AETC AIDS Education & Training Center Program Mountain West

2020 Updates:
PrEP failures and HIV testing
PrEP-hormones interactions

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Disclosures

- I attended Gilead's 2018 U.S. Latinx/Hispanic PrEP Advisory Program.
- Only FTC/TDF and now FTC/TAF are approved by the FDA and only for use as daily PrEP in some but not all populations.

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Case #1: “Use of Drug-Level Testing and Single-Genome Sequencing to Unravel a Case of HIV Seroconversion on PrEP”

44 yo man

- 12/2017: starts PrEP after negative Ag-Ab combo test
- 12/2017-4/2019: quarterly HIV tests negative
- 6/2019: reports HA, ST, chills
  - WBC 2.8k, plt 99k, HIV Ag-Ab test positive, Geenius negative
  - Because he reported 100% adherence, told likely false positive
  - HIV RNA resulted two weeks later at 3.1 million copies/mL
- When VL returned, started on BIC/TAF/FTC

Spinelli et al. CID 2020

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Case #1: "Use of Drug-Level Testing and Single-Genome Sequencing to Unravel a Case of HIV Seroconversion on PrEP"

Enrolled in UCSF SeroPrEP study of PrEP seroconversion

- Mass spectrometry tests from treatment visit (2wks after sx)
  - 4cm long hair sample
    - Proximal 1cm 0.035ng/mg = est 7 doses/wk last 4 wks
    - Next 1cm 0.028ng/mg = 5-6 doses/wk in 4-8wks prior
  - DBS→1683 femtomole/punch = est 7d/wk adherence/last 6 wks
- Stored serum sample from initial positive visit sent for single genome sequencing (SGS)
  - Homogeneous population
  - Genotype: M184V, K70N, V179R, P225H

Spinelli et al. CID 2020

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Case #1: "Use of Drug-Level Testing and Single-Genome Sequencing to Unravel a Case of HIV Seroconversion on PrEP"

Discussion

- HIV acquisition can happen in setting of 100% adherence.
  - (Be suspicious of "false positives" with AHI symptoms)
- All but one of the well-documented cases of PrEP failure are associated with TDF/TAF and/or FTC resistance.
- "Targeted outreach to people living with HIV with unsuppressed viral loads who are harboring resistance mutations to PrEP's components could be considered to prevent transmission of potentially PrEP-resistant viruses."

Spinelli et al. CID 2020

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Case #1: “Use of Drug-Level Testing and Single-Genome Sequencing to Unravel a Case of HIV Seroconversion on PrEP”

Poll: Should HIV providers counsel patients with detectable viral loads and FTC and/or TAF/TDF resistance specifically about the possibility of transmission in the setting of PrEP?

1) No

2) Yes, but only if the resistance was detectable on the most recent genotype

3) Yes, but only if the viral load is > 3,000 copies

4) Yes, if the patient has a partner on PrEP

5) Yes, in all cases

Spinelli et al. CID 2020

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Case #2: “Failure of PrEP with daily tenofovir/emtricitabine and the scenario of delayed seroconversion.”

24 yo man on TDF/FTC as part of clinical trial in Hong Kong

Wk	Regimen	HIV test	Result
0	Daily	POC Ag-Ab	Negative
4		POC Ag-Ab	Negative
10		POC Ag-Ab	Negative
18	2-1-1	POC Ag-Ab	Negative
20		POC Ag-Ab	Negative
26		POC Ag-Ab	Ab Positive

POC=point-of-care

Shul-Shan Lee et al, Intl J Inf Dis, 2020

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Case #2: “Failure of PrEP with daily tenofovir/emtricitabine and the scenario of delayed seroconversion.”

