# The Effect of Prolonged Breast-feeding on the Development of Postmenopausal Osteoporosis in Population with Insufficient calcium intake and vitamin D level

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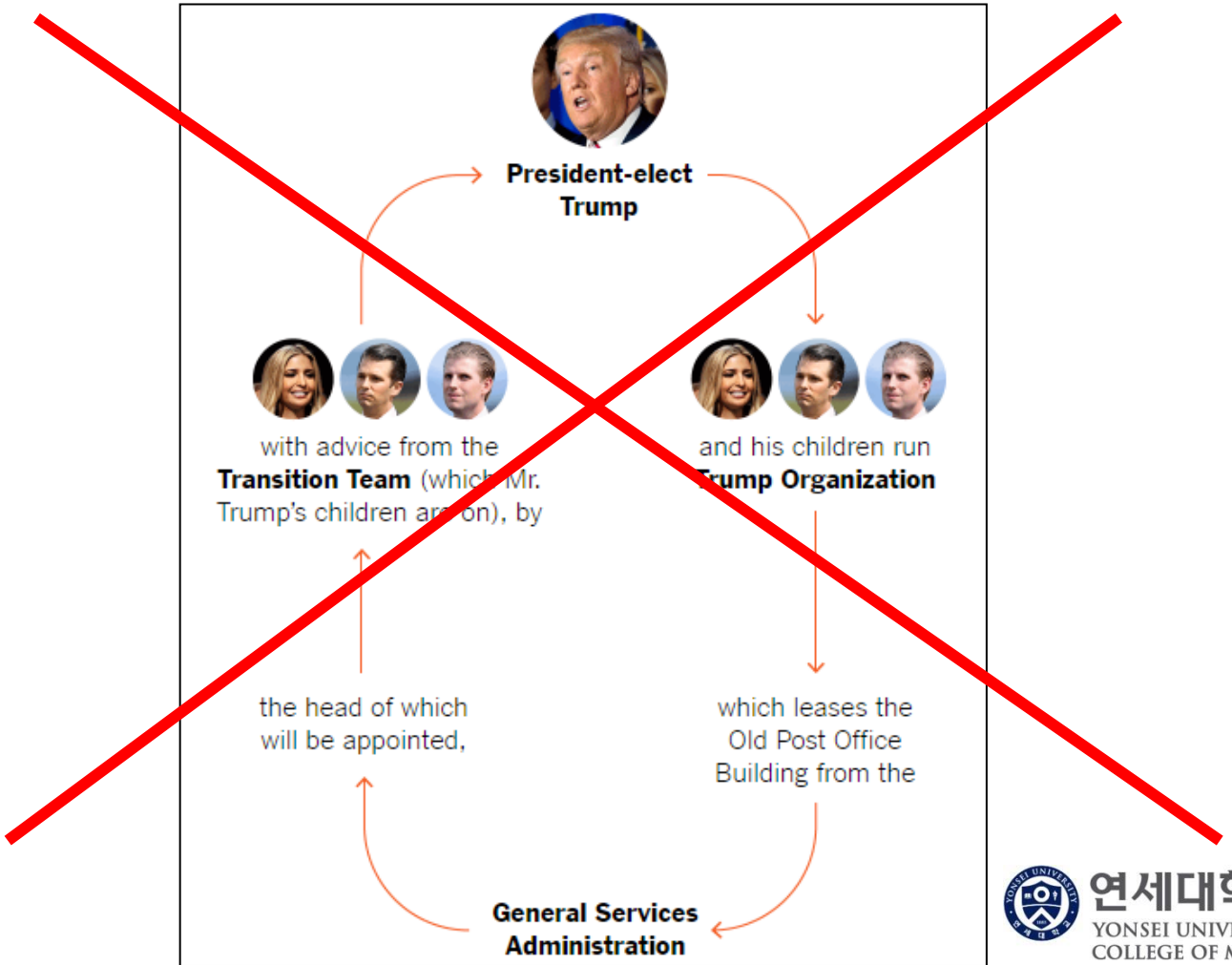
- I have no conflict of interest to declare.



