

Supplemental Table 1. Change in sex hormones, stratified by weight loss (%).

| | | | | Baseline | 12-months | | | | |
|-------|-------------------------|-------------------|----|----------------------------|----------------------------|------------|------------|----------------------|----------------------|
| Group | Biomarker | | N | Geometric Mean (95% CI) | Geometric Mean (95% CI) | Δ^a | % Δ | P-Value [†] | P-value [‡] |
| Diet | Estrone (pg/mL) | CONTROL | 80 | 32.0 (28.6, 35.8) | 34.6 (31.4, 38.1) | 2.6 | 8.1 | Ref. | |
| | | Weight Loss <5% | 28 | 38.2 (33.4, 43.7) | 36.7 (31.6, 42.6) | -1.6 | -4.1 | 0.05 | Ref. |
| | | Weight Loss 5-10% | 27 | 35.0 (30.2, 40.5) | 33.2 (28.0, 39.2) | -1.8 | -5.1 | 0.02 | 0.85 |
| | | Weight Loss >10% | 46 | 31.8 (28.4, 35.6) | 28.4 (25.7, 31.5) | -3.3 | -10.5 | <0.001 | 0.22 |
| | | | | | | | | (<0.001*) | 0.20** |
| | Estradiol (pg/mL) | CONTROL | 80 | 10.9 (9.6-12.3) | 11.4 (10.2, 12.8) | 0.5 | 4.9 | Ref. | |
| | | Weight Loss <5% | 28 | 13.3 (11.7,15.2) | 12.5 (10.5, 14.9) | -0.8 | -6.3 | 0.09 | Ref. |
| | | Weight Loss 5-10% | 27 | 10.6 (9.0, 12.5) | 9.4 (7.8, 11.4) | -1.3 | -11.7 | 0.03 | 0.42 |
| | | Weight Loss >10% | 46 | 10.7 (9.4, 12.3) | 8.6 (7.7,9.5) | -2.2 | -20.4 | <0.0001 | <0.01 |
| | | | | | | | | (<0.0001*) | <0.01** |
| | Testosterone (ng/dL) | CONTROL | 80 | 22.8 (20.2, 25.7) | 23.2 (20.8, 25.9) | 0.4 | 1.8 | Ref. | |
| | | Weight Loss <5% | 28 | 26.8 (22.8, 31.6) | 25.7 (21.7, 30.5) | -1.1 | -4.0 | 0.14 | Ref. |

| | | | | Baseline | 12-months | | | | |
|-------|----------------------------|-------------------|----|----------------------------|----------------------------|------------|------------|-------------------------|-----------------------|
| Group | Biomarker | | N | Geometric Mean (95% CI) | Geometric Mean (95% CI) | Δ^a | % Δ | P-Value [†] | P-value [‡] |
| | | Weight Loss 5-10% | 27 | 21.9 (19.0, 25.1) | 21.2 (18.1, 24.9) | -0.6 | -2.9 | 0.35 | 0.83 |
| | | Weight Loss >10% | 46 | 23.5 (20.4, 27.0) | 23.8 (20.8, 27.3) | 0.4 | 1.6 | 0.91 | 0.19 |
| | | | | | | | | (0.81 [*]) | 0.18 ^{**} |
| | Androstenedione (ng/dL) | CONTROL | 80 | 48.7 (43.9, 54.0) | 49.4 (45.4, 53.7) | 0.7 | 1.5 | Ref. | |
| | | Weight Loss <5% | 28 | 49.8 (42.9, 57.8) | 45.8 (39.8, 52.7) | -4.0 | -8.1 | 0.16 | Ref. |
| | | Weight Loss 5-10% | 27 | 55.9 (46.4, 67.4) | 56.6 (46.3, 69.2) | 0.7 | 1.2 | 0.96 | 0.29 |
| | | Weight Loss >10% | 46 | 50.5 (44.4, 57.4) | 53.0 (47.7, 59.0) | 2.5 | 5.0 | 0.62 | 0.09 |
| | | | | | | | | (0.57 [*]) | 0.10 ^{**} |
| | SHBG (nmol/L) | CONTROL | 80 | 34.7 (31.5, 38.2) | 33.7 (30.3, 37.5) | -0.9 | -2.7 | Ref. | |
| | | Weight Loss <5% | 28 | 36.9 (31.9, 42.8) | 37.2 (32.6, 42.5) | 0.3 | 0.8 | 0.32 | Ref. |
| | | Weight Loss 5-10% | 27 | 37.3 (30.7, 45.4) | 43.5 (36.4, 52.0) | 6.2 | 16.6 | <0.0001 | <.01 |
| | | Weight Loss >10% | 46 | 34.4 (30.4, 39.0) | 47.8 (42.7, 53.5) | 13.4 | 38.9 | <0.0001 | <0.0001 |
| | | | | | | | | (<0.0001 [*]) | <0.0001 ^{**} |
| | Free Estradiol (pg/mL) | CONTROL | 80 | 0.30 (0.27, 0.34) | 0.32 (0.29, 0.36) | 0.02 | 6.3 | Ref. | |

| | | | | Baseline | 12-months | | | | |
|----------|------------------------------|-------------------|----|----------------------------|----------------------------|------------|------------|----------------------|----------------------|
| Group | Biomarker | | N | Geometric Mean (95% CI) | Geometric Mean (95% CI) | Δ^a | % Δ | P-Value [†] | P-value [‡] |
| | | Weight Loss <5% | 28 | 0.35 (0.31, 0.41) | 0.33 (0.27, 0.40) | - 0.02 | -6.2 | 0.07 | Ref. |
| | | Weight Loss 5-10% | 27 | 0.28 (0.23, 0.34) | 0.23 (0.19, 0.29) | - 0.04 | -15.8 | <0.01 | 0.12 |
| | | Weight Loss >10% | 46 | 0.29 (0.25, 0.34) | 0.21 (0.18, 0.24) | - 0.08 | -28.6 | <0.0001 | <0.0001 |
| | | | | | | | | (<0.0001*) | <0.0001** |
| | Free Testosterone (pg/mL) | CONTROL | 80 | 4.9 (4.4, 5.6) | 5.1 (4.6, 5.7) | 0.1 | 2.6 | Ref. | |
| | | Weight Loss <5% | 28 | 5.7 (4.8, 6.7) | 5.5 (4.6, 6.5) | -0.2 | -4.1 | 0.10 | Ref. |
| | | Weight Loss 5-10% | 27 | 4.6 (3.7, 5.5) | 4.1 (3.3, 5.1) | -0.4 | -9.6 | 0.02 | 0.30 |
| | | Weight Loss >10% | 46 | 5.1 (4.4, 5.9) | 4.4 (3.9, 5.1) | -0.7 | -13.4 | <0.001 | 0.03 |
| | | | | | | | | (<0.001*) | 0.03** |
| Exercise | Estrone (pg/mL) | CONTROL | 80 | 32.0 (28.6, 35.8) | 34.6 (31.4, 38.1) | 2.6 | 8.1 | Ref. | |
| | | Weight Loss <5% | 72 | 33.6 (30.7, 36.8) | 33.2 (30.3, 36.4) | -0.4 | -1.2 | 0.06 | Ref. |
| | | Weight Loss >=5% | 27 | 35.4 (30.5, 41.0) | 31.4 (27.5, 35.9) | -3.9 | -11.1 | <0.01 | 0.11 |
| | | | | | | | | (<0.01*) | |
| | Estradiol (pg/mL) | CONTROL | 80 | 10.9 (9.6, 12.3) | 11.4 (10.2, 12.8) | 0.5 | 4.9 | Ref. | |

| | | | | Baseline | 12-months | | | | |
|-------|-------------------------|-----------------------|----|-------------------------|-------------------------|------------|------------|-----------------------|----------------------|
| Group | Biomarker | | N | Geometric Mean (95% CI) | Geometric Mean (95% CI) | Δ^a | % Δ | P-Value [†] | P-value [‡] |
| | | Weight Loss <5% | 72 | 11.1 (10.0, 12.3) | 11.3 (10.2, 12.6) | 0.2 | 2.1 | 0.75 | Ref. |
| | | Weight Loss \geq 5% | 27 | 12.0 (10.3, 14.0) | 9.9 (8.6, 11.3) | -2.1 | -17.8 | <0.001 | <0.001 |
| | | | | | | | | (<0.01 [*]) | |
| | Testosterone (ng/dL) | CONTROL | 80 | 22.8 (20.2, 25.7) | 23.2 (20.8, 25.9) | 0.4 | 1.8 | Ref. | |
| | | Weight Loss <5% | 72 | 23.5 (21.5, 25.6) | 23.5 (21.2, 25.9) | 0.0 | -0.0 | 0.63 | Ref. |
| | | Weight Loss \geq 5% | 27 | 25.5 (21.8, 29.9) | 23.4 (19.3, 28.3) | -2.1 | -8.3 | 0.09 | 0.17 |
| | | | | | | | | (0.12 [*]) | |
| | Androstenedione (ng/mL) | CONTROL | 80 | 48.7 (43.9, 54.0) | 49.4 (45.4, 53.7) | 0.7 | 1.5 | Ref. | |
| | | Weight Loss <5% | 72 | 47.3 (43.3, 51.6) | 48.8 (44.5, 53.6) | 1.5 | 3.2 | 0.76 | Ref. |
| | | Weight Loss \geq 5% | 27 | 54.7 (46.4, 64.4) | 51.9 (42.7, 63.1) | -2.8 | -5.0 | 0.33 | 0.19 |
| | | | | | | | | (0.50 [*]) | |
| | SHBG (nmol/L) | CONTROL | 80 | 34.7 (31.5, 38.2) | 33.7 (30.3, 37.5) | -0.9 | -2.7 | Ref. | |
| | | Weight Loss <5% | 72 | 39.4 (35.3, 43.9) | 38.0 (34.2, 42.2) | -1.4 | -3.5 | 0.91 | Ref. |
| | | Weight Loss \geq 5% | 27 | 38.1 (33.2, 43.8) | 40.3 (34.5, 47.1) | 2.2 | 5.7 | 0.05 | 0.03 |
| | | | | | | | | (0.11 [*]) | |

