Appendix

(1) Chronological aging reflected by follow-up visit and ovarian aging

To study the associations of 6-year changes in body composition with ovarian and chronological aging, we used the following form of the mixed effects model:

$$y_{ij} = \beta_0 + \beta_1 t_{ij} + \beta_2 t_{ij}^2 + \beta_3 y_{i0} + \beta_4 A_{i0} + \beta_5 O_{ij} + Interactions + b_{i0} + b_{i1} t_{ij} + b_{i2} t_{ij}^2 + \varepsilon_{ij} \quad \text{(A.1)}$$

$$i = 1,2,...,N\ ,\ \ j = 1,2,...,6$$

where $N = 543$ was the total number of participants in the study and t_{ij} was the j^{th} follow-up visit for participant i. The time variable was centered for models including a quadratic time term to reflect change with time. y_{ij} was the appropriately transformed body composition measure of interest measured at time j for i^{th} participant; y_{i0} was the appropriately transformed baseline measure for i^{th} participant; A_{i0} was the baseline age for i^{th} participant; O_{ij} was the measure of ovarian aging for i^{th} participant at time j. The measure of ovarian aging could be represented by the natural log-transformed FSH_{ij} (i.e., $_{\log}(FSH_{ij})$) or menopausal status classification based on self-reported frequency of menses. Interaction terms were included in the model as appropriate. In these models, the assumptions for the random effects and error terms for participant i were:

$$\mathbf{b}_i \sim N(\mathbf{0},\mathbf{G}),\ \ \boldsymbol{\varepsilon}_i \sim N(\mathbf{0},\mathbf{R}_i),\ \mathbf{b}_1,\mathbf{b}_2,...,\mathbf{b}_N \text{ and } \boldsymbol{\varepsilon}_1,\boldsymbol{\varepsilon}_2,...,\boldsymbol{\varepsilon}_N \text{ are independent.}$$

By fitting the mixed-effects model, we obtained the marginal models for the following three primary body composition measures.

a. $_{\log}$ (Waist circumference):

$$-0.1513 + 1.0317 \cdot y_{i0} + 0.0005 \cdot A_{i0} + 0.0930 \cdot \log(FSH_{ij}) + \left[0.0709 - 0.0136 \cdot y_{i0}\right] \cdot t_{ij} - 0.0212 \cdot \log(FSH_{ij}) \cdot y_{i0}$$

(A.2)

b. $_{\log}$ (Skeletal muscle mass):

$$0.1894 + 0.9479 \cdot y_{i0} + 0.0002 \cdot A_{i0} - 0.0113 \cdot \log(FSH_{ij}) + \left[0.0325 - 0.0110 \cdot y_{i0}\right] \cdot t_{ij}$$

(A.3)

c. $_{\log}$ (Fat mass):

$$0.2997 + 0.9278 \cdot y_{i0} - 0.0010 \cdot A_{i0} + 0.0082 \cdot \log(FSH_{ij}) + \left[0.0629 - 0.0143 \cdot y_{i0}\right] \cdot (t_{ij} - 3) + \left[0.0314 - 0.0080 \cdot y_{i0}\right] \cdot (t_{ij} - 3)^2$$

(A.4)

Baseline age was evaluated in these models to be consistent with our hypotheses, but the baseline age variable was not statistically significant at $\alpha = 0.05$ level.

(2) Adjusted model

The adjusted model for $_{\log}$ **(fat mass)** with a median baseline age of 45 years and a median baseline fat mass of 33.21 kg was:

$$3.4885 + 0.0082 \cdot \log(FSH_{ij}) - 0.0075 \cdot t_{ij} + 0.0034 \cdot t_{ij}^2$$

(A.5)

This information is shown in Figure 2b.

(3) Ovarian aging reflected by time since FMP

In order to examine the dynamics of body composition measures at or near FMP, three approaches were considered:

1) fitting an overall linear/quadratic model;

2) fitting a piecewise linear trend model; and

3) fitting separate models by cutting the dataset into two sub-datasets.

