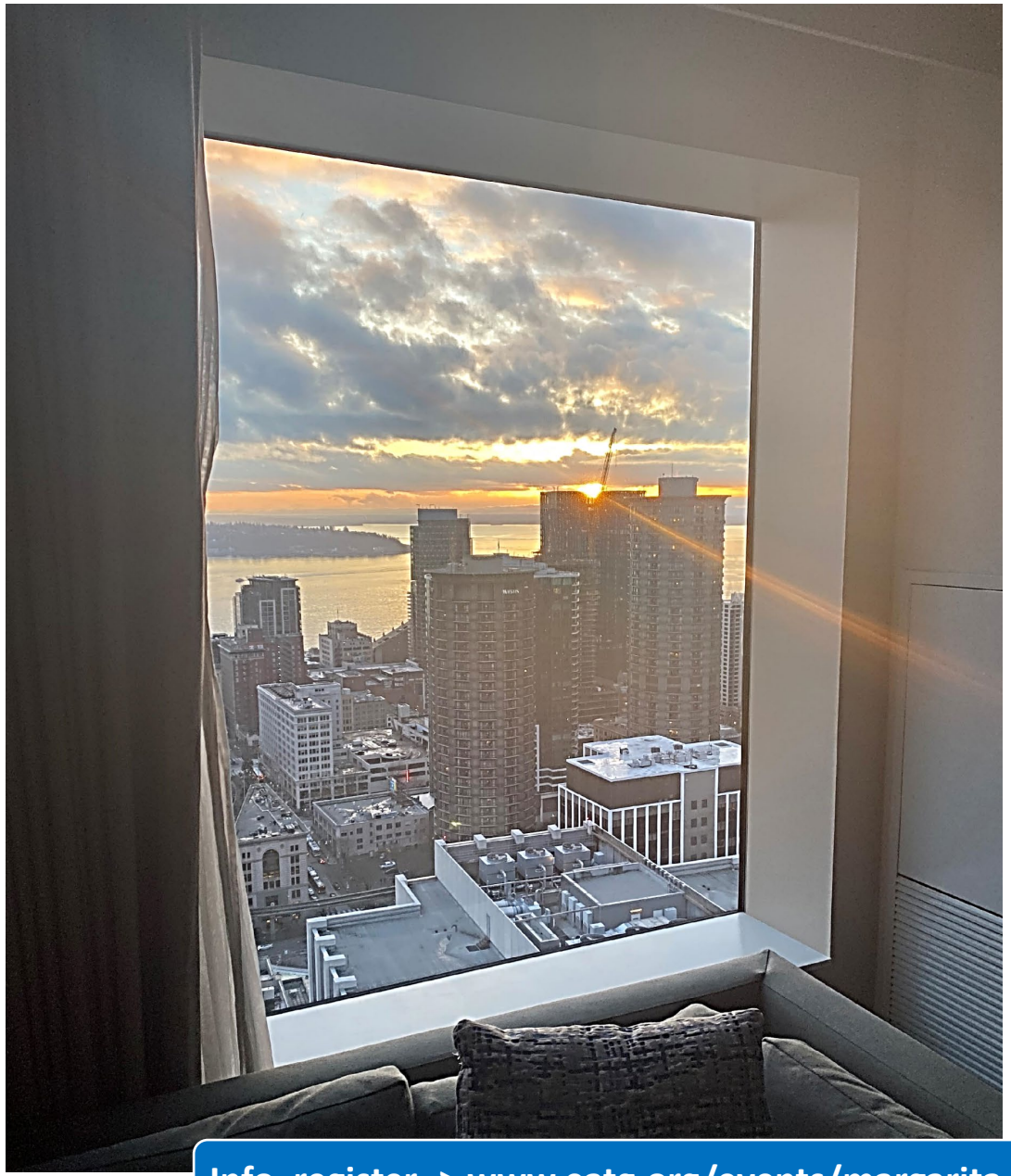

DAILY COMMUNITY RESEARCH UPDATES FROM CROI2023

MARGARITA BREAKFAST CLUBS

AT #CROI2023

FEBRUARY 20-22 2023

7:00 – 8:00 AM PST
16:00 – 17:00 CET

REGISTER AT ZOOM

MONDAY FEBRUARY 20: ARRESTED DEVELOPMENT: DISCONTINUATION OF THE MOSAICO TRIAL, ITS LEGACY AND EXPECTATIONS FOR HIV VACCINE RESEARCH DR. SUSAN BUCHBINDER AND RICHARD JEFFERYS

TUESDAY FEBRUARY 21: MOVING FORWARD: UPCOMING STRATEGIES ON STI PREVENTION JEAN-MICHEL MOLINA AND JONATHAN AYALA

WEDNESDAY FEBRUARY 22: THE DATA GAP: FILLING IN THE MISSING PERSPECTIVES ON WOMEN AND CHILDREN IN HIV RESEARCH PROFESSOR LEE FAIRLIE, JANE KABAMI AND IMELDA MAHAKA

