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**hereby submit this original work as part of the requirements for the degree of:**

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The Effects of Dietary Phytoestrogens on

Waist-to-Hip and Waist-to-Height Ratios in Prepubescent Girls

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# The Effects of Dietary Phytoestrogens on Waist-to-Hip and Waist-to-Height Ratios in Prepubescent Girls

A thesis submitted to the graduate school of the University of Cincinnati in partial fulfillment of the requirements for the degree of Master's of Science.

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**ABSTRACT**

***Objective:*** Develop three phytoestrogen exposure metrics based on a dietary questionnaire, 24-hour diet recall, and urinary biomarkers and determine the correlation of these metrics. Evaluate the relationship between phytoestrogen consumption and central adiposity in prepubescent girls in regression models with metrics developed from each of the three different phytoestrogen measurement tools.

***Methods:*** A cross-sectional study design was used for this analysis, using participants in the Growing up Female study as the frame for the population. Girls with urinary biomarker measurements, questionnaire data, and diet recalls administered within 24 hours of the urine sample were eligible (n=46). Exposure metrics were developed and analyzed to determine correlations. Waist-to-hip and waist-to-height ratios were calculated and linear regression was used to examine the relationship between these ratios and the biomarker and diet recall data.

***Results:*** No relationship was found between the questionnaire data and the urinary biomarkers. Linear regression analysis examined 3 different regression models with waist-to-height and waist-to-hip ratios and BMI percentile, weekly activity, age, and race. In all final models BMI percentile was significant with $p<.0001$. R squared values showed the strongest correlations between the waist-to-height ratios and variables in the full model of the analysis, specifically the model with daidzein urinary biomarker with R square= 0.777.

***Conclusion:*** No statistical significance was found between any of the biomarker exposure metrics and either waist-to-hip or waist-to-height ratios. This was a well designed study that can be improved with a larger sample size and more descriptive questionnaire data. Future studies should focus on the temporality of the different exposure metrics to better determine their correlation with waist-to-hip and waist-to-height ratios.

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## INTRODUCTION

Breast cancer is the second most common type of cancer in women and is the 7th leading cause of death among women.[1] Dietary phytoestrogen intake has been thought to decrease breast cancer risk.[2] Phytoestrogens are chemical compounds found in plants and structurally resemble estrogens. When phytoestrogens are in the presence of estrogen receptors in humans they can produce estrogenic or anti-estrogenic effects. This implies phytoestrogens can either mimic estrogens or block the effect of estrogens. Dietary phytoestrogens are divided into two groups, isoflavones and lignans.[2] The main sources of dietary isoflavones include legumes, soybeans, and soy-based products. Lignans are typically found in cereal grains and flax seeds.[2] This study will be specifically looking at daidzein and genistein, which are two major isoflavones**.**

Digestion of daidzein results in the release of the sugar molecule daidzin and may be absorbed back into the blood or metabolized by intestinal bacteria into two different metabolites, equol and O-desmethylangolensin (O-DMA). It is estimated between 30-50% of the population are able to produce equol.[9] The metabolite equol is similar in structure to the endogenous hormone estradiol.[10] It has been shown that equol has a higher binding affinity to estrogen receptors when compared to daidzein or genistein. A high soy diet for an equol producer may be beneficial for post-menopausal women, but based on this information could increase levels of estrogen in developing girls. [11]

Waist-to-hip and waist-to-height ratios are measurements of central adiposity[12], which can contribute to increased estrogen levels. Exposure to

estrogen at an earlier age may be related to early breast development, which is a known risk for breast cancer.[3] The incidence rate of early breast development has been on the rise in the United States.[3] It has been hypothesized that diet and increased body mass index (BMI) in young girls are the main contributing factors to this phenomenon.[4,5] Girls who exhibit early breast development have been shown to have higher total body mass and central mass fat throughout the different stages of puberty.[6] Similarly, an increased waist-to-hip ratio in post-menopausal women has been identified as a risk factor for post-menopausal breast cancer.[7]