| | | | | Baseline | 12-months | | | | |
|-------------------|------------------------------|-----------------------|----|----------------------------|----------------------------|------------|------------|----------------------|----------------------|
| Group | Biomarker | | N | Geometric Mean (95% CI) | Geometric Mean (95% CI) | Δ^a | % Δ | P-Value [†] | P-value [‡] |
| | Free Estradiol (pg/mL) | CONTROL | 79 | 0.30 (0.27, 0.34) | 0.32 (0.29, 0.36) | 0.02 | 6.3 | Ref. | |
| | | Weight Loss <5% | 72 | 0.29 (0.25, 0.32) | 0.30 (0.26, 0.33) | 0.01 | 3.5 | 0.97 | Ref. |
| | | Weight Loss \geq 5% | 27 | 0.32 (0.27, 0.37) | 0.26 (0.22, 0.29) | - 0.06 | -19.6 | <0.0001 | <0.0001 |
| | | | | | | | | (0.001*) | |
| | Free Testosterone (pg/mL) | CONTROL | 80 | 4.9 (4.4, 5.6) | 5.1 (4.6, 5.7) | 0.1 | 2.6 | Ref. | |
| | | Weight Loss <5% | 72 | 4.8 (4.4, 5.2) | 4.9 (4.4, 5.4) | 0.1 | 1.9 | 0.78 | Ref. |
| | | Weight Loss \geq 5% | 27 | 5.3 (4.6, 6.3) | 4.7 (4.0, 5.7) | -0.6 | -11.1 | 0.02 | 0.02 |
| | | | | | | | | (0.04*) | |
| Diet+ Exercise | Estrone (pg/mL) | CONTROL | 80 | 32.0 (28.6, 35.8) | 34.6 (31.4, 38.1) | 2.6 | 8.1 | Ref. | |
| | | Weight Loss <5% | 18 | 39.0 (33.2, 45.7) | 36.1 (30.4, 42.9) | -2.8 | -7.3 | 0.02 | Ref. |
| | | Weight Loss 5- 10% | 21 | 34.3 (27.4, 42.9) | 29.5 (24.3, 35.7) | -4.8 | -14.0 | 0.002 | 0.33 |
| | | Weight Loss >10% | 69 | 33.2 (30.2, 36.4) | 29.0 (26.5, 31.8) | -4.1 | -12.5 | <.0001 | 0.30 |
| | | | | | | | | (<.0001*) | 0.43** |
| | Estradiol (pg/mL) | CONTROL | 80 | 10.9 (9.6, 12.3) | 11.4 (10.2, 12.8) | 0.5 | 4.9 | Ref. | |

| | | | | Baseline | 12-months | | | | |
|-------|----------------------------|-------------------|----|----------------------------|----------------------------|------------|------------|------------------------|----------------------|
| Group | Biomarker | | N | Geometric Mean (95% CI) | Geometric Mean (95% CI) | Δ^a | % Δ | P-Value [†] | P-value [‡] |
| | | Weight Loss <5% | 18 | 13.4 (11.2, 16.0) | 12.2 (10.1, 14.7) | -1.2 | -8.7 | 0.07 | Ref. |
| | | Weight Loss 5-10% | 21 | 11.4 (8.9, 14.6) | 8.8 (7.0, 11.0) | -2.7 | -23.2 | <.0001 | 0.04 |
| | | Weight Loss >10% | 69 | 11.3 (10.2, 12.6) | 8.6 (7.8, 9.6) | -2.7 | -23.7 | <.0001 | 0.01 |
| | | | | | | | | (<.0001 [*]) | 0.03 ^{**} |
| | Testosterone (ng/dL) | CONTROL | 80 | 22.8 (20.2, 25.7) | 23.2 (20.8, 25.9) | 0.4 | 1.8 | Ref. | |
| | | Weight Loss <5% | 18 | 29.0 (24.1, 35.0) | 26.1 (22.2, 30.7) | -2.9 | -10.1 | 0.14 | Ref. |
| | | Weight Loss 5-10% | 21 | 20.6 (17.2, 24.6) | 19.7 (16.8, 23.2) | -0.8 | -4.0 | 0.30 | 0.49 |
| | | Weight Loss >10% | 69 | 24.2 (22.0, 26.5) | 22.5 (20.4, 24.9) | -1.6 | -6.7 | 0.02 | 0.67 |
| | | | | | | | | (0.04 [*]) | 0.78 ^{**} |
| | Androstenedione (ng/mL) | CONTROL | 80 | 48.7 (43.9, 54.0) | 49.4 (45.4, 53.7) | 0.7 | 1.5 | Ref. | |
| | | Weight Loss <5% | 18 | 59.3 (49.2, 71.4) | 50.5 (39.8, 64.2) | -8.7 | -14.7 | 0.07 | Ref. |
| | | Weight Loss 5-10% | 21 | 45.8 (37.7, 55.6) | 48.8 (41.7, 57.2) | 3.1 | 6.7 | 0.53 | 0.04 |
| | | Weight Loss >10% | 69 | 54.7 (50.6, 59.1) | 51.4 (47.1, 56.2) | -3.3 | -6.0 | 0.17 | 0.30 |
| | | | | | | | | (0.31 [*]) | 0.63 ^{**} |

| | | | | Baseline | 12-months | | | | |
|-------|------------------------------|-------------------|----|----------------------------|----------------------------|------------|------------|----------------------|----------------------|
| Group | Biomarker | | N | Geometric Mean (95% CI) | Geometric Mean (95% CI) | Δ^a | % Δ | P-Value [†] | P-value [‡] |
| | SHBG (nmol/L) | CONTROL | 80 | 34.7 (31.5, 38.2) | 33.7 (30.3, 37.5) | -0.9 | -2.7 | Ref. | |
| | | Weight Loss <5% | 18 | 35.6 (30.4, 41.9) | 36.0 (30.8, 42.0) | 0.3 | 0.9 | 0.24 | Ref. |
| | | Weight Loss 5-10% | 21 | 37.5 (32.1, 43.8) | 41.6 (35.8, 48.3) | 4.1 | 10.8 | <.01 | 0.07 |
| | | Weight Loss >10% | 69 | 33.5 (30.5,30.7) | 42.0 (42.0, 48.8) | 11.8 | 35.3 | (<.0001 | <.0001 |
| | | | | | | | | (<.0001*) | <.0001** |
| | Free Estradiol (pg/mL) | CONTROL | 79 | 0.30 (0.27, 0.34) | 0.32 (0.29, 0.36) | 0.02 | 6.3 | Ref. | |
| | | Weight Loss <5% | 18 | 0.36 (0.30, 0.43) | 0.33 (0.27, 0.39) | -0.03 | -8.9 | 0.05 | Ref. |
| | | Weight Loss 5-10% | 21 | 0.30 (0.24, 0.39) | 0.22 (0.18, 0.28) | -0.08 | -25.7 | <.0001 | 0.03 |
| | | Weight Loss >10% | 69 | 0.31 (0.28, 0.35) | 0.22 (0.19, 0.24) | -0.1 | -30.7 | <.0001 | 0.0001 |
| | | | | | | | | (<.0001*) | <.001** |
| | Free Testosterone (pg/mL) | CONTROL | 80 | 4.9 (4.4, 5.6) | 5.1 (4.6, 5.7) | 0.1 | 2.6 | Ref. | |
| | | Weight Loss <5% | 18 | 6.3 (5.2, 7.6) | 5.6 (4.8, 6.6) | -0.7 | -10.4 | 0.11 | Ref. |
| | | Weight Loss 5-10% | 21 | 4.3 (3.7, 5.1) | 4.0 (3.5, 4.5) | -0.4 | -8.6 | 0.06 | 0.83 |

| | | | | Baseline | 12-months | | | | |
|-------|-----------|------------------|----|----------------------------|----------------------------|------------|------------|------------------------|----------------------|
| Group | Biomarker | | N | Geometric Mean (95% CI) | Geometric Mean (95% CI) | Δ^a | % Δ | P-Value [†] | P-value [‡] |
| | | Weight Loss >10% | 69 | 5.4 (4.9, 5.9) | 4.3 (3.9, 4.8) | -1.0 | -19.2 | <.0001 [†] | 0.23 |
| | | | | | | | | (<.0001 [*]) | 0.10 ^{**} |

Abbreviations: CI, confidence interval; SHBG, sex hormone-binding globulin; Δ , change.

^a: Change from baseline to 12-months

[†]Testing difference in change from baseline to 12 months in hormones compared to Controls.

[‡]Testing difference in change from baseline to 12 months in hormones compared to Weight Loss <5% Group, excluding Controls

^{*}Testing for a trend in change from baseline to 12 months in hormones from Controls through Weight Loss \geq 10% Group

^{**}Testing for a trend in change from baseline to 12 months in hormones from >5% Weight Loss Group through Weight Loss \geq 10% Group

Supplemental Table 2. Change in sex hormones measures, stratified by **body fat loss (%)**

| Group | Biomarker | | N | Baseline Geometric Mean (95% CI) | 12-months Geometric Mean (95% CI) | Δ | % Δ | P-Value [†] | P-value [‡] |
|-------|-------------------------------|--------------------|----|--|---|----------|-------------------------|------------------------|----------------------|
| Diet | Estrone (pg/mL) | CONTROL | 80 | 32.0 (28.6, 35.8) | 34.6 (31.4, 38.1) | 2.6 | 8.1 | Ref. | |
| | | Decrease <0.9% | 25 | 40.9 (35.5, 47.1) | 37.2 (31.7, 43.5) | -3.7 | -9.1 | 0.007 | Ref. |
| | | Decrease <0.9-4.4% | 31 | 34.5 (30.5, 38.9) | 32.9 (28.2, 38.3) | -1.6 | -5.0 | 0.02 | 0.42 |
| | | Decrease > 4.4% | 45 | 31.0 (27.5, 34.9) | 28.5 (25.6, 31.7) | -2.5 | -8.1 | 0.003 | 0.85 |
| | | | | | | | (0.003*) | (0.95**) | |
| | Estradiol (pg/mL) | CONTROL | 80 | 10.9 (9.6-12.3) | 11.4 (10.2, 12.8) | 0.5 | 4.9 | Ref. | |
| | | Decrease <0.9% | 25 | 14.1 (12.2,16.3) | 13.5 (11.3, 16.0) | -0.7 | -4.7 | 0.12 | Ref. |
| | | Decrease <0.9-4.4% | 31 | 10.6 (9.0, 12.5) | 9.4 (7.8, 11.4) | -1.3 | -11.7 | 0.005 | 0.10 |
| | | Decrease > 4.4% | 45 | 10.7 (9.4, 12.3) | 8.6 (7.7,9.5) | -2.2 | -20.4 | <0.0001 | 0.002 |
| | | | | | | | (<0.0001 [†]) | (<0.01 ^{**}) | |
| | Total Testosterone (ng/dL) | CONTROL | 80 | 22.8 (20.2, 25.7) | 23.2 (20.8, 25.9) | 0.4 | 1.8 | Ref. | |
| | | Decrease <0.9% | 25 | 29.1 (25.1, 33.9) | 27.6 (23.6, 32.3) | -1.5 | -5.3 | 0.06 | Ref. |
| | | Decrease <0.9-4.4% | 31 | 23.5 (20.1, 27.4) | 23.5 (19.9, 27.7) | 0.0 | 0.0 | 0.67 | 0.21 |
| | | Decrease > 4.4% | 45 | 21.7 (19.0, 25.8) | 21.7 (19.0, 25.9) | 0.1 | 0.2 | 0.70 | 0.20 |