Open to everyone!
CROI registration is not required

ation with AVAC, EATG and

CROI AVAC EATG European AIDS Treatment Group

Info, register -> www.eatg.org/events/margarita-breakfast-clubs-at-croi-2023/


There were 2 main lineages of SARS-CoV-2 in the early epidemic, A and B

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30th CROI 2023

ANRS 174 DOXYVAC
An Open-Label Randomized trial to Prevent STIs in MSM on PrEP

Jean-Michel Molina

University of Paris Cité, St-Louis/Lariboisière Hospitals, APHP, Paris, France

Disclosure: *Laboratory support from Roche*

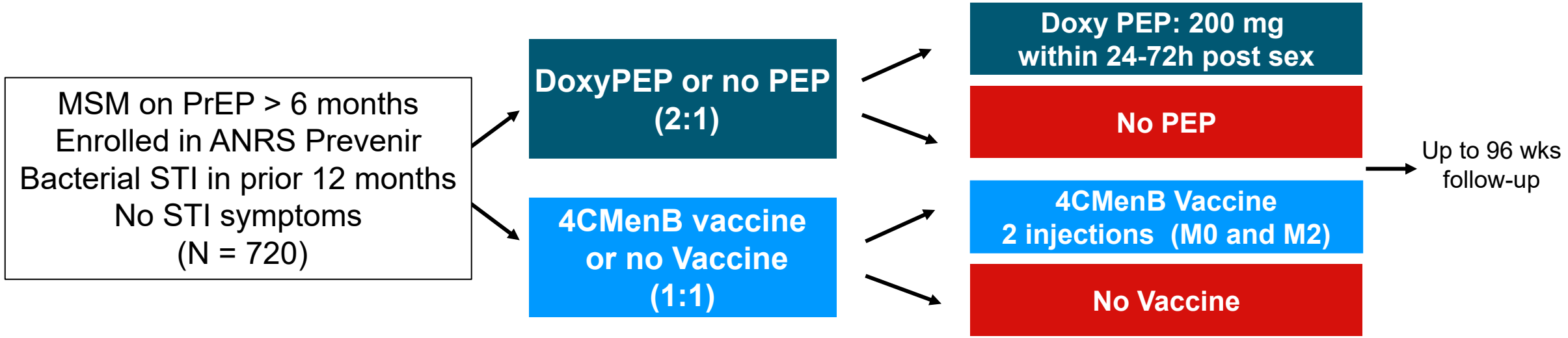
Background

- High rate of bacterial STIs among men who have sex with men (MSM) on PrEP: cumulative incidence of 75.8/100 PY in the ANRS Prevenir study.
- Doxycycline PEP reduced chlamydia and syphilis incidence by ~70% in the ANRS Ipergay trial, but no significant effect on gonorrheae (tetracycline resistance rate in France in 2021: 65.7%).
- Meningococcal B vaccines associated with 26-46% reduction of gonorrhoae in observational studies.
- 4CMenB vaccine contains OMV proteins shared with *N. gonorrheae* with 44-99% genetic homology and 69% homology for NHBA protein.
- Need for confirmation studies and assessment of antibiotic resistance before implementation

Molina Lancet HIV 2022, Molina Lancet Inf Dis 2018, Petoussis-Harris et al. Lancet 2017; Folaranmi CID 2017; Semchenko EA et al. CID 2019; Semchenko EA et al. JID 2020; Abara et al Lancet ID 2022; Wang et al. Lancet ID 2022 ; Bruxvoort KJ. et al. CID 2022

Study Design

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



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

ANRS 174 DOXYVAC
Premature Study Discontinuation

- August 2022 DOXYPEP results: 65% reduction in STIs incidence (CT and syphilis ~ 80%; GC ~ 55%)
- September 2, 2022: DOXYVAC DSMB requested unblinded analysis on participants enrolled from 01/19/2021 to 07/15/2022
- Significant effectiveness of both interventions and DSMB recommended to:
  - stop enrollment of new participants (last enrolment: 09/19/2022)
  - offer Doxy PEP and 4CMenB vaccine to all (last visit up to 01/2023).
- Recommendations endorsed by the scientific committee and ANRS

Luetkemeyer A. et al. AIDS 2022 Montreal 29 July-2 August, 2022. Canada

Participants Baseline Characteristics

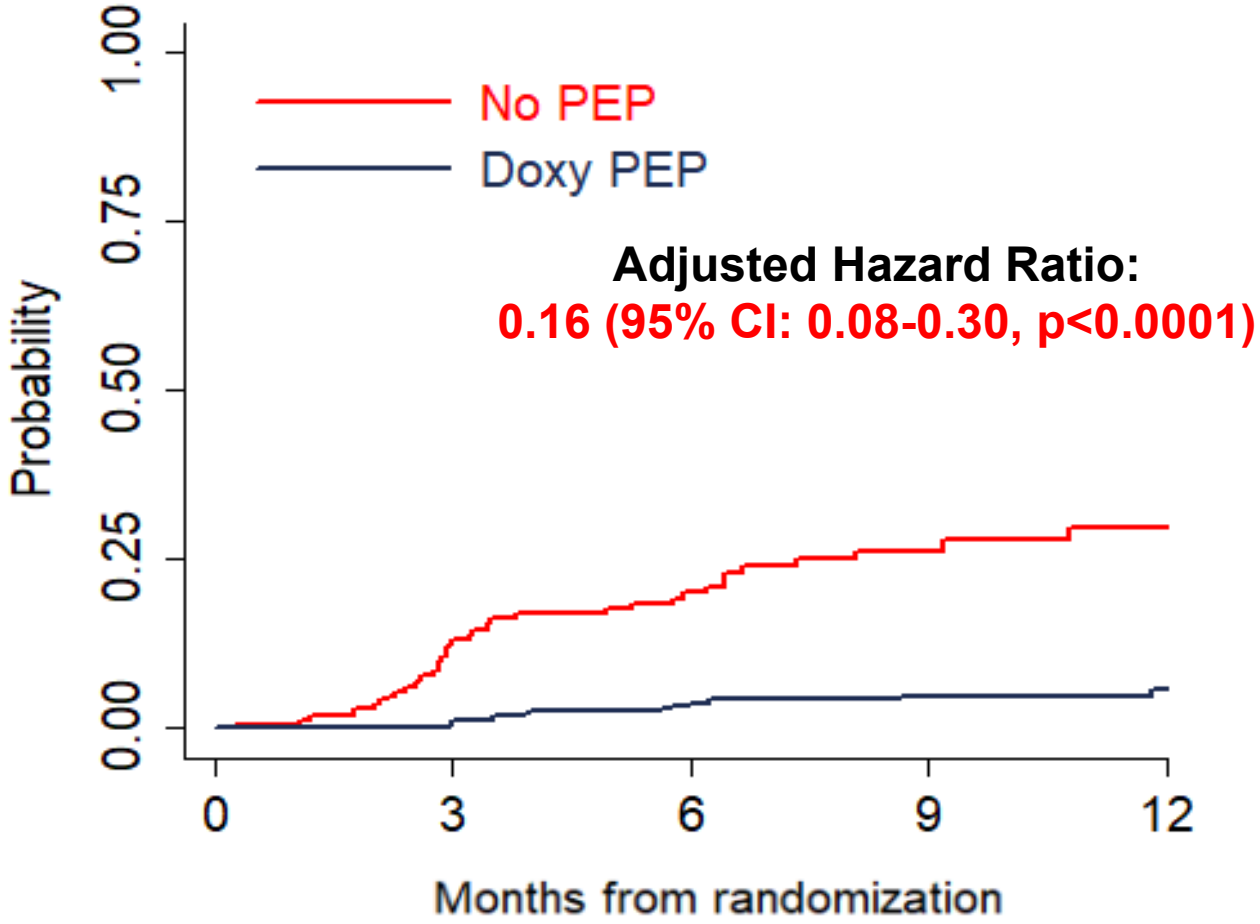
Median (IQR) or %	Doxy PEP (n = 332)	No PEP (n = 170)	4CMenB vaccine (n = 257)	No Vaccine (n = 245)	Total (n=502)
Age, years	40 (33-48)	39 (33-47)	40 (33-47)	39 (33-48)	**39 (33-47)**
White	79.2	82.9	75.9	85.3	**80.5**
Born in France	84.8	81.7	82.7	84.8	**83.8**
Secondary education	89.1	88.4	90.7	87.0	**88.9**
Employed	87.0	87.5	89.6	84.6	**87.2**
PrEP use, months	42 (32-55)	43 (35-55)	43 (32-55)	42 (33-54)	**42 (32-55)**
No. STIs in prior 12 months	2 (1-2)	2 (1-2)	2 (1-3)	2 (1-2)	**2 (1-2)**
Gonorrheae	67.3	70.1	67.5	69.0	**68.2**
Chlamydiae	50.3	47.9	52.5	46.3	**49.5**
Syphilis	21.5	17.4	20.4	19.8	**20.1**
M. genitalium	3.9	4.2	3.5	4.5	**4.0**
Condomless sex (4 weeks) no.	5 (3-10)	5 (2-10)	5 (2-10)	5 (3-10)	**5 (2-10)**
Partners (last 3 months) no.	10 (5-20)	10 (5-20)	10 (5-20)	10 (5-20)	**10 (5-20)**
Chemsex at last sex act	11.8	10.6	12.5	10.2	**11.4**

