Supplemental Table 1. Variance changes for specific femoral bone traits in 5-month-old mice versus 19-month-old mice

|          | 5m.o. mean | 19m.o. mean | P (t-test) | 5m.o. variance | 19m.o. variance | P (Levene test) |
|----------|------------|-------------|------------|----------------|-----------------|-----------------|
| TV       | 4.8        | 5.7         | 5.9E-12    | 0.5            | 0.2             | 4.8E-03         |
| BV       | 2.4        | 2.5         | 2.7E-03    | 0.1            | 0.1             | 0.4             |
| BV.TV    | 49.5       | 44.3        | 8.2E-22    | 4.8            | 5.7             | 0.4             |
| TS       | 18.8       | 20.7        | 5.6E-09    | 3.2            | 1.4             | 3.2E-03         |
| TS.per.  | 13.6       | 14.7        | 6.0E-09    | 1.1            | 0.5             | 8.4E-04         |
| BS       | 28.4       | 31.4        | 2.0E-07    | 10.1           | 4.9             | 2.4E-02         |
| BS.per.  | 23.9       | 26.5        | 2.8E-09    | 5.3            | 2.6             | 6.6E-03         |
| BS.BV    | 12.0       | 12.5        | 1.0E-03    | 0.2            | 1.0             | 5.9E-03         |
| T.Ar     | 1.9        | 2.3         | 5.9E-12    | 0.1            | 3.7E-02         | 4.8E-03         |
| T.Pm     | 5.4        | 5.9         | 6.0E-09    | 0.2            | 0.1             | 8.4E-04         |
| B.Ar     | 0.9        | 1.0         | 2.7E-03    | 1.3E-02        | 1.0E-02         | 0.4             |
| B.Pm     | 9.6        | 10.6        | 2.8E-09    | 0.8            | 0.4             | 6.6E-03         |
| Ecc      | 0.8        | 0.8         | 1.5E-18    | 3.2E-04        | 8.5E-04         | 1.4E-03         |
| Cs.Th    | 0.2        | 0.2         | 2.8E-03    | 6.8E-05        | 2.2E-04         | 1.7E-03         |
| Po.cl.   | 50.2       | 55.0        | 4.1E-14    | 6.8            | 10.6            | 0.4             |
| endosteal| 4.1        | 4.7         | 1.4E-08    | 0.3            | 0.2             | 0.1             |
| Med.area | 1.0        | 1.3         | 1.5E-17    | 2.7E-02        | 1.4E-02         | 1.4E-02         |

**abbreviations**: TV - total volume; BV - bone volume; BV.TV - percent bone volume; TS - tissue surface; TS.per. - tissue surface percent; BS - bone surface; BS.per. bone surface percent; BS.BV - bone surface/volume ratio; T.Ar - mean total crosssectional tissue area; T.Pm - mean total crosssectional tissue perimeter; B.Ar mean total crosssectional bone area; B.Pm - mean total crosssectional bone perimeter; Ecc - eccentricity; Cs.Th - cross sectional thickness; Po.cl. - closed porosity; endosteal - endosteal perimeter; Med.area - medullary area. N=50 for 5 month old animals, N=64 19 month old animals.
Supplemental table 2. Age-related metrics for mid diaphysis femoral cortical bone in male 19-36 month old untreated animals.

| Phenotype | N  | β   | SE  | P      |
|-----------|----|-----|-----|--------|
| TV        | 50 | 0.143 | 0.008 | 7.0E-23 |
| BV        | 50 | -0.064 | 0.009 | 9.7E-09 |
| BV.TV     | 50 | -1.838 | 0.133 | 3.0E-16 |
| TS        | 50 | 0.657 | 0.037 | 1.2E-21 |
| TS.per.   | 50 | 0.208 | 0.009 | 1.4E-27 |
| BS        | 50 | 1.426 | 0.172 | 8.3E-10 |
| BS.per.   | 50 | 0.931 | 0.120 | 3.9E-09 |
| BS.BV     | 50 | 0.856 | 0.068 | 8.6E-15 |
| T.Ar      | 50 | 0.057 | 0.003 | 6.8E-23 |
| T.Pm      | 50 | 0.083 | 0.004 | 1.4E-27 |
| B.Ar      | 50 | -0.026 | 0.004 | 9.7E-09 |
| B.Pm      | 50 | 0.373 | 0.048 | 3.9E-09 |
| Ecc       | 50 | -0.005 | 0.001 | 2.5E-04 |
| Cs.Th     | 50 | -0.009 | 0.001 | 7.9E-15 |
| Po.cl.    | 50 | 1.213 | 0.312 | 3.5E-04 |
| endosteal | 50 | 0.282 | 0.045 | 4.1E-07 |
| Med.area  | 50 | 0.086 | 0.005 | 2.1E-20 |

**Abbreviations:** TV - total volume; BV - bone volume; BV.TV - percent bone volume; TS - tissue surface; TS.per. - tissue surface percent; BS - bone surface; BS.per. bone surface percent; BS.BV - bone surface/volume ratio; T.Ar - mean total crosssectional tissue area; T.Pm - mean total crosssectional tissue perimeter; B.Ar mean total crosssectional bone area; B.Pm - mean total crosssectional bone perimeter; Ecc - eccentricity; Cs.Th - cross sectional thickness; Po.cl. - closed porosity; endosteal - endosteal perimeter; Med.area - medullary area; N - total number of male animals measured; β - calculated mean outcome of phenotype per 100 days between 19 and 36 months of age; SE - standard error of the mean; P - p value
Supplemental table 3. Age-related metrics for mid diaphysis femoral cortical bone in female 19-36 month old untreated animals.

| Phenotype | N  | β    | SE_females | P       |
|-----------|----|------|------------|---------|
| TV        | 39 | 0.221| 0.015      | 6.5E-17 |
| BV        | 39 | -0.033| 0.012      | 0.007   |
| BV.TV     | 39 | -2.144| 0.174      | 5.4E-14 |
| TS        | 39 | 0.800| 0.077      | 7.2E-12 |
| TS.per.   | 39 | 0.310| 0.023      | 1.6E-15 |
| BS        | 39 | 1.228| 0.302      | 2.7E-04 |
| BS.per.   | 39 | 0.874| 0.212      | 2.3E-04 |
| BS.BV     | 39 | 0.727| 0.115      | 4.1E-04 |
| T.Ar      | 39 | 0.088| 0.006      | 6.5E-17 |
| T.Pm      | 39 | 0.124| 0.009      | 1.6E-15 |
| B.Ar      | 39 | -0.013| 0.005      | 0.007   |
| B.Pm      | 39 | 0.350| 0.085      | 2.3E-04 |
| Ecc       | 39 | -0.012| 0.001      | 1.5E-09 |
| Cs.Th     | 39 | -0.008| 0.001      | 8.7E-08 |
| Po.cl.    | 39 | 1.550| 0.581      | 0.012   |
| endosteal | 39 | 0.223| 0.078      | 0.007   |
| Med.area  | 39 | 0.102| 0.006      | 6.6E-20 |