Wolff et al (2008) examined phytoestrogen exposure and the onset of puberty using breast development as the indicator for puberty. They found that increased dietary intake of phytoestrogens had no association with pubertal development.[13] A cross-sectional study from the Breast Cancer and the Environment Research Centers (BCERC) recently examined phytoestrogens and other environmental exposures and their relation to pubertal onset**.** Three different environmental exposures were examined including phytoestrogens, phenols, and phthalates and their varying urinary concentrations at different stages of development. Enterolactone and bisphenol A (BPA) were higher among girls with higher BMI compared to those with a lower BMI. This study suggests these environmental biomarkers may be relevant in pubertal development.[14] Teitelbaum et al (2008) examined the temporal variability in urinary biomarkers, specifically focusing on quantifying endocrine disrupters. A reasonable degree of temporal reliability was found, leading to the conclusion

that phthalates, phytoestrogens, and phenols are reliable biomarkers to use in studies examining environmental exposures in children.[15]

The CDC identified a sample of urine as an adequate method of measuring levels of chemicals that have entered the body and were transformed into metabolites. The metabolites measured in urine are presented with and without the creatinine correction. Creatinine correction corrects for differences in urinary dilution.[2] Urine samples alone do not necessarily explain the source, amount, or route of phytoestrogen exposure.[2] Phytoestrogens remain in plasma for approximately 24 hours and are excreted in the urine and feces.[16] This implies a urine sample only captures a small window of time regarding a persons total phytoestrogen consumption. Different phytoestrogen estimation tools like questionnaires and diet recalls are often used to fill in those gaps.

Food frequency questionnaires (FFQ) are a common tool used to measure dietary phytoestrogen intake. Three studies have examined the effectiveness of measuring phytoestrogen intake using a FFQ. A study of Asian women in the UK compared the results from a FFQ with those from a 24-hour diet recall. They found phytoestrogen intake to be slightly higher using the FFQ, but determined both measurement tools to be valid.[17] The other two studies compared the results of the FFQ with a urine sample. Both studies concluded the FFQ was effective in measuring dietary phytoestrogen intake.[17, 18]

## METHODS

### Exposure Metrics

A cross-sectional study design was utilized, using participants in the Growing up Female study as the frame for the population**.** This population consists of 379 girls between the ages of 6 and 9 living in the Cincinnati area. A total of 46 girls had data for all three exposure metrics and made up the subset population for this analysis. Although thousands of diet recalls have been administered over the course of this study, only 46 girls had diet recalls administered within 24 hours of their second year study visit. Exposure metrics were developed for the three different phytoestrogen measurement tools. The first exposure metric was acquired through a urine sample. Urinary concentrations of genistein and daidzein were measured by the CDC in an environmental laboratory and examined for correlation.

A 24-hour timed diet recall was the second exposure metric. This diet recall was administered via phone call by the Cincinnati Center for Nutritional Research and Analysis with the parent and daughter within 24 hours of the urine sample. The genistein and daidzein biomarkers data were retrieved from the nutrient analysis reports from the Nutrition Data System for Research (NDSR) Dietary intake data were collected and analyzed using Nutrient Data System for Research software version 2009 developed by the Nutrition Coordinating Center (NCC), University of Minnesota, Minneapolis, MN.[20] This system takes the information from the diet recall and produces a quantitative measure of different nutritional elements based on the information provided by the subject and the subject's parent. The total value the NDSR calculates for daidzein and genistein intake is the exposure metric for 24-hour diet recall.

The third and final exposure metric was developed using a food frequency questionnaire. For each of the foods in the Product Use section of the BCERC questionnaire that contain phytoestrogens, the response to that item is either YES, NO, or Don't know. There was no time frame given for this question. Phytoestrogen content, specifically genistein and daidzein, was calculated using the NDRS for each item on this food list. After this calculation, 6 items on the food list were found to contain either genistein, daidzein, or both. The food items of interest consist of peas and lima beans, soy products, eggrolls, tea, coffee, and instant breakfast drink. The number of yes answers for each girl represents the non-weighted exposure metric for the food frequency questionnaire.

