

Recovery of bone mineral density in adolescents following the use of depot medroxyprogesterone acetate (DMPA) contraceptive injections

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DMPA

Progestin-only contraceptive method



Relative estrogen deficiency



Bone loss

Questions remain re:

- 1. Exact mechanisms of bone loss**
- 2. Clinical implications of bone loss**

Purpose:

**To examine the impact
of DMPA use on
adolescents' bone
mineral density**

Study Design

- Design
 - Open-label, nonrandomized, prospective, multicenter study
- Subjects
 - Females aged 12 to 18 years
- Assessment during treatment and after D/C
 - DMPA-IM every 12 wks for up to 240 wks
 - F/U after DMPA D/C for up to 240 wks

Study Design (cont)

- BMD of the lumbar spine and hip was measured at baseline and every 6 months by dual energy x-ray absorptiometry (DXA)
- Bone formation markers (serum osteocalcin and bone-specific alkaline phosphatase), bone resorption marker (urinary N-telopeptide), and serum estradiol were measured at baseline and every 6 months
- Serum PTH and 25 (OH) vitamin D levels were obtained from adolescents with $\geq 5\%$ BMD loss from baseline

Study Design

- Participants

- 181 adolescents provided data during DMPA use
- 98 of these adolescents provided data after discontinuation (D/C) of DMPA

Unanswered Question #1

**Why are some
adolescent DMMPA users
loosing more bone than
others?**

Purpose

To identify and characterize adolescents on DMPA-IM who experienced a BMD loss of $\geq 5\%$ from baseline in comparison with adolescents who lost $<5\%$

Lumbar Spine BMD During DMPA use

	< 5% BMD loss	≥ 5% BMD loss
n (%)	136 (75)	45 (25)
No. of injections		
Median	7	12 (p < 0.001)
Time to confirmed loss of ≥5% (wk)		
Median	N/A	123
Range		83-209

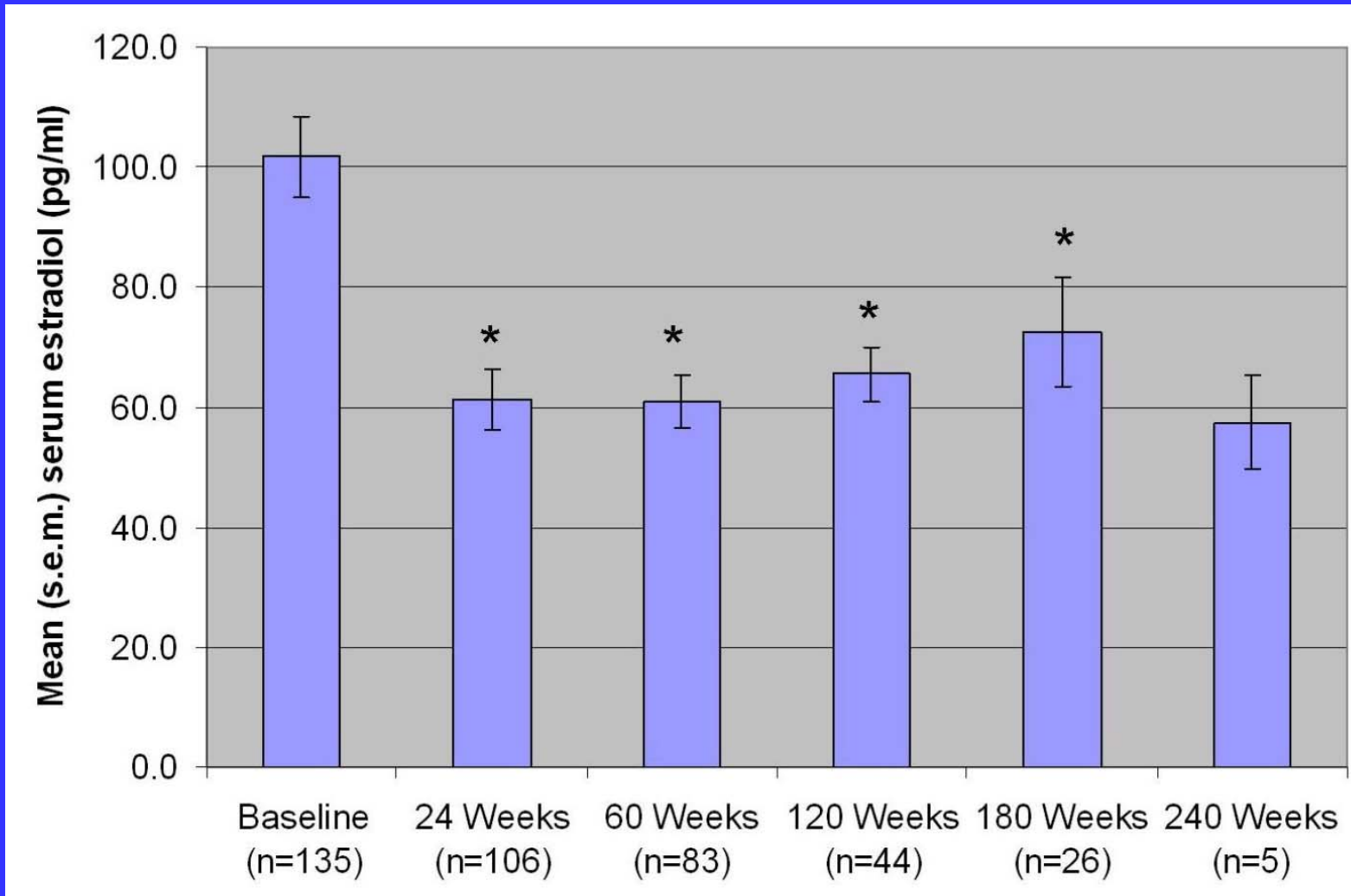
	< 5% BMD loss (n=136)	≥ 5% BMD loss (n=45)
Age, yr, (SE)	15.5 (0.1)	15.7 (0.03)
Gyn age, months (SE)	46.5 (1.9)	48.5 (3.3)
Race		
Black (%)	55	60
Other (%)	45	40
Mean BMI (SE)	23.7 (0.4)	23.1 (0.7)
Calcium serving/wk	24.4 (2.2)	20.7 (2.4)
Activity score	3.0	3.3
Smoker (%)	29	33
% Alcohol user	30	47 (p=0.043)

