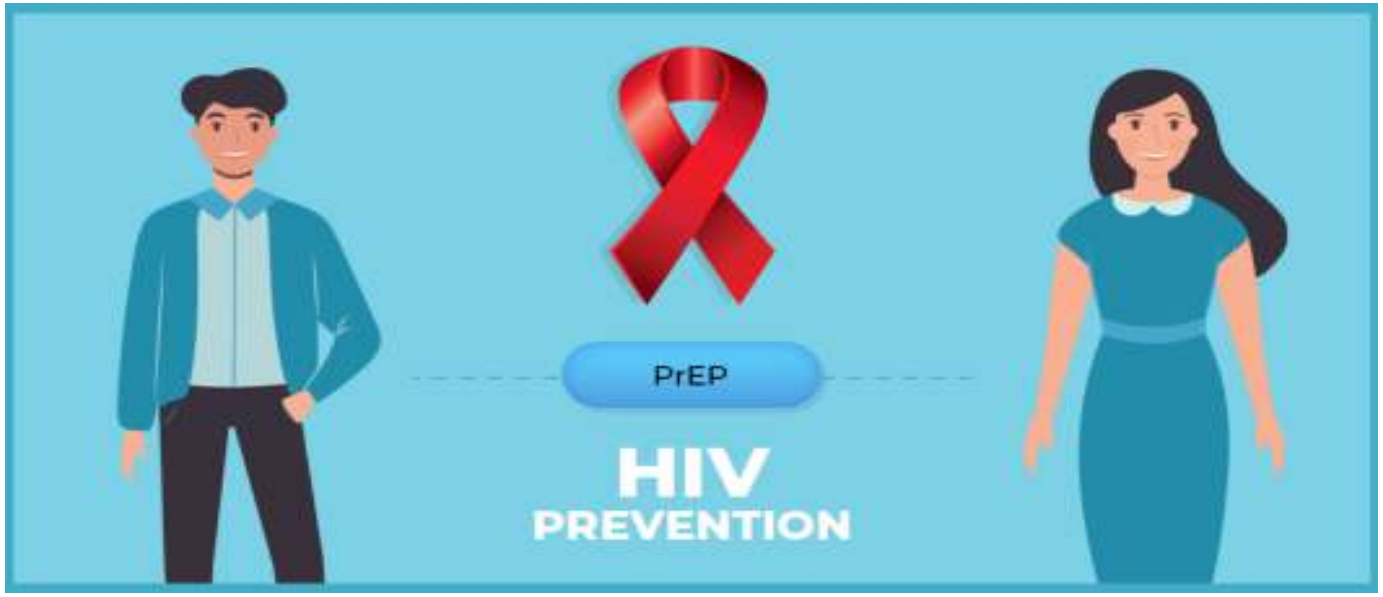


PrEP
Uygulamada Püf Noktalar

Dr Özlem Altuntaş Aydın

Başakşehir Çam ve Sakura Şehir SUAM

PrEP etkin ama ilaca uyum varsa

- Maksimum koruma
- Uyumsuzluk nedenli ilaca dirençli suşların seçilimi

Table 4: Measures of Efficacy, by Medication Adherence, Percentage Reduction in HIV Incidence in Randomized Clinical Trials (95% Confidence Interval)

Study	Modified Intent-to-Treat Efficacy			Efficacy by Self-report Adherence Measures	Efficacy by Pill-count Adherence Measures	Efficacy by Blood Detection of Drug Measures[a]
iPrEx (TDF/FTC)	44% (15–63%)			>50% 50% (18–70%) >90% 73% (41–88%)		92% (40–99%)
Partners PrEP	All TDF: 67% TDF/FTC: 75%	Men TDF: 63% TDF/FTC: 84%	Women TDF: 71% TDF/FTC: 66%	NR	100% (87–100%)	TDF: 86% (67–94%) TDF/FTC: 90% (58–98%)
TDF2 (TDF/FTC)	All 63%	Men 80%	Women 49%[b]	NR	NR	TDF detected: 85%[b]
FEM-PrEP (TDF/FTC)	NR			NR	NR	NR
VOICE (TDF,TDF/FTC)	NR			NR	NR	NR
BTS (TDF)	49%			NR	56% (-19 to 86%)[c]	74% (17–94%)

NR, not reported.

[a] Tenofovir detection assays were done in subsets of persons randomly assigned to receive TDF or TDF/FTC

[b] Finding not statistically significant

[c] Among participants on directly observed therapy

Etkin koruma için yüksek düzeyde uyum gerekli

Risk azaltma

- 7 doz/hf %99
- 4 doz/hf %96
- 2 doz/hf %76

Randomized Controlled Trial > Sci Transl Med. 2012 Sep 12;4(151):151ra125.
doi: 10.1126/scitranslmed.3004006.

Emtricitabine-tenofovir concentrations and pre-exposure prophylaxis efficacy in men who have sex with men

Peter L Anderson [1], David V Glidden, Albert Liu, Susan Buchbinder, Javier R Lama, Juan Vicente Guanira, Vanessa McMahan, Lane R Bushman, Martín Casapía, Orlando Montoya-Herrera, Valdilea G Veloso, Kenneth H Mayer, Suwat Chariyalertsak, Mauro Schechter, Linda-Gail Bekker, Esper Georges Kallás, Robert M Grant, iPrEx Study Team

Affiliations + expand

PMID: 22972843 PMCID: PMC3721979 DOI: 10.1126/scitranslmed.3004006
Free PMC article

Abstract

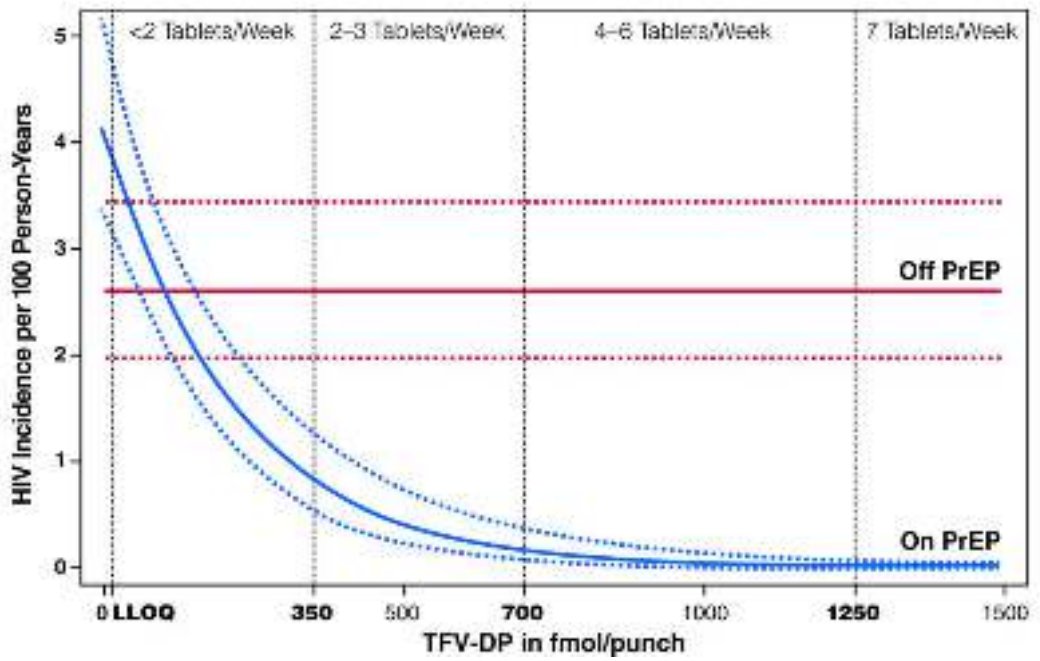
Drug concentrations associated with protection from HIV-1 acquisition have not been determined. We evaluated drug concentrations among men who have sex with men in a substudy of the iPrEx trial (1). In this randomized placebo-controlled trial, daily oral doses of emtricitabine/tenofovir disoproxil fumarate were used as pre-exposure prophylaxis (PrEP) in men who have sex with men. Drug was detected less frequently in blood plasma and in viable cryopreserved peripheral blood mononuclear cells (PBMCs) in HIV-infected cases at the visit when HIV was first discovered compared with controls at the matched time point of the study (8% versus 44%; $P < 0.001$) and in the 90 days before that visit (11% versus 51%; $P < 0.001$). An intracellular concentration of the active form of tenofovir, tenofovir-diphosphate (TFV-DP), of 16 fmol per million PBMCs was associated with a 90% reduction in HIV acquisition relative to the placebo arm. Directly observed dosing in a separate study, the STRAND trial, yielded TFV-DP concentrations that, when analyzed according to the iPrEx model, corresponded to an HIV-1 risk reduction of 76% for two doses per week, 96% for four doses per week, and 99% for seven doses per week. Prophylactic benefits were observed over a range of doses and drug concentrations, suggesting ways to optimize PrEP regimens for this population.

iPrEx OLE

1603 HIV(-) kişi, %76'sı PrEP

PrEP kullanmayanlarda HIV insidansı 4.7/100 py

PrEP etkisi uyum ile artmakta



Lancet Infect Dis. 2014 September ; 14(9): 820–829. doi:10.1016/S1473-3099(14)70847-3.

An observational study of preexposure prophylaxis uptake, sexual practices, and HIV incidence among men and transgender women who have sex with men