A weighted questionnaire exposure metric was developed using the food frequency questionnaires and takes into account the amount of daidzein and genistein content in each questionnaire food item. Table 1 shows the amount of daidzein and genistein in the food items. Each food item was weighted according to the content of daidzein and genistein. Table 2 shows the weighted values used for genistein and daidzein.

Regression analysis

Waist to hip and waist to height ratios were calculated on the subset population. BMI percentile was calculated using the CDC website.[24] Linear regression was used to examine the relationship between these ratios and the biomarker and diet recall data. Genistein and daidzein were analyzed separately and then their amounts summed for a total measure for both the urinary biomarker and the diet recall data. The subjects' BMI percentile, age, race, and

total weekly activity were also added to the model. The waist to hip and waist to height ratios act as the dependent variables. Regression techniques were then applied to obtain final models. Models were also run without BMI percentile, and with BMI percentile as the dependent variable.

**Results**

Descriptive Statistics

The subset population used for this study consisted of 20 African Americans, 24 Caucasians, and 2 Hispanics. The race variable was later re-coded into a dichotomous variable, African American (20) versus all others (26). The mean BMI percentile for the cohort (n=46) was 65.57%. The mean waist-to-hip and waist-to-height ratios were 0.83 and 0.50 respectively. Biomarker descriptive statistics are shown in Table 3.

Creatinine Correction

The urine samples were creatinine corrected by dividing the level of the phytoestrogen biomarker by the level of creatinine in the urine. This correction was only going to be used if there was an existing correlation. In this particular case a correlation did not exist, so the creatinine corrected urine was not utilized for the analysis. R squared values for correlation of genistein and daidzein with creatinine were 0.325 and 0.344 respectively.

Questionnaire Data

The weighted and non weighted questionnaire data were analyzed to determine if a correlation existed between the questionnaire data and the urinary biomarkers as well as the diet recall biomarkers. No correlation was found

between the urinary biomarker data and the weighted and non weighted questionnaire data or between urinary biomarker data and diet recall (Table 4).

Linear Regression

The first set of analyses used the waist-to-hip and waist-to-height terms as the dependent variables. Urinary biomarker genistein (GEN) and daidzein (DAZ) were analyzed individually and as a combined term (GENDAZ). The diet recall data were also analyzed with the genistein and daidzein separately and then again as a combined term. Race, age, weekly activity, and BMI percentile were also included in the full model. Full and final models were generated and are shown in Tables 5-8. In both final models BMI percentile was significant in every situation with $p<.0001$. R squared values served as the model-fit statistic for this analysis. Tables 9 and 10 show these values. Strongest correlations can be seen between the waist-to-height ratios and variables from the full model of the analysis, specifically the daidzein urinary biomarker.

Because of the strong correlation between the anthropometric measurements and BMI percentile, BMI was first removed from the model and then evaluated as the dependent variable (Table 11). The final model for waist-to-hip ratio with BMI percentile removed from the model shows weekly activity to be significant in the 3 urinary biomarker variables (Table 12). The waist-to-height final model with BMI percentile removed from the model showed age to be significant with the genistein diet recall and the combined diet recall data (tables 13 and 14). R squared values for model fit showed no significance without BMI in the model (Tables 15 and 16). With BMI percentile as the dependent variable,

all terms proved to be insignificant and fell out of the model, leaving only the biomarker term. R squared values for model fit also showed no significance (Tables 17-19). A post hoc power analysis was conducted to determine the power for detecting a correlation between the waist-to-hip ratio and genistein and daidzein. This analysis showed genistein and daidzein to have a power of 7.9% and 7.2% respectively. .

**Discussion**

No statistical significance was found between any of the biomarker exposure metrics and either waist-to-hip or waist-to-height ratios. The post-hoc power analysis indicated this study was significantly underpowered. Waist-to-hip and waist-to-height ratios were chosen as the dependent variables because we were interested in finding how the biomarker data would associate with the measures of central obesity, and the fit of the models to the data when different measures of phytoestrogens exposures were used. The subject's BMI percentile, age, race, and weekly activity were added to the model because these variables may also affect the girl's central obesity measurement. BMI percentile showed to be very significant in the model, which is why this term was first removed from the model and then analyzed as the dependent variable.

