

Adolescents and Oral PrEP: Results and Lessons from ATN 113

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Conflicts of Interest

- No conflicts to disclose

Background

- Blinded and open label studies among adult MSM support the efficacy of TDF/FTC for HIV prevention
- No PrEP data available on adolescent MSM to date
- Additional safety and behavioral data in adolescents are needed to support a PrEP indication
- Paired PrEP demonstration and safety studies
 - ATN 110 (ages 18-22); in press JAIDS
 - ATN 113 (ages 15-17): presented AIDS 2016

Primary Objectives

- To provide additional safety data regarding TDF/FTC use among HIV-uninfected YMSM ages 15-17.
- To examine acceptability, patterns of use, rates of adherence and measured levels of drug exposure when YMSM are provided open label TDF/FTC.
- To examine patterns of sexual behavior when YMSM are provided a behavioral intervention as well as open label TDF/FTC

Secondary Objectives



ELSEVIER

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Original article

Adolescent Self-Consent for Biomedical Human Immunodeficiency Virus Prevention Research



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AJPH LAW & ETHICS

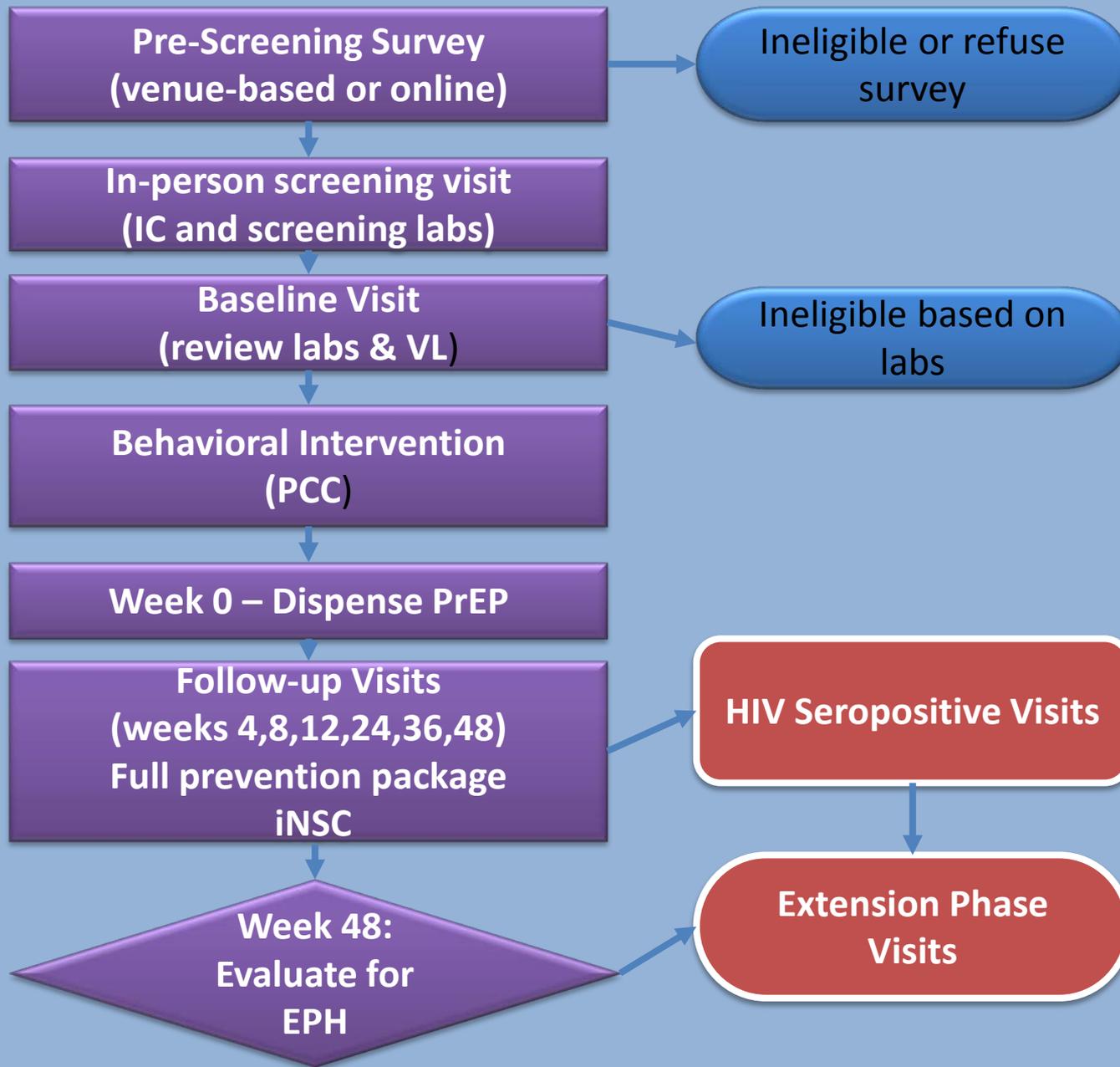
Legal Barriers to Adolescent Participation in Research About HIV and Other Sexually Transmitted Infections

Whether adolescents can participate in clinical trials of *Quianta L. Moore, MD, JD, Mary E. Paul, MD, Amy L. McGuire, JD, PhD, and Mary A. Majumder, JD, PhD*

Inclusion Criteria

- Ages 15-17; born male
- Self-reports evidence of high risk for acquiring HIV, including at least one of the following in the last 6 months:
 - Condomless anal intercourse with an HIV-infected male partner or a male partner of unknown HIV status;
 - Anal intercourse with 3 or more male sex partners;
 - Exchange of money, gifts, shelter, or drugs for anal sex with a male partner;
 - Sex with a male partner and has had a STI;
 - Sexual partner of an HIV-infected male with whom condoms were not consistently used; or
 - At least one episode of anal intercourse where the condom broke or slipped off
- Tests HIV antibody negative at time of screening

