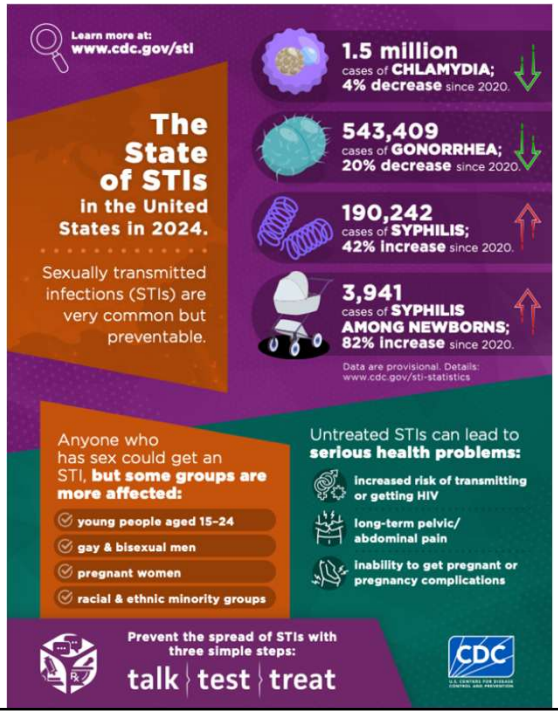
Sexually Transmitted Infection Management & Prevention: 2026 Update

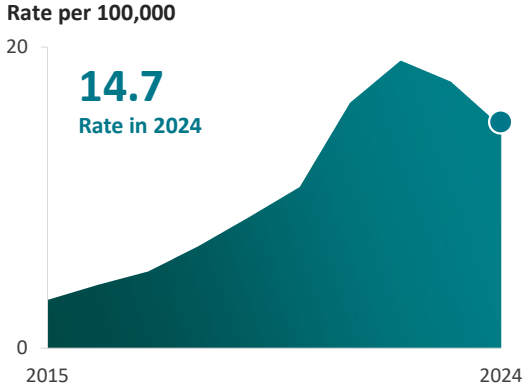
Jeanne Marrazzo, MD, MPH
CEO, Infectious Diseases Society of America
Prior Director, NIAID/NIH

November, 2026

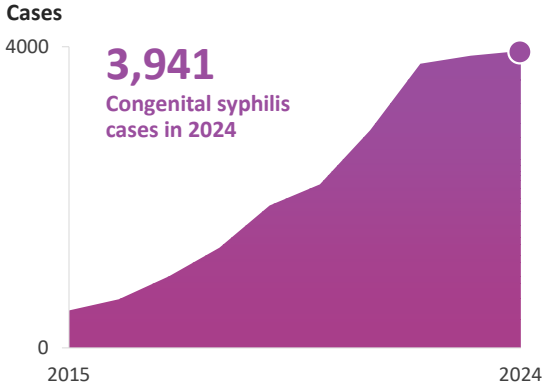


Congenital Syphilis Cases in 2024 Continue to Mirror Changes of Primary and Secondary Syphilis Among Females Aged 15-44 Years

Primary and Secondary Syphilis Rate Among Females Aged 15–44 Years

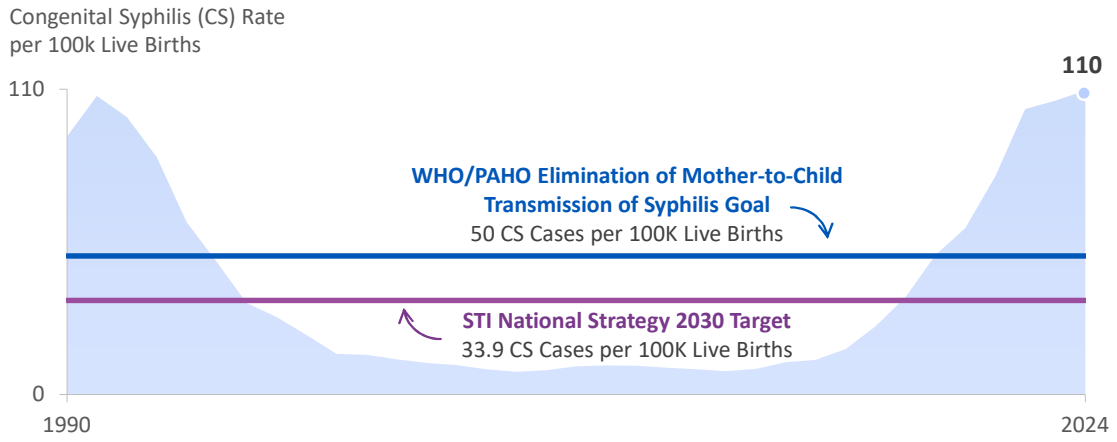


Reported Congenital Syphilis (CS) Cases by Year of Birth



2024 data are provisional as of August 14, 2025.

Congenital Syphilis Cases Increased for the 12th Year, with Slower Rate of Increase



2024 data are provisional as of August 14, 2025.