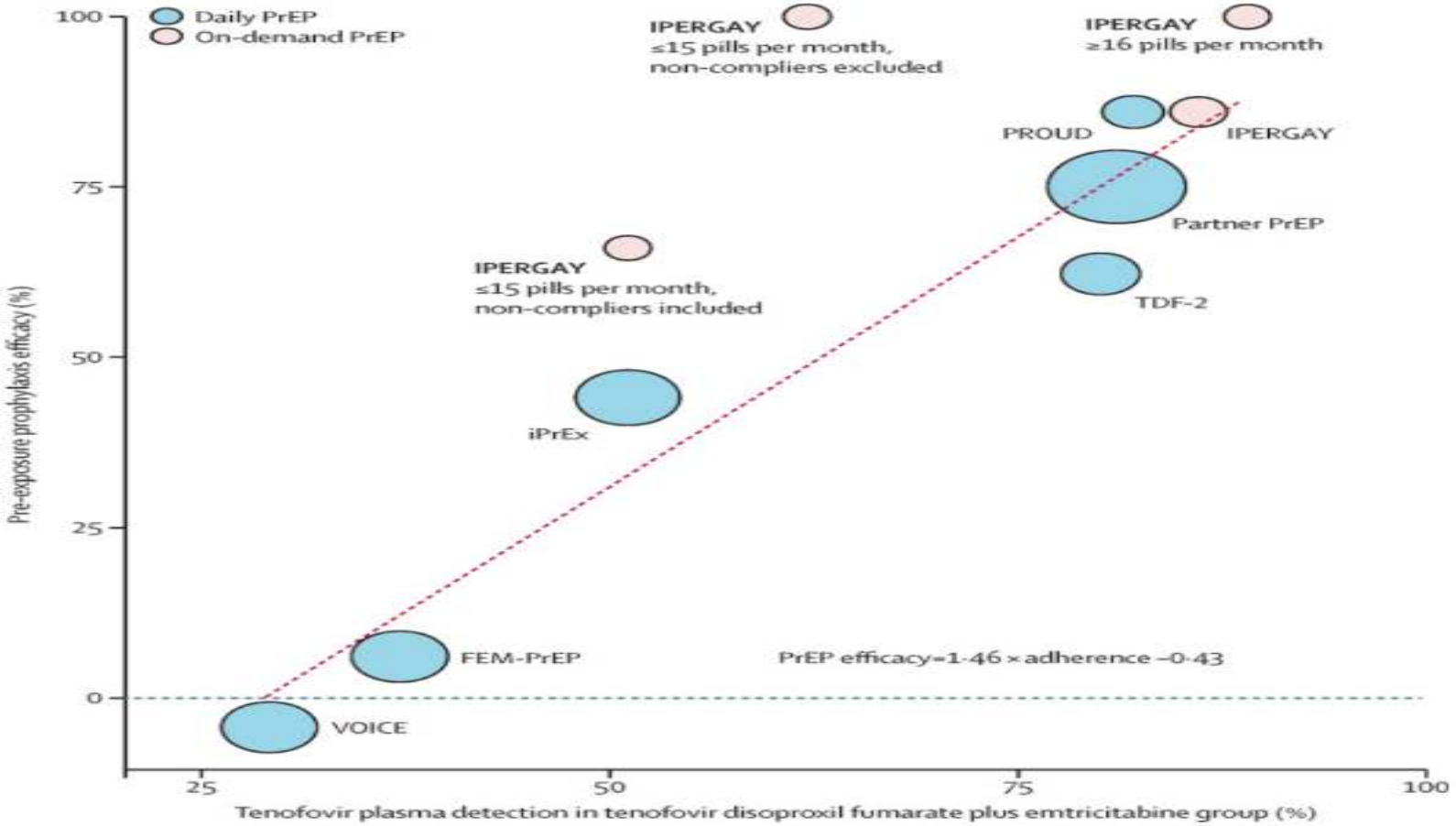
Robert M Grant, MD[1,2,3], Peter L. Anderson, PharmD[4], Vanessa McMahan, BS[1], Albert Liu, MD[2,5], K. Rivet Amico, PhD[6], Megha Mehrotra, MPH[1], Sybil Hosek, PhD[7], Carlos Mosquera, MD[8], Martin Casapia, MD[9], Orlando Montoya[10], Susan Buchbinder, MD[2,5], Valdilea G. Veloso, MD[11], Kenneth Mayer, MD[12], Suwat Chariyalertsak, MD[13], Linda-Gail Bekker, PhD[14], Esper G. Kallas, MD[15], Mauro Schechter, MD[16], Juan Guanira, MD[8], Lane Bushman, BChem[4], David N. Burns, MD[17], James F. Rooney, MD[18], David V. Glidden, PhD[2], and for the iPrEx study team

On-demand PrEP efficacy: forgiveness or timely dosing?

Lancet HIV 2019
Published Online
November 26, 2019
https://doi.org/10.1016/S2352-3018(19)30332-7
See Online/Articles
https://doi.org/10.1016/S2352-3018(19)30341-8

Oral daily pre-exposure prophylaxis (PrEP) containing tenofovir disoproxil fumarate plus emtricitabine can be highly protective against HIV infection. However, its effectiveness is dependent on drug intake. In large randomised placebo-controlled trials,[1,2] objective measures of adherence have closely predicted the extent of protection against HIV in the intention-to-treat

frequent sexual intercourse, Antoni and colleagues[3] reviewed the pill uptake of tenofovir disoproxil fumarate plus emtricitabine and data from self-reported adherence questionnaires in the ANRS IPERGAY trial to identify a specific pattern of PrEP use: 15 pills of fewer per month with consistent event-driven PrEP use. 270 participants had at least one

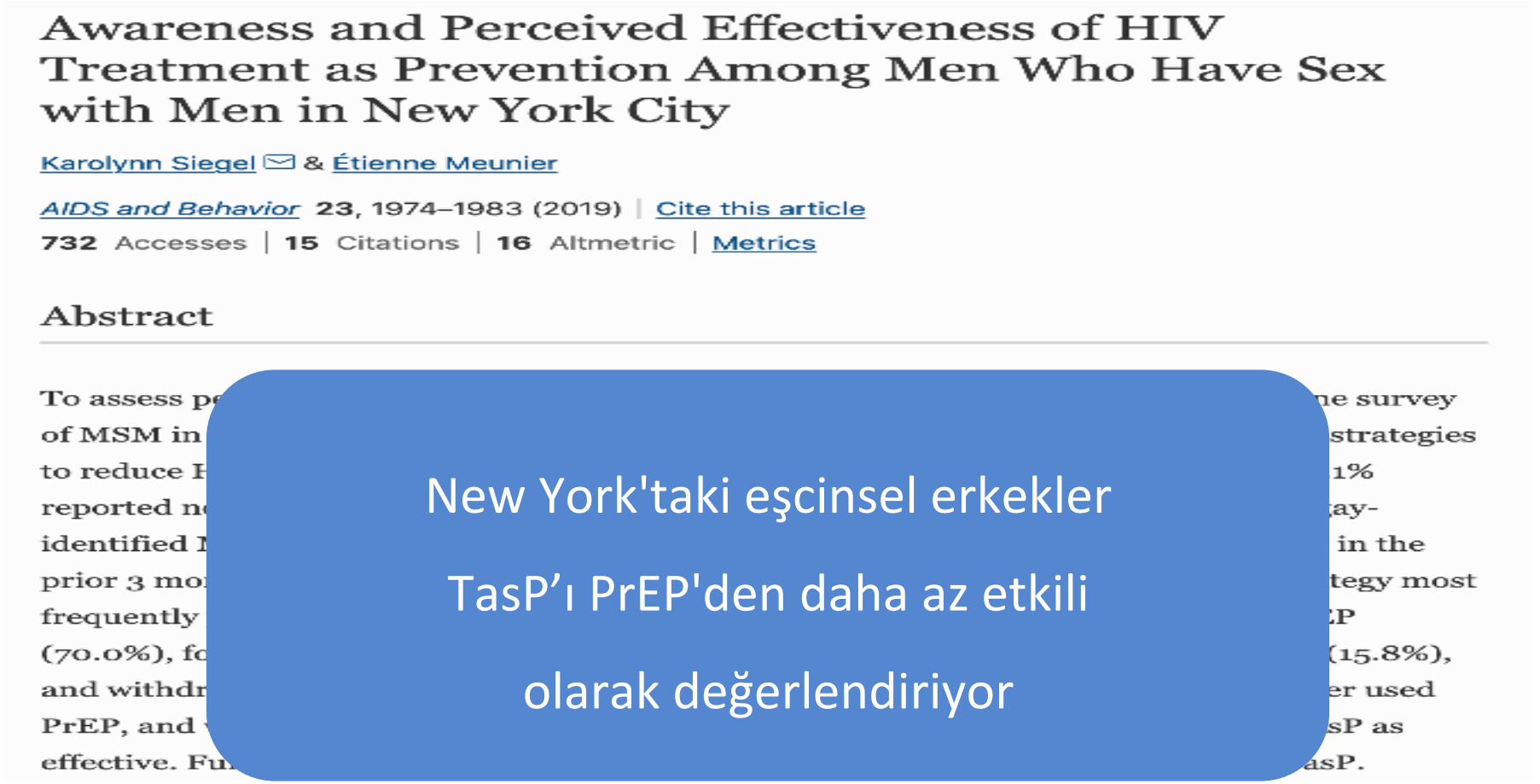


2-1-1 PrEP

Eşcinsel erkeklerde
istek üzerine PrEP
rastgele alınan
aynı miktarda
günlük PrEP'den
daha koruyucu olabilir

İstek üzerine > Günlük

PrEP ortaya çıktığından beri, eşcinsel erkeklerin en güvenli HIV önleme stratejisi



Awareness and Perceived Effectiveness of HIV Treatment as Prevention Among Men Who Have Sex with Men in New York City

Karolynn Siegel & Étienne Meunier

AIDS and Behavior **23**, 1974–1983 (2019) | Cite this article

Abstract

To assess p… …e survey
of MSM in … …strategies
to reduce H… …1%
reported n… …ay-
identified M… … in the
prior 3 mo… …tegy most
frequently … …P
(70.0%), fo… …(15.8%),
and withdr… …er used
PrEP, and … …sP as
effective. Fu… …asP.

New York'taki eşcinsel erkekler TasP'ı PrEP'den daha az etkili olarak değerlendiriyor

Danışmanlık

- İlacı tanıtmak, amacı anlatmak, ne zaman, kaç tane ilaç alınacak?
- Uyumun önemi (uyumun önündeki engellerin tanımlanması)
- İlaç alımı unutuldu ise

Sonraki dozun zamanı gelmediği sürece, unutulan dozun hatırladıkları anda alınması

Bir sonraki dozun zamanı yaklaştıysa, kaçırılan dozu atlamalı ve düzenli programa devam

- Yan etkiler ve yönetimi
- HIV enfeksiyonu bulguları
- Risk azaltma

Risk azaltma

- Bekleme odasında video, broşür vb bilgilendirme araçları
- Güvenli şırınga kullanımı
- CYBE
- Kondom kullanımı

PrEP’in CYBE’den korumadığı anlatılmalı

HIV enf dışındaki CYBE’ler artmaktadır

Özellikle PrEP kullanımından sonra artış daha belirgin!

PrEP mi CYBE’leri arttırıyor, CYBE riski yüksek kişiler mi PrEP kullanıyor?

PrEP kullanıcıları daha sıkı takip ediliyor, test yapılıyor, daha çok mu tanı konuyor?

- Gonore ve klamidya 6 ayda bir – MSM'lerde NAAT farenks, rektal ve idrarda
- Kadınlarda vajinal sıvı ve riski olanlarda rektal örnek - NAAT

HIV (+) kadınların %29'u biseksüel erkeklerle birlikte

kadınların 1/3'ünden fazlasının anal seks deneyimi mevcut

Published in final edited form as:

AIDS Behav. 2015 July ; 19(7): 1327–1337. doi:10.1007/s10461-014-0992-8.