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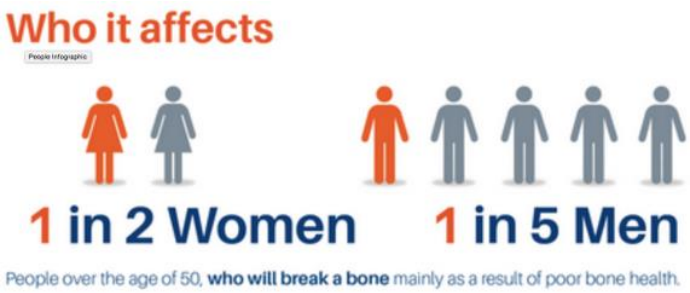
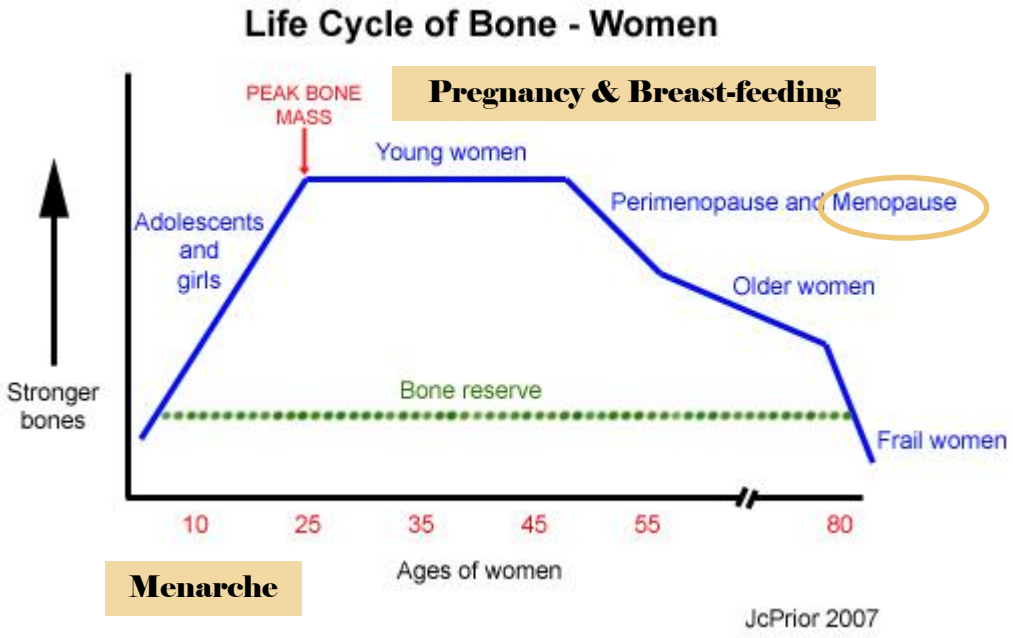
# Introduction

