Long-Term Body Weight Trajectories and Health in Older Adults: Hierarchical Clustering of Functional Curves.

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ABSTRACT

Background. The relationship between body mass index (BMI) and health develops over the life course. There is increasing interest among researchers in modeling long-term changes in BMI and indentifying distinct BMI trajectory types in the population. Traditionally, researchers have used fully parametric (regression) or semi-parametric (latent class) models, which required difficult-to-justify decisions that sometimes yielded conflicting findings.

Objective. The aim is to identify clusters of long-term BMI curves among older adults and associated health correlates, using a novel nonparametric functional-data approach.

Methods. Data are from the Health and Retirement Study (N=9,893), a nationally representative panel survey of adults born in 1931-41. BMI was collected in up to 10 waves between 1992 and 2010. We utilize a cutting-edge functional data analysis for sparse longitudinal data, specifically hierarchical clustering of BMI functions estimated via the PACE algorithm.

Results. Three BMI trajectory clusters emerged for each gender: normal stable, overweight gaining, and overweight losing. The initial health of the overweight gaining group in both genders was poorer than that of the normal stable group but their mortality was comparable. The overweight losing cluster experienced significantly poorer health at baseline and higher risk of mortality.

Conclusions. The BMI trajectories among older adults cluster into distinct types, with differing health risks. The study highlights the potential of functional data analysis for BMI trajectories, as well as many other developmental and age-dependent processes relevant to obesity and health.

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The relationship between body weight and health evolves gradually over the life course [1]. Correspondingly, researchers are increasingly examining long-term weight changes using longitudinal data with multiple BMI data points. This represents a marked improvement over analyses using a measure of BMI at a single time point as a predictor of health outcomes. However, methodologically there is room for innovative, more precise approaches to model weight trajectories. We analyze long-term BMI trajectories in an 18-year longitudinal study of a nationally-representative sample of older adults, using a new methodology: hierarchical clustering of functional curves.

Studies have often used approaches that *a priori* categorized initial BMI level and BMI change. Researchers created multiple categories of BMI change, such as 'gaining from normal weight to overweight' or 'losing weight from obese to overweight range' to capture both level and change in weight [2-7]. Although this approach allows for nuanced modeling of the level and change in BMI, results can vary depending on the selected thresholds. Additionally, the approach does not reveal patterns of typical weight trajectories. Discovering such typical trajectories is important in order to classify individuals into various risk levels and target interventions accordingly.

It is known that distinct BMI trajectory types exist among older adults [8-9] and at younger ages [10-11]. However, the number of the distinct BMI trajectory types, their shapes, and their health correlates remain open questions. This is largely because the growth mixture models used to estimate the trajectory classes require analysts to make critical and difficult-to-justify assumptions (and thus decisions) about the data.

For instance, two recent studies [12-13] used the same data on older adults from the Health and Retirement Study. Both estimated latent growth mixture models to determine BMI trajectory

groups in the older population. However, the two studies made different assumptions in the models – in particular, Zheng et al. [13] restricted the residual variance of the growth factors in the trajectory groups to zero while Zajacova and Ailshire [12] did not. These different approaches resulted in fundamentally different findings. The first study reported five BMI trajectory classes with relatively modest change over time; the second study found three BMI trajectory classes with one relatively stable BMI group over time, and the other two marked by pronounced weight gain and loss, respectively.

The present analysis uses hierarchical clustering of functional curves estimated via the PACE algorithm, a powerful, cutting-edge, nonparametric approach to analyzing longitudinal data. The methodology has only recently been developed in the statistical literature and, to the best of our knowledge, this study is its first application for substantive (applied) questions. The BMI curves are estimated using Principal Components via Conditional Expectations (PACE) algorithm and clustered to identify typical BMI curves in the sample. We examine the health differences across these clusters. The findings thus provide a clear, data-driven and empirically grounded analysis of typical patterns of body weight trajectories in older adults, which can help inform public-health and clinical recommendations.

