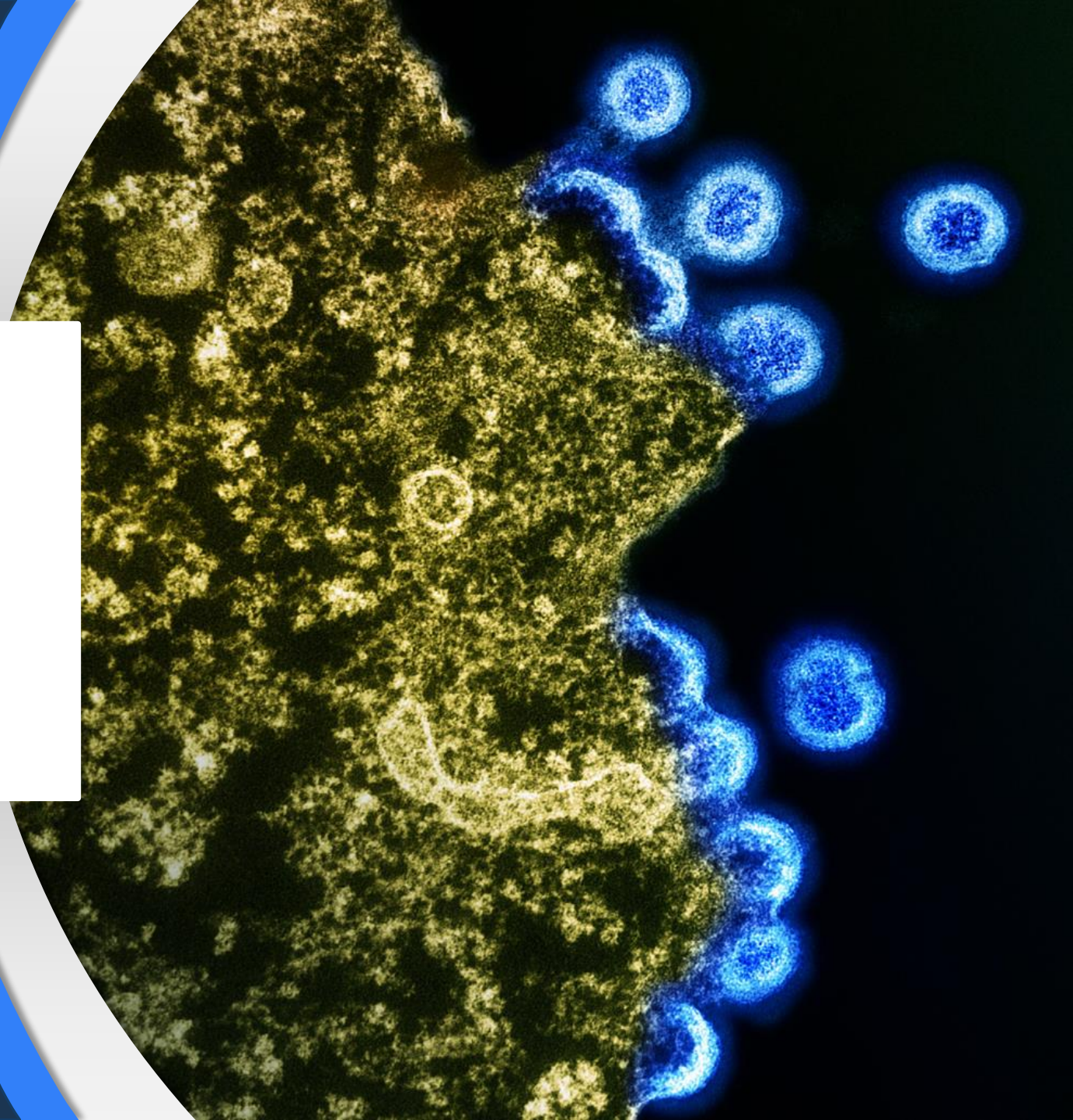
National Institute of Allergy and Infectious Diseases

2024 HPTN Annual Meeting

June 18, 2024

JEANNE MARRAZZO, MD, MPH
DIRECTOR, NIAID



Framework for Presentation

- Budget Update
- Shaping the Future
- Opportunities in Infectious Disease Research
- HPTN's Vital Role

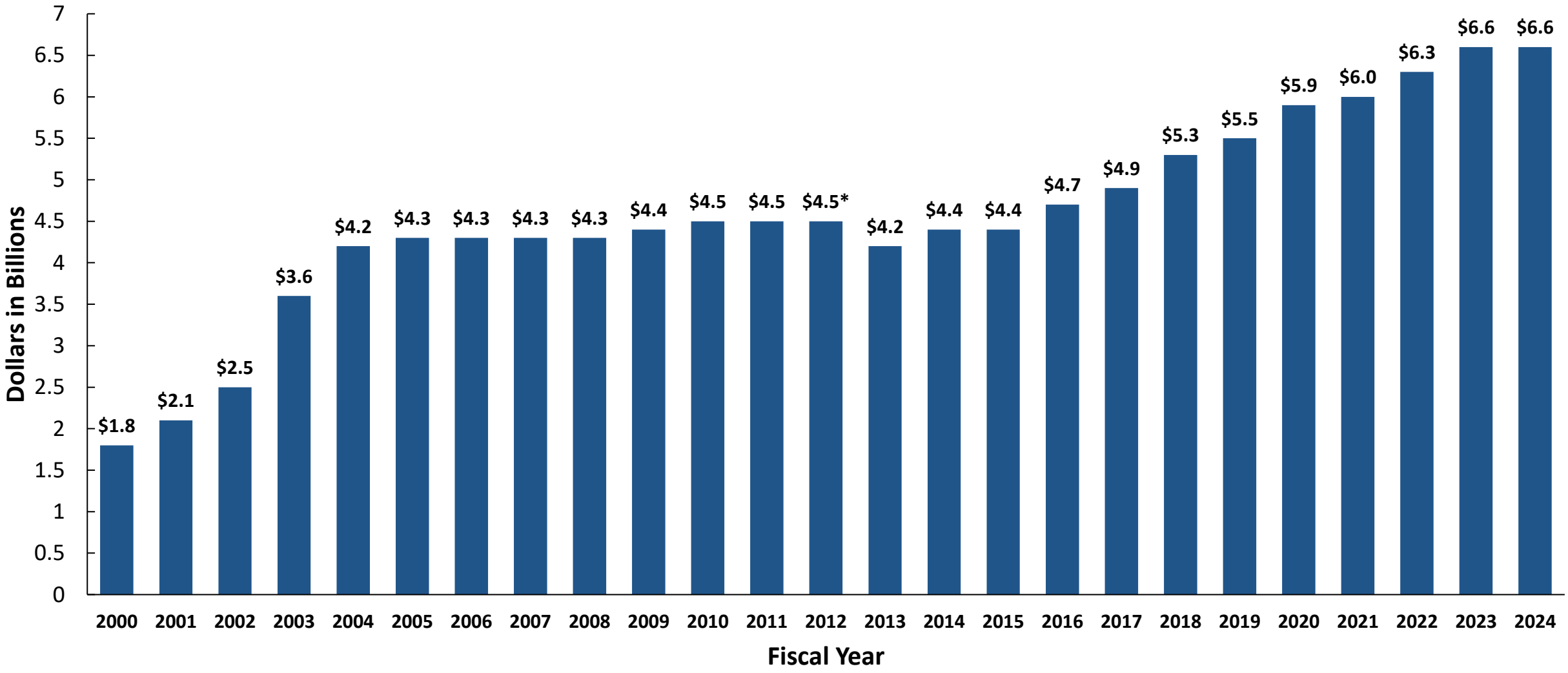
NIH Budget Comparison by Institute/Center