Hip BMD During DMPA use

	< 5% BMD loss	≥ 5% BMD loss
n (%)	91 (50)	90 (50)
No. of injections		
Median	7	12
		(p < 0.001)
Time to confirmed loss of ≥5% (wk)		
Median	N/A	126
Range		53-243

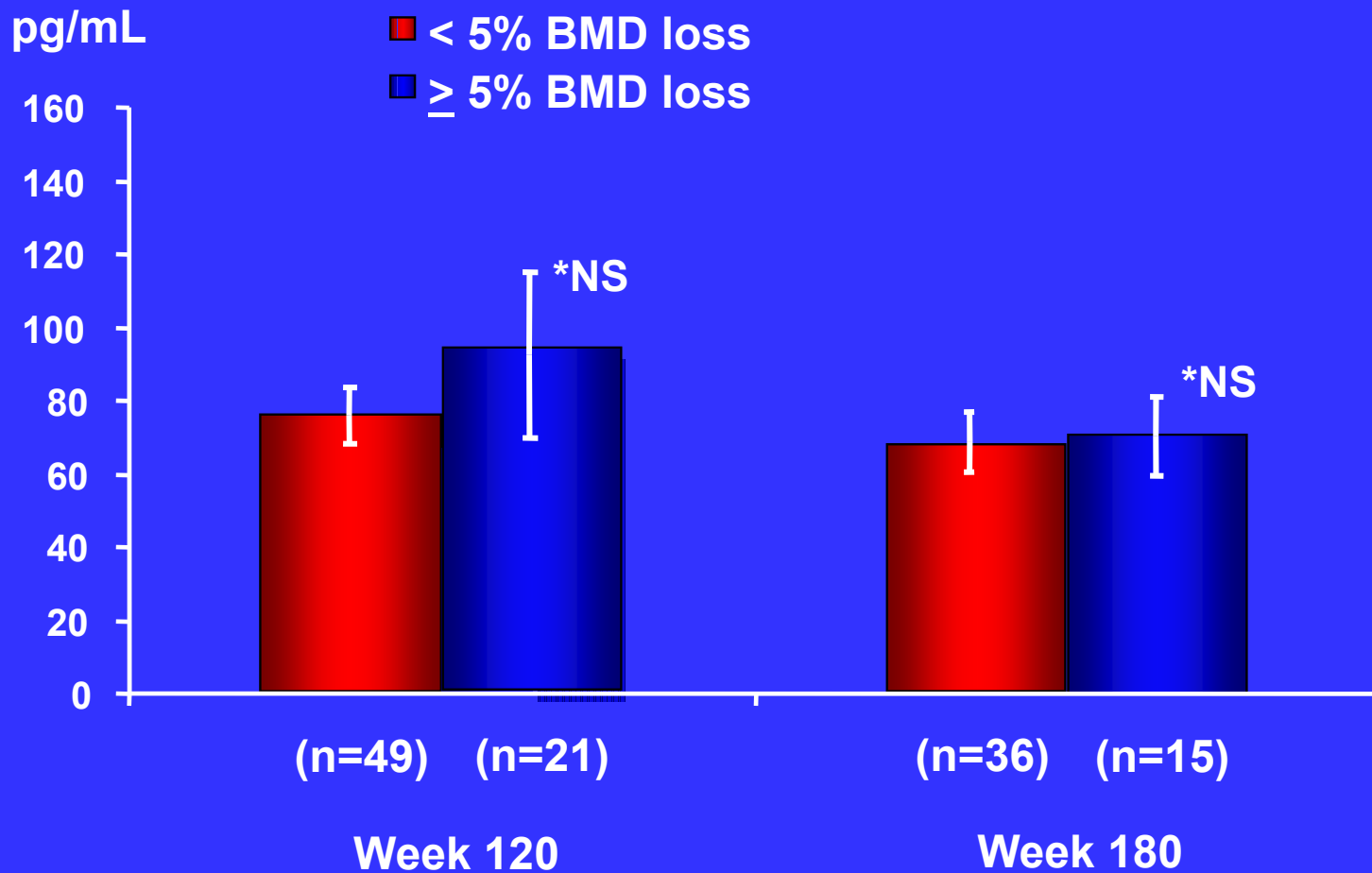
	< 5% BMD loss (n=91)	≥ 5% BMD loss (n=90)
Age, yr, (SE)	15.5 (0.2)	15.6 (0.02)
Gyn age, months (SE)	49.3 (2.2)	44.7 (2.5)
Race		
Black (%)	54	59
Other (%)	46	41
Mean BMI (SE)	24.6 (0.6)	22.4 (0.04) (p=0.002)
Calcium serving/wk	27.3 (2.9)	20.6 (2.0) (p=0.002)
Activity score	3.0	3.2
Smoker (%)	26	33
% Alcohol user	28	41

