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## The Association Between Dairy Consumption and Insulin Resistance

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A thesis submitted to the faculty of
Brigham Young University
in partial fulfillment of the requirements for the degree of

Master of Science

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#### **ABSTRACT**

The Association Between Dairy Consumption and Insulin Resistance

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**Background:** A cross-sectional design was employed to ascertain the relationship between dairy consumption and insulin resistance (IR) in 272 middle-aged, nondiabetic women. Methods: Participants kept a seven-day weighed food record to report their diets, including consumption of dairy foods. IR was assessed using the homeostatic model assessment (HOMA), using the following formula: fasting plasma insulin ( $\mu$ U/ml) x fasting plasma glucose (mg/dL)/405. The Bod Pod was used to examine body fat percentage, and accelerometry over a seven-day period was used to assess physical activity. HOMA values were log-transformed and regression analysis and the General Linear Model procedure were used to determine how mean HOMA differed across low, moderate, and high dairy intake groups. **Results:** (Mean  $\pm$  SD) age: 40.1  $\pm$  3.0 years, physical activity (average activity counts for one week, divided by 1,000): 2700.1  $\pm$  781.9, body fat percentage:  $31.7 \pm 6.9$ , weight (kg):  $66.1 \pm 10.0$ , fasting glucose (mg/dL):  $86.7 \pm 5.9$ , fasting insulin ( $\mu$ U/mL): 7.0 ± 4.2, energy intake (kcal/day): 2051.9 ± 319.1, kcal from carbohydrate (%):  $55.7 \pm 6.2$ , kcal from protein (%):  $13.8 \pm 2.5$ , kcal from fat (%):  $30.5 \pm 5.8$ , soluble fiber (g per 1,000 kcal):  $1.7 \pm 0.9$ , insoluble fiber (g per 1,000 kcal):  $3.8 \pm 1.9$ , dairy intake (servings/day):  $1.1 \pm 1.0$ , HOMA:  $1.5 \pm 1.0$ , log-transformed HOMA:  $0.3 \pm 0.6$ . Those in the highest quartile for dairy consumption had significantly higher log-transformed HOMA  $(0.41 \pm 0.53)$  than those in the moderate  $(0.22 \pm 0.55)$  or low  $(0.19 \pm 0.58)$  consumption categories (F = 6.90, p = 0.0091). This relationship remained significant after controlling for all covariates (F = 4.71, p = 0.030). Controlling for physical activity strengthened the relationship between dairy consumption and IR by 7%. Adjusting for body weight, percent of kcal from fat, and insoluble and soluble fiber intake also strengthened the relationship. Controlling for energy intake and body fat percentage weakened the relationship by 32% and 13%, respectively, though it remained significant. Conclusion: High dairy consumption is significantly associated with IR in middle-aged, nondiabetic women.

Keywords: milk, diet, type 2 diabetes mellitus, T2DM



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#### Introduction

Increasing rates of overweight and obesity worldwide have generated concern about a diabetes epidemic, with associated negative effects on quality of life, life expectancy, and healthcare costs. Recent data from the United States suggests that more than 21 million people (8.7% of the population) are affected by diabetes, with more than 90% of these suffering from type 2 diabetes mellitus (T2DM). Danaei et al. reported that the number of individuals with diabetes worldwide has nearly doubled over the past 30 years. The substantial economic and healthcare burdens placed on society by T2DM demonstrate a need for improved prevention efforts, particularly given its largely avertable nature.

To better control T2DM, considerable effort has been devoted to research aimed at isolating the determinants of this widespread disorder. To date, many modifiable risk factors of T2DM have been identified. <sup>4-7</sup> Of these contributors, diet has become a primary focus. <sup>8,9</sup> Consumption of a healthy diet, commonly characterized by sensible intakes of unsaturated fats and fiber, and low intakes of saturated and trans fats and foods with a high glycemic load, has been associated with a decreased risk of developing T2DM. <sup>6,10,11</sup>

Several studies have also investigated the impact of milk and dairy products on the development of T2DM. Many epidemiological investigations have identified an inverse relationship between dairy consumption, as part of an overall healthy diet, and T2DM<sup>12-14</sup> and the metabolic syndrome (MetS). However, an inverse association has not always been found. leaving the relationship inconclusive.