Median levels of genistein were slightly lower then those of other children in the US but median daidzein levels were very comparable. According to the CDC's Fourth national report on human exposure to environmental chemicals median levels in children living in the US for genistein and daidzein were 0.029

mg and 0.0067 respectively.[22] This is valuable information because it can be used to better educate parents regarding their child's dietary intake in comparison to the rest of the country.

Overall, associations were not found between the waist-to-hip and waist-to-height ratios and the biomarker data. However correlations were found between the anthropometric ratios and BMI percentile. Although this was to be expected, it validated our modeling techniques and demonstrated that these ratios are valuable measurements and could be analyzed with BMI in the future.

Limitations

All the anthropometric measurements and urine samples used in this analysis were taken from the second year visit. Parents were instructed to fill out the questionnaire within 24 hours of the study visit. However, the question itself did not specify a time period, but rather just listed the foods and asked for a yes or no response. The questionnaire data were very limited in soy food options and certain questions combined two or more food options into one question. For example peas and lima beans were grouped together, however only lima beans contain genistein. The question itself was limiting in that the required answer was only a yes or no response. A better way to word this question in the future would be to ask about the quantity of food product consumed.

The Growing up Female study population is a community based population, with the majority of the subjects recruited through local elementary schools. Because this is a volunteer population it is not necessarily representative of the general population. A smaller subset population had to be

used for the analysis because a limited number of girls had timed diet recall data. For future studies an analysis with more power would be more appropriate. This subset analysis leads to further bias due to the temporality of the diet recall. Timed diet recalls were only obtained during certain months throughout the year. This could potentially alter the subject's diet depending on whether or not she was in school at the time. For example, school lunches may offer a soy burger, which contain high levels of genistein and daidzein, and might not be something the girl would typically eat at home. In this instance, her daidzein and genistein levels would be higher if she was in school during the time of the urine collection and 24-hour diet recall.

Future studies

Future studies on this topic may want to further examine phytoestrogen intake in its entirety and not just the isoflavones. Enterolactone is another phytoestrogen and is considered part of the lignan class. Common foods containing enterolactone are whole grains and flaxseed. In a recent study comparing the relationship between urinary biomarkers and pubertal development, an inverse association between enterolactone levels and BMI was found. They also examined genistein and daidzein, but found limited associations between the urinary biomarkers and pubertal development.[23]

Another interesting variable to examine for future studies would be the girl's daily caloric intake. The total calories from phytoestrogen could then be calculated using the NDRS and compared with the girl's total caloric intake. This

would require an extremely accurate 24-hour diet recall and would need to be done multiple times in order to increase the validity of this test.

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**Table 1. Non Weighted Food Exposure Metric**

| Food Item | Serving size | Daidzein per serving | Genistein per serving | Number of YES answers |
|---|---|---|---|---|
| Instant breakfast drink | 1 Packet | 0.416 | 0.718 | 1 |
| Tofu or any soy products such as soy milk or veggie burgers | 2 OZ | 9.042 | 13.747 | 3 |
| Eggrolls | 1 | 0.068 | 0.064 | 2 |
| Peas and Lima Beans | 0.5 CP | 0.000 | 0.003 | 8 |
| Coffee | 1 CP | 0.118 | 0.000 | 2 |
| Tea | 1 CP | 0.024 | 0.018 | 8 |
| Total | | | | 24 |

**Table 2. Weighted Food Exposure Metric**

| Food Item | Weighted Daidzein (mg) | Weighted Genistein (mg) |
|---|---|---|
| Instant breakfast drink | 0.416 | 0.718 |
| Tofu or any soy products such as soy milk or veggie burgers | 9.042 | 13.747 |
| Eggrolls | 0.068 | 0.064 |
| Peas and Lima Beans | 0.000 | 0.003 |
| Coffee | 0.118 | 0.000 |
| Tea | 0.024 | 0.018 |

