

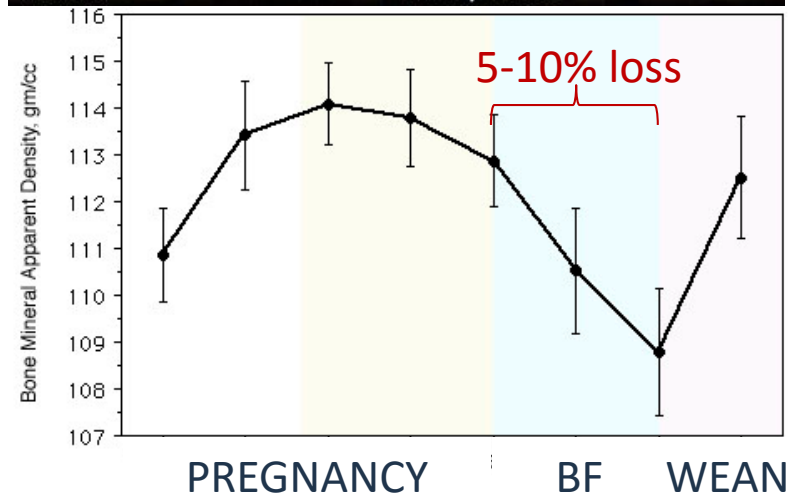
# Safety Update: Impact of tenofovir-containing triple antiretroviral therapy (ART) on bone mineral density in