2099 kadının %38'i son 6 ay içinde kondomsuz anal seks

Pre-exposure prophylaxis to prevent the acquisition of HIV-1 infection (PROUD): effectiveness results from the pilot phase of a pragmatic o

Sheena McCormack*, David T Dunn*,
Gabriel Schembri, Nicola Mackie, Chris
Saye H Khoo, James Rooney, Anthony

Summary

Background Randomised place
tenofovir–emtricitabine reduc
compensation in users of PrEI

Methods PROUD is an open-l
negative gay and other men wi

Clinical Infectious Diseases

MAJOR ARTICLE

Effects of Pre-exposure Prophylaxis for the Prevention of Human Immunodeficiency Virus Infection on Sexual Risk Behavior in Men Who Have Sex With Men: A Systematic Review and Meta-analysis

Michael W. Traeger,[1,2] Sophia E. Schroeder,[1,3] Edwina J. Wright,[1,4,5,6] Margaret E. Hellard,[1,4,5] Vincent J. Cornelisse,[5,7,8] Joseph S. Doyle,[1,5,a] and Mark A. Stoové[1,4,a]

[1]Disease Elimination Progra
Sciences, Lund University, M
[6]Peter Doherty Institute of I
Australia

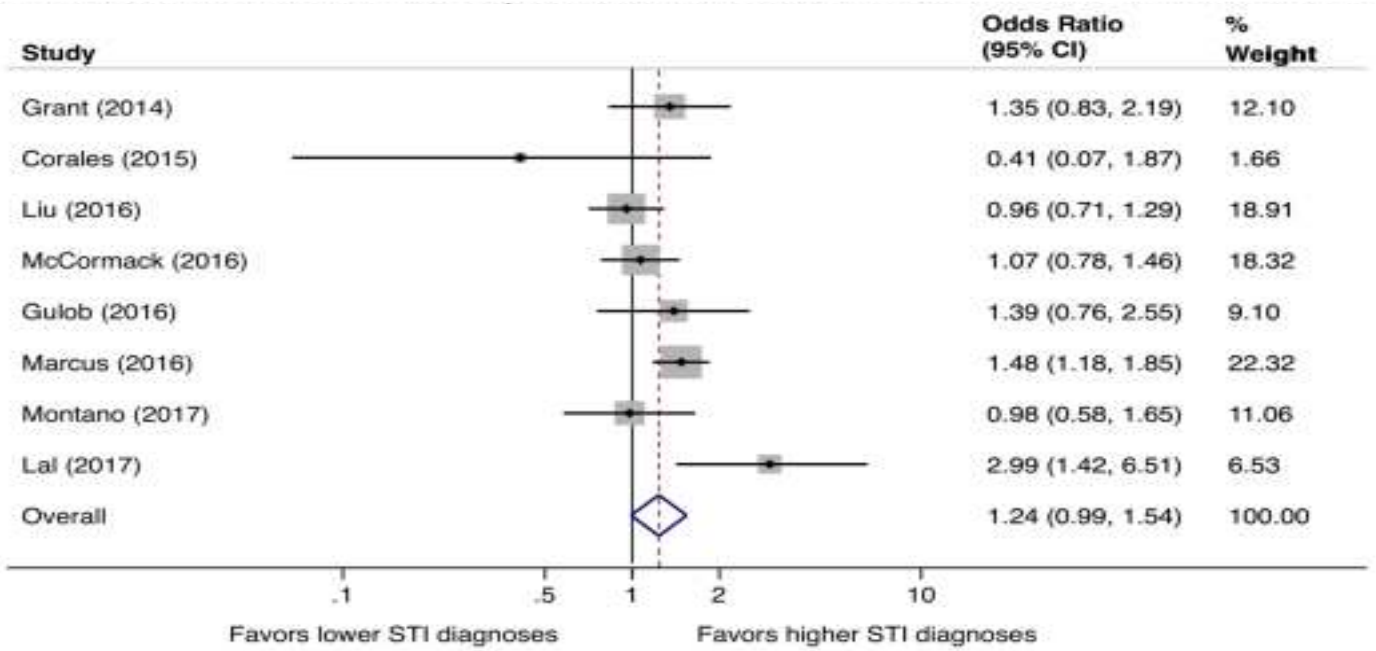
[3]Department of Clinical
Alfred and Monash University,
Health Centre, Carlton, Victoria,

Background. I
who have sex with
and increased inci

Methods. We
in the context of d
random-effects me

Results. Sixtee
reported STI preva
use was associated
and an increase in
later studies. Most

Conclusion. F
Monitoring of risk
health of MSM and



ducing HIV risk in men
decreased condom use
risk outcomes in MSM
ed sexual risk outcomes
s were calculated using

otal of 4388 participants
e-exposure prophylaxis
nterval [CI], 1.19–2.13
agnoses was stronger in

their sexual partners
t of PrEP on the sexua

Hollanda’da modelleme çalışması

- PrEP kriterlerine uyan MSM’lerin %75’ine
- 3 ayda bir HIV ve CYBE testleri yapılırsa
- HIV enf ve gonore insidansında %70 azalma

Preexposure prophylaxis for men who have sex with men in the Netherlands: impact on HIV and *Neisseria gonorrhoeae* transmission and cost-effectiveness

Maarten Reitsema[a,b], Albert Jan van Hoek[a], Maarten Schim van der Loeff[c,d], Elske Hoornenborg[c], Ard van Sighem[e], Jacco Wallinga[a,b], Birgit van benthem[a] and Maria Xiridou[a]

Objectives: To assess the impact of a preexposure prophylaxis (PrEP) programme for high-risk men who have sex with men (MSM), which includes gonorrhoea testing and treatment, on the transmission of HIV and *Neisseria* among MSM in the Netherlands and the cost-effectiveness of such programme with and without risk compensation (in the form of reduced condom use).

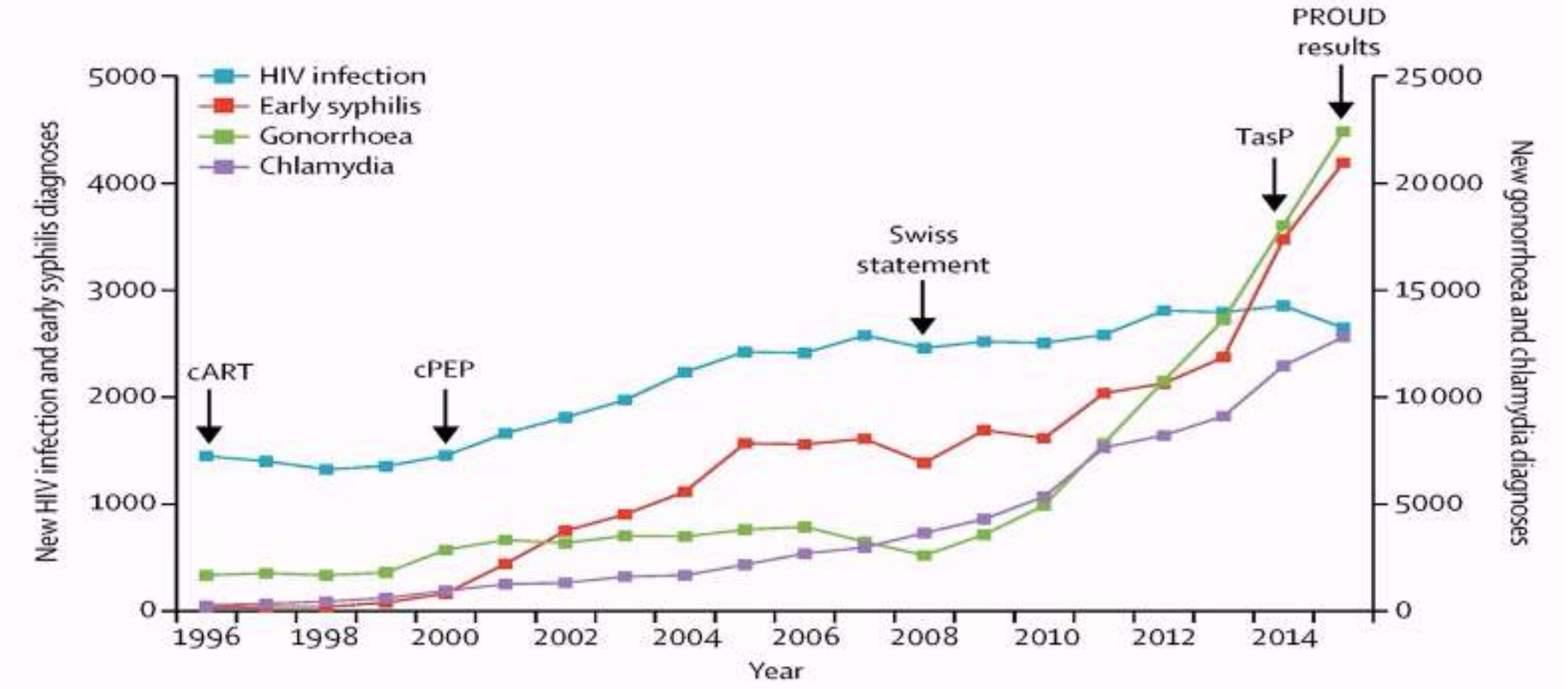
Methods: We developed a stochastic agent-based transmission model of HIV and gonorrhoea. We simulated a capped (max 2.5% of MSM) and uncapped (5.5% of MSM in 2018 declining to 3% in 2027) daily PrEP programme for high-risk MSM, with 3-monthly HIV and gonorrhoea testing, with and without risk compensation. Epidemiological outcomes were calculated from the transmission model and used in an economic model to calculate costs, quality-adjusted life-years (QALY), and incremental cost-effectiveness ratios (ICER), over 2018–2027, taking a healthcare payer perspective.

Results: Without risk compensation, PrEP can lead to a reduction of 61 or 49% in the total number of new HIV infections in 2018–2027, if the programme is uncapped or capped to 2.5% of MSM, respectively. With risk compensation, this reduction can be 63 or 46% in the uncapped and capped programmes, respectively. In all scenarios, gonorrhoea prevalence decreased after introducing PrEP. Without risk compensation, 92% of simulations were cost-effective (of which 52% cost-saving). With risk compensation, 73% of simulations were cost-effective (of which 23% was cost-saving).

Conclusion: A nationwide PrEP programme for high-risk MSM can result in substantial reductions in HIV and gonorrhoea transmission and be cost-effective, even with risk compensation.