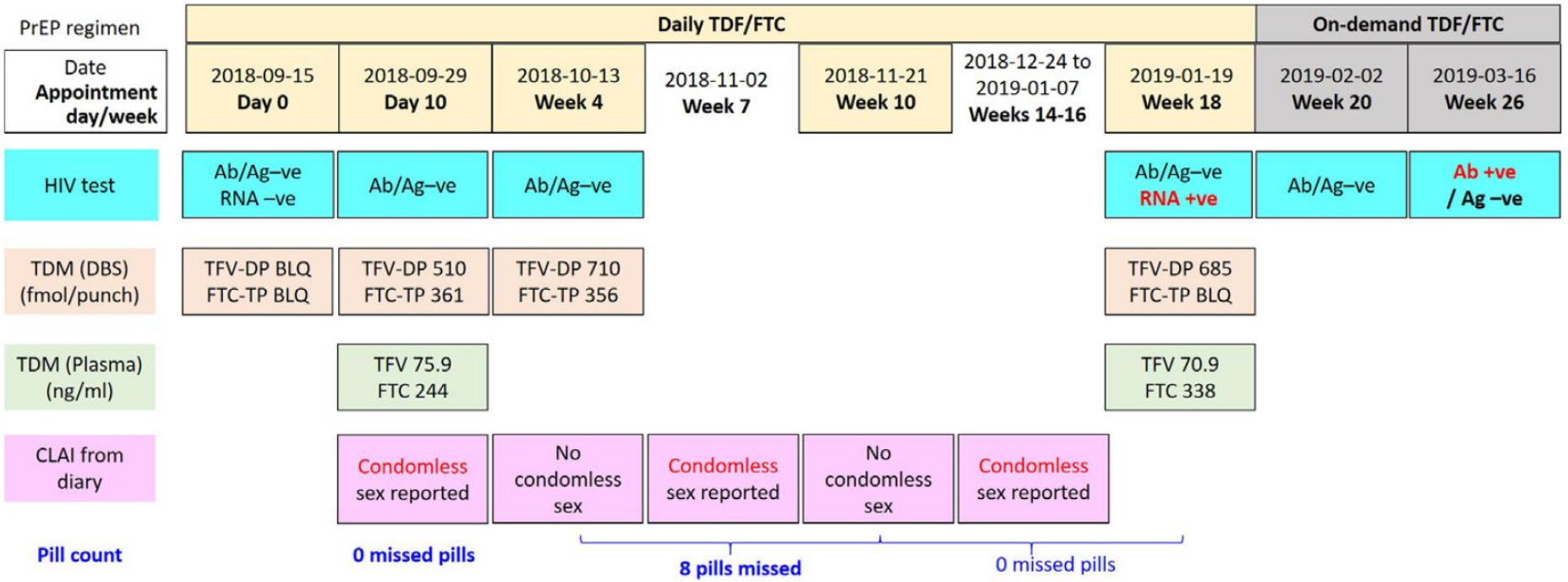

Figure 1. Summary of laboratory and point-of-care test results at baseline and following pre-exposure prophylaxis.

Shul-Shan Lee et al, Intl J Inf Dis, 2020

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Case #2: “Failure of PrEP with daily tenofovir/emtricitabine and the scenario of delayed seroconversion.”

Discussion

- Delayed detection seroconversion has been noted previously, particularly when using point-of-care tests performed on oral fluid and even on fingerstick, whole blood.
- Delayed seroconversion makes it challenging to determine whether PrEP failure was due to suboptimal adherence.
- The authors suggest that delayed seroconversion is one rationale for keeping HIV testing to Q3 month monitoring.
- Laboratory-based antigen-antibody assays continue to be the preferred HIV test, when available.

Shul-Shan Lee et al, Intl J Inf Dis, 2020

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"Sex Hormone Therapy and Tenofovir Diphosphate Concentration in Dried Blood Spots: Primary Results of the iBrEATHe Study."

Background

- Previous studies have shown slightly lower levels of tenofovir diphosphate (TFV-DP) among transgender women (TGW) receiving feminizing hormones.
- No prior studies have evaluated PrEP levels among transgender men (TGM) receiving masculinizing hormones.
- Prior studies have shown that PrEP does not impact hormone levels.
- Because these medications have different metabolic pathways, drug-drug interactions are not expected.

Grant et al, 2020, CID (accepted)

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"Sex Hormone Therapy and Tenofovir Diphosphate Concentration in Dried Blood Spots: Primary Results of the iBrEATHe Study."

Methods

- TGM/TGW on >6 months of stable hormone therapy containing either testosterone or estradiol
- No recent PrEP use
- 4 wks of daily observed FTC/TDF (video or in-person)
  - Weekly measurement of TFV-DP in DBS
  - Sex hormones in serum
- Results compared to DOT-DBS, a prior study of cisgender men and women
  - New extraction procedure led to new threshold of 800 fmol/punch for ≥4 doses/week as associated with high PrEP efficacy.

Grant et al, 2020, CID (accepted)

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"Sex Hormone Therapy and Tenofovir Diphosphate Concentration in Dried Blood Spots: Primary Results of the iBrEATHe Study."

Population characteristics (24 TGM, 24 TGW)

- Median age 31
- 57% White, 21% Black, 32% Latinx
- TGW: hormones
  - oral estradiol 83%
  - injected estradiol 17%
  - oral progesterone 12.5%
  - spironolactone 37.5%
- TGM: hormones
  - injected testosterone cypionate 75%
  - injected testosterone enanthate 8%
  - topical testosterone gel 8%
  - implanted testosterone pellets 4%
  - finasteride 12.5%
- sCr higher in TGM (1.0 v 0.8), so eCrCl lower, than TGW