Additional Challenges

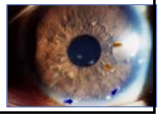
- Still using the same diagnostic approach (albeit with methodologic improvements) for the last several decades
  - Serology: limited ability to distinguish past from recent infection, treatment failure, re-infection
  - Imperfect surrogate to gauge treatment response
  - Especially problematic for accurate diagnosis of congenital/neonatal syphilis
- Missed diagnosis is common!
- Slow progress to a vaccine
- Variable supply of PCN formulations
  - Due to Bicillin L-A shortages, alternate, approved, imported supplies (e.g., Extencillin) were authorized by the FDA in 2024
  - July 2025 product recall by Pfizer due to particulate matter in solution

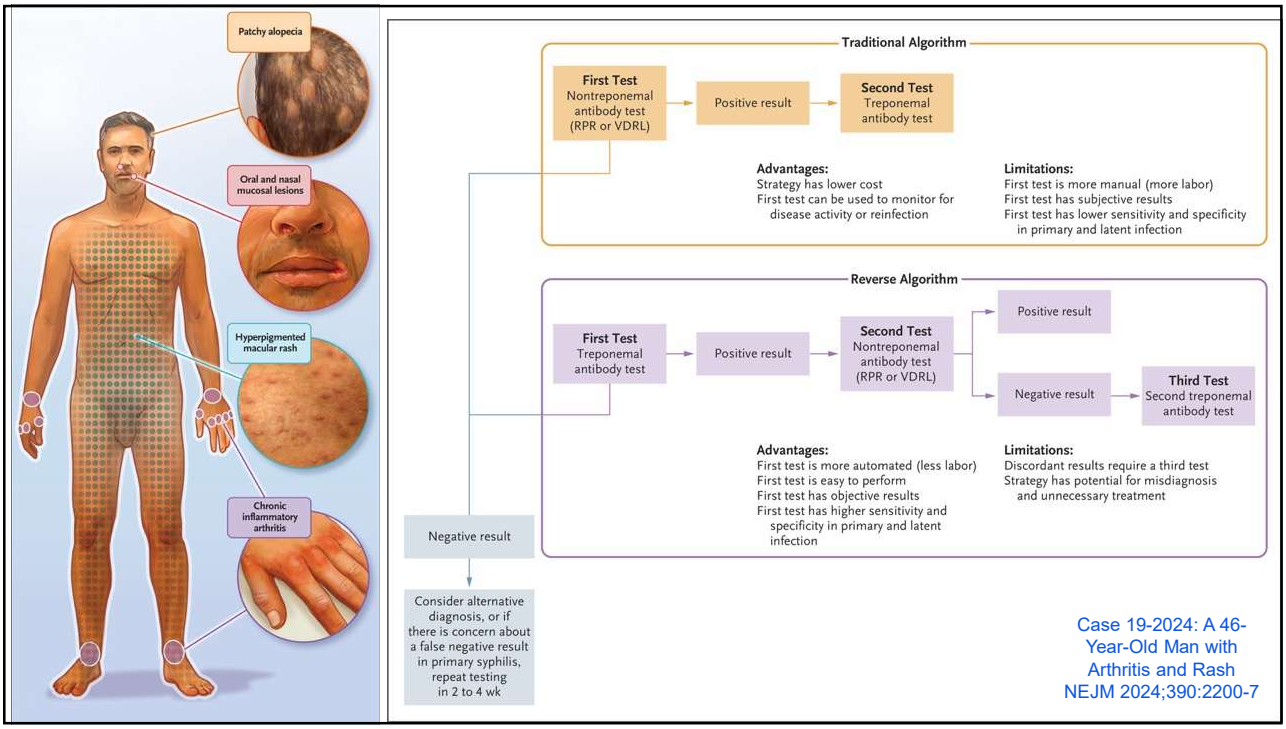






Case 19-2024: A 46-Year-Old Man with Arthritis and Rash
NEJM 2024;390:2200-7

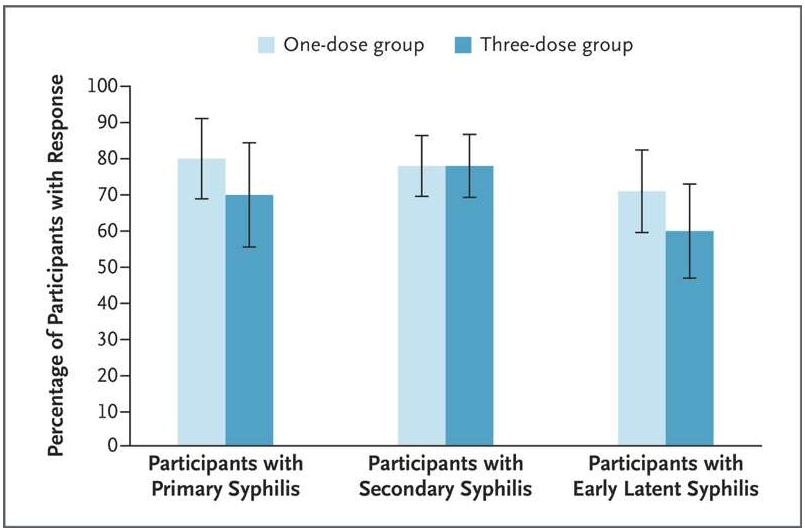




Case 19-2024: A 46-Year-Old Man with Arthritis and Rash
NEJM 2024;390:2200-7

One Dose (2.4M units IM) versus Three Doses of Benzathine Penicillin G in Early Syphilis