- Osteoporosis





**ESTROGEN**



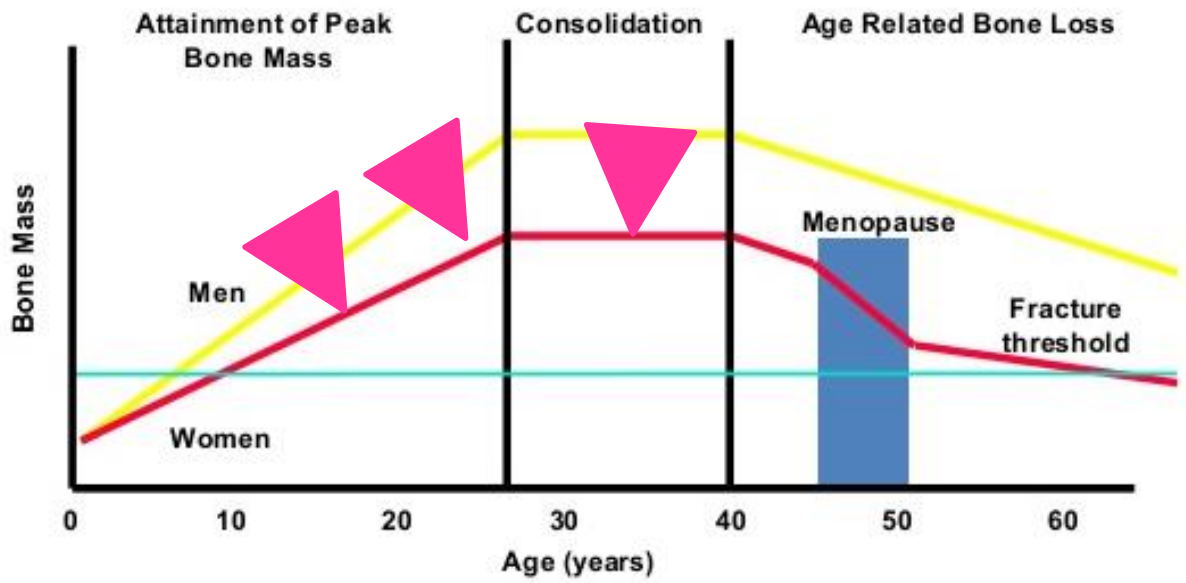
- Breast-feeding
  - ✓ Directly affects bone metabolism and calcium homeostasis.
  - ✓ Potentially negative effects of breast-feeding on osteoporosis are abrogated soon after cesession.

**Calcium losses ↑** :
via the breast milk and bone reabsorption increases

**Prolactin level ↑** :
suppresses the secretion of estrogen and stimulates parathyroid hormone related protein synthesis

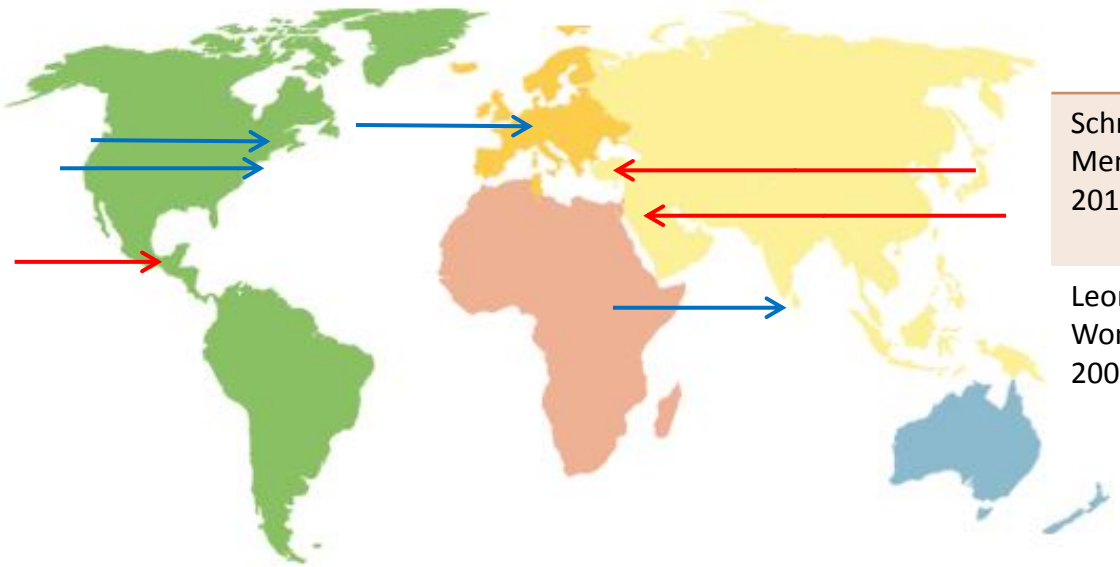
**Estrogen level ↓** :
triggers bone resorption, which increases the calcium level in the bloodstream

suppresses parathyroid hormone production




*Compston et al., Clin Endocrinol 1990*

By Interrupting the bone mass accumulation, breast-feeding may affect the bone health later on.