The piecewise linear trend model was formulated as:

$$y_{ij} = \beta_0 + \beta_1 t_{ij} + \sum_{k=1}^{K} \beta_{k+1} \left[\left(t_{ij} - t_{(k)}^{*} \right) \cdot 1_{\{t_{ij} > t_{(k)}^{*}\}} \right] + b_{i0} + b_{i1} t_{ij} + \varepsilon_{ij}, \quad t_{(k)}^{*} \in \Omega$$

(A.6)

where $1_{\{\bullet\}}$ was the indicator function and $\Omega = \left\{ t_{(k)}^{*}, 1 \le k \le K \middle| t_{(1)}^{*} < t_{(2)}^{*} < \ldots < t_{(K)}^{*} \right\}$ was a division of the variable of interest (e.g., years since FMP). The decomposed components $t_{ij} \cdot 1_{\{t_{ij} > t_{(k)}^{*}\}}$ and $t_{(k)}^{*} \cdot 1_{\{t_{ij} > t_{(k)}^{*}\}}$ described the change of slope and change of intercept compared to those in the previous interval, respectively. This piecewise linear trend model has the advantage of being able to capture pattern changes at designated points, incorporate covariates, and use all data for parameter estimates and inferences. In the following selected marginal models t = number of years since FMP, $t \in [-5,5]$ and t=0 was the date of FMP. The information is shown in graphs on the right side of Figure 1.

a. $_{\log}$ (Waist circumference):

- Overall linear trend model:

$$4.5589 + 0.0096 \cdot t, -5 \le t \le 5$$

(A.7)

- Piecewise linear trend model:

$$4.5614 + 0.0117 \cdot t - 0.0074^{*}(t - 1.53)1_{\{t>1.53\}} = \begin{cases} 4.5614 + 0.0117 \cdot t & , -5 \le t \le 1.53 \\ 4.5727 + 0.0043 \cdot t & , 1.53 < t \le 5 \end{cases} \quad \text{(A.8)}$$

Note: * statistically significant at α = 0.05.

- Separate models before and after a certain year since FMP:

$$\begin{cases} 4.5563 + 0.0093 \cdot t, -5 \le t \le 1 \\ 4.5718 + 0.0056 \cdot t, 1 < t \le 5 \end{cases} \quad \text{(A.9)}$$

Within the study time frame, waist circumference continued to increase but at some time around one year following the FMP ($t \approx 1.53$), the rate of increase slowed down by 0.0074 (S.E.= 0.0037).

b. $_{\log}$(Skeletal muscle mass):

- Overall linear trend model:

$$3.0382 - 0.0018^{*} \cdot t, -5 \le t \le 5$$

(A.10)

- Piecewise linear trend model:

$$3.0347 - 0.0037 \cdot t + 0.0054^{*}(t - 0.8)1_{\{t>0.8\}} = \begin{cases} 3.0347 - 0.0037 \cdot t & , -5 \le t \le 0.8 \\ 3.0304 + 0.0017 \cdot t & , 0.8 < t \le 5 \end{cases}$$

(A.11)

Note: * statistically significant at $\alpha = 0.10$.

- Separate models before and after a certain year since FMP:

$$\begin{cases} 3.0360 - 0.0043 \cdot t, t \le 0 \\ 3.0338, t > 0 \end{cases}$$

(A.12)

Within the study time frame, women lost skeletal muscle mass till 0.8 years after FMP and remained relatively stable after that time.

c. $_{\log}$ (Fat mass):

- Overall linear trend model:

$$3.5306 + 0.0137 \cdot t, -5 \le t \le 5$$

(A.13)

- No critical point in the study time frame was identified from the piecewise linear trend model.

- Separate models before and after certain year since FMP:

$$\begin{cases} 3.5241 + 0.0110 \cdot t, t \le 0.1 \\ 3.5392 + 0.0141 \cdot t, t > 0 \end{cases} \tag{A.14}$$

Within the study time frame, women continued to gain fat mass. There was no statistically significant point identified in which the rate of change increased or decreased.

(4) When FSH values were considered in relation to time and FMP, the average $_{\log}$FSH increased as a cubic line

$$3.7884 + 0.2341 \cdot t - 0.0178 \cdot t^2 - 0.0049 \cdot t^3 \tag{A.15}$$

where t was the number of years since FMP, $t \in [-5,5]$ and t=0 was the date of FMP. The point of inflection was around $t \approx -1.21$, which was approximately one year before the FMP. This information is shown in Figure 3.

<u>Note: We are glad to provide the models/figures for other body composition measures or the equations of how to calculate the various kinds of changes in body composition measures to interested readers upon request.</u>