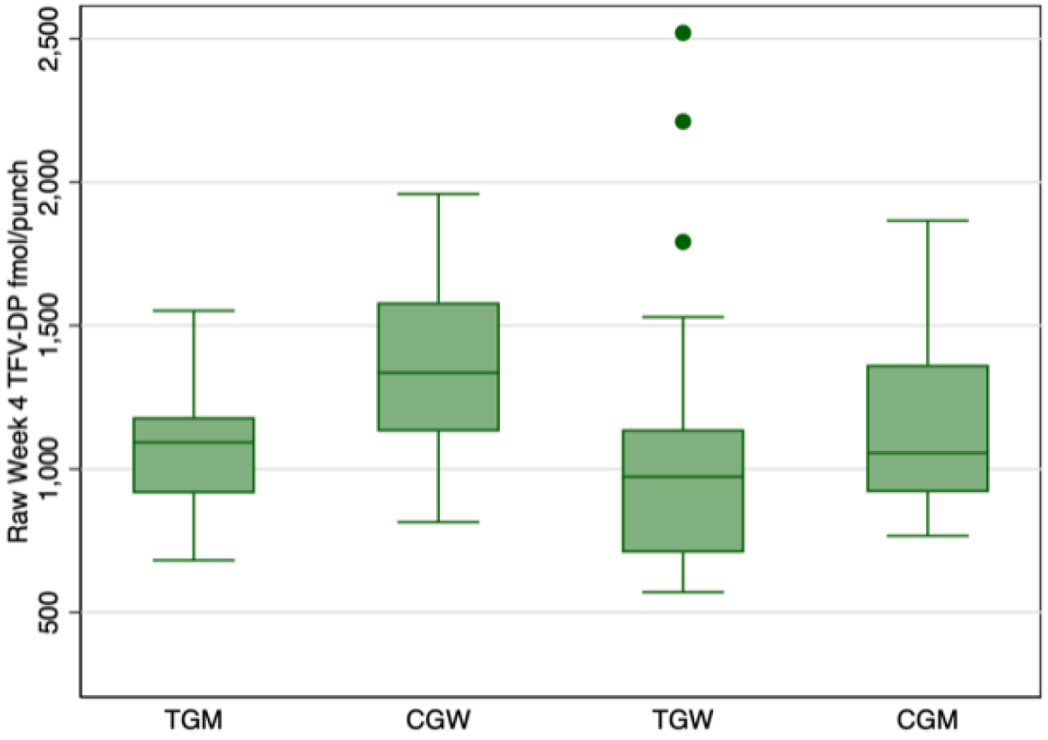
Grant et al, 2020, CID (accepted)

MWAETC

"Sex Hormone Therapy and Tenofovir Diphosphate Concentration in Dried Blood Spots: Primary Results of the iBrEATHe Study."

Comparisons

- Levels lower by 23% in TGM v 17 CGW
- No difference in wk 4 TFV-FP levels in TGW v 15 CGM
- All participants expected to reach TFV-DP > 800 by 8 weeks



Grant et al, 2020, CID (accepted)

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"Sex Hormone Therapy and Tenofovir Diphosphate Concentration in Dried Blood Spots: Primary Results of the iBrEATHe Study."

Discussion

- TGW, TGM, CGM had similar TFV-DP levels at 4 weeks, and CGW had higher concentrations.
- Lower TFV-DP levels in TGW observed in iPrEx trial due to adherence and not differences in metabolism.
- Gender affirming hormones are not expected to reduce PrEP efficacy. However, the relationship between TFV-DP in DBS and risk for acquisition is most confidently known for CGM.
- Results may not apply to TAF.

Grant et al, 2020, CID (accepted)

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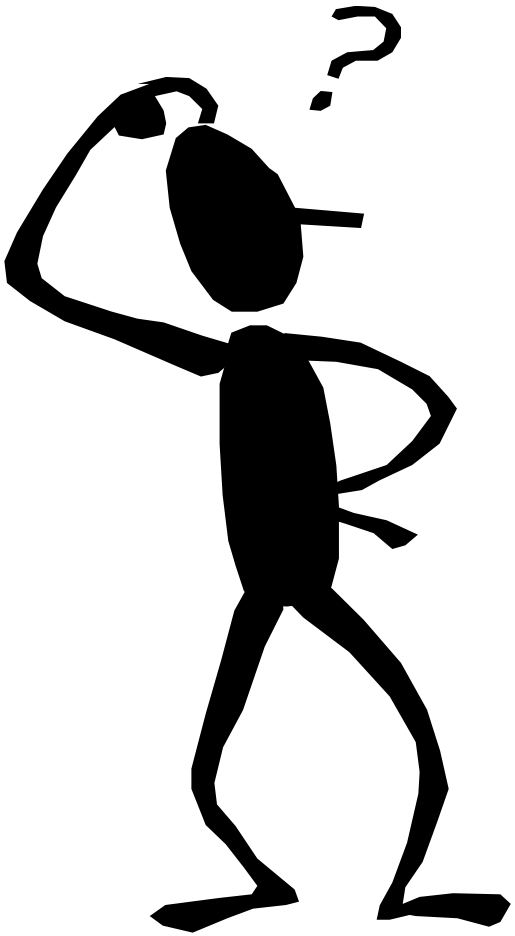
Questions?



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