

II Curso de **Infecciones de Transmisión Sexual** *ITS*



Doble cara de Doxy-pep:
Reducción nuevas infecciones e impacto en resistencia

Oskar Ayerdi Aguirrebengoa. Hospital Universitario Donostia, Osakidetza.

Índice

- ¿Qué es Doxy-pep?
- Evidencia de la eficacia preventiva
- Posicionamiento de las principales guías
- Doble cara: beneficios y riesgos
- Conclusiones

Doxycycline for STIs

¿Qué es la Doxy-pep?

Doxy-pep = Doxycycline para prevenir ITS

Antibiótico de amplio espectro

Usado para prevención de malaria y enfermedad de Lyme

Primer estudio publicado en 2015

Published in final edited form as:

Sex Transm Dis. 2015 February ; 42(2): 98–103. doi:10.1097/OLQ.0000000000000216.

Doxycycline Prophylaxis to Reduce Incident Syphilis among HIV-Infected Men who have Sex with Men who Continue to Engage in High Risk Sex: A Randomized, Controlled Pilot Study

Robert K. Bolan, MD^{*}, Matthew R. Beymer, MPH^{*,†}, Robert E. Weiss, PhD^{††}, Risa P. Flynn^{*}, Arleen A. Leibowitz, PhD^{**}, and Jeffrey D. Klausner, MD, MPH[‡]

^{*}Los Angeles LGBT Center (The Center)

N=30, doxy 100 mg once daily

Post-exposure prophylaxis with doxycycline to prevent sexually transmitted infections in men who have sex with men: an open-label randomised substudy of the ANRS IPERGAY trial

Jean-Michel Molina, Isabelle Charreau, Christian Chidiac, Gilles Pialoux, Eric Cua, Constance Delaugerre, Catherine Capitant, Daniela Rojas-Castro, Julien Fonsart, Béatrice Bercot, Cécile Bébér, Laurent Cotte, Olivier Robineau, François Raffi, Pierre Charbonneau, Alexandre Aslan, Julie Chas, Laurence Niedbalski, Bruno Spire, Luis Sagaon-Teyssier, Diane Carette, Soizic Le Mestre, Veronique Doré, Laurence Meyer, for the ANRS IPERGAY Study Group*

Lancet, 2018

Molina JM, Charreau I, Chidiac C, et al; ANRS IPERGAY Study Group. Post-exposure prophylaxis with doxycycline to prevent sexually transmitted infections in men who have sex with men: an open-label randomised substudy of the ANRS IPERGAY trial. Lancet Infect Dis. 2018 Mar;18(3):308-317. doi: 10.1016/S1473-3099(17)30725-9. Epub 2017 Dec 8. PMID: 29229440.

- Open-label aleatorizado en usuarios de PrEP (232 HSH y mujeres trans)
- 1:1_Doxiciclina 200 mg<24 horas después de rel.sex (n=116) vs no intervention (n=116)
- Media de seguimiento 8.7 meses/persona (7.8-9.7), cribado de ITS cada 2 meses
- Objetivo primario: suceso de primera ITS

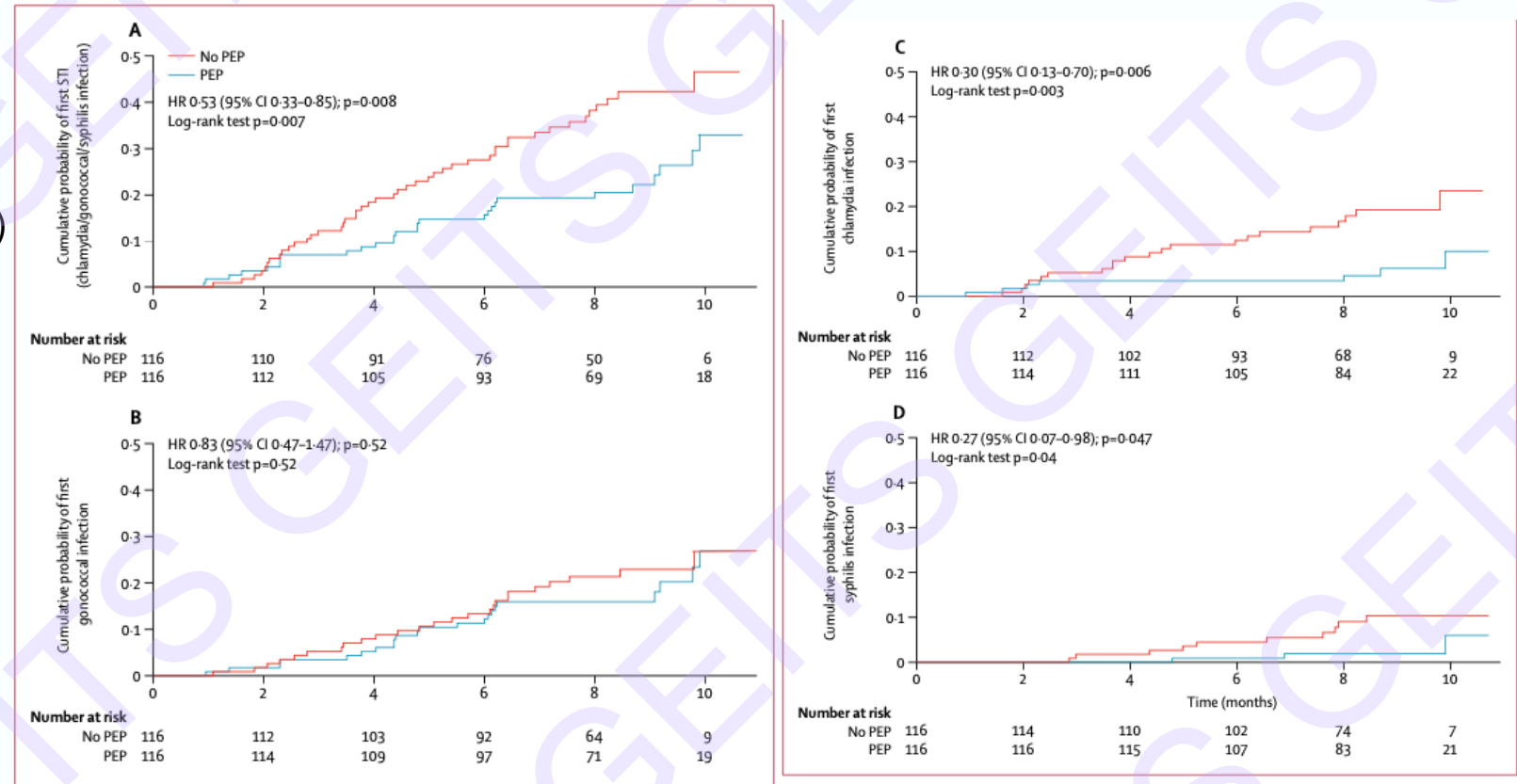
Resultados: 73 participantes presentaron ITS