| Group | Biomarker | | N | Baseline Geometric Mean (95% CI) | 12-months Geometric Mean (95% CI) | Δ | %Δ | P-Value [†] | P-value [‡] |
|-------|----------------------------|------------------------|----|--|---|------|-------|-------------------------|--------------------------|
| | | | | | | | | (0.73 [*]) | (0.27 ^{**}) |
| | Androstenedione (ng/dL) | CONTROL | 80 | 48.7 (43.9, 54.0) | 49.4 (45.4, 53.7) | 0.7 | 1.5 | Ref. | |
| | | Decrease <0.9% | 25 | 55.7 (47.3, 65.6) | 52.2 (44.2, 61.6) | -3.5 | -6.3 | 0.30 | Ref. |
| | | Decrease <0.9- 4.4% | 31 | 45.6 (39.8, 52.4) | 48.5 (42.4, 55.6) | 2.9 | 6.3 | 0.53 | 0.17 |
| | | Decrease > 4.4% | 45 | 54.1 (46.9, 62.3) | 54.0 (47.3, 61.7) | -0.1 | 0.2 | 0.79 | 0.46 |
| | | | | | | | | (0.97 [*]) | (0.59 ^{**}) |
| | SHBG (nmol/L) | CONTROL | 80 | 34.7 (31.5, 38.2) | 33.7 (30.3, 37.5) | -0.9 | -2.7 | Ref. | |
| | | Decrease <0.9% | 25 | 33.5 (28.0, 40.2) | 35.1 (30.2, 40.9) | 1.6 | 4.8 | 0.11 | Ref. |
| | | Decrease <0.9- 4.4% | 31 | 35.0 (29.5, 41.4) | 40.4 (34.8, 46.8) | 5.4 | 15.4 | <0.0001 | 0.09 |
| | | Decrease > 4.4% | 45 | 37.9 (33.6, 42.7) | 51.6 (46.5, 57.2) | 13.7 | 36.1 | <0.0001 | <0.0001 |
| | | | | | | | | (<0.0001 [*]) | (<0.0001 ^{**}) |
| | Free Estradiol (pg/mL) | CONTROL | 80 | 0.30 (0.27, 0.34) | 0.32 (0.29, 0.36) | 0.02 | 6.3 | Ref. | |
| | | Decrease <0.9% | 25 | 0.39 (0.33, 0.44) | 0.36 (0.30, 0.44) | - | -5.5 | 0.08 | Ref. |
| | | Decrease <0.9- 4.4% | 31 | 0.31 (0.27, 0.37) | 0.26 (0.21, 0.32) | - | -17.7 | 0.0001 | 0.03 |
| | | Decrease > 4.4% | 45 | 0.26 (0.22, 0.30) | 0.19 (0.17, 0.21) | - | -27.5 | <0.0001 | <0.0001 |
| | | | | | | | | (<0.0001 [*]) | (<0.0001 ^{**}) |

| | | | | Baseline | 12-months | | | | |
|----------|---------------------------|--------------------|----|-------------------------|-------------------------|------|-------|------------------------|-----------------------|
| Group | Biomarker | | N | Geometric Mean (95% CI) | Geometric Mean (95% CI) | Δ | %Δ | P-Value [†] | P-value [‡] |
| | Free Testosterone (pg/mL) | CONTROL | 80 | 4.9 (4.4, 5.6) | 5.1 (4.6, 5.7) | 0.1 | 2.6 | Ref. | |
| | | Decrease <0.9% | 28 | 6.4 (5.4, 7.6) | 6.0 (5.1, 7.1) | -0.4 | -6.6 | 0.03 | Ref. |
| | | Decrease <0.9-4.4% | 27 | 5.1 (4.2, 6.1) | 4.8 (3.9, 5.8) | -0.3 | -6.0 | 0.04 | 0.88 |
| | | Decrease > 4.4% | 46 | 4.5 (4.0, 5.2) | 4.0 (3.4, 4.5) | -0.6 | -14.1 | <0.001 | 0.10 |
| | | | | | | | | (<0.001 [*]) | (0.08 ^{**}) |
| Exercise | Estrone (pg/mL) | CONTROL | 80 | 32.0 (28.6, 35.8) | 34.6 (31.4, 38.1) | 2.6 | 8.1 | Ref. | |
| | | Decrease <0.9% | 45 | 36.7 (32.7, 41.2) | 35.1 (31.4, 39.2) | -1.6 | -4.4 | 0.01 | Ref. |
| | | Decrease <0.9-4.4% | 43 | 31.0 (27.8, 34.5) | 29.6 (27.5, 35.9) | -1.4 | -4.4 | 0.04 | 0.10 |
| | | Decrease > 4.4% | 11 | 36.6 (28.5, 47.1) | 36.3 (30.8, 42.9) | -0.3 | -0.8 | 0.35 | 0.67 |
| | | | | | | | | (0.05 [*]) | (0.73 ^{**}) |
| | Estradiol (pg/mL) | CONTROL | 80 | 10.9 (9.6, 12.3) | 11.4 (10.2, 12.8) | 0.5 | 4.9 | Ref. | |
| | | Decrease <0.9% | 45 | 12.0 (10.6, 13.6) | 11.9 (10.4, 13.6) | -0.1 | -0.6 | 0.43 | Ref. |
| | | Decrease <0.9-4.4% | 43 | 10.4 (9.1, 11.9) | 10.0 (8.8, 11.2) | -0.4 | -4.2 | 0.20 | 0.52 |
| | | Decrease > 4.4% | 11 | 12.8 (9.8, 16.7) | 11.0 (9.1, 13.4) | -1.8 | -14.0 | 0.01 | 0.04 |
| | | | | | | | | (0.04 [*]) | (0.08 ^{**}) |

| | | | | Baseline | 12-months | | | | |
|-------|-------------------------------|--------------------|----|----------------------------|----------------------------|------|------|----------------------|-----------------------|
| Group | Biomarker | | N | Geometric Mean (95% CI) | Geometric Mean (95% CI) | Δ | %Δ | P-Value [†] | P-value [‡] |
| | Total Testosterone (ng/dL) | CONTROL | 80 | 22.8 (20.2, 25.7) | 23.2 (20.8, 25.9) | 0.4 | 1.8 | Ref. | |
| | | Decrease <0.9% | 45 | 24.3 (21.9, 26.9) | 23.4 (21.0, 26.1) | -0.9 | -3.6 | 0.14 | Ref. |
| | | Decrease <0.9-4.4% | 43 | 23.2 (20.6, 26.1) | 22.9 (19.6, 26.8) | -0.3 | -1.2 | 0.60 | 0.68 |
| | | Decrease > 4.4% | 11 | 26.2 (19.3, 35.7) | 25.8 (20.3, 32.9) | -0.4 | -1.6 | 0.66 | 0.80 |
| | | | | | | | | (0.51 [*]) | (0.67 ^{**}) |
| | Androstenedione (ng/mL) | CONTROL | 80 | 48.7 (43.9, 54.0) | 49.4 (45.4, 53.7) | 0.7 | 1.5 | Ref. | |
| | | Decrease <0.9% | 45 | 46.0 (41.0, 51.5) | 47.4 (42.3, 53.1) | 1.4 | 3.1 | 0.79 | Ref. |
| | | Decrease <0.9-4.4% | 43 | 50.5 (44.5, 57.0) | 49.0 (42.5, 56.5) | -1.4 | -2.7 | 0.47 | 0.30 |
| | | Decrease > 4.4% | 11 | 59.4 (49.3, 71.6) | 63.3 (50.3, 79.7) | 3.9 | 6.6 | 0.64 | 0.74 |
| | | | | | | | | (0.85 [*]) | (0.84 ^{**}) |
| | SHBG (nmol/L) | CONTROL | 80 | 34.7 (31.5, 38.2) | 33.7 (30.3, 37.5) | -0.9 | -2.7 | Ref. | |
| | | Decrease <0.9% | 45 | 38.2 (34.1, 42.8) | 36.9 (33.1, 41.3) | -1.3 | -3.3 | 0.96 | Ref. |
| | | Decrease <0.9-4.4% | 43 | 40.7 (34.8, 47.5) | 40.0 (34.3, 46.7) | -0.7 | -1.6 | 0.66 | 0.63 |
| | | Decrease > 4.4% | 11 | 36.2 (29.6, 44.2) | 40.2 (32.0, 50.6) | 4.0 | 11.1 | 0.002 | 0.002 |
| | | | | | | | | (0.09 [*]) | (0.02 ^{**}) |

| | | | | Baseline | 12-months | | | | |
|---------------|---------------------------|--------------------|----|-------------------------|-------------------------|------|-------|----------------------|-----------------------|
| Group | Biomarker | | N | Geometric Mean (95% CI) | Geometric Mean (95% CI) | Δ | %Δ | P-Value [†] | P-value [‡] |
| | Free Estradiol (pg/mL) | CONTROL | 80 | 0.30 (0.27, 0.34) | 0.32 (0.29, 0.36) | 0.02 | 6.3 | Ref. | |
| | | Decrease <0.9% | 45 | 0.32 (0.28,0.36) | 0.32 (0.27, 0.37) | 0.00 | 0.53 | 0.54 | Ref. |
| | | Decrease <0.9-4.4% | 43 | 0.26 (0.23, 0.31) | 0.25 (0.22, 0.29) | - | -3.6 | 0.20 | 0.46 |
| | | Decrease > 4.4% | 11 | 0.35 (0.26, 0.46) | 0.29 (0.23, 0.36) | -0.1 | -17.1 | 0.002 | 0.008 |
| | | | | | | | | (0.02 [*]) | (0.03 ^{**}) |
| | Free Testosterone (pg/mL) | CONTROL | 80 | 4.9 (4.4, 5.6) | 5.1 (4.6, 5.7) | 0.1 | 2.6 | Ref. | |
| | | Decrease <0.9% | 45 | 5.1 (4.5, 5.7) | 5.0 (4.5, 5.5) | -0.1 | -1.9 | 0.20 | Ref. |
| | | Decrease <0.9-4.4% | 43 | 4.6 (4.1, 5.2) | 4.6 (4.0, 5.3) | -0.0 | -0.4 | 0.57 | 0.78 |
| | | Decrease > 4.4% | 11 | 5.6 (4.0, 7.9) | 5.3 (4.1, 6.8) | -0.4 | -6.8 | 0.23 | 0.53 |
| | | | | | | | | (0.29 [*]) | (0.74 ^{**}) |
| Diet+Exercise | Estrone (pg/mL) | CONTROL | 80 | 32.0 (28.6, 35.8) | 34.6 (31.4, 38.1) | 2.6 | 8.1 | Ref. | |
| | | Decrease <0.9% | 12 | 46.1 (36.9, 57.7) | 39.6 (31.2, 50.4) | -6.5 | -14.1 | 0.006 | Ref. |
| | | Decrease <0.9-4.4% | 31 | 37.3 (32.5, 42.8) | 32.8 (29.3, 36.9) | -4.5 | -12.0 | <0.001 | 0.77 |
| | | Decrease > 4.4% | 65 | 31.2 (28.2, 34.4) | 27.6 (25.0, 30.4) | -3.6 | -11.5 | <0.0001 | 0.70 |