(Dollars in thousands)

Institute	FY 2023 Enacted	FY 2024 Enacted	FY24 versus FY23 Change
NCI	$7,317,241	$7,104,159	-2.9%
NIAID	$6,562,279	$6,562,279	0.0%
NHLBI	$3,985,158	$3,982,345	-0.1%
NHGRI	$660,510	$663,200	0.4%
NCATS	$923,323	$923,323	0.0%
NIGMS	$3,239,679	$3,239,679	0.0%
NIA	$4,412,090	$4,407,623	-0.1%
NIDA	$1,663,365	$1,662,695	0.0%
Other ICs	$15,499,259	$15,228,218	-1.7%
Subtotal	$44,262,277	$43,773,521	-1.1%
OD	$3,066,208	$2,885,514	-5.9%
B & F	$350,000	$350,000	0.0%
NIH Program Level**	$47,678,485	$47,009,035	-1.4%

***Includes Type 1 Diabetes, Non-HHS Appro. (Superfund), and excludes NIH-OAR AIDS transfers*

NIAID Funding, FY 2000-2024



**Beginning in FY 2012, budget no longer passes through funds to the Global Fund*

FY 2025 President's Budget Request

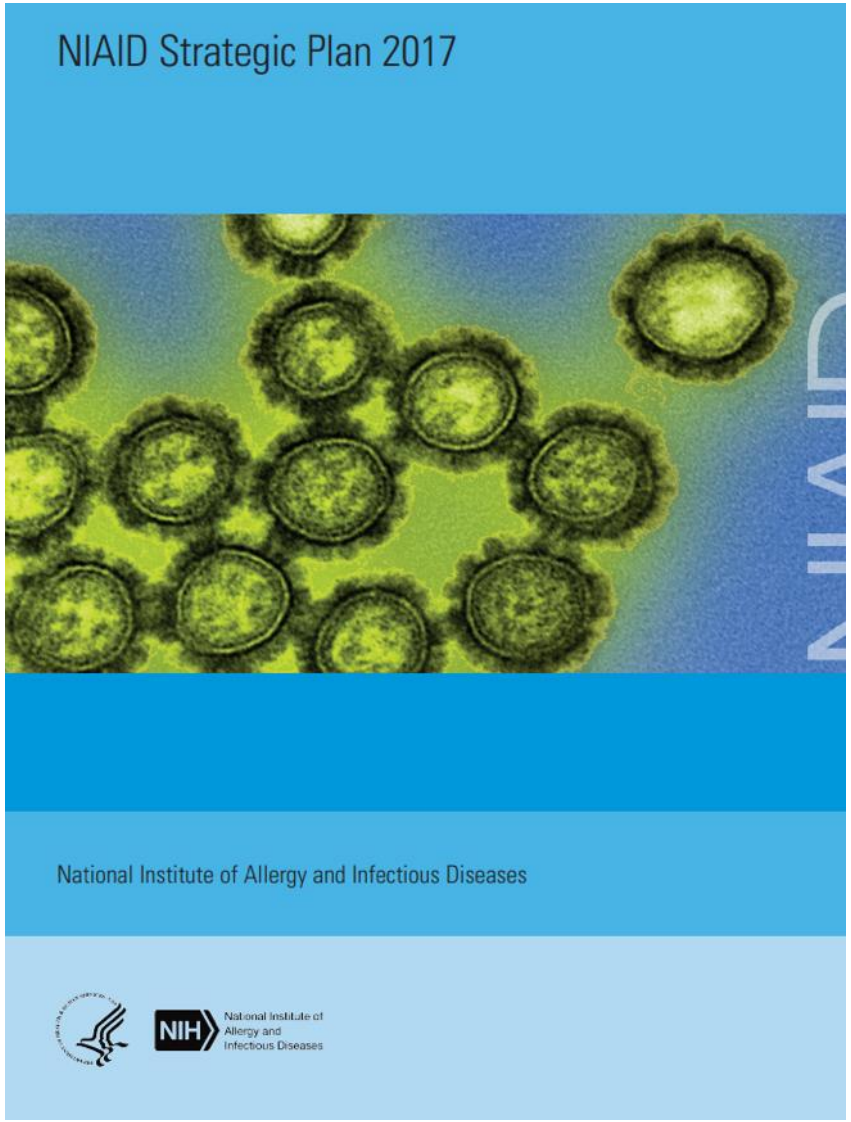
- Released March 11, 2024
- NIH Proposed Program level budget $50.1 billion (excluding ARPA-H)
  - NIAID budget request $6.581B ($19M over FY 2024)

NIH Budget Comparison by Institute/Center

(Dollars in thousands)

Institute	FY 2024 Enacted	FY 2025 President's Budget	% Change
NCI	$7,224,159	$9,287,141	28.6%
NIAID	$6,562,279	$6,581,291	0.3%
NHLBI	$3,982,345	$3,997,086	0.4%
NHGRI	$663,200	$663,660	0.1%
NCATS	$928,323	$926,086	-0.2%
NIGMS	$3,244,679	$3,249,375	0.1%
NIA	$4,507,623	$4,425,295	-1.8%
NIDA	$1,662,695	$1,668,343	0.3%
Other ICs	$15,390,650	$15,923,785	3.5%
Subtotal	$44,165,953	$46,722,062	5.8%
ARPA-H	$1,500,000	$1,500,000	0.0%
OD	$2,885,514	$3,044,455	5.5%
B&F	$350,000	$350,000	0.0%
NIH Program Level*	$48,901,467	$51,616,517	5.6%

Includes Type I Diabetes and Non-HHS/Labor Appropriation (Superfund). Excludes OAR transfers



Shaping the future

NIAID is in the process of reevaluating the Institute's priorities:

- Infectious and Immune-Mediated Diseases Research
- Pandemic Preparedness
- Training/Workforce
- Infrastructure
- Community Engagement

We welcome your feedback!

NIAID Strategic Plan Crosscutting Themes

Addressing Health Disparities

Understand, reduce, and ultimately prevent health disparities in disadvantaged populations, including

- Racial and ethnic minorities
- Sexual and gender minorities
- People with low SES
- Rural communities
- People with disabilities

Advancing Women's Health

Address the health of all women and individuals assigned female at birth.

Expanding Research Inclusivity

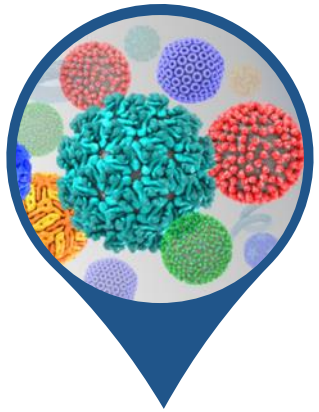
Intentional and appropriate inclusion of diverse populations in human subjects' research.