MATERIALS AND METHODS

Data

We used data from the Health and Retirement Survey (HRS) [14]. The HRS, one of the leading sources of information on the health of older Americans, is a nationally representative panel survey of U.S. adults born between 1931 and 1941. The sample cohort was first interviewed in 1992 and re-interviewed every two years thereafter. We use data through the 2010 interview, the most recent wave available, which provides up to ten measures of BMI and mortality follow-up over 18 years of the study period. We used version L of the dataset available from the RAND Corporation [15].

Sample definition. After excluding 3 individuals who had no BMI information at any wave and 286 individuals (2.8 percent) who had BMI values considered to be outliers (above 45 or below 15 at any interview wave), the final sample size was N=9,893.

Variables

Body mass index (BMI) was calculated as weight (kg)/height (m) squared. Height was self-reported at the first interview; weight was self-reported at every interview. For each individual, all available BMI data points were included to define the weight functions.

Mortality followup has been collected throughout the study duration by HRS staff who obtained information about a respondent's death from a spouse, another family member, friend, or other sources. Individuals were coded as 0 if they survived or were believed to be alive through wave 10 in 2010; 1 if they were known or believed to have died. There were no missing values on this variable.

Covariates included age, sex, and initial health status. Age was included as a time-varying measure and served as the time axis for the BMI curves. Sex was dichotomized; all analyses were estimated independently for men and women. Initial health status was captured with two self-reported indicators. Self-rated health (SRH) was measured on the standard 5-point scale from excellent (=1) to poor (=5). The number of chronic conditions, which included highly prevalent conditions like hypertension, arthritis, cancer, and diabetes, was a count variable ranging from 0 up to 7. Both health variables were included in analyses as continuous.

Approach

Hierarchical clustering of functional curves estimated via the PACE algorithm was used to identify groups of similar BMI curves. We describe the method in a broad conceptual way and include references for readers interested in additional information about the methodology.

Functional data analysis (FDA) for sparse longitudinal data. FDA is a flexible, nonparametric approach to modeling longitudinal data. FDA was originally developed for dense data with thousands of measurements over time as may be available with weather information or from fMRI [16-17]. In contrast, social research longitudinal data, including the repeated BMI measurements in the Health and Retirement Study, is sparse in comparison and measured with error. These characteristics necessitate a specific set of methods to estimate the functional curves from the observed data points, the PACE algorithm. The statistical theory and computing algorithms for sparse data have only been developed in recent years [18-20].

We assume that a smooth (twice-differentiable) process generates body mass index (BMI) trajectories across age [21]. The individual –unobserved-- BMI curves are considered random (i.i.d.) realizations of that process and the observed BMI data points are considered snapshots of those individual curves at the times of measurement. The goal of FDA is to estimate the individual BMI curves from the observed BMI data points. These reconstructed curves are the unit of FDA analysis.

Functional principal component analysis (FPCA) via PACE. FPCA is the core dimension-reduction tool in FDA [22]. Analogous to multivariate principal components analysis, FPCA decomposes the covariance surface into eigenvalues and eigenfunctions, which are then used in further analyses [23]. The mean function (mean BMI function by age in our case) is estimated with a local linear scatterplot smoother fitted to the aggregated BMI data plotted against age. The mean function is combined with the raw data to calculate raw covariances of pairwise time points of BMI measurements for each individual. A final smooth covariance surface is estimated by fitting a 2-dimensional smoother over the combination of the raw covariances for all individuals. Using the estimated mean function and covariance surface, principal component scores can be obtained for each individual for use in further analysis. A small number of first eigenfunctions are chosen such that a high percentage of the variation, as given by the

eigenvalues, is explained. The FPC scores for each individual then can be obtained using the mean function and the eigenfunctions.