| Group | Biomarker | | N | Baseline Geometric Mean (95% CI) | 12-months Geometric Mean (95% CI) | Δ | % Δ | P-Value [†] | P-value [‡] |
|-------|----------------------------------|------------------------|----|--|---|----------|------------|-------------------------|-----------------------|
| | | | | | | | | (<0.0001 [*]) | (0.72 ^{**}) |
| | Estradiol (pg/mL) | CONTROL | 80 | 10.9 (9.6, 12.3) | 11.4 (10.2, 12.8) | 0.5 | 4.9 | Ref. | |
| | | Decrease <0.9% | 12 | 15.3 (11.6, 20.2) | 13.6 (10.4, 17.9) | -1.7 | -10.9 | 0.08 | Ref. |
| | | Decrease <0.9- 4.4% | 31 | 12.8 (11.1, 14.8) | 10.4 (9.0, 11.9) | -2.4 | -19.0 | <0.001 | 0.30 |
| | | Decrease > 4.4% | 65 | 10.6 (9.5, 11.9) | 8.0 (7.2, 9.0) | -2.6 | -24.1 | <0.0001 | 0.07 |
| | | | | | | | | (<0.0001 [*]) | (0.07 ^{**}) |
| | Total Testosterone (ng/dL) | CONTROL | 80 | 22.8 (20.2, 25.7) | 23.2 (20.8, 25.9) | 0.4 | 1.8 | Ref. | |
| | | Decrease <0.9% | 12 | 32.1 (24.4, 42.3) | 27.6 (21.6, 35.4) | -4.5 | -14.0 | 0.15 | Ref. |
| | | Decrease <0.9- 4.4% | 31 | 24.2 (21.3, 27.4) | 22.8 (20.2, 25.8) | -1.3 | -5.5 | 0.11 | 0.43 |
| | | Decrease > 4.4% | 65 | 22.9 (20.7, 25.3) | 21.5 (19.4, 23.9) | -1.4 | -6.0 | 0.04 | 0.45 |
| | | | | | | | | (0.05 [*]) | (0.51 ^{**}) |
| | Androstenedione (ng/mL) | CONTROL | 80 | 48.7 (43.9, 54.0) | 49.4 (45.4, 53.7) | 0.7 | 1.5 | Ref. | |
| | | Decrease <0.9% | 12 | 68.7 (53.9, 87.5) | 51.2 (36.3, 72.0) | - | -25.5 | 0.006 | Ref. |
| | | Decrease <0.9- 4.4% | 31 | 49.1 (43.2, 55.7) | 50.9 (45.3, 57.1) | 1.8 | 3.6 | 0.75 | 0.004 |
| | | Decrease > 4.4% | 65 | 53.3 (48.9, 58.2) | 50.6 (46.1, 55.6) | -2.7 | -5.0 | 0.25 | 0.03 |

| Group | Biomarker | | N | Baseline Geometric Mean (95% CI) | 12-months Geometric Mean (95% CI) | Δ | % Δ | P-Value [†] | P-value [‡] |
|-------|------------------------------|--------------------|----|--|---|----------|------------|-------------------------|--------------------------|
| | | | | | | | | (0.46 [*]) | (0.24 ^{**}) |
| | SHBG (nmol/L) | CONTROL | 80 | 34.7 (31.5, 38.2) | 33.7 (30.3, 37.5) | -0.9 | -2.7 | Ref. | |
| | | Decrease <0.9% | 12 | 34.1 (26.5, 43.9) | 35.7 (28.8, 44.2) | 1.6 | 4.6 | 0.09 | Ref. |
| | | Decrease <0.9-4.4% | 31 | 33.5 (29.6, 37.8) | 37.0 (33.0, 41.5) | 3.6 | 10.6 | <0.001 | 0.27 |
| | | Decrease > 4.4% | 65 | 35.2 (32.3, 38.3) | 47.5 (44.3, 51.0) | 12.3 | 35.0 | (<0.0001) | (<0.0001) |
| | | | | | | | | (<0.0001 [*]) | (<0.0001 ^{**}) |
| | Free Estradiol (pg/mL) | CONTROL | 80 | 0.30 (0.27, 0.34) | 0.32 (0.29, 0.36) | 0.02 | 6.3 | Ref. | |
| | | Decrease <0.9% | 12 | 0.42 (0.31, 0.56) | 0.37 (0.28, 0.48) | -0.05 | -11.7 | 0.06 | Ref. |
| | | Decrease <0.9-4.4% | 31 | 0.35 (0.30, 0.41) | 0.28 (0.24, 0.32) | 0.08 | -21.3 | <0.0001 | 0.02 |
| | | Decrease > 4.4% | 65 | 0.29 (0.25, 0.32) | 0.20 (0.18, 0.22) | 0.09 | -31.2 | <0.0001 | 0.006 |
| | | | | | | | | (<0.0001 [*]) | (<0.01 ^{**}) |
| | Free Testosterone (pg/mL) | CONTROL | 80 | 4.9 (4.4, 5.6) | 5.1 (4.6, 5.7) | 0.1 | 2.6 | Ref. | |
| | | Decrease <0.9% | 12 | 7.0 (5.3, 9.4) | 6.0 (4.6, 7.7) | -1.1 | -15.3 | 0.10 | Ref. |
| | | Decrease <0.9-4.4% | 31 | 5.4 (4.8, 6.1) | 4.9 (4.3, 5.5) | -0.5 | -9.6 | 0.01 | 0.59 |

| | | | | Baseline | 12-months | | | | |
|-------|-----------|-----------------|----|-------------------------|-------------------------|----------|------------|-------------------------|-----------------------|
| Group | Biomarker | | N | Geometric Mean (95% CI) | Geometric Mean (95% CI) | Δ | % Δ | P-Value [†] | P-value [‡] |
| | | Decrease > 4.4% | 65 | 5.0 (4.5, 5.5) | 4.0 (3.6, 4.5) | -0.9 | -18.7 | <0.0001 | 0.73 |
| | | | | | | | | (<0.0001 [*]) | (0.32 ^{**}) |

[†]Testing difference in change from baseline to 12 months in hormones compared to Controls.

[‡]Testing difference in change from baseline to 12 months in hormones compared to Weight Loss <5% Group, excluding Controls

^{*}Testing for a trend in change from baseline to 12 months in hormones from Controls through Weight Loss \geq 10% Group

^{**}Testing for a trend in change from baseline to 12 months in hormones from >5% Weight Loss Group through Weight Loss \geq 10% Group

| Group | Biomarker | | N | Baseline Geometric Mean (95% CI) | 12-months Geometric Mean (95% CI) | Δ | % Δ | P-Value† | P-value‡ |
|-------|-------------------------|-----------|----|----------------------------------|-----------------------------------|----------|------------|-------------------------|-------------------------|
| | | | | | | | | (0.33 [*]) | (0.67 ^{**}) |
| | Androstenedione (ng/mL) | CONTROL | 80 | 0.49 (0.44, 0.54) | 0.49 (0.45, 0.54) | 0.01 | 1.5 | Ref. | |
| | | <84.3% | 41 | 0.46 (0.41, 0.51) | 0.44 (0.38, 0.52) | -0.01 | -2.8 | 0.39 | Ref. |
| | | 84.3-106% | 36 | 0.53 (0.47, 0.61) | 0.55 (0.49, 0.63) | 0.02 | 3.8 | 0.72 | 0.29 |
| | | >= 106% | 38 | 0.55 (0.47, 0.65) | 0.55 (0.48, 0.63) | 0 | -0.8 | 0.75 | 0.68 |
| | | | | | | | | (0.93 [*]) | (0.76 ^{**}) |
| | SHBG (nmol/L) | CONTROL | 80 | 34.7 (31.5, 38.2) | 33.7 (30.3, 37.5) | -0.9 | -2.7 | Ref. | |
| | | <84.3% | 41 | 36.1 (31.5, 41.4) | 39.9 (34.2, 46.5) | 3.8 | 10.5 | 0.02 | Ref. |
| | | 84.3-106% | 36 | 34.1 (29.3, 39.8) | 42.7 (38.0, 48.0) | 8.6 | 25.1 | <0.0001 | 0.004 |
| | | >= 106% | 38 | 37.0 (32.4, 42.3) | 48.1 (41.6, 55.6) | 11.0 | 29.8 | <0.0001 | 0.0004 |
| | | | | | | | | (<0.0001 [*]) | (<0.001 ^{**}) |
| | Free Estradiol (pg/mL) | CONTROL | 79 | 0.30 (0.27, 0.34) | 0.32 (0.29, 0.36) | 0.02 | 6.3 | Ref. | |
| | | <84.3% | 41 | 0.34 (0.29, 0.39) | 0.28 (0.23, 0.35) | -0.05 | -15.2 | 0.002 | Ref. |
| | | 84.3-106% | 36 | 0.31 (0.27, 0.36) | 0.24 (0.21, 0.28) | -0.07 | -21.4 | <0.0001 | 0.20 |
| | | >= 106% | 38 | 0.28 (0.24, 0.34) | 0.22 (0.18, 0.26) | -0.07 | -24.2 | <0.0001 | 0.05 |
| | | | | | | | | (<0.0001 [*]) | (0.05 ^{**}) |

| Group | Biomarker | | N | Baseline Geometric Mean (95% CI) | 12-months Geometric Mean (95% CI) | Δ | % Δ | P-Value† | P-value‡ |
|---------------|---------------------------|-----------|----|----------------------------------|-----------------------------------|----------|------------|-------------------------|-----------------------|
| | Free Testosterone (pg/mL) | CONTROL | 80 | 4.9 (4.4, 5.6) | 5.1 (4.6, 5.7) | 0.1 | 2.6 | Ref. | |
| | | <84.3% | 41 | 5.0 (4.3, 5.8) | 4.8 (4.0, 5.8) | -0.2 | -4.1 | 0.003 | Ref. |
| | | 84.3-106% | 36 | 5.2 (4.5, 6.2) | 4.9 (4.2, 5.6) | -0.4 | -7.6 | 0.08 | 0.76 |
| | | >= 106% | 38 | 5.1 (4.3, 5.9) | 4.2 (3.6, 5.0) | -0.9 | -16.8 | <0.0001 | 0.02 |
| | | | | | | | | (0.0001 [*]) | (0.01 ^{**}) |
| Diet+Exercise | Estrone (pg/mL) | CONTROL | 80 | 32.0 (28.6, 35.8) | 34.6 (31.4, 38.1) | 2.6 | 8.1 | Ref. | |
| | | <84.3% | 33 | 36.9 (31.5, 43.1) | 33.2 (28.2, 39.0) | -3.7 | -10.0 | 0.0005 | Ref. |
| | | 84.3-106% | 43 | 33.2 (29.6, 37.3) | 29.8 (26.5, 33.5) | -3.4 | -10.3 | 0.0004 | 0.38 |
| | | >= 106% | 40 | 32.5 (28.5, 36.9) | 28.8 (25.5, 32.6) | -3.6 | -11.2 | 0.0001 | 0.47 |
| | | | | | | | | (0.0001 [*]) | (0.52 ^{**}) |
| | Estradiol (pg/mL) | CONTROL | 80 | 10.9 (9.6, 12.3) | 11.4 (10.2, 12.8) | 0.5 | 4.9 | Ref. | |
| | | <84.3% | 33 | 12.6 (10.5, 15.1) | 10.7 (8.8, 12.9) | -1.9 | -15.4 | 0.0003 | Ref. |
| | | 84.3-106% | 43 | 11.0 (9.8, 12.5) | 9.2 (8.1, 10.5) | -1.8 | -16.4 | 0.0001 | 0.47 |
| | | >= 106% | 40 | 11.2 (9.6, 13.0) | 8.3 (7.2, 9.7) | -2.9 | -25.8 | <0.0001 | 0.44 |
| | | | | | | | | (<0.0001 [*]) | (0.36 ^{**}) |