Supporting Global Health

Invest in international research and collaborations and build global research capacities.

People are the Unifying Element for Combating Disease

Pandemic Preparedness

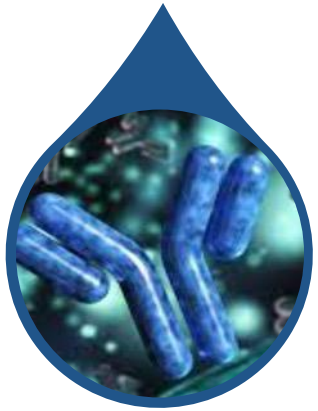


HIV-Related Research

Research Infrastructure

PIPELINE OF RESEARCHERS

Allergy & Immunology



Diversity, Equity, Inclusion, and Accessibility

Strengthening the Investigator Pipeline is Imperative

Number of **Infectious Disease fellows** is declining

- ~67% of ID positions filled in 2023*

Number of **NIH-supported postdoctoral scholars** is declining**

Number of **U.S. citizens & permanent resident biological/biomedical postdoctoral scholars** is declining

- 10% drop from 2021 to 2022***

*NRMP 2024 SMS Fellowship Matches **NIH Office of Extramural Research *** NSF Survey of Graduate Students and Postdoctorates in Science and Engineering

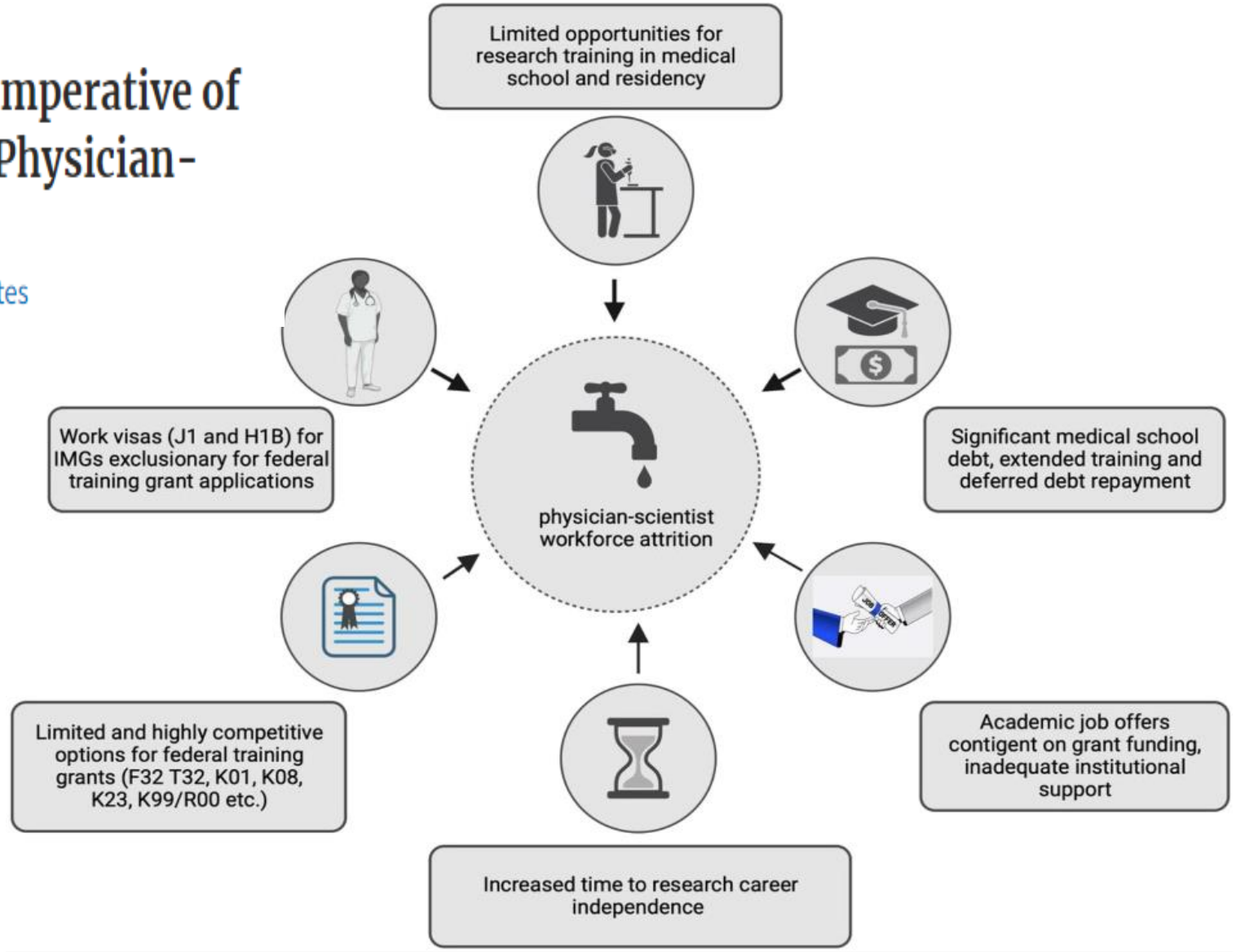
Addressing the Challenges

JOURNAL ARTICLE CORRECTED PROOF EDITOR'S CHOICE

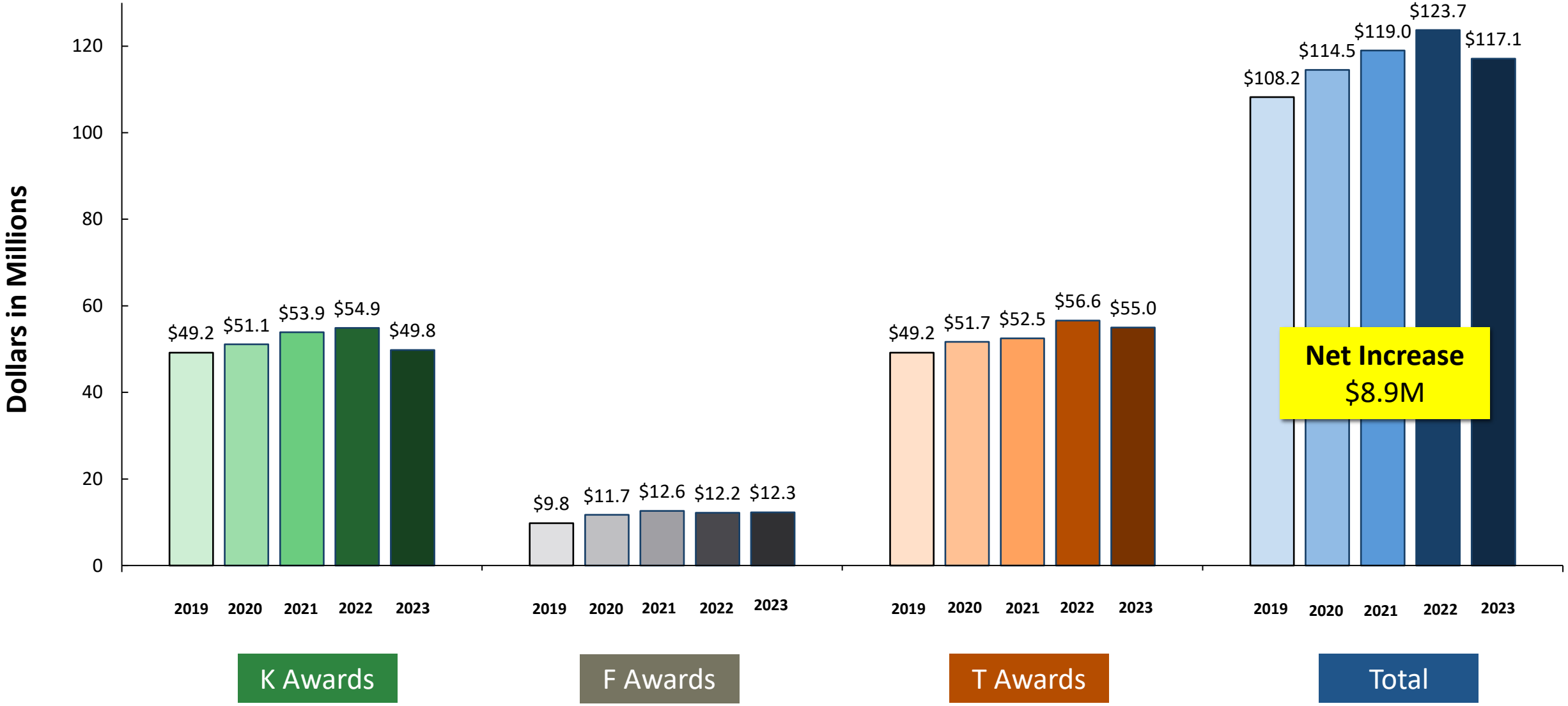
Culturing the Future of Medicine: The Imperative of Strengthening the Infectious Diseases Physician-Scientist Pipeline FREE