**Abbreviations:** TV - total volume; BV - bone volume; BV.TV - percent bone volume; TS - tissue surface; TS.per. - tissue surface percent; BS - bone surface; BS.per. bone surface percent; BS.BV - bone surface/volume ratio; T.Ar - mean total crosssectional tissue area; T.Pm - mean total crosssectional tissue perimeter; B.Ar mean total crosssectional bone area; B.Pm - mean total crosssectional bone perimeter; Ecc - eccentricity; Cs.Th - cross sectional thickness; Po.cl. - closed porosity; endosteal - endosteal perimeter; Med.area - medullary area; N - total number of male animals measured; β - calculated mean outcome of phenotype per 100 days between 19 and 36 months of age; SE - standard error of the mean; P - p value
Supplemental Tables 4-26; Power calculation of clinically relevant age-related phenotypes.

Power calculation to determine the sample size in each group needed to detect various treatment effects expressed as percent change increase compared to the untreated controls. Power of 0.8 and an alpha level of 0.05 was used, and repeated numbers of measures (N) every 100 days from 19 months of age through 36 months of age to calculate group sizes. Power calculations are based on estimated within and between variation from repeated measures in our control population of aging C57BL/6J mice (max N=138). Variances, and the corresponding power calculations, change for different age-related phenotypes. Supplemental Tables 5-16 (metabolic power tables), show equivalent calculations for multiple metrics over late life. Tables 17-27; femoral bone

| Supplemental Table 4. Bone volume percent (BV.TV) |
|-----------------------------------------------|
| δ   | N_9times | N_8times | N_7times | N_6times | N_5times | N_4times | N_3times |
|-----|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
| 0.05| 402       | 406       | 412       | 423       | 446       | 499       | 659       |
| 0.1 | 100       | 101       | 103       | 106       | 112       | 125       | 165       |
| 0.15| 45        | 45        | 46        | 47        | 50        | 55        | 73        |
| 0.2 | 25        | 25        | 26        | 26        | 28        | 31        | 41        |
| 0.25| 16        | 16        | 16        | 17        | 18        | 20        | 26        |
| 0.3 | 11        | 11        | 11        | 12        | 12        | 14        | 18        |
| 0.35| 8         | 8         | 8         | 9         | 9         | 10        | 13        |
| 0.4 | 6         | 6         | 6         | 7         | 7         | 8         | 10        |

| Supplemental Table 5. Blood glucose (BG) |
|-----------------------------------------|
| δ   | N_9times | N_8times | N_7times | N_6times | N_5times | N_4times | N_3times |
|-----|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
| 0.05| 644       | 666       | 702       | 768       | 900       | 1208      | 2131      |
| 0.1 | 161       | 166       | 176       | 192       | 225       | 302       | 533       |
| 0.15| 72        | 74        | 78        | 85        | 100       | 134       | 237       |
| 0.2 | 40        | 42        | 44        | 48        | 56        | 75        | 133       |
| 0.25| 26        | 27        | 28        | 31        | 36        | 48        | 85        |
| 0.3 | 18        | 18        | 20        | 21        | 25        | 34        | 59        |
| 0.35| 13        | 14        | 14        | 16        | 18        | 25        | 43        |
| 0.4 | 10        | 10        | 11        | 12        | 14        | 19        | 33        |
power tables. If more than ~100 animals per group were calculated to detect significant

Supplemental Table 6. EE.BMN (energy expenditure/body mass at night)

| δ  | N_9times | N_8times | N_7times | N_6times | N_5times | N_4times | N_3times |
|----|----------|----------|----------|----------|----------|----------|----------|
| 0.05 | 2820     | 2850     | 2900     | 2990     | 3169     | 3588     | 4845     |
| 0.1  | 705      | 713      | 725      | 747      | 792      | 897      | 1211     |
| 0.15 | 313      | 317      | 322      | 332      | 352      | 399      | 538      |
| 0.2  | 176      | 178      | 181      | 187      | 198      | 224      | 303      |
| 0.25 | 113      | 114      | 116      | 120      | 127      | 144      | 194      |
| 0.3  | 78       | 79       | 81       | 83       | 88       | 100      | 135      |
| 0.35 | 58       | 58       | 59       | 61       | 65       | 73       | 99       |
| 0.4  | 44       | 45       | 45       | 47       | 50       | 56       | 76       |

Supplemental Table 7. EE.LBMN (energy expenditure/lean body mass night)

| δ  | N_9times | N_8times | N_7times | N_6times | N_5times | N_4times | N_3times |
|----|----------|----------|----------|----------|----------|----------|----------|
| 0.05 | 4110     | 4141     | 4192     | 4284     | 4469     | 4898     | 6187     |
| 0.1  | 1028     | 1035     | 1048     | 1071     | 1117     | 1225     | 1547     |
| 0.15 | 457      | 460      | 466      | 476      | 497      | 544      | 687      |
| 0.2  | 257      | 259      | 262      | 268      | 279      | 306      | 387      |
| 0.25 | 164      | 166      | 168      | 171      | 179      | 196      | 247      |
| 0.3  | 114      | 115      | 116      | 119      | 124      | 136      | 172      |
| 0.35 | 84       | 85       | 86       | 87       | 91       | 100      | 126      |
| 0.4  | 64       | 65       | 66       | 67       | 70       | 77       | 97       |

changes, these variables are not shown. Red box, main text example.
### Supplemental table 8. EE (energy expenditure by night)

| Δ   | N_9times | N_8times | N_7times | N_6times | N_5times | N_4times | N_3times |
|-----|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
| 0.05| 1348      | 1381      | 1436      | 1535      | 1734      | 2196      | 3583      |
| 0.1 | 337       | 345       | 359       | 384       | 433       | 549       | 896       |
| 0.15| 150       | 153       | 160       | 171       | 193       | 244       | 398       |
| 0.2 | 84        | 86        | 90        | 96        | 108       | 137       | 224       |
| 0.25| 54        | 55        | 57        | 61        | 69        | 88        | 143       |
| 0.3 | 37        | 38        | 40        | 43        | 48        | 61        | 100       |
| 0.35| 28        | 28        | 29        | 31        | 35        | 45        | 73        |
| 0.4 | 21        | 22        | 22        | 24        | 27        | 34        | 56        |

