for Tuberculosis

S.E. Dorman, P. Nahid, E.V. Kurbatova, P.P.J. Phillips, K. Bryant, K.E. Dooley, M. Engle, S.V. Goldberg, H.T.T. Phan, J. Hakim, J.L. Johnson, M. Lourens, N.A. Martinson, G. Muzanyi, K. Narunsky, S. Nerette, N.V. Nguyen, T.H. Pham, S. Pierre, A.E. Purfield, W. Samaneka, R.M. Savic, I. Sanne, N.A. Scott, J. Shenje, E. Sizemore, A. Vernon, Z. Waja, M. Weiner, S. Swindells, and R.E. Chaisson, for the AIDS Clinical Trials Group and the Tuberculosis Trials Consortium

ABSTRACT

48

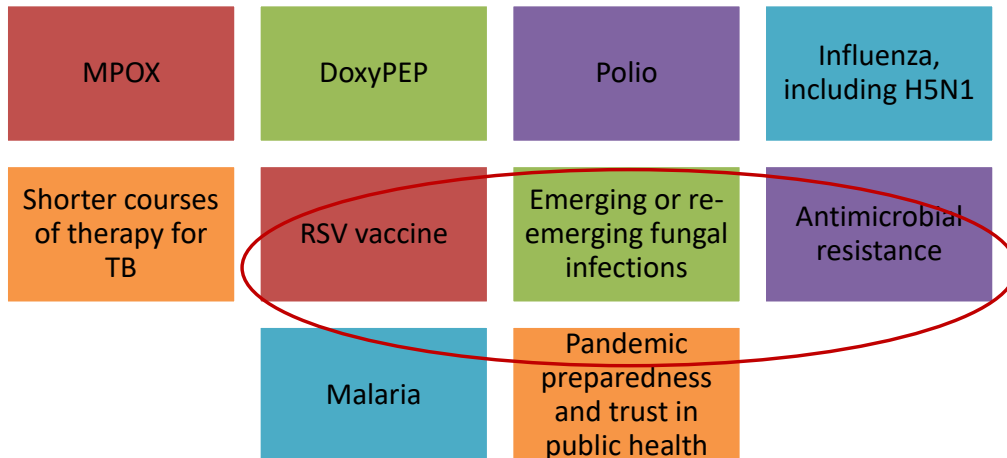
RIPE (INH, Rif, PZA, EMB) x 8 weeks, then INH/Rif x 18 weeks	Rifapentine/INH/PZA/EMB x 8 weeks + Rifapentine/INH x 9 weeks				Rifapentine/INH/PZA/Moxi x 8 weeks + Rifapentine/Moxi/INH x 9 weeks			
Table 2. Primary Efficacy Analysis in the Microbiologically Eligible and the Assessable Populations.*								
Outcome	Microbiologically Eligible Population				Assessable Population			
	Control (N=768)	Rifapentine-Moxifloxacin (N=791)	Rifapentine (N=784)	Total (N=2343)	Control (N=726)	Rifapentine-Moxifloxacin (N=756)	Rifapentine (N=752)	Total (N=2234)
Favorable								
Participants with outcome — no. (%)	656 (85.4)	668 (84.5)	645 (82.3)	1969 (84.0)	656 (90.4)	668 (88.4)	645 (85.8)	1969 (88.1)
Adjusted difference from control — percentage points (95% CI)	NA	1.0 (-2.6 to 4.5)	3.0 (-0.6 to 6.6)	NA	NA	2.0 (-1.1 to 5.1)	4.4 (1.2 to 7.7)	NA
Participant had negative culture at month 12 — no. (%)	643 (83.7)	656 (82.9)	636 (81.1)	1935 (82.6)	643 (88.6)	656 (86.8)	636 (84.6)	1935 (86.6)
Participant was seen at month 12 but no sputum was produced or cultures were contaminated but without evidence of <i>M. tuberculosis</i> — no. (%)	13 (1.7)	12 (1.5)	9 (1.1)	34 (1.5)	13 (1.8)	12 (1.6)	9 (1.2)	34 (1.5)
Unfavorable								
Participants with outcome — no. (%)	112 (14.6)	123 (15.5)	139 (17.7)	374 (16.0)	DISCUSSION In this phase 3 trial, the efficacy of the 4-month regimen containing rifapentine and moxifloxacin was noninferior to that of the standard 6-month regimen. Noninferiority of the rifapentine-moxifloxacin regimen to the control regimen was confirmed across analysis populations as well as in sensitivity and prespecified subgroup analyses. The efficacy of the 4-month regimen			
Outcome related to tuberculosis — no. (%)	24 (3.1)	45 (5.7)	75 (9.6)	144 (6.2)				
Two consecutive positive cultures at or after week 17 [†]	11 (1.4)	34 (4.3)	63 (8.0)	108 (4.6)				
Participant not seen at month 12 but had positive culture when last seen	11 (1.4)	3 (0.4)	4 (0.5)	18 (0.8)				