HIV-infected breastfeeding women in sub- Saharan Africa

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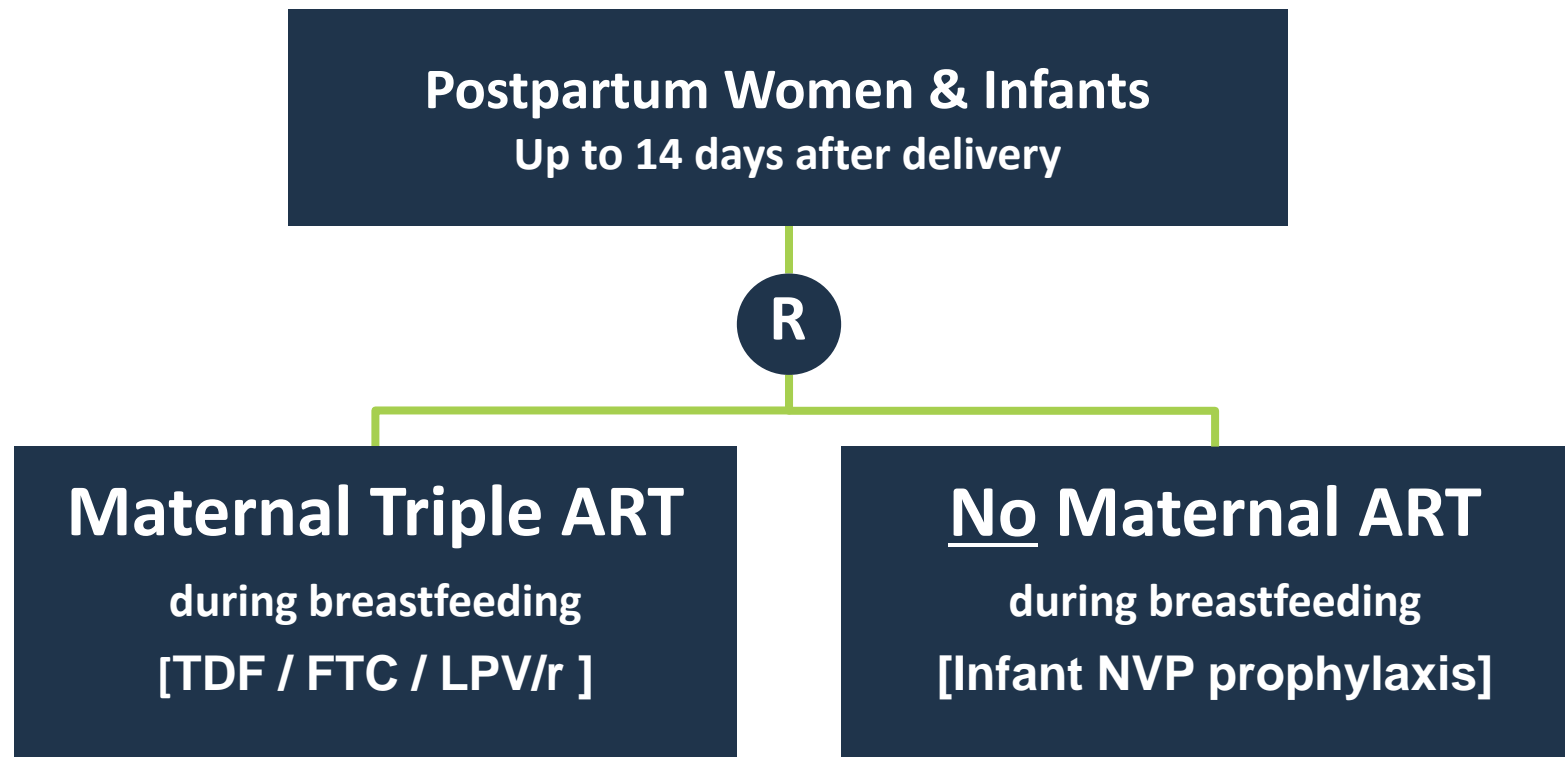