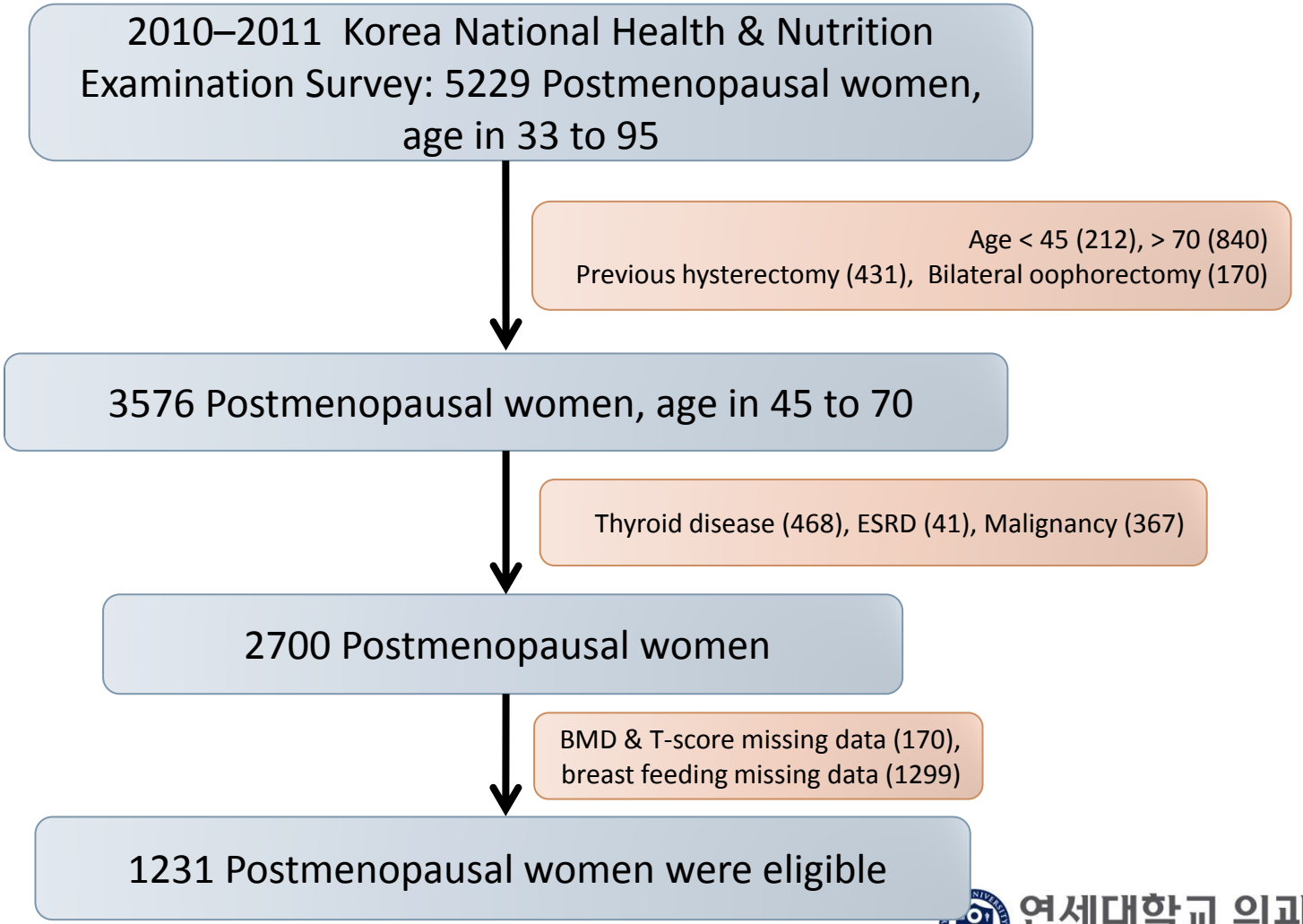


| No harm | Risk for postmenopausal osteoporosis |
|---|---|
| Schnatz, PF et al. Menopause 2010;17(6):1161-6 **(New York, USA)** | Tsvetov, G et al. Maturitas 2014;77(3):249-54 **(Tel Aviv, ISRAEL)** |
| Leonora, J et al. BMC Womens health 2009;9:19 **(Colombo, Sri Lanka)** | Okyay, DO et al. Maturitas 2013;74(3):270-275 **(Izmir, Turkey)** |
| | Dursan,N et al. Osteoporos Int 2006;17(5):651-655 **(Kocaeli, Turkey)** |
| Grimes, JP et al. Curr Womens Health Rep 2003;3(3):193-198 **(New Jursey, USA)** | Rajano-Mejia,D et al. Menopause 2011;18(3):302-306 **(Mexico-city, Mexico)** |
| Hadji, P et al. Climacteric 2002;5:277-285 **(Hamburg, Germany)** | |

## Main Question

May Breast-feeding duration be a risk factor for postmenopausal osteoporosis, on terms with Calcium intake and vitamin D level?

# Materials & Methods



## Measurements

- ✓ Physical examinations
- ✓ Body mass index (BMI)
- ✓ Serum vitamin D [25-hydroxy(OH)-D] levels
- ✓ Bone mineral density (BMD)

## Interviews

- ✓ Smoking histories
- ✓ Exercise levels
- ✓ Nutritional intakes

- ✓ Reproductive factors

(Ages at menarche and menopause, histories of taking OC and HT, gravidity)

- ✓ Breast-feeding histories

## Statistical analysis

- Student's *t*-test
- Mann-Whitney U test
- Chi-square test
- ANOVA with post-hoc analysis using Bonferroni's method
- Logistic regression analyses