Hook, et al.
N Engl J Med
393(9):869-878,
2025



- 249 randomized
- Mean age 35 y
- 97% men
- 61% with HIV (77% CD4>350)
- 19% primary
- 47% secondary
- 33% early latent
- Overall serologic response 76% (68,82) in single dose vs. 70% (61,77) in 3-dose
- Same in HIV

Serologic Response at 6 Months to Treatment with Benzathine Penicillin G

Other Treatment Issues for Syphilis

Unpublished data to help guide tough choices

- RCT in pregnancy compared 1 to 3 doses of BPG for early syphilis- no difference
- RCT doxy vs. BPG in France - no difference
- "RCT" comparing cefixime to BPG in early syphilis in non-pregnant adults- cefixime may be ok but data are complex, will need to see the study to understand the limitations

Open Forum Infectious Diseases

BRIEF REPORT

A Pilot Study of Linezolid for Early Syphilis Treatment

Ryan M. Nguyen,[1,a] Chrysovalantis Stafylis,[1,a] Kelika A. Konda,[1] E. Michael Reyes-Diaz,[2] Kori Keith,[1] Keith Stokes,[3] Catherine Creticos,[4] Candice J. McNeil,[5] Philip A. Chan,[6] James B. Brock,[7] Byron Buck,[3] Ebony Warren,[4] Rica M. Abbott,[5] Jennifer L. Nall,[5] Peter Salhaney,[6] Takila Keys,[7] and Jeffrey D. Klausner[1]

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In a study of oral linezolid among 18 patients with early syphilis, 15 showed adequate serological response by 6 months. Among 6 patients treated with benzathine penicillin G, 5 showed adequate serological response. There were no serious adverse events. Linezolid shows promise for the treatment of early syphilis.

Keywords. linezolid; repurposing; syphilis; treatment.

Gonorrhea: Treatment 2026

Uncomplicated Gonococcal Infection of the Cervix, Urethra, or Rectum

Recommended Regimen for Uncomplicated Gonococcal Infection of the Cervix, Urethra, or Rectum Among Adults and Adolescents

Ceftriaxone 500 mg* IM in a single dose for persons weighing <150 kg

If chlamydial infection has not been excluded, treat for chlamydia with doxycycline 100 mg orally 2 times/day for 7 days.

* For persons weighing ≥150 kg, 1 g ceftriaxone should be administered.

Alternative Regimens if Ceftriaxone Is Not Available

Gentamicin 240 mg IM in a single dose
plus
Azithromycin 2 g orally in a single dose
or
Cefixime* 800 mg orally in a single dose

* If chlamydial infection has not been excluded, providers should treat for chlamydia with doxycycline 100 mg orally 2 times/day for 7 days.

Uncomplicated Gonococcal Infection of the Pharynx

Recommended Regimen for Uncomplicated Gonococcal Infection of the Pharynx Among Adolescents and Adults

Ceftriaxone 500 mg* IM in a single dose for persons weighing <150 kg

* For persons weighing ≥150 kg, 1 g ceftriaxone should be administered.

- No reliable alternative treatments are available for pharyngeal gonorrhea.
- For persons with a history of a beta-lactam allergy, thorough assessment of the reaction is recommended
- If partner treatment w/ IM CTX not possible, consider cefixime 800 mg PO (single dose)

Gepotidacin "Gepo"



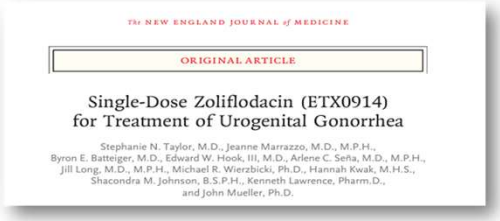
Oral gepotidacin for the treatment of uncomplicated urogenital gonorrhoea (EAGLE-1): a phase 3 randomised, open-label, non-inferiority, multicentre study

Jonathan D C Ross, Janet Wilson, Kimberly A Workowski, Stephanie N Taylor, David A Lewis, Sally Gatsi, William Flight, Nicole E Scangarella-Oman, Charles Jakielaszek, Dan Lythgoe, Marcy Powell, Salim Janmohamed, Judith Absalon, Caroline Perry

- First-in-class triazaacenaphthylene Dual-targeting: inhibits DNA gyrase (GyrA) and topoisomerase IV (ParC)
- Prevents DNA replication
- Dual-targeting reduces likelihood of resistance

Ross, Lancet 2025

Zoliflodacin "Zoli"



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

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

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

- First-in-class spiropyrimidinetrione Inhibits DNA gyrase (GyrB subunit)
- Blocks DNA biosynthesis→ GC death
- Active against GC strains resistant to cephalosporins and fluoroquinolones