Doxycycline PEP
Time to First CT or Syphilis Infection

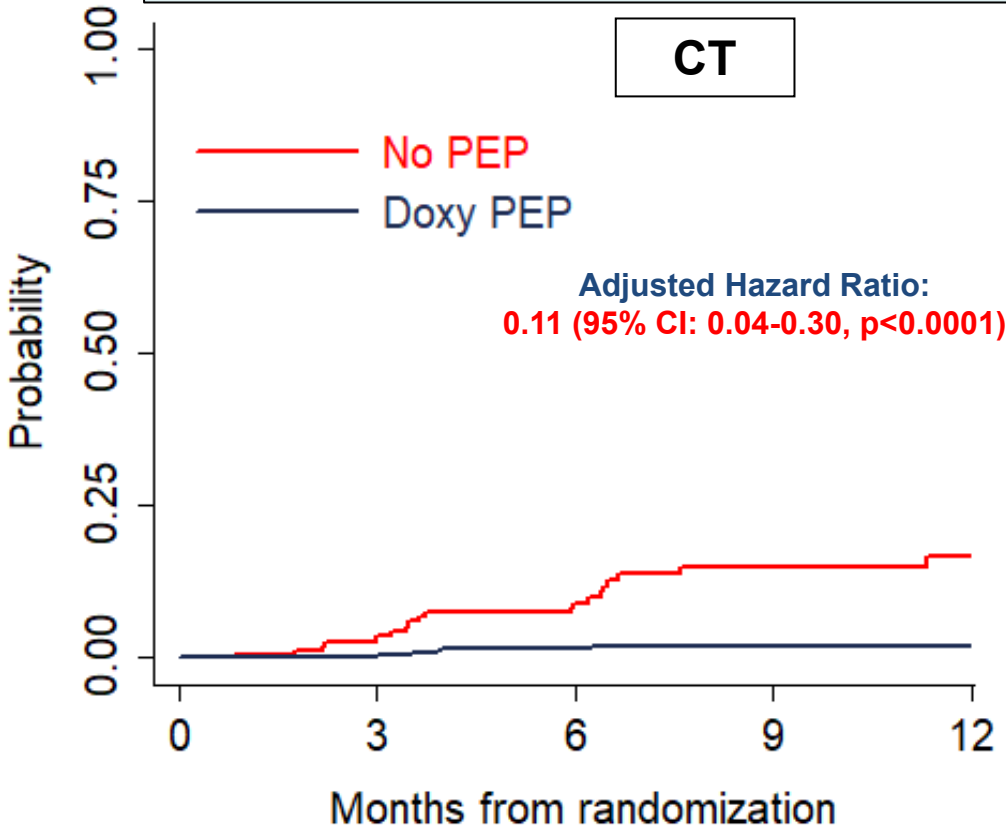
No interaction between Doxy PEP and 4CMenB vaccine (p=0.99)

Median follow-up: **9 months**
(IQR: 6 to 12)

49 subjects infected
36 in No PEP arm
(incidence: 35.4/100 PY),
13 in Doxy PEP arm
(incidence: 5.6/100 PY)



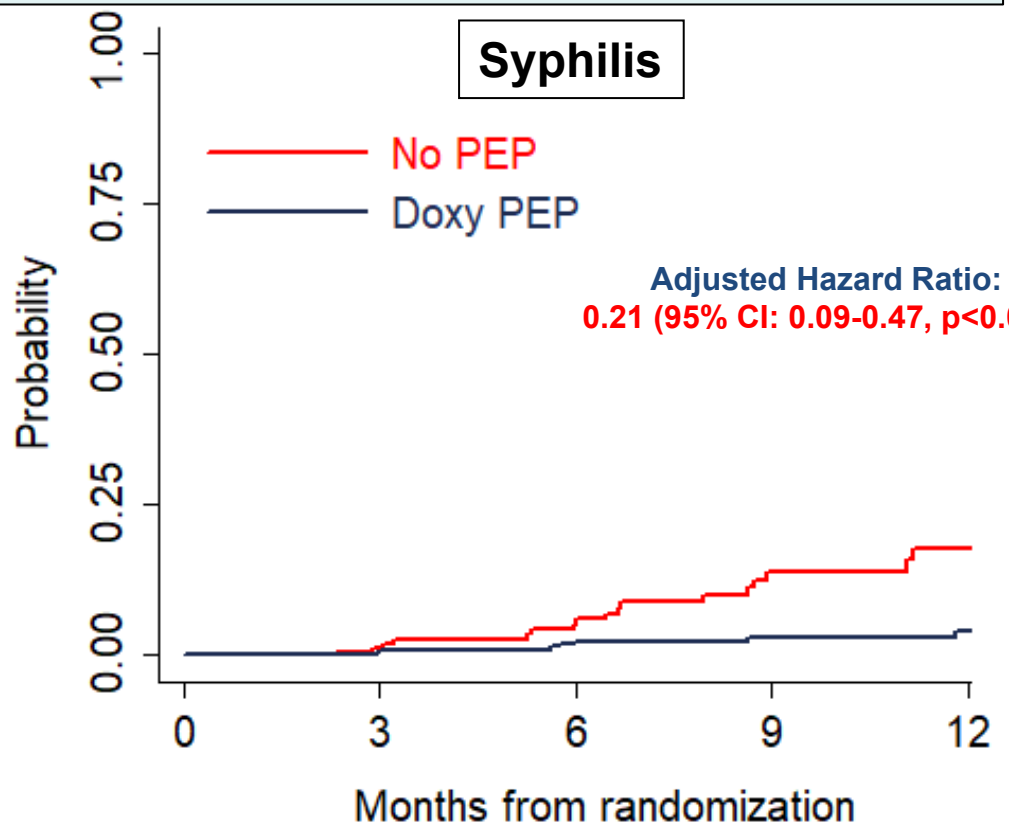
Doxycycline PEP
Time to First CT and Syphilis Infection



Number at risk

No PEP	170	139	105	58	30
Doxy PEP	332	274	223	147	86

26 subjects infected
21 in No PEP arm (incidence: 19.3/100 PY),
5 in Doxy PEP arm (incidence: 2.1/100 PY)