*IBM®SPSS® software version 20*

- Dietary calcium intake
  - Lower intake group: <800mg/day
  - Higher intake group: ≥800mg/day

- Level of serum vitamin D
  - Deficiency: <20ng/mL
  - Insufficiency: 20ng/mL≤, < 30ng/mL
  - Sufficiency: ≥30ng/mL
  - Quartiles

| | |
|---|---|
| Q1 | 3.26-12.85ng/mL |
| Q2 | 12.86-16.39ng/mL |
| Q3 | 16.40-21.55ng/mL |
| Q4 | 21.56-42.9ng/mL |

# Results

# Baseline characteristics

| | Osteoporosis group (*n*=304) | Non-osteoporosis group (*n*=927) | p-value |
|---|---|---|---|
| **Age, years** | 62.69 (5.65) | 58.32 (5.95) | <0.0001 |
| **BMI, kg/m2** | 23.39 (2.92) | 24.58 (3.25) | <0.0001 |
| **Age at menarche, years** | 16.28 (2.07) | 15.80 (1.96) | <0.0001 |
| **Age at menopause, years** | 50.93 (2.92) | 50.90 (2.86) | 0.868 |
| **Time since menopause, years** | 11.76 (6.16) | 7.42 (5.72) | <0.0001 |
| **Gravidity, *n*** | 5.78 (8.87) | 6.07 (11.23) | 0.682* |
| **Time from menarche to first delivery, years** | 7.97 (3.57) | 8.46 (3.89) | 0.055 |
| **Calcium intake, mg/day** | 431.96 (274.51) | 480.81 (331.57) | 0.025 |
| **Exercise, days/week** | 1.77 (2.90) | 2.11 (3.01) | 0.082 |
| **Total duration of breast-feeding, months** | 51.79 (36.41) | 39.94 (31.42) | <0.0001 |
| **Smoking status, *n* (%)** | | | 0.213 |
| **Never smoked** | 290 (23.6) | 859 (69.8) | |
| **Current smoker** | 9 (0.7) | 37 (3) | |
| **Past smoker** | 5 (0.4) | 31 (2.5) | |