The natural disease progression of T2DM is characterized by the inability of the body to respond to consumption of a glycemic load with the appropriate amount of insulin to mediate



glucose uptake.<sup>23,24</sup> This is known as insulin resistance (IR). IR has been identified as an independent risk factor for T2DM, obesity, and cardiovascular disease.<sup>25,26</sup>

Milk and dairy products have been identified as potent insulin-secratagogues, as their consumption stimulates acute hyperinsulinemia.<sup>27-31</sup> The hyperinsulinemia resulting from milk and dairy consumption may be considered a beneficial and even protective effect for regulating blood glucose levels, particularly in individuals with elevated levels or those with T2DM.<sup>32</sup> However, consumption of milk and dairy products and resultant hyperinsulinemia may produce less-than-desirable long-term effects in healthy individuals, including IR. Research in humans<sup>33</sup> and in rats<sup>34</sup> suggests that hyperinsulinemia can lead to IR.

Prevention of T2DM may best be accomplished by avoiding the development of IR. Several modifiable risk factors of IR have been identified, 35-38 among which diet plays a principal role. 37,38 Given several studies show that consumption of dairy products tends to be inversely related to T2DM, it seems that there would be a similar association between dairy intake and IR. Unfortunately, the dairy and IR relationship has not been extensively investigated, 39-42 and results have been contradictory.

Measurement method shortcomings are common among studies that have investigated the role of milk and dairy products on disease outcomes. To date, body weight has largely been self-reported or the body mass index (BMI) has been employed to estimate body composition. Both of these strategies result in considerable measurement error and frequent misclassification. <sup>43</sup> In addition, questionnaires have been used almost exclusively to assess physical activity levels in participants. Unfortunately, self-reported physical activity is known to be highly biased. <sup>44</sup>

The present study was designed to overcome these measurement deficiencies. A high quality measurement method, air-displacement plethysmography, was employed to evaluate body fat, rather than body weight. Moreover, physical activity was measured objectively using accelerometers, rather than relying on self-reported estimates of activity.

In conclusion, studies designed to examine the relationship between dairy intake and IR are sparse. New research on the association between dairy intake and IR in women is warranted. Use of high quality measurement methods employed in the present study should enhance our understanding of the role of dairy consumption on IR in women.

#### **Methods and Procedures**

Design

A cross-sectional design was employed to examine the relationship between dairy intake and insulin resistance (IR) in a sample of 272 middle-aged women. In addition, the extent to which age, weight, body fat percentage, total energy intake, physical activity level, education, percent of kcal from carbohydrate, protein, and fat, and insoluble and soluble fiber intake influenced the relationship between dairy consumption and IR was investigated.

## Pre-Existing Data

Data for the present study were pre-existing and were collected as part of the Brigham Young University (BYU) Lifestyle Project directed by Larry Tucker, Ph.D. The BYU Lifestyle Project is a prospective cohort study spanning ten years. Over the course of the epidemiological study, dozens of students assisted with collecting data every other year on the cohort, covering five different phases of the investigation. The present study represents data collected during one

of the five phases. The author took an additional graduate course, Hlth 602 Epidemiology, to substitute for not participating in the data collection process.

Subjects

Potential subjects were recruited through advertisements and e-mails for the BYU Lifestyle Project from approximately 20 cities in Utah and Wyoming. Initial inclusion screening was conducted via telephone. In order to be included as a participant in the Lifestyle Project participants were required to be female, aged 35-45 years, not pregnant, nondiabetic, nonsmoking, and apparently healthy. Using nondiabetic subjects allowed for a greater opportunity to investigate potential prevention strategies for T2DM. Informed consent was obtained from each subject prior to study commencement and was approved by the University's Institutional Review Board.