The FPCA for sparse longitudinal data involves an additional conditional expectation and uses the Principal Analysis by Conditional Expectation (PACE) algorithm. The Principal Analysis by Conditional Expectation (PACE) approach to FPCA was recently developed as a non-parametric approach to predicting the individual FPC scores from sparse longitudinal data [20, 24]. Due to the small number of observations per individual function, the FPC scores cannot be estimated effectively using the data alone but require an additional model step that combines the available individual data points with data from the whole sample [20]. In the PACE approach, we assume that the FPC scores and the errors are jointly normal and thus, instead of the scores, the conditional expectation of the scores is estimated based on the estimated mean and eigenfunctions [25]. The predicted FPC scores can be used to predict complete individual functions or can be used in other analyses.

Hierarchical clustering for sparse functional data. Cluster analysis is an exploratory approach for sorting objects into meaningful groups. In general, the clustering procedure comprises two steps; first, a dissimilarity matrix is calculated, then clustering algorithms are used to group various features of the functional data. Dissimilarity among functions is defined using the L^2 distance, analogous to Euclidian distance for multivariate data [26]. The resulting dissimilarity matrix consists of distances between BMI trajectories. To aid visualization and interpretation, multidimensional scaling is applied to the dissimilarity matrix to project all individual trajectories onto a 2-dimensional space. These locations are then entered into a hierarchical clustering algorithm.

For this analysis, we used Ward's linkage [27] and a squared Euclidean metric to obtain a solution with the optimal number of clusters. Matlab hierarchical clustering supports an agglomerative method (bottom - up) in which smaller clusters are joined to create larger clusters as the

algorithm proceeds. The process is usually visualized by a dendrogram, a branching diagram where clusters at one level are grouped into larger clusters at a higher level, to represent the dissimilarity across clusters or arrangement of clusters produced by hierarchical clustering. The bottom row represents collapsed data (if we had fewer than 30 observations, the original data would be shown); the other nodes represent the corresponding clusters. The length of the vertical lines represents the dissimilarity (distance) of the cluster from other clusters. The horizontal distance is irrelevant. For a clustering analysis of dense functional data, see Huzurbazar and Humphrey [28]. Documentation for the hierarchical clustering in Matlab is available online [29].

Finally, we compare the health correlates across the clusters. All analyses are stratified by gender. Stata 11.2 [30] was used for descriptives and for comparing the characteristics of the clusters; PACE 2.16 package in Matlab [24] was used for functional data analysis.

RESULTS

Table 1 summarizes sample characteristics. There are slightly more women (52%) than men; the mean year of birth for both groups is in 1936 – that is, they were 56 years old, on average, at the baseline interview wave. Men and women started with mean BMI of 27 and on average gained about one BMI point during the 18 years of followup.

Figure 1 illustrates the steps of the FPCA. The FPCA via PACE first estimated the mean BMI trajectories, the covariance surface, eigenfunctions, and the individuals' estimated principal component scores. The top row plots of Figure 1 show the estimated mean BMI curve for men and women in the sample, both of which increase slightly from age 50 to about 70-75 and then begin to decrease. The middle row of Figure 1 shows the estimated correlation surface, and the bottom row a scree plot from the FPCA. The scree plot displays the cumulative proportion of total variance in the data due to each added functional principal component. For both genders, the first two principal components explain approximately 97 percent of the total variance in BMI.

Figure 2 shows the dendrograms for male and female BMI functions, The plots summarize the formation of the clusters by displaying the vertical distances between the hierarchically-formed clusters. We can identify the number of clusters associated with a particularly large vertical distance values of the cluster formation. The visual inspection indicated the 3-cluster solution as the optimal choice for both genders. Once individuals are clustered, we can obtain the mean BMI curves for each cluster.