### Supplemental Table 9. PMN (meters walked at night)

| Δ   | N_9times | N_8times | N_7times | N_6times | N_5times | N_4times | N_3times |
|-----|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
| 0.05| 259       | 312       | 400       | 559       | 878       | 1620      | 3848      |
| 0.1 | 65        | 78        | 100       | 140       | 219       | 405       | 962       |
| 0.15| 29        | 35        | 44        | 62        | 98        | 180       | 428       |
| 0.2 | 16        | 19        | 25        | 35        | 55        | 101       | 240       |
| 0.25| 10        | 12        | 16        | 22        | 35        | 65        | 154       |
| 0.3 | 7         | 9         | 11        | 16        | 24        | 45        | 107       |
| 0.35| 5         | 6         | 8         | 11        | 18        | 33        | 79        |
| 0.4 | 4         | 5         | 6         | 9         | 14        | 25        | 60        |
### Supplemental Table 10. PSD (speed of walking in day)

| δ   | N_9times | N_8times | N_7times | N_6times | N_5times | N_4times | N_3times |
|-----|----------|----------|----------|----------|----------|----------|----------|
| 0.05| 626      | 652      | 696      | 775      | 933      | 1301     | 2407     |
| 0.1 | 156      | 163      | 174      | 194      | 233      | 325      | 602      |
| 0.15| 70       | 72       | 77       | 86       | 104      | 145      | 267      |
| 0.2 | 39       | 41       | 43       | 48       | 58       | 81       | 150      |
| 0.25| 25       | 26       | 28       | 31       | 37       | 52       | 96       |
| 0.3 | 17       | 18       | 19       | 22       | 26       | 36       | 67       |
| 0.35| 13       | 13       | 14       | 16       | 19       | 27       | 49       |
| 0.4 | 10       | 10       | 11       | 12       | 15       | 20       | 38       |

### Supplemental Table 11. PSN (speed of walking at night)

| δ   | N_9times | N_8times | N_7times | N_6times | N_5times | N_4times | N_3times |
|-----|----------|----------|----------|----------|----------|----------|----------|
| 0.05| 662      | 702      | 768      | 887      | 1125     | 1680     | 3345     |
| 0.1 | 166      | 175      | 192      | 222      | 281      | 420      | 836      |
| 0.15| 74       | 78       | 85       | 99       | 125      | 187      | 372      |
| 0.2 | 41       | 44       | 48       | 55       | 70       | 105      | 209      |
| 0.25| 26       | 28       | 31       | 35       | 45       | 67       | 134      |
| 0.3 | 18       | 20       | 21       | 25       | 31       | 47       | 93       |
| 0.35| 14       | 14       | 16       | 18       | 23       | 34       | 68       |
| 0.4 | 10       | 11       | 12       | 14       | 18       | 26       | 52       |
### Supplemental Table 12. RQN (respiratory quotient at night)

| δ   | N_9times | N_8times | N_7times | N_6times | N_5times | N_4times | N_3times |
|-----|----------|----------|----------|----------|----------|----------|----------|
| 0.05| 717      | 748      | 799      | 892      | 1078     | 1512     | 2813     |
| 0.1 | 179      | 187      | 200      | 223      | 270      | 378      | 703      |
| 0.15| 80       | 83       | 89       | 99       | 120      | 168      | 313      |
| 0.2 | 45       | 47       | 50       | 56       | 67       | 94       | 176      |
| 0.25| 29       | 30       | 32       | 36       | 43       | 60       | 113      |
| 0.3 | 20       | 21       | 22       | 25       | 30       | 42       | 78       |
| 0.35| 15       | 15       | 16       | 18       | 22       | 31       | 57       |
| 0.4 | 11       | 12       | 12       | 14       | 17       | 24       | 44       |

### Supplemental Table 13. VO2N (VO2 at night)

| δ   | N_9times | N_8times | N_7times | N_6times | N_5times | N_4times | N_3times |
|-----|----------|----------|----------|----------|----------|----------|----------|
| 0.05| 587.17   | 613.92   | 658.51   | 738.77   | 899.28   | 1273.81  | 2397.39  |
| 0.1 | 146.79   | 153.48   | 164.63   | 184.69   | 224.82   | 318.45   | 599.35   |
| 0.15| 65.24    | 68.21    | 73.17    | 82.09    | 99.92    | 141.53   | 266.38   |
| 0.2 | 36.7     | 38.37    | 41.16    | 46.17    | 56.2     | 79.61    | 149.84   |
| 0.25| 23.49    | 24.56    | 26.34    | 29.55    | 35.97    | 50.95    | 95.9     |
| 0.3 | 16.31    | 17.05    | 18.29    | 20.52    | 24.98    | 35.38    | 66.59    |
| 0.35| 11.98    | 12.53    | 13.44    | 15.08    | 18.35    | 26       | 48.93    |
| 0.4 | 9.17     | 9.59     | 10.29    | 11.54    | 14.05    | 19.9     | 37.46    |
### Supplemental Table 14. WMN (wheel meters run at night)

| δ   | N_9times | N_8times | N_7times | N_6times | N_5times | N_4times | N_3times |
|-----|----------|----------|----------|----------|----------|----------|----------|
| 0.05| 1102     | 1118     | 1144     | 1192     | 1287     | 1509     | 2176     |
| 0.1 | 275      | 279      | 286      | 298      | 322      | 377      | 544      |
| 0.15| 122      | 124      | 127      | 132      | 143      | 168      | 242      |
| 0.2 | 69       | 70       | 72       | 74       | 80       | 94       | 136      |
| 0.25| 44       | 45       | 46       | 48       | 51       | 60       | 87       |
| 0.3 | 31       | 31       | 32       | 33       | 36       | 42       | 60       |
| 0.35| 22       | 23       | 23       | 24       | 26       | 31       | 44       |
| 0.4 | 17       | 17       | 18       | 19       | 20       | 24       | 34       |

### Supplemental Table 15. WSN (wheel speed run at night)

| δ   | N_9times | N_8times | N_7times | N_6times | N_5times | N_4times | N_3times |
|-----|----------|----------|----------|----------|----------|----------|----------|
| 0.05| 1312     | 1324     | 1342     | 1376     | 1443     | 1600     | 2071     |
| 0.1 | 328      | 331      | 336      | 344      | 361      | 400      | 518      |
| 0.15| 146      | 147      | 149      | 153      | 160      | 178      | 230      |
| 0.2 | 82       | 83       | 84       | 86       | 90       | 100      | 129      |
| 0.25| 52       | 53       | 54       | 55       | 58       | 64       | 83       |
| 0.3 | 36       | 37       | 37       | 38       | 40       | 44       | 58       |
| 0.35| 27       | 27       | 27       | 28       | 29       | 33       | 42       |
| 0.4 | 21       | 21       | 21       | 22       | 23       | 25       | 32       |
Supplemental Table 16. BV (bone volume)

| $\delta$ | N_9times | N_8times | N_7times | N_6times | N_5times | N_4times | N_3times |
|----------|----------|----------|----------|----------|----------|----------|----------|
| 0.05     | 1445     | 1468     | 1507     | 1577     | 1717     | 2044     | 3024     |
| 0.1      | 361      | 367      | 377      | 394      | 429      | 511      | 756      |
| 0.15     | 161      | 163      | 167      | 175      | 191      | 227      | 336      |
| 0.2      | 90       | 92       | 94       | 99       | 107      | 128      | 189      |
| 0.25     | 58       | 59       | 60       | 63       | 69       | 82       | 121      |
| 0.3      | 40       | 41       | 42       | 44       | 48       | 57       | 84       |
| 0.35     | 29       | 30       | 31       | 32       | 35       | 42       | 62       |
| 0.4      | 23       | 23       | 24       | 25       | 27       | 32       | 47       |