# Baseline characteristics –*continued*

| | Osteoporosis group (*n*=304) | Non-osteoporosis group (*n*=927) | p-value |
|---|---|---|---|
| **History of HT use, *n* (%)** | | | 0.002 |
| **Yes** | 41 (13.5) | 199 (21.5) | |
| **No** | 263 (86.5) | 728 (78.5) | |
| **History of OC use, *n* (%)** | | | 0.061 |
| **Yes** | 64 (21.1) | 245 (26.4) | |
| **No** | 240 (78.9) | 682 (73.6) | |

* Mann-Whitney *U* test was performed on the continuous variables that did not show normal distributions. The data presented are the means with standard deviations unless otherwise noted.
The *p* values were obtained using Student's *t*-test or the chi-square test, as appropriate.
*BMI* body mass index, *HT* hormone treatment, *OC* oral contraceptive

# Osteoporosis development according to the total breast-feeding duration

| | Never (*n*=104) | <24 months (*n*=451) | ≥24 months (*n*=673) | *p* value |
|---|---|---|---|---|
| **Femoral neck BMD, g/cm2** | 0.68 (0.10)* | 0.67 (0.09)# | 0.64 (0.98)*# | <0.0001 |
| **Lumbar spine BMD, g/cm2** | 0.86 (0.14)* | 0.85 (0.12)# | 0.81 (0.13)*# | <0.0001 |
| **Femoral neck T score** | -1.19 (0.94)* | -1.26 (0.87)# | -1.51 (0.92)*# | <0.0001 |
| **Lumbar spine T score** | -1.24 (1.21)* | -1.33 (1.08)# | -1.69 (1.17)*# | <0.0001 |
| **Osteoporosis of the femoral neck, *n* (%)** | | | | 0.01 |
| **Osteoporosis group** | 7 (5.9) | 31 (26.1) | 81 (68.1) | |
| **Non-osteoporosis group** | 96 (8.7) | 419 (37.9) | 591 (53.4) | |
| **Osteoporosis of the lumbar spine, *n* (%)** | | | | <0.0001 |
| **Osteoporosis group** | 12 (4.8) | 66 (26.3) | 173 (68.9) | |
| **Non-osteoporosis group** | 91 (9.5) | 382 (39.8) | 487 (50.7) | |
| **Osteoporosis, *n* (%)** | | | | <0.0001 |
| **Present** | 15 (5.0) | 83 (18.4) | 205 (67.7) | |
| **Absent** | 89 (9.6) | 368 (39.8) | 468 (50.6%) | |

# Comparison of the groups in relation to the serum vitamin D levels & quartiles

| | Osteoporosis group (*n*=304) | Non-osteoporosis group (*n*=927) | *p* value |
|---|---|---|---|
| **Mean (standard deviation) serum vitamin D (25[OH]D), ng/mL** | 17.21 (6.55) | 17.85 (6.70) | 0.154 |
| **Serum vitamin D quartile, *n* (%)** | | | |
| **Q1, 3.26–12.85 ng/mL** | 85 (29.9) | 210 (23.5) | |
| **Q2, 12.86–16.39 ng/mL** | 70 (24.6) | 224 (24.6) | |
| **Q3, 16.40–21.55 ng/mL** | 63 (22.2) | 231 (25.9) | |
| **Q4, 21.56–42.9 ng/mL** | 66 (23.2) | 228 (25.5) | |
| **Serum vitamin D status, *n* (%)** | | | 0.534 |
| **Deficient** | 203 (71.5) | 607 (68.0) | |
| **Insufficient** | 66 (23.2) | 235 (26.3) | |
| **Sufficient** | 15 (5.3) | 51 (5.7) | |