Taylor, NEJM 2023

Gepo and Zoli vs Ceftriaxone

	Gepotidacin (Nuzolvence)	Zoliflodacin (Blujepa)
Dosing	3g, two doses, 10-12 hrs apart	3g, Single dose
Efficacy: urogenital	**ME: 100% (TD, 0%)**	**ME: 96.8% (TD, 3.16%)**
Efficacy: rectal	**ME: 100% (26/26), (TD, 0%)**	**ME (n=103): 95.8%, (TD, 4.17%)**
Efficacy: pharyngeal	**ME: 87.5% (14/16), (TD, -12.5%), 2 bacterial persistence**	**ME (n=69): 91.3% (TD, 4.35%)**
Side effect profile	Mild; GI (67%) – diarrhea, nausea	Comparable to CRO-AZI; headache
FDA approval	**Yes** (3/2025, uncomplicated UTI, 12/2025 for uncomplicated GC)	**Yes** (12/2025, uncomplicated GC)
Indication	Uncomplicated urogenital GC in people >12 yo & >35 kg	Uncomplicated urogenital GC in people >12 yo & ≥45 kg w/limited or no alternative treatment options
Cost	Unknown	Unknown

ME: Microbiologic efficacy, **TD**=Treatment Difference

Mycoplasma genitalium treatment

Recommended Regimens if *M. genitalium* Resistance Testing Is Available
If macrolide sensitive: Doxycycline 100 mg orally 2 times/day for 7 days, followed by **azithromycin** 1 g orally initial dose, followed by 500 mg orally daily for 3 additional days (2.5 g total)
If macrolide resistant: Doxycycline 100 mg orally 2 times/day for 7 days followed by **moxifloxacin** 400 mg orally once daily for 7 days

Recommended Regimen if *M. genitalium* Resistance Testing Is Not Available
If *M. genitalium* **is detected by an FDA-cleared NAAT: Doxycycline** 100 mg orally 2 times/day for 7 days, followed by **moxifloxacin** 400 mg orally once daily for 7 days

Treatment failure is common

- Patients who test positive for MG, complete treatment with doxy/moxi, and then return with signs/symptoms of recurrent or persistent NGU, cervicitis, or proctitis
- **Retest patients, ideally at least 3 weeks after treatment** to avoid false positive results (due to residual Mgen genetic material) and false negatives (due to low organism load from antibiotics)

- STD Clinical Consultation Network 2015-2024:
  - 332 MG consults, 75% reported after 1/2023
  - 35% were treatment failures (McLean 2026, Open Forum Infect Dis)
- Mycoplasma Genitalium Treatment Failure Registry, 2022-2024:
  - 120 reports, 50 confirmed failures after doxy plus moxi
  - Half required 2 or 3 more courses of antibiotics (range 1-8 courses)
  - Some with ongoing treatment failure

(Penney J. ISSTDR 2025)

Minocycline is second-line therapy for treatment failure

- **Second line therapy: minocycline 100 mg PO BID x 14 days**
- % cured= **68%-71%** of macrolide resistant MG infections (among people who took it and had low risk for reinfection)
- >90% took ALL doses of the minocycline
- Mild side effects: dizziness (9%), nausea (6%), headache (6%), fatigue (4%), "brain fog" (4%)

- Follow-up study 2024: **Minocycline together with metronidazole x 14 days**
- **80%** microbiologic cure in patients with MRM (<10% d/c for side effects)

- From Denmark, reported success with minocycline plus metronidazole plus methenamine plus pristinamycin for up to 28 days

Clarke EJ . Open Forum Infect Dis. 2023
Doyle M. Open Forum Infect Dis. 2020
Htaik K. J Antimicrob Chemother 2025

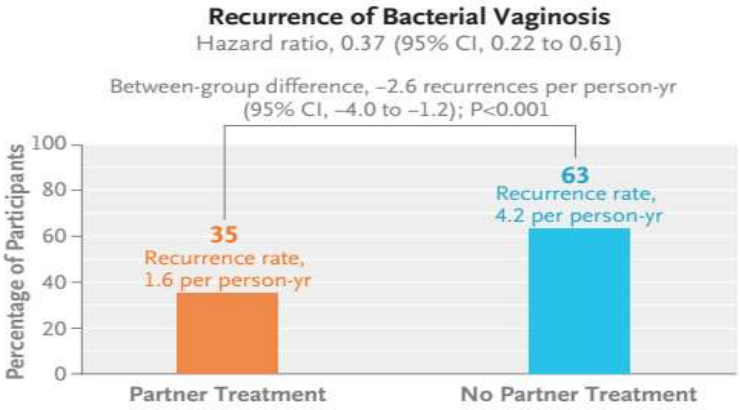
Get ready to travel for that *M. genitalium* Treatment

- Other drugs used successfully for moxifloxacin treatment failures include sitafloxacin, pristinamycin, and spectinomycin. **None are available in the US.**
  - Pristinamycin is available in France and Ireland, (or as a study drug in Australia) with limited and unpredictable availability in other parts of EU
  - Sitafloxacin is available in Japan and Ireland
  - Spectinomycin is available in some parts of Africa, Asia and Latin America

PLEASE REPORT TO THE CDC REGISTRY



BV Partner Treatment: Will it work in the US?



