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| **Supplemental table 1.** Cross-sectional associations between reproductive characteristics and sRANKL concentrations (geometric means; pmol/L) by menopausal status and PMH use at blood collection. Excluding women with sRANKL concentrations below the assays lower limit of detection. | | | | | | |
|  | **Premenopausal women** | | **Postmenopausal women** | | | |
|  | *No PMH* | | *PMH* | |
|  | n (%)a | Geometric mean  (95%CI) | n (%)a | Geometric mean  (95%CI) | n (%)a | Geometric mean  (95%CI) |
| **Full study population\*** | 447 (100%) | 0.07 (0.06-0.08) | 707 (100%) | 0.08 (0.07-0.10) | 651 (100%) | 0.06 (0.05-0.08) |
| **Age at blood collection, years** |  |  |  |  |  |  |
| <50 | 357 (80%) | 0.11 (0.09-1.14) | 12 (2%) | 0.09 (0.06-0.14) | 28 (4%) | 0.12 (0.08-0.18) |
| 50-55 | 87 (19%) | 0.09 (0.07-1.12) | 116 (16%) | 0.11 (0.10-0.14) | 176 (27%) | 0.11 (0.09-0.13) |
| 50-60 | 3 (1%) | *ǂ* | 259 (37%) | 0.10 (0.08-0.11) | 261 (40%) | 0.11 (0.09-0.14) |
| 60+ | 0 0%) | *ǂ* | 320 (45%) | 0.09 (0.08-0.10) | 186 (29%) | 0.10 (0.08-0.13) |
| Ptrendb |  | 0.20 |  | <0.01 |  | 0.45 |
| **Age at menarche, years** |  |  |  |  |  |  |
| <12 | 79 (18%) | 0.11 (0.09-0.15) | 97 (14%) | 0.10 (0.08-0.13) | 100 (15%) | 0.10 (0.08-0.13) |
| 12-14 | 310 (69%) | 0.10 (0.08-0.13) | 455 (64%) | 0.10 (0.09-0.11) | 421 (65%) | 0.11 (0.09-0.13) |
| ≥15 | 56 (13%) | 0.09 (0.07-0.12) | 147 (21%) | 0.09 (0.07-0.10) | 122 (19%) | 0.11(0.09-0.14) |
| Ptrendb |  | 0.29 |  | 0.25 |  | 0.84 |
| **Oral contraceptive (OC) use** |  |  |  |  |  |  |
| Never | 159 (36%) | 0.11 (0.09-0.14) | 442 (63%) | 0.10 (0.08-0.11) | 240 (37%) | 0.11 (0.09-0.13) |
| < 5 years | 169 (59%) | 0.11 (0.09-0.13) | 145 (56%) | 0.10 (0.09-0.11) | 200 (49%) | 0.11 (0.09-0.13) |
| 5-9 years | 74 (26%) | 0.10 (0.08-0.13) | 44 (17%) | 0.09 (0.07-0.12) | 67 (16%) | 0.09 (0.07-0.11) |
| ≥ 10 years | 45 (16%) | 0.08 (0.06-0.11) | 71 (27%) | 0.07 (0.06-0.09) | 140 (30%) | 0.11 (0.08-0.11) |
| Ptrendc including never users |  | 0.54 |  | 0.01 |  | 0.51 |
| Ptrendbd among ever users |  | 0.03 |  | 0.08 |  | 0.51 |
| **Full-term pregnancy (FTP)** |  |  |  |  |  |  |
| Never | 53 (12%) | 0.11 (0.08-0.15) | 87 (12%) | 0.10 (0.08-0.12) | 73 (11%) | 0.10 (0.08-0.13) |
| Ever | 388 (87%) | 0.11 (0.09-0.14) | 618 (87%) | 0.10 (0.08-0.11) | 562 (86%) | 0.11 (0.09-0.13) |
| 1 FTP | 83 (21%) | 0.11 (0.08-0.14) | 98 (16%) | 0.10 (0.08-0.12) | 101 (18%) | 0.09 (0.07-0.12) |
| 2 FTPs | 210 (54%) | 0.11 (0.08-0.14) | 288 (47%) | 0.10 (0.08-0.11) | 276 (49%) | 0.11 (0.09-0.14) |
| ≥ 3 FTPs | 94 (24%) | 0.10 (0.08-0.14) | 232 (38%) | 0.09 (0.08-0.11) | 184 (33%) | 0.10 (0.08-0.13) |
| Pcatc ever/never |  | 0.98 |  | 0.88 |  | 0.48 |
| Pcatce number |  | 0.99 |  | 0.66 |  | 0.11 |
| **Age at first FTPe** |  |  |  |  |  |  |
| < 25 years | 187 (48%) | 0.11 (0.08-0.14) | 287 (46%) | 0.10 (0.08-0.11) | 322 (57%) | 0.11 (0.09-0.13) |