# HIV-infected mothers in resource limited settings at risk of low bone mineral density

- Low BMD in HIV infected pregnant/BF women the result of:
  - HIV infection itself
  - Lactation
  - Antiretroviral drug use
- AIM: To evaluate the effect of postnatal ARV exposure on BMD

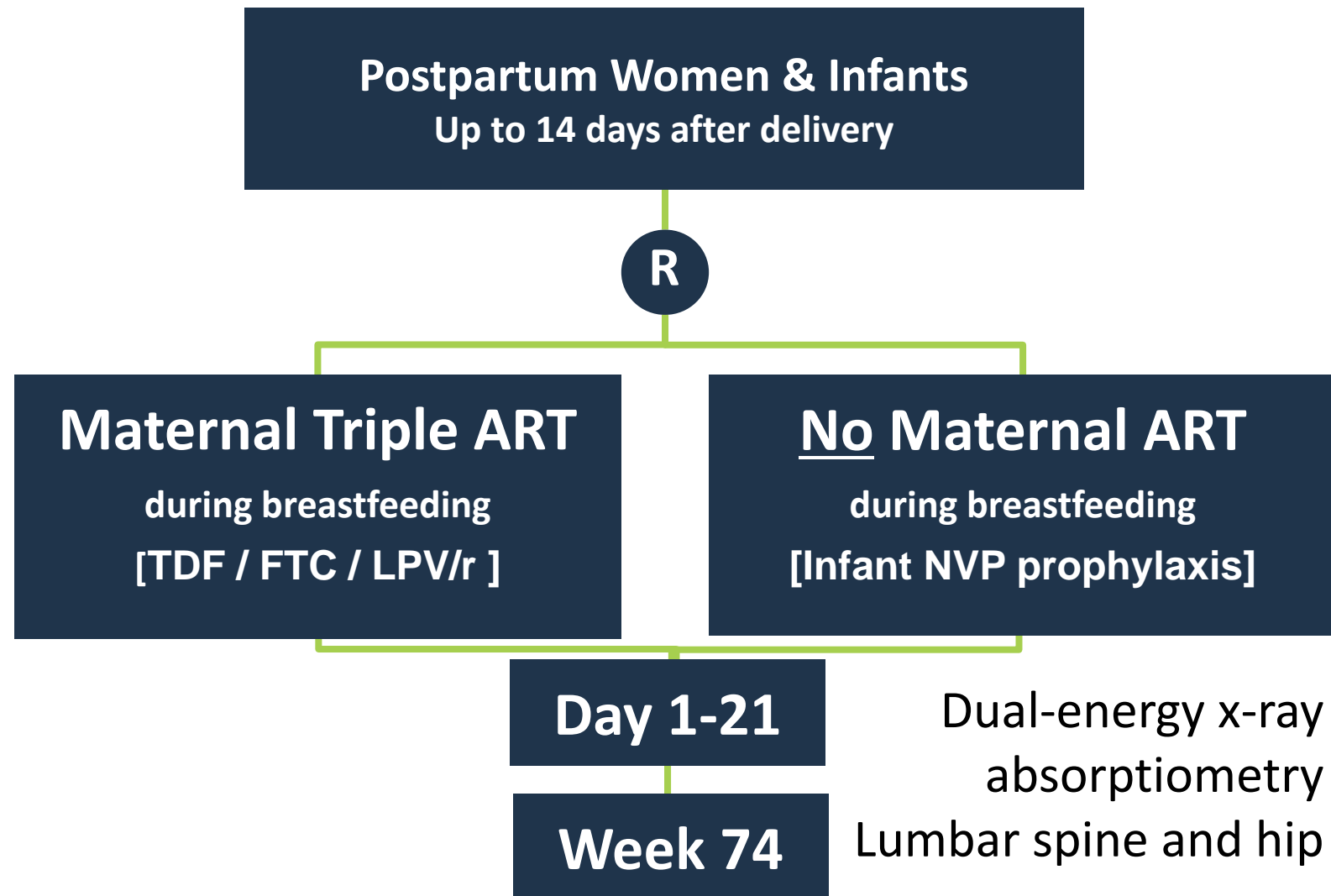


# Subset of 1077BP pairs co-enrolled in P1084s



Co-enrolment offered to randomised women in Zimbabwe, Uganda, South Africa, Malawi sites with available DXA