Doxy-pep:

- 28/116 al menos 1 ITS
- Probabilidad 22% (15-32)
- Hazard ratio **0.53** (0.33-0.85, p=0.008)
 - Clamidia: HR 0.30 (0.13-0.70)
 - Sífilis: HR 0.27 (0.07-0.98)
 - Gonorrea: HR 0.83 (0.47-1.47)

No intervención

- 45/116 al menos 1 ITS
- Probabilidad 42% (33-53) p=0.007



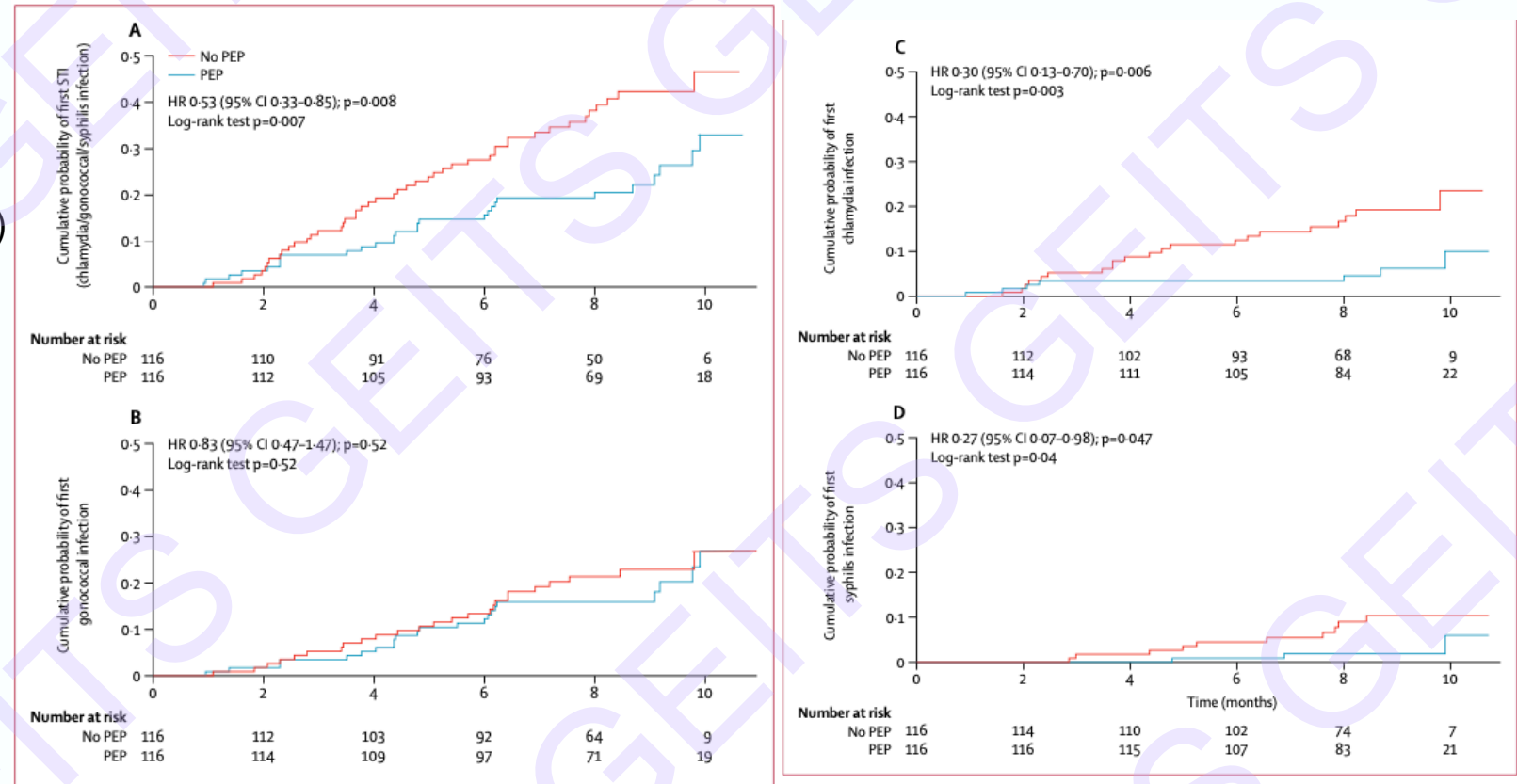
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Resultados de resistencias

- Solo PCR, no se testaron cepas de ITS.
- No se testaron otras cepas.



The NEW ENGLAND JOURNAL of MEDICINE

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 Grabow, M.P.H., Clare E. Brown, Ph.D., Cheryl Malinski, B.S.,
Rodney Perkins, R.N., M.P.H., Melody Nasser, B.A., Carolina Lopez, B.A.,
Eric Vittinghoff, Ph.D., Susan P. Buchbinder, M.D., Hyman Scott, M.D., M.P.H.,
Edwin D. Charlebois, Ph.D., M.P.H., Diane V. Havlir, M.D., Olusegun O. Soge, Ph.D.,
and Connie Celum, M.D., M.P.H., for the DoxyPEP Study Team*

New England, 2023

Luetkemeyer AF, Donnell D, Dombrowski JC, et al.; DoxyPEP Study Team. Postexposure Doxycycline to Prevent Bacterial Sexually Transmitted Infections. N Engl J Med. 2023 Apr 6;388(14):1296-1306. doi: 10.1056/NEJMoa2211934. PMID: 37018493; PMCID: PMC10140182.