| Group | Biomarker | | N | Baseline Geometric Mean (95% CI) | 12-months Geometric Mean (95% CI) | Δ | %Δ | P-Value† | P-value‡ |
|-------|----------------------------|-----------|----|----------------------------------|-----------------------------------|-------|------|-------------------------|-----------------------|
| | Total Testosterone (ng/dL) | CONTROL | 80 | 22.8 (20.2, 25.7) | 23.2 (20.8, 25.9) | 0.4 | 1.8 | Ref. | |
| | | <84.3% | 33 | 24.8 (20.9, 29.5) | 22.8 (19.4, 26.7) | -2.1 | -8.3 | 0.02 | Ref. |
| | | 84.3-106% | 43 | 23.3 (20.8, 26.2) | 22.8 (20.4, 25.3) | -0.6 | -2.5 | 0.30 | 0.11 |
| | | >= 106% | 40 | 23.8 (21.1, 26.9) | 22.1 (19.1, 25.5) | -1.7 | -7.3 | 0.04 | 0.42 |
| | | | | | | | | (0.08 [*]) | (0.54 ^{**}) |
| | Androstenedione (ng/mL) | CONTROL | 80 | 0.49 (0.44, 0.54) | 0.49 (0.45, 0.54) | 0.01 | 1.5 | Ref. | |
| | | <84.3% | 33 | 0.5 (0.43, 0.58) | 0.47 (0.39, 0.56) | -0.03 | -5.9 | 0.15 | Ref. |
| | | 84.3-106% | 43 | 0.53 (0.47, 0.59) | 0.51 (0.46, 0.57) | -0.01 | -2.8 | 0.48 | 0.39 |
| | | >= 106% | 40 | 0.55 (0.50, 0.60) | 0.53 (0.47, 0.59) | -0.02 | -3.9 | 0.42 | 0.5 |
| | | | | | | | | (0.43 [*]) | (0.56 ^{**}) |
| | SHBG (nmol/L) | CONTROL | 80 | 34.7 (31.5, 38.2) | 33.7 (30.3, 37.5) | -0.9 | -2.7 | Ref. | |
| | | <84.3% | 33 | 32.6 (28.6, 37.2) | 40.0 (34.9, 45.9) | 7.4 | 22.7 | 0.0001 | Ref. |
| | | 84.3-106% | 43 | 33.6 (30.4, 37.2) | 40.6 (36.7, 45.0) | 7.0 | 21.0 | <0.0001 | 0.62 |
| | | >= 106% | 40 | 35.8 (32.0, 40.1) | 47.4 (43.2, 51.9) | 11.5 | 32.2 | <0.0001 | 0.03 |
| | | | | | | | | (<0.0001 [*]) | (0.02 ^{**}) |

| Group | Biomarker | | N | Baseline Geometric Mean (95% CI) | 12-months Geometric Mean (95% CI) | Δ | %Δ | P-Value† | P-value‡ |
|-------|---------------------------|-----------|----|----------------------------------|-----------------------------------|-------|-------|------------|----------|
| | Free Estradiol (pg/mL) | CONTROL | 80 | 0.30 (0.27, 0.34) | 0.32 (0.29, 0.36) | 0.02 | 6.3 | Ref. | |
| | | <84.3% | 33 | 0.35 (0.29, 0.42) | 0.28 (0.22, 0.34) | -0.07 | -20.5 | <0.0001 | Ref. |
| | | 84.3-106% | 43 | 0.30 (0.27, 0.34) | 0.24 (0.21, 0.27) | -0.06 | -21.3 | <0.0001 | 0.60 |
| | | >= 106% | 40 | 0.30 (0.26, 0.36) | 0.20 (0.17, 0.24) | -0.1 | -32.2 | <0.0001 | 0.25 |
| | | | | | | | | (<0.0001*) | (0.20**) |
| | Free Testosterone (pg/mL) | CONTROL | 80 | 4.9 (4.4, 5.6) | 5.1 (4.6, 5.7) | 0.1 | 2.6 | Ref. | |
| | | <84.3% | 33 | 5.6 (4.7, 6.6) | 4.7 (4.0, 5.5) | -0.9 | -16.5 | 0.0007 | Ref. |
| | | 84.3-106% | 43 | 5.2 (4.6, 5.8) | 4.6 (4.1, 5.2) | -0.6 | -10.9 | 0.002 | 0.20 |
| | | >= 106% | 40 | 5.1 (4.5, 5.8) | 4.2 (3.6, 4.8) | -1.0 | -18.9 | <0.0001 | 0.94 |
| | | | | | | | | (<0.0001*) | (0.74**) |

†Testing difference in change from baseline to 12 months in hormones compared to Controls.

‡Testing difference in change from baseline to 12 months in hormones compared to the lowest adherence Group, excluding Controls

*Testing for a trend in change from baseline to 12 months in hormones from Controls through the highest adherence Group

**Testing for a trend in change from baseline to 12 months in hormones from the lowest adherence Group through the highest adherence Group.

Supplementary Table 4: Change in sex hormone levels, stratified by percent change in absolute VO₂ MAX (L/min)

| Group | Biomarker | | N | Baseline Geometric Mean (95% CI) | 12-months Geometric Mean (95% CI) | Δ | %Δ | P-Value† | P-value‡ |
|----------|----------------------------|----------------------------|----|----------------------------------|-----------------------------------|------|------|----------|----------|
| Exercise | Estrone (pg/mL) | CONTROL | 80 | 32.0 (28.6, 35.8) | 34.6 (31.4, 38.1) | 2.6 | 8.1 | Ref. | |
| | | Decrease or increase <3.5% | 24 | 32.7 (27.8, 38.4) | 34.2 (29.6, 39.5) | 1.6 | 4.8 | 0.58 | Ref. |
| | | Increase <3.5-14.3% | 37 | 34.1 (29.9, 38.8) | 31.1 (27.5, 35.3) | -2.9 | -8.6 | 0.0024 | 0.01 |
| | | Increase > 14.3% | 31 | 35.2 (30.8, 40.1) | 34.6 (30.3, 39.4) | -0.6 | -1.7 | 0.14 | 0.31 |
| | | | | | | | | (0.02*) | (0.41**) |
| | Estradiol (pg/mL) | CONTROL | 80 | 10.9 (9.6-12.3) | 11.4 (10.2, 12.8) | 0.5 | 4.9 | Ref. | |
| | | Decrease or increase <3.5% | 24 | 11.7 (9.9,13.9) | 11.5 (9.8, 13.5) | -0.2 | -1.5 | 0.32 | Ref. |
| | | Increase <3.5-14.3% | 37 | 10.6 (9.2, 12.3) | 10.3 (9.1, 11.7) | -0.3 | -3.2 | 0.23 | 0.73 |
| | | Increase > 14.3% | 31 | 11.6 (9.9, 13.6) | 11.1 (9.4,13.1) | -0.5 | -4.2 | 0.28 | 0.68 |
| | | | | | | | | (0.20*) | (0.70**) |
| | Total Testosterone (ng/dL) | CONTROL | 80 | 22.8 (20.2, 25.7) | 23.2 (20.8, 25.9) | 0.4 | 1.8 | Ref. | |
| | | Decrease or increase <3.5% | 24 | 20.1 (17.2, 23.4) | 21.1 (17.3, 25.9) | 1.1 | 5.4 | 0.68 | Ref. |

| Group | Biomarker | | N | Baseline Geometric Mean (95% CI) | 12-months Geometric Mean (95% CI) | Δ | % Δ | P-Value† | P-value‡ |
|-------|----------------------------|-------------------------------|----|---|--|----------|------------|----------------------|-----------------------|
| | | Increase <3.5-14.3% | 37 | 25.6 (22.9, 28.8) | 25.0 (22.1, 28.3) | -0.7 | -2.6 | 0.34 | 0.33 |
| | | Increase > 14.3% | 31 | 26.0 (22.5, 30.1) | 24.7 (20.9, 29.2) | -1.3 | -5.0 | 0.19 | 0.22 |
| | | | | | | | | (0.14 [*]) | (0.22 ^{**}) |
| | Androstenedione (ng/mL) | CONTROL | 80 | 0.49 (0.44, 0.54) | 0.49 (0.45, 0.54) | 0.01 | 1.5 | Ref. | |
| | | Decrease or increase <3.5% | 24 | 0.44 (0.4, 0.48) | 0.49 (0.43, 0.56) | 0.05 | 11.2 | 0.14 | Ref. |
| | | Increase <3.5-14.3% | 37 | 0.51 (0.44, 0.59) | 0.5 (0.44, 0.57) | -0.01 | -1.8 | 0.58 | 0.05 |
| | | Increase > 14.3% | 31 | 0.55 (0.47, 0.63) | 0.55 (0.47, 0.65) | 0 | 0.6 | 0.88 | 0.13 |
| | | | | | | | | (0.68 [*]) | (0.17 ^{**}) |
| | SHBG (nmol/L) | CONTROL | 80 | 34.7 (31.5, 38.2) | 33.7 (30.3, 37.5) | -0.9 | -2.7 | Ref. | |
| | | Decrease or increase <3.5% | 24 | 35.4 (29.7, 42.2) | 34.9 (29.4, 41.3) | -0.5 | -1.4 | 0.72 | Ref. |
| | | Increase <3.5-14.3% | 37 | 38.4 (33.4, 44.2) | 37.8 (32.9, 43.4) | -0.6 | -1.6 | 0.64 | 0.97 |
| | | Increase > 14.3% | 31 | 42.6 (35.9, 50.5) | 42.5 (35.7, 50.7) | -0.08 | -0.2 | 0.42 | 0.81 |
| | | | | | | | | (0.42 [*]) | (0.79 ^{**}) |
| | Free Estradiol (pg/mL) | CONTROL | 79 | 0.30 (0.27, 0.34) | 0.32 (0.29, 0.36) | 0.02 | 6.3 | Ref. | |