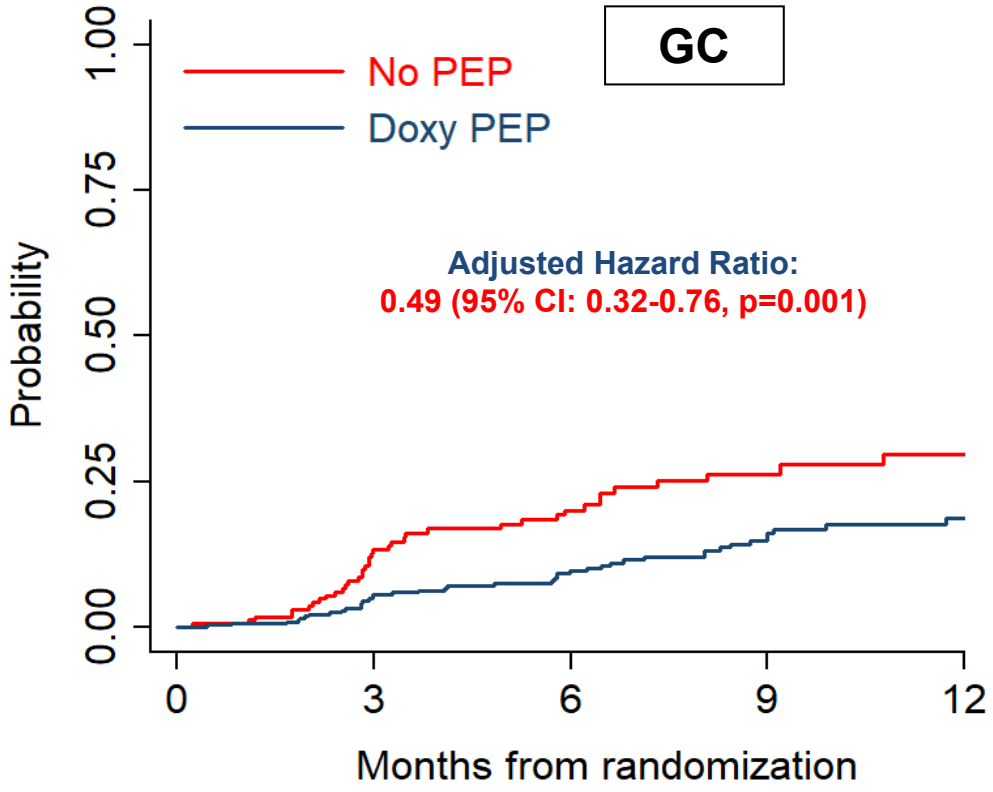


Number at risk

No PEP	170	142	109	56	27
Doxy PEP	332	272	224	147	85

26 subjects infected
18 in No PEP arm (incidence: 16.3/100 PY),
8 in Doxy PEP arm (incidence: 3.4/100 PY)

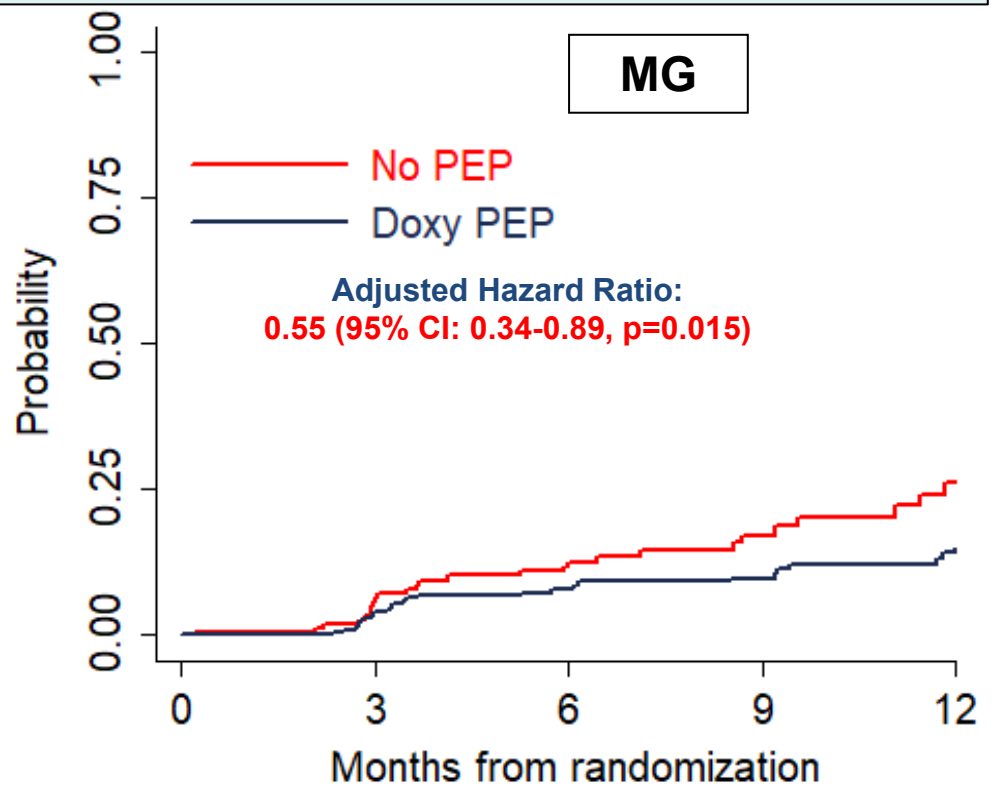
Doxycycline PEP
Time to First GC and MG infection



Number at risk

No PEP	170	125	90	47	20
Doxy PEP	332	259	201	128	66

84 subjects infected
40 in No PEP arm (incidence: 41.3/100 PY),
44 in Doxy PEP arm (incidence: 20.5/100 PY)