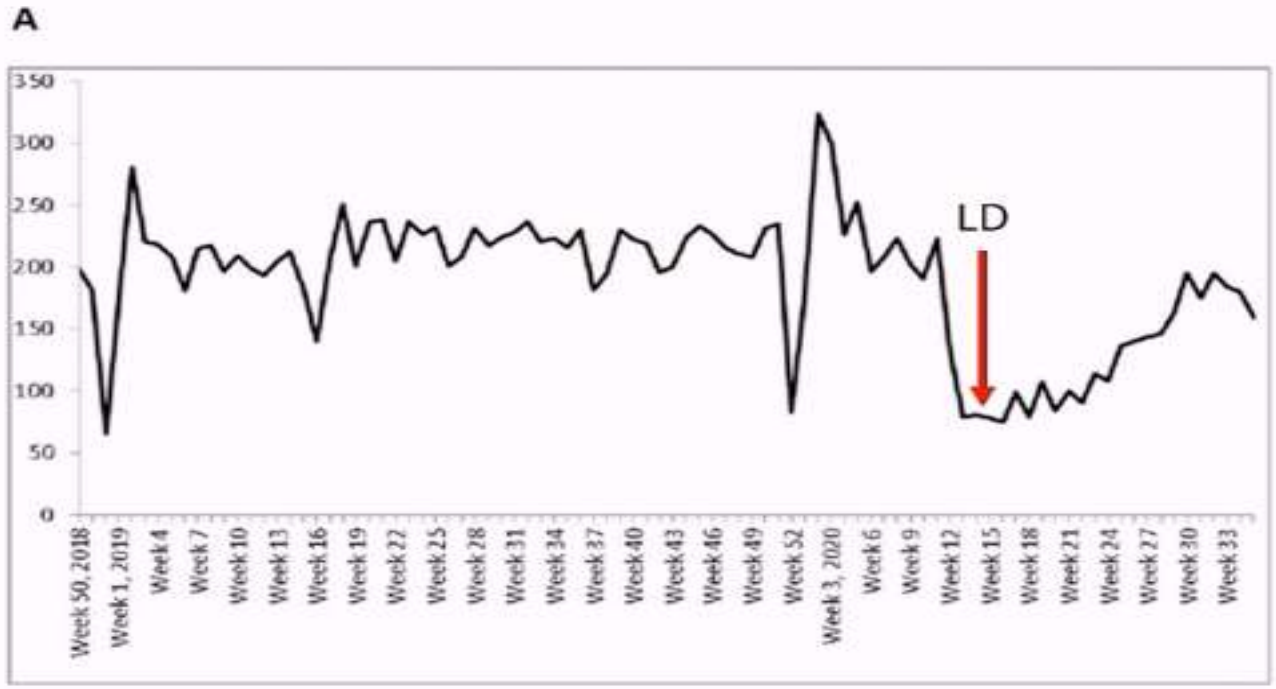
AIDS 2020, **34**:621–630

New diagnoses of STIs from 1996 to 2015 in MSM in England

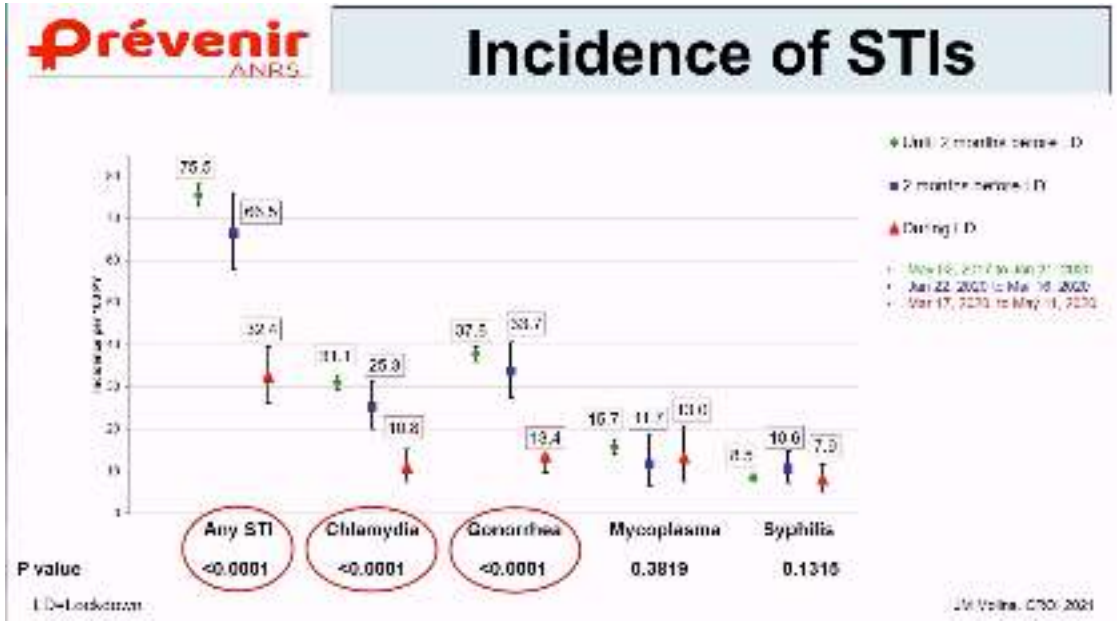


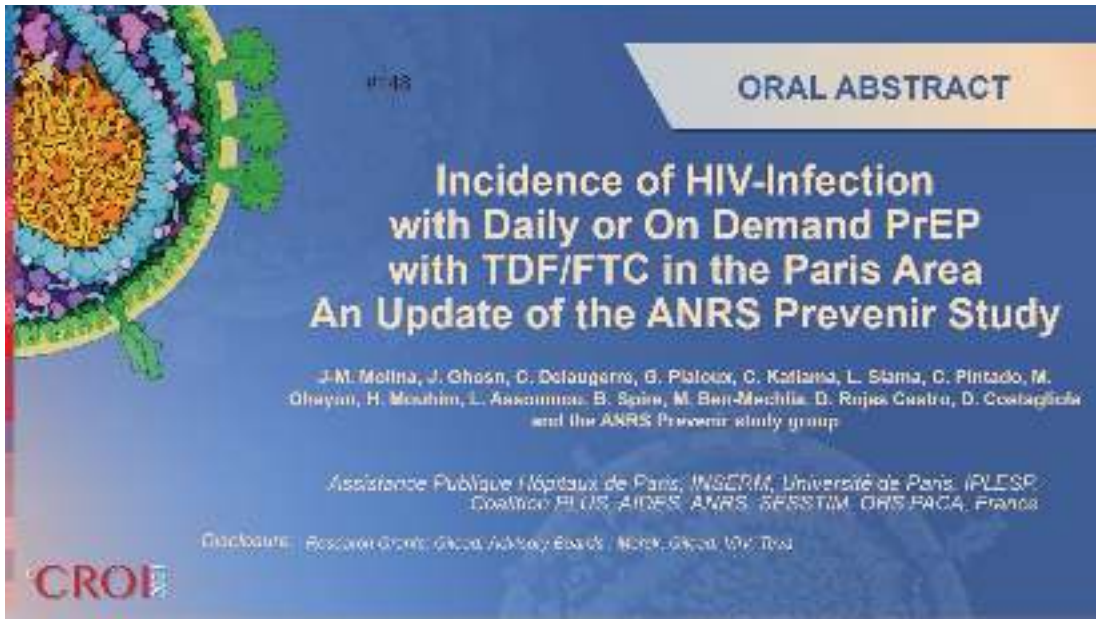
Unemo M et al. Lancet Infect Dis 2017

Weekly number of individuals diagnosed with Neisseria gonorrhoeae at 56 Dean Street, London, UK from week 50 (2018) to week 35 (2020).



Gary George Whitlock et al. Sex Transm Infect
doi:10.1136/sextrans-2020-054943


Prévenir
ANRS
Incidence of STIs
Any STI
Chlamydia
Gonorrhea
Mycoplasma
Syphilis
P value
<0.0001
<0.0001
<0.0001
0.3819
0.1316

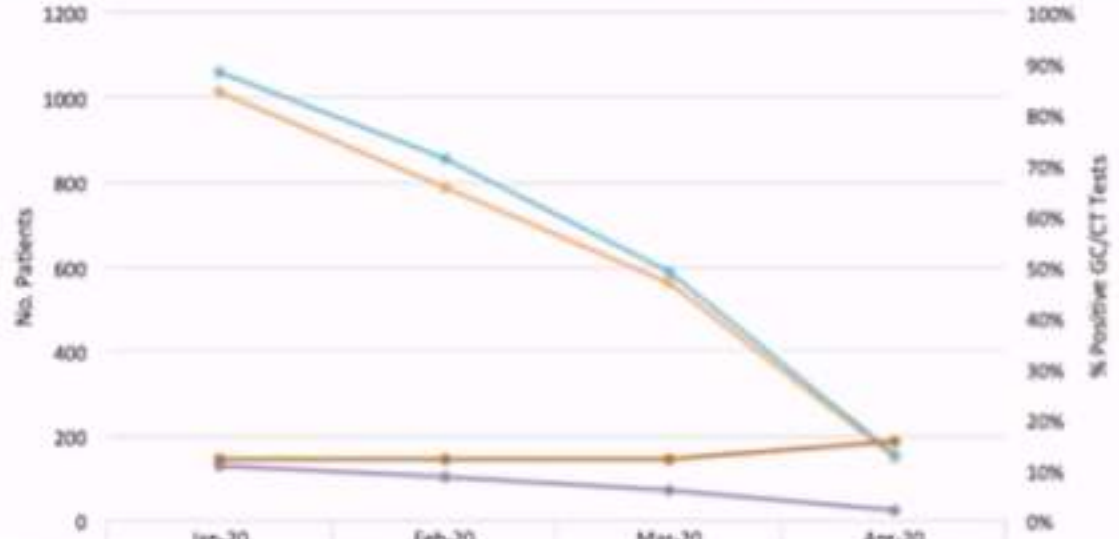

ORAL ABSTRACT
Incidence of HIV-Infection with Daily or On Demand PrEP with TDF/FTC in the Paris Area An Update of the ANRS Prevenir Study
J-M. Molina, J. Ghosn, C. Delaugerre, G. Pialoux, C. Katlama, L. Slama, C. Pintado, M. Ghayan, H. Mouhim, L. Assoumou, B. Spire, M. Ben-Mechlia, D. Rojas Castro, D. Costagliola and the ANRS Prevenir study group
Assistance Publique Hôpitaux de Paris, INSERM, Université de Paris, IPLESP
CROI

IMPACT OF COVID-19 ON HIV PREEXPOSURE PROPHYLAXIS CARE AT A BOSTON COMMUNITY HEALTH CENTER

Douglas S. Krakower, Patricia Solleveld, Ken Levine, Kenneth H. Mayer

Abstract OACLB0104

Gonorrhea/chlamydia test positivity increased by 3.5 percentage points



	Jan-20	Feb-20	Mar-20	Apr-20
HIV Tests Performed	1014	786	562	151
GC/CT Tests Performed	1058	854	590	158
Positive GC/CT Tests	130	103	72	25
% Positive GC/CT Tests	12.3%	12.1%	12.2%	15.8%

Increased of 3.5 percentage points (28.5% increase)

PrEP ve HCV enfeksiyonu

- 376 MSM ve TGW
- HCV prevalansı %4.8
- İnsidans 1/100 py
- Reenfeksiyon 25.5/100 py
- %75'i kimyasal seks

- PrEP
  - kondom kullanımında azalma
  - HIV (+) ve (-) kişiler arasında cinsel aktivitede artış
- HIV (-) kişilerde HCV insidansında artış olabilir!!!

Reenfeksiyonlara da dikkat!!

PrEP kişinin cinsel aktivite modeline göre planlanmalı

Kondom kullanmak istemese de koruyucu TDF

düzeyi olana kadar kullanmalı

- Rektal dokuda max konsantrasyona 7 gün
- Servikovajinal dokuda 21 gün

Risk – tatil planı

Planlanan kondomsuz cinsel temastan 7 gün önce

Kadınlarda 3 hf önce - 1 ay daha devam et

Klinik koruma

- Anal temasta 2 tb alındıktan 2-24 h sonra

Vajinal temasta istek üzerine PrEP kullanımı önerilmez (dokularda ilaçların koruyucu seviyesi?)

Yan etkiler

Table 2. Adverse Events.*

Adverse Event	FTC–TDF (N = 1251)		Placebo (N = 1248)		P Value†
	no. of patients (%)	no. of events	no. of patients (%)	no. of events	
Any adverse event	862 (69)	2330	877 (70)	2511	0.50
Any serious adverse event	62 (5)	76	67 (5)	87	0.57
Any grade 3 or 4 event	151 (12)	248	164 (13)	285	0.51
Grade 3 event	110 (9)	197	117 (9)	225	0.65
Grade 4 event	41 (3)	51	47 (4)	60	0.57
Elevated creatinine level	25 (2)	28	14 (1)	15	0.08
Headache	56 (4)	66	41 (3)	55	0.10
Depression	43 (3)	46	62 (5)	68	0.07
Nausea	20 (2)	22	9 (<1)	10	0.04
Unintentional weight loss (>5%)	22 (2)	24	14 (1)	19	0.04
Diarrhea	46 (4)	49	55 (4)	61	0.36
Bone fracture	15 (1)	16	12 (<1)	12	0.41
Death	1 (<1)‡	1	4 (<1)	4	0.18
Discontinuation of study drug					
Permanently	25 (2)	26	27 (2)	33	0.82
Permanently or temporarily	74 (6)	99	72 (6)	97	0.49

* A listing of all laboratory abnormalities and clinical adverse events of grade 2 or higher that were reported in 25 or more subjects (1%) is provided in Tables S6 and S10 in the Supplementary Appendix. FTC–TDF denotes emtricitabine and tenofovir disoproxil fumarate.
† P values were calculated by the log-rank test.
‡ This death was due to a motorcycle accident.