| Group | Biomarker | | N | Baseline Geometric Mean (95% CI) | 12-months Geometric Mean (95% CI) | Δ | % Δ | P-Value† | P-value‡ |
|---------------|---------------------------------|-------------------------------|----|---|--|----------|------------|-----------|----------|
| | | Decrease or increase <3.5% | 24 | 0.31 (0.26, 0.38) | 0.31 (0.26, 0.37) | 0 | -0.9 | 0.3 | Ref. |
| | | Increase <3.5- 14.3% | 37 | 0.28 (0.24, 0.33) | 0.27 (0.23, 0.31) | -0.01 | -2.6 | 0.24 | 0.72 |
| | | Increase > 14.3% | 31 | 0.29 (0.24, 0.35) | 0.28 (0.23, 0.34) | -0.01 | -4.3 | 0.26 | 0.61 |
| | | | | | | | | (0.18*) | (0.62**) |
| | Free Testosterone (pg/mL) | CONTROL | 80 | 4.9 (4.4, 5.6) | 5.1 (4.6, 5.7) | 0.1 | 2.6 | Ref. | |
| | | Decrease or increase <3.5% | 24 | 4.3 (3.6, 5.1) | 4.6 (3.8, 5.6) | 0.3 | 6.4 | 0.69 | Ref. |
| | | Increase <3.5- 14.3% | 37 | 5.3 (4.7, 6.0) | 5.2 (4.6, 5.9) | -0.1 | -1.8 | 0.33 | 0.31 |
| | | Increase > 14.3% | 31 | 5.1 (4.4, 5.9) | 4.8 (4.1, 5.7) | -0.3 | -5.1 | 0.12 | 0.15 |
| | | | | | | | | (0.10*) | (0.16**) |
| Diet+Exercise | Estrone (pg/mL) | CONTROL | 80 | 32.0 (28.6, 35.8) | 34.6 (31.4, 38.1) | 2.6 | 8.1 | Ref. | |
| | | Decrease or increase <3.5% | 41 | 35.5 (31.5, 40.0) | 30.4 (26.8, 34.4) | -5.1 | -14.4 | <0.0001 | Ref. |
| | | Increase <3.5- 14.3% | 32 | 32.7 (27.9, 38.3) | 29.6 (25.6, 34.3) | -3.1 | -9.4 | 0.001 | 0.22 |
| | | Increase > 14.3% | 31 | 33.6 (29.2, 38.7) | 30.5 (26.5, 35.2) | -3.2 | -9.4 | 0.002 | 0.26 |
| | | | | | | | | (<0.001*) | (0.23**) |

| Group | Biomarker | | N | Baseline Geometric Mean (95% CI) | 12-months Geometric Mean (95% CI) | Δ | % Δ | P-Value† | P-value‡ |
|-------|----------------------------------|-------------------------------|----|---|--|----------|------------|-----------|----------|
| | Estradiol (pg/mL) | CONTROL | 80 | 10.9 (9.6, 12.3) | 11.4 (10.2, 12.8) | 0.5 | 4.9 | Ref. | |
| | | Decrease or increase <3.5% | 41 | 11.9 (10.3, 13.8) | 8.7 (7.5, 10.2) | -3.2 | -26.9 | <0.0001 | Ref. |
| | | Increase <3.5- 14.3% | 32 | 10.6 (9.0, 12.4) | 8.4 (7.2, 10.0) | -2.1 | -20.1 | <0.0001 | 0.23 |
| | | Increase > 14.3% | 31 | 12.3 (10.5, 14.4) | 10.6 (9.1, 12.4) | -1.7 | -13.7 | 0.006 | 0.05 |
| | | | | | | | | (<0.001*) | (0.05**) |
| | Total Testosterone (ng/dL) | CONTROL | 80 | 22.8 (20.2, 25.7) | 23.2 (20.8, 25.9) | 0.4 | 1.8 | Ref. | |
| | | Decrease or increase <3.5% | 41 | 24.6 (21.7, 27.9) | 22.6 (20.0, 25.6) | -2.0 | -8.1 | 0.02 | Ref. |
| | | Increase <3.5- 14.3% | 32 | 22.6 (19.8, 25.8) | 20.5 (17.7, 23.7) | -2.1 | -9.4 | 0.007 | 0.76 |
| | | Increase > 14.3% | 31 | 23.3 (20.4, 26.7) | 23.9 (20.7, 27.6) | 0.6 | 2.7 | 0.90 | 0.025 |
| | | | | | | | | (0.48*) | (0.04**) |
| | Androstenedione (ng/mL) | CONTROL | 80 | 0.49 (0.44, 0.54) | 0.49 (0.45, 0.54) | 0.01 | 1.5 | Ref. | |
| | | Decrease or increase <3.5% | 41 | 0.54 (0.48, 0.61) | 0.49 (0.44, 0.56) | -0.05 | -9.0 | 0.11 | Ref. |
| | | Increase <3.5- 14.3% | 32 | 0.51 (0.45, 0.58) | 0.48 (0.43, 0.54) | -0.03 | -6.5 | 0.19 | 0.71 |

| Group | Biomarker | | N | Baseline Geometric Mean (95% CI) | 12-months Geometric Mean (95% CI) | Δ | % Δ | P-Value† | P-value‡ |
|-------|---------------------------------|-------------------------------|----|---|--|----------|------------|------------------------------------|-------------------------------|
| | | Increase > 14.3% | 31 | 0.54 (0.48, 0.62) | 0.57 (0.48, 0.66) | 0.02 | 4.3 | 0.72 (0.95 [*]) | 0.09 (0.10 ^{**}) |
| | SHBG (nmol/L) | CONTROL | 80 | 34.7 (31.5, 38.2) | 33.7 (30.3, 37.5) | -0.9 | -2.7 | Ref. | |
| | | Decrease or increase <3.5% | 41 | 34.8 (31.5, 38.6) | 41.2 (36.9, 45.9) | 6.3 | 18.1 | <0.0001 | Ref. |
| | | Increase <3.5- 14.3% | 32 | 34.0 (29.9, 38.8) | 43.3 (38.5, 48.8) | 9.3 | 27.4 | <0.0001 | 0.15 |
| | | Increase > 14.3% | 31 | 33.3 (29.2, 38.0) | 43.4 (39.1, 48.3) | 10.1 | 30.4 | <0.0001 (<0.0001 [†]) | 0.07 (0.06 ^{**}) |
| | Free Estradiol (pg/mL) | CONTROL | 79 | 0.30 (0.27, 0.34) | 0.32 (0.29, 0.36) | 0.02 | 6.3 | Ref. | |
| | | Decrease or increase <3.5% | 41 | 0.32 (0.28, 0.38) | 0.22 (0.19, 0.26) | -0.1 | -30.8 | <0.0001 | Ref. |
| | | Increase <3.5- 14.3% | 32 | 0.29 (0.24, 0.34) | 0.21 (0.18, 0.26) | -0.07 | -26.0 | <0.0001 | 0.40 |
| | | Increase > 14.3% | 31 | 0.34 (0.28, 0.40) | 0.27 (0.23, 0.32) | -0.07 | -20.4 | 0.0001 (<0.0001 [†]) | 0.11 (0.12 ^{**}) |
| | Free Testosterone (pg/mL) | CONTROL | 80 | 4.9 (4.4, 5.6) | 5.1 (4.6, 5.7) | 0.1 | 2.6 | Ref. | |
| | | Decrease or increase <3.5% | 41 | 5.4 (4.8, 6.0) | 4.6 (4.0, 5.1) | -0.8 | -15.4 | <0.0001 | Ref. |

| Group | Biomarker | | N | Baseline Geometric Mean (95% CI) | 12-months Geometric Mean (95% CI) | Δ | % Δ | P-Value† | P-value‡ |
|-------|-----------|-------------------------|----|---|--|----------|------------|-----------|----------|
| | | Increase <3.5- 14.3% | 32 | 5.0 (4.4, 5.7) | 4.0 (3.4, 4.7) | -1.0 | -19.2 | <0.0001 | 0.35 |
| | | Increase > 14.3% | 31 | 5.2 (4.4, 6.1) | 4.7 (4.0, 5.5) | -0.5 | -9.0 | 0.01 | 0.16 |
| | | | | | | | | (<0.001*) | (0.21**) |

†Testing difference in change from baseline to 12 months in hormones compared to Controls.

‡Testing difference in change from baseline to 12 months in hormones compared to Decrease or Increase <3.5% Group, excluding Controls

*Testing for a trend in change from baseline to 12 months in hormones from Controls through increase \geq 14.3% Group

**Testing for a trend in change from baseline to 12 months in hormones from Decrease or Increase <3.5% Group through Increase \geq 14.3% Group.

Supplementary Table 5: Change in sex hormone levels, stratified by change in steps/day

| Group | Biomarker | | N | Baseline Geometric Mean (95% CI) | 12-months Geometric Mean (95% CI) | Δ | % Δ | P-Value† | P-value‡ |
|-------------------------|----------------------------------|------------------------|----|---|--|----------|------------|----------------------|-----------------------|
| Exercise (steps/day) | Estrone (pg/mL) | CONTROL | 80 | 32.0 (28.6, 35.8) | 34.6 (31.4, 38.1) | 2.6 | 8.1 | Ref. | |
| | | <2000 steps/day | 26 | 33.7 (29.2, 38.9) | 33.1 (28.5, 38.4) | -0.6 | -1.9 | 0.11 | Ref. |
| | | 2000-5000 steps/day | 35 | 33.2 (28.9, 38.1) | 32.0 (27.9, 36.8) | -1.1 | -3.4 | 0.03 | 0.77 |
| | | >5000 steps/day | 21 | 34.1 (28.8, 40.5) | 35.1 (30.3, 40.7) | 1.0 | 2.9 | 0.48 | 0.49 |
| | | | | | | | | (0.15 [†]) | (0.52 ^{**}) |
| | Estradiol (pg/mL) | CONTROL | 80 | 10.9 (9.6-12.3) | 11.4 (10.2, 12.8) | 0.5 | 4.9 | Ref. | |
| | | <2000 steps/day | 26 | 11.3 (9.6,13.3) | 11.4 (9.9, 13.2) | 0.1 | 1.0 | 0.67 | Ref. |
| | | 2000-5000 steps/day | 35 | 11.3 (9.6, 13.3) | 10.7 (9.2, 12.5) | -0.6 | -5.5 | 0.10 | 0.26 |
| | | >5000 steps/day | 21 | 10.0 (8.3, 12.1) | 10.1 (8.3,12.3) | 0.09 | 0.9 | 0.71 | 0.99 |
| | | | | | | | | (0.31 [†]) | (0.93 ^{**}) |
| | Total Testosterone (ng/dL) | CONTROL | 80 | 22.8 (20.2, 25.7) | 23.2 (20.8, 25.9) | 0.4 | 1.8 | Ref. | |
| | | <2000 steps/day | 26 | 24.9 (21.9, 28.3) | 25.3 (22.3, 28.7) | 0.4 | 1.7 | 0.95 | Ref. |