Boghuma K Titanji ✉, Irini Sereti, Benjamin D Singer Author Notes

The Journal of Infectious Diseases



NIAID Training Budget Trends (FY 2019 – 2023)



NIAID Efforts to Balance the Training Portfolio

Overall NIAID Training Budget

Maintain Innovative T32 Program

- Examine priorities for T32 portfolio
- Conduct an annual review of **institutions with multiple T32 grants**

F Budget

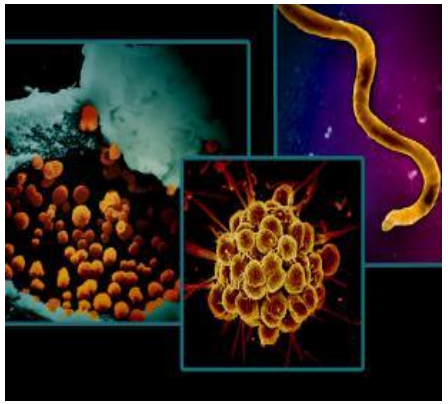
*increase **success rates** and **diversity***

K Budget

Increase success rates
Increase salary and research budgets

NIAID Training Working Group to Assess the Portfolio Annually

WHO Situation Report on HIV, Hepatitis and Sexually Transmitted Diseases



~1.3 million new HIV infections; higher incidence among MSM, IDUs, sex workers, transgenders, people in prisons; 630,000 HIV-related deaths

~8 million new syphilis cases among adults aged 15-49 years; increases in congenital syphilis; 220,000 syphilis-associated deaths

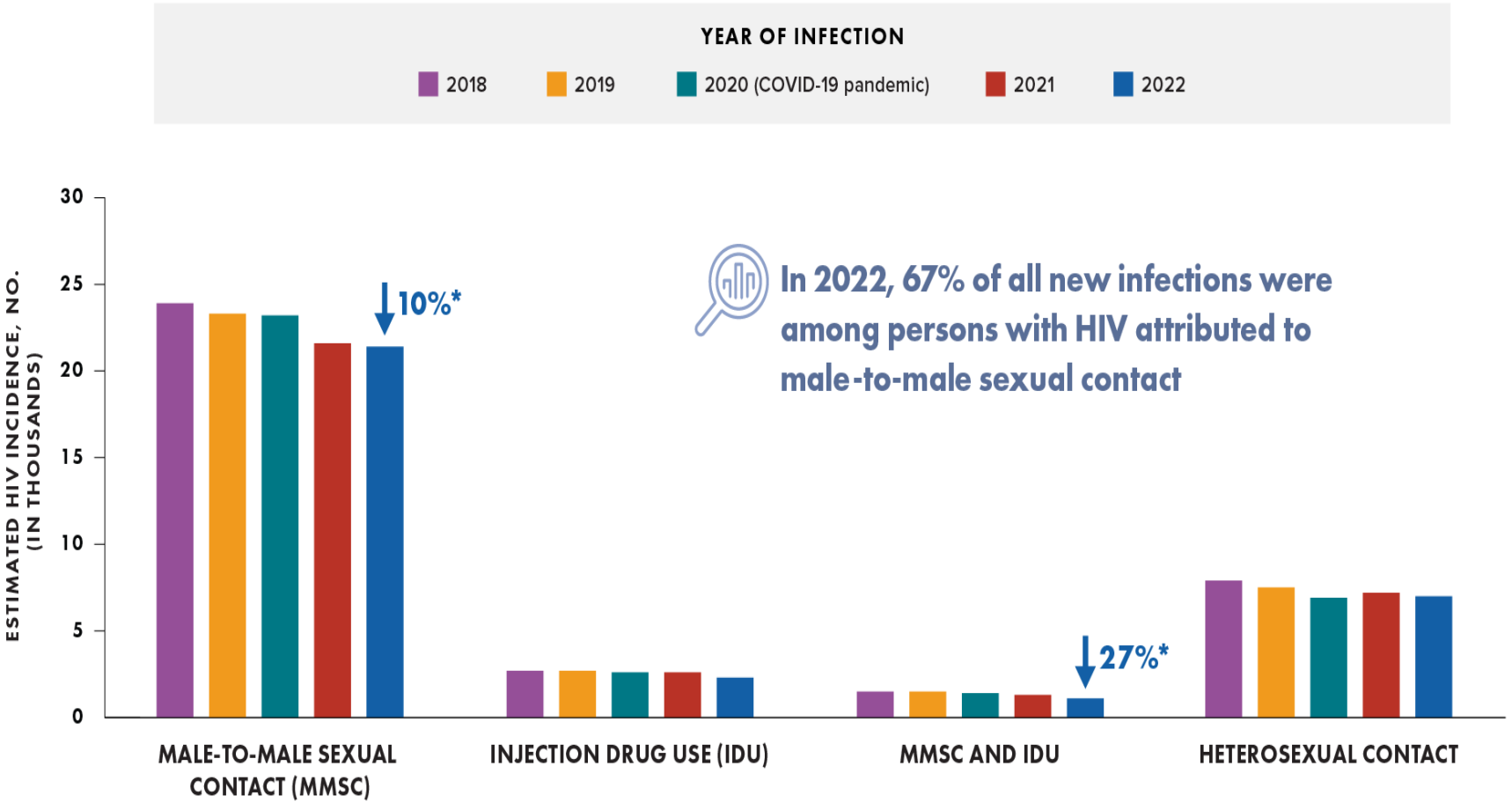
>1 million infections daily of four curable STIs – syphilis, gonorrhea, chlamydia, and trichomoniasis