- Recurrence rate **35% vs 63%, -2.6 recurrences/person/year**

Vodstrcil L. NEJM 2025



vs



- 80% European/Western
- 80% Uncircumcised
- 100% Hetero-monogamous
- 1/3 had IUDs

- BV prevalence by race
  - -50% of Black women
  - -40% of Hispanic women
  - -25% of White women
  - -11% Asian women (Allsworth, 2007)
- 70-80% men are circumcised
- 1 in 10 men have concurrent partners

(Adimora AA. Am J Public Health)

Treatment and Suppression of genital herpes in ~~1996~~ 2026

- Same drugs for **30+ years (Acyclovir, valacyclovir, famciclovir)**
- No new dosages in the 2015, 2021 CDC guidelines
- General principle: Suppressive therapy daily vs. episodic therapy during outbreaks
- Even 3 g of valacyclovir daily (6x the typical suppressive dose) does not fully suppress shedding (Johnston C et al, Lancet 2012)





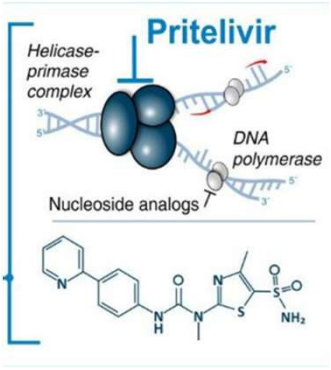



The NEW ENGLAND JOURNAL of MEDICINE
CURRENT ISSUE
SPECIALTIES
ORIGINAL ARTICLE

Helicase–Primase Inhibitor Pritelivir for HSV-2 Infection

Authors: Anna Wald, M.D., M.P.H., Lawrence Corey, M.D., Burkhard Timmler, M.D., Amalia Magaret, Ph.D., Warren, M.N., Stephen Tyring, M.D., Ph.D., Christine Johnston, M.D., M.P.H., +8, and Alexander Birkman Ph.D. Author Info & Affiliations

Published January 16, 2014 | N Engl J Med 2014;370:201-210 | DOI: 10.1056/NEJMoa1301150 | VOL. 37



Targets the viral helicase-primase complex

• In contrast to existing drugs, does not require activation by viral enzymes (thymidine kinase), thus can prevent infection of uninfected cells

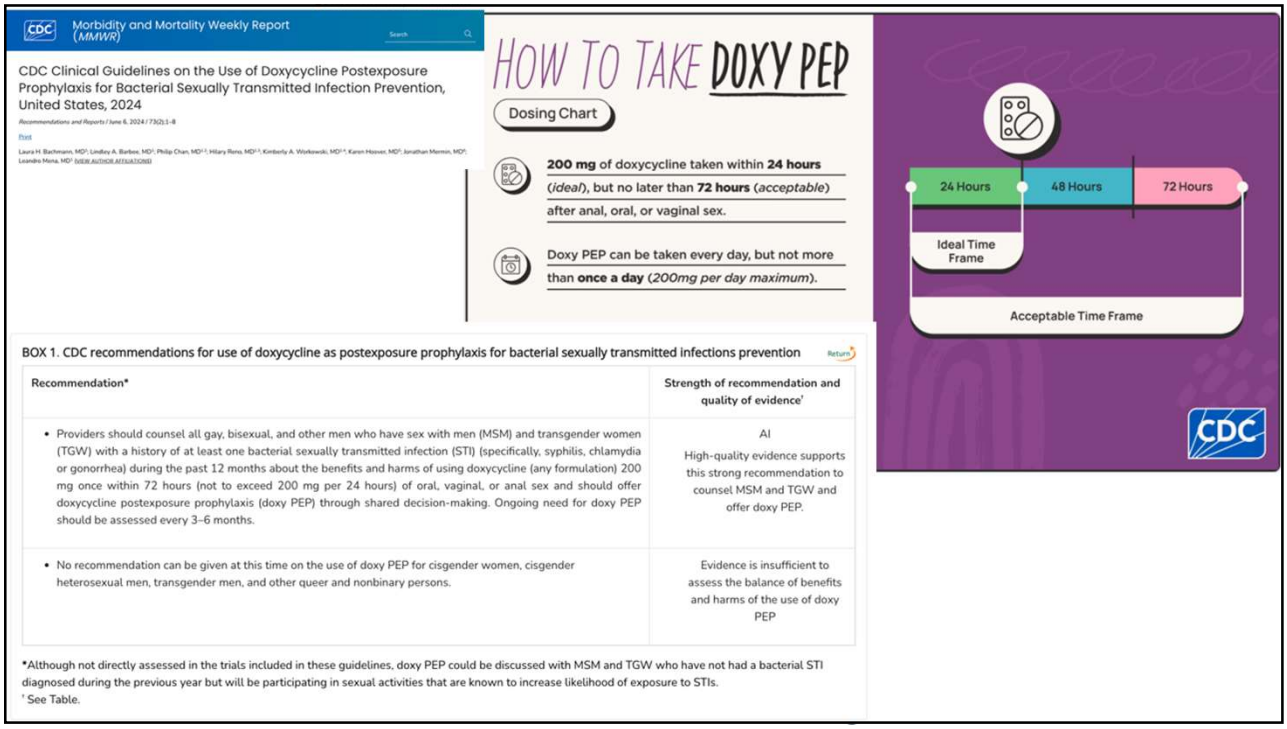
• Pritelivir is active against HSV-1 and HSV-2 including acyclovir or foscarnet resistant viruses in vitro