| Group | Biomarker | | N | Baseline Geometric Mean (95% CI) | 12-months Geometric Mean (95% CI) | Δ | %Δ | P-Value† | P-value‡ |
|-------|----------------------------|------------------------|----|---|--|-------|------|----------------------|------------------------|
| | | 2000-5000 steps/day | 35 | 24.3 (21.0, 28.3) | 24.8 (21.0, 29.3) | 0.5 | 2.0 | 1.0 | 0.96 |
| | | >5000 steps/day | 21 | 25.3 (21.3, 30.0) | 24.6 (21.0, 28.9) | -0.6 | -2.6 | 0.37 | 0.51 |
| | | | | | | | | (0.56 [†]) | (0.53 ^{**}) |
| | Androstenedione (ng/mL) | CONTROL | 80 | 0.49 (0.44, 0.54) | 0.49 (0.45, 0.54) | 0.01 | 1.5 | Ref. | |
| | | <2000 steps/day | 26 | 0.53 (0.44, 0.63) | 0.54 (0.45, 0.65) | 0.01 | 1.9 | 0.97 | Ref. |
| | | 2000-5000 steps/day | 35 | 0.48 (0.43, 0.54) | 0.47 (0.42, 0.53) | -0.01 | -1.3 | 0.61 | 0.67 |
| | | >5000 steps/day | 21 | 0.56 (0.49, 0.65) | 0.59 (0.51, 0.69) | 0.03 | 4.7 | 0.67 | 0.75 |
| | | | | | | | | (0.95 [†]) | (0.79 ^{**}) |
| | SHBG (nmol/L) | CONTROL | 80 | 34.7 (31.5, 38.2) | 33.7 (30.3, 37.5) | -0.9 | -2.7 | Ref. | |
| | | <2000 steps/day | 26 | 42.9 (34.5, 53.4) | 40.7 (33.1, 50.1) | -2.2 | -5.0 | 0.56 | Ref. |
| | | 2000-5000 steps/day | 35 | 42.6 (37.8, 47.9) | 43.1 (38.1, 48.8) | 0.5 | 1.2 | 0.17 | 0.06 |
| | | >5000 steps/day | 21 | 35.1 (29.2, 42.2) | 37.7 (31.4, 45.3) | 2.7 | 7.6 | 0.01 | 0.003 |
| | | | | | | | | (0.01 [†]) | (<0.01 ^{**}) |
| | Free Estradiol (pg/mL) | CONTROL | 79 | 0.30 (0.27, 0.34) | 0.32 (0.29, 0.36) | 0.02 | 6.3 | Ref. | |
| | | <2000 steps/day | 26 | 0.28 (0.23, 0.34) | 0.29 (0.24, 0.35) | 0.01 | 3.2 | 0.94 | Ref. |

| Group | Biomarker | | N | Baseline Geometric Mean (95% CI) | 12-months Geometric Mean (95% CI) | Δ | %Δ | P-Value† | P-value‡ |
|------------------------------|---------------------------------|------------------------|----|---|--|-------|-------|------------------------|-----------------------|
| | | 2000-5000 steps/day | 35 | 0.29 (0.24, 0.34) | 0.27 (0.23, 0.32) | -0.02 | -6.1 | 0.07 | 0.11 |
| | | >5000 steps/day | 21 | 0.27 (0.22, 0.34) | 0.27 (0.21, 0.34) | 0 | -1.3 | 0.51 | 0.57 |
| | | | | | | | | (0.18 [†]) | (0.51 ^{**}) |
| | Free Testosterone (pg/mL) | CONTROL | 80 | 4.9 (4.4, 5.6) | 5.1 (4.6, 5.7) | 0.1 | 2.6 | Ref. | |
| | | <2000 steps/day | 26 | 4.8 (4.3, 5.4) | 5.0 (4.4, 5.7) | 0.2 | 4.8 | 0.79 | Ref. |
| | | 2000-5000 steps/day | 35 | 4.8 (4.2, 5.6) | 4.9 (4.2, 5.7) | 0.06 | 1.3 | 0.76 | 0.63 |
| | | >5000 steps/day | 21 | 5.5 (4.6, 6.6) | 5.2 (4.4, 6.1) | -0.3 | -5.8 | 0.08 | 0.08 |
| | | | | | | | | (0.20 [†]) | (0.09 ^{**}) |
| Diet+Exercise (steps/day) | Estrone (pg/mL) | CONTROL | 80 | 32.0 (28.6, 35.8) | 34.6 (31.4, 38.1) | 2.6 | 8.1 | Ref. | |
| | | <2000 steps/day | 24 | 34.5 (29.7, 40.1) | 30.1 (25.1, 36.0) | -4.4 | -12.9 | 0.0006 | Ref. |
| | | 2000-5000 steps/day | 36 | 34.2 (29.4, 39.8) | 29.4 (25.5, 33.8) | -4.9 | -14.3 | <0.0001 | 0.78 |
| | | >5000 steps/day | 38 | 32.9 (29.0, 37.4) | 30.5 (27.1, 34.3) | -2.4 | -7.3 | 0.003 | 0.28 |
| | | | | | | | | (0.0004 [†]) | (0.21 ^{**}) |
| | Estradiol (pg/mL) | CONTROL | 80 | 10.9 (9.6, 12.3) | 11.4 (10.2, 12.8) | 0.5 | 4.9 | Ref. | |

| Group | Biomarker | | N | Baseline Geometric Mean (95% CI) | 12-months Geometric Mean (95% CI) | Δ | %Δ | P-Value† | P-value‡ |
|-------|----------------------------------|------------------------|----|---|--|-------|-------|------------------------|-----------------------|
| | | <2000 steps/day | 24 | 11.6 (9.8, 13.8) | 9.0 (7.5, 10.8) | -2.6 | -22.5 | <0.0001 | Ref. |
| | | 2000-5000 steps/day | 36 | 12.6 (10.9, 14.6) | 9.7 (8.3, 11.4) | -2.9 | -23.0 | <0.0001 | 0.92 |
| | | >5000 steps/day | 38 | 10.7 (9.1, 12.5) | 8.6 (7.4, 9.9) | -2.1 | -19.7 | 0.002 | 0.69 |
| | | | | | | | | (0.0001 [†]) | (0.67 ^{**}) |
| | Total Testosterone (ng/dL) | CONTROL | 80 | 22.8 (20.2, 25.7) | 23.2 (20.8, 25.9) | 0.4 | 1.8 | Ref. | |
| | | <2000 steps/day | 24 | 22.9 (19.9, 26.5) | 21.4 (18.7, 24.6) | -1.5 | -6.6 | 0.12 | Ref. |
| | | 2000-5000 steps/day | 36 | 24.2 (21.2, 27.6) | 22.3 (19.4, 25.6) | -1.9 | -7.9 | 0.02 | 0.82 |
| | | >5000 steps/day | 38 | 23.3 (20.4, 26.7) | 23.0 (19.9, 26.6) | -0.4 | -1.5 | 0.43 | 0.36 |
| | | | | | | | | (0.20 [†]) | (0.29 ^{**}) |
| | Androstenedione (ng/mL) | CONTROL | 80 | 0.49 (0.44, 0.54) | 0.49 (0.45, 0.54) | 0.01 | 1.5 | Ref. | |
| | | <2000 steps/day | 24 | 0.54 (0.45, 0.64) | 0.49 (0.41, 0.60) | -0.04 | -8.1 | 0.25 | Ref. |
| | | 2000-5000 steps/day | 36 | 0.50 (0.44, 0.56) | 0.48 (0.42, 0.55) | -0.01 | -2.7 | 0.51 | 0.54 |
| | | >5000 steps/day | 38 | 0.57 (0.50, 0.63) | 0.54 (0.49, 0.60) | -0.02 | -4.3 | 0.39 | 0.67 |
| | | | | | | | | (0.39 [†]) | (0.71 ^{**}) |

| Group | Biomarker | | N | Baseline Geometric Mean (95% CI) | 12-months Geometric Mean (95% CI) | Δ | %Δ | P-Value† | P-value‡ |
|-------|---------------------------------|------------------------|----|---|--|-------|-------|-------------------------|--------------------------|
| | SHBG (nmol/L) | CONTROL | 80 | 34.7 (31.5, 38.2) | 33.7 (30.3, 37.5) | -0.9 | -2.7 | Ref. | |
| | | <2000 steps/day | 24 | 33.8 (28.4, 40.3) | 37.6 (32.4, 43.7) | 3.8 | 11.2 | 0.005 | Ref. |
| | | 2000-5000 steps/day | 36 | 36.2 (32.8, 40.1) | 44.2 (40.0, 48.8) | 7.9 | 21.9 | <0.0001 | 0.09 |
| | | >5000 steps/day | 38 | 32.8 (29.6, 36.4) | 45.3 (41.3, 49.7) | 12.4 | 37.9 | <0.0001 | 0.0002 |
| | | | | | | | | (<0.0001 [†]) | (<0.0001 ^{**}) |
| | Free Estradiol (pg/mL) | CONTROL | 79 | 0.30 (0.27, 0.34) | 0.32 (0.29, 0.36) | 0.02 | 6.3 | Ref. | |
| | | <2000 steps/day | 24 | 0.32 (0.26, 0.38) | 0.24 (0.19, 0.29) | -0.08 | -24.6 | <0.0001 | Ref. |
| | | 2000-5000 steps/day | 36 | 0.34 (0.29, 0.40) | 0.25 (0.21, 0.29) | -0.1 | -27.9 | <0.0001 | 0.54 |
| | | >5000 steps/day | 38 | 0.30 (0.25, 0.35) | 0.21 (0.18, 0.25) | -0.08 | -27.5 | <0.0001 | 0.68 |
| | | | | | | | | (<0.0001 [†]) | (0.72 ^{**}) |
| | Free Testosterone (pg/mL) | CONTROL | 80 | 4.9 (4.4, 5.6) | 5.1 (4.6, 5.7) | 0.1 | 2.6 | Ref. | |
| | | <2000 steps/day | 24 | 5.0 (4.5, 5.7) | 4.5 (4.0, 5.1) | -0.5 | -10.6 | 0.001 | Ref. |
| | | 2000-5000 steps/day | 36 | 5.2 (4.5, 6.0) | 4.4 (3.7, 5.1) | -0.9 | -16.4 | <0.0001 | 0.27 |
| | | >5000 steps/day | 38 | 5.3 (4.6, 6.0) | 4.4 (3.8, 5.2) | -0.8 | -15.5 | <0.0001 | 0.32 |

| Group | Biomarker | | N | Baseline Geometric Mean (95% CI) | 12-months Geometric Mean (95% CI) | Δ | % Δ | P-Value† | P-value‡ |
|-------|-----------|--|---|----------------------------------|-----------------------------------|----------|------------|-------------------------|-----------------------|
| | | | | | | | | (<0.0001 [†]) | (0.37 ^{**}) |

[†]Testing difference in change from baseline to 12 months in hormones compared to Controls.