- Estudio abierto-aleatorizado, en usuarios de PrEP y PQVIH con alguna ITS < 1 año (N=501 HSH y mujeres trans)
- 2:1_Doxiclina 200 mg<72h de la rel. sex (n=327) vs no PEP (n=174)
- Media en el estudio: 8,9 meses, cribado de ITS cada 3 meses.
- Objetivo primario: Incidencia de al menos una ITS bacteriana por trimestre

Resultados incidencia de ITS bacterianas

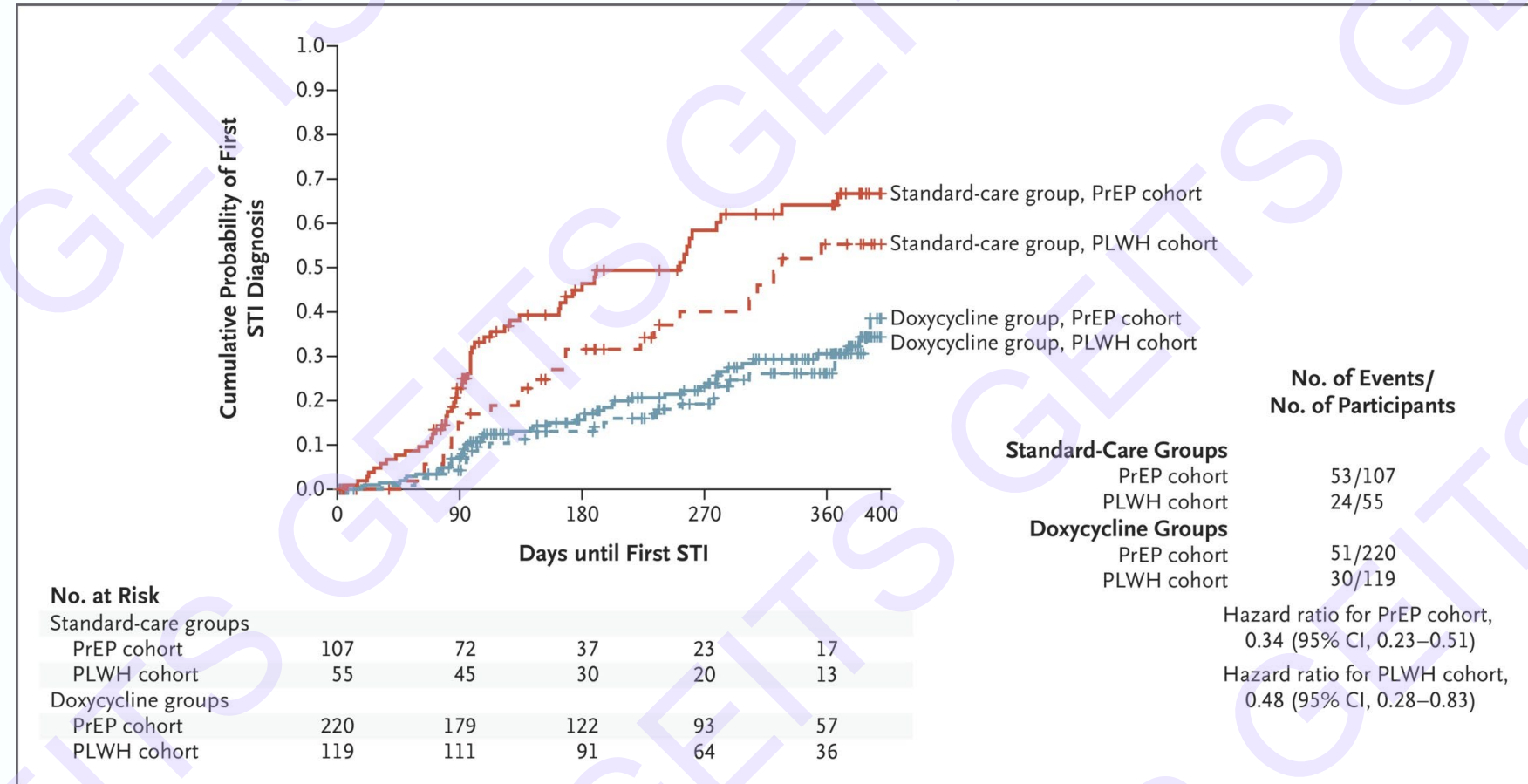
Doxy-pep

- 10-11% una ITS/trimestre;
- RR 0.34 (0.24-0.49, $p < 0.001$)

Clamidiasis	
Usuario PrEP	RR 0,12 (0,05-0,25)
PQVIH	RR 0,26 (0,12-0,57)
Sífilis	
Usuario PrEP	RR 0,13 (0,03-0,59)
PQVIH	RR 0,23 (0,04-1,29)
Gonococia	
Usuario PrEP	RR 0,45 (0,32-0,65)
PQVIH	RR 0,43 (0,26-0,71)