| ≥ 25 years | 199 (51%) | 0.11 (0.08-0.14) | 329 (53%) | 0.09 (0.08-0.11) | 234 (42%) | 0.10 (0.08-0.12) |
| Ptrendb |  | 0.69 |  | 0.49 |  | 0.33 |
| *a percentages may not add up to 100% due to missing data; b P value for linear trend assessed using type III F statistics from linear regression models with continuous exposure variables; c P value for difference in geometric mean concentration of OPG across categories of the exposure variable. Assessed using type III F statistics from linear regression models; d among those who ever used OCs; e Among those who ever had a FTP; ǂ Not evaluated; Generalized linear models adjusted for: age (continuous), fasting status ((<3, 3-6, >6 hours, missing), time of day (continuous), and menstrual cycle phase at blood collection (premenopausal women: early follicular, late follicular, ovulatory, early luteal, mid luteal, late luteal, missing), and country (as a proxy for study center).\* P value comparing pre- to postmenopausal at blood collection=0.91; comparing PMH to no PMH use at blood collection <0.01.* | | | | | | |

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| **Supplemental table 2.** Cross-sectional associations between lifestyle characteristics and sRANKL concentrations (geometric means; pmol/L) by menopausal status and PMH use at blood collection. Excluding women with sRANKL concentrations below the assays lower limit of detection. | | | | | | |
|  | **Premenopausal women** | | **Postmenopausal women** | | | |
|  | *No PMH* | | *PMH* | |
|  | n (%)a | Geometric mean  (95%CI) | n (%)a | Geometric mean  (95%CI) | n (%)a | Geometric mean  (95%CI) |
| **Baseline BMI** |  |  |  |  |  |  |
| < 20 kg/m2 | 27 (6%) | 0.09 (0.06-0.13) | 42 (6%) | 0.09 (0.07-0.11) | 56 (9%) | 0.09 (0.07-0.12) |
| 20-24.9 kg/m2 | 242 (54%) | 0.09 (0.08-0.12) | 295 (42%) | 0.09 (0.08-0.11) | 354 (54%) | 0.10 (0.08-0.12) |
| 25-29.9 kg/m2 | 134 (30%) | 0.11 (0.09-0.14) | 267 (38%) | 0.10 (0.09-0.12) | 191 (29%) | 0.12 (0.10-0.15) |
| ≥ 30 kg/m2 | 44 (10%) | 0.14 (0.10-0.19) | 103 (15%) | 0.09 (0.08-0.11) | 50 (8%) | 0.11 (0.09-0.15) |
| Ptrendb |  | <0.01 |  | 0.46 |  | 0.02 |
| **Baseline smoking status** |  |  |  |  |  |  |
| Never smoker | 239 (54%) | 0.10 (0.08-0.13) | 404 (57%) | 0.10 (0.09-0.12) | 348 (53%) | 0.11 (0.09-0.14) |
| Former smoker | 107 (24%) | 0.10 (0.08-0.13) | 165 (23%) | 0.09 (0.08-0.11) | 169 (26%) | 0.10 (0.08-0.12) |
| Current smoker | 96 (21%) | 0.10 (0.8-0.13) | 132 (19%) | 0.08 (0.07-0.10) | 112 (17%) | 0.11 (0.09-0.14) |
| ≤ 10 yearsc | 44 (10%) | 0.13 (0.10-0.19) | 39 (6%) | 0.09 (0.06-0.12) | 45 (7%) | 0.09 (0.06-0.13) |
| 11-20 yearsc | 61 (14%) | 0.13 (0.09-0.18) | 37 (5%) | 0.07 (0.05-0.10) | 44 (7%) | 0.09 (0.06-0.14) |
| 21-30 yearsc | 81 (18%) | 0.13 (0.09-0.17) | 63 (9%) | 0.09 (0.06-0.12) | 67 (11%) | 0.10 (0.07-0.15) |