>80 countries reporting gonorrhea antimicrobial resistance

~1.2 million new hepatitis B infections; ~1 million new hepatitis C infections; 1.3 million deaths associated with viral hepatitis

WHO, 2024

Estimated HIV incidence among persons aged ≥ 13 years, by transmission category, 2018–2022—United States



- In 2022, an estimated 31,800 new HIV infections occurred, representing a 12% decline from 36,200 new infections in 2018
- ~1.2 million people in the U.S. have HIV; about 13% do not know their HIV serostatus
- HIV continues to disproportionately impact certain populations, particularly racial and ethnic minorities and gay, bisexual, and other MSM
- New HIV diagnoses are not evenly distributed across States and regions with highest rates continuing in the South

Source: Estimated HIV Incidence and Prevalence in the United States, 2018–2022 Report, 2024, CDC

EDITORIAL

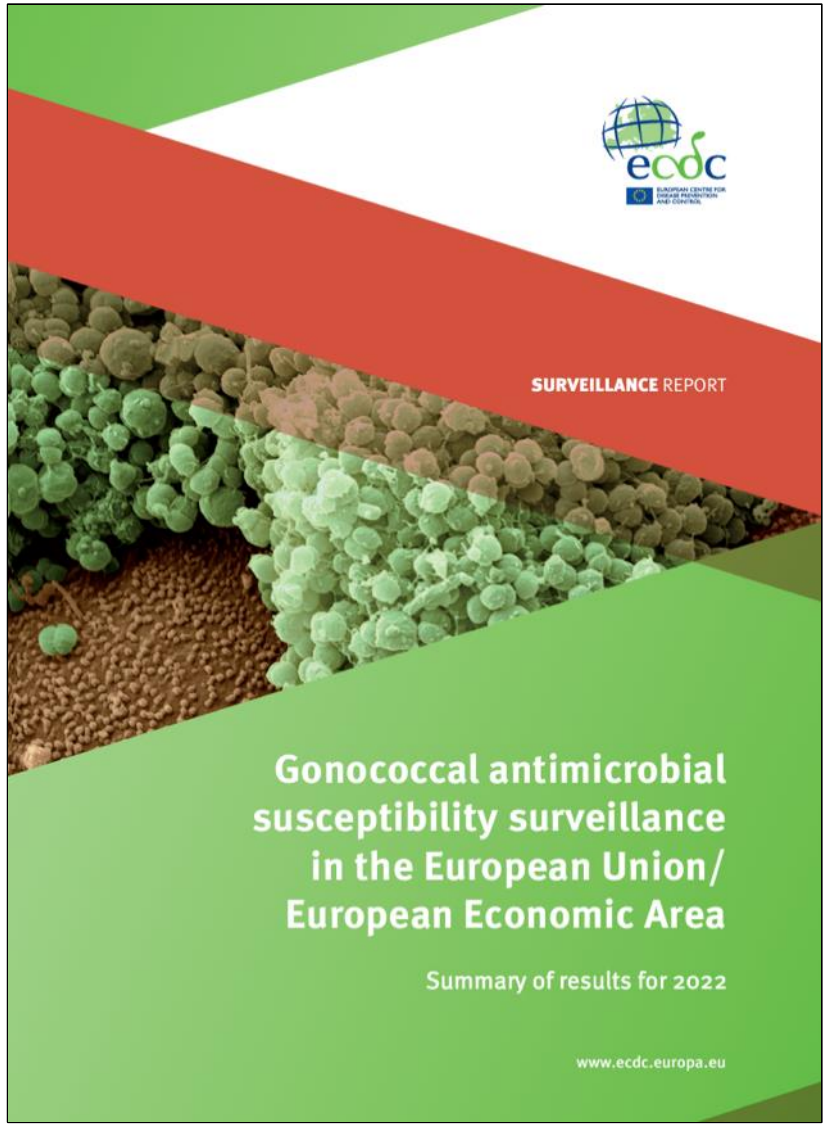
Doxycycline Postexposure Prophylaxis for STIs in Women — Uncertain Benefit, Urgent Need

J Marrazzo

The NEW ENGLAND JOURNAL of MEDICINE

2023 Dec 20; VOL. 389 NO. 25

"…opportunity to reconsider how to strategically inform the design and conduct of biomedical intervention trials involving women of reproductive age."



Increasing Threat of Antimicrobial Resistance in *Neisseria gonorrhoeae*

- In 2022, 70,881 cases of gonorrhea reported from 28 EU/EEA nations reflects 48% increase over 2021
- 25.6% of 4,396 isolates resistant to azithromycin compared to 14.2% in 2021
- 65.9% of 4,396 isolated resistant to ciprofloxacin compared to 62.8% in 2021
- Resistance to cefixime remains low at 0.3%
- Continued detection of occasional ceftriaxone resistance
- Critical need for enhanced surveillance, quality-assured antimicrobial susceptibility testing, antibiotic stewardship, early treatment, more therapeutic options, safer sexual practices and prevention strategies

ECDC, May 2024

Zoliflodacin Approved for Uncomplicated Gonorrhea

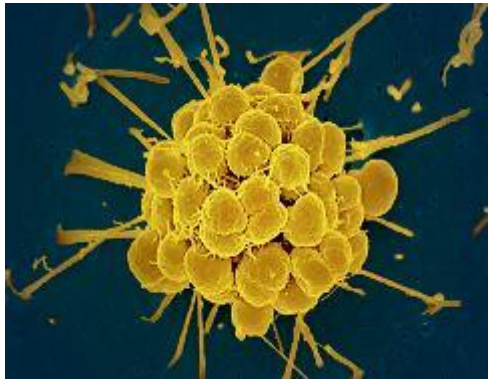
Gonorrhea afflicts more than 80 million adults worldwide each year

Demonstrated resistance to treatment options

NIAID sponsored three clinical studies to evaluate safety, pharmacokinetics, and antimicrobial activity

Phase 3 Non-Inferiority Trial of Zoliflodacin Completed

- Sponsor: Global Antibiotic Research & Development Partnership
- Oral antibiotic that inhibits replication of bacterial DNA
- Safe and as effective as standard therapy



What if We Had a Vaccine that Prevents *Neisseria gonorrhoeae*? Inspiration, Assumptions, and Aspirations

Myron S. Cohen[1] **and Jeanne M. Marrazzo**[2]

[1]UNC Chapel Hill, SOM Institute for Global Health and Infectious Diseases, Chapel Hill, NC, USA; and [2]The National Institute of Health, The National Institute of Allergy and Infectious Diseases, Bethesda, MD USA

"The [mathematical] models presented suggest that successful deployment of a vaccine with even modest efficacy could reduce the spread of *N. gonorrhoeae*."