No intervencion

- 30-32% una ITS por trimestre



Resultados de resistencias

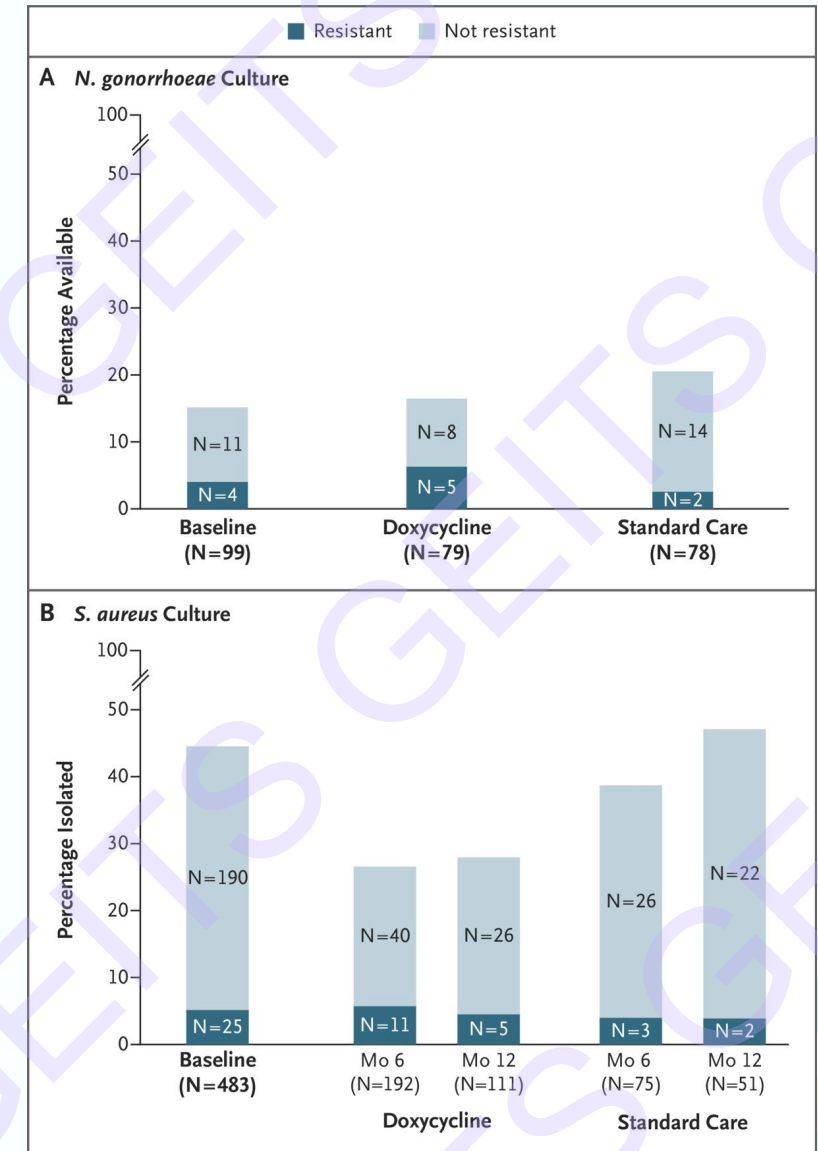
N. gonorrhoeae:

Resistencia a la tetraciclina probada en cultivo, si la PCR NG (+):

- Basal: 4/15 (27%) aislamientos resistentes a la tetraciclina
- Seguimiento:
 - 5/13 (38%) en el grupo doxyPEP
 - 2/16 (12%) en el grupo estándar.

S. aureus:

- Basal: el 45% fue positivo, el 12% cepa resistente a doxiciclina
- Seguimiento:
 - Positivo: 28 % (doxyPEP) frente al 47 % fue positivo
 - Resistencia a doxiciclina 6 M: 27,5% (doxyPEP) frente a 11,5% (no PEP)
 - Resistencia a doxiciclina 12 M: 19,2% (doxyPEP) frente a 9,1% (no PEP)
- En general: % de personas con una cepa de *S. aureus* resistente fue similar: 5 % frente a 4 %

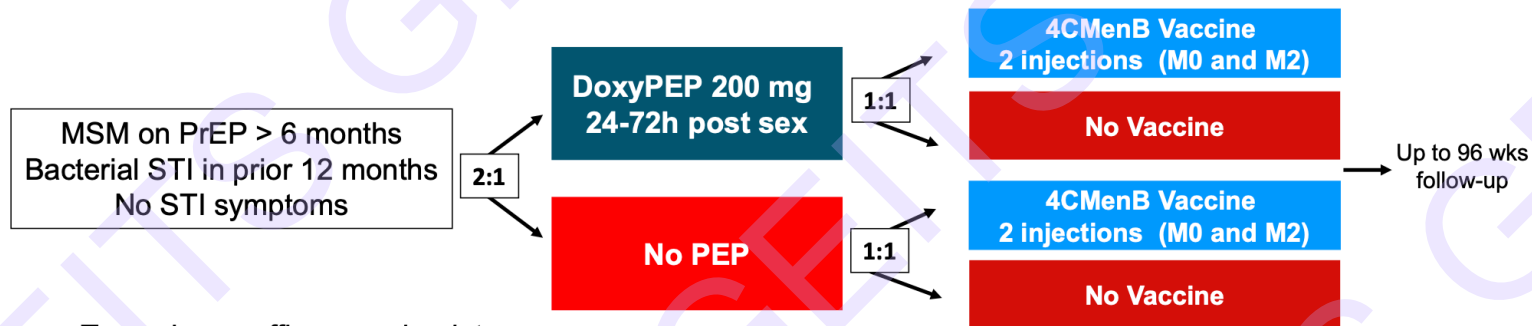


ANRS 174 DoxyVaC (The Lancet_2024)

CROI 2024

ANRS DOXYVAC Study Design

- Multicenter, 2 x 2 factorial randomized, open-label, superiority, phase III trial (NCT04597424)



- Two primary efficacy end-points:
 - Impact of DoxyPEP on time to a first episode of syphilis or chlamydia
 - Impact of the 4CMenB vaccine on time to a first episode of *N. gonorrhoeae* infection.
- Sample size: based on vaccine effectiveness assuming no impact of Doxy on GC: **720** subjects needed for an HR: **0.70** (Estimated probability of a first GC episode over 18 months: 52%, power 85%, 18% lost to FU).
- Quarterly visits with PCR tests (Roche dual target Cobas^o) for GC/CT/MG (3 sites) and serology for TP
- Doxycycline monohydrate purchased from Mylan and 4CMenB vaccine purchased from GSK

ANRS 174 DoxyVaC (The Lancet_2024)

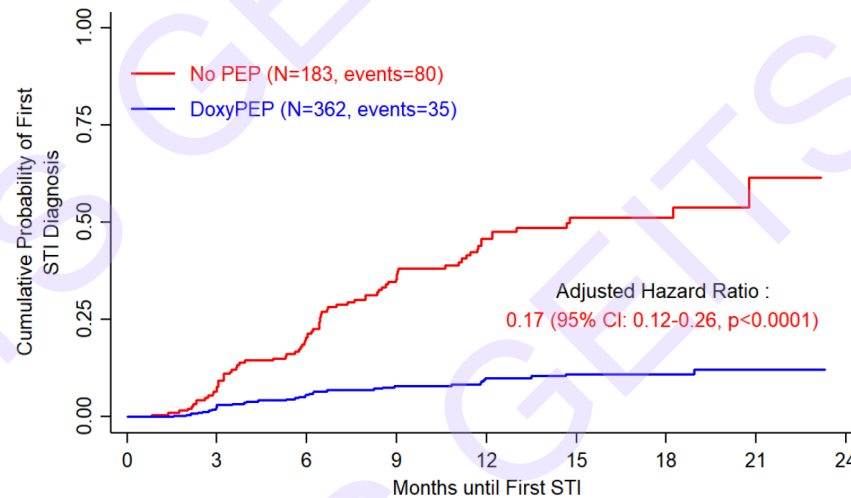
Doxycycline PEP Time to First CT or Syphilis Infection