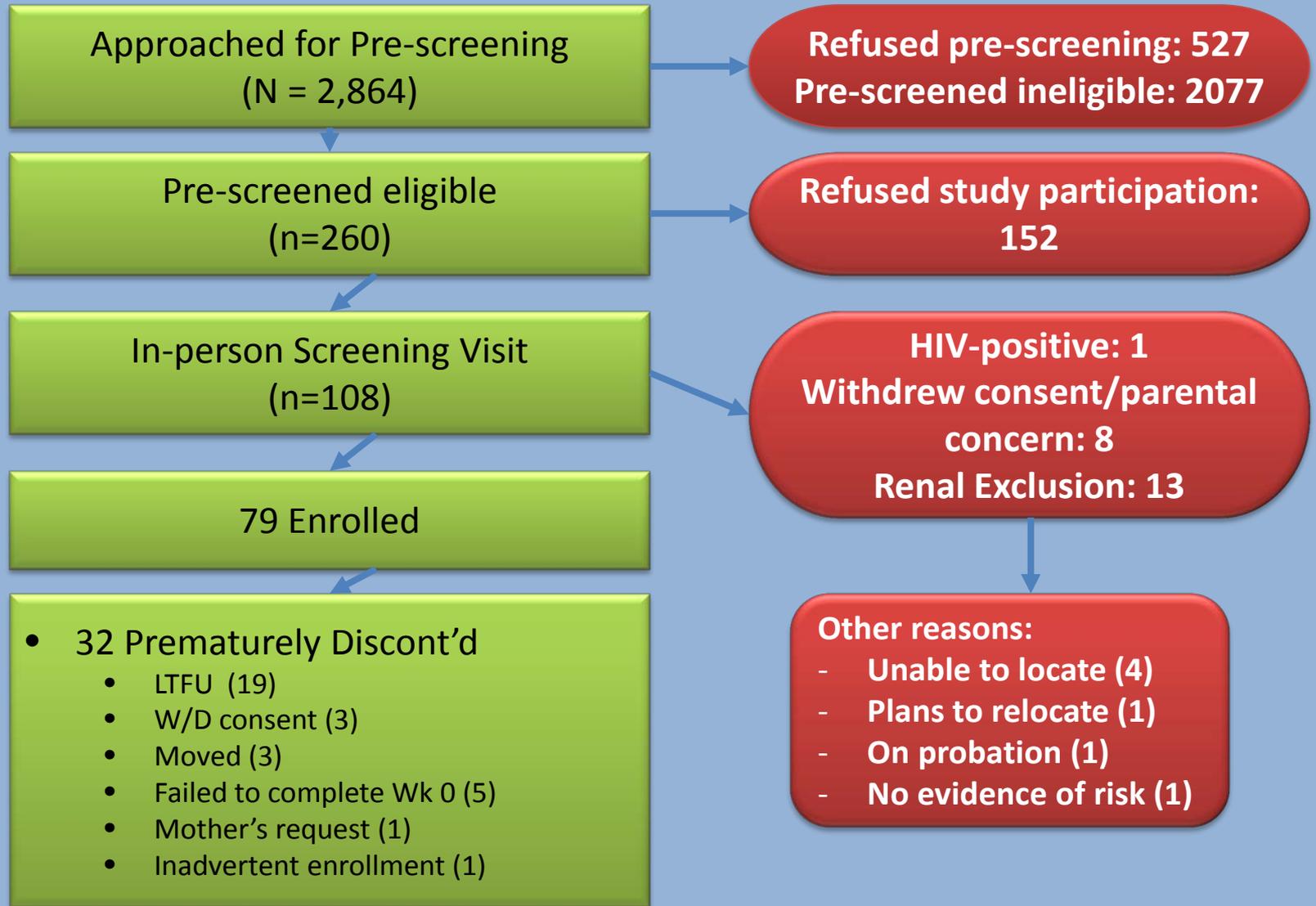
Study Flow



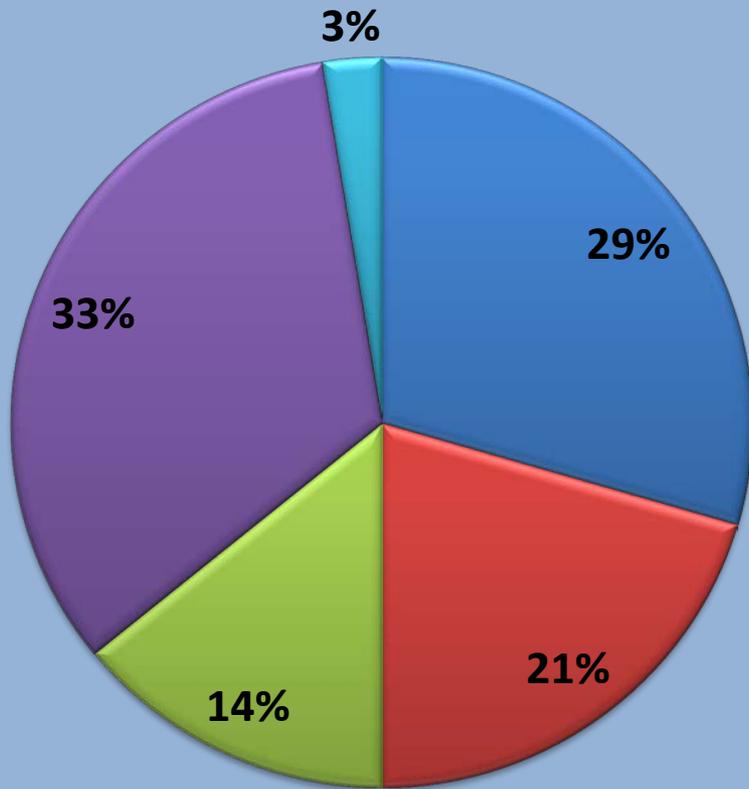
ATN 113 Study Sites



Consort Diagram



Baseline Demographics



- Black
- Hispanic/Latino
- White
- Other/Mixed
- Asian/PI

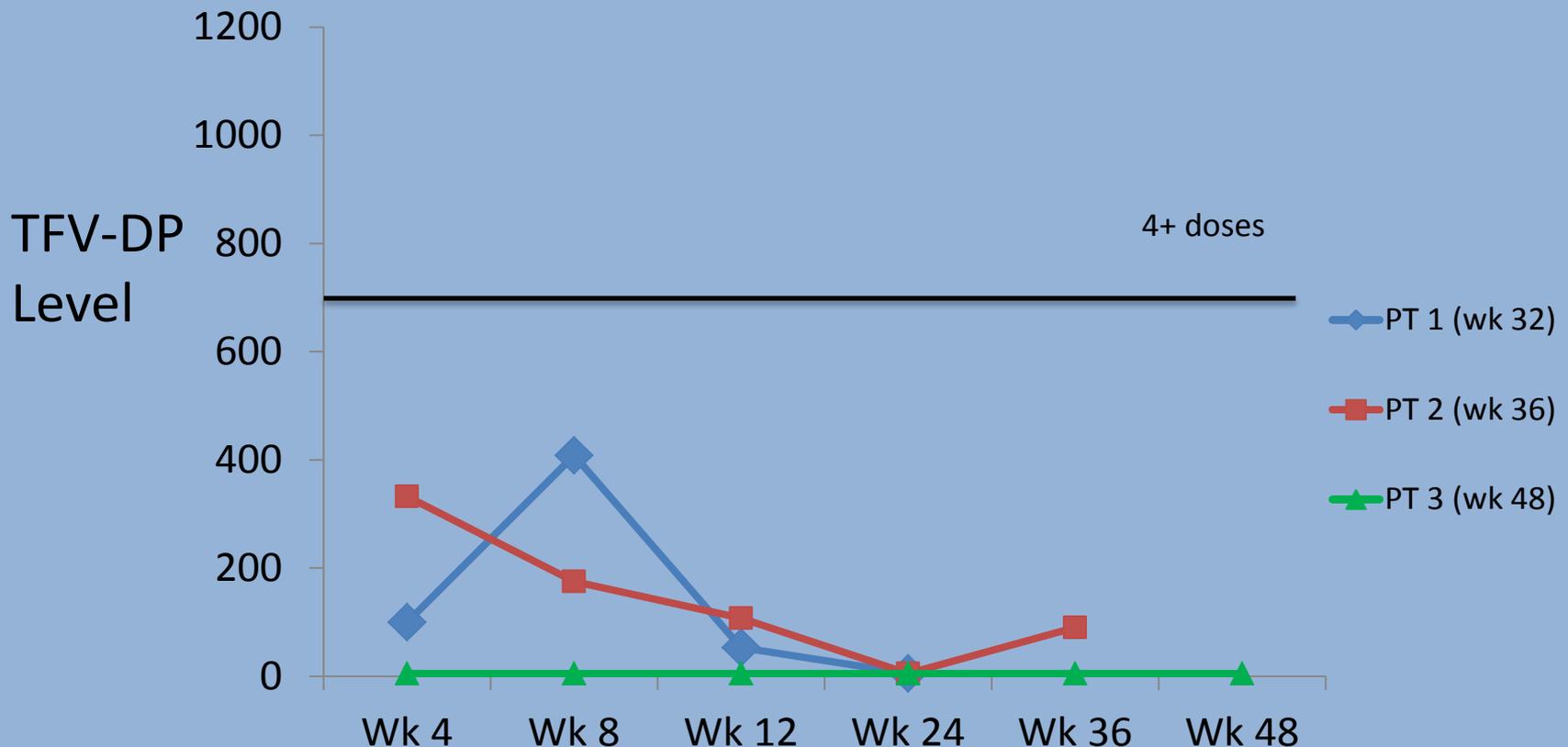
| | |
|--------------------------------------|---|
| Mean age | 16.5 |
| Sexual Identity | Gay – 58% Bisexual – 28% Questioning – 6% |
| Completed high school | 18.4% |
| Currently living with parents/family | 88.5% |
| Received public aid | 76.9% |
| Kicked out of house for being gay | 15% |
| Ever been paid for sex | 17% |
| Partners in past mo | 2 |
| CRAI w/last partner | 60% |
| Any positive STI test | 15.4% |

Safety

- Well-tolerated overall
 - No documented discontinuations due to side effects
- Adverse Events
 - Three Grade 3 adverse events (weight loss) in 2 participants deemed related to study drug
 - Grade 3 weight loss = 10-19%
- No abnormal laboratory results
- Bone Mineral Density
 - DXA data still being analyzed