### Procedures

Subject information and measurements were gathered at the University. Measurements and instructions lasted approximately 60 to 90 minutes. Height and weight were measured for each participant during the initial appointment while wearing a one-piece lab-issued swimsuit. While wearing the same swimsuit and a swim cap, a Bod Pod test (Life Measurements Instruments, Concord, CA) was performed on each subject to estimate body fat percentage. Subjects were taught how to accurately measure food intake using a digital food scale (Ohaus 2000, Florham Park, NJ), and were instructed to keep a seven-day weighed food record. A nine-page diet log, including specific directions for recording dietary intake, a sample page, and blank records for each day of the week, was given to each subject. Each subject was asked to read the instructions. Common recording mistakes were drawn to the attention of the subjects to improve



detail and compliance. Next, each subject was given written and verbal instructions regarding the proper way to weigh food with the Ohaus 2000 portable electronic scale using plastic food models.

Each subject received an Actigraph accelerometer (Health One Technology, formerly CSA, Pensacola, FL), which they were instructed to wear continuously over the left hip for seven consecutive days, with the exception of bathing or water events. Participants were encouraged to maintain their normal lifestyle and to avoid implementing new dietary or exercise practices. Explanations of proper techniques were provided to all participants so that they understood correct procedures.

During the seven-day period participants were contacted by study personnel by telephone two to three times to ensure that they were accurately recording everything consumed, that they were maintaining a typical diet and physical activity levels, and to answer procedural questions. Participants were given a blood requisition form, which they took to a local hospital during the seven days following a 12-hour fast to have their blood drawn by lab phlebotomists. At the end of the seven days the subjects returned the food record, food scale, and accelerometer. Subjects were weighed again wearing a one-piece lab-issued swimsuit. Once it was determined that the data obtained was accurate and complete, subjects were mailed a thank you letter with a \$25 gift certificate.

#### Instrumentation and Measurements

The criterion variable for this study was IR, assessed using the homeostatic model assessment (HOMA). The primary predictor variable was dairy consumption, which was measured using seven-day weighed food records. Statistical analysis was used to determine the



extent to which potential confounding variables impacted the dairy-IR relationship, namely age, education, total energy intake, dietary fat intake, intake of other dietary components, physical activity level, and body fat percentage.

Insulin Resistance. Lab phlebotomists withdrew a blood sample from the antecubetal vein after the subjects had been fasting for at least 12 hours. The samples were stored at about -20°C after being centrifuged for 15 minutes at 2000g at 4°C. The Access Ultrasensitive Insulin assay (Beckman Coulter, Brea, CA) was used to determine fasting insulin ( $\mu$ U/L). Dimension Vista System and Flex reagent cartridges (Siemens, Deerfield, IL) were used to measure fasting glucose levels (mg/dL). HOMA was used to assess IR using the following formula: fasting plasma insulin ( $\mu$ U/ml) x fasting plasma glucose (mg/dL)/405. HOMA has been shown to be comparable to the euglycemic clamp as a means of assessing IR (r = 0.82, p = 0.0002), and is considered valid and reliable.

<u>Dietary Intake</u>. Seven-day weighed food records were used to measure dairy consumption, total energy intake, percent of calories from carbohydrate, protein, and fat, and insoluble and soluble fiber intake. This method minimizes subject recall bias and effectively represents an individual's normal dietary patterns by covering weekdays and weekends.<sup>47</sup>
Weighed food records have frequently been employed as a standard for comparison when assessing the validity of other dietary intake measurements, <sup>48,49</sup> and seven days has been shown to be an adequate length of time to accurately assess intake.<sup>47</sup>

Subjects were issued a digital food scale and were instructed how to properly weigh and record foods and beverages using plastic food models and printed directions. The food records were returned following the seven-day recording period and were examined for accuracy. If a



participant's food record indicated her daily intake was less than 130% of her estimated resting metabolic rate, determined using the Ravussin formula,<sup>50</sup> she was required to repeat the weighed food record. Seven subjects were dropped from the study for refusing to comply with the dietary assessment requirements. A registered dietician input all food records into the ESHA Research software, (ESHA Research Inc., Salem, OR) for further analysis.