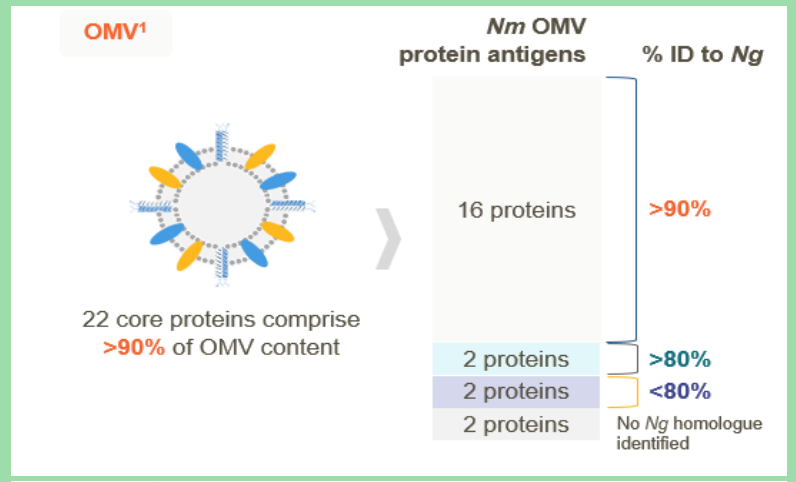
The Journal of Infectious Diseases

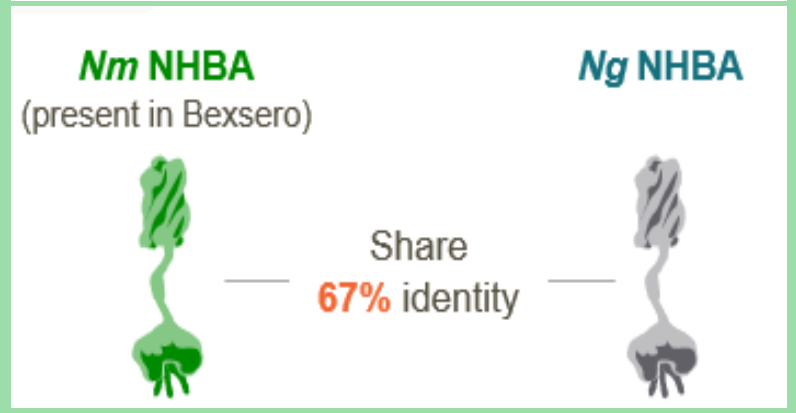
EDITORIAL COMMENTARY

2024 April 17; published online ahead of print

New Knowledge of the Anti-Bacterial Immune Response and Bacterial Antigens Supports Novel Vaccine Development: Gonorrhea

Cross Protection Against *N. gonorrhoeae* from *N. meningitidis* Vaccines





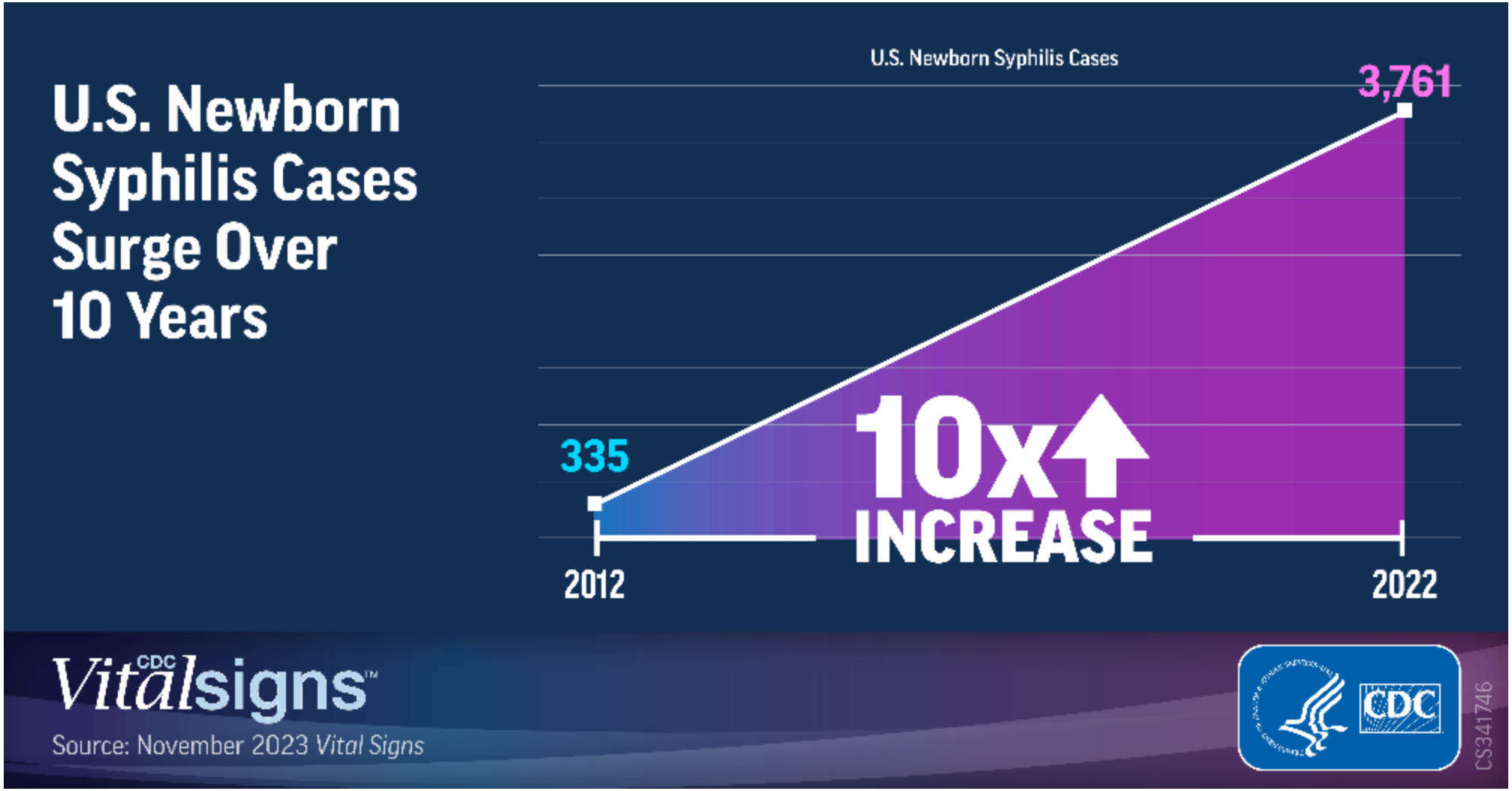
1. Semchenko EA *et al. Clin Infect Dis* 2019;69:1101–1111
2. Semchenko EA *et al. J Infect Dis* 2020;221:1612-1622

Phase 2 Clinical Trial: Testing 4CMenB as a Gonococcal Vaccine (MAGI Study)