49

CDC		Interim Guidance: 4-Month Rifapentine-Moxifloxacin Regimen for the Treatment of Drug-Susceptible Pulmonary Tuberculosis — United States, 2022			
Weekly / February 25, 2022 / 71(8):285-289					
TABLE 1. Dosing recommendation for a 4-month rifapentine-moxifloxacin regimen for patients aged ≥12 years with pulmonary tuberculosis caused by drug-susceptible organisms — United States, 2022					
Medication*	Body weight, kg	Dose	Intensive phase	Continuation phase	Total doses
Rifapentine	≥40	1,200 mg	7 days/wk for 56 doses (8 wks)	7 days/wk for 63 doses (9 wks)	119
Moxifloxacin	≥40	400 mg			
Isoniazid [†]	≥40	300 mg			
Pyrazinamide	40–<55	1,000 mg	NA		
	≥55–75	1,500 mg			
	>75 kg	2,000 mg			

50

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



51

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

52



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

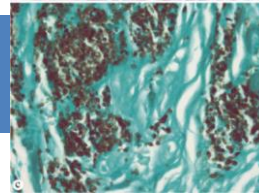
RSV Vaccine Guidance for Older Adults

WHAT TO KNOW

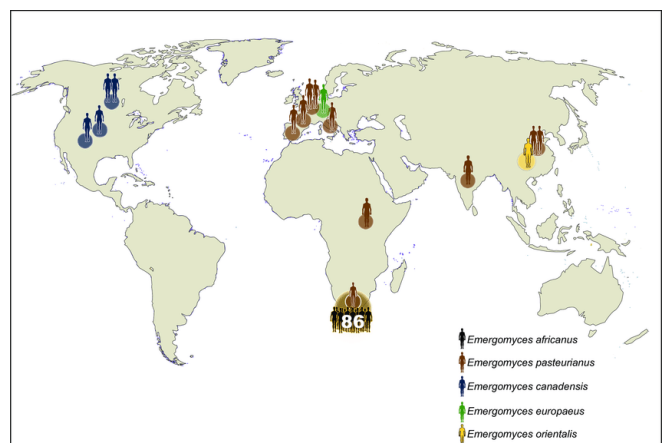
- CDC recommends a single dose of any FDA-licensed RSV vaccine for all adults ages 75 and older and adults ages 60–74 at increased risk of severe RSV.
- Three RSV vaccines are currently available for adults ages 60 and older: GSK's Arexvy, Moderna's mResvia, and Pfizer's Abrysvo. Eligible older adults 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.

53

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

54

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

55

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.

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. Previous publications have estimated the effect of AMR on incidence, deaths, hospital length of stay, and health-care costs for specific pathogen–drug combinations in select locations. To our knowledge, this study presents the most comprehensive estimates of AMR burden to date.

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

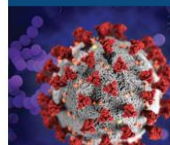
Media Statement

For Immediate Release: Tuesday, July 12, 2022

Contact: Media Relations
(404) 639-3286

COVID-19 CREATED A PERFECT STORM

The U.S. lost progress combating antimicrobial resistance in 2020



↑15% Antimicrobial-resistant infections and deaths increased in hospitals in 2020.

~80% Patients hospitalized with COVID-19 who received an antibiotic March–October 2020.



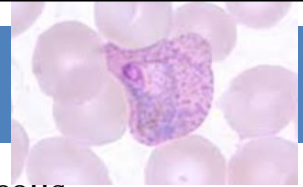
Delayed or unavailable data, leading to resistant infections spreading undetected and untreated.

Setbacks to fighting antimicrobial resistance can and must be temporary.