Supplemental Table 17. TV (total volume)

| $\delta$ | N_9times | N_8times | N_7times | N_6times | N_5times | N_4times | N_3times |
|----------|----------|----------|----------|----------|----------|----------|----------|
| 0.05     | 566      | 567      | 570      | 575      | 585      | 608      | 678      |
| 0.1      | 141      | 142      | 143      | 144      | 146      | 152      | 170      |
| 0.15     | 63       | 63       | 63       | 64       | 65       | 68       | 75       |
| 0.2      | 35       | 35       | 36       | 36       | 37       | 38       | 42       |
| 0.25     | 23       | 23       | 23       | 23       | 23       | 24       | 27       |
| 0.3      | 16       | 16       | 16       | 16       | 16       | 17       | 19       |
| 0.35     | 12       | 12       | 12       | 12       | 12       | 12       | 14       |
| 0.4      | 9        | 9        | 9        | 9        | 9        | 10       | 11       |
## Supplemental Table 18. BV.TV (Bone volume/total volume)

| $\delta$ | N\_9times | N\_8times | N\_7times | N\_6times | N\_5times | N\_4times | N\_3times |
|----------|------------|------------|------------|------------|------------|------------|------------|
| 0.05     | 402        | 406        | 412        | 423        | 446        | 499        | 659        |
| 0.1      | 100        | 101        | 103        | 106        | 112        | 125        | 165        |
| 0.15     | 45         | 45         | 46         | 47         | 50         | 55         | 73         |
| 0.2      | 25         | 25         | 26         | 26         | 28         | 31         | 41         |
| 0.25     | 16         | 16         | 16         | 17         | 18         | 20         | 26         |
| 0.3      | 11         | 11         | 11         | 12         | 12         | 14         | 18         |
| 0.35     | 8          | 8          | 8          | 9          | 9          | 10         | 13         |
| 0.4      | 6          | 6          | 6          | 7          | 7          | 8          | 10         |

## Supplemental Table 19. TS (Tissue surface)

| $\delta$ | N\_9times | N\_8times | N\_7times | N\_6times | N\_5times | N\_4times | N\_3times |
|----------|------------|------------|------------|------------|------------|------------|------------|
| 0.05     | 61         | 67         | 75         | 90         | 120        | 191        | 403        |
| 0.1      | 15         | 17         | 19         | 23         | 30         | 48         | 101        |
| 0.15     | 7          | 7          | 8          | 10         | 13         | 21         | 45         |
| 0.2      | 4          | 4          | 5          | 6          | 8          | 12         | 25         |
| 0.25     | 2          | 3          | 3          | 4          | 5          | 8          | 16         |
| 0.3      | 2          | 2          | 2          | 3          | 3          | 5          | 11         |
| 0.35     | 1          | 1          | 2          | 2          | 2          | 4          | 8          |
| 0.4      | 1          | 1          | 1          | 1          | 2          | 3          | 6          |
### Supplemental Table 20. TS.per. (Tissue percent)

| δ  | N_9times | N_8times | N_7times | N_6times | N_5times | N_4times | N_3times |
|----|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
| 0.05 | 244       | 246       | 250       | 258       | 273       | 307       | 410       |
| 0.1  | 61        | 62        | 63        | 64        | 68        | 77        | 103       |
| 0.15 | 27        | 27        | 28        | 29        | 30        | 34        | 46        |
| 0.2  | 15        | 15        | 16        | 16        | 17        | 19        | 26        |
| 0.25 | 10        | 10        | 10        | 10        | 11        | 12        | 16        |
| 0.3  | 7         | 7         | 7         | 7         | 8         | 9         | 11        |
| 0.35 | 5         | 5         | 5         | 5         | 6         | 6         | 8         |
| 0.4  | 4         | 4         | 4         | 4         | 4         | 5         | 6         |

### Supplemental Table 21. BS.BV (Bone surface/Bone volume)

| δ  | N_9times | N_8times | N_7times | N_6times | N_5times | N_4times | N_3times |
|----|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
| 0.05 | 1056      | 1064      | 1076      | 1097      | 1140      | 1240      | 1541      |
| 0.1  | 264       | 266       | 269       | 274       | 285       | 310       | 385       |
| 0.15 | 117       | 118       | 120       | 122       | 127       | 138       | 171       |
| 0.2  | 66        | 66        | 67        | 69        | 71        | 78        | 96        |
| 0.25 | 42        | 43        | 43        | 44        | 46        | 50        | 62        |
| 0.3  | 29        | 30        | 30        | 30        | 32        | 34        | 43        |
| 0.35 | 22        | 22        | 22        | 22        | 23        | 25        | 31        |
| 0.4  | 17        | 17        | 17        | 17        | 18        | 19        | 24        |
### Supplemental Table 22. TA (Tissue area)

| δ  | N_9times | N_8times | N_7times | N_6times | N_5times | N_4times | N_3times |
|----|-----------|----------|----------|----------|----------|----------|----------|
| 0.05 | 566       | 567      | 570      | 575      | 585      | 608      | 678      |
| 0.1  | 141       | 142      | 143      | 144      | 146      | 152      | 170      |
| 0.15 | 63        | 63       | 63       | 64       | 65       | 68       | 75       |
| 0.2  | 35        | 35       | 36       | 36       | 37       | 38       | 42       |
| 0.25 | 23        | 23       | 23       | 23       | 23       | 24       | 27       |
| 0.3  | 16        | 16       | 16       | 16       | 16       | 17       | 19       |
| 0.35 | 12        | 12       | 12       | 12       | 12       | 12       | 14       |
| 0.4  | 9         | 9        | 9        | 9        | 9        | 10       | 11       |