- Phase 2, randomized, observer-blinded, multi-site trial of 4CMenB (Bexsero)
- Objective: Demonstrate efficacy in prevention of urogenital and/or anorectal gonococcal infection
- Enrollment: ~2,200 participants (MSW, MSM, & women) to achieve >202 evaluable cases; complete enrollment in Summer 2024
- Sites: 9 sites in U.S.; 2 sites in Bangkok; 1 site in Lilongwe, Malawi
- Collaboration: NIAID, WRAIR/AFRIMS, USU, and GSK

https://clinicaltrials.gov/ct2/show/NCT04350138

CDC Recommends Action to Stop the Increase in Newborn Syphilis Cases

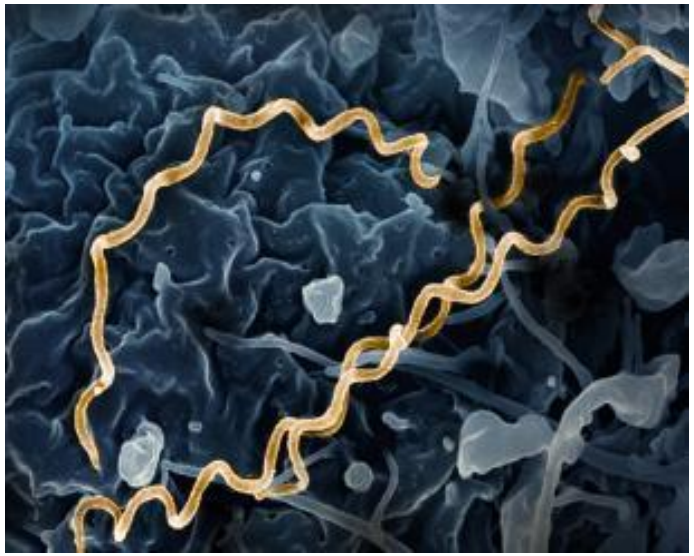


Advancing *T. pallidum* Diagnostics

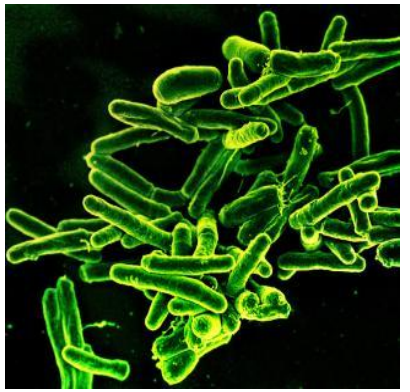
RFA-AI-23-039: Advancing Development of Diagnostics for Congenital and Adult Acquired Syphilis

- 10 awards expected

- Focus on:
  - ❑ Advancing new technologies
  - ❑ Ultra-sensitive detection
  - ❑ Differentiating current and previous infections
    - ○ Multi-omic approaches, genome and amplicon sequencing
  - ❑ Congenital syphilis diagnosis
    - ○ Immune signatures, protein breakdown products, biomarkers
  - ❑ Diagnosis in point-of-care settings using various sample types, including blood and ulcer swabs



Recent NIAID TB Vaccine highlights



- Subunit vaccine candidate H107:CAF10b is moving to Phase 1 trial

Phase 1 trial will be supported by the Gates Foundation in South Africa

- Phase 1 trial of a temperature stable form of TB vaccine candidate ID93-GLA-SE, shows it is safe and prompts immune response

Thermostable vaccines are desirable in settings where maintaining cold or frozen vaccines for long periods can be costly and difficult

Active Clinical TB Vaccine Trials

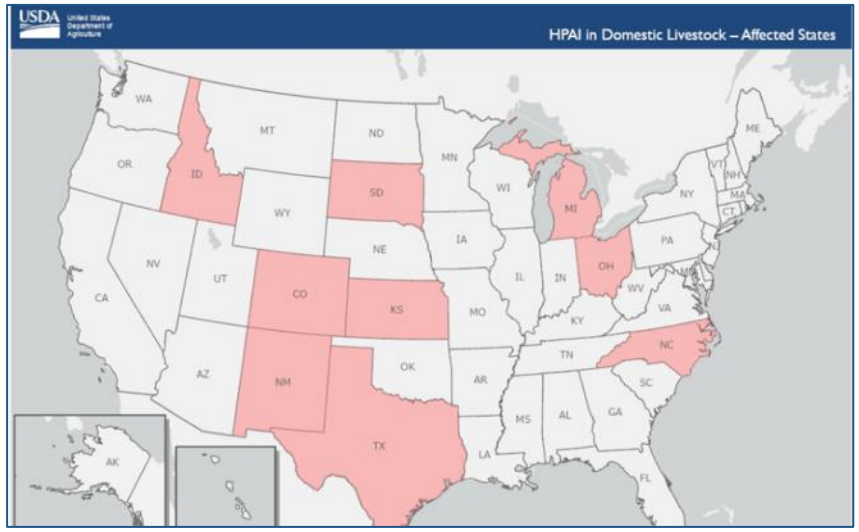
Phase 1	Phase 2	Phase 3
BNT164a1	**AEC/BC02**	**GamTBvac**
BNT164b1	**RUTI**	**MTBVAC**
TB/FLU-05E	**H56/IC31**	**VPM1002**
H107:CAF10b	**BCG – revaccination**	**M72/AS01E**
		Immuvac
		BCG$_{travelers}$

Concepts or candidate vaccines which NIAID has contributed support at some point in development.

TB Vaccine Pipeline - Working Group on New TB Vaccines

Highly Pathogenic Avian Influenza H5N

June 18, 2024



- 3/25/2024: USDA reports H5 HPAI (2.3.4.4b) detected in clinical samples of unpasteurized milk isolated from sick dairy cows in Kansas and Texas
- 4/1/2024 & 5/22/2024: Human infections reported in dairy farm workers in Texas and Michigan (**conjunctivitis**)
- 5/30/2024: Human infection reported in Michigan in a dairy farm worker (**respiratory**)
- No live virus detected in pasteurized milk
- Multiple other mammalian species infected in this outbreak: alpacas, domestic cats, house mice, goats
- Some genetic mutations favoring mammalian adaptation identified in bovine and human viral isolates
- Rare genetic markers of antiviral resistance in human or bovine isolates

Centers of Excellence for Influenza Research and Response (CEIRR)

- **Sample collection** – St. Jude's
  - CEIRR veterinarians allowed access to affected farm in Ohio, potentially Kansas
  - 900 samples and swabs collected, milk and nasal swabs analyzed on site with FluDETECT AIV strips
  - Deceased cat from affected farms collected for necropsy- revealed hemorrhagic pneumonia
- **Virus isolation and amplification from positive milk samples** – St. Jude, CRIPT
- **Viral characterization and risk assessment studies** - St. Jude, CRIPT, Emory, Penn
  - Replication in human cells
  - Antigenic analysis, sequence analysis
  - Pathogenicity and transmission (mice, ferrets)
  - Test antiviral drug sensitivity/resistance
  - Testing sera from H5 clinical trials to determine potential protection (how well stockpile vaccines will protect)
  - Phylogenetic analysis of goat, cattle, contemporary wild bird and human isolate sequences
  - Generate recombinant bovine H5 HA based on sequence data
  - Establish reverse genetics plasmids for generating RG viruses of A/dairycattle/Texas/24008749001/2024 strain

CEIRR Current and Planned Activities (continued)

- **Milk studies** - CRIPT, Emory, St. Jude
  - Replicate pasteurization conditions on spiked milk samples to determine if virus still infectious
  - Fractionate milk and determine viral prevalence/ stability in each component (whole milk, skim milk, casein, whey)
  - Determine virus stability in aerosolized milk and on metallic surfaces as function of time, humidity, and temperature
  - Feed animals (mice/ferrets) infected milk to determine if viable route of infection

- **Cattle studies** – St. Jude, Penn
  - Identify site of viral replication, clinical signs, shedding and transmission (cow to cow, cow to calf via milk consumption)
  - Preparing H5 mRNA-LNP vaccines for testing in cattle

Future activities (Centers have capacity, but studies not planned yet)

- HA receptor-preference assessment (virus histochemistry with animal tissues and glycan work)
- Polymerase functionality studies

HPTN – Yesterday, Today, and Tomorrow

- Advancing research to improve HIV prevention including long-acting ARVs and delivery systems for PrEP; MPTs to concurrently prevent HIV and pregnancy, STIs or opioid dependence; bNAbs, alone and in combination, for PrEP; and integrated strategies for HIV prevention.