Number at risk

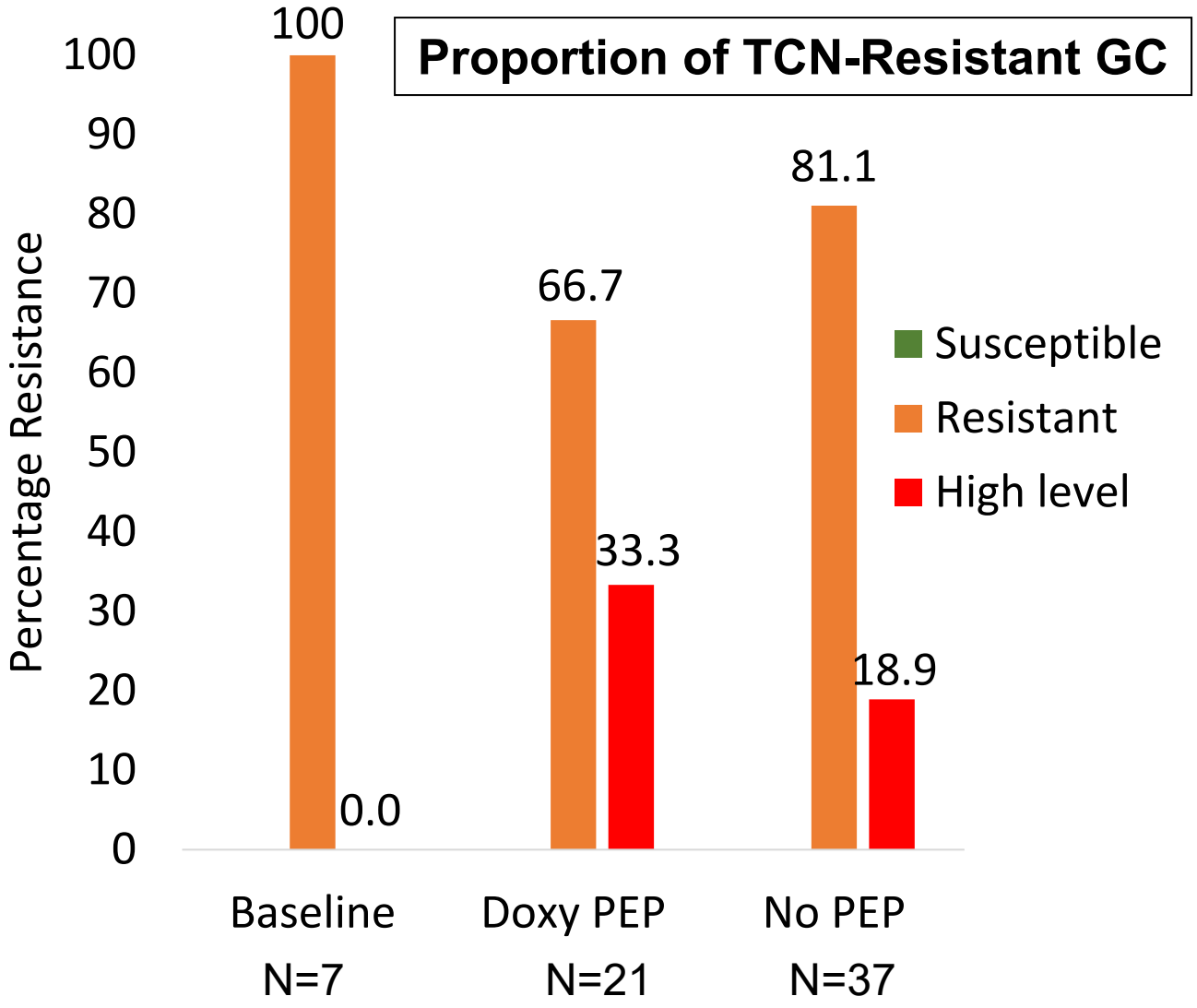
No PEP	170	148	110	67	38
Doxy PEP	332	298	234	157	89

68 subjects infected
31 in No PEP arm (incidence: 29.4/100 PY),
37 in Doxy PEP arm (incidence: 16.8/100 PY)

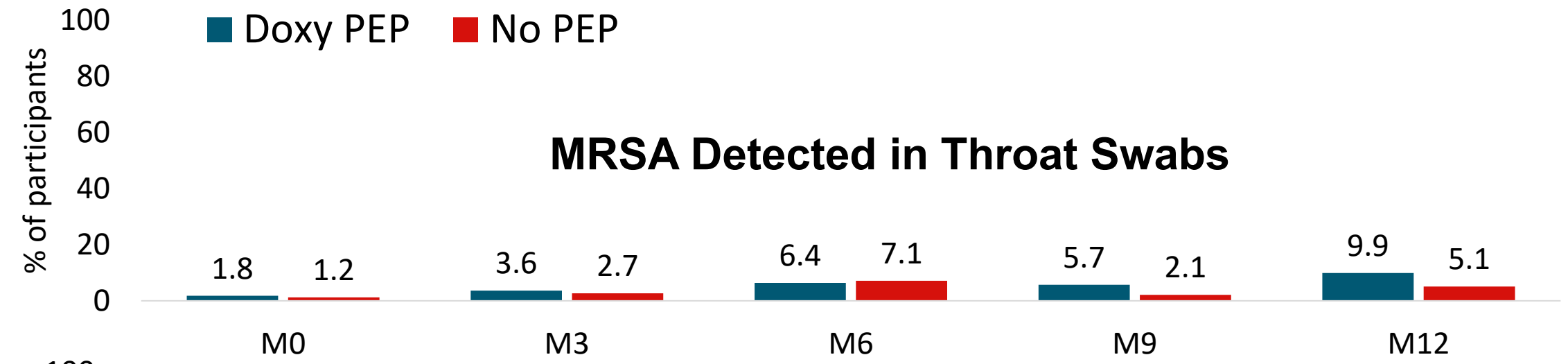
Tetracycline (TCN) Resistance for GC and CT

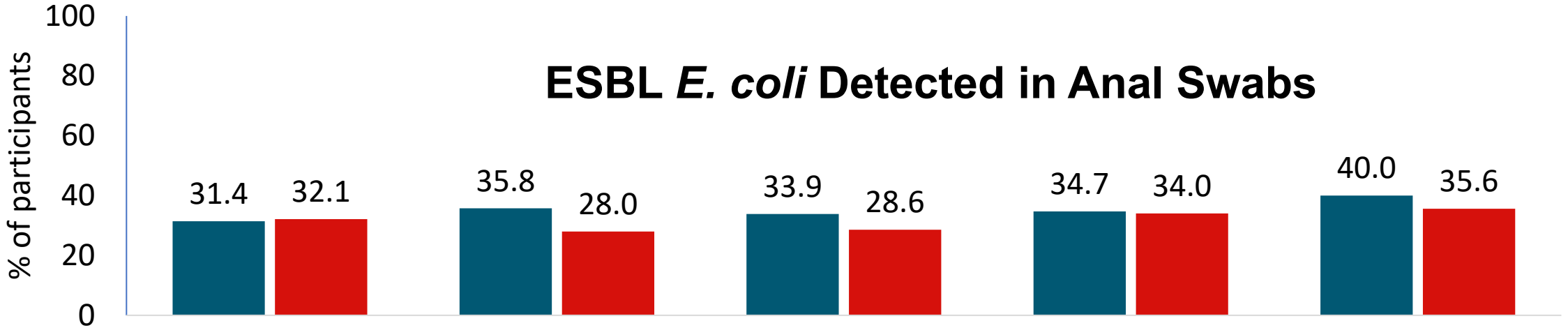
- **GC:**
  - 65 cultures available for resistance testing (15% of PCR positive samples)
  - Tetracycline MICs determined by Etest
  - Resistance using EUCAST 2023 breakpoints
    - Resistance: MIC > 0.5 mg/L
    - High level resistance: MIC > 8 mg/L

- **CT**:
  - 4/23 strains tested for TCN-R in culture: no resistance (but none from PEP arm)
  - 53/65 PCR+ swabs with16S rRNA sequenced: no TCN-R mutation (only 3 from PEP arm)