Dietary analysis categorized dairy intake based on the 2003-2007 American Dietetic Association (now Academy of Nutrition and Dietetics) and American Diabetic Association (ADA) Exchange Lists program. In the Exchange Lists program, a fat-free/low-fat serving of dairy is defined as 12 g of carbohydrate, 8 g of protein, 0-3 g of fat, and approximately 90 kilocalories. Reduced-fat or whole fat dairy exchanges contain the same amount of carbohydrate and protein, but differ regarding fat content. To separate the effect of dairy and dietary fat, for any dairy exchange that included more than 3 g of fat, the extra fat grams were added to the ADA fat exchange category. Partial servings were calculated to within 0.1 serving.

Physical Activity. Physical activity was assessed using Actigraph accelerometers. Accelerometers provide an objective method to measure physical activity, making them superior to self-reported physical activity, which is known to be biased. The accelerometers used in the present study have been tested with adults and are considered valid and reliable. A study by Bassett et al. compared the correlations of four different accelerometers, one of which was used in the present investigation, to an indirect calorimetry process, which estimated energy expenditure. The Actigraph accelerometer was the only one of the four that did not differ significantly from the energy expenditure findings (p = 0.473).

A pilot study testing 15 women from the present investigation evaluated the reliability of the accelerometers as they took part in 17 different activities, such as walking, jogging, and stair climbing at different speeds and grades. The same assessments were performed one week following the baseline tests. The test-retest reliability for each activity was greater than 0.90, and was greater than 0.98 for the sum of the seventeen activities.

Following the testing period, participants returned the accelerometers and investigators downloaded their activity data and checked for accuracy. Any participant who failed to wear the accelerometer for at least 12 hours during waking times was required to re-wear it for the corresponding day(s) of the week as the noncompliant day(s).

Body Fat Percentage. Air-displacement plethysmography (Bod Pod) was used to estimate body fat percentage. The Bod Pod was also used to assess thoracic lung volume, which was subtracted from body volume. Subjects were instructed to fast and avoid exercise for at least three hours before their appointment. They were given a lab-issued swimsuit and a swim cap to complete the test in and were asked to void, if possible, before the assessment. Body composition was measured in the Bod Pod at least twice. If the body fat results differed by more than one percentage point, then another measurement was taken. This process was repeated until two results were within one percentage point, and then the average of these two outcomes were used to index body fat percentage. Only two measures were taken 75% of the time.

The Bod Pod has been shown to be valid and reliable in estimating body fat percentage. Maddalozzo et al.<sup>53</sup> demonstrated concurrent validity for the Bod Pod compared to dual energy x-ray absorptiometry (DEXA). Concurrent validity of the body fat percentage measure resulting from the Bod Pod and DEXA was also established with a sample of 100 women from the current



study, with an intraclass correlation of 0.97 (p < 0.0001). In addition, test-retest with the Bod Pod of the same sample indicated an intraclass correlation of 0.99 (p < 0.0001). Estimating body fat percentage with the Bod Pod is a much more valid technique than using self-reported weight or measured BMI, as these methods often produce misclassification. Statistical Analysis

Statistical analysis was conducted using the SAS software program, version 9.3 (Cary, NC). Because HOMA values deviated significantly from a normal distribution, they were log-transformed. To avoid redundancy, the log-transformed values are referred to as HOMA and not log-transformed HOMA throughout the article. Bivariate associations were determined using Pearson correlations. The extent to which mean HOMA levels differed across categories of dairy intake was determined using regression analysis and the General Linear Model (GLM) procedure. For these computations, dairy intake was divided into quartiles and the middle-two quartiles were combined forming three categories: Low (0 to 0.5 servings of dairy per day), Moderate (0.6 to 1.5 servings of dairy per day), and High (1.6 to 6 servings of dairy per day). To examine the influence of specific potential confounders, such as age, education, body weight, diet, body fat percentage, and physical activity, considered individually and collectively, on the relationship between dairy intake and HOMA, partial correlations were computed using the GLM procedure. Adjusted means were calculated using the least-squares means procedure.