**Table 3. Descriptive Statistics**

| | Mean | Median | SD |
|---|---|---|---|
| Daidzein Biomarker (mg) | 0.14 | 0.06 | 0.24 |
| Genistein Biomarker (mg) | 0.25 | 0.17 | 0.38 |
| Combined Genistein and Daidzein Biomarker (mg) | 0.39 | 0.26 | 0.60 |
| kcal | 1836.75 | 1732.99 | 469.33 |
| Daidzein Diet Recall (mg) | 0.07 | 0.04 | 0.12 |
| Genistein Diet Recall (mg) | 0.13 | 0.08 | 0.19 |
| Combined Genistein and Daidzein Diet Recall (mg) | 0.21 | 0.14 | 0.30 |
| Waist to hip ratio | 0.83 | 0.83 | 0.04 |
| Waist to height ratio | 0.50 | 0.44 | 0.05 |
| BMI % | 65.57 | 71.20 | 30.17 |
| Age (months) | 104.11 | 104.00 | 8.58 |
| Activity each week (min) | 835.82 | 730.00 | 725.83 |

**Table 4. Urinary biomarker data versus the weighted and non weighted questionnaire data**

| **Correlations: R and P values** | | | |
|---|---|---|---|
| | | **R values** | **P Values** |
| | GEN from diet recall and GEN from non-weighted q metric | 0.09391 | 0.5592 |
| | DAZ from diet recall and DAZ from non-weighted q metric | 0.01605 | 0.9207 |
| | GEN from diet recall and GEN from weighted q metric | 0.09193 | 0.5676 |
| | DAZ from diet recall and DAZ from weighted q metric | 0.04180 | 0.7952 |
| | GEN from diet recall and urinary biomarker GEN | 0.06588 | 0.6636 |
| | DAZ from diet recall and urinary biomarker DAZ | -0.15414 | 0.3064 |
| | GEN from urinary biomarker and GEN from non-weighted q metric | 0.00995 | 0.9576 |
| | DAZ from urinary biomarker and DAZ from non-weighted q metric | -0.18923 | 0.3080 |
| | GEN from urinary biomarker and GEN from weighted q metric | -0.06959 | 0.7099 |
| | DAZ from urinary biomarker and DAZ from weighted q metric | -0.10708 | 0.5664 |

**Table 5. Full model (waist-to-hip)**

| | Biomarker | | BMIPCT | | Age | | Activity | | Race | |
|---|---|---|---|---|---|---|---|---|---|---|
| | beta | p | beta | p | beta | p | beta | p | beta | p |
| GEN Biomarker | 0.00788 | 0.7182 | 0.00085 | 0.0002 | -0.00002 | 0.9748 | 0.00001 | 0.0989 | 0.00070 | 0.9538 |
| GEN Diet Recall | 0.00243 | 0.9442 | 0.00084 | 0.0002 | -0.00003 | 0.9668 | 0.00001 | 0.1012 | 0.00109 | 0.9280 |
| DAZ Biomarker | 0.03468 | 0.3570 | 0.00087 | <.0001 | 0.00001 | 0.9939 | 0.00002 | 0.0854 | 0.00035 | 0.9763 |
| DAZ Diet Recall | 0.02844 | 0.6427 | 0.00086 | 0.0002 | -0.00001 | 0.9922 | 0.00002 | 0.0945 | 0.00094 | 0.9376 |
| GEN and DAZ Biomarker | 0.00873 | 0.5505 | 0.00086 | 0.0001 | -0.00001 | 0.9866 | 0.00001 | 0.0945 | 0.00045 | 0.9704 |
| GEN and DAZ Diet Recall | 0.00508 | 0.8255 | 0.00085 | 0.0002 | -0.00002 | 0.9755 | 0.00001 | 0.0990 | 0.00097 | 0.9356 |
| | | | | | | | | | | |