**No interaction between
Doxy PEP and 4CMenB
vaccine (p=0.83)**

Median follow-up:
14 months (IQR: 9-18)

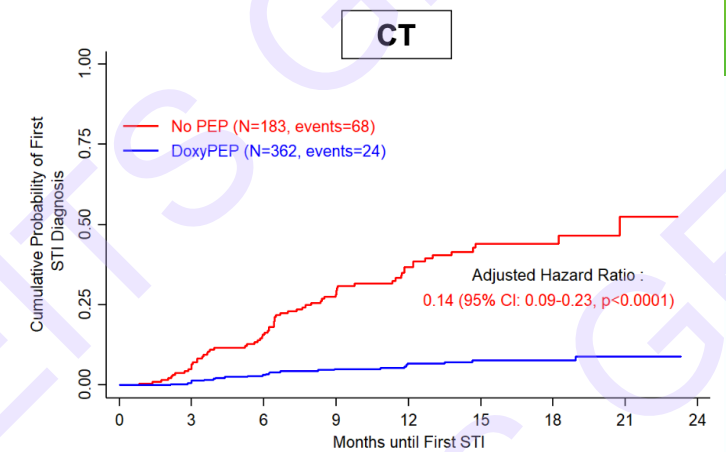
115 subjects infected
80 in No PEP arm
(incidence: 53.2/100 PY),
35 in Doxy PEP arm
(incidence: 8.8/100 PY)

Interim analysis:
49 subjects infected, aHR: 0.16



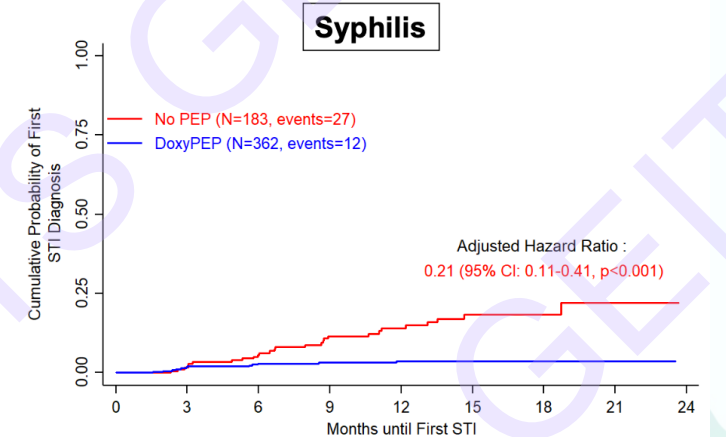
Number at risk	No PEP	183	164	135	92	60	32	20	4	0
DoxyPEP	362	339	316	264	206	146	90	19	0	0

For CT multi-sites infection = 1 single event



Number at risk	No PEP	183	166	143	104	71	37	25	6	0
DoxyPEP	362	345	324	271	213	150	94	19	0	0