Estradiol levels in adolescents during use of DMPA – Mean (SE)

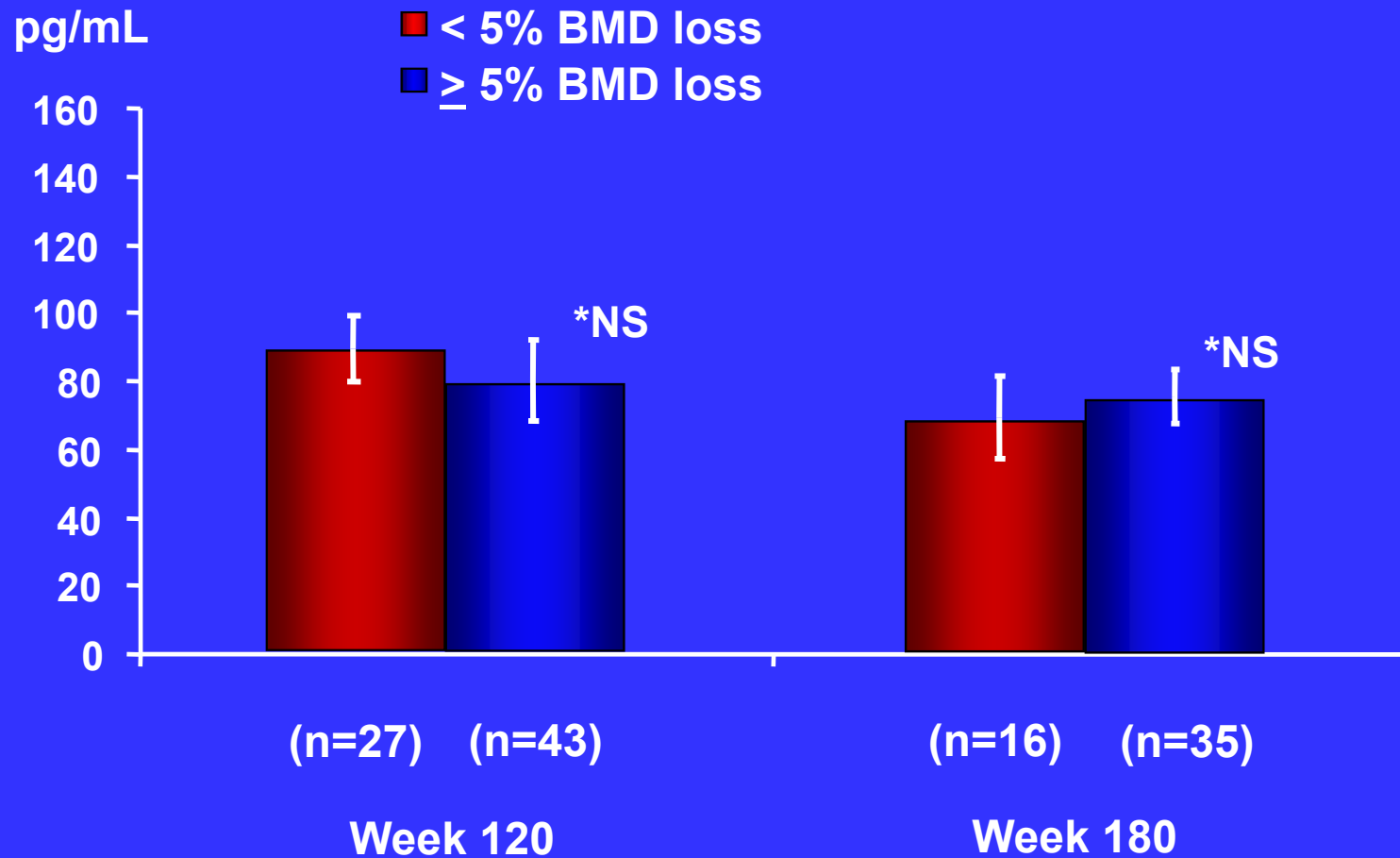


*p<0.05

