NORTHWEST AIDS EDUCATION AND TRAINING CENTER

CROI Update 2014: Prevention

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Outline

- Risk of HIV Transmission with Suppressed Viral Load
- Maternal Tenofovir and Newborn Bone Mineral Content
- New Medications for Pre-Exposure Prophylaxis (PrEP)

Risk of HIV Transmission with Suppressed Viral Load

PARTNER Study: HIV Transmission Risk with Condomless Sex if Positive Partner on Suppressive ART

- **Background:**
  - Absolute risk of HIV transmission with condomless sex and suppressed viral load unknown
  - Knowing risk would help inform counseling & PrEP decisions
- **PARTNER Study:**
  - Observational study of serodiscordant couples at 75 sites in 14 European countries to try to estimate risk

Roger A et al. CROI 2014, Boston, MA. Abstract 153LB.

PARTNER Study: Methods and Results

- **Methods:**
  - Every 6 month behavioral questionnaire, HIV RNA (positive partner), HIV test (negative partner)
  - Counseling and informed consent at each study contact
  - Eligible CYFU: condomless sex, no PEP or PrEP, positive partner VL <200 copies/mL
- **Results:**
  - 1,110 couples recruited by Nov 1st, 2013
  - 767 couples provided 894 CYFU

PARTNER Study: Baseline Characteristics
HIV Negative Partners

	MSM Couples (N=282)	Heterosexual, M –ve (N=245)	Heterosexual, W –ve, (N=240)
Age, median	40	45	40
Yrs condomless sex, median	**1.5**	2.7	3.5
Yrs in study, median	1.1	1.5	1.5
Dx with STI	**16%**	5%	6%
Condomless sex with other partners	**34%**	3%	4%
Condomless sex acts/year, median	43	37	38
Estimated total # condomless sex acts	16,400	14,000	14,000

PARTNER Study: Baseline Characteristics
HIV Positive Partners

	MSM Couples (N=282)	Heterosexual, M –ve (N=245)	Heterosexual, W –ve, (N=240)
Age, median	42	40	45
Yrs on ART, median	**5**	7	10
Self-reported adherence >90%	97%	94%	94%
Self-reported VL undetectable	**94%**	86%	85%
CD4 >350	90%	88%	84%
Missed ART >4 consecutive days	2%	7%	4%
Dx with STI	**16%**	4%	5%

PARTNER Study:
Key Results

- Phylogenetically linked transmissions: **none**
  - Absolute transmission rate: 0
  - 10-year risk of transmission: 0
- *However*, due to limited # of CYFU, uncertainty exists:

	CYFU	Upper bound 95% CI	Upper estimate of 10-year risk
Any sex	894	0.4/100 CYFU	**4%**
Anal sex	374	0.96/100 CYFU	**10%**
Receptive anal sex with ejaculation	93	4/100 CYFU	**32%**

PARTNER Study: Interpretation

- Conclusions:
  - Zero linked transmissions over 894 CYFU
  - However, uncertainty remains over upper limit of risk
  - More data needed; PARTNER2 study through 2017 for MSM
  - Will this change your practice or how you counsel patients?

Maternal Tenofovir Use and Newborn Bone Mineral Content

Lower Newborn Bone Mineral Content Associated With Maternal Use of Tenofovir (TDF)

- **Background**:
  - TDF affects BMD more than other ARV's in adults and children with HIV; also affects BMD in HIV-negative persons (PrEP)
  - TDF use in pregnancy increasing
  - Limited data for effects on fetal bone growth
    - Animal studies show bone undermineralization (?dose related)
    - One small study showed TDF exposure *in utero* had no effect on children age 1-5 using bone ultrasound and biomarkers

Siberry GK et al. CROI 2014, Boston, MA. Abstract 71.

Tenofovir and Newborn Bone Mineral Content: Methods

- Pediatric HIV AIDS Cohort Study (PHACS)
- 14 sites in US and Puerto Rico
- Compared 2 groups of HIV-negative newborns:
  - TDF-exposed: TDF used for ≥8 weeks in 3rd trimester
  - TDF-unexposed: no TDF in pregnancy
  - Within 4 weeks of birth: whole body DXA scan