Figure 3 shows the mean BMI curves in each cluster for men and women. The results for both genders are substantively similar. One group remains in the normal BMI range (high-normal for men) with a relatively stable levels, especially for me: a slight increase of less than 2 BMI points from age 50 until about age 75 when the mean declines somewhat; we call this group the normal-stable cluster. The second group starts in the overweight range and increases to the obese range; we call this group the overweight-gaining cluster. For women, this cluster starts with the mean BMI of about 29 and increases to about 31 by age 70 when the BMI begins to decline slightly; the men's cluster starts with the mean BMI of about 27 and increases to almost 32. The third group is characterized by BMI curves that start in the overweight/obese range and decline fairly steeply with age; we refer to this group as the overweight-losing cluster. For men, the decline is about 5 BMI points from about 31 to 27; the average BMI for women in this cluster declines about 7 BMI points from 28 to 21.

Table 2 compares basic characteristics of these three groups for men and women. The overweight-gaining and overweight-losing clusters are compared against the normal-stable group using regression-based Wald tests. Unsurprisingly, the mean BMI levels at the start (1992) and end of followup (2010), as well as BMI change over time, were significantly different in both overweight non-stable groups, compared to the reference cluster.

Baseline health as measured by self-rated health and number of conditions was significantly worse for both overweight groups in both genders (P <.001 in seven out of the 8 comparisons,

the exception was SRH in the overweight-gaining group for men, where *P* =.07). The differences were quite pronounced: for instance, the normal stable groups averaged 0.8 chronic conditions in both genders in 1992 while the overweight-losing cluster started with 1.3 and 1.4 conditions for men and women, respectively. In terms of survival during the study duration, the overweight gaining cluster was either statistically equivalent (for women, *P* =.66) to the normal stable cluster or even experienced a lower proportion of deaths (for men, *P* =.02). In contrast, the overweight losing group experienced a significantly higher proportion of loss to death. Among men, 37 percent of the overweight losing cluster died through 2010, compared to 28 percent in the normal stable cluster (*P* <.001). The difference was particularly large for women: the overweight losing cluster lost over 36 percent of the sample to death, compared to just 17 percent in the normal stable group (*P* <.001).

DISCUSSION

The aim of this study was to determine typical body mass index (BMI) trajectories among older adults and to assess the health correlates of the different trajectory groups. The analysis used a novel nonparametric approach: hierarchical clustering of functional curves estimated via the PACE algorithm for sparse longitudinal data. To the best of our knowledge, this is the first applied study using this approach in any field.

We found that BMI curves among older adults fall into three groups: one cluster is mostly in the normal-weight range and remains fairly stable or increases moderately across age; a second cluster is mostly in the overweight range and characterized by gradual weight gain; a third cluster is also mostly in the overweight range but is characterized by steady weight loss. Interestingly, both the optimal number of clusters and the mean BMI trajectories in each cluster were similar for men and women, which suggests common underlying biological determinants for these three different BMI patterns.

The three BMI trajectory clusters differed substantially in terms of initial health and survival through the end of the study period. The overweight gaining cluster started with significantly worse health than the normal stable cluster – despite their poorer health, individuals in this cluster experienced similar (among women) or even slightly lower (among men) risks of dying over time. This discrepancy between health and mortality results might be related to the obesity paradox [3] whereby overweight (and sometimes even obese older individuals) have comparable or lower mortality than the normative group with BMIs between 18.5 and 25,One possible explanation posits that continued weight gain signifies substantial physiological reserve that allow older adults to function with their health problems over the long-term [31-32].

Individuals in the overweight losing cluster started, on average, with significantly worse health than those in the normal stable group; they also experienced significantly greater mortality: about a third higher among men and over twice as high among women. This findings supports well-known research on the high mortality associated with weight loss among older adults [33-35]. However, our approach indicates that the typical weight loss patterns among older adults occurs at relatively high BMI levels, from overweight/obese levels toward the normal weights. This is an important factor because weight loss from overweight levels could be viewed as a positive changed from the perspective of clinicians or the individuals themselves. This paradox, therefore, needs to be further examined with additional evidence.