# Unadjusted odds ratios of the risk factors for postmenopausal osteoporosis

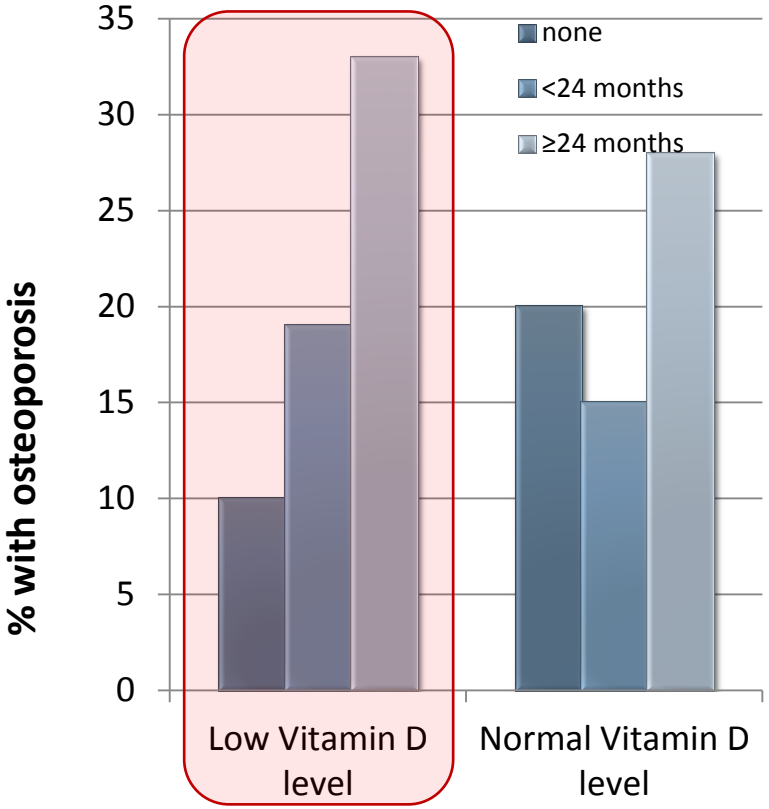
| | Unadjusted OR (95 % CI) | *p* value |
|---|---|---|
| Age | 1.132 (1.106–1.159) | <0.0001 |
| BMI | 1.611 (1.221–2.126) | 0.001 |
| Calcium intake | 0.948 (0.905–0.994) | 0.026 |
| Serum vitamin D status | | |
| Deficient | 1.137 (0.626–2.066) | 0.673 |
| Insufficient | 0.955 (0.505–1.806 | 0.887 |
| Sufficient | 1 | |
| Serum vitamin D quartiles | | |
| Q1 | 1.398 (0.964–2.029) | 0.078 |
| Q2 | 1.080 (0.736–1.584) | 0.696 |
| Q3 | 0.942 (0.637–1.393) | 0.765 |
| Q4 | 1 | |
| HT | 0.570 (0.396–0.821) | 0.003 |
| OC | 0.742 (0.543–1.014) | 0.061 |
| Exercise | 0.960 (0.917–1.005) | 0.083 |
| Total breast-feeding duration | | |
| Never | 1 | |
| <24 months | 1.338 (0.737–2.430) | 0.339 |
| ≥24 months | 2.599 (1.468–4.601) | 0.001 |
| Smoking status | | |
| Never smoked | 1 | |
| Past smoker | 0.478 (0.184–1.24) | 0.129 |
| Current smoker | 0.721 (0.344–1.511) | 0.386 |
| Age at menarche | 1.128 (1.056–1.204) | <0.0001 |
| Age at menopause | 1.004 (0.959–1.050) | 0.867 |
| Time since menopause | 1.125 (1.10–1.15) | <0.0001 |
| Gravidity | 0.997 (0.985–1.01) | 0.683 |
| Time from menarche to first delivery | 0.966 (0.933–1.001) | 0.055 |