# BMD assessed at weeks 1 and 74 by DXA

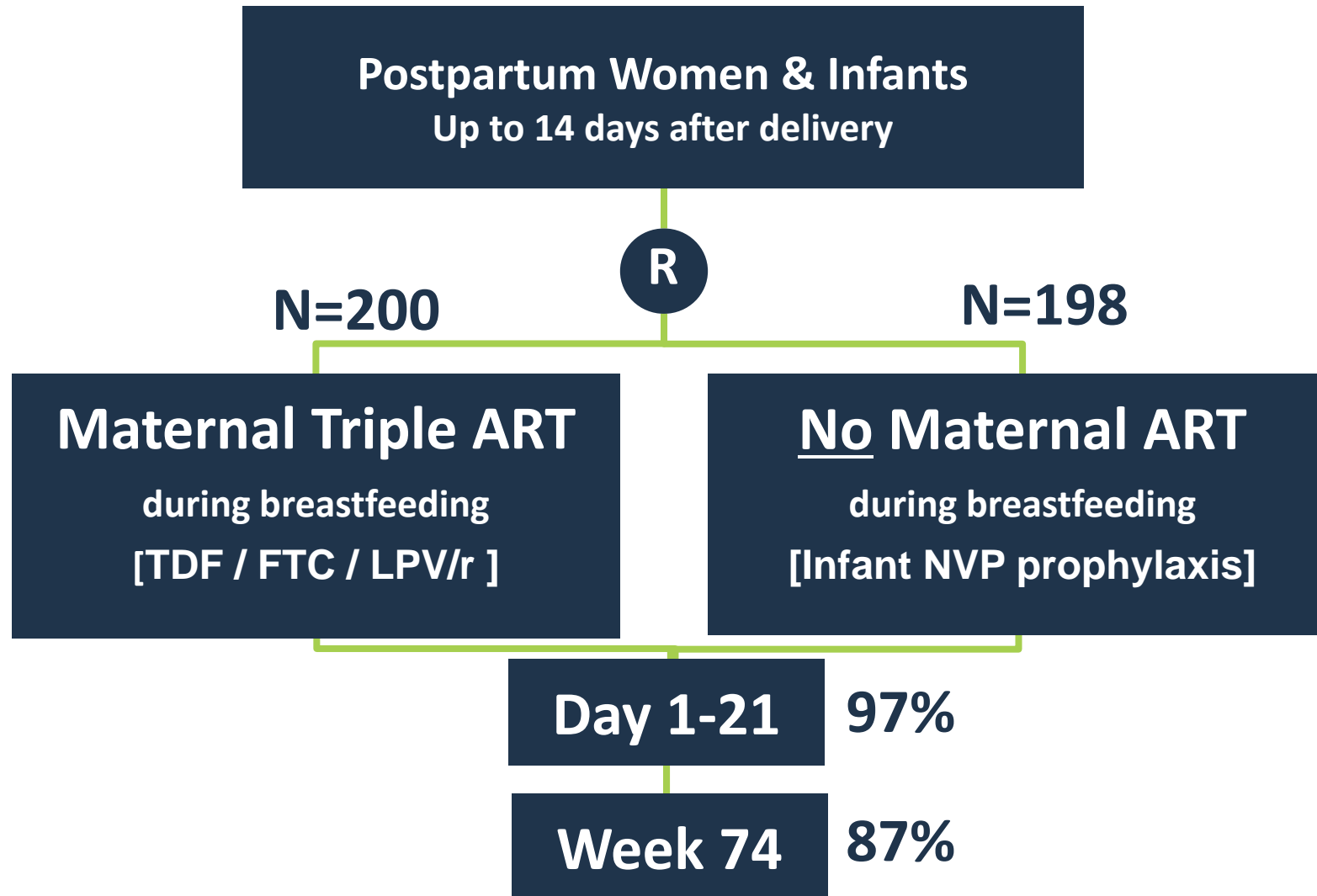


# Data Analysis

- Percent change in hip and spine BMD between weeks 1 and 74 were compared between women who received ART while breastfeeding and women who did not
- Student t-tests (two-sided)
- Modification of the effect by subgroups assessed via linear regression
- Comparisons of other data applied Wilcoxon/Kruskal-Wallis for continuous data,  $\chi^2$ /exact tests for categorical data, as appropriate
- Multivariate analyses to adjust for other covariates
- Mean and 95% confidence interval (CI) are presented

# Accrual and DXA completeness

N=398



# Baseline Characteristics

Characteristic	Median	Q1 – Q3
Age	26.5 years	23.2 – 30.0
Body Mass Index	24.8 kg/m <sup>2</sup>	22.4 – 28.0
CD4 count	671 cells/mm <sup>3</sup>	544 – 855
Viral Load	400 copies/mL	83 – 2289
Characteristic	Frequency	
First or second pregnancy	46%	
Alcohol use ever	12%	
Smoking history ever	1%	

# Baseline Characteristics

Characteristic	ART	No ART	
Aged 18-<30yrs	79%	71%	p=0.046
Undetectable HIV RNA	40%	26%	p=0.003

- Median duration of breastfeeding 14 months
- Most women weaned <24 wks before week 74 DXA

Weeks since weaning		Median	Q1 – Q3
	ART	17.29	9.07 – 24.71
	No ART	17.00	9.86 – 23.36