Our results also corroborate findings from one of the recent studies that modeled heterogeneity in BMI trajectories among older adults and associated health and/or mortality [12]. That study used a joint growth mixture-survival (proportional hazard) model. Despite the different methodologies used, with fundamentally different assumptions (in particular, the FDA approach makes no parametric assumptions about the age effects while the growth mixture analysis was parametric –linear-- with respect to time), the findings of these two studies were substantively similar, which strengthens the validity of both sets of results. However, we argue that the FDA

approach should be used in future analysis, as it is more responsive to data patterns and less restrictive in its assumptions.

Several caveats should be noted. First, we did not distinguish between voluntary and involuntary weight loss (we did not have this data). However, given the modest (at best) success rates of voluntary weight loss programs in the U.S. [36-37], we can safely assume the bulk of the weight loss observed in our data was involuntary. Second, all BMI information was self-reported, potentially biasing the results. However, while we can expect that respondents tend to underreport their body weight [38-39], the underreporting tendencies are likely to remain relatively unchanged over the multiple interviews. Thus the shape of the described trajectories is likely unbiased, but their overall levels may be biased slightly downward.

There is growing interest in examining heterogeneity in BMI trajectories, that is, identifying distinct trajectory types. The growth mixture methodology used in the available studies, however, depends heavily on assumptions and modeling decisions, sometimes yielding contradictory results. We introduced functional data approach as a compelling alternative methodology to identify such BMI trajectory types. The approach can be used for a wide variety of substantive issues, from physical and mental development in early life to health changes across the lifecourse. The nonparametric nature of the FDA allows the detection of subtle but possibly important features of the data, such as acceleration or deceleration of changes at specific ages or time points. For instance, in supplementary analyses (not shown), we found a systematic acceleration of weight loss starting at least several years prior to death, a pattern that's difficult to capture in parametric models. New tools and applications for FDA for sparse longitudinal data are being developed. We urge researchers to explore FDA to examine diverse substantive questions because its flexibility and assumptions that differ from most standard approaches can reveal new and important findings.

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Table 1. Characteristics of the HRS cohort 1992-2010, by sex (N=9,893).