### Supplemental Table 23. T.Pm (Tissue perimeter)

| δ  | N_9times | N_8times | N_7times | N_6times | N_5times | N_4times | N_3times |
|----|-----------|----------|----------|----------|----------|----------|----------|
| 0.05 | 244       | 247      | 251      | 258      | 273      | 307      | 411      |
| 0.1  | 61        | 62       | 63       | 65       | 68       | 77       | 103      |
| 0.15 | 27        | 27       | 28       | 29       | 30       | 34       | 46       |
| 0.2  | 15        | 15       | 16       | 16       | 17       | 19       | 26       |
| 0.25 | 10        | 10       | 10       | 10       | 11       | 12       | 16       |
| 0.3  | 7         | 7        | 7        | 7        | 8        | 9        | 11       |
| 0.35 | 5         | 5        | 5        | 5        | 6        | 6        | 8        |
| 0.4  | 4         | 4        | 4        | 4        | 4        | 5        | 6        |
### Supplemental Table 24. Ecc. (Eccentricity)

| δ     | N_9times | N_8times | N_7times | N_6times | N_5times | N_4times | N_3times |
|-------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
| 0.05  | 350       | 396       | 472       | 609       | 882       | 1520      | 3433      |
| 0.1   | 88        | 99        | 118       | 152       | 220       | 380       | 858       |
| 0.15  | 39        | 44        | 52        | 68        | 98        | 169       | 381       |
| 0.2   | 22        | 25        | 29        | 38        | 55        | 95        | 215       |
| 0.25  | 14        | 16        | 19        | 24        | 35        | 61        | 137       |
| 0.3   | 10        | 11        | 13        | 17        | 25        | 42        | 95        |
| 0.35  | 7         | 8         | 10        | 12        | 18        | 31        | 70        |
| 0.4   | 5         | 6         | 7         | 10        | 14        | 24        | 54        |

### Supplemental Table 25. Cs.Th (cross sectional thickness)

| δ     | N_9times | N_8times | N_7times | N_6times | N_5times | N_4times | N_3times |
|-------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
| 0.05  | 812       | 819       | 831       | 852       | 893       | 990       | 1280      |
| 0.1   | 203       | 205       | 208       | 213       | 223       | 247       | 320       |
| 0.15  | 90        | 91        | 92        | 95        | 99        | 110       | 142       |
| 0.2   | 51        | 51        | 52        | 53        | 56        | 62        | 80        |
| 0.25  | 33        | 33        | 33        | 34        | 36        | 40        | 51        |
| 0.3   | 23        | 23        | 23        | 24        | 25        | 27        | 36        |
| 0.35  | 17        | 17        | 17        | 17        | 18        | 20        | 26        |
| 0.4   | 13        | 13        | 13        | 13        | 14        | 15        | 20        |
Supplemental Table 26. Med.area (medullary area)

| δ   | N_9times | N_8times | N_7times | N_6times | N_5times | N_4times | N_3times |
|-----|----------|----------|----------|----------|----------|----------|----------|
| 0.05| 494      | 495      | 497      | 501      | 508      | 526      | 577      |
| 0.1 | 124      | 124      | 124      | 125      | 127      | 131      | 144      |
| 0.15| 55       | 55       | 55       | 56       | 57       | 58       | 64       |
| 0.2 | 31       | 31       | 31       | 31       | 32       | 33       | 36       |
| 0.25| 20       | 20       | 20       | 20       | 20       | 21       | 23       |
| 0.3 | 14       | 14       | 14       | 14       | 14       | 15       | 16       |
| 0.35| 10       | 10       | 10       | 10       | 10       | 11       | 12       |
| 0.4 | 8        | 8        | 8        | 8        | 8        | 8        | 9        |
Supplemental Table 27. Metabolic measures assayed

| Phenotype     | Units       | Description                                         |
|---------------|-------------|-----------------------------------------------------|
| BG            | mg/dl       | Blood glucose levels (fasted)                       |
| BMD           | g           | Body mass by day (average)                          |
| BMN           | g           | Body mass by night (average)                        |
| EE.BMD        | kcal/hr/g   | Energy expenditure by day/body mass (average)       |
| EE.BMN        | kcal/hr/g   | Energy expenditure/body mass by night (average)     |
| EE.LBMD       | kcal/hr/g   | Energy expenditure/lean body mass by day (average)  |
| EE.LBMN       | kcal/hr/g   | Energy expenditure/lean body mass by night (average)|
| EED           | kcal/hr     | Energy expenditure by day (average)                 |
| EEN           | kcal/hr     | Energy expenditure by night (average)               |
| FBM           | g           | Fat mass (estimated by QMR)                         |
| FD            | g           | Food consumed by day (average)                      |
| FN            | g           | Food consumed by night (average)                    |
| LBM           | g           | Lean body mass                                      |
| PMD           | m           | Meters walked by day (average)                      |
| PMN           | m           | Meters walked by night (average)                    |
| PSD           | m/s         | Mean speed of walking by day (average)              |
| PSN           | m/s         | Mean speed of walking by night (average)            |
| RQD           | Dimensionless number | Respiratory quotient by day (average)     |
| RQN           | Dimensionless number | Respiratory quotient by night (average) |
| SD            | hours(h)    | Sleep by day (average)                              |
| SN            | hours(h)    | Sleep by night (average)                            |
| VCD           | ml/min      | VCO₂ by day (average)                               |
| VCN           | ml/min      | VCO₂ by night (average)                             |
| VOD           | ml/min      | VO₂ by day (average)                                |
| VON           | ml/min      | VO₂ by night (average)                              |
| WD            | g           | Water drunk by day (average)                        |
| WN            | g           | Water drunk by night (average)                      |
| WMD           | m           | Meters run in a wheel by day (average)              |
| WMN           | m           | Meters run in a wheel by night (average)            |
| WSD           | m/s         | Speed of running in a wheel by day (average)        |
| WSN           | m/s         | Speed of running a wheel by night (average)         |
Supplemental Table 28. Metabolic changes with age; males

| Phenotype | Total N | $\beta$ | SE    | P    | N (5 months old) | N (19 months old) |
|-----------|---------|--------|-------|------|------------------|-------------------|
| BG        | 52      | 5.340  | 9.516 | 0.577| 16               | 36                |
| EE.BMD    | 28      | -0.001 | 4.0E-04 | 0.085| 16               | 12                |
| EE.BMN    | 28      | -0.003 | 0.001 | 0.001| 16               | 12                |
| EE.LBMD   | 28      | -3.2E-04 | 4.5E-04 | 0.478| 16               | 12                |
| EE.LBMN   | 28      | -0.003 | 0.001 | 0.001| 16               | 12                |
| EED       | 28      | 0.024  | 0.018 | 0.185| 16               | 12                |
| EEN       | 28      | -0.032 | 0.026 | 0.217| 16               | 12                |
| FBM       | 52      | 2.419  | 0.615 | 2.6E-04| 16               | 36                |
| FD        | 28      | -0.174 | 0.172 | 0.323| 16               | 12                |
| FN        | 28      | 0.321  | 0.262 | 0.232| 16               | 12                |
| LBM       | 52      | 1.238  | 0.546 | 0.028| 16               | 36                |
| PMD       | 28      | 6.720  | 4.936 | 0.185| 16               | 12                |
| PMN       | 28      | -4.966 | 8.420 | 0.560| 16               | 12                |
| PSD       | 28      | -0.001 | 0.001 | 0.427| 16               | 12                |
| PSN       | 28      | -0.001 | 0.001 | 0.125| 16               | 12                |
| RQD       | 28      | -0.051 | 0.024 | 0.044| 16               | 12                |
| RQN       | 28      | -0.053 | 0.018 | 0.007| 16               | 12                |
| SD        | 28      | -0.432 | 0.706 | 0.546| 16               | 12                |
| SN        | 28      | -0.144 | 0.272 | 0.601| 16               | 12                |
| VCD       | 28      | -0.005 | 0.070 | 0.938| 16               | 12                |
| VCN       | 28      | -0.203 | 0.096 | 0.044| 16               | 12                |
| VOD       | 28      | 0.102  | 0.057 | 0.084| 16               | 12                |
| VON       | 28      | -0.080 | 0.083 | 0.347| 16               | 12                |
| WD        | 28      | 0.091  | 0.117 | 0.444| 16               | 12                |
| WMD       | 27      | -160   | 97    | 0.112| 15               | 12                |
| WMN       | 27      | -1080  | 530   | 0.052| 15               | 12                |
| WN        | 28      | -0.325 | 0.232 | 0.174| 16               | 12                |
| WSD       | 26      | -0.011 | 0.016 | 0.521| 15               | 11                |
| WSN       | 26      | -0.025 | 0.014 | 0.083| 15               | 11                |