Table 5: Evidence Summary of Randomized Clinical Trials — Safety and Toxicity

Study	Outcome Analyses	
	Agent	Control
Grade 3/4 Adverse Clinical Events*		
iPrEx	52 events	59 events
ATN 082	1 event	1 event
TDF2	9 events	10 events
West African Trial	NR	NR
Grade 3/4 Adverse Laboratory Events *		
iPrEx	59 events	48 events
ATN 082	3 events	0 events
TDF2	32 events	32 events
West African Trial	1 event	5 events
Grade 3/4 Adverse Events (Clinical and Laboratory)*		
Partners PrEP	TDF: 323 events TDF/FTC: 337 events	307 events
FEM-PrEP	NR	NR
US MSM Safety Trial	36 events	26 events
VOICE	NR	NR
BTS	175 events	173 events

NR, not reported.

* RDBPCT = randomized, double blind, prospective clinical trial

2-1-1 PrEP

Clinical Infectious Diseases

BRIEF REPORT

Early Adopters of Event-driven Human Immunodeficiency Virus Pre-exposure Prophylaxis in a Large Healthcare System in San Francisco

J. Carlo Hojilla,[1,2] Julia L. Marcus,[1] Michael J. Silverberg,[1,3] C. Bradley Hare,[4] Rachel Herbers,[4] Leo Hurley,[1] Derek D. Satre,[1,2] and Jonathan E. Volk[4]

[1]Division of Research, Kaiser Permanente Northern California, Oakland, California, USA, [2]Weill Institute for Neurosciences, Department of Psychiatry, University of California, San Francisco, California, USA, [3]Department of Population Medicine, Harvard Medical School and Harvard Pilgrim Health Care Institute, Boston, Massachusetts, USA, and [4]Department of Adult and Family Medicine, Kaiser Permanente San Francisco Medical Center, San Francisco, California, USA

Among 279 patients within a large healthcare system in San Francisco, event-driven HIV pre-exposure prophylaxis using a 2–1–1 regimen was a desirable alternative to daily dosing. Problems with adherence, planning sex in advance, or side effects were infrequent (13.9%). We found no new HIV infections over 136 person-years of follow-up.

Table 1. Patients Prescribed 2–1–1 PrEP at Kaiser Permanente San Francisco, Assessed at the 3-Month Follow-up Visit

	No. (%)
Dosing regimen in the prior 3 months	
Exclusively 2–1–1	140 (51.3)
Daily	53 (19.4)
Combination of 2–1–1 and daily	41 (15.0)
Stopped PrEP	20 (7.3)
Other nondaily dosing	11 (4.0)
Never started PrEP	8 (2.9)
Reasons for selecting 2–1–1	
Infrequent sex	158 (57.9)
Concerns around side effects from daily dosing	11 (4.0)
Cost	7 (2.6)
Difficulty with daily adherence	6 (2.2)
Advice by medical provider	3 (1.1)
Challenges with 2–1–1 PrEP	
Adherence/difficulty with dosing pattern	16 (5.9)
Unable to plan sex in advance	13 (4.8)
Side effects	8 (2.9)
Cost	1 (0.4)
Reasons for stopping PrEP	
Lost health ins	14 (5.1)
Reduction in se	4 (1.5)
Side effects	2 (0.7)

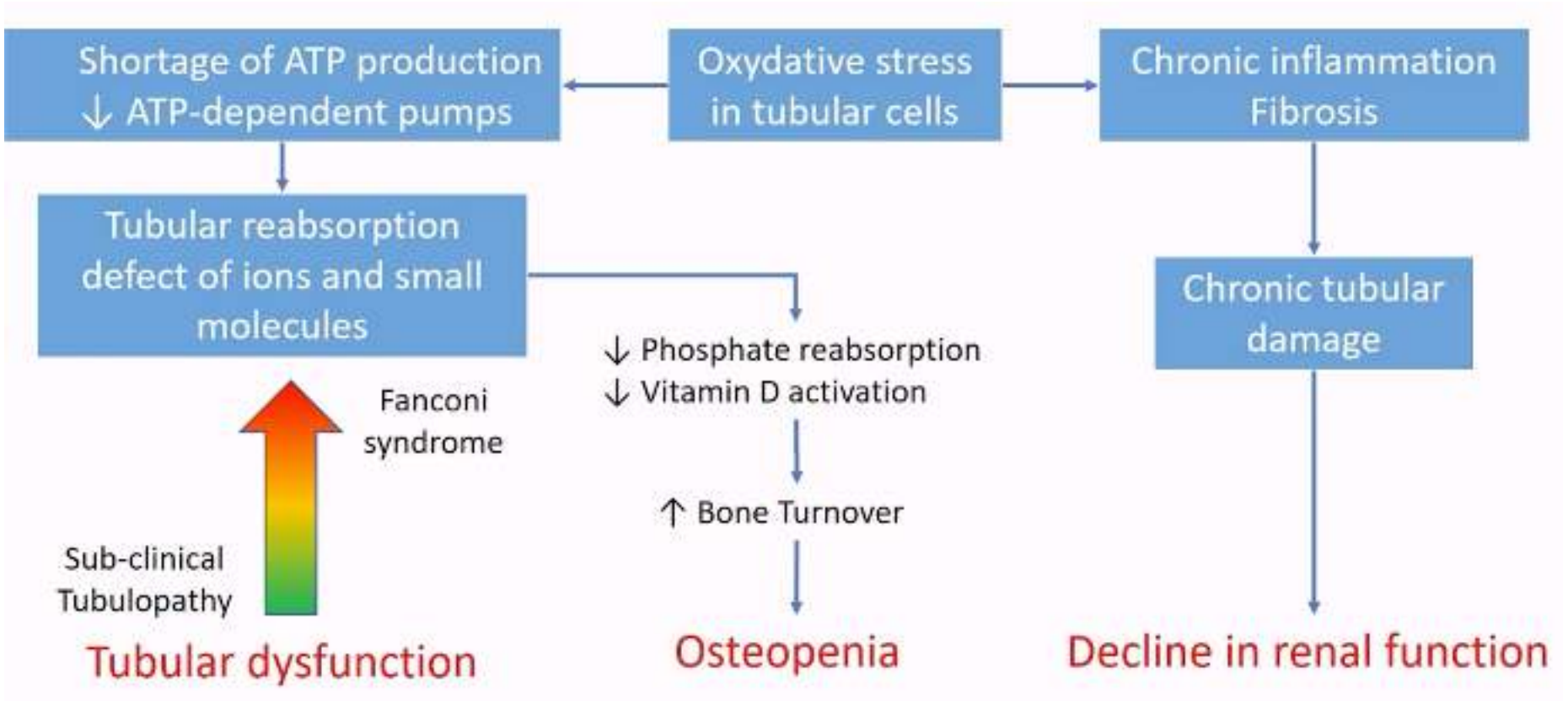
N = 273.

Abbreviation: PrEP,

kreaCl azalma
Kc enz artış

Nefrotoksisite

TFV renal tubuler hücrelerde mitokondriyal toksisiteye, oksidatif strese neden olur



Published in final edited form as:
J Acquir Immune Defic Syndr. 2016 April 1; 71(4): e115–e118. doi:10.1097/QAI.0000000000000906.

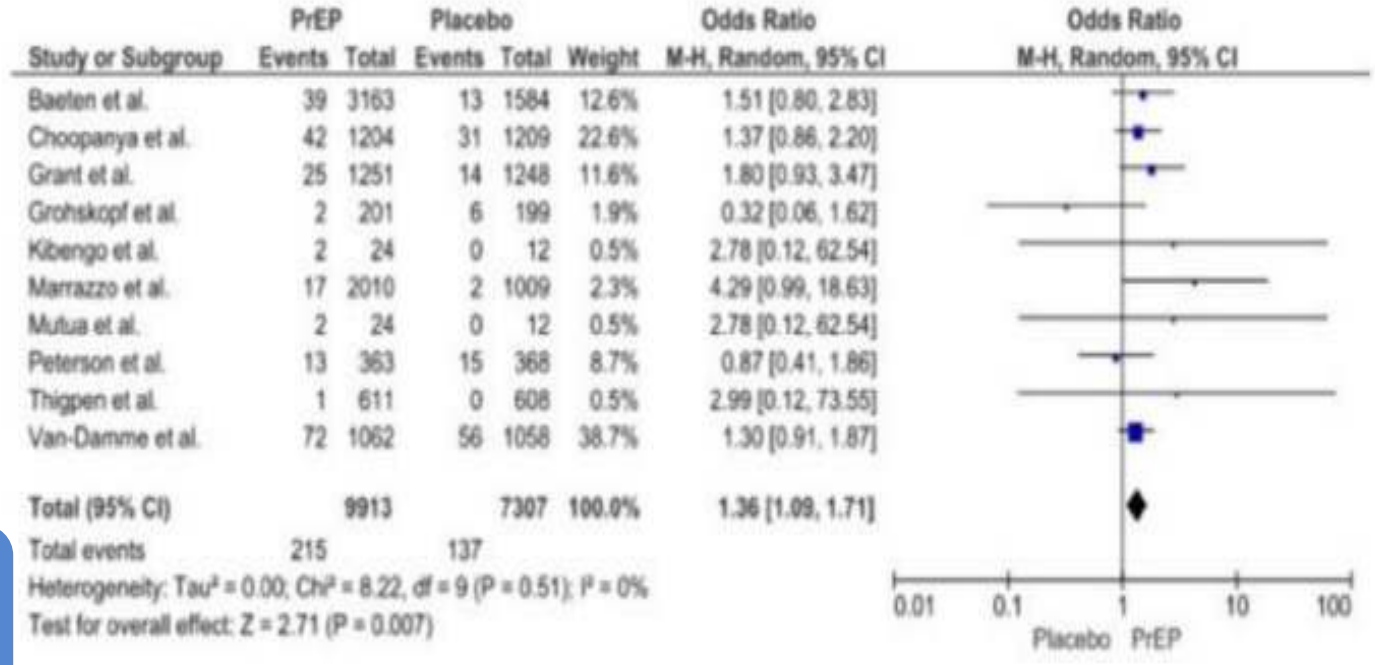
Elevations in Serum Creatinine with Tenofovir-Based HIV Pre-exposure Prophylaxis: A Meta-Analysis of Randomized Placebo-Controlled Trials

Rabi Yacoub, MD[1,*], Girish N. Nadkarni, MD, MPH, CPH[2,*], Damian Weikum, BS[3], Ioannis Konstantinidis, MD[2], Anna Boueilh, MD[4], Robert M. Grant, MD MPH[5], Kenneth K. Mugwanya, MBChB, MS[6], Jared M. Baeten, MD[7], and Christina M. Wyatt, MD[2]

Metanalysis – 10 placebo-controlled PrEP clinical trials – 19 507 participants

Creatinine elevation	TDF N=9913	Placebo N=7307
Total	215 (2.2%)	137 (1.9%)
Grade 1 1,1 – 1,3 X ULN* No. (%)	195 (2%)	126 (1.7%)
Grade 2 1,4-1,8 X ULN No. (%)	16 (1.6‰)	7 (1‰)
Grade 3 ou 4 1,9 X ULN No. (%)	4 (0.4‰)	4 (0.5‰)