A power analysis was conducted using the PASS 6.0 statistical software (NCSS, Kaysville, UT, USA) to determine the number of participants needed to achieve 0.80 power with alpha set at 0.05 when evaluating mean differences across three categories (Low, Moderate, and

High) using ANOVA to detect a small effect size of 0.20. Results showed that 240 subjects would be sufficient. Overall, with more than 270 participants, the study had excellent power.

#### Results

A total of 272 women participated in the present investigation. Subjects were primarily Caucasian (approximately 90%), middle-aged ( $40.1 \pm 3.0$  years), working either full- or part-time (approximately 60%), married (approximately 80%), with about 32% having had at least some college education. Table 1 shows additional descriptive characteristics for the study participants, including total physical activity, body fat percentage, weight, fasting glucose, fasting insulin, total energy intake, percent of total calories from carbohydrate, protein, and fat, insoluble fiber intake per 1,000 calories, soluble fiber intake per 1,000 calories, average servings of dairy consumed per day, HOMA, and log-transformed HOMA. Means, standard deviations, minimum and maximum values, and quartiles are also displayed in Table 1. Average dairy intake for these women was  $1.1 \pm 1.0$  servings per day and average HOMA was  $0.3 \pm 0.6$ . The low consumption category had an average of  $0.2 \pm 0.2$  servings of dairy per day, while the moderate consumption category had  $1.0 \pm 0.4$  servings per day, and the high consumption category had  $2.4 \pm 0.9$  servings per day.

Table 2 displays the mean differences in HOMA across the three dairy consumption categories. As shown, when no variables were controlled, significant differences in mean HOMA were seen across the three dairy consumption categories (F = 6.90, p = 0.0091). Those in the high dairy consumption category had significantly higher HOMA ( $0.41 \pm 0.53$ ) than those in the moderate consumption ( $0.22 \pm 0.55$ ) or the low consumption categories ( $0.19 \pm 0.58$ ). Differences in the potential confounding factors, including age, weight, body fat percentage,



energy intake, total physical activity, education, percent of calories from carbohydrate, protein, and fat, insoluble fiber intake, and soluble fiber intake, failed to influence appreciably the relationship between dairy consumption and HOMA. (Table 2)

The relationship was attenuated slightly after controlling for age (F = 6.77, p = 0.0098), education (F = 6.48, p = 0.0114), and percent of calories from protein (F = 5.87, p = 0.0160), yet it remained statistically significant. Adjusting for differences in energy intake weakened the relationship by 32% (F = 4.68, p = 0.0315). Controlling for several other variables strengthened the relationship, including weight (F = 9.18, p = 0.0027), body fat percentage (F = 7.67, p = 0.0060), total physical activity (F = 7.47, p = 0.0067), percent of calories from fat (F = 8.40, p = 0.0041), intake of insoluble fiber (F = 7.45, p = 0.0068), and intake of soluble fiber (F = 7.69, p = 0.0059). After controlling for all of the potential confounding factors simultaneously, the dairy and HOMA relationship was weakened, but remained significant (F = 4.71, p = 0.0309) (Table 2).

The associations between HOMA and potential confounders, including age (r = 0.02, p = 0.7515), physical activity (r = -0.09, p = 0.1201), percent of total calories from carbohydrate (r = -0.09, p = 0.1562), protein (r = 0.07, p = 0.2367), and fat (r = 0.06, p = 0.3238), and insoluble fiber intake (r = -0.06, p = 0.3045) were not statistically significant. However, there were significant relationships between HOMA and body fat percentage (r = 0.47, p < 0.0001), body weight (r = 0.39, p < 0.0001), fasting plasma glucose (r = 0.45, p < 0.0001), fasting plasma insulin (r = 0.91, p < 0.0001), total energy intake (r = 0.23, p < 0.0001), and soluble fiber intake (r = -0.17, p = 0.0040).