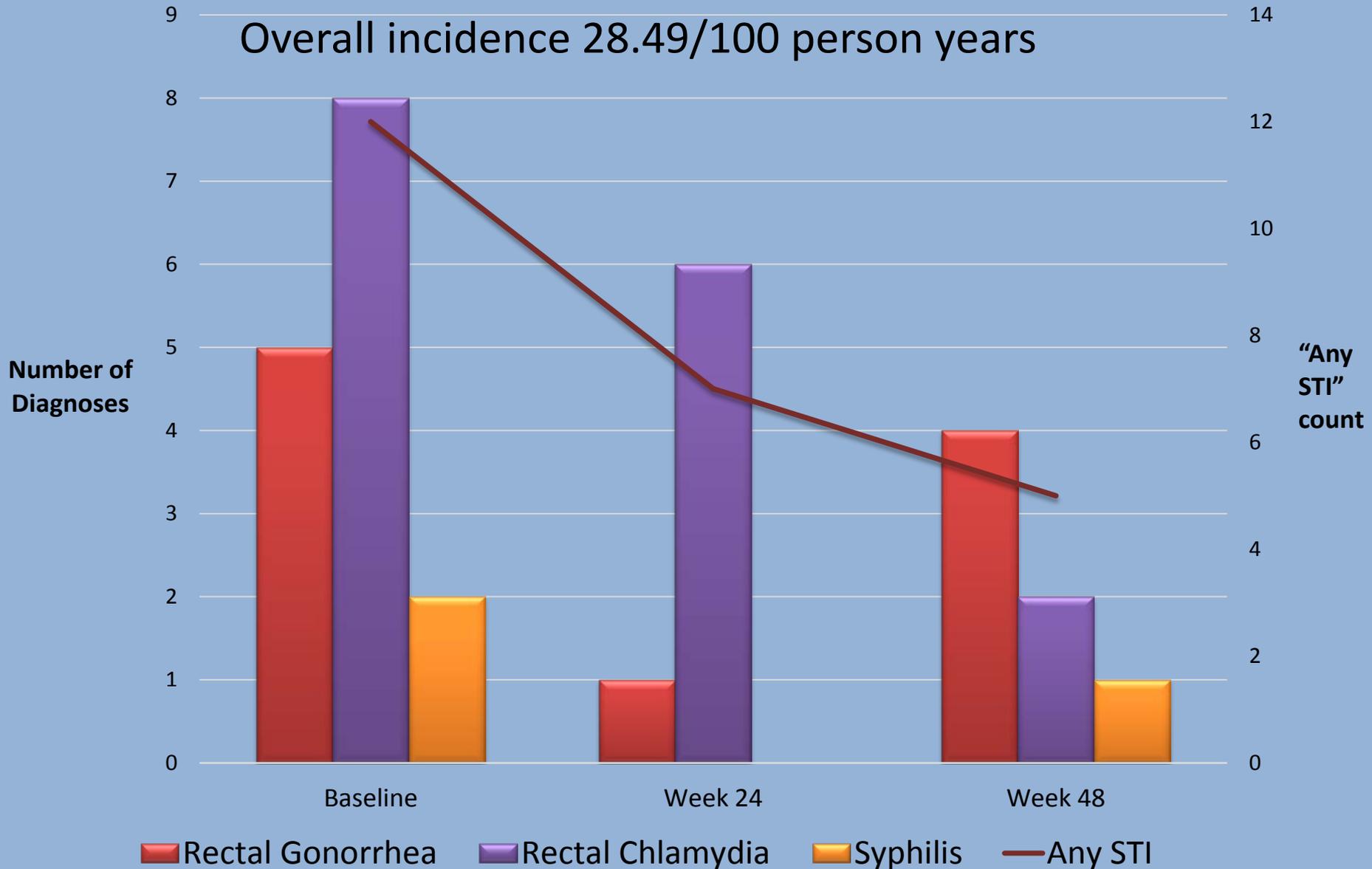
HIV Incidence

- 3 seroconversions through week 48
- HIV incidence = 6.41 per 100 person-years (95% CI: 0.0-13.66)