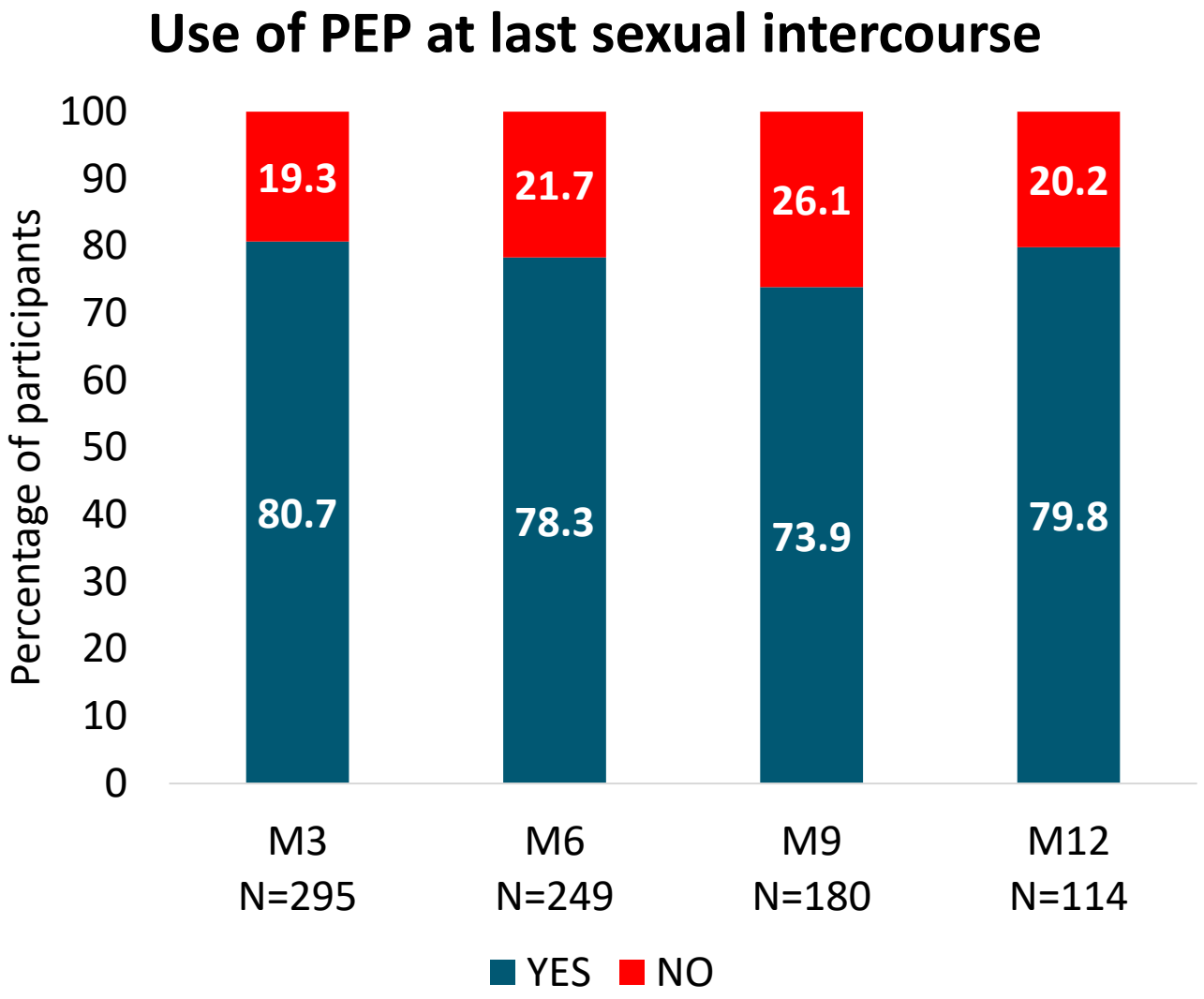
Microbiome Analysis





	M0	M3	M6	M9	M12
Doxy PEP	331	304	251	193	121
No PEP	168	150	126	94	59

Self-Reported Adherence to Doxy PEP

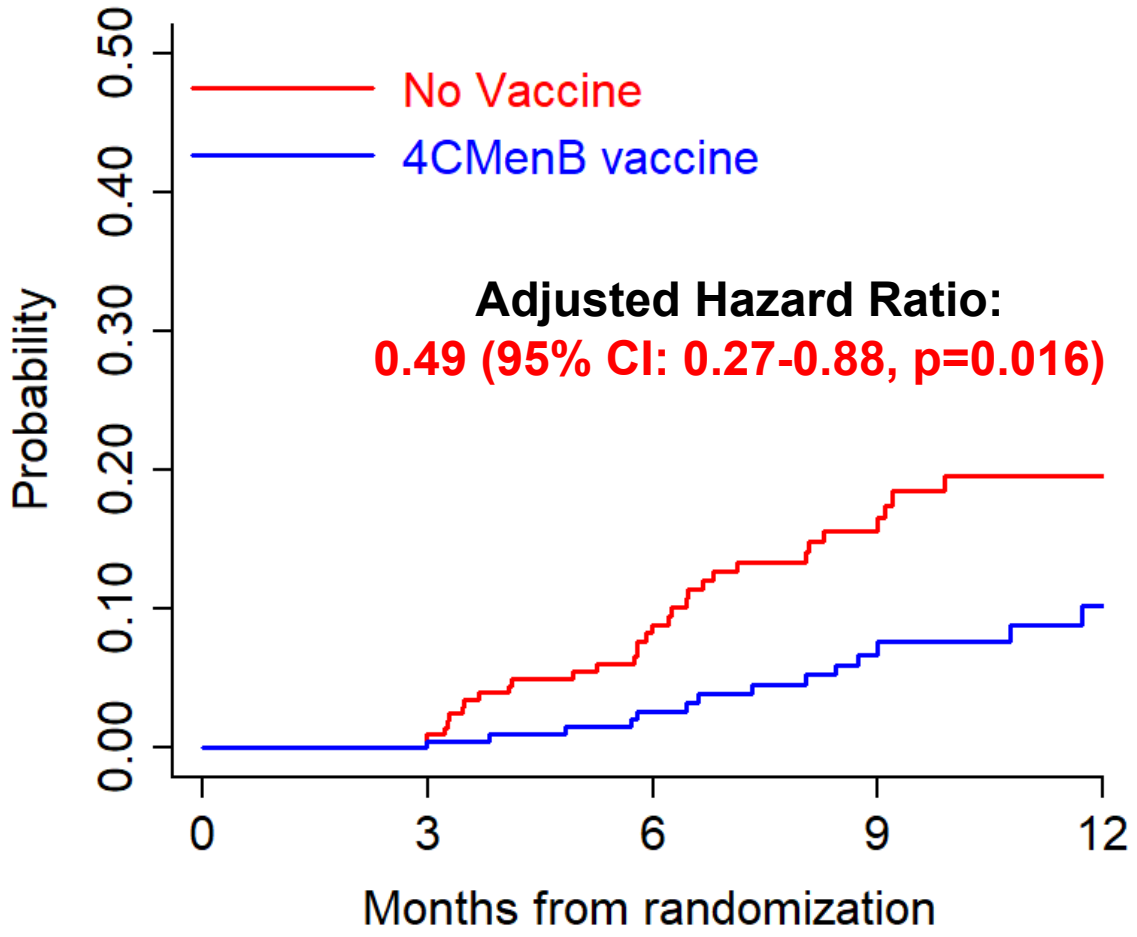


- **Median (IQR) time to PEP intake: 27h** (5-33) after sex
- **Median (IQR) PEP use: 83% (50-100%)** per participant during follow-up
- **Median no. of pills/month (IQR): 7 pills** (4-11)
- **3 (0.9%) discontinued PEP:** GI AEs (n=2) and fear of AEs (n= 1)

4CMenB Vaccine
Time to First GC infection

No interaction between Doxy PEP and 4CMenB vaccine (p=0.41)

49 subjects infected