• High bioavailability with half-life of 60 hours allowing once-daily dosing for treatment

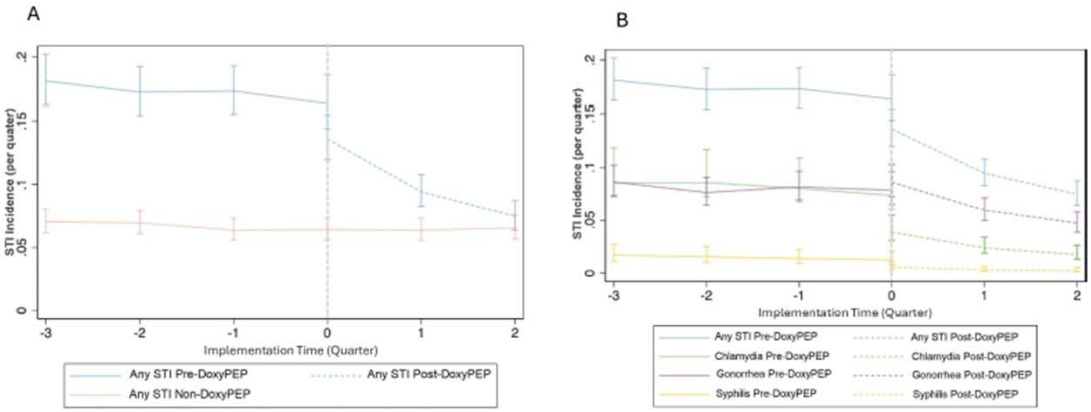
Wald A. NEJM 2014
Birkman, *J. Med. Chem.* 2022

FDA Approval & Indication OCT 2026: Oral pritelivir (marketed as HOVILPRI) is indicated for immunocompromised adults suffering from mucocutaneous HSV lesions refractory or resistant to standard therapies, including people with HIV

Phase 3 PRIOH-1 Data Highlights: Late-breaking data presented at IDWeek 2026 showed that oral pritelivir significantly improved lesion healing and reduced hospitalizations down to 29.4% compared to 76% with investigator's choice therapies



Effect of Doxy-PEP in San Francisco

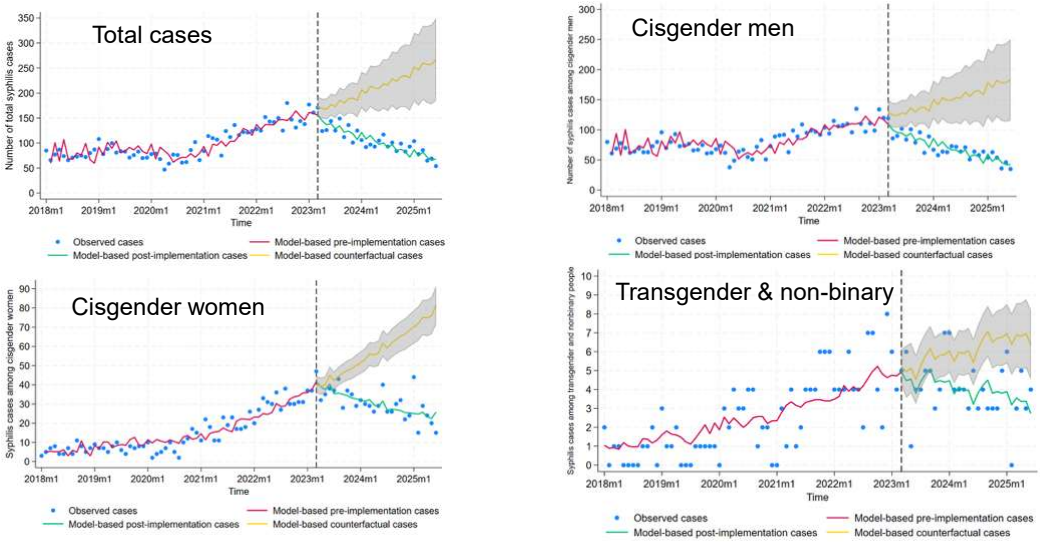


Incident chlamydia, syphilis and gonorrhea infections / quarter among DoxyPEP users & non-users (A), and (B) among PrEP users at San Francisco AIDS Foundation Sexual Health Clinic

Scott HM, Sex Transm Infect doi:10.1136/sextrans-2025-056674

Menza TW, CID 2026

Effect of Doxy-PEP on Syphilis in Seattle



Observed monthly syphilis cases & model-based pre- & post-implementation observed & counterfactual trends relative to doxy-PEP implementation in PHSKC Sexual Health Clinic beginning March 2023, 2018-2025