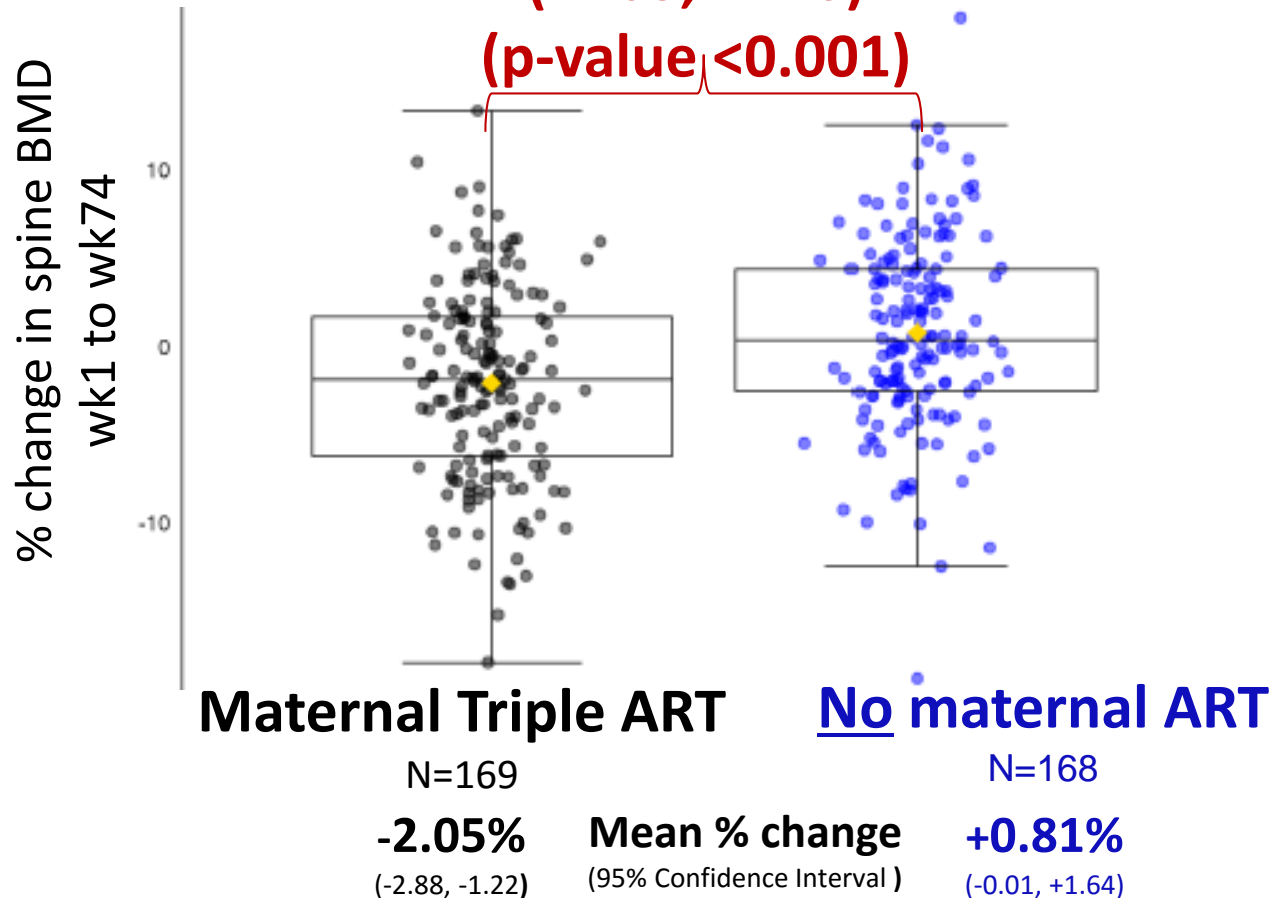


# Lumbar spine BMD % decline week 1 to 74 greater in maternal ART study arm

Mean difference of -2.86%

(-4.03, -1.70)

(p-value < 0.001)