| 31-40 yearsc | 12 (3%) | 0.09 (0.05-0.15) | 86 (12%) | 0.08 (0.06-0.10) | 70 (11%) | 0.10 (0.07-0.15) |
| > 40 yearsc | 0 (0%) | *ǂ* | 54 (8%) | 0.07 (0.05-0.10) | 33 (5%) | 0.10 (0.06-0.16) |
| Pcatd never vs. current smoking |  | 0.97 |  | 0.03 |  | 0.21 |
| Ptrendbc duration of smoking |  | 0.19 |  | 0.13 |  | 0.55 |
| **Baseline physical activity** |  |  |  |  |  |  |
| Inactive | 73 (16%) | 0.10 (0.07-0.13) | 72 (10%) | 0.09 (0.07-0.12) | 128 (20%) | 0.12 (0.09-0.15) |
| Moderately inactive | 142 (32%) | 0.11 (0.09-0.14) | 220 (31%) | 0.09 (0.08-0.11) | 276 (42%) | 0.12 (0.09-0.15) |
| Moderately active | 185 (41%) | 0.10 (0.08-0.12) | 362 (51%) | 0.10 (0.08-0.11) | 193 (30%) | 0.11 (0.09-0.13) |
| Active | 47 (11%) | 0.10 (0.08-0.14) | 53 (8%) | 0.10 (0.08-0.12) | 53 (8%) | 0.09 (0.07-0.12) |
| Pcatd inactive vs. active |  | 0.63 |  | 0.74 |  | 0.08 |
| **Lifetime alcohol consumption** |  |  |  |  |  |  |
| Non-drinker | 38 (9%) | 0.12 (0.09-0.18) | 75 (11%) | 0.09 (0.07-0.11) | 21 (3%) | 0.11 (0.07-0.17) |
| Former drinker | 13 (3%) | 0.11 (0.07-0.19) | 38 (5%) | 0.06 (0.05-0.08) | 9 (1%) | 0.16 (0.09-0.29) |
| Current drinker | 384 (88%) | 0.11 (0.08-0.14) | 576 (84%) | 0.09 (0.08-0.11) | 603 (95%) | 0.11 (0.08-0.13) |
| < 6 gram/daye | 141 (32%) | 0.11 (0.08-0.14) | 198 (29%) | 0.09 (0.08-0.11) | 155 (25%) | 0.10 (0.08-0.13) |
| 6-12 gram/daye | 162 (37%) | 0.12 (0.09-0.15) | 277 (40%) | 0.09 (0.08-0.11) | 294 (46%) | 0.11 (0.08-0.13) |
| ≥12 gram daye | 81 (19%) | 0.09 (0.07-0.13) | 101 (15%) | 0.10 (0.08-0.12) | 154 (24%) | 0.10 (0.08-0.12) |
| Pcatd never vs. current alcohol use |  | 0.31 |  | 0.48 |  | 0.72 |
| Ptrendb gram/daye |  | 0.92 |  | 0.95 |  | 0.62 |
| *a percentages may not add up to 100% due to missing data; b P value for linear trend assessed using type III F statistics from linear regression models with continuous exposure variables; c  In current and former smokers; d P value for difference in geometric mean concentration of sRANKL across categories of the exposure variable. Assessed using type III F statistics from linear regression models; e among current drinkers; ǂ Not evaluated; Generalized linear models adjusted for: age (continuous), fasting status ((<3, 3-6, >6 hours, missing), time of day (continuous), and menstrual cycle phase at blood collection (premenopausal women: early follicular, late follicular, ovulatory, early luteal, mid luteal, late luteal, missing), and country (as a proxy for study center).* | | | | | | |

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| **Supplemental table 3.** Cross-sectional associations between fasting status, breastfeeding, and menstrual cycle phase and sRANKL concentrations (geometric means; pmol/L) by menopausal status and PMH use at blood collection. | | | | | | |
|  | **Premenopausal women** | | **Postmenopausal women** | | | |
|  | *No PMH* | | *PMH* | |