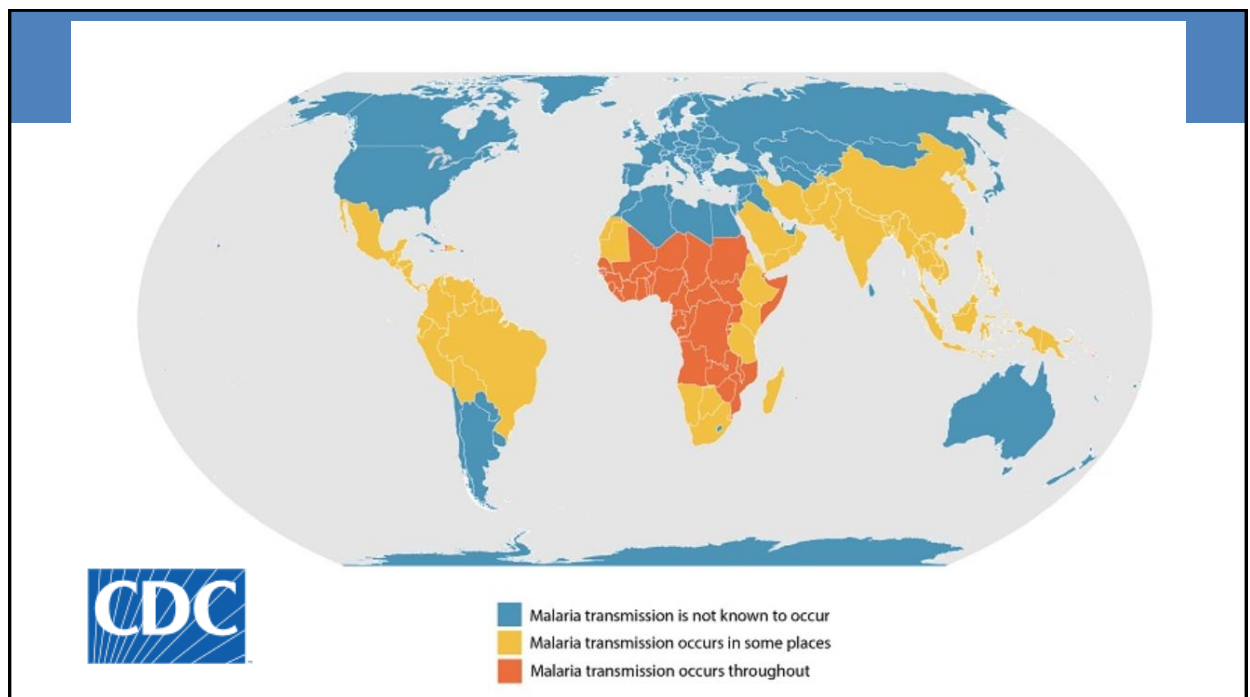
56

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.

57



58

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



59







Pandemic Preparedness

60

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

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	<ul style="list-style-type: none"> Pathogens can go to new niches, have access to new hosts
 Interaction with animals (hunting, eating, pets)	<ul style="list-style-type: none"> Zoonoses is when a microbe jumps from nonhuman to human hosts
 Changes in agriculture	<ul style="list-style-type: none"> New crops attract new pests
 Encroachment on animal habitats	<ul style="list-style-type: none"> Other animals crowded, microbes can mutate, mix Destruction of rain forests bring humans into contact with unfamiliar microbes
 Urbanization	<ul style="list-style-type: none"> People more crowded together, contagious diseases
 Other	<ul style="list-style-type: none"> 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.

61

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.



62

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%

Public trust in sources of health information among US adults, by degree of trust, 2022

Source	A great deal	Somewhat	Not very much	Not at all
Doctors	54%	48%	1%	0%
Nurses	48%	48%	2%	0%
Scientists working on health issues	37%	48%	10%	5%
Pharmacists	37%	48%	10%	5%
American Cancer Society	37%	48%	10%	5%
Health researchers	37%	48%	10%	5%
Centers for Disease Control and Prevention	37%	48%	10%	5%
National Institutes of Health	33%	48%	10%	9%
Surgeon General	33%	48%	10%	9%
Food and Drug Administration	30%	48%	10%	12%
American Red Cross	30%	48%	10%	12%
Their local public health department	30%	48%	10%	12%
Their state public health department	30%	48%	10%	12%
Their friends and family	15%	48%	25%	12%
Their religious leaders	15%	48%	25%	12%
Their state elected officials	15%	48%	25%	12%
Their local elected officials	15%	48%	25%	12%

63

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

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

64

Monica Gandhi, MD
Top 10 Updates in Infectious Disease

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.

Response	Oct '23	Apr '21
Definitely true	32%	34%
Probably true	39%	43%
Not sure	13%	14%
Probably false	10%	6%
Definitely false	6%	6%

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

Exemptions for required vaccines for US kindergartners reach record high
November 9, 2023

65

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

66

Zimbabwe Says Measles Outbreak Has Killed 700 Children



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

11 May, 2023

67

SARS-CoV-2 History¹⁻³



- 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](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)

68

Company or name	Type of vaccine	Reference	
Moderna	mRNA vaccine (US)	Baden NEJM , Feb 4, 2021	<p>There are actually 8 unique vaccines approved by WHO for COVID-19 (Sputnik V pending), three authorized in U.S.</p>
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	

69

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



NO ONE IS SAFE UNTIL EVERYONE IS SAFE.