**Table 6. Final Model (waist-to-hip)**

| | Biomarker | | BMIPCT | | Age | |
|---|---|---|---|---|---|---|
| | beta | p | beta | p | beta | p |
| GEN Biomarker | -0.01391 | 0.3062 | 0.00079 | <0.0001 | | |
| GEN Diet Recall | -0.02723 | 0.3196 | 0.00078 | <0.0001 | | |
| DAZ Biomarker | 0.03475 | 0.3359 | 0.00087 | <0.0001 | 0.00002 | 0.0447 |
| DAZ Diet Recall | 0.02876 | 0.6251 | 0.00086 | <0.0001 | 0.00002 | 0.0506 |
| GEN and DAZ Biomarker | 0.00881 | 0.5293 | 0.00086 | <0.0001 | 0.00002 | 0.0515 |
| GEN and DAZ Diet Recall | 0.00530 | 0.8105 | 0.00085 | <0.0001 | 0.00001 | 0.0544 |

**Table 7. Full Model (waist-to height)**

| | Biomarker | | BMIPCT | | Age | | Activity | | Race | |
|---|---|---|---|---|---|---|---|---|---|---|
| | beta | p | beta | p | beta | p | beta | p | beta | p |
| GEN Biomarker | 0.00103 | 0.9576 | 0.00150 | <0.0001 | -0.00020 | 0.7390 | 0.000002 | 0.7772 | 0.00133 | 0.9018 |
| GEN Diet Recall | 0.00023 | 0.9941 | 0.00150 | <0.0001 | -0.00021 | 0.7380 | <0.00001 | 0.7784 | 0.00138 | 0.8976 |
| DAZ Biomarker | 0.01675 | 0.6189 | 0.00152 | <0.0001 | -0.00019 | 0.7584 | <0.00001 | 0.7508 | 0.00010 | 0.9256 |
| DAZ Diet Recall | 0.01414 | 0.7957 | 0.00151 | <0.0001 | -0.00019 | 0.7529 | <0.00001 | 0.7636 | 0.00130 | 0.9049 |
| GEN and DAZ Biomarker | 0.00297 | 0.8200 | 0.00151 | <0.0001 | -0.00020 | 0.7457 | <0.00001 | 0.7703 | 0.00115 | 0.9151 |
| GEN and DAZ Diet Recall | 0.00210 | 0.9187 | 0.00150 | <0.0001 | -0.00020 | 0.7430 | <0.00001 | 0.7732 | 0.00132 | 0.9027 |

**Table 8. Final Model (waist-to-height)**

| | Biomarker | | BMIPCT | |
|---|---|---|---|---|
| | beta | p | beta | p |
| GEN Biomarker | -0.010573 | 0.3261 | 0.00146 | <0.0001 |
| GEN Diet Recall | -0.017271 | 0.4261 | 0.00145 | <0.0001 |
| DAZ Biomarker | -0.019927 | 0.2350 | 0.00146 | <0.0001 |
| DAZ Diet Recall | -0.037702 | 0.2867 | 0.00144 | <0.0001 |
| GEN and DAZ Biomarker | -0.007351 | 0.2751 | 0.00146 | <0.0001 |
| GEN and DAZ Diet Recall | -0.012755 | 0.3561 | 0.00145 | <0.0001 |

**Table 9. Model Fit (waist-to-height**

| | Full Model | Final Model | |
|---|---|---|---|
| | R squared | R squared | p value |
| GEN Biomarker | 0.774972 | 0.741794 | 0.3261 |
| GEN Diet Recall | 0.774948 | 0.739823 | 0.4261 |
| DAZ Biomarker | 0.777039 | 0.744429 | 0.2350 |
| DAZ Diet Recall | 0.775516 | 0.742807 | 0.2867 |
| GEN and DAZ Biomarker | 0.775387 | 0.743137 | 0.2751 |
| GEN and DAZ Diet Recall | 0.775036 | 0.741126 | 0.3561 |

**Table 10. Model Fit (waist-to-hip)**

| | Full Model | Final Model | |
|---|---|---|---|
| | R squared | R squared | p value |
| GEN Biomarker | 0.515950 | 0.364219 | 0.3062 |
| GEN Diet Recall | 0.513655 | 0.363393 | 0.3196 |
| DAZ Biomarker | 0.528891 | 0.528875 | 0.3359 |
| DAZ Diet Recall | 0.517500 | 0.517378 | 0.6251 |
| GEN and DAZ Biomarker | 0.520064 | 0.520029 | 0.5293 |
| GEN and DAZ Diet Recall | 0.514456 | 0.514299 | 0.8105 |