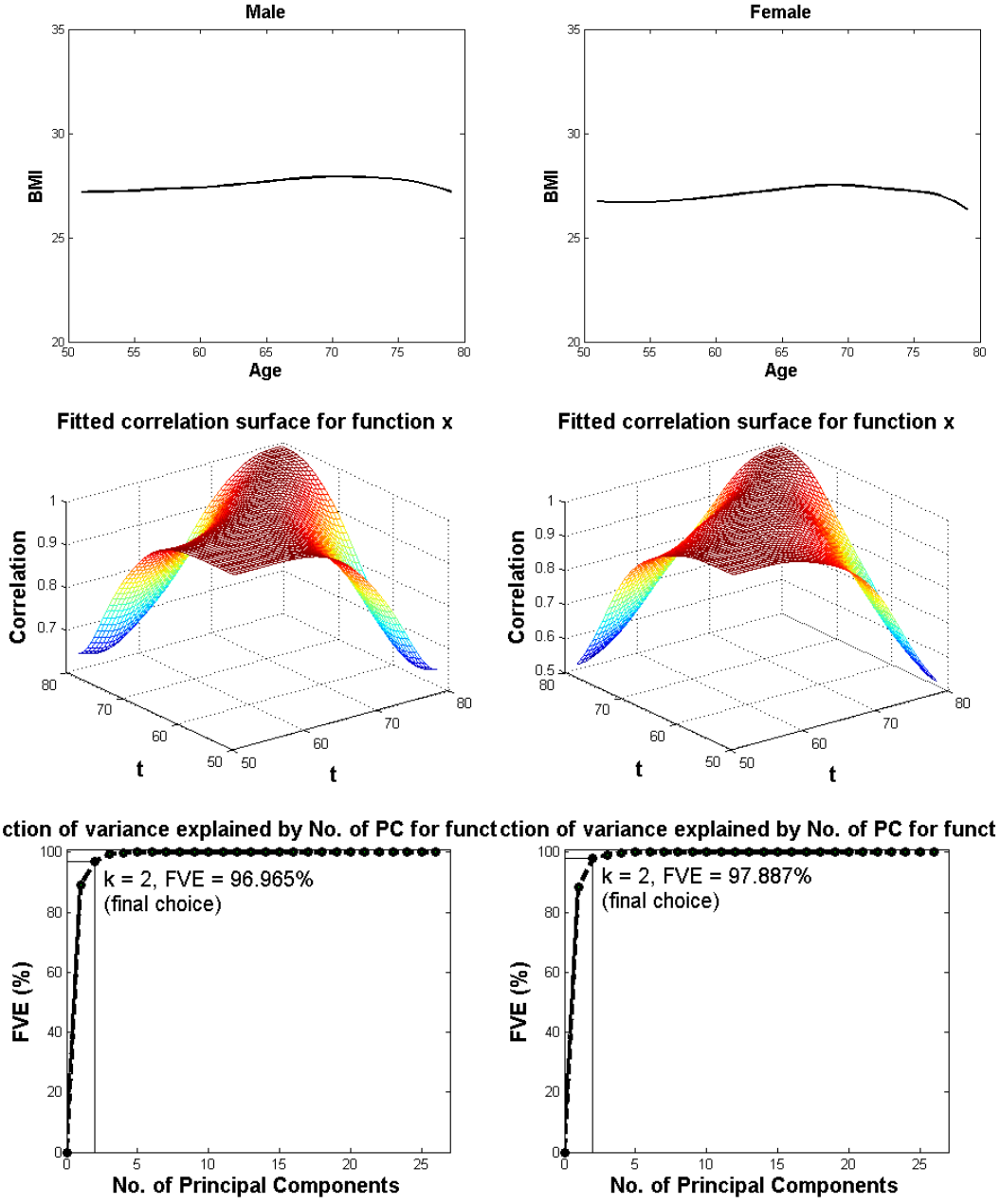
	Men	Women
Proportion of sample at baseline	48.2%	51.8%
Mean year of birth (s.d.)	1936.1 (3.1)	1936.2 (3.1)
Mean body mass index (BMI), in kg/m^2		
In 1992	27.1 (4.0)	26.6 (4.9)
In 2010	28.0 (4.6)	27.5 (5.3)
Self-rated health at baseline		
Excellent	23.1%	21.3%
Very good	27.7%	28.6%
Good	28.4%	27.1%
Fair	12.8%	15.4%
Poor	8.0%	7.6%
Number of conditions at baseline (s.d.)	1.0 (1.1)	1.1 (1.1)
Mortality followup		
Proportion died by 2010 (wave 10)	29.2%	20.5%
Proportion died between waves 9 & 10	7.2%	5.8%
N	4,764	5,129

Table 2. Three-cluster solution for BMI curves: sample means and group comparisons

	Stable normal		Overweight gaining		Overweight losing	
Men						
% in each class	39.1%		32.1%		28.8%	
BMI at 1992 baseline	24.1	Ref.	27.4	*P* <.001	30.7	*P* <.001
BMI at 2010 interview	24.6	Ref.	31.5	*P* <.001	29.1	*P* <.001
BMI change 1992 to 2010	0.2	Ref.	3.4	*P* <.001	-1.5	*P* <.001
Year of birth	1935.8	Ref.	1936.5	*P* <.001	1936.3	*P* <.001
Self-rated health	2.4	Ref.	2.5	*P* =.075	2.8	*P* <.001
Number of conditions	0.8	Ref.	1.0	*P* <.001	1.25	*P* <.001
Proportion died by 2010	27.7%	Ref.	24.2%	*P* =.023	36.6%	*P* <.001
Women						
% in each class	33.9%		50.9%		15.1%	
BMI at 1992 baseline	22.2	Ref.	29.3	*P* <.001	27.5	*P* <.001
BMI at 2010 interview	23.5	Ref.	31.0	*P* <.001	22.7	*P* <.001
BMI change 1992 to 2010	1.1	Ref.	2.1	*P* <.001	-4.6	*P* =.001
Year of birth	1936.1	Ref.	1936.3	*P* =.236	1936.3	*P* =.223
Self-rated health	2.3	Ref.	2.7	*P* <.001	2.9	*P* <.001
Number of conditions	0.8	Ref.	1.2	*P* <.001	1.4	*P* <.001
Proportion died by 2010	17.4%	Ref.	17.9%	*P* =.664	36.1%	*P* <.001