**abbreviations:** Total N; Total numbers of animals per measured phenotype are shown; $\beta$ - change relative to young animals; SE - standard error; P - P value; (Phenotype)D - average by day; (Phenotype)N - average by night; BG - fasted blood glucose level; BM - body mass; EE.BM - energy expenditure/body mass; EE.LBM - energy expenditure/lean body mass; EE - energy expenditure; FBM - fat; F - food consumed; LBM - lean body mass; PM - meters walked; PS - mean speed of walking; RQ - respiratory quotient; S - sleep; VC - VCO2; VO - VO2; W - water drunk; WM - wheel meters run; WS - wheel speed while running.
Supplemental Table 29. Metabolic changes with age; females

| Phenotype | Total N | β     | SE  | P     | N (5 months old) | N (19 months old) |
|-----------|---------|-------|-----|-------|------------------|-------------------|
| BG        | 45      | 0.7   | 8.4 | 0.938 | 16               | 29                |
| EE.BMD    | 28      | -0.001| 0.001 | 0.188 | 16               | 12                |
| EE.BMN    | 28      | -0.006| 0.001 | 4.9E-05 | 16               | 12                |
| EE.LBMD   | 28      | -0.001| 0.001 | 0.240 | 16               | 12                |
| EE.LBMN   | 28      | -0.006| 0.001 | 1.4E-04 | 16               | 12                |
| EED       | 28      | 0.025 | 0.016 | 0.128 | 16               | 12                |
| EEN       | 28      | -0.068| 0.032 | 0.046 | 16               | 12                |
| FBM       | 45      | 2.1   | 0.4  | 7.3E-06 | 16               | 29                |
| FD        | 28      | -0.483| 0.238 | 0.053 | 16               | 12                |
| FN        | 28      | -0.769| 0.337 | 0.031 | 16               | 12                |
| LBM       | 45      | 1.8   | 0.3  | 1.3E-07 | 16               | 29                |
| PMD       | 28      | -4.9  | 2.6  | 0.075 | 16               | 12                |
| PMN       | 28      | -5.5  | 13.4 | 0.685 | 16               | 12                |
| PSD       | 28      | -0.001| 0.001 | 0.134 | 16               | 12                |
| PSN       | 28      | -0.001| 0.001 | 0.387 | 16               | 12                |
| RQD       | 28      | -0.234| 0.023 | 1.3E-10 | 16               | 12                |
| RQN       | 28      | -0.232| 0.027 | 4.5E-09 | 16               | 12                |
| SD        | 28      | 0.618 | 0.480 | 0.209 | 16               | 12                |
| SN        | 28      | 1.548 | 0.364 | 2.4E-04 | 16               | 12                |
| VCD       | 28      | -0.194| 0.063 | 0.005 | 16               | 12                |
| VCN       | 28      | -0.586| 0.129 | 1.1E-04 | 16               | 12                |
| VOD       | 28      | 0.158 | 0.050 | 0.004 | 16               | 12                |
| VON       | 28      | -0.122| 0.102 | 0.246 | 16               | 12                |
| WD        | 28      | 0.019 | 0.169 | 0.913 | 16               | 12                |
| WMD       | 26      | -121  | 123  | 0.332 | 14               | 12                |
| WMN       | 26      | -5448 | 740  | 1.3E-07 | 14               | 12                |
| WN        | 28      | -0.217| 0.177 | 0.231 | 16               | 12                |
| WSD       | 26      | -0.056| 0.023 | 0.021 | 14               | 12                |
| WSN       | 26      | -0.102| 0.015 | 2.7E-07 | 14               | 12                |

**Abbreviations:** Total N; Total numbers of animals per measured phenotype are shown; β - change relative to young animals; SE - standard error; P - P value; (Phenotype)D - average by day; (Phenotype)N - average by night; BG - fasted blood glucose level; BM - body mass; EE.BM - energy expenditure/body mass; EE.LBM - energy expenditure/lean body mass; EE - energy expenditure; FBM - fat; F - food consumed; LBM - lean body mass; PM - meters walked; PS - mean speed of walking; RQ - respiratory quotient; S - sleep; VC - VCO2; VO - VO2; W - water drunk; WM - wheel meters run; WS - wheel speed while running.
### Supp. Table 30. Metabolic changes with advanced age