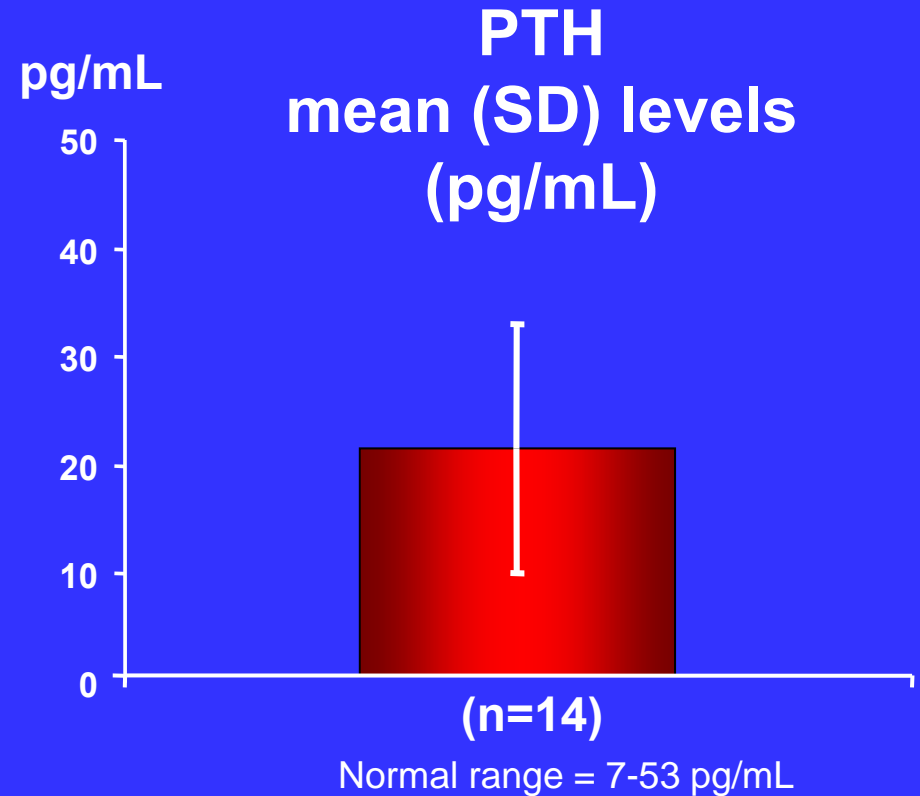
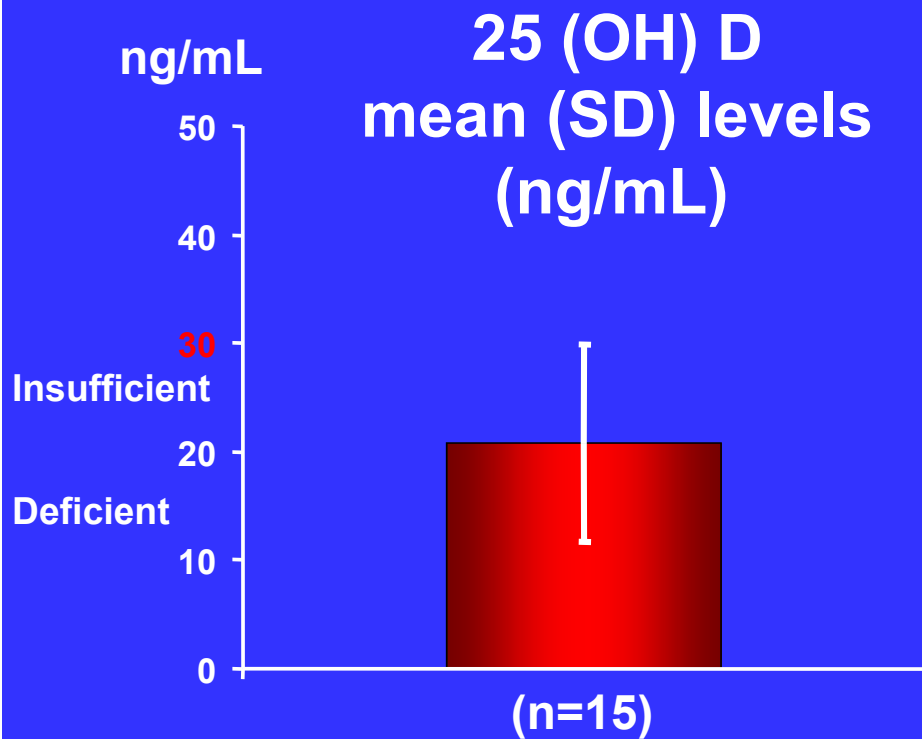
Estradiol Levels in Adolescents by Lumbar Spine BMD Change - Mean (SE)