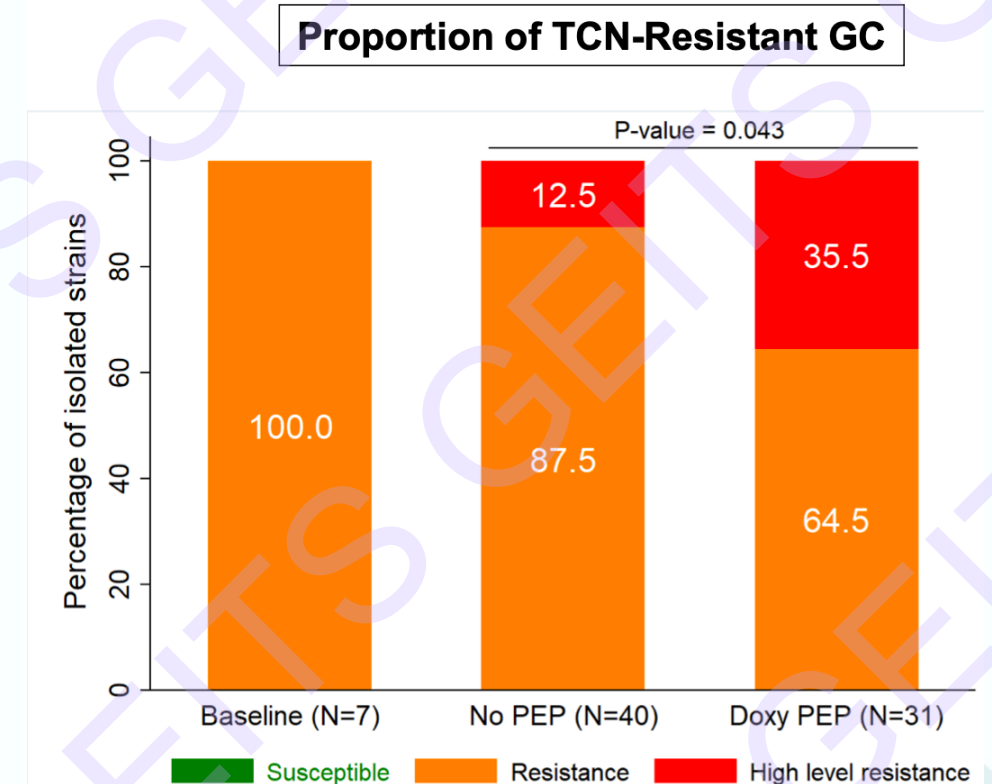
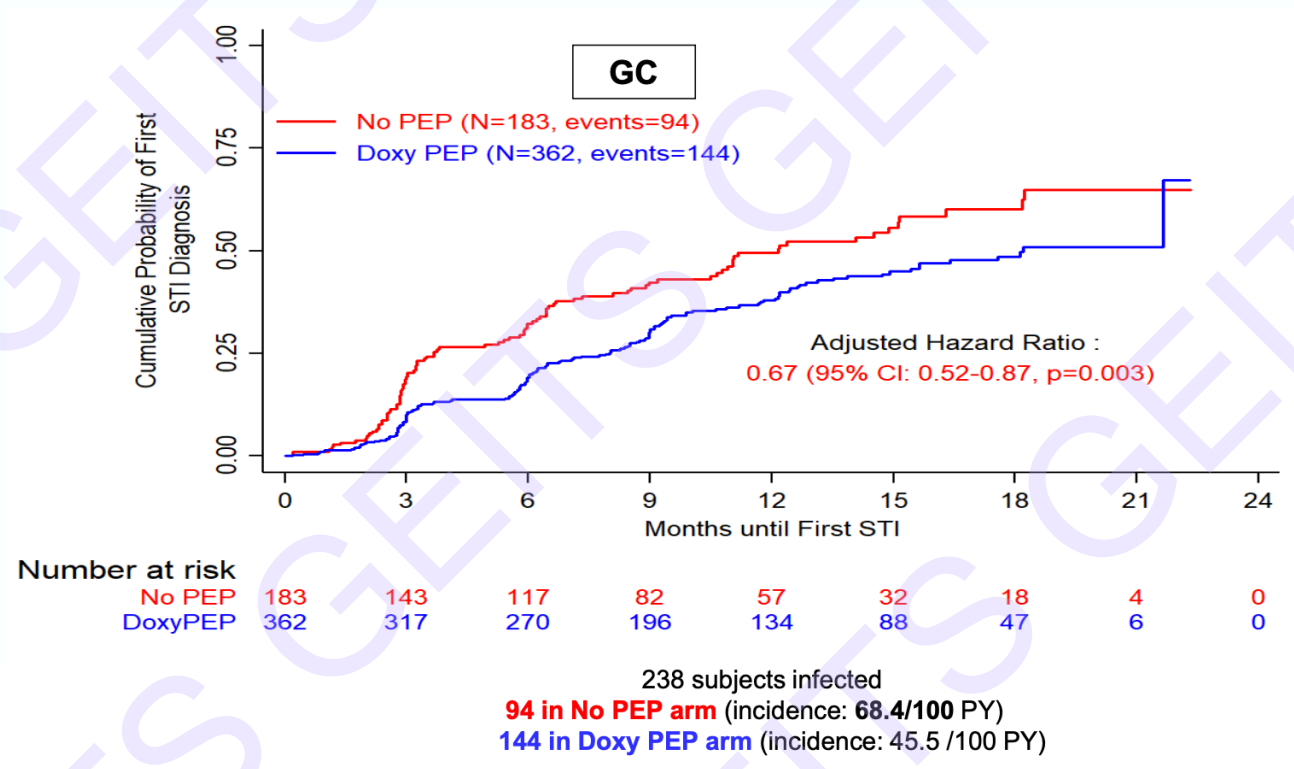
92 subjects infected
68 in No PEP arm (incidence: 42.1/100 PY),
24 in Doxy PEP arm (incidence: 5.9/100 PY)



Number at risk	No PEP	183	175	161	124	94	53	33	10	0
DoxyPEP	362	343	324	277	221	157	96	22	0	0

39 subjects infected
27 in No PEP arm (incidence: 14.5/100 PY),
12 in Doxy PEP arm (incidence: 2.9/100 PY)

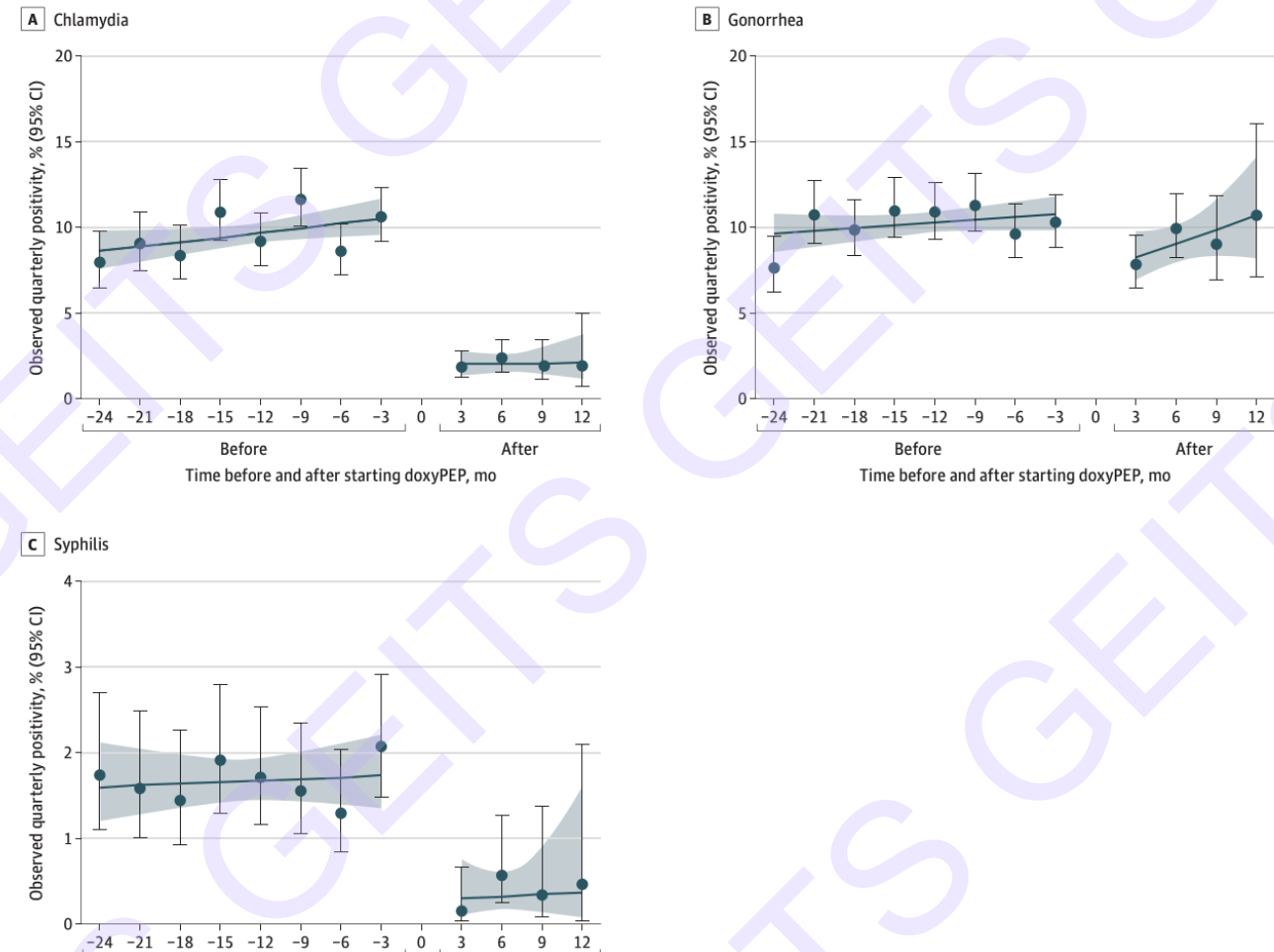
ANRS 174 DoxyVaC: incidencia de NG y resistencias