| Phenotype  | N  | β  | SE  | P    | P (Sex Interaction) |
|------------|----|----|-----|------|---------------------|
| BG         | 69 | -12| 1.461| 7.1E-12 | 0.477               |
| EE.BMD     | 37 | 5.8E-05 | 1.2E-04 | 0.628 | 0.004               |
| EE.BMN     | 37 | -0.001 | 1.7E-04 | 0.001 | 0.527               |
| EE.LBMD    | 36 | 0.000 | 2.1E-04 | 0.971 | 0.000               |
| EE.LBMN    | 36 | -0.002 | 4.3E-04 | 0.001 | 0.003               |
| EED        | 40 | 0.004 | 0.055 | 0.395 | 6.1E-08             |
| EEN        | 40 | -0.020 | 0.005 | 2.4E-04 | 8.3E-05             |
| FBM        | 69 | -0.610 | 0.121 | 2.7E-06 | 0.075               |
| FD         | 41 | 0.053 | 0.037 | 0.160 | 0.429               |
| FN         | 41 | 0.002 | 0.081 | 0.982 | 0.898               |
| LBM        | 69 | 0.077 | 0.093 | 0.411 | 0.440               |
| PMD        | 41 | -4.205 | 0.987 | 1.4E-04 | 0.012               |
| PMN        | 41 | -7.342 | 1.870 | 3.5E-04 | 0.231               |
| PSD        | 41 | -0.001 | 1.3E-04 | 1.6E-05 | 0.079               |
| PSN        | 41 | -0.001 | 1.7E-04 | 1.1E-04 | 0.247               |
| RQD        | 40 | 0.013 | 0.004 | 0.004 | 0.633               |
| RQN        | 40 | 0.017 | 0.004 | 1.9E-05 | 0.782               |
| SD         | 41 | -0.106 | 0.160 | 0.512 | 0.002               |
| SN         | 41 | 0.184 | 0.124 | 0.147 | 0.109               |
| VCD        | 40 | 0.022 | 0.016 | 0.171 | 5.5E-07             |
| VCN        | 40 | -0.035 | 0.016 | 0.040 | 0.001               |
| VOD        | 40 | 0.012 | 0.018 | 0.495 | 8.6E-08             |
| VON        | 40 | -0.075 | 0.016 | 3.9E-05 | 6.9E-05             |
| WD         | 41 | 0.105 | 0.047 | 0.032 | 0.094               |
| WMD        | 40 | -14 | 6.446 | 0.036 | 0.404               |
| WMN        | 40 | -604 | 100.906 | 3.7E-07 | 0.365               |
| WN         | 41 | 0.152 | 0.102 | 0.146 | 0.024               |
| WSD        | 36 | -0.011 | 0.004 | 0.004 | 0.512               |
| WSN        | 37 | -0.019 | 0.003 | 5.1E-07 | 0.947               |

**Abbreviations:** Total N; Total numbers of animals per measured phenotype are shown; β - mean change in outcome over 100 days; SE - standard error; P - P value; P(Sex interaction) - P < 0.05 β significantly different by sex; (Phenotype)D - average by day; (Phenotype)N - average by night; BG - fasted blood glucose level; BM - body mass; EE.BM - energy expenditure/body mass; EE.LBM - energy expenditure/lean body mass; EE - energy expenditure; FBM - fat; F - food consumed; LBM - lean body mass; PM - meters walked; PS - mean speed of walking; RQ - respiratory quotient; S - sleep; VC - VCO2; VO - VO2; W - water drunk; WM - wheel meters run; WS - wheel speed while running.
Supplemental Table 31. Metabolic changes in males of advanced age

| Phenotype  | N  | β    | SE  | P     |
|------------|----|------|-----|-------|
| BG         | 41 | -11.2| 1.7 | 1.1E-07 |
| EE.BMD     | 18 | -2.2E-04 | 1.1E-04 | 0.079 |
| EE.BMN     | 18 | -0.001 | 1.5E-04 | 2.8E-04 |
| EE.LBMD    | 18 | -0.001 | 2.2E-04 | 0.009 |
| EE.LBMN    | 18 | -0.003 | 4.9E-04 | 1.3E-04 |
| EED        | 21 | -0.014 | 0.004 | 0.003 |
| EEN        | 21 | -0.032 | 0.005 | 1.0E-05 |
| FBM        | 41 | -0.755 | 0.129 | 1.2E-06 |
| FD         | 21 | 0.030 | 0.042 | 0.496 |
| FN         | 21 | -0.015 | 0.065 | 0.823 |
| LBM        | 41 | 0.029 | 0.118 | 0.808 |
| PMD        | 21 | -6.1 | 1.4 | 0.001 |
| PMN        | 21 | -5.9 | 2.2 | 0.018 |
| PSD        | 21 | -4.7E-04 | 1.6E-04 | 0.011 |
| PSN        | 21 | -5.9E-04 | 2.2E-04 | 0.020 |
| RQD        | 21 | 0.010 | 0.005 | 0.094 |
| RQN        | 21 | 0.017 | 0.004 | 0.001 |
| SD         | 21 | 0.262 | 0.198 | 0.203 |
| SN         | 21 | 0.349 | 0.168 | 0.058 |
| VCD        | 21 | -0.032 | 0.014 | 0.038 |
| VCN        | 21 | -0.072 | 0.017 | 0.001 |
| VOD        | 21 | -0.051 | 0.013 | 0.002 |
| VON        | 21 | -0.117 | 0.017 | 4.2E-06 |
| WD         | 21 | 0.046 | 0.042 | 0.295 |
| WMD        | 20 | -18 | 9 | 0.056 |
| WMN        | 20 | -515 | 117 | 4.9E-04 |
| WN         | 21 | -0.018 | 0.103 | 0.865 |
| WSD        | 17 | -0.013 | 0.004 | 0.014 |
| WSN        | 19 | -0.019 | 0.003 | 0.000 |

**Abbreviations:** Total N; Total numbers of animals per measured phenotype are shown; β - mean change in outcome over 100 days; SE - standard error; P - P value; (Phenotype)D - average by day; (Phenotype)N - average by night; BG - fasted blood glucose level; BM - body mass; EE.BM - energy expenditure/body mass; EE.LBM - energy expenditure/lean body mass; EE - energy expenditure; FBM - fat; F - food consumed; LBM - lean body mass; PM - meters walked; PS - mean speed of walking; RQ - respiratory quotient; S - sleep; VC - VCO2; VO - VO2; W - water drunk; WM - wheel meters run; WS - wheel speed while running.
Supplemental Table 32. Metabolic changes in females of advanced age

| Phenotype | N  | ß   | SE  | P     |
|-----------|----|-----|-----|-------|
| BG        | 28 | -14 | 3   | 2.8E-04 |
| EE.BMD    | 19 | 0.000 | 2.2E-04 | 0.054 |
| EE.BMN    | 19 | -0.000 | 3.5E-04 | 0.204 |
| EE.LBMD   | 18 | 0.001 | 3.8E-04 | 0.005 |
| EE.LBMN   | 18 | -0.000 | 0.001 | 0.899 |
| EED       | 19 | 0.032 | 0.008 | 0.001 |
| EEN       | 19 | 0.006 | 0.009 | 0.533 |
| FBM       | 28 | -0.304 | 0.263 | 0.257 |
| FD        | 20 | 0.091 | 0.070 | 0.216 |
| FN        | 20 | 0.008 | 0.186 | 0.965 |
| LBM       | 28 | 0.225 | 0.152 | 0.152 |
| PMD       | 20 | -0.933 | 0.881 | 0.308 |
| PMN       | 20 | -10 | 3   | 0.012 |
| PSD       | 20 | -0.001 | 2.3E-04 | 0.001 |
| PSN       | 20 | -0.001 | 2.4E-04 | 0.001 |
| RQD       | 19 | 0.015 | 0.006 | 0.038 |
| RQN       | 19 | 0.016 | 0.007 | 0.046 |
| SD        | 20 | -0.735 | 0.204 | 0.003 |
| SN        | 20 | -0.057 | 0.176 | 0.752 |
| VCD       | 19 | 0.100 | 0.021 | 3.3E-04 |
| VCN       | 19 | 0.047 | 0.033 | 0.167 |
| VOD       | 19 | 0.108 | 0.026 | 0.001 |
| VON       | 19 | 0.013 | 0.030 | 0.674 |
| WD        | 20 | 0.206 | 0.107 | 0.075 |
| WMD       | 20 | -10 | 9   | 0.299 |
| WMN       | 20 | -813 | 234 | 0.003 |
| WN        | 20 | 0.440 | 0.190 | 0.037 |
| WSD       | 19 | -0.012 | 0.007 | 0.102 |
| WSN       | 18 | -0.018 | 0.006 | 0.008 |