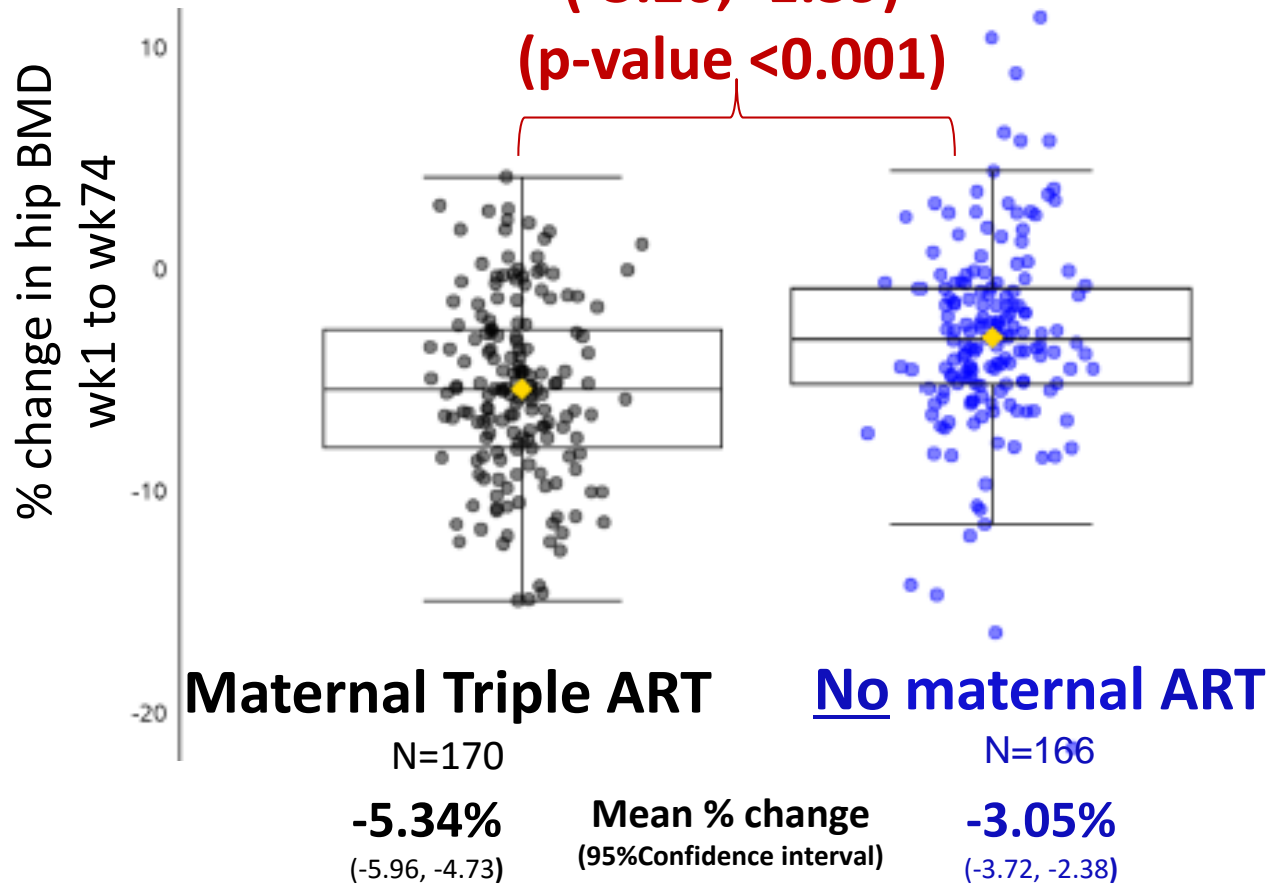


# Hip BMD % decline week 1 to 74 greater in maternal ART study arm

Mean difference of -2.29%

(-3.20, -1.39)

(p-value <0.001)



# Conclusions

- Significant decline in BMD seen at 74 weeks post delivery for PROMISE mothers randomized to receive ART compared to mothers whose infants received infant NVP prophylaxis during breastfeeding
- Planned IMPAACT research will evaluate alternative ART regimens that may lessen the risk of BMD decreases seen with TDF/PI based ART in P1084s
  - IMPAACT 2010

# Conclusions

- Future research will also focus on 5 year follow up of PROMISE mothers to assess if life time ART is associated with further BMD decreases with repeat pregnancy/breastfeeding
  - PEPFAR PROMOTE observational cohort
- These safety findings may also be relevant to HIV uninfected women who use PrEP during lactation
  - IMPAACT 2009

# P1084s Protocol Team and Site Investigators

*The PROMISE study team gratefully acknowledges the dedication and commitment of the more than 3,500 mother-infants pairs without whom this study would not have been possible.*

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