*ULN Upper limit of normal



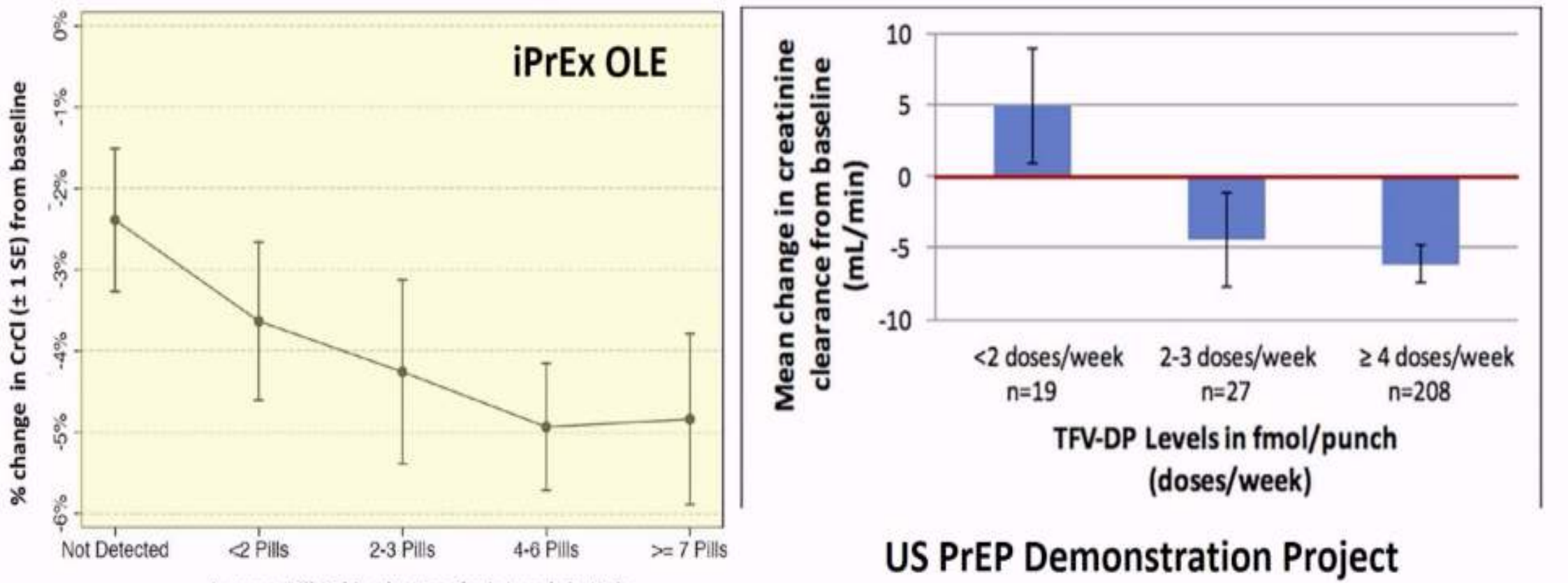
PrEP ile renal toksisite nadir ve ciddi değil

Clinical Trials	Population	No. of participants	Adherence	Mean eGFR reduction (mL/min/1.73m²) from baseline between TDF and placebo arms			
				M1	M6	M12	M24
iPrEx	MSM	2499	45%	-1.27	-1.31	-2.04	-0.80
Partners PrEP	Heterosexual couples	4747	82%	-2.42	-1.42	-2.01	-0.42
BTS*	PWID	2413	51%			-1.70	-2.60

*Bangkok Tenofovir Study

Günlük PrEP, plasebo ile karşılaştırıldığında eGFR'de azalma ~ 2 mL/dk/1.73 m^2

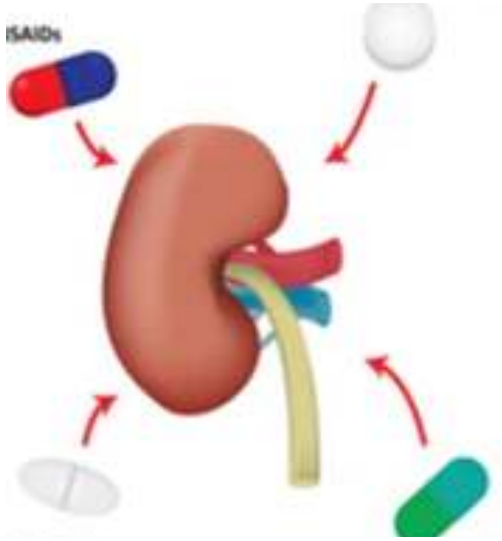
Solomon, *AIDS*, 2014; Martin, *CID*, 2014; Mugwanya, *JAMA Intern Med*, 2015



eGFR’de azalma TDF’ye maruziyet ile koreledir

Gandhi, *Lancet HIV*, 2016; Tang, *JAIDS*, 2017

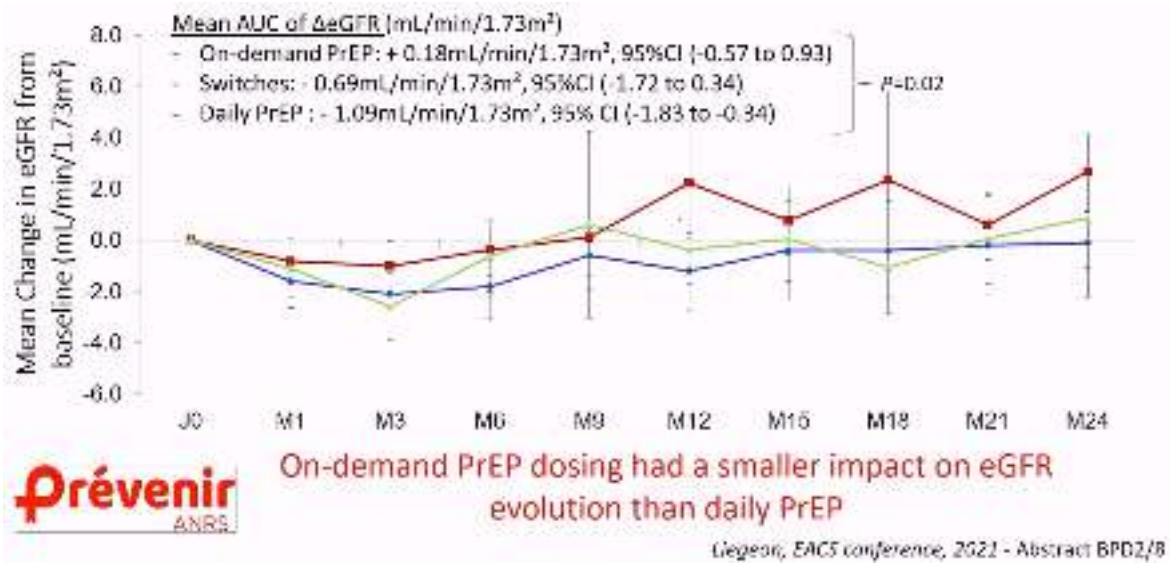
- 6 ayda bir eCrCl
- Bazal eCrCl < 90 ml/dk veya 40 yaşın üzerindeyse yakın takip
- HT, DM varsa daha sık ve ek testler (proteinüri takibi)
- eCrCl ≥ 60 ml/dk ise serum kreatinindeki artış ilacı kesmeyi gerektirmez, ancak azalmaya meyilli ise nefrolog görüşü



İstek üzerine (on-demand) PrEP daha mı az renal toksisiteye neden oluyor?

BPD2/8 | Renal safety of on-demand and daily TDF-FTC for HIV pre-exposure prophylaxis in the ANRS-PREVENIR Study

G. Liegeon[1]; L. Assoumou[2]; J. Ghosn[3]; M. El Mouhebb[2]; C. Katlama[4]; G. Pialoux[5]; J.-P. Viard[6]; K. Lacombe[7]; M. Genin[2]; L. Beniguel[2]; J. Lourenco[8]; D. Rojas Castro[9]; D. Costagliola[2]; J.-M. Molina[1]; for the ANRS PREVENIR Study Group

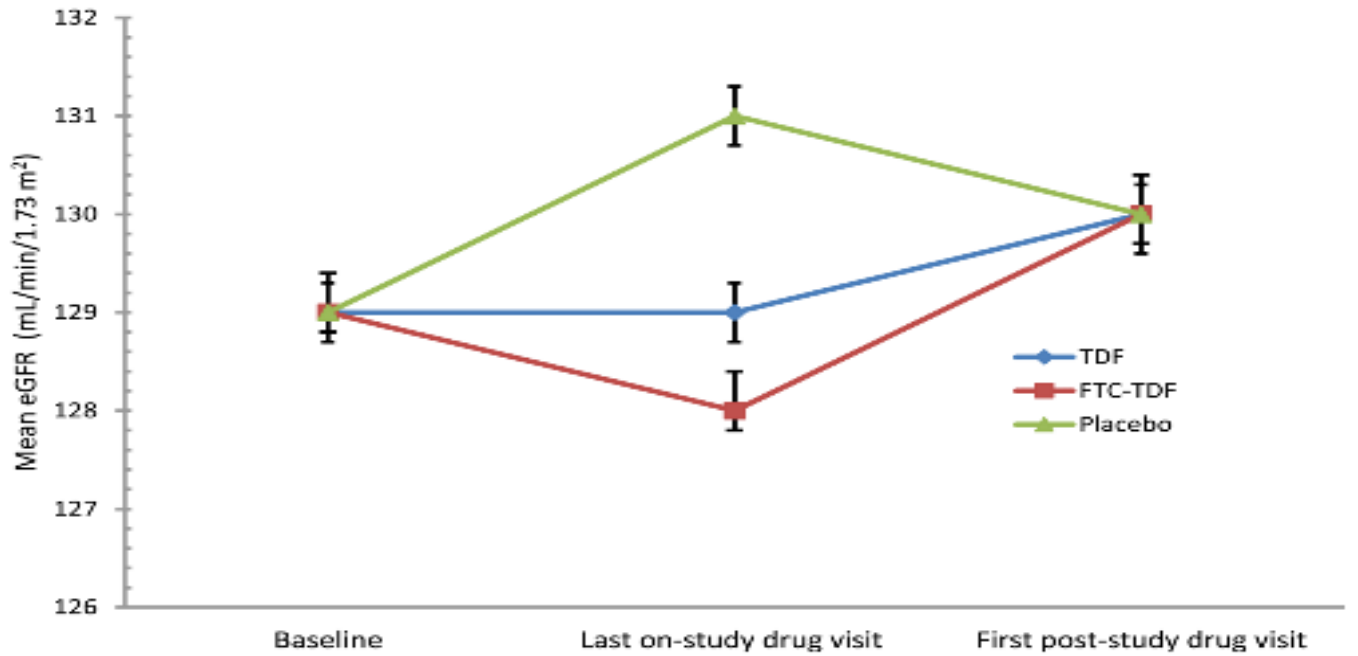


J Acquir Immune Defic Syndr. 2016 April 1; 71(4): 374–380. doi:10.1097/QAI.0000000000000868.