Estradiol Levels in Adolescents by Hip BMD Change – Mean (SE)



25 (OH) D and PTH levels in adolescents with substantial ($\geq 5\%$) BMD loss



Conclusions

Substantial BMD decreases of $\geq 5\%$ were observed in

- 25% of adolescents at the lumbar spine
- 50% of adolescents at the hip

DMPA-IM induced a relative estrogen deficiency, but the decrease did not correlate with the magnitude of BMD loss

Lower BMI, insufficient calcium and vitamin D intake, and alcohol use, were associated with a greater BMD loss

Unanswered Question #2

**What is the pattern of
BMD recovery after
discontinuation of
DMPA?**

Recovery of lumbar spine (LS) bone mineral density after DMPA D/C

- Mean LS BMD recovered to pre-treatment levels 60 weeks after the last DMPA injection, and then continued to increase at all subsequent time points to 240 weeks
- By 240 weeks after DMPA discontinuation, 84% of participants had a LS BMD value that exceeded their baseline value, and the mean LS BMD value was 4.7% greater than at baseline

Recovery of hip bone mineral density after DMPA Discontinuation (D/C)

- BMD changes following DMPA D/C occurred more slowly at the hip.
- Full recovery of mean BMD to baseline value at the total hip (TH) required 240 weeks and at the femoral neck (FN) at least 180 weeks
- By 240 weeks after DMPA D/C:
 - 56% of participants had a TH BMD value that exceeded their baseline value,
 - 40% had a FN BMD value that exceeded their baseline value