#### **Discussion**

It has been shown previously that T2DM is primarily a function of IR. <sup>24-26</sup> While many have investigated the role of dairy intake on reducing risk of T2DM or the MetS, <sup>12-22</sup> results have been divergent. In addition, the effect of milk and dairy consumption on IR has not been thoroughly analyzed, especially with the use of valid and objective measurements. <sup>39-42</sup> The present cross-sectional investigation aimed to assess the relationship between dairy consumption and IR in middle-aged, nondiabetic women, while controlling for several important variables by employing high-quality measurement techniques.

There was a significant relationship between dairy consumption and IR. Namely, women who were in the high category for dairy intake (top 25%) had significantly higher HOMA levels than women who were below the top 25% for dairy intake. (Table 2) This association remained significant after statistically controlling for several potential confounding variables, including age, weight, body fat percentage, energy intake, total physical activity, education, percent of kcal from carbohydrate, protein or fat, insoluble fiber intake, and soluble fiber consumption.

These findings are in line with an intervention by Hoppe et al.<sup>40</sup> who studied 24 8-year-old boys. HOMA increased significantly after one week in those given a dairy supplement, but did not change in those given a meat supplement. Unfortunately, this study lacked strong control over important confounding factors, including energy intake, body composition, and physical activity.

Also in agreement with the present study were findings from Snijder et al.<sup>56</sup> who found that higher dairy consumption was significantly associated with higher fasting glucose levels in a population from the Netherlands, where dairy consumption is generally high. In addition, Lawlor



et al.<sup>57</sup> examined the relationship between milk consumption and insulin resistance and the MetS in 4,024 British women. It was observed that women who never drank milk had lower HOMA, were less likely to have T2DM, and were less likely to manifest the MetS than women who regularly drank milk. Lawlor et al. noted that the number of women who never drank milk was relatively small, making it possible that some of these women were lactose malabsorbers. Milk consumption was measured nominally (yes milk intake vs. no milk intake), thus preventing the determination of a dose-response relationship.

Contradictory to the present results, Rideout et al.<sup>42</sup> found that HOMA levels improved in overweight or obese subjects with higher dairy consumption (4 servings per day of milk or yogurt v. fewer than 2 servings per day of milk or yogurt) over the course of 12 months in a crossover trial of 23 adults. Body fat was assessed using DEXA; however, the study lacked control of the subjects' physical activity levels and total energy intake.

Akter et al.<sup>41</sup> found results conflicting with the present study in a cross-sectional investigation of 496 Japanese adults, where higher intake of full-fat milk or yogurt was associated with lower HOMA. Body composition was controlled through BMI, physical activity was assessed using a self-reported questionnaire, and dietary intake was assessed using a food frequency questionnaire, each of which tends to include significant measurement error. Akter et al.<sup>41</sup> point out that this population, in general, consumes considerably less dairy than Western populations, and that only a small percentage regularly consume low-fat or fat-free dairy.

Previous investigations into the relationship between dairy consumption and IR have largely relied on BMI to account for the effects of body composition. Unfortunately, this method frequently produces error through misclassification.<sup>43</sup> Obesity is a known contributor to IR,<sup>58</sup>



even among nondiabetic populations,<sup>59</sup> and therefore must be carefully controlled. The present study assessed body fat percentage to estimate and control for body composition. Results for this study showed that controlling for body fat percentage weakened the relationship between dairy consumption and HOMA-IR by 13%. In other words, if all of the women of the present study would have had the same level of body fat, the relationship between dairy and IR would have been slightly weaker.