Tenofovir and Newborn Bone Mineral Content:
Baseline Characteristics

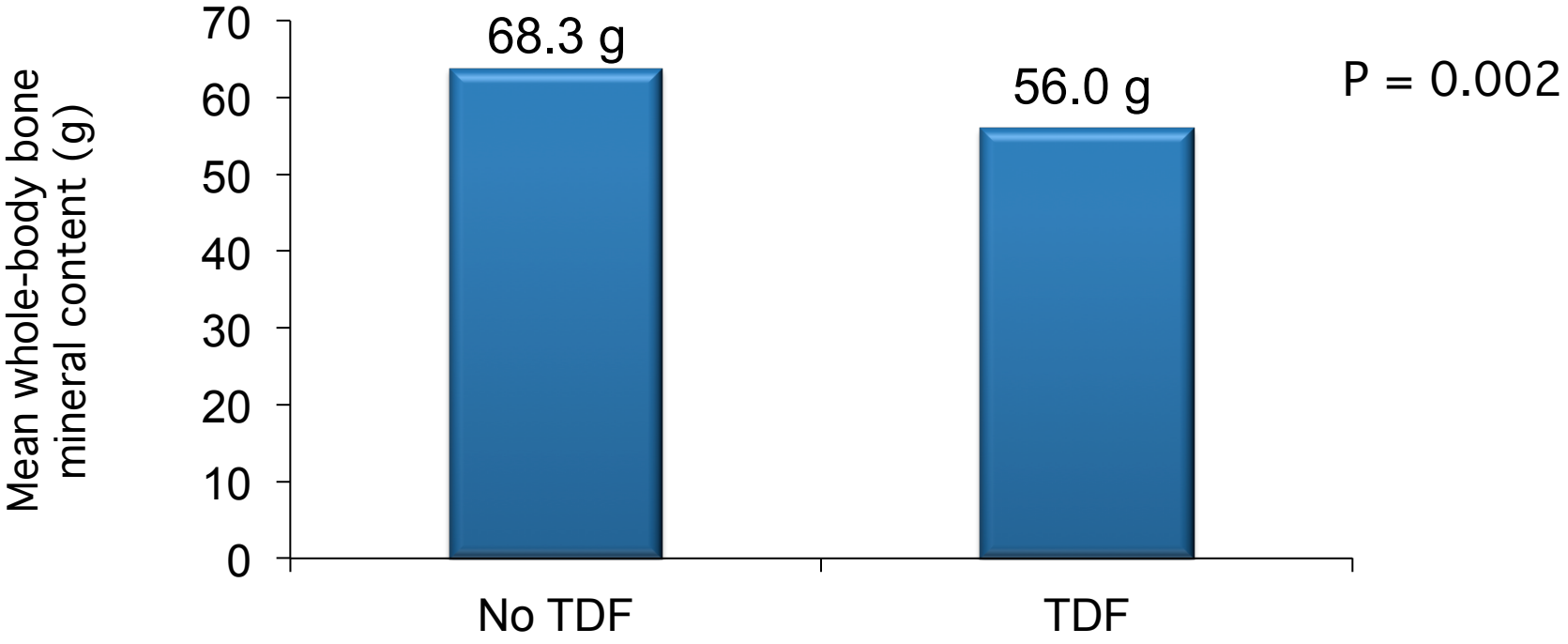
	No-TDF (N=69)	TDF (N=74)	P Value
Maternal age, median	28 yrs	30 yrs	**0.10**
Married	15 (22%)	23 (31%)	**0.04**
Any substance use	25 (37%)	19 (26%)	**0.19**
Black, Hispanic	58%, 32%	70%, 19%	0.25
Boosted PI	44 (64%)	64 (86%)	**0.005**
CD4 >250	58/63 (94%)	41/44 (93%)	0.92
VL <400	56/62 (90%)	45/50 (90%)	0.95
Gest. age wks, mean	38.1	38.2	0.60
Infant female sex	34 (49%)	28 (38%)	**0.17**

*Bold = included in multivariate analysis

Tenofovir and Newborn Bone Mineral Content: Maternal ARV Regimens

Study Arm	Maternal ARV Regimen	N (%)
TDF (N=74)	TDF-FTC-ATZ-r	38 (52%)
	TDF-FTC-DRV-r	12 (16%)
	TDF-FTC-RAL	6 (8%)
	TDF-FTC-LPV/r	4 (5)
	Other	14 (19%)
No TDF (N=69)	AZT-3TC-LPV/r	27 (41%)
	AZT-ABC-3TC	14 (21%)
	AZT-3TC-DRV/r	4 (6%)
	Other	24 (32%)

Tenofovir and Newborn Bone Mineral Content: Key Results



Difference remained significant in multivariate model that adjusted for: infant gestational age, body length, race/ethnicity, site, age at DXA, maternal age, boosted PI use, and smoking

Tenofovir and Newborn Bone Mineral Content

- **Limitations**:
  - Non-randomized
  - High use of AZT-ABC-3TC in no-TDF arm (21%)
  - Cross-sectional study → does effect persist?
- **Next steps:**
  - Duration and clinical significance will be evaluated in longitudinal studies
  - Plans for testing stored specimens to examine mechanism of maternal TDF on infant bone

Tenofovir and Newborn Bone Mineral Content

- Will the study change guidelines? How about your practice?
- Systematic review, Sept. 2013: “Five studies that followed in utero TDF-exposed infants showed **no increased risk of growth or bone abnormalities**...”
- “More evidence collected prospectively, ideally with bone density measurements and randomized trial design, will be optimal to determine the effects of antenatal TDF exposure on children's health.”

Wang L et al. Clin Infect Dis. 2013 Dec;57(12):1773-81.

New Medications for PrEP

New Meds for PrEP: The Highlights

- **GSK-744-LA:**
  - One injection protected 12 male macaques from weekly rectal SHIV challenges for at least 5 weeks
  - Two monthly injections protected 6 female macaques from low-dose vaginal SHIV challenges (and high-dose, poster)
- **Dapivirine and maraviroc intravaginal rings:**
  - Safe in healthy HIV-neg women, though only dapivirine reached protective levels in genital tissues
- **Dapivirine film:**
  - Safe in healthy HIV-neg women and provides similar plasma and genital tissue levels as gel and ring, but difficult to insert

Andrews CD et al. Abstract 941LB. Radzio J et al. Abstract 40LB. Chen BA et al. Abstract 41. Bunge KE et al. Abstract 42.

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Conclusions

- Best data yet for risk of HIV transmission with suppressed viral load, but uncertainty remains
- Concern for adverse effects of maternal tenofovir on fetal bone but awaiting longitudinal data
- New medications and delivery methods for PrEP are promising and may offer choice of method in the future