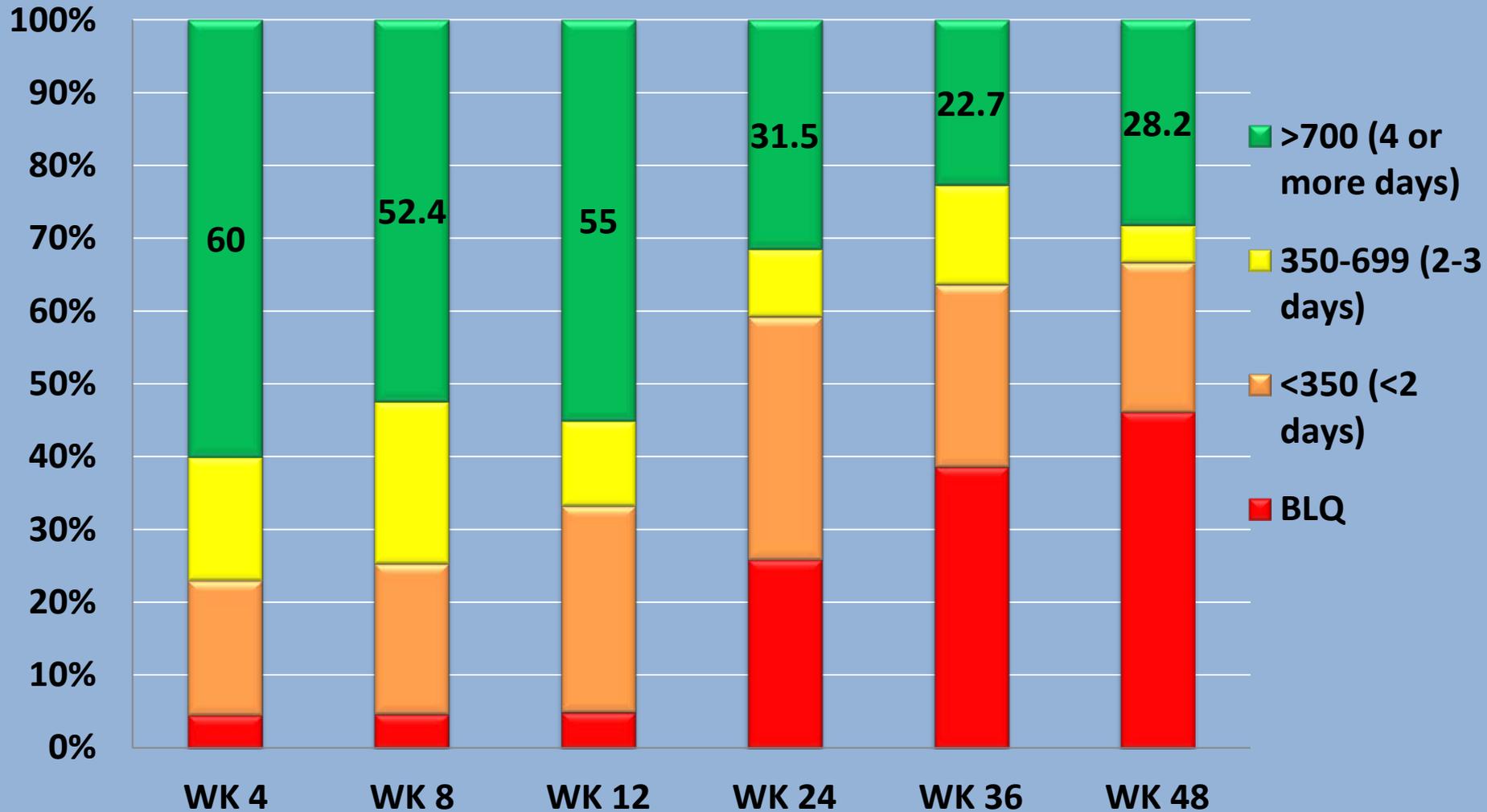


STI Diagnoses

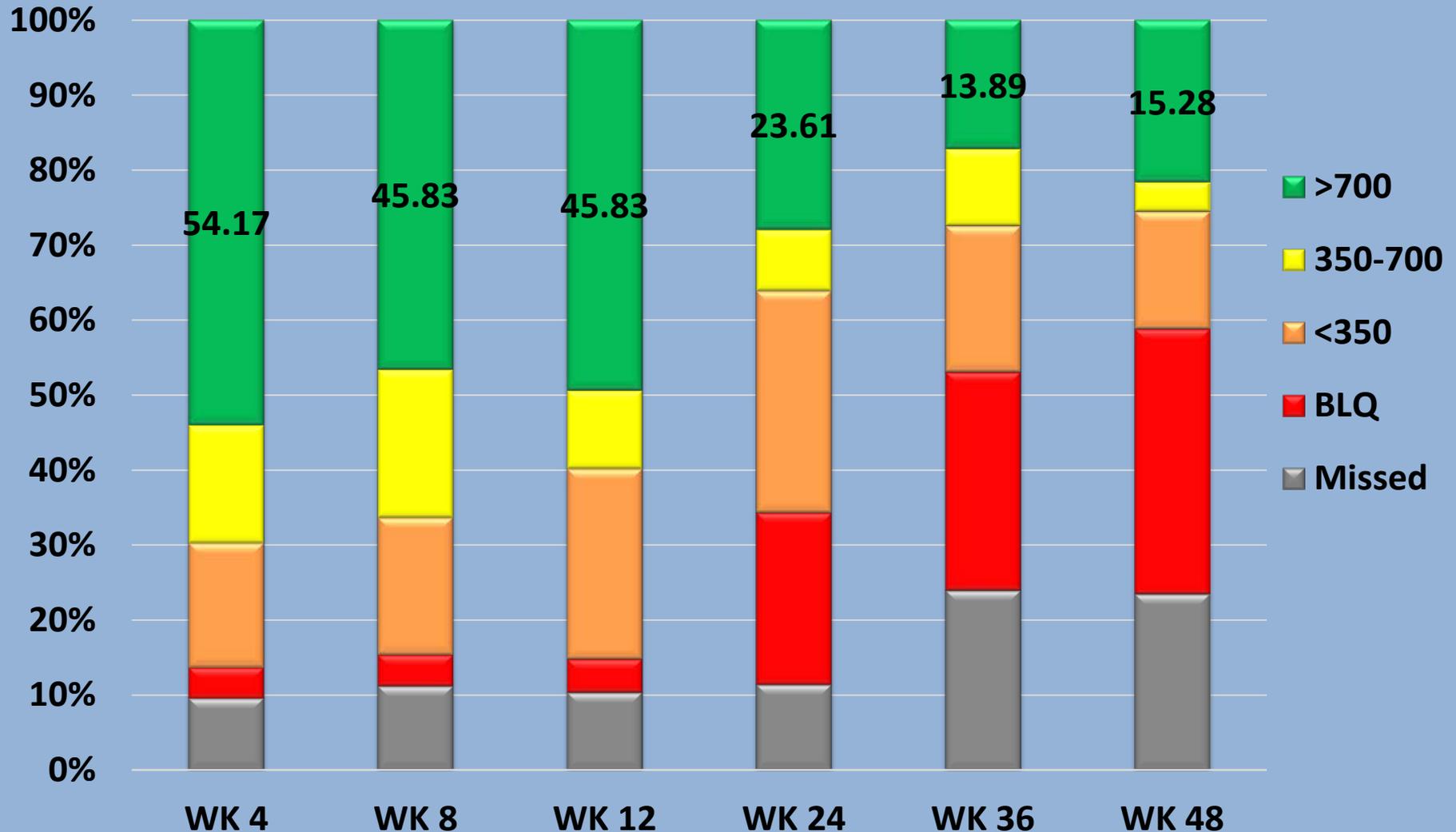
Overall incidence 28.49/100 person years