Physical activity is another important variable that affects IR and should be controlled objectively. It is widely accepted that participation in physical activity reduces risk of IR and T2DM. <sup>60,61</sup> Both regular physical activity and single bouts of exercise have been shown to improve insulin sensitivity. <sup>62</sup> To date, no investigation of the relationship between dairy intake and IR has objectively controlled for differences in physical activity. Questionnaires are typically administered to gather information on participation in physical activity; however, subject responses to questionnaires regarding physical activity are generally skewed. <sup>44</sup> The present study employed accelerometry over a period of seven days in order to more objectively assess engagement in physical activity. The relationship between dairy consumption and IR remained significant and was strengthened by 7% after controlling for physical activity.

While the association between dairy consumption and IR remained significant after controlling for several potential confounders, it is worth noting that some variables did not produce the same effect as controlling for body composition or physical activity. Adjusting statistically for differences in body weight strengthened the relationship by 12%. Other variables that appreciably strengthened the relationship were percent of kcal from carbohydrate



(strengthened by 13%), percent of kcal from fat (strengthened by 21%), and insoluble (strengthened by 8%) and soluble fiber intake (strengthened by 8%).

Consistent with the present findings, it has been shown previously that dietary fiber intake is generally associated with improved insulin sensitivity,  $^{63-65}$  particularly with higher intake of soluble fiber. There was a significant positive relationship between soluble fiber intake and physical activity (r = 0.15, p = 0.0114), but soluble fiber was negatively associated with HOMA (r = -0.17, p = 0.0040). These relationships may partly explain why controlling for soluble fiber intake strengthened the association between dairy consumption and IR. Namely, women who ate more soluble fiber also participated in greater amounts of physical activity and had lower levels of IR.

Controlling for total daily energy intake weakened the relationship between dairy consumption and IR by 32%. Further analyses showed that energy intake was significantly and positively related to dairy intake (r = 0.21, p = 0.0006), physical activity (r = 0.16, p = 0.0101), body weight (r = 0.40, p < 0.0001), and HOMA (r = 0.23, p < 0.0001). Thus, women with higher total energy intakes were more likely to have higher consumption of dairy products, participate in greater amounts of physical activity, have higher body weights, and be more insulin resistant than women with lower total energy intakes.

An important strength of the present study was its use of direct and objective assessments to control several potential confounding variables. The Bod Pod was used to estimate body composition rather than BMI, accelerometry was used to assess physical activity instead of a questionnaire, and seven-day weighed food records were used to quantify dietary intake instead of a questionnaire, thereby reducing the negative influence of measurement error.



This study also had weaknesses. The present study was limited by its cross-sectional design, thus preventing the establishment of a cause-and-effect relationship. Also, the focus of the study was on nondiabetic, middle-aged, nonsmoking women, and the sample was largely homogeneous, being predominately Caucasian and well-educated women. Hence, generalization of the findings may be limited to populations with similar characteristics.

Diets categorized by a consistently high glycemic load have been correlated with IR and subsequent T2DM in both men<sup>66</sup> and women,<sup>10</sup> as chronically high requirements of insulin to mediate glucose uptake can lead to reduced insulin sensitivity over time. Therefore, consumption of diets with a low glycemic index (GI) is recommended to prevent T2DM. Dairy is considered to have a relatively low GI (15-60),<sup>67</sup> inferring that it may not adversely affect insulin requirements. However, the insulinemic index has been shown to be three to six times higher than expected based on the GI of dairy foods,<sup>28,30</sup> suggesting that there is an insulinotropic component in milk products.<sup>28-31</sup> Thus, while it has been established that chronic hyperglycemia can lead to IR,<sup>68</sup> research indicates that chronic hyperinsulinemia may also lead to IR.<sup>33,34</sup>

High intake of animal protein has been linked to increased risk of T2DM.<sup>69</sup> Elevated levels of amino acids interfere with normal glucose metabolism, particularly in individuals with reduced insulin sensitivity, leading to IR.<sup>69-71</sup> High consumption of dairy protein could correspondingly exacerbate IR.

Beta cell function should be taken into account when discussing insulin secretion.