|  | n (%)a | Geometric mean  (95%CI) | n (%)a | Geometric mean  (95%CI) | n (%)a | Geometric mean  (95%CI) |
| **Fasting status at blood collection** |  |  |  |  |  |  |
| <3 hours | 166 (36%) | 0.08 (0.07-0.09) | 382 (50%) | 0.09 (0.07-0.10) | 398 (53%) | 0.06 (0.05-0.08) |
| 3-6 hours | 66 (14%) | 0.10 (0.08-0.14) | 137 (18%) | 0.08 (0.06-0.10) | 197 (26%) | 0.07 (0.05-0.08) |
| ≥7 hours | 226 (49%) | 0.09 (0.07-0.11) | 232 (31%) | 0.08 (0.06-0.10) | 151 (20%) | 0.06 (0.05-0.09) |
| Ptrendb |  | 0.15 |  | 0.45 |  | 0.96 |
| **Breastfeedingc** |  |  |  |  |  |  |
| Never | 121 (26%) | 0.09 (0.07-0.13) | 195 (26%) | 0.08 (0.06-0.10) | 184 (24%) | 0.07 (0.05-0.09) |
| Ever | 332 (72%) | 0.10 (0.08-0.14) | 547 (72%) | 0.08 (0.06-0.09) | 538 (71%) | 0.07 (0.05-0.09) |
| < 3 months | 89 (27%) | 0.11 (0.08-0.15) | 129 (24%) | 0.07 (0.05-0.09) | 127 (24%) | 0.07 (0.05-0.10) |
| 3-6 months | 61 (18%) | 0.11 (0.08-0.16) | 117 (21%) | 0.08 (0.06-0.11) | 127 (24%) | 0.07 (0.05-0.11) |
| 6-12 months | 109 (33%) | 0.10 (0.07-0.14) | 163 (30%) | 0.09 (0.07-0.11) | 163 (30%) | 0.07 (0.05-0.09) |
| ≥12 months | 72 (22%) | 0.10 (0.07-0.14) | 132 (24%) | 0.07 (0.05-0.09) | 111 (21%) | 0.06 (0.04-0.09) |
| Pcatd never vs. ever breastfeeding |  | 0.26 |  | 0.83 |  | 0.83 |
| Ptrendb duration of breastfeeding |  | 0.03 |  | 0.55 |  | 0.70 |
| **Menstrual cycle phase at blood collection** | |  |  |  |  |  |
| Early follicular | 93 (20%) | 0.12 (0.08-0.16) |  | *ǂ* |  | *ǂ* |
| Late follicular | 51 (11)% | 0.12 (0.09-0.17) |  | *ǂ* |  | *ǂ* |
| Ovulatory | 81 (17%) | 0.11 (0.08-0.15) |  | *ǂ* |  | *ǂ* |
| Early luteal | 33 (7%) | 0.11 (0.07-0.16) |  | *ǂ* |  | *ǂ* |
| Mid luteal | 65 (14%) | 0.08 (0.06-0.12) |  | *ǂ* |  | *ǂ* |
| Late luteal | 61 (13%) | 0.11 (0.08-0.15) |  | *ǂ* |  | *ǂ* |
| Pcat |  | 0.27 |  |  |  |  |
| *a percentages may not add up to 100% due to missing data; b P value for linear trend assessed using type III F statistics from linear regression models with continuous exposure variables; c Among women with at least one full term pregnancy; d P value for difference in geometric mean concentration of sRANKL across categories of the exposure variable. Assessed using type III F statistics from linear regression models; ǂ Not evaluated; Generalized linear models adjusted for: age (continuous), fasting status ((<3, 3-6, >6 hours, missing), time of day (continuous), and menstrual cycle phase at blood collection (premenopausal women: early follicular, late follicular, ovulatory, early luteal, mid luteal, late luteal, missing), and country (as a proxy for study center).* | | | | | | |

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| **Supplemental table 4.** Cross-sectional associations between fasting status, breastfeeding, and menstrual cycle phase and sRANKL concentrations (geometric means; pmol/L) by menopausal status and PMH use at blood collection. Excluding women with sRANKL concentrations below the assays lower limit of detection. | | | | | | |