- **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.

70

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

71

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](https://doi.org/10.1016/S0140-6736(21)02796-3)

THE LANCET

72

nature human behaviour

Article <https://doi.org/10.1038/s41562-022-01411-1>

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)

Country	19/21	19/20	20/21	Avg ₁₅₋₁₉
Bulgaria	-43.0	-17.8	-25.1	+1.6
Slovakia	-33.1	-9.2	-23.9	+3.1
United States	-28.2	-25.5	-2.7	+2.0
Poland	-26.6	-14.5	-12.1	+2.0
Lithuania	-25.7	-17.8	-7.9	+5.8
Hungary	-24.6	-8.2	-16.4	+2.8
Estonia	-23.2	-1.8	-21.5	+3.5
Czech Republic	-21.9	-11.6	-10.4	+2.2
Chile	-21.1	-13.1	-8.0	.
Croatia	-21.0	-9.4	-11.6	+3.3
Greece	-15.5	-3.2	-12.4	+1.9
Scotland	-9.6	-8.9	-0.7	+0.8
Northern Ireland	-9.5	-8.6	-0.9	+2.0
England and Wales	-9.3	-11.5	+2.1	+1.7
Portugal	-7.6	-8.3	+0.7	+1.7
Austria	-7.6	-8.1	+0.5	+2.5
Italy	-7.4	-12.6	+5.1	+3.1
Netherlands	-7.4	-7.7	+0.3	+1.8
Spain	-7.4	-15.0	+7.6	+2.9
Slovenia	-7.3	-10.4	+3.1	+2.4
Germany	-5.7	-2.6	-3.1	+2.3
Iceland	-2.1	-3.2	+1.0	+1.8
France	-1.2	-6.2	+5.0	+1.8
Belgium	-1.2	-12.0	+10.8	+3.0
Switzerland	-0.5	-8.2	+7.7	+3.0
Denmark	-0.4	+1.1	-1.5	+2.1
Finland	-0.3	-0.4	+0.1	+1.8
Sweden	-0.1	-7.6	+7.5	+2.5
Norway	+1.7	+2.0	-0.3	+2.3

73

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

74

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

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

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.

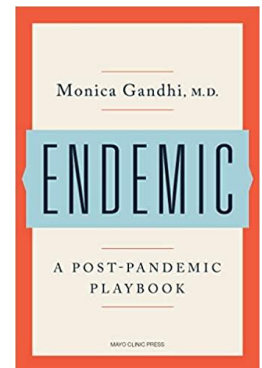
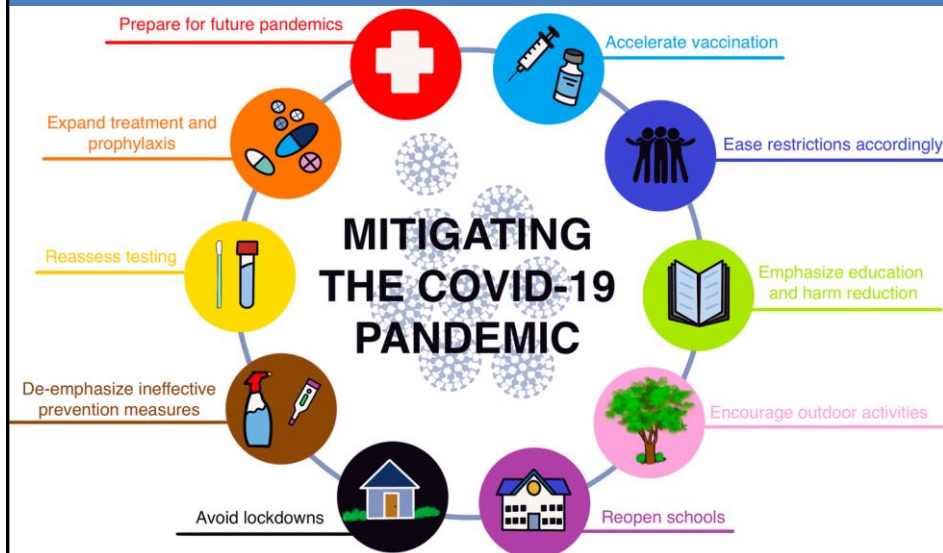
- Vaccines mainstay for any pathogen
- Those at risk want vaccines
- Targeted messaging campaign towards those at risk, safety, health

75

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

BMC Public Health

Halperin D....Gandhi M



76