32 in No Vaccine arm
(incidence: 19.7/100 PY),
17 in 4CMenB vaccine arm
(incidence: 9.8/100 PY)

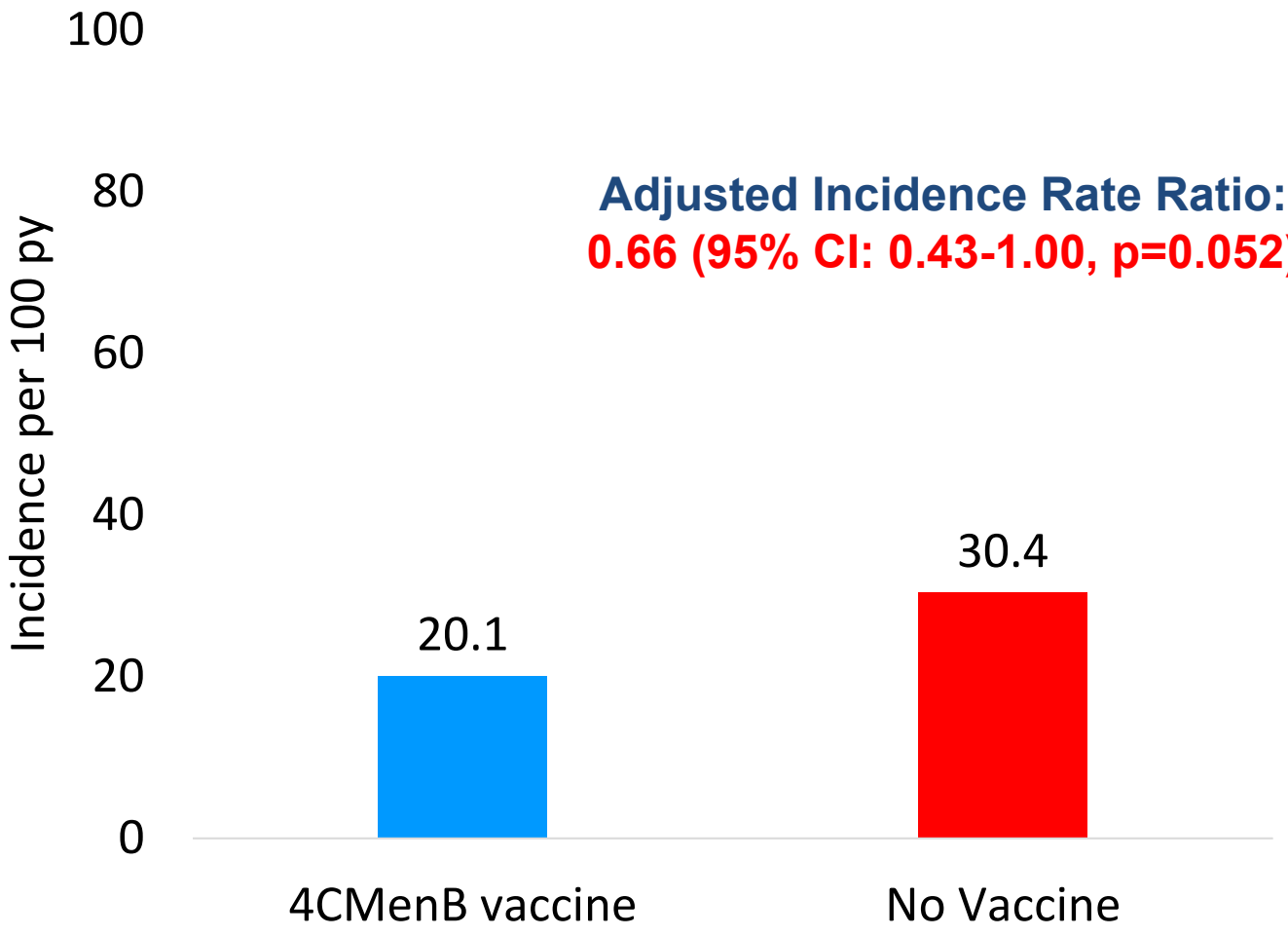


GC infections were considered from M3 visit (1 month after 2nd vaccine dose)

Number at risk					
No Vaccine	245	208	150	91	49
4CMenB vaccine	257	208	170	102	49

4CMenB Vaccine
Cumulative Incidence of GC Infections

90 GC infections
54 in No Vaccine arm,
36 in 4CMenB vaccine arm



Adjusted Incidence Rate Ratio:
0.66 (95% CI: 0.43-1.00, p=0.052)

GC infections were considered from M3 visit (1 month after 2nd vaccine dose)

4CMenB Vaccine - What is Next ?