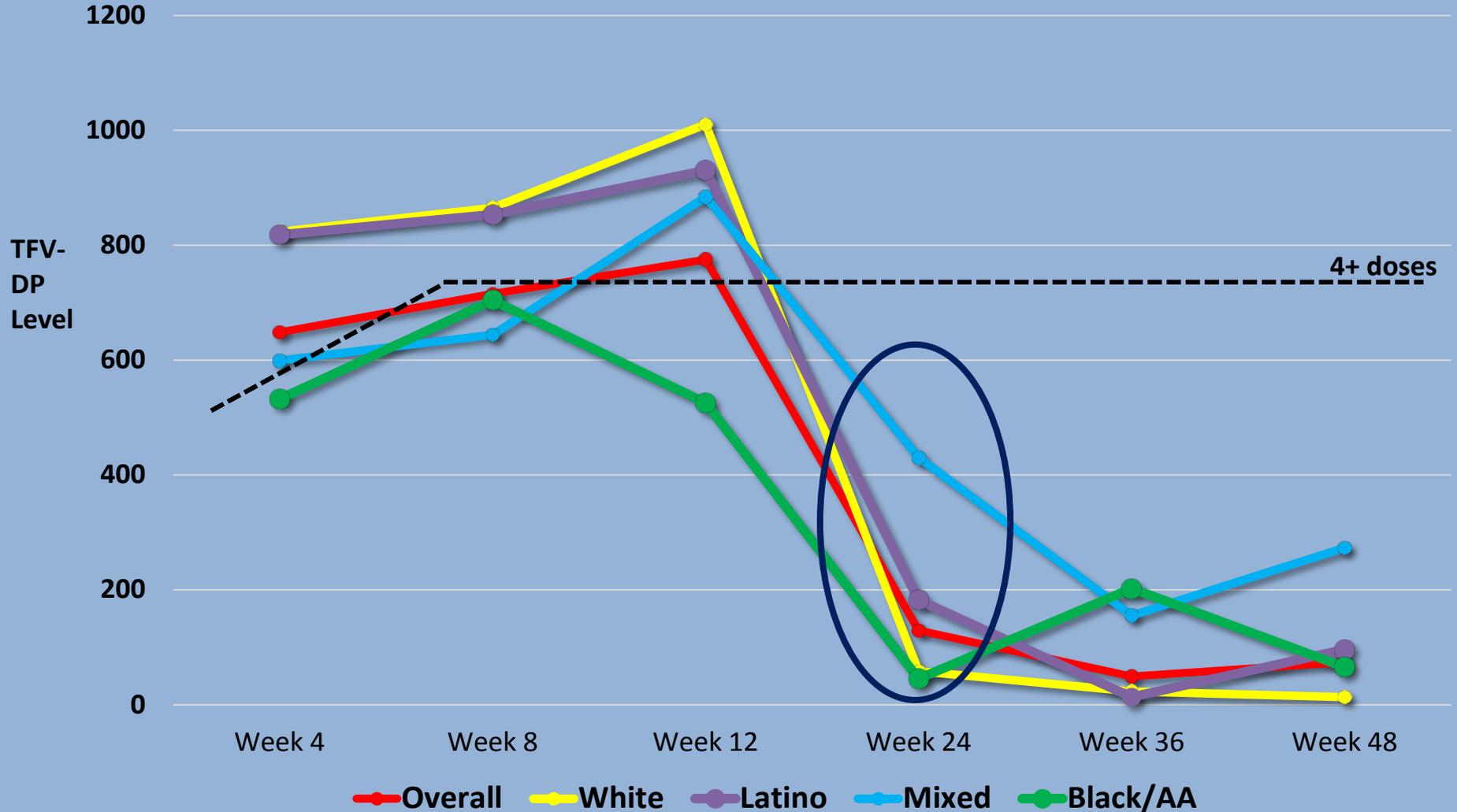
Adherence: TFV-DP (fmol/punch) via DBS w/Dosing Estimates



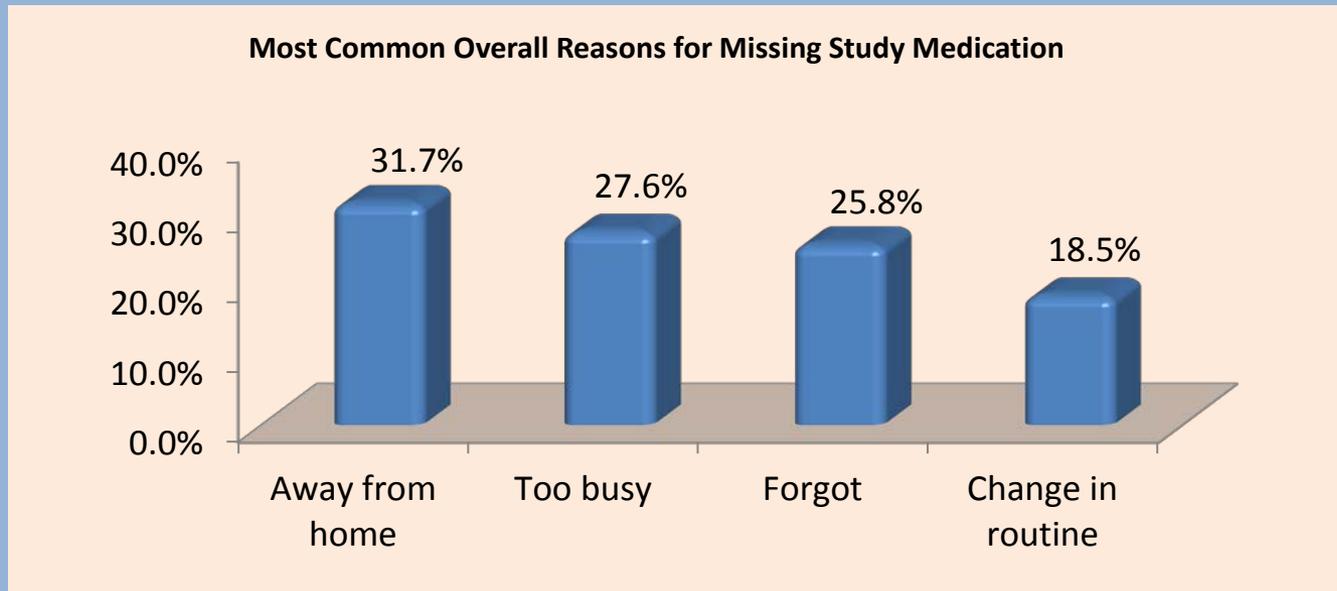
Adherence: DBS w/Dosing Estimates including Missed Visits