Reversibility of Glomerular Renal Function Decline in HIV Uninfected Men and Women Discontinuing Emtricitabine-Tenofovir Disoproxil Fumarate Pre-exposure Prophylaxis

Kenneth K. Mugwanya, MBChB, MS[1,2], Christina Wyatt, MD, MS[3], Connie Celum, MD, MPH[1,4,5], Deborah Donnell, PhD[4,6], James Kiarie, MBChB, MPH[4,7], Allan Ronald, MD[8], Jared M. Baeten, MD, PhD[1,4,5], and the Partners PrEP Study Team*

PrEP bırakıldıktan sonra renal fonksiyon düzelmektedir



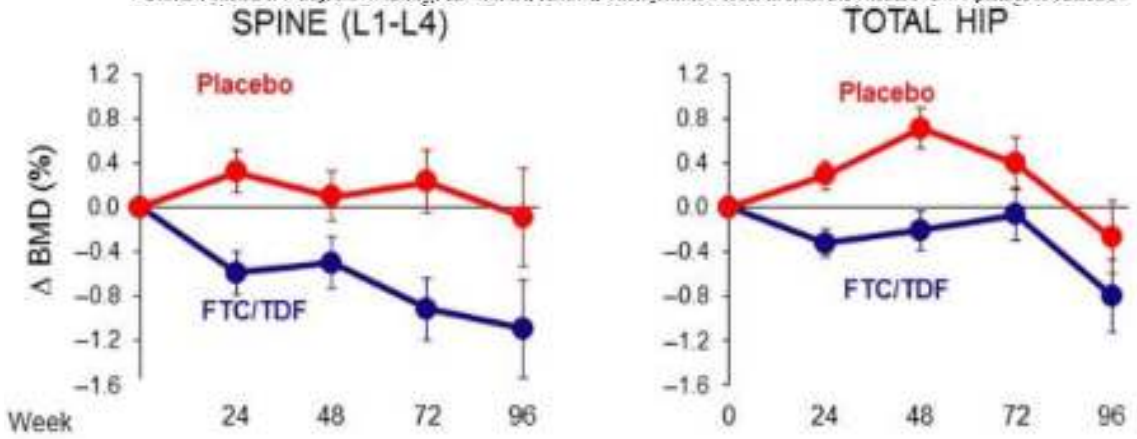
Kemik toksisitesi

- TDF kemik mineral yoğunluğunda azalma ile ilişkili (öz ilk 6 ayda)
- Osteoporoz/peni varsa yarar-zarar hesabı. TAF olabilir

Effects of Emtricitabine/Tenofovir on Bone Mineral Density in HIV-Negative Persons in a Randomized, Double-Blind, Placebo-Controlled Trial

Kathleen Mulligan,[1] David V. Glidden,[1] Peter L. Anderson,[2] Albert Liu,[1,3] Vanessa McMahan,[4] Pedro Gonzales,[5] Maria Esther Ramirez-Cardich,[6] Sirianong Namwongprom,[1] Piotr Chodacki,[7] Laura Maria Carvalo de Mendonca,[8] Furong Wang,[1] Javier R. Lama,[9] Suwat Chariyalertsak,[1,10] Juan Vicente Guanira,[9] Susan Buchbinder,[1,3] Linda-Gail Bekker,[6] Mauro Schechter,[8,11] Valdilea G. Veloso,[12] and Robert M. Grant[1,4]; for the Preexposure Prophylaxis Initiative Study Team

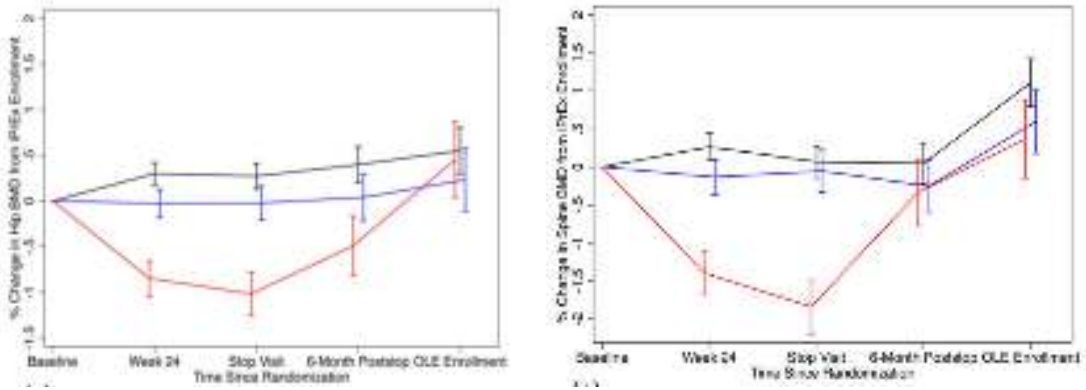
[1]University of California, San Francisco, [2]University of Colorado Denver, Aurora, [3]Bridge HIV, San Francisco Department of Public Health, California, and [4]Gladstone Institute of Virology and Immunology, San Francisco, California, [5]Asociación Civil Impacta Salud y Educación



J Acquir Immune Defic Syndr. Author manuscript; available in PMC 2018 Oct 1.
Published in final edited form as:
J Acquir Immune Defic Syndr. 2017 Oct 1; 76(2): 177–182.
doi: 10.1097/QAI.0000000000001475
PMCID: PMC5597476
NIHMSID: NIHMS884871
PMID: 28639995

Recovery of Bone Mineral Density Following Discontinuation of Tenofovir-Based HIV Pre-Exposure Prophylaxis

David V. Glidden, Ph.D., Kathleen Mulligan, Ph.D., Vanessa McMahan, M.S., Peter L Anderson, Pharm.D., Juan Guanira, M.D., M.P.H., Suwat Chariyalertsak, M.D., Dr.P.H., Susan P. Buchbinder, M.D., Linda Gail Bekker, M.B., Ch.B., Ph.D., Mauro Schechter, M.D., Ph.D., Beatriz Grinsztejn, M.D., Ph.D., and Robert M. Grant, M.D., M.P.H.



Akut HIV enfeksiyonu

Table 8: Clinical Signs and Symptoms of Acute (Primary) HIV Infection[75]

Features	Overall (n = 375) %	Sex		Route of transmission	
		Male (n = 355) %	Female (n = 23) %	Sexual (n = 324) %	Injection Drug Use (n = 34) %
Fever	75	74	83	77	50
Fatigue	68	67	78	71	50
Myalgia	49	50	26	52	29
Skin rash	48	48	48	51	21
Headache	45	45	44	47	30
Pharyngitis	40	40	48	43	18
Cervical adenopathy	39	39	39	41	27
Arthralgia	30	30	26	28	26
Night sweats	28	28	22	30	27
Diarrhea	27	27	21	28	23

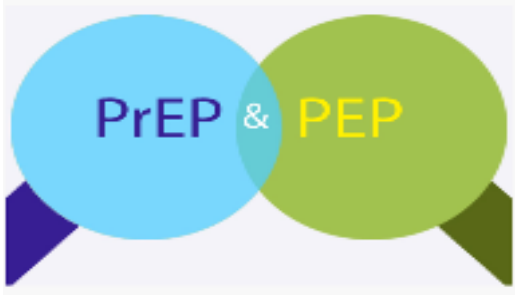
- CD4, HIVRNA, genotipik direnç testi
- Rehberlere uygun ART

TDF/FTC + DTG veya DRV/r

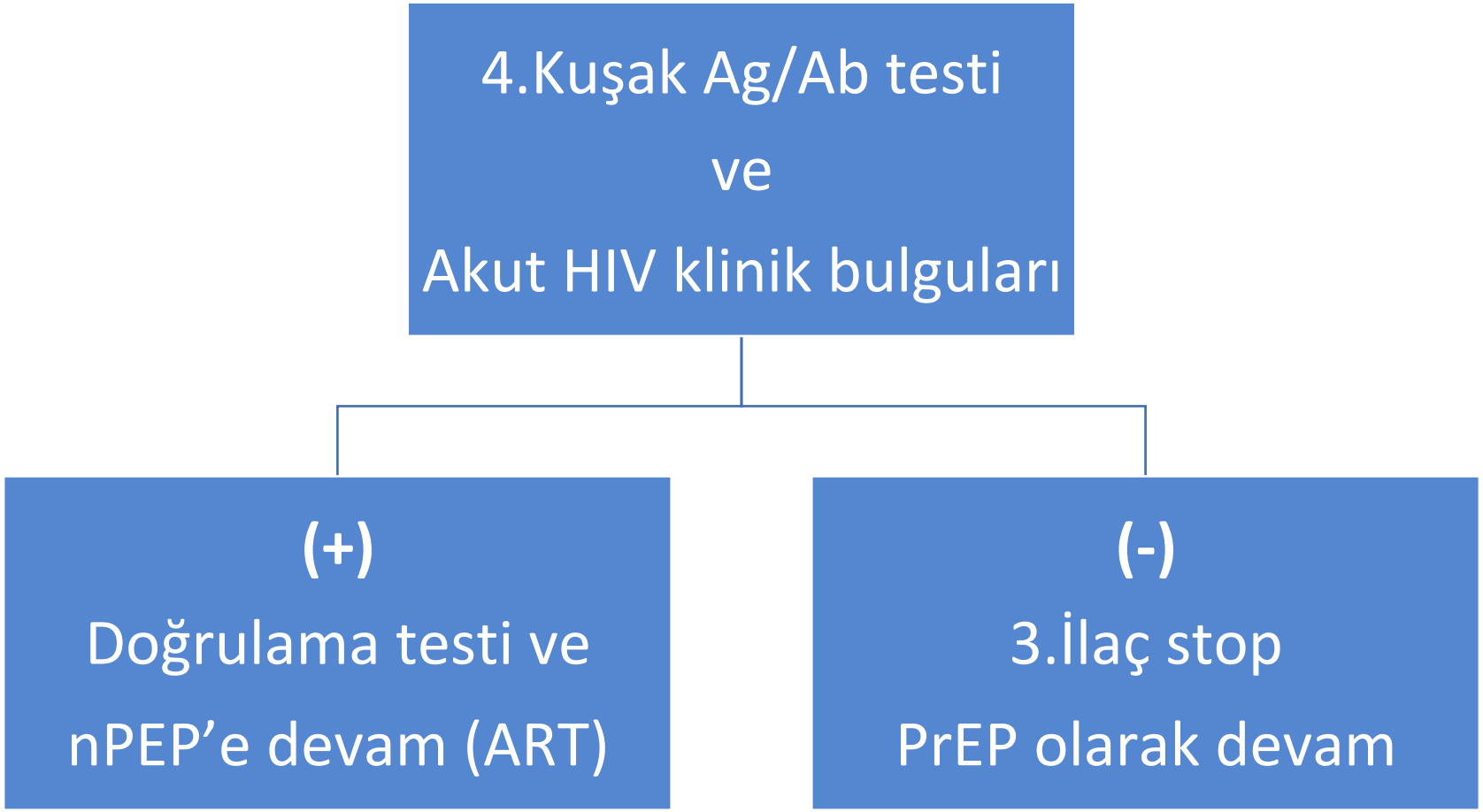
- Direnç sonucuna göre ART modifikasyonu
- Partnerlerin de test edilmesi, son 72 h içinde kondomsuz temas veya enjektör kullanımı varsa PEP

Mesleki olmayan temas sonrası proflaksiden (nPEP) sonra PrEP adayları

1. Önceki 72 saatte HIV maruziyeti olanlar
2. Yakın bir dönemde tekrarlanan nPEP talep edenler (6 ayda > 2)



- nPEP endike ve kişi PrEP için uygunsa, 28 günlük nPEP verilmelidir
- nPEP sonunda PrEP'e geçiş için değerlendirilir


4.Kuşak Ag/Ab testi
ve
Akut HIV klinik bulguları
(+)
Doğrulama testi ve
nPEP'e devam (ART)
(-)
3.İlaç stop
PrEP olarak devam