[‡]Testing difference in change from baseline to 12 months in hormones compared to <2000 Steps/Day Group, excluding Controls

^{*}Testing for a trend in change from baseline to 12 months in hormones from Controls through > 5000 Steps/Day Group

^{**}Testing for a trend in change from baseline to 12 months in hormones from <2000 Steps/Day Group through > 5000 Steps/Day Group.

| Group | Biomarker | | N | Baseline Geometric Mean (95% CI) | 12-months Geometric Mean (95% CI) | Δ | % Δ | P-Value† | P-value‡ |
|-------|-------------------------|-----------------|----|----------------------------------|-----------------------------------|----------|------------|----------------------|-----------------------|
| | | | | | | | | (0.50 [†]) | (0.39 ^{**}) |
| | Androstenedione (ng/mL) | CONTROL | 80 | 0.49 (0.44, 0.54) | 0.49 (0.45, 0.54) | 0.01 | 1.5 | Ref. | |
| | | <= 154 mins/wk | 38 | 0.48 (0.43, 0.55) | 0.44 (0.38, 0.51) | -0.04 | -8.4 | 0.46 | Ref. |
| | | 154-196 mins/wk | 38 | 0.49 (0.43, 0.57) | 0.49 (0.42, 0.57) | -0.01 | -1.1 | 0.67 | 0.81 |
| | | >196 mins/wk | 34 | 0.53 (0.47, 0.60) | 0.56 (0.49, 0.63) | 0.02 | 4.0 | 0.69 | 0.31 |
| | | | | | | | | (0.85 [†]) | (0.29 ^{**}) |
| | SHBG (nmol/L) | CONTROL | 80 | 34.7 (31.5, 38.2) | 33.7 (30.3, 37.5) | -0.9 | -2.7 | Ref. | |
| | | <= 154 mins/wk | 38 | 39.8 (34.2, 46.3) | 38.8 (32.3, 46.6) | -0.9 | -2.4 | 0.95 | Ref. |
| | | 154-196 mins/wk | 38 | 35.0 (30.5, 40.2) | 36.0 (31.3, 41.4) | 1.0 | 2.8 | 0.06 | 0.16 |
| | | >196 mins/wk | 34 | 43.4 (37.5, 50.4) | 42.3 (36.9, 48.5) | -1.1 | -2.6 | 0.88 | 0.86 |
| | | | | | | | | (0.44 [†]) | (0.91 ^{**}) |
| | Free Estradiol (pg/mL) | CONTROL | 79 | 0.30 (0.27, 0.34) | 0.32 (0.29, 0.36) | 0.02 | 6.3 | Ref. | |
| | | <= 154 mins/wk | 38 | 0.33 (0.29, 0.39) | 0.31 (0.27, 0.37) | -0.02 | -6.5 | 0.08 | Ref. |
| | | 154-196 mins/wk | 38 | 0.32 (0.27, 0.37) | 0.31 (0.26, 0.36) | -0.01 | -2.8 | 0.20 | 0.44 |
| | | >196 mins/wk | 34 | 0.25 (0.21, 0.29) | 0.24 (0.21, 0.29) | 0 | -1.6 | 0.39 | 0.40 |
| | | | | | | | | (0.30 [†]) | (0.42 ^{**}) |

| Group | Biomarker | | N | Baseline Geometric Mean (95% CI) | 12-months Geometric Mean (95% CI) | Δ | % Δ | P-Value† | P- value‡ |
|---------------|---------------------------------|-----------------|----|---|--|----------|------------|-------------------------|-----------------------|
| | Free Testosterone (pg/mL) | CONTROL | 80 | 4.9 (4.4, 5.6) | 5.1 (4.6, 5.7) | 0.1 | 2.6 | Ref. | |
| | | <= 154 mins/wk | 38 | 5.4 (4.7, 6.1) | 4.7 (4.0, 5.4) | -0.7 | -13.0 | 0.05 | Ref. |
| | | 154-196 mins/wk | 38 | 5.1 (4.5, 5.7) | 5.2 (4.4, 6.0) | 0.07 | 1.3 | 0.77 | 0.19 |
| | | >196 mins/wk | 34 | 4.7 (4.1, 5.5) | 4.7 (4.1, 5.3) | -0.08 | -1.7 | 0.29 | 0.26 |
| | | | | | | | | (0.45 [*]) | (0.29 ^{**}) |
| Diet+Exercise | Estrone (pg/mL) | CONTROL | 80 | 32.0 (28.6, 35.8) | 34.6 (31.4, 38.1) | 2.6 | 8.1 | Ref. | |
| | | <= 154 mins/wk | 39 | 34.7 (30.7, 39.3) | 30.1 (27.1, 33.4) | -4.7 | -13.4 | <0.0001 | Ref. |
| | | 154-196 mins/wk | 36 | 34.0 (29.4, 39.2) | 32.1 (28.0, 36.7) | -1.9 | -5.6 | 0.01 | 0.03 |
| | | >196 mins/wk | 41 | 33.2 (29.1, 37.9) | 28.7 (25.0, 32.9) | -4.5 | -13.5 | <0.0001 | 0.54 |
| | | | | | | | | (<0.0001 [*]) | (0.67 ^{**}) |
| | Estradiol (pg/mL) | CONTROL | 80 | 10.9 (9.6-12.3) | 11.4 (10.2, 12.8) | 0.5 | 4.9 | Ref. | |
| | | <= 154 mins/wk | 39 | 11.5 (9.9,13.4) | 9.3 (7.9, 10.9) | -2.2 | -19.4 | <0.0001 | Ref. |
| | | 154-196 mins/wk | 36 | 11.4 (9.7, 13.3) | 9.5 (8.1, 11.3) | -1.8 | -16.2 | 0.0002 | 0.26 |
| | | >196 mins/wk | 41 | 11.7 (10.1, 13.4) | 8.8 (7.7,10.1) | -2.9 | -24.5 | 0.0001 | 0.68 |
| | | | | | | | | (<0.0001 [*]) | (0.62 ^{**}) |

| Group | Biomarker | | N | Baseline Geometric Mean (95% CI) | 12-months Geometric Mean (95% CI) | Δ | % Δ | P-Value† | P- value‡ |
|-------|----------------------------------|-----------------|----|---|--|----------|------------|-------------------------|-----------------------|
| | Total Testosterone (ng/dL) | CONTROL | 80 | 22.8 (20.2, 25.7) | 23.2 (20.8, 25.9) | 0.4 | 1.8 | Ref. | |
| | | <= 154 mins/wk | 39 | 25.9 (22.4, 30.0) | 23.3 (20.7, 26.3) | -2.6 | -10.0 | 0.004 | Ref. |
| | | 154-196 mins/wk | 36 | 22.5 (19.6, 25.8) | 22.8 (19.8, 26.2) | 0.3 | 1.2 | 0.84 | 0.008 |
| | | >196 mins/wk | 41 | 23.4 (20.8, 26.3) | 21.7 (18.9, 24.9) | -1.7 | -7.1 | 0.03 | 0.21 |
| | | | | | | | | (0.13 [†]) | (0.29 ^{**}) |
| | Androstenedione (ng/mL) | CONTROL | 80 | 0.49 (0.44, 0.54) | 0.49 (0.45, 0.54) | 0.01 | 1.5 | Ref. | |
| | | <= 154 mins/wk | 39 | 0.54 (0.47, 0.63) | 0.51 (0.46, 0.56) | -0.04 | -6.8 | 0.04 | Ref. |
| | | 154-196 mins/wk | 36 | 0.51 (0.45, 0.59) | 0.54 (0.47, 0.63) | 0.03 | 5.8 | 0.56 | 0.02 |
| | | >196 mins/wk | 41 | 0.52 (0.48, 0.57) | 0.48 (0.42, 0.55) | -0.04 | -8.1 | 0.13 | 0.66 |
| | | | | | | | | (0.35 [†]) | (0.82 ^{**}) |
| | SHBG (nmol/L) | CONTROL | 80 | 34.7 (31.5, 38.2) | 33.7 (30.3, 37.5) | -0.9 | -2.7 | Ref. | |
| | | <= 154 mins/wk | 39 | 35.1 (31.4, 39.2) | 43.4 (38.9, 48.6) | 8.4 | 23.9 | <0.0001 | Ref. |
| | | 154-196 mins/wk | 36 | 31.6 (28.0, 35.8) | 39.4 (34.9, 44.4) | 7.7 | 24.5 | <0.0001 | 0.32 |
| | | >196 mins/wk | 41 | 35.4 (31.8, 39.4) | 45.7 (41.6, 50.2) | 10.4 | 29.3 | <0.0001 | 0.1 |
| | | | | | | | | (<0.0001 [†]) | (0.09 ^{**}) |

| Group | Biomarker | | N | Baseline Geometric Mean (95% CI) | 12-months Geometric Mean (95% CI) | Δ | % Δ | P-Value† | P-value‡ |
|-------|---------------------------|-----------------|----|----------------------------------|-----------------------------------|----------|------------|------------|----------|
| | Free Estradiol (pg/mL) | CONTROL | 79 | 0.30 (0.27, 0.34) | 0.32 (0.29, 0.36) | 0.02 | 6.3 | Ref. | |
| | | <= 154 mins/wk | 39 | 0.31 (0.27, 0.36) | 0.24 (0.20, 0.27) | -0.08 | -24.7 | <0.0001 | Ref. |
| | | 154-196 mins/wk | 36 | 0.32 (0.27, 0.38) | 0.25 (0.21, 0.30) | -0.07 | -21.6 | <0.0001 | 0.40 |
| | | >196 mins/wk | 41 | 0.32 (0.27, 0.37) | 0.22 (0.19, 0.26) | -0.1 | -30.6 | <0.0001 | 0.48 |
| | | | | | | | | (<0.0001*) | (0.42**) |
| | Free Testosterone (pg/mL) | CONTROL | 80 | 4.9 (4.4, 5.6) | 5.1 (4.6, 5.7) | 0.1 | 2.6 | Ref. | |
| | | <= 154 mins/wk | 39 | 5.7 (4.9, 6.5) | 4.6 (4.1, 5.2) | -1.1 | -18.8 | <0.0001 | Ref. |
| | | 154-196 mins/wk | 36 | 5.1 (4.4, 5.9) | 4.7 (4.0, 5.4) | -0.4 | -8.5 | 0.02 | 0.03 |
| | | >196 mins/wk | 41 | 5.1 (4.5, 5.7) | 4.2 (3.6, 4.8) | -0.9 | -17.9 | <0.0001 | 0.59 |
| | | | | | | | | (<0.0001*) | (0.73**) |

†Testing difference in change from baseline to 12 months in hormones compared to Controls.

‡Testing difference in change from baseline to 12 months in hormones compared to the lowest adherence Group, excluding Controls

*Testing for a trend in change from baseline to 12 months in hormones from Controls through the highest adherence Group

**Testing for a trend in change from baseline to 12 months in hormones from the lowest adherence Group through the highest adherence Group.