|  | **Premenopausal women** | | **Postmenopausal women** | | | |
|  | *No PMH* | | *PMH* | |
|  | n (%)a | Geometric mean  (95%CI) | n (%)a | Geometric mean  (95%CI) | n (%)a | Geometric mean  (95%CI) |
| **Fasting status at blood collection** |  |  |  |  |  |  |
| <3 hours | 155 (35%) | 0.10 (0.08-0.11) | 355 (50%) | 0.11 (0.10-0.12) | 339 (50%) | 0.09 (0.08-0.11) |
| 3-6 hours | 65 (15%) | 0.11 (0.09-0.14) | 119 (17%) | 0.11 (0.09-0.13) | 169 (26%) | 0.10 (0.08-0.12) |
| ≥7 hours | 222 (50%) | 0.11 (0.09-0.13) | 224 (32%) | 0.10 (0.08-0.12) | 134 (21%) | 0.09 (0.07-0.11) |
| Ptrendb |  | 0.34 |  | 0.46 |  | 0.98 |
| **Breastfeedingc** |  |  |  |  |  |  |
| Never | 63 (16%) | 0.09 (0.07-0.13) | 96 (16%) | 0.09 (0.07-0.11) | 85 (15%) | 0.10 (0.08-0.13) |
| Ever | 321 (83%) | 0.11 (0.08-0.14) | 509 (82%) | 0.09 (0.08-0.11) | 465 (83%) | 0.10 (0.09-0.13) |
| < 3 months | 87 (27%) | 0.11 (0.09-0.15) | 117 (23%) | 0.09 (0.07-0.11) | 107 (23%) | 0.10 (0.08-0.13) |
| 3-6 months | 59 (18%) | 0.11 (0.08-0.15) | 111 (22%) | 0.10 (0.08-0.12) | 113 (24%) | 0.11 (0.08-0.14) |
| 6-12 months | 104 (32%) | 0.11 (0.09-0.15) | 155 (30%) | 0.11 (0.09-0.13) | 143 (31%) | 0.10 (0.08-0.13) |
| ≥12 months | 70 (22%) | 0.10 (0.07-0.13) | 121 (24%) | 0.09 (0.07-0.11) | 93 (20%) | 0.10 (0.08-0.13) |
| Pcatd never vs. ever breastfeeding |  | 0.17 |  | 0.75 |  | 0.60 |
| Ptrendb duration of breastfeeding |  | 0.01 |  | 0.69 |  | 0.86 |
| **Menstrual cycle phase at blood collection** | |  |  |  |  |  |
| Early follicular | 89 (17%) | 0.15 (0.11-0.20) |  | *ǂ* |  | *ǂ* |
| Late follicular | 51 (11%) | 0.14 (0.10-0.18) |  | *ǂ* |  | *ǂ* |
| Ovulatory | 80 (18%) | 0.12 (0.09-0.16) |  | *ǂ* |  | *ǂ* |
| Early luteal | 32 (7%) | 0.13 (0.09-0.19) |  | *ǂ* |  | *ǂ* |
| Mid luteal | 62 (14%) | 0.11 (0.08-0.14) |  | *ǂ* |  | *ǂ* |
| Late luteal | 58 (13%) | 0.14 (0.10-0.18) |  | *ǂ* |  | *ǂ* |
| Pcatd |  | 0.18 |  |  |  |  |
| *a percentages may not add up to 100% due to missing data; b P value for linear trend assessed using type III F statistics from linear regression models with continuous exposure variables; c Among women with at least one full term pregnancy; d P value for difference in geometric mean concentration of sRANKL across categories of the exposure variable. Assessed using type III F statistics from linear regression models; ǂ Not evaluated; Generalized linear models adjusted for: age (continuous), fasting status ((<3, 3-6, >6 hours, missing), time of day (continuous), and menstrual cycle phase at blood collection (premenopausal women: early follicular, late follicular, ovulatory, early luteal, mid luteal, late luteal, missing), and country (as a proxy for study center).* | | | | | | |