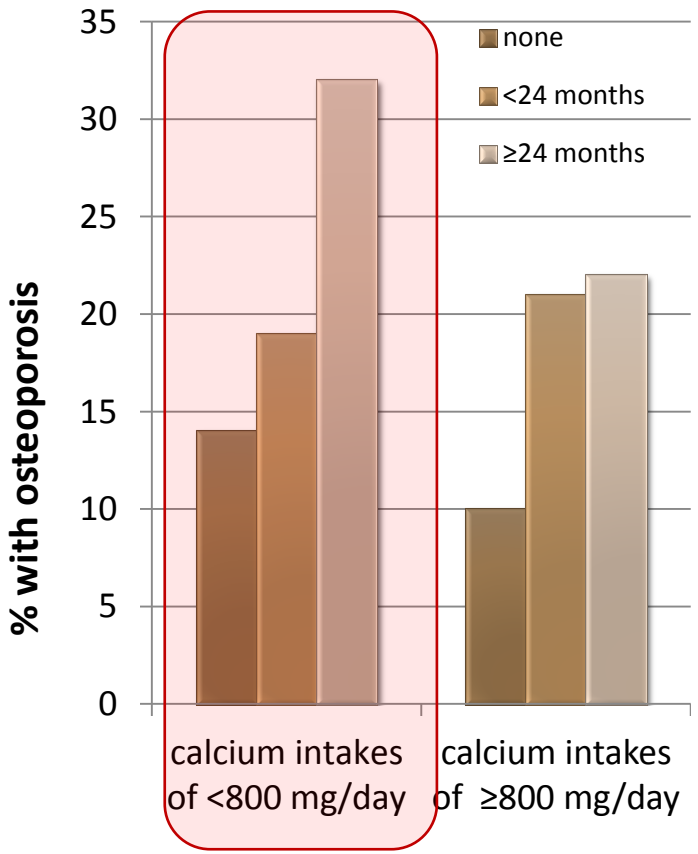
# Adjusted odds ratios of the risk factors for postmenopausal osteoporosis

| | Total breast-feeding duration | Adjusted OR (95 % CI) | *p* value |
|---|---|---|---|
| **Model 1** | Never | 1 | |
| | <24 months | 1.996 (0.901–4.422) | 0.089 |
| | ≥24 months | 2.489 (1.111–5.578) | 0.027 |
| **Model 2** | Never | 1 | |
| | <24 months | 2.005 (0.906–4.436) | 0.086 |
| | ≥24 months | 2.503 (1.118–5.602) | 0.026 |
| **Model 3** | Never | 1 | |
| | <24 months | 2.212 (0.843–5.808) | 0.107 |
| | ≥24 months | 2.825 (1.056–7.56) | 0.039 |

**Model 1** was adjusted for age, BMI, calcium intake, exercise, smoking status, age at menarche, age at menopause, years since menopause, time from menarche to first delivery, hormone treatment, oral contraceptives use, gravidity, and the serum vitamin D status (deficient, insufficient, or sufficient).
**Model 2** was adjusted for the same variables used in model 1, **except for the vitamin D status**, which was substituted for **the vitamin D quartiles.**
**Model 3** was adjusted for the same variables used in model 1, but the regression analysis was performed **only on the cases that were vitamin D deficient.**

- **Breast-feeding for ≥24 months** → Increase in the development of osteoporosis in the participants with **deficient and insufficient vitamin D levels and daily calcium intakes lower than 800 mg.**




**Low vitamin D** denotes the participants who had deficient and insufficient serum vitamin D levels.
**Normal** vitamin D denotes the participants who had sufficient serum vitamin D levels.

# Discussion

- Total breast-fed duration more than 24 months lifelong are associated with the development of osteoporosis in postmenopausal women.

- **Total breast-feeding durations may contribute as a** risk factor of osteoporosis in particular countries, including Korea, **where vitamin D deficiencies and inadequate calcium intakes** are prevalent.

- Limitations of the study
  - ✓ Probability of selective bias: elder women has a tendency to have longer breast-feeding duration.
  - ✓ Retrospective, comparative design.

# Conclusion

- Breast-feeding may increase the risk of postmenopausal osteoporosis, especially those with insufficient vitamin D levels and calcium intakes.

- Although nutritional deficiency is a modifiable factor, caution should be exercised when assessing women who give birth and breast-feed in certain areas.

THANK YOU FOR YOUR

ATTENTION !