**abbreviations:** Total N; Total numbers of animals per measured phenotype are shown; ß - mean change in outcome over 100 days; SE - standard error; P - P value; (Phenotype)D - average by day; (Phenotype)N - average by night; BG - fasted blood glucose level; BM - body mass; EE.BM - energy expenditure/body mass; EE.LBM - energy expenditure/lean body mass; EE - energy expenditure; FBM - fat; F - food consumed; LBM - lean body mass; PM - meters walked; PS - mean speed of walking; RQ - respiratory quotient; S - sleep; VC - VCO2; VO - VO2; W - water drunk; WM - wheel meters run; WS - wheel speed while running.
Supplemental Table 33. Statistically significant metabolic changes with late life

| Phenotype | Intervention | N Control | N Intervention | \( \beta \) | SE  | P      | P (sex interaction) |
|-----------|--------------|-----------|----------------|--------|-----|--------|---------------------|
| BG        | Clioquinol   | 69        | 17             | 13     | 4   | 0.001  | 0.075               |
| EE.BMD    | Lithium      | 37        | 7              | 0.001  | 0.000 | 0.042  | 0.007               |
| FD        | HBX          | 41        | 10             | -0.216 | 0.096| 0.029  | 0.040               |
| PSN       | HBX          | 41        | 10             | -0.001 | 4.7E-04| 0.017  | 0.169               |
| RQD       | Lithium      | 40        | 7              | -0.054 | 0.010| 3.2E-06| 0.722               |
| RQD       | HBX          | 40        | 10             | -0.021 | 0.009| 0.024  | 0.126               |
| RQN       | Lithium      | 40        | 9              | -0.044 | 0.010| 1.1E-04| 0.488               |
| RQN       | HBX          | 40        | 10             | -0.021 | 0.008| 0.015  | 0.756               |
| SD        | Beta sitosterol | 41    | 20             | -0.605 | 0.256| 0.022  | 1.4E-07             |
| SD        | HBX          | 41        | 10             | -0.972 | 0.388| 0.015  | 3.1E-06             |
| VOD       | Lithium      | 40        | 7              | 0.101  | 0.048| 0.043  | 1.8E-06             |
| WMD       | Lithium      | 40        | 7              | -38    | 17   | 0.031  | 0.248               |
| WMN       | Lithium      | 40        | 9              | -1043  | 273  | 3.5E-04| 0.148               |
| WN        | Lithium      | 41        | 9              | 0.707  | 0.307| 0.026  | 0.022               |
| WN        | Clioquinol   | 41        | 6              | -0.998 | 0.304| 0.002  | 0.027               |
| WSN       | Lithium      | 37        | 9              | -0.021 | 0.008| 0.008  | 0.847               |

**abbreviations:** N Control - number of untreated controls for specified intervention; N Intervention - number of animals treated with that intervention for specified assay; \( \beta \) - mean change in outcome per 100 days over late life for the specified intervention relative to untreated controls; SE - standard error; P - P value; (Phenotype)D - average by day; (Phenotype)N - average by night; BG - fasted blood glucose level; EE.BM - energy expenditure/body mass; F - food consumed; PS - mean speed of walking; RQ - respiratory quotient; S - sleep; VC - VCO\(_2\); VO - VO\(_2\); W - water drunk; WM - wheel meters run; WS - wheel speed while running; P (sex interaction) \( P < 0.05 \) effect of intervention on \( \beta \) was significantly different by sex.
Supplemental Table 35. Doses used for each intervention

| Intervention | Dosage in food |
|--------------|----------------|
| BS           | 2%             |
| CQ           | 210 ppm        |
| HBX          | 1ppm           |
| Li₂CO₃       | 0.064%         |

Supplemental Table 36. Numbers of animals purchased and enrolled

| Group   | Male | Female | Age (mo) |
|---------|------|--------|----------|
| Young   | 25   | 25     | 5        |
| BS      | 60   | 60     | 18       |
| CQ      | 60   | 60     | 18       |
| HBX     | 60   | 60     | 18       |
| Li₂CO₃  | 60   | 60     | 18       |
| Controls| 120  | 120    | 18       |

abbreviations: BS - Beta Sitosterol; CQ - Clioquinol; HBX - (2-(2-hydroxyphenyl) benzoxazole); Li₂CO₃

Supplemental Table 34. Tortuosity measures kyphosis in 5-month old versus 19-month-old mice

| Sex   | n_total | β       | SE      | P       | n_5months | n_19months |
|-------|---------|---------|---------|---------|-----------|------------|
| M & F | 122     | 0.026   | 0.005   | 7.1E-07 | 50        | 72         |
| F     | 61      | 0.019   | 0.006   | 0.001   | 25        | 36         |
| M     | 61      | 0.034   | 0.008   | 1.3E-04 | 25        | 36         |

abbreviations: M - Males; F - Females; n_total - total number of animals measured, β - average difference in 19-months-old versus 5-months-old in tortuosity; SE - standard error of the mean; P - P value; n_5months - number of animals measured for tortuosity at 5-months-old; n_19months - number of animals measured for tortuosity at 19-months-old.
Supplemental Table 37. Femoral bone measures assayed

| Phenotype | Units    | Description                          |
|-----------|----------|--------------------------------------|
| TV        | mm³      | Total volume                         |
| BV        | mm³      | Bone volume                          |
| BV.TV     | %        | Percent bone volume                  |
| TS        | mm²      | Tissue surface                       |
| TS.per.   | %        | Tissue surface (%)                   |
| BS        | mm²      | Bone surface                         |
| BS.per.   | %        | Bone surface percent                 |
| BS.BV     | mm⁻¹     | Bone surface/volume ratio            |
| T.Ar      | mm²      | Mean total crosssectional tissue area|
| T.Pm      | mm       | Mean total crosssectional tissue perimeter|
| B.Ar      | mm²      | Mean total crosssectional bone area  |
| B.Pm      | mm       | Mean total crosssectional bone perimeter|
| Ecc       | Dimensionless number | Mean eccentricity                     |
| Cs.Th     | mm       | Crosssectional thickness             |
| Po.cl.    | %        | Closed porosity                      |
| endosteal | mm       | Endosteal perimeter                  |
| Med.area  | mm²      | Medullary area                       |