Adherence: Median TFV-DP by Race/Ethnicity



Adherence and PrEP Beliefs



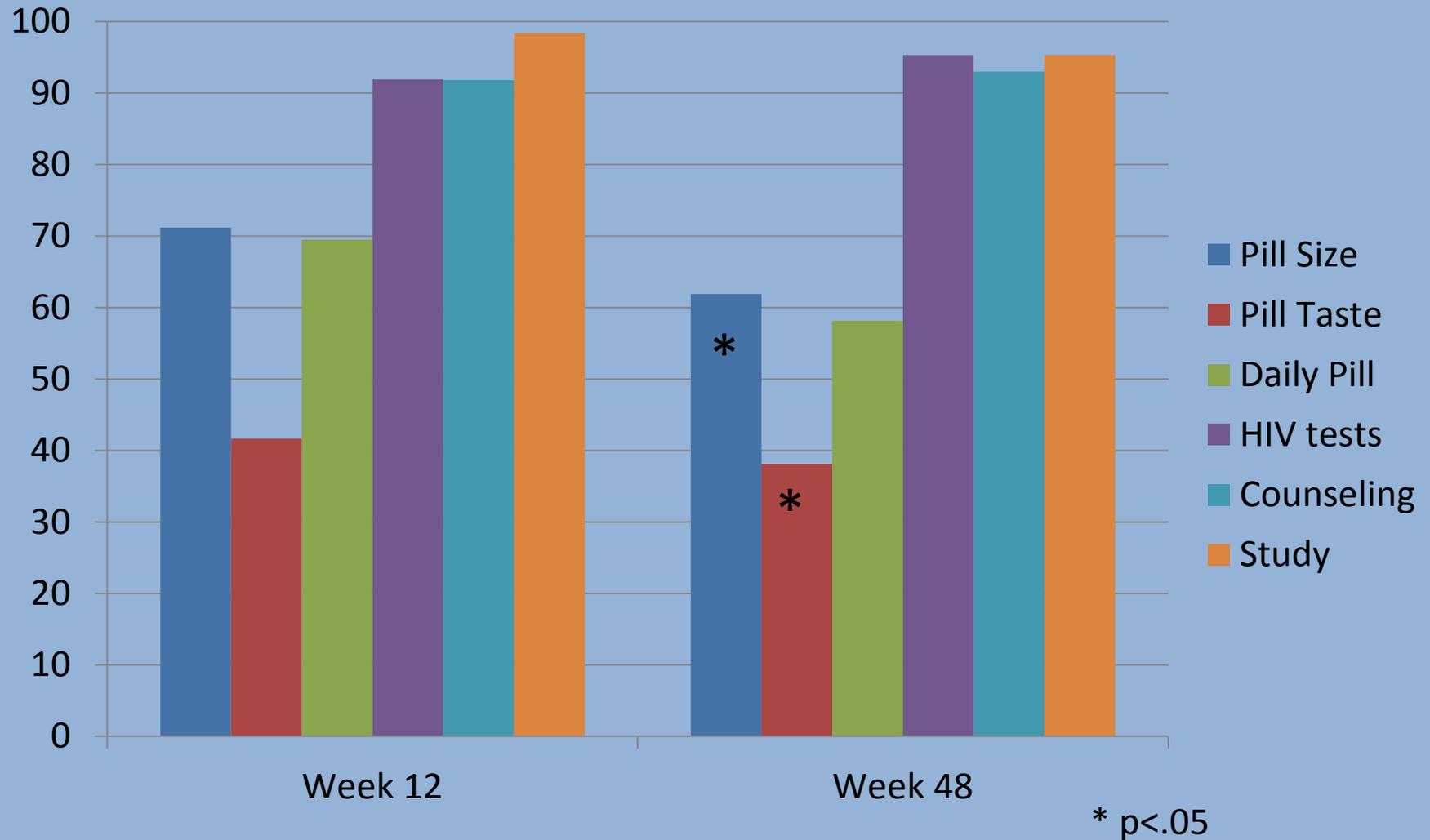
- Non-adherent participants were more likely to endorse the following beliefs than adherent participants:
 - “I worry others will see me taking pills and think I am HIV-positive” (p=.03)
 - “I am concerned people will know I have sex with other men because I’m taking PrEP” (p=.06)
 - “I don’t like taking pills” (p=.06)

Adherence: In their words...

“Honestly it was harder than I thought it was going to be. I set an alarm and I made it a certain time every day and I would try and keep extra pills. I’m in a long distance relationship so every weekend I would be traveling to see my partner. It was harder to keep on track of it than I thought it would be. It was manageable, I think. It was just something that I had to keep that in mind or I would forget.”

“I was pretty good about it. I never missed a day other than I think it was like a week or two that I didn’t take it. But other than that, I was good taking it every day. Yeah. And then they gave me that little black box so then they knew I was taking it every day.”

Acceptability: Participants Liked/Liked A lot



Acceptability: In their words...