**Table 11. Full Model (waist-to-hip) without BMI**

| | Biomarker | | Age | | Activity | | Race | |
|---|---|---|---|---|---|---|---|---|
| | beta | p | beta | p | beta | p | beta | p |
| GEN Biomarker | -0.01445 | 0.5959 | -0.00091 | 0.2826 | 0.00002 | 0.0301 | -0.00751 | 0.6242 |
| GEN Diet Recall | -0.03829 | 0.3682 | -0.00091 | 0.2814 | 0.00002 | 0.0351 | -0.00688 | 0.6499 |
| DAZ Biomarker | 0.00001 | 0.9599 | 0.00199 | 0.2771 | 0.00862 | 0.0287 | 0.00052 | 0.5736 |
| DAZ Diet Recall | -0.04495 | 0.5526 | -0.00093 | 0.2761 | 0.00002 | 0.0340 | -0.00790 | 0.6037 |
| GEN and DAZ Biomarker | -0.00684 | 0.7083 | -0.00093 | 0.2802 | -0.00092 | 0.0304 | -0.00789 | 0.6071 |
| GEN and DAZ Diet Recall | -0.02309 | 0.4133 | -0.00091 | 0.2792 | 0.00002 | 0.0354 | -0.00718 | 0.6358 |

**Table 12. Final Model (waist-to-hip) without BMI**

| | Biomarker | | Activity | |
|---|---|---|---|---|
| | beta | p | beta | p |
| GEN Biomarker | -0.01684 | 0.5275 | 0.00002 | 0.0522 |
| GEN Diet Recall | -0.05205 | 0.1100 | | |
| DAZ Biomarker | -0.00517 | 0.9121 | 0.00002 | 0.0523 |
| DAZ Diet Recall | -0.08212 | 0.1243 | | |
| GEN and DAZ Biomarker | -0.00833 | 0.6417 | 0.00002 | 0.0536 |
| GEN and DAZ Diet Recall | -0.03358 | 0.1057 | | |

**Table 13. Full Model (waist-to-height) without BMI**

| | Biomarker | | Age | | Activity | Race | | |
|---|---|---|---|---|---|---|---|---|
| | beta | p | beta | p | beta | p | beta | p |
| GEN Biomarker | -0.03842 | 0.2914 | -0.00178 | 0.1187 | 0.00002 | 0.1840 | -0.01317 | 0.5177 |
| GEN Diet Recall | -0.07273 | 0.2009 | -0.00178 | 0.1155 | 0.00002 | 0.2098 | -0.01289 | 0.5218 |
| DAZ Biomarker | -0.04776 | 0.4540 | -0.00181 | 0.1157 | 0.00002 | 0.1906 | -0.01465 | 0.4747 |
| DAZ Diet Recall | -0.11508 | 0.2546 | -0.00181 | 0.1116 | 0.00002 | 0.2108 | -0.01428 | 0.4791 |
| GEN and DAZ Biomarker | -0.02429 | 0.3198 | -0.00179 | 0.1173 | 0.00002 | 0.1906 | -0.01347 | 0.5090 |
| GEN and DAZ Diet Recall | -0.04802 | 0.2025 | -0.00179 | 0.1137 | 0.00002 | 0.2144 | -0.01311 | 0.5116 |

**Table 14. Final Model (waist-to-height) without BMI**

| | Biomarker | | Age | |
|---|---|---|---|---|
| | beta | p | beta | p |
| GEN Biomarker | -0.02396 | 0.2434 | | |
| GEN Diet Recall | 0.00712 | 0.0939 | 0.00961 | 0.0529 |
| DAZ Biomarker | -0.03709 | 0.2488 | | |
| DAZ Diet Recall | -0.10859 | 0.1015 | | |
| GEN and DAZ Biomarker | -0.01536 | 0.2328 | | |
| GEN and DAZ Diet Recall | 0.043531 | 0.0824 | -0.00168 | 0.0533 |