  - Cabotegravir maintains protective efficacy in the setting of bacterial STIs:

    HPTN 083
  - Site-based HIV testing assay performance for Cabotegravir and TDF-FTC PrEP Failure in HPTN 083
  - No increased risk for hypertension with CAB-LA compared to TDF/FTC for HIV PrEP in HPTN 083

Innovating HIV Prevention and Care: HPTN 111 (TRIM) Launches in Uganda Barbershops

HPTN 111

TRIM

Testing a Barbershop-based HIV Prevention Initiative Among Men

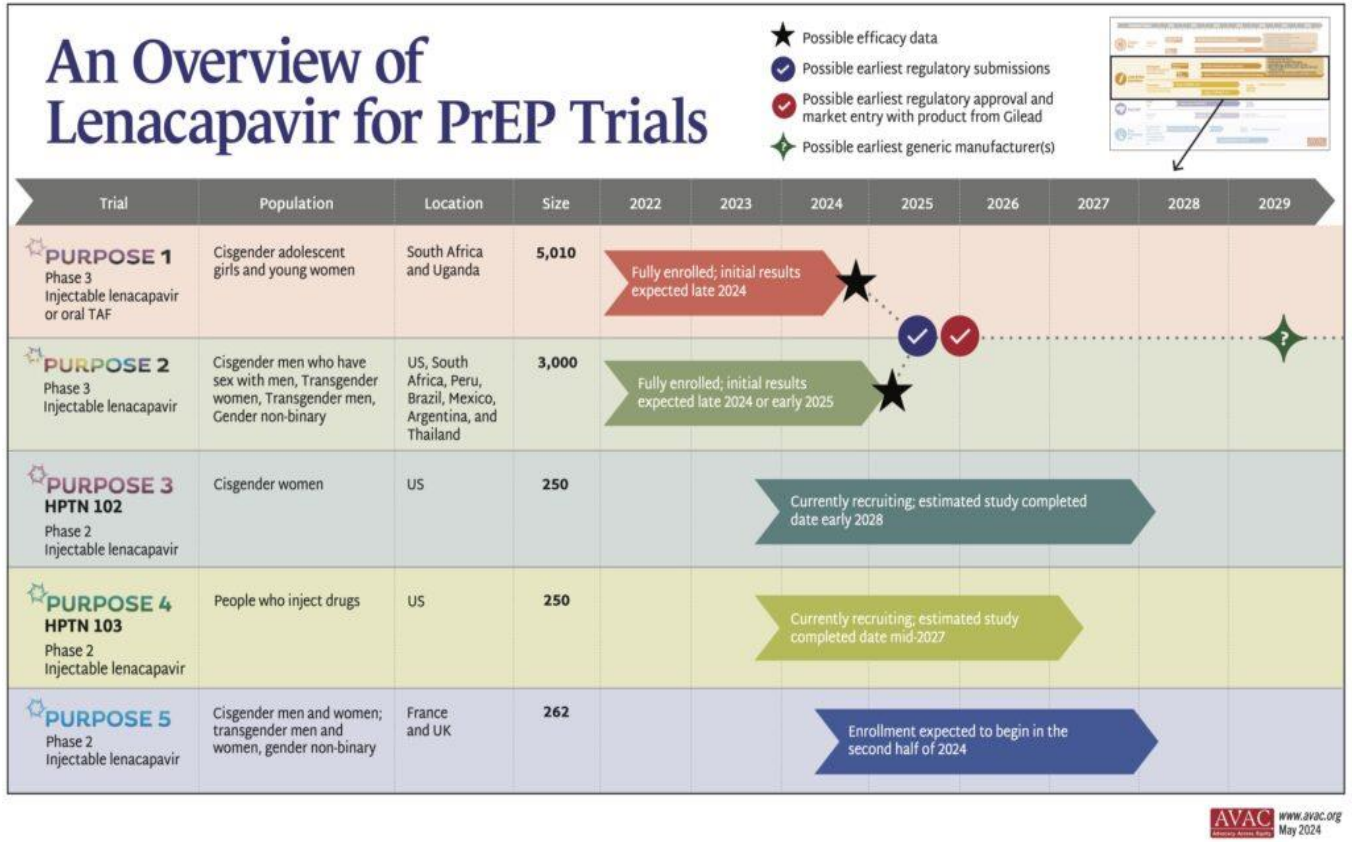
HPTN 012: Improving HIV prevention among heterosexual men seeking STI services in Malawi: examining the benefits, acceptability, and associated costs of a systems-navigator-delivered integrated prevention package

Njira

HPTN 112 Navigated Journey to Improve Reduction of HIV in African Men

PURPOSE 3 (HPTN-102) and PURPOSE 4 (HPTN-103) Trials to Test Effectiveness of Lenacapavir in Cisgender Women and People Who Inject Drugs

- Assess safety, acceptability, & pharmacokinetics of lenacapavir as PrEP
- Twice-yearly injection
- Priority populations (cisgender woman & people who inject drugs) with meaningful inclusion of diverse and representative populations
- Both studies began enrolling patients in June 2024



HPTN – Yesterday, Today, and Tomorrow

- Crucial pillar of NIAID's comprehensive strategy for novel treatments and a cure for HIV and its associated comorbidities

- Key component of NIAID's future response to public health emergencies and development and testing of medical countermeasures





Thank You!

NIAID Network TB Vaccine Trials in Development

HVTN 605/ACTG 5421: Phase 2a, safety and immunogenicity study of MTBVAC in HIV-infected and HIV–uninfected adolescents and adults

IMPAACT 2035/HVTN 604: Phase 1/2 evaluation of safety, immunogenicity of BCG revaccination or VPM1002 in HIV-infected and HIV-uninfected pediatric participants

ACTG 5397/HVTN 603: Phase 2a/b, evaluation of safety and immunogenicity of therapeutic ID93/GLA-SE vaccination in HIV-infected and HIV–uninfected adults with DS pulmonary TB

HVTN 606: Phase 1 trial to evaluate safety and immunogenicity of VIR-1778 in HIV-uninfected adults with overall good health

ACTG AIDS CLINICAL TRIALS GROUP

HIV VACCINE TRIALS NETWORK

IMPAACT International Maternal Pediatric Adolescent AIDS Clinical Trials Network