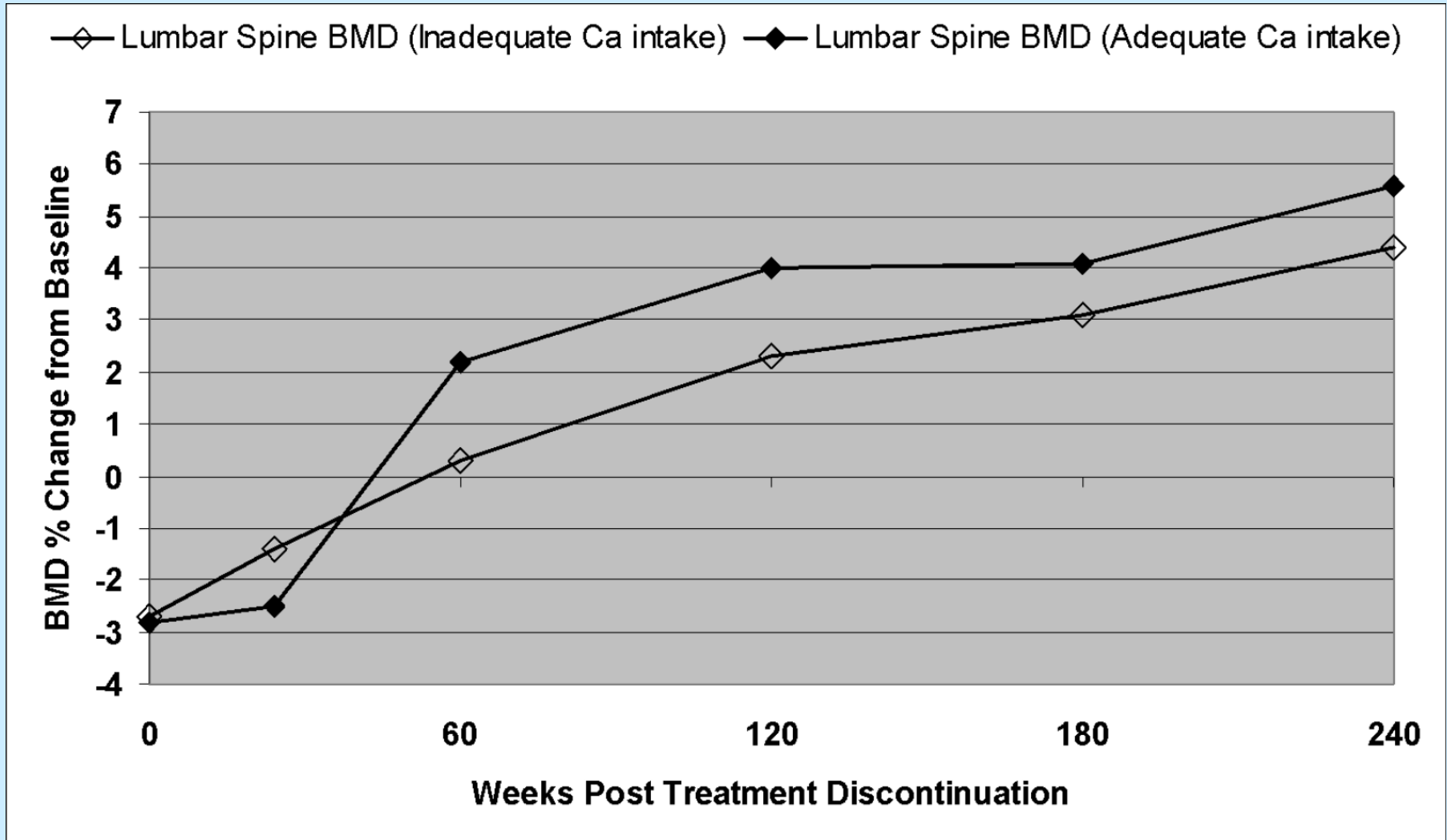
Conclusions

BMD loss in female adolescents receiving DMPA for contraception is substantially or fully reversible in most girls following discontinuation of DMPA, with faster recovery at the LS than at the hip