Note: The first column for each group summarizes each characteristic within the group. The second column shows the p-value comparing the second and third groups with the first one with respect to each characteristic. The results are from regression models (linear models, ordered logistic models for SRH and logistic models for proportion who died) of a characteristic on the categorical cluster variable, with the “stable normal” group as the reference category.
The summarized mean BMI levels in each cluster listed in this table are not identical to the estimated mean cluster BMI trajectories.

Figure 1. Mean BMI curves, fitted correlation surfaces, and scree plots.



Note: the left and right panel show results for men and women, respectively.

Figure 2. Dendrograms for male and female clustering, respectively.

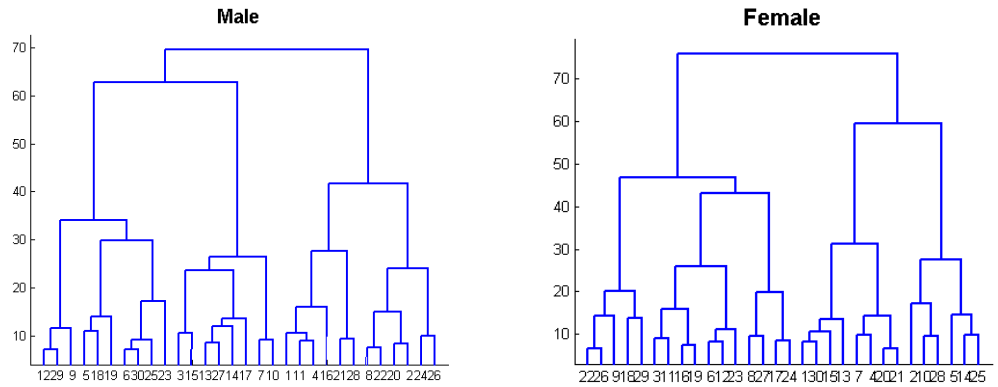
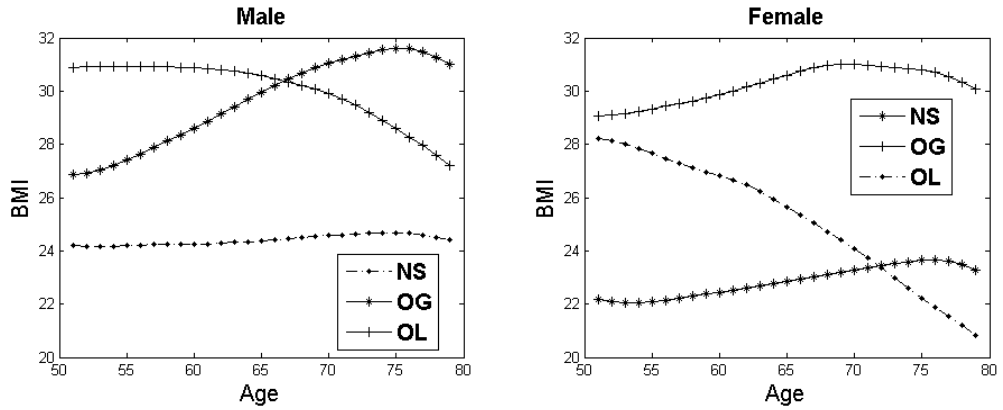


Figure 3. The mean BMI curves of each clusters for men and women



Note: NS = normal stable cluster; OG = overweight gaining cluster; OL = overweight-losing cluster.