Estudio retrospectivo cohorte PrEP Kaiser, California (JAMA, 2025)

- Estudio de cohorte retrospectivo: PrEP +/-doxyPEP
- Cribado de ITS trimestral
- 11.551 usuarios de PrEP → 2253 (19,5%) doxyPEP y 1096 (48,6%) habían tenido una ITS en el año previo.
- Positividad trimestral:
 - CT: **9.6%** (IC 95%, 9.0%-10.3%) vs **2.0%** (IC 95%, 1.5%-2.6%) (RR, 0.21; IC 95%, 0.16-0.27; $P < .001$),
 - NG: **10.2%** (IC 95%, 9.6%-10.9%) vs **9.0%** (IC 95%, 8.0%-10.1%) (RR, 0.88; IC 95%, 0.77-1.00; $P = .048$).
 - Sífilis: **1.7%** (IC 95%, 1.4%-1.9%) a **0.3%** (IC 95%, 0.2%-0.6%) después de iniciar doxyPEP (RR, 0.20; IC 95%, 0.11-0.37; $P < .001$).

Figure 1. Quarterly Sexually Transmitted Infection Positivity From 24 Months Before to 12 Months After Starting Doxycycline Postexposure Prophylaxis (DoxyPEP) Among HIV Preexposure Prophylaxis Users Dispensed DoxyPEP at Least Once (n = 2253)



Posicionamiento frente a Doxy-PEP

- ASHM (2023)
- CDC (2024)
- BASHH (2025)
- EACS (2025)
- SEIMC (2024 - GEITS)

Posicionamiento frente a Doxy-PEP_ASHM (2023)



ashm

2023 Consensus Statement on doxycycline prophylaxis (Doxy-PEP) for the prevention of syphilis, chlamydia and gonorrhoea among gay, bisexual, and other men who have sex with men in Australia.

- Doxy-PEP should be considered primarily for the prevention of **syphilis** in GBMSM who are at risk of this STI, although for some individuals the reduction in chlamydia, and the lesser reduction of gonorrhoea might be important. Some stakeholders held the view that Doxy-PEP should be considered **only** for the prevention of syphilis in GBMSM, for the reasons listed above.
- While evidence for appropriate suitability criteria for commencing Doxy-PEP is limited, the following might be appropriate for considering doxy-PEP until further data emerges:
 1. GBMSM with a recent syphilis diagnosis (e.g., within the previous six or twelve months); or
 2. GBMSM with two or more recent other (i.e., not syphilis) bacterial STI diagnoses (e.g., within the previous six or twelve months); or
 3. GBMSM who identify an upcoming period of heightened STI risk, for example, attendance at a sex event, or holiday plans that likely involve sexual activity with multiple casual sexual partners; or
 4. GBMSM with concurrent male and cisgender female sexual partners or other sexual partners with a uterus, recognising the additional health risks posed by chlamydia, gonorrhoea and syphilis for people with a uterus.
 5. GBMSM who present for HIV PEP can also consider Doxy-PEP, although the indications for HIV PEP do not necessarily indicate a need for Doxy-PEP.

Posicionamiento frente a Doxy-PEP_CDC (5/Dic/2024)

- Comentar los pros y contras del Doxy-pep con GBHSH y mujeres trans que hayan tenido una ITS bacteriana en el último año.
- Pauta de doxy-PEP →
- Ofrecimiento en el contexto de un enfoque integral de salud sexual.

<https://www.cdc.gov/sti/hcp/doxy-pep/index.html>

CDC Sexually Transmitted Infections (STIs)

EXPLORAR ESTE TEMA ▾

HOW TO TAKE DOXY PEP

Dosing Chart

- 200 mg** of doxycycline taken within **24 hours** (*ideal*), but no later than **72 hours** (*acceptable*) after anal, oral, or vaginal sex.
- Doxy PEP can be taken every day, but not more than **once a day** (200mg per day maximum).

Example

SEX ON SATURDAY:

Ideal: Take doxy PEP on Sunday

Acceptable: Take doxy PEP no later than Tuesday

Timeline diagram showing Ideal Time Frame (0 to 24 hours) and Acceptable Time Frame (0 to 72 hours).

CDC

Posicionamiento frente a Doxy-PEP_BASHH (2022; 2025)

BASHH updated position statement on doxycycline as prophylaxis for sexually transmitted infections

Manik Kohli ^{1,2}, Nicholas Medland,^{3,4} Helen Fifer ⁵,
John Saunders ^{1,5}

to advise patients about STI prophylaxis. Importantly, it remains the case that doxycycline taken as PEP or pre-exposure prophylaxis (PrEP) for STIs is not endorsed by BASHH or UKHSA.