- Efficacy Studies of 4CMenB (Bexsero®) vs. Placebo to Prevent Gonorrhoea
  - in Gay and Bisexual Men (GoGoVax), n= 730 MSM on PrEP or HIV+ in Australia. Study Chair: Pr Kate Seib. (NCT 04415424) Started in 07/2021
  - in Men and Women, n= 2200 in the US and Thailand, NIAID. Study Chair: Pr. J. Marrazzo. (NCT 04350138) Started in 12/2020 (700 enrolled)
- Modeling studies:
  - A vaccine with modest efficacy would reduced NG prevalence among MSM by 62% within 2 years with possible elimination in 8 years (Hui BB et al. JID 2022)

Summary

- **Doxycycline PEP:**
  - 3 large studies have shown significant reductions of STIs among MSM
  - Doxycycline PEP is well tolerated with high self-reported adherence
  - Evaluation of full impact on antibiotic resistance is underway (STIs, microbiome)
- **4CMenB Vaccine:**
  - 4CMenB vaccine reduced GC incidence among MSM on PrEP
- **There is no magic bullet:** Interest for combined approaches
- **STI research:** a scientific priority to meet 2030 WHO/UNAIDS targets to reduce incidence of HIV and STIs by 90%

Acknowledgments

Participants

Sites investigators

Scientific committee

DSMB: M. Resche-Rigon, O. Chosidow, L. Cotte, C. Alauzet, H. Pollard

AIDES: D. Michels

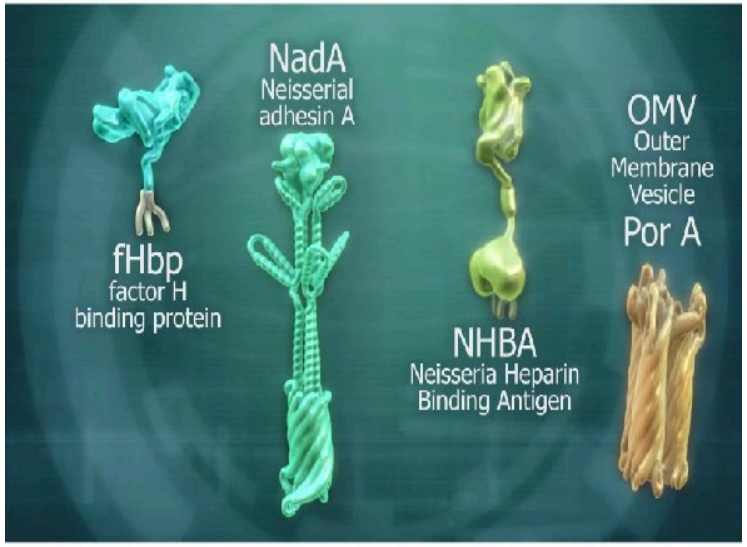
ANRS/MIE: V. Petrov, S. Lemestre, C. Birkle

Study team: JM Molina, B. Bercot, L. Assoumou, M. Algarte-Genin, E. Rubenstein G. Pialoux, C. Katlama, L. Surgers, C. Bebear, N. Dupin, JP. Viard, J. Pavie C. Duvivier, J. Ghosn, and D. Costagliola

@jmmolinaparis

Potential Cross-Protection against Gonorrhoea with Meningococcal B Vaccine

- Meningococcal group B vaccines may affect incidence of gonorrhoea
  - 31% reduction of gonorrhea in a case-control study in NZ
  - Similar ecological evidence in Cuba, Norway and Canada
  - 26-46% reduction of gonorrhoae in retrospective observational studies in USA and Australia
- Meningococcal B vaccine (4CMen B: Bexsero°) contains Outer Membrane Vesicle (OMV) proteins (Por A) and 3 recombinant proteins



- 20 OMV proteins shared with NG with 44-99% genetic homology and 69% homology for NHBA
- NHBA is surface exposed in NG and contributes to colonization and survival of NG
- Bexsero° vaccine elicits antibodies to NG OMV and NHBA in human serum, mainly IgG
- Bexsero° vaccine accelerated clearance and reduced bacterial burden in a murine model

Petoussis-Harris et al. Lancet 2017; Folaranmi CID 2017; Semchenko EA et al. CID 2019; Semchenko EA et al. JID 2020; Abara et al Lancet ID 2022; Wang et al. Lancet ID 2022 ; Bruxvoort KJ. et al. CID 2022

Moving Forward: Upcoming Strategies on STI Prevention

NMAC
leads with race

National HIV & Aging Advocacy Network

GMOC FELLOWSHIP | GAY MEN OF COLOR FELLOWSHIP
BIOMEDICAL HIV PREVENTION

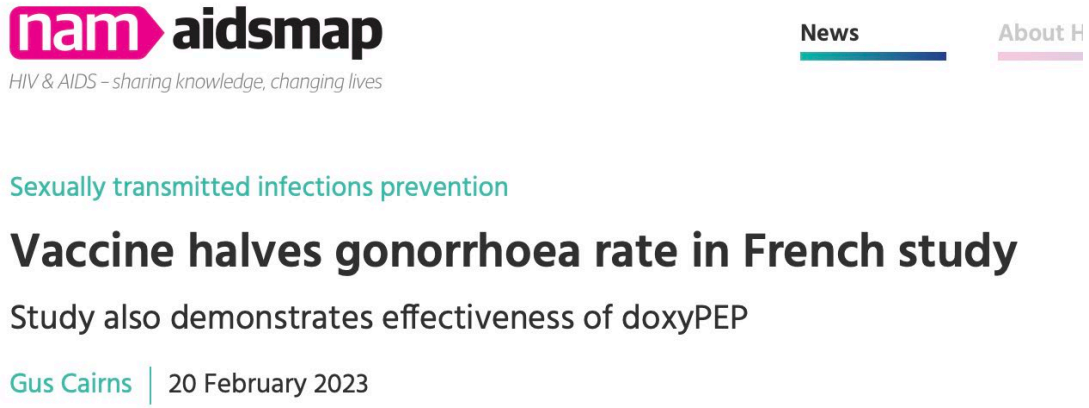
HIV50+
STRONG & HEALTHY

General Impressions as a Non-Scientist

- Doxy-PEP is a useful tool for people to maintain their physical and sexual health
- Substantially reduce the frequency of STIs for cisgender men and trans women
- Important that it's been shown to be effective both for PLWH and people not LWH
- Potential to frame this tool within a sex-positive framework
- Folks can use it when it fits their needs (AKA not a daily pill)

Questions, Comments, Concerns

- **Lack of public education around Doxy-PEP**
  - Not a ton of familiarity, yet.
  - Need be more and clear reporting and guidance from trusted sources + trusted messengers
  - Need to be in the language that community uses
  - Guidance + messages need to be available in Spanish and other languages.



Questions, Comments, Concerns

- **Some thoughts around messaging. Explain that:**
  - This a post-exposure tool, but different from HIV PEP (i.e., not 28 days).
  - You don’t have to take it every day, like PrEP
  - There are potential benefit in reducing bacterial STIs
  - Research is ongoing around treatment resistance concerns
  - Antibiotics are used as prophylaxis for other health conditions and there is a difference between prophylaxis and misuse of antibiotics

Questions, Comments, Concerns

- **Keep in mind:**
  - Can’t discount people’s hesitation around a new intervention. Instead, provide clear, precise information.
  - We need to be clear and upfront in all messaging that cisgender women are being left out of this tool. Any new research + product development needs to center needs of Black cisgender women.
  - There will be questions about who is eligible, where to go, how to take it, side effects, how to pay for it. Intentional about the implementation

Questions, Comments, Concerns

- **Talk to folks with institutional power:**
  - Providers need to be trained on this intervention + how to appropriately offer the tool to folks.
  - Researchers need to work with urgency to develop tools for cisgender women
  - How long will it take CDC to get onboard?