**Table15. Model fit (waist-to-hip) without BMI**

| | Full Model | Final Model | |
|---|---|---|---|
| | R squared | R squared | p value |
| GEN Biomarker | 0.173405 | 0.134382 | 0.5275 |
| GEN Diet Recall | 0.189131 | 0.055784 | 0.1100 |
| DAZ Biomarker | 0.164985 | 0.122950 | 0.9121 |
| DAZ Diet Recall | 0.175546 | 0.051689 | 0.1243 |
| GEN and DAZ Biomarker | 0.169148 | 0.129004 | 0.6417 |
| GEN and DAZ Diet Recall | 0.184981 | 0.057126 | 0.1057 |

**16. Model fit (waist-to-height) without BMI**

| | Full Model | Final Model | |
|---|---|---|---|
| | R squared | R squared | p value |
| GEN Biomarker | 0.149637 | 0.030116 | 0.2434 |
| GEN Diet Recall | 0.165631 | 0.131569 | 0.0939 |
| DAZ Biomarker | 0.132383 | 0.029439 | 0.2488 |
| DAZ Diet Recall | 0.155318 | 0.101500 | 0.1015 |
| GEN and DAZ Biomarker | 0.145813 | 0.031483 | 0.2328 |
| GEN and DAZ Diet Recall | 0.165288 | 0.135757 | 0.0824 |

**Table 17. Full Model with BMI as Dependent Variable**

| | Biomarker | | Age | | Activity | | Race | |
|---|---|---|---|---|---|---|---|---|
| | beta | p | beta | p | beta | p | beta | p |
| GEN Biomarker | -26.26992 | 0.2084 | -1.0498654 | 0.1078 | 0.01147 | 0.1702 | -9.65572 | 0.4074 |
| GEN Diet Recall | -48.64075 | 0.1354 | -1.0499465 | 0.1038 | 0.01069 | 0.1972 | -9.51598 | 0.4077 |
| DAZ Biomarker | -42.47727 | 0.2441 | -1.0707398 | 0.1025 | 0.01116 | 0.1854 | -10.30131 | 0.3769 |
| DAZ Diet Recall | -85.44204 | 0.1387 | -1.0695908 | 0.0979 | 0.01058 | 0.2032 | -10.28342 | 0.3694 |
| GEN and DAZ Biomarker | -18.06205 | 0.1962 | -1.0556061 | 0.1054 | 0.01123 | 0.1794 | -9.68108 | 0.4051 |
| GEN and DAZ Diet Recall | -33.29999 | 0.1223 | -1.0555415 | 0.1011 | 0.01052 | 0.2039 | -9.64043 | 0.3997 |

**Table 18. Final Model with BMI as Dependent Variable**

| | Biomarker | |
|---|---|---|
| | beta | p |
| GEN Biomarker | -9.19359 | 0.4447 |
| GEN Diet Recall | -31.79385 | 0.1799 |
| DAZ Biomarker | 11.78523 | 0.5319 |
| DAZ Diet Recall | -49.07947 | 0.2071 |
| GEN and DAZ Biomarker | -5.49906 | 0.4659 |
| GEN and DAZ Diet Recall | -20.34839 | 0.1782 |

**Table 19. Model Fit with BMI as Dependent Variable**

| | Full Model | Final Model | |
|---|---|---|---|
| | R Squared | R Squared | p value |
| GEN Biomarker | 0.174938 | 0.013040 | 0.4447 |
| GEN Diet Recall | 0.194104 | 0.194104 | 0.1799 |
| DAZ Biomarker | 0.168131 | 0.008741 | 0.5319 |
| DAZ Diet Recall | 0.193008 | 0.035129 | 0.2071 |
| GEN and DAZ Biomarker | 0.177554 | 0.011878 | 0.4659 |
| GEN and DAZ Diet Recall | 0.198735 | 0.039913 | 0.1782 |