Kohli M, et al. *Sex Transm Infect* May 2022 Vol 98 No 3

BASHH Guidelines

British Association for Sexual Health and HIV (BASHH) UK national guideline for the use of doxycycline post-exposure prophylaxis (DoxyPEP) for the prevention of syphilis, 2025

John Saunders¹ , Joseph Deering², Claire Dewsnap³, Rachel Drayton⁴, John Gilmore⁵, Alison Grant⁶, Dwayne-Wilson Hunt⁷, Manik Kohli^{8,9} , Fiona Lyons¹⁰, Hamish Mohammed¹, Phil Samba¹¹, Benjamin Weil¹¹, John White¹², Nicholas Medland¹³ and Helen Fifer¹ 

Abstract

This guideline provides evidence-based recommendations for the use of doxycycline post exposure prophylaxis (doxyPEP) for the prevention of syphilis. DoxyPEP should be part of a comprehensive approach to the prevention of STIs, along with condom use, appropriate HIV prevention interventions, vaccination, STI testing, treatment and management, and appropriate risk reduction advice and psychological interventions if indicated.

Saunders J, Deering J, Dewsnap C, et al. H. British Association for Sexual Health and HIV (BASHH) UK national guideline for the use of doxycycline post-exposure prophylaxis (DoxyPEP) for the prevention of syphilis, 2025. *Int J STD AIDS*. 2025 Sep;36(10):756-764. doi: 10.1177/09564624251352053. Epub 2025 Jun 12. PMID: 40505019.

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Posicionamiento frente a Doxy-PEP_EACS (1/Oct/2025)

EACS Guidelines

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Prophylaxis for Bacterial STIs - DoxyPEP

last updated Oct 1, 2025

Prophylaxis for Bacterial STIs

- Multiple randomized clinical trials have shown that administration of doxycycline after condomless sexual contact (Doxy-PEP) is effective in reducing the incidence of chlamydial infections and syphilis in gay and bisexual men who have sex with men (GBMSM) and transgender women (TGW) compared to standard of care. Effectiveness against *N. gonorrhoeae* was observed only in some studies and may depend on local antimicrobial susceptibility profiles.
- GBMSM and TGW with history of a recent (<12 months) STI should be counselled on the benefits and risks of Doxy-PEP. Limited data are available on the effectiveness and safety of Doxy-PEP in populations other than GBMSM and TGW.
- Doxy-PEP should be administered as a single, oral 200 mg doxycycline dose taken as soon as possible and within 72 hours after sexual contact. The cumulative dose should not exceed 200 mg in 24 hours.
- At the initial visit, individuals initiating doxy-PEP should be screened and appropriately treated for any diagnosed STIs.
- Doxy-PEP should be part of a holistic approach aimed at improving sexual health, and individuals should be counselled on additional STI risk reduction strategies.
- The need for ongoing doxy-PEP should be routinely re-evaluated at follow-up visits.

Posicionamiento frente a Doxy-PEP_SEIMC (2024)



**DOCUMENTO DE POSICIONAMIENTO
SOBRE EL USO PROFILÁCTICO DE DOXICICLINA PARA PREVENIR LAS ITS (DOXI-PEP)
DE LA SOCIEDAD ESPAÑOLA DE ENFERMEDADES INFECCIOSAS Y MICROBIOLOGÍA CLÍNICA (SEIMC)
A TRAVÉS DEL GRUPO DE ESTUDIO EN INFECCIONES DE TRANSMISIÓN SEXUAL (GEITS), DEL GRUPO DE ESTUDIO DEL SIDA
(GESIDA) Y DEL GRUPO DE ESTUDIO DE LOS MECANISMOS DE ACCIÓN Y DE LA RESISTENCIA A LOS ANTIMICROBIANOS
(GEMARA)**

Marzo, 2024

EVIDENCIA CIENTÍFICA DEL USO DE LA DOXI-PEP

La profilaxis antibiótica se usa habitualmente en distintas situaciones clínicas y epidemiológicas como prevención secundaria de distintas enfermedades infecciosas. Dado el aumento en la incidencia de las infecciones de transmisión sexual (ITS) a nivel mundial y, en particular en Europa, se han intensificado los esfuerzos para identificar nuevas estrategias de prevención efectivas. Hasta la fecha, diversos estudios han evaluado el impacto del uso profiláctico postexposición de la doxiciclina (doxi-PEP) para la prevención de las ITS de origen bacteriano (tabla 1), evidenciando una reducción significativa en el riesgo de adquisición de infecciones como la sífilis, la clamidiasis y, en menor medida, la gonococia.¹⁻⁵



Posicionamiento frente a Doxy-PEP_SEIMC (2024)

- El uso de la Doxiciclina para prevención de ITS se considera fuera de indicación.
- Valorar únicamente y de manera individualizada en HSH o MTG que tienen sexo con hombres y que han presentado reiteradas ITS en el último año (no en mujeres cisgénero ni en hombres trans).
- Doxi-PEP (200 mg/día) <24h (<72h) del contacto sexual (oral, anal o vaginal sin psvt).
- Informar sobre la efectividad, beneficios y riesgos que conlleva su administración, decisión compartida.
- Fundamental informar al paciente sobre la importancia y la necesidad de mantener relaciones sexuales con protección.
- Necesidad de estudios longitudinales para conocer el impacto en la selección y diseminación de resistencia a tetraciclinas u otras familias de antimicrobianos.

Doxy-pep: beneficios vs riesgos

Beneficios

- Seguro y bien tolerado.
- Responde a una necesidad salud pública
- Reduce incidencia de sífilis
- Reduce incidencia de CT
- La gente ya lo hace, mejor con receta
- Reducción moderada frente NG ¿Limitación?

Limitaciones

- Se seleccionan y transmiten cepas resistentes (NG frente a tetraciclinas)
- Efectos de la presión antibiótica en el microbioma desconocidos
- La serología de sífilis es menos interpretable
- Si estuviera disponible, su uso se extenderá a más personas de las que lo necesitan
- Resultados a largo plazo desconocidos

Conclusiones

- Varios ensayos clínicos han mostrado una fuerte reducción de infecciones por clamidia y sífilis entre HSH y mujeres trans. Buena tolerancia y alta adherencia.
- Menos eficaz contra la gonococia, con una tasa creciente de resistencia de alto nivel a las tetraciclinas.
- Se están llevando a cabo estudios de implementación con monitoreo de la resistencia a antibióticos.
- Valorar de forma individualizada la conveniencia de la Doxy-pep, una decisión compartida que se integra con en una estrategia de prevención combinada.



Muchas gracias