“They [study staff] were just really genuine, just really genuine from the heart type of people. I'm the type of person that can find out if you're fake, but I definitely didn't get that vibe from them. I just felt like I was in a safe, loving, genuine, caring situation. I definitely grew relationships with the doctors, with the counselors, and the nurses. I feel like that was the best part.”

“[I had] peace of mind knowing that I could have a sex life and not have to worry about contracting HIV because I feel like know the rates and I'm like one of the key demographics of people who would get it. It was just really reassuring that I could sort of like take good care of my body and make decision that I'm going to take this every day so I'd never get HIV or spread it to anyone else.”

Was there anyone that you wish had been part of the consent process?

“It was kind of cool just like with me and the doctor. At that time, I also wasn't out about my identity, so it was kind of like I didn't want to really talk about it to other parties.”

“I feel like my relationship with my dad isn't the best. So I'm kind of like independent in that sense. I never discussed it with my dad so I wouldn't say him. Like I said, my mom even since she was not knowledgeable in the area I didn't really feel the need to inform her in the process.”

“No. No, not really. I feel like if I had to have a parent or guardian or someone there, it would have just been a little bit awkward, and it probably wouldn’t have happened because my mom doesn’t have time for all that.”

“I found it to be a really personal decision. I did discuss it with my mom but it wasn’t like she had a lot of input in it. It was more like I just let her know. She had never heard of PrEP. I told her the case study and that it was voluntary and she was fine with it. I discussed it with my partner as well. He was fine with it as well. I discussed it with people at [RESEARCH SITE]. I think a lot of it was just my own decision and me doing research online and like my prior knowledge.”

Study Conclusions

- Adolescents need access to PrEP!
 - Despite decreasing STIs, HIV incidence was high compared to other open label trials; 2x HIV incidence seen in ATN 110
 - We must decrease regulatory and financial barriers
- PrEP was well tolerated with minimal safety concerns
 - DXA data may be difficult to interpret
- Acceptability of PrEP, the overall study, and HIV testing and counseling was high
- More work is needed to address traditional adherence barriers, plus additional stigma-related concerns

Managing Expectations

- “Since this didn’t work, should we just focus on the injectables?”

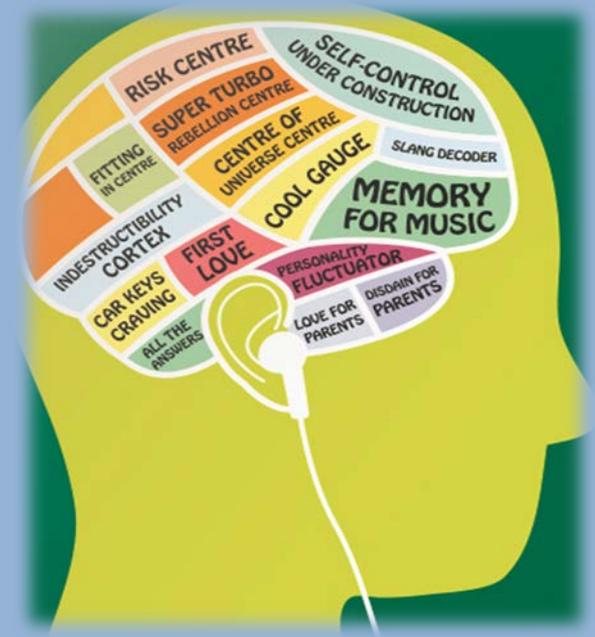
Gay and Bi Teens Adhere Poorly to PrEP

Gay and Bi Teens May Need Monthly Monitoring to Adhere Well to PrEP

- Adherence in youth is challenging regardless of prevention vs. treatment
- Always remember the adolescent brain...

Key Points on Adolescent Brain

- Still developing into 20s
- Compared to adults, poorer:
 - executive functioning,
 - decision-making,
 - processing speed,
 - insight
- Mismatch in development timeline between reward centers of brain and impulse-control centers
- Heightened emotionality, increased sensitivity and self-consciousness
- BUT increased capacity for learning, desire for social interaction, exploration and limit testing are necessary for independence



Dear, Mom and Dad

During science class this week we read an article and watched a video. They were both about the teenage brain. The article is titled *The Teen Brain: It's Just Not Grown Up*

I have learned that my brain as a teenager is not fully developed. My frontal lobe is not fully connected to the rest of my brain. This can result in poor or not well thought out decisions. In addition to the frontal lobe not being fully connected, my nerve cells are "sluggish". This results in a lack of proper communication within my brain. Apparently, the fully connected frontal lobe is needed for good judgement and insight.

As a teenager I will make dumb decisions. This is partly due to my lack of fully developed brain. I hope that I will think twice about the consequences of my actions before I do something. Now you know that it is hard for me to think twice before I do something. So in the future remember this letter before you yell or get mad at me.

DO NOT OPEN UNTIL AGE 25!



The Way Forward...

- Despite knowing the differences between the adolescents and adults, we still design studies with adults in mind
 - My biggest regret...
- Adolescent PrEP implementation must use developmentally-appropriate strategies
 - Youth need enhanced visit schedules and/or more frequent interactions (in-person or via mobile technology)
 - Clinical guidelines for contraception recommend more frequent visits
 - “Adolescents are identified throughout this document as a special population that might benefit from more frequent follow-up.” (CDC MMWR: U.S. Selected Practice Recommendations for Contraceptive Use, 2013)

- Drop-outs were substantial, highlighting need for ongoing retention/engagement strategies
 - Peer support groups or buddies, adherence clubs
- We must be willing to give adolescents the time, attention and resources that they need to succeed, both in clinical practice AND in clinical trials.

**IF YOU DON'T HAVE
TIME TO DO IT
RIGHT, WHEN WILL
YOU HAVE TIME TO
DO IT OVER.**

- JOHN WOODEN

Acknowledgements

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THANK YOU!