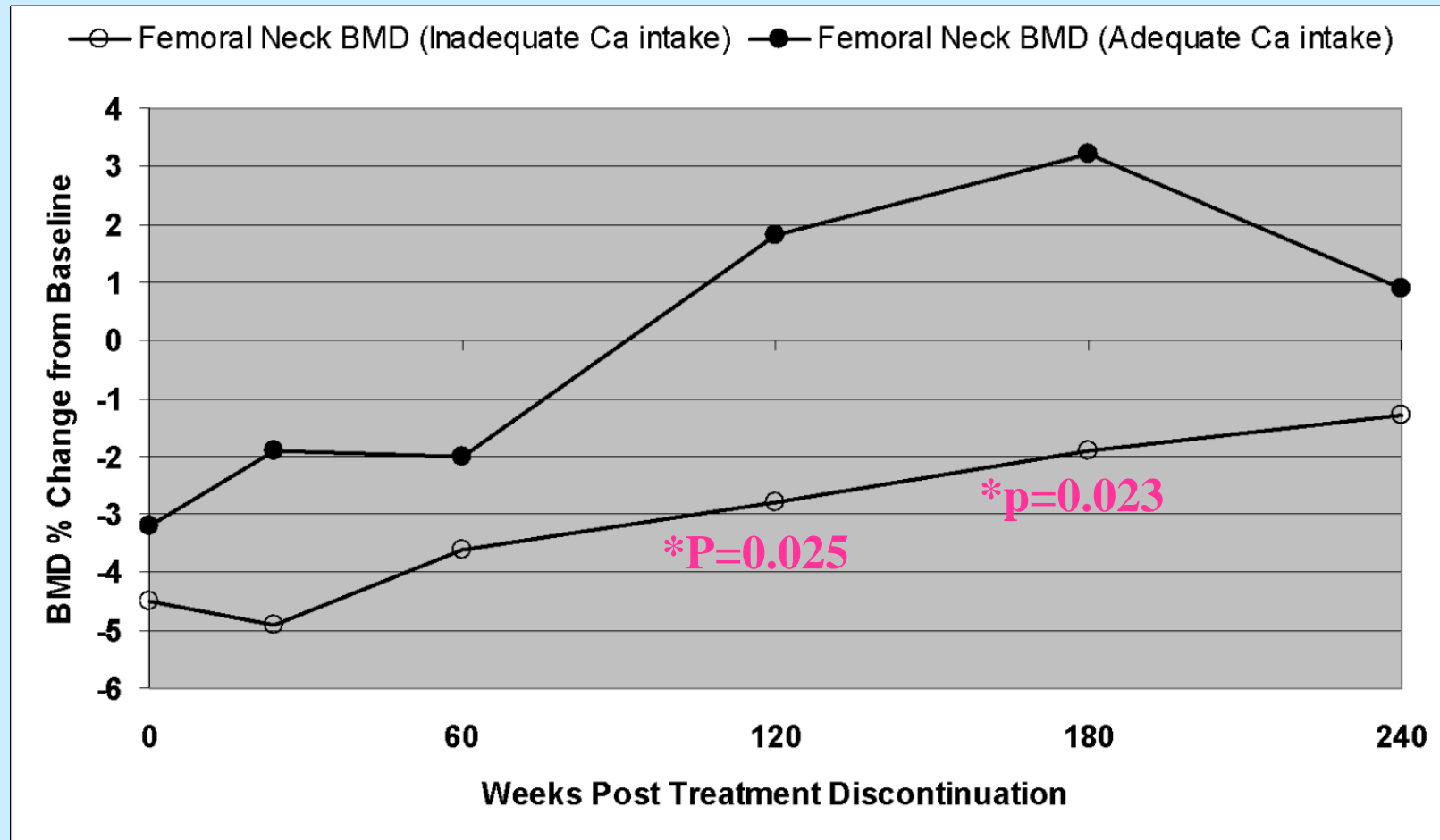
Unanswered Question #3

**Does calcium intake
affect the extent of BMD
recovery after DMPA
discontinuation?**

Mean % change from baseline in Lumbar Spine BMD after DMPA D/C, by calcium intake



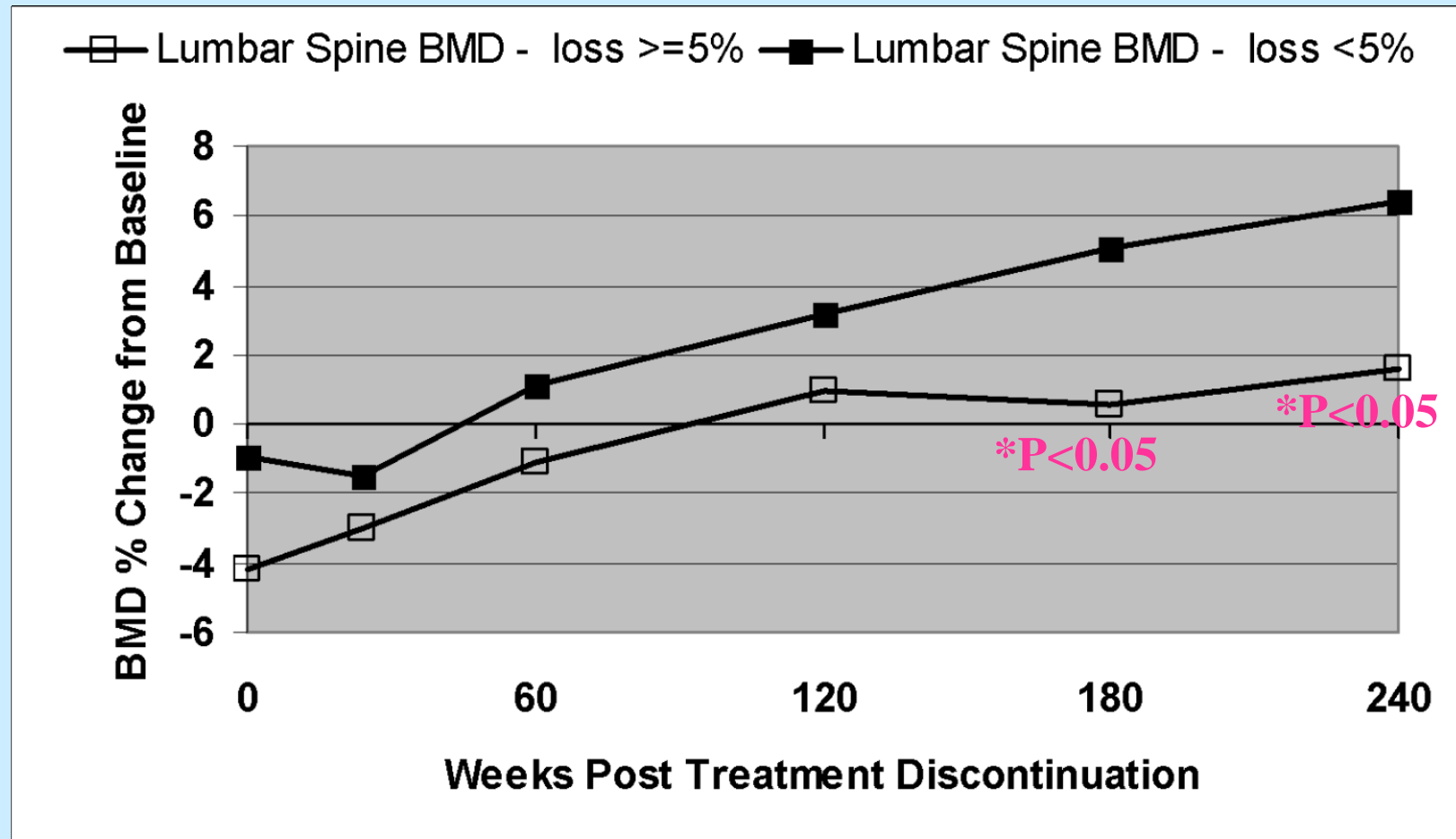
Mean % change from baseline in Femoral Neck BMD after DMPA D/C, by calcium intake