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| **Supplemental table 5.** Cross-sectional associations between fasting status, breastfeeding, and menstrual cycle phase and OPG concentrations (geometric means; pmol/L) by menopausal status and PMH use at blood collection. | | | | | | |
|  | **Premenopausal women** | | **Postmenopausal women** | | | |
|  | *No PMH* | | *PMH* | |
|  | n (%)a | Geometric mean  (95%CI) | n (%)a | Geometric mean  (95%CI) | n (%)a | Geometric mean  (95%CI) |
| **Fasting status at blood collection** |  |  |  |  |  |  |
| <3 hours | 168 (36%) | 8.26 (7.92-8.61) | 396 (50%) | 10.16 (9.78-10.56) | 397 (52%) | 9.96 (9.55-10.38) |
| 3-6 hours | 66 (14%) | 8.38 (7.86-8.93) | 144 (18%) | 10.41 (9.89-10.95) | 197 (26%) | 10.16 (9.67-10.67) |
| ≥7 hours | 225 (48%) | 7.85 (7.41-8.31) | 246 (31%) | 10.61 (10.07-11.19) | 151 (20%) | 9.58 (9.04-10.15) |
| Ptrendb |  | 0.24 |  | 0.34 |  | 0.18 |
| **Breastfeedingc** |  |  |  |  |  |  |
| Never | 122 (26%) | 8.12 (7.56-8.73) | 207 (26%) | 10.00 (9.31-10.73) | 183 (24%) | 9.70 (9.05-10.40) |
| Ever | 332 (72%) | 8.18 (7.68-8.72) | 571 (72%) | 9.87 (9.38-10.37) | 538 (71%) | 9.80 (9.31-10.32) |
| < 3 months | 88 (27%) | 8.27 (7.61-8.99) | 130 (23%) | 9.82 (9.19-10.49) | 127 (24%) | 9.92 (9.29-10.59) |
| 3-6 months | 61 (18%) | 8.09 (7.39-8.85) | 119 (21%) | 9.74 (9.10-10.43) | 127 (24%) | 9.52 (8.91-10.18) |
| 6-12 months | 109 (33%) | 8.37 (7.73-9.07) | 175 (31%) | 9.79 (9.20-10.41) | 163 (31%) | 10.03 (9.42-10.69) |
| ≥12 months | 73 (22%) | 8.35 (7.67-9.09) | 141 (25%) | 10.00 (9.37-10.66) | 111 (21%) | 9.81 (9.16-10.50) |
| Pcatc never vs. ever breastfeeding |  | 0.94 |  | 0.65 |  | 0.72 |
| Ptrendb duration of breastfeeding |  | 0.27 |  | 0.99 |  | 0.94 |
| **Menstrual cycle phase at blood collection** | |  |  |  |  |  |
| Early follicular | 93 (20%) | 8.40 (7.74-9.11) |  | *ǂ* |  | *ǂ* |
| Late follicular | 51 (11%) | 8.22 (7.53-8.96) |  | *ǂ* |  | *ǂ* |
| Ovulatory | 81 (17%) | 7.85 (8.24-8.52) |  | *ǂ* |  | *ǂ* |
| Early luteal | 33 (7%) | 8.30 (7.48-9.22) |  | *ǂ* |  | *ǂ* |
| Mid luteal | 65 (14%) | 8.38 (7.68-9.13) |  | *ǂ* |  | *ǂ* |
| Late luteal | 63 (14%) | 7.82 (7.19-8.52) |  | *ǂ* |  | *ǂ* |
| Pcatd |  | 0.28 |  |  |  |  |
| *a percentages may not add up to 100% due to missing data; b P value for linear trend assessed using type III F statistics from linear regression models with continuous exposure variables; c Among women with at least one full term pregnancy; d P value for difference in geometric mean concentration of sRANKL across categories of the exposure variable. Assessed using type III F statistics from linear regression models; ǂ Not evaluated; Generalized linear models adjusted for: age (continuous), fasting status ((<3, 3-6, >6 hours, missing), time of day (continuous), and menstrual cycle phase at blood collection (premenopausal women: early follicular, late follicular, ovulatory, early luteal, mid luteal, late luteal, missing), and country (as a proxy for study center).* | | | | | | |