Weekly doxy DOT likely prevents chlamydia among cisgender women

Incident chlamydia rate with **weekly doxycycline: 11.2** per 100 person years
Incident chlamydia rate in **dPEP Kenya SOC group: 29.6** per 100 person years

Analysis	Endpoint	Weekly DoxyDOT (N=60)	SOC dPEP Kenya (N=225)	RR	95% CI	P-value
GEE Censoring Clinical Hold Time	All STIs	6/57 (10.5%)	31/220 (14.1%)	0.73	0.28-1.91	0.52
	Chlamydia	**3/57 (5.3%)**	**29/220 (13.2%)**	**0.39**	**0.12-1.25**	**0.11**
	Gonorrhea	4/57 (7.0%)	5/220 (2.3%)	3.03	0.637-14.40	0.16

* Two additional cases of chlamydia and 3 additional gonorrhea cases among people on holds

Stewart et al. ISSTDR, 2025.



Now Enrolling!



8 Cities: Baltimore, Chicago, Houston, Memphis, New Orleans, San Francisco, Tampa and Washington DC

https://atnresearch.org/our-studies/#ATN173

Randomized, double-blind, placebo-controlled trial evaluated whether the 4CMenB meningococcal vaccine prevents Neisseria gonorrhoeae infection among men who have sex with men (MSM) at high risk for infection.

- **No Efficacy:** First infection was 48.1 cases per 100 person-years in 4CMenB group and 47.8 cases per 100 person-years in placebo group (−0.5%; 95% CI, −26.2 to 19.9).
- **Consistency with Trials:** Findings align with other recent randomized trials (ANRS 174 DOXYVAC)
- **Contrasting Observational Data:** While earlier retrospective and case-control observational studies suggested around a 38% risk reduction, those findings were likely subject to residual confounding

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CURRENT ISSUE SPECIALTIES TOI

ORIGINAL ARTICLE

Meningococcal B Vaccine to Prevent *Neisseria gonorrhoeae* Infection

Authors: Kate L. Seib, Ph.D., Basil Donovan, M.D., Fengyi Jin, Ph.D., Caroline Thng, M.B., B.S., Barbara Yeung, M.P.H., Nicholas Comninos, M.D., Rohan I. Bopage, M.Med., +26, for the GoGoVax Study Team* Author Info & Affiliations

Published July 8, 2026 | N Engl J Med 2026;395:349-361 | DOI: 10.1056/NEJMoa2516739 | VOL. 395 NO. 4
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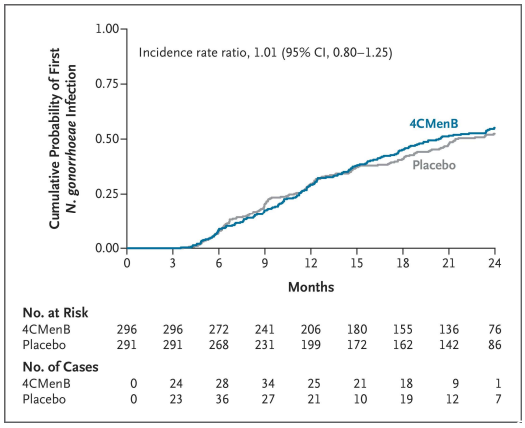

No. at Risk									
4CMenB	296	296	272	241	206	180	155	136	76
Placebo	291	291	268	231	199	172	162	142	86
No. of Cases									
4CMenB	0	24	28	34	25	21	18	9	1
Placebo	0	23	36	27	21	10	19	12	7

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Noninferiority of One HPV Vaccine Dose to Two Doses

A Research Summary based on Kreimer AR et al. | 10.1056/NEJMoa2506765 | Published on December 3, 2025

WHY WAS THE TRIAL DONE?

Vaccination against human papillomavirus (HPV) in adolescence can prevent most cervical cancers, but only about 27% of eligible girls worldwide have received the vaccine. Emerging data suggest that a single dose may provide some protection. Whether a single dose of HPV vaccine would provide protection similar to two doses is uncertain.

HOW WAS THE TRIAL CONDUCTED?

Girls 12 to 16 years of age were randomly assigned to receive either a bivalent or a nonavalent HPV vaccine. They were then assigned to receive either the second dose of the assigned vaccine or a vaccine for tetanus, diphtheria, and pertussis as a control. The primary end point was new HPV16 or HPV18 infection that occurred during follow-up and persisted for at least 6 months. The noninferiority margin was 1.25 infections per 100 participants.

TRIAL DESIGN

- Double-blind
- Randomized
- Controlled
- Noninferiority
- Location: Costa Rica

RESULTS

During 5 years of follow-up, one dose of either HPV vaccine was noninferior to two doses in preventing HPV16 or HPV18 infection. No safety concerns were identified; serious adverse events that were assessed by the investigator as being potentially related to HPV vaccination occurred in 0.03% of the participants.