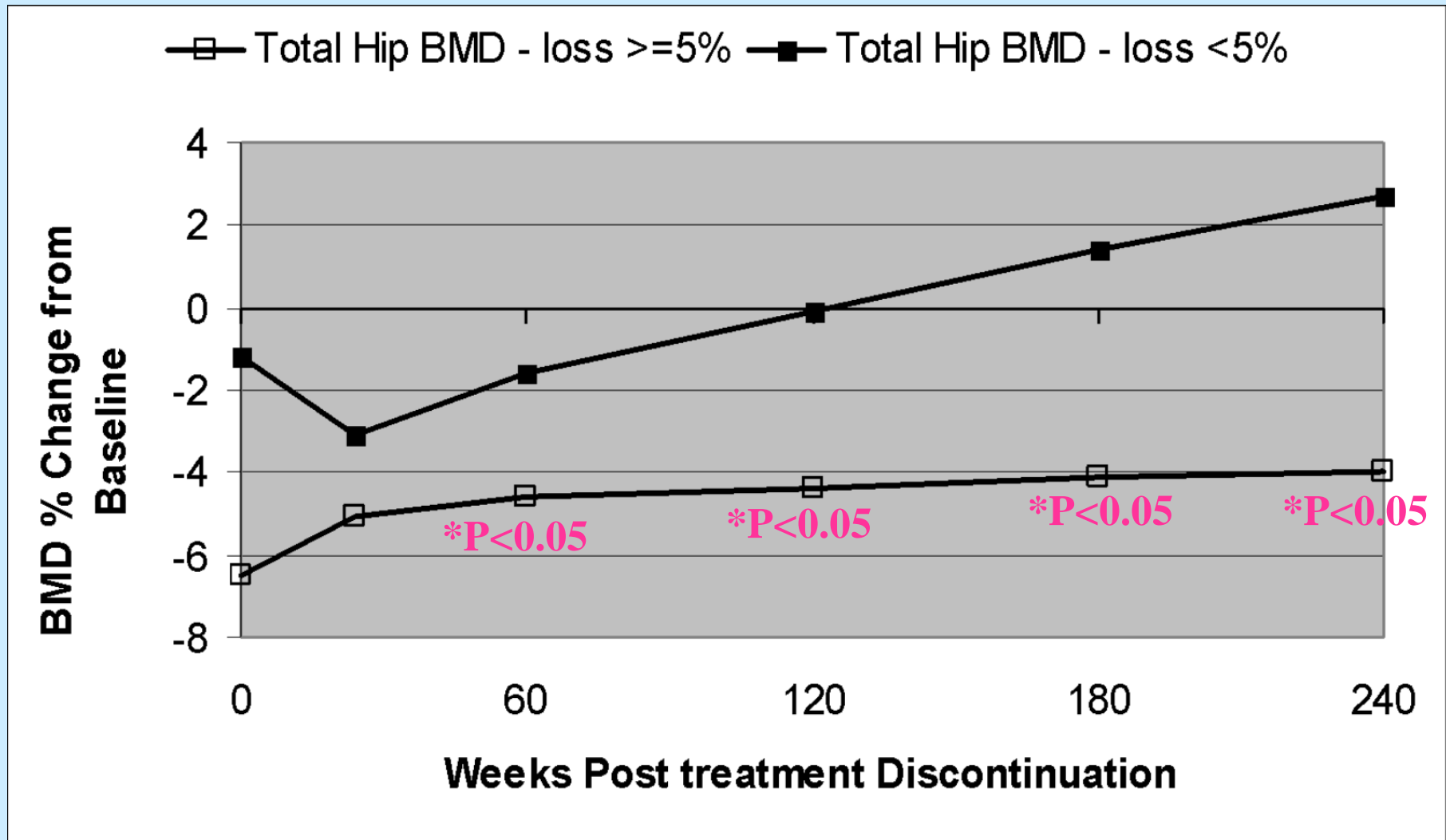
Unanswered Question #4

**Does the extent of BMD
loss during use of DMMPA
affect the extent of BMD
recovery after
discontinuation?**

Mean % Change from Baseline in Lumbar Spine BMD after DMPA D/C in participants with and without BMD losses of $\geq 5\%$ during DMPA use



Mean % Change from Baseline in Total Hip BMD after DMPA D/C in participants with and without BMD losses of $\geq 5\%$ during DMPA use



The final question

**Do we need to minimize
the BMD loss during use
of DMMPA in
adolescents?**

Ways of minimizing the decrease in bone mineral density

- (+) Adequate calcium intake (1300 mg/day)**
- (+) Adequate vitamin D intake (400 IU or more)**
 - Assess serum total 25OH vitamin D level**
- (+) Regular weight bearing physical activity**
- (+) Avoid smoking and alcohol**
- (?) Periodic add-back of estrogen**
- (?) Phytoestrogens**



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