Direnç

Table 6: Evidence Summary of Randomized Clinical Trials — HIV Resistance Findings (TDF or FTC Drug Resistant Virus Detected)

Study	Outcome Analyses	
	Agent	Control
iPrEx	2 resistant viruses among 2 persons infected at baseline 0 resistant viruses among 36 persons infected after baseline	1 resistant virus among 8 persons infected at baseli 0 resistant viruses among 64 persons infected after baseline
US MSM Safety Trial	0 resistant viruses among 3 persons infected after baseline (in delayed arm before starting drug)	1 resistant virus among 1 person infected at baseline 0 resistant viruses among 3 persons infected after baseline
Partners PrEP	s among 5 persons infected at baseline and randomly 1 resistant virus among 3 persons infected at baseline and randomly F/FTC among 27 persons infected after baseline	0 resistant viruses among 6 persons infected at base 0 resistant viruses among 51 persons infected after baseline
TDF2	1 resistant virus in 1 person infected at baseline es among 9 persons infected after baseline	1 resistant virus in 1 person infected at baseline (very low frequency and transient detection) 0 resistant viruses among 24 persons infected after baseline
FEM-PrEP	4 resistant viruses among 33 persons infected after baseline	1 resistant virus in 35 persons infected after baselir
West African Trial	0 resistant viruses among 2 persons infected while on TDF	NR
VOICE TDF	NR	—
BTS	0 resistant viruses among 49 persons infected after baseline	

M184V/I

n=1251

n=1248

n=201

n=199

M184V/I

n=1589

n=1586

K65R

n=1583

n=611

M184V/I

n=608

n=1062

n=1058

n=469

n=467

n=1204

n=1207

NR, not reported.

PrEP alırken,

- FTC’nin genetik bariyeri düşük, M184V/I ortaya çıkması olasıdır
- TFV genetik bariyeri yüksek, TFV direnci (K65R mutasyonu) olasılığı daha düşüktür

PrEP alanlar dirençli HIV ile enfekte olabilir!

Case Reports > N Engl J Med. 2017 Feb 2;376(5):501-502. doi: 10.1056/NEJMc1611639.

Multidrug–Resistant HIV–1 Infection despite Preexposure Prophylaxis

Multipl direnç mutasyonları içeren HIV ile enfekte

PrEP ve uyum ile tutarlı kan TFV seviyelerine rağmen bulaşma meydana gelmiştir

PrEP'e ek olarak **KONDOM KULLANIMI** önemli

- Kişi dirençli HIV'e maruz kaldıysa, aktif antiretroviraller içeren PEP başlatılmalıdır

WHAT ARE THE POTENTIAL RISKS OF ED-PREP IN MEN WHO HAVE SEX WITH MEN?

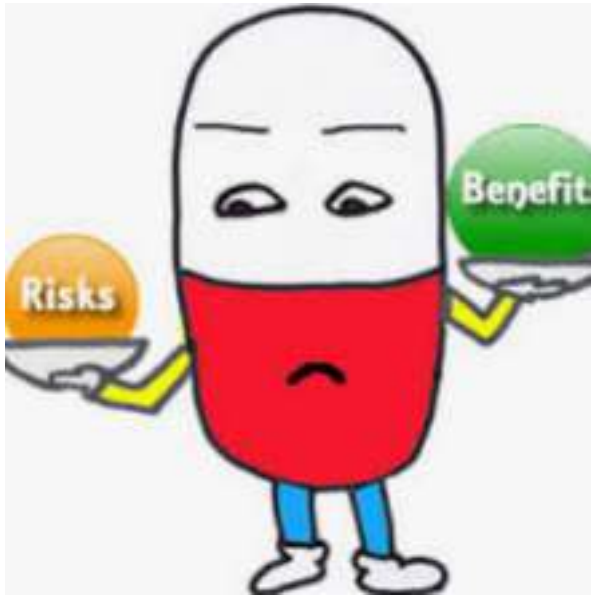
İstek üzerine PrEP'de

- İlaca epizodik maruz kalma
- PrEP'den önce HIV testi yapılmaması ile

direnç riski daha yüksek olabilir

İstek üzerine PrEP'i seyrek olarak alan kişiler

- PrEP'den çıktıkları dönemlerde HIV ile enfekte olabilirler
- HIV enfeksiyonunu dışlamadan PrEP alınırsa direnç riski artar



Gebelik

- VL yüksek HIV (+) partneri olan kadınlar PrEP kullanırken kondom kullanımını bırakıp gebe kaldıklarında HIV enfeksiyonu riskinde artış
- Serodiskordan çiftler PrEP öncesi bilgilendirilmeli HIV (+) partnerin efektif ART kullanımı sağlanmalı

Panel's Recommendations

- Health care providers should offer and promote oral combination tenofovir disoproxil fumarate/emtricitabine (TDF/FTC) pre-exposure prophylaxis (PrEP) to individuals who are at risk for HIV and are trying to conceive or are pregnant, postpartum, or breastfeeding (**AII**). Indications for PrEP include any risk factors for acquiring HIV, such as condomless sex with a partner with HIV whose HIV-RNA level is detectable or unknown, recent sexually transmitted infection (STI), or injection drug use. Because risk factors may be underreported, those who report feeling at risk for HIV acquisition should be counseled on the benefits and risks of and be offered PrEP.

- People who become pregnant while using TDF/FTC as PrEP can continue PrEP throughout their pregnancy. Risk for HI acquisition should be reassessed and people should be counseled regarding benefits and risks of PrEP use in pregnancy (**AII**).

- Gebelik öncesi
- Gebelik
- Postpartum
- [illegible]nzirmede

TDF/FTC

TDF/FTC kullanırken gebelik
- Devam edilebilir
- Risk değerlendirmesi ile karar

- Providers should counsel patients about the benefits of PrEP to reduce the risk of maternal HIV acquisition and perinatal HIV transmission (**AI**) and about potential risks of PrEP to mother and fetus or infant during periconception, pregnancy, postpartum, and breastfeeding periods (**AII**).
- In cases when the individual's risk factor is one identified partner with HIV and that partner is on antiretroviral therapy (ART) with sustained viral suppression, PrEP may be optional because condomless sexual intercourse is associated with effectively no risk of sexual HIV transmission when HIV viral load is suppressed (**AI**) (see Reproductive Options for Couples When One or Both Partners Have HIV).
- Providers should counsel patients about the importance of daily adherence to oral PrEP in preventing HIV acquisition (**AI**). Women should be counseled to take a once-daily pill of coformulated TDF/FTC PrEP for 20 days prior to being protected from HIV and therefore should use back-up protection in the interim (**B**II). No data support on-demand PrEP use for people exposed to HIV through vaginal exposure.
- Providers should offer routine PrEP follow-up, including testing for HIV every 3 months and counseling on signs and symptoms of acute retroviral syndrome (**AI**) (see the Centers for Disease Prevention and Control Guidelines for HIV Pre-Exposure Prophylaxis and Maternal HIV Testing and Identification of Perinatal HIV Exposure). More frequent testing may be appropriate when clinically indicated (e.g., adherence challenges, nonstandard visit schedule).

Other novel PrEP agents including oral tenofovir alafenamide (TAF)/FTC and injectable agents are not yet recommended for people exposed to HIV through receptive vaginal sex.

B=B
PrEP opsiyonel

Reproductive Options for Couples When One or Both Partners Have HIV

(Last updated December 29, 2020; last reviewed December 29, 2020)

Panel's Recommendations

For Couples Who Want to Conceive When One or Both Partners Have HIV:

- Expert consultation is recommended to tailor guidance to couples' specific needs **(AIII)**.
- Both partners should be screened and treated for genital tract infections before attempting to conceive **(AII)**.
- Partners with HIV should achieve sustained viral suppression (e.g., two recorded measurements of plasma viral loads that are below the limits of detection at least 3 months apart) before attempting conception to maximize their health, prevent HIV sexual transmission **(AI)** and, for pregnant persons with HIV, to minimize the risk of HIV transmission to the infant **(AI)**.
- When partners have different HIV statuses, sexual intercourse without a condom allows conception with effectively no risk of sexual HIV transmission to the partner without HIV if the partner with HIV is on antiretroviral therapy (ART) and

- HIV (+) partnerde viral supresyon sağlanmadıysa/bilinmiyorsa
- Partnerin ART uyumu kötüyse

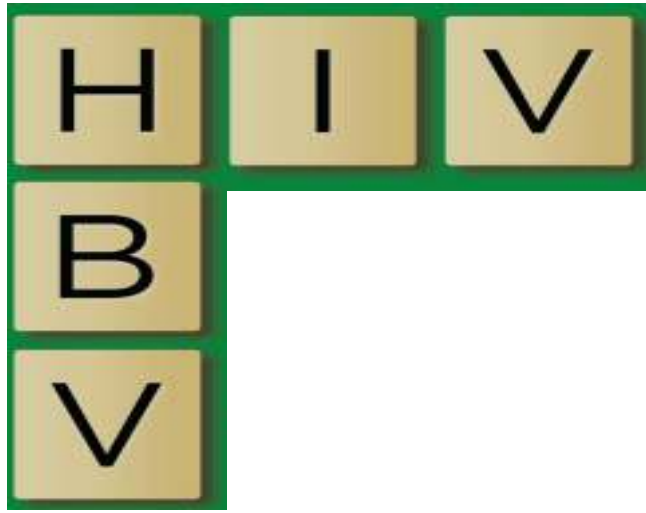
Ovulasyon döneminde kondomsuz cinsel temas PrEP ile optimize edilebilir

- Timing condomless sex to coincide with ovulation (peak fertility) is an approach that can optimize the probability of conception **(AIII)**.
- When partners with different HIV statuses attempt conception, the partner without HIV can choose to take PrEP even if the partner with HIV has achieved viral suppression **(CIII)**.

PrEP’i bırakmak

- Kişisel istek
- Yaşam şekli değişikliği
- Yan etkiler
- İlaca Kronik uyumsuzluk
- HIV enfeksiyonu

- HIV enfeksiyonundan korunma, günlük PrEP kullanımını bıraktıktan sonra 7-10 gün içinde azalacaktır
- Anal seks için kullanılan PrEP’de TDF/FTC <7 gün duraklatıldıysa tekrar 1 tb/gün olarak başlanabilir
- Bıraktığı zamanki HIV statüsü ???
- Bırakıp tekrar başlamak??



HBV ko-enfekte ise

- TDF potent, yüksek direnç bariyeri
- Reaktivasyondan korunmak için düzenli kullanım önemli (İstek üzerine PrEP kullanımı önerilmez)
- PrEP ihtiyacı kalmazsa

    - HBV tedavisine TDF veya diğer potent ajanlar ile devam

    - HBV alevlenmesi takibi

Son sözler…

- Güvenli ve etkili bir HIV önleme seçeneği, ancak UYGUN kullanılırsa
- Reseptif vajinal seks, DİİK'da sadece günlük PrEP onaylı
- Eşcinsel erkeklerde, istek üzerine (2-1-1) PrEP de kullanılabilir ve rastgele alınan aynı miktarda günlük PrEP'den daha koruyucu olabilir
- Kullanmak isteyen kişinin özelliklerine, yaşam şekline uygun şekilde düzenlenmeli
- Klinisyenler PrEP'in DOĞRU ve UYUMLU şekilde kullanılmasında önemli rol oynamakta


#PrEPWORKS