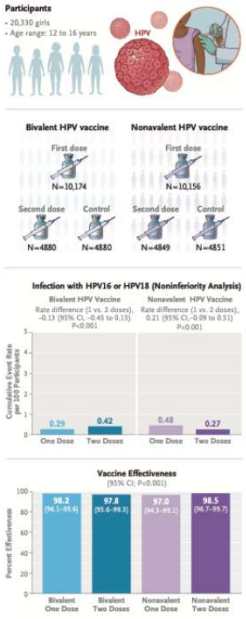
LIMITATIONS AND REMAINING QUESTIONS

- Estimates of vaccine effectiveness were determined on the basis of a control group of participants who did not undergo randomization.
- Longer-term durability of response would require additional monitoring.
- The prespecified noninferiority margin, which considered a vaccine efficacy of 80% to be noninferior to 94.0%, may be too broad.

CONCLUSIONS

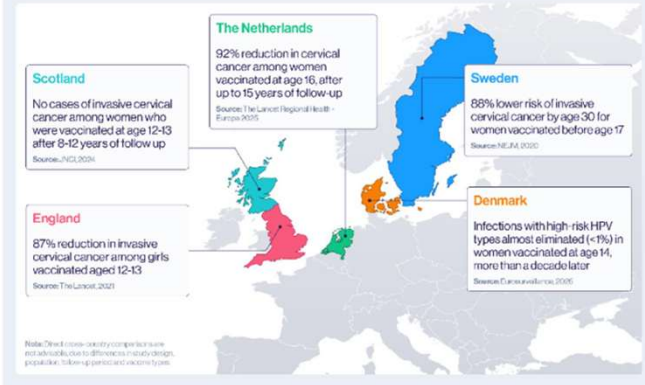
One dose of either a bivalent or a nonavalent HPV vaccine provided protection against HPV16 or HPV18 infection that was similar to that of the standard two-dose series.

NEJM QUICK TAKE | EDITORIAL



Real-world efficacy of HPV vaccines

Across countries with long-running HPV vaccination programmes, real-world data show strong reductions in cervical cancer and precancer – particularly when vaccination occurs before age 17.



Across countries with long-running HPV vaccination programmes, real-world data shows strong reductions in cervical cancer and precancer – particularly when vaccination occurs before age 17.

Final Thoughts

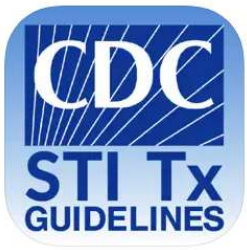
- Congenital syphilis occurs because the infection is not detected and/or treated correctly during pregnancy; screen, treat, & ensure serologic response
- Remember to presumptively treat sex partners (see guidelines for exposure timeframes), regardless of whether they can be evaluated and tested
- Doxy-PEP may be changing the landscape quicker than expected
- Wait to see what AAP says about 1 dose HPV vaccine after reviewing data
- Two new oral alternatives for GC, gepo and zoli Minocycline is the alternative therapy we have for M genitalium treatment failure, adding metronidazole at the same time may help boost efficacy
- Pritelivir approved for HSV

Ina Park
Kim Workowski
Tim Menza, University of Washington
Laura Quilter, CDC
Kenneth Lawrence, Aicuris



Thank You!

Get the CDC Treatment Guidelines App



STI Tx Guide 12+
Centers For Disease Control and Prevention
Designed for iPhone
★★★★★ 4.3 • 25 Ratings
Free

App Store (Apple)

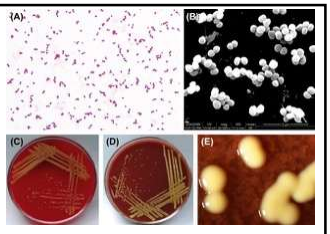
Google Play (Android)

https://www.cdc.gov/std/treatment-guidelines/default.htm



STDCCN.org

Invasive Meningococcal Disease



- Serogroup C outbreaks in MSM, regardless of HIV status
- People w/ HIV are at 11x – 24x increased risk; higher with low CD4 or high viral load
  - Most caused by serogroups C, W or Y
- Two pentavalent (MenABCWY) vaccines in the U.S.; indicated for intrinsic or induced complement deficiency, asplenia, routine exposure (microbiologists)
  - Penbraya
  - Penmenvy
- Two quadrivalent conjugate (MenACWY) vaccines in U.S.; indicated for HIV, outbreak (including MSM)
  - MenACWY-CRM (Menveo)
  - MenACWY-TT (MenQuadfi)
- Two serogroup B (MenB) vaccines in U.S; indications as per pentavalent
  - MenB-FHbp (Trumenba)
  - MenB-4C (Bexsero)

CDC Morbidity and Mortality Weekly Report (*MMWR*) Search

Use of the GSK MenACWY-CRM/MenB-4C Pentavalent Meningococcal Vaccine Among Persons Aged ≥10 Years: Recommendations of the Advisory Committee on Immunization Practices — United States, 2025

Weekly / January 8, 2026 / 75(1);7–14

- On April 16, 2025, the Advisory Committee on Immunization Practices recommended that, when both quadrivalent (serogroups A, C, W, and Y) and serogroup B meningococcal (MenB) vaccine are indicated concurrently for persons aged ≥10 years, MenACWY-CRM/MenB-4C may be administered instead.