Persistent consumption of foods categorized by either a high GI or a high insulinemic index causes beta cells to release more insulin in order to initiate glucose uptake into body cells, leading to insulin insensitivity. <sup>10,66</sup> According to Leahy et al. <sup>68</sup> and Polonsky et al., <sup>72</sup> this could



lead to IR and eventual T2DM as the pancreatic beta cells hypersecrete insulin to maintain normal blood glucose levels. Thereafter, glucose-stimulated insulin release underperforms, leading to beta cell failure, a key feature of T2DM.<sup>68,72</sup>

The hyperinsulinemic response associated with dairy consumption<sup>27-31</sup> may be considered a beneficial and even protective effect for regulating blood glucose levels, particularly in individuals with T2DM.<sup>32</sup> However, this does not mean that the effects of chronic milk and dairy intake on insulin levels in healthy individuals necessarily follow a similar pattern. Similarly, perhaps the short-term benefits of milk and dairy consumption for blood glucose regulation produce adverse long-term effects, including IR.

The present study uncovered a significant relationship between dairy consumption and IR in middle-aged, nondiabetic women, suggesting that higher intake of dairy products may be associated with greater IR. This relationship was partly explained by differences in body composition, body weight, physical activity, and dietary fiber intake. High dairy consumption remained a significant predictor of IR after adjusting for all covariates. Future research on the relationship between dairy consumption and IR should be conducted using objective measures, particularly of body composition, physical activity, and diet. Prevention of T2DM may be aided by additional research into the relationship between dairy intake and IR.



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Table 1 Descriptive Characteristics for all Participants

				Percentile			
Variables	Mean	SD	Min	25th	50th	75th	Max
Age (years)	40.1	3.0	34.0	38.0	40.0	43.0	46.0
Total PA (counts/week)*	2700.1	781.9	827.8	2103.9	2669.6	3166.6	4945.9
Body fat (%)	31.7	6.9	14.6	27.2	32.2	36.8	44.8
Weight (kg)	66.1	10.0	42.1	58.9	65.2	72.0	95.5
Fasting glucose (mg/dL)	86.7	5.9	73.0	82.0	87.0	90.0	111.0
Fasting insulin ( $\mu U/mL$ )	7.0	4.2	1.2	4.3	6.1	8.3	34.8
Energy intake (kcal/day)	2051.9	319.1	1504.0	1822.1	2004.4	2230.4	3495.1
kcal from CHO (%)	55.7	6.2	25.4	51.7	56.0	59.4	73.3
kcal from PRO (%)	13.8	2.5	8.5	12.3	13.5	15.1	25.5
kcal from FAT (%)	30.5	5.8	11.6	27.1	30.3	34.5	51.6
Insoluble fiber (g/1000 kcal)	3.8	1.9	0.5	2.5	3.4	4.7	12.6
Soluble fiber (g/1000 kcal)	1.7	0.9	0.2	1.1	1.6	2.0	6.3
Dairy intake (serv/day)**	1.1	1.0	0.0	0.5	1.0	1.6	6.0
HOMA***	1.5	1.0	0.2	0.9	1.3	1.8	8.3
LHOMA****	0.3	0.6	-1.5	-0.1	0.3	0.6	2.1

Min, minimum or lowest individual value for each variable; Max, maximum or highest individual value for each variable.

<sup>\*</sup>Average activity counts for 1 week objectively measured using accelerometers, divided by 1,000.



\*\*One serving of dairy, according the ADA Exchange Lists, included 12 grams (g) of carbohydrate, 8 g of protein, and 0-3 g of fat. Partial servings were calculated to within 0.1 serving.

\*\*\*\*HOMA, homeostasis model assessment of insulin resistance. Formula for HOMA is fasting plasma glucose (mg/dL) x fasting plasma insulin ( $\mu$ U/mL)/405.

\*\*\*\*\*LHOMA, log-transformed HOMA.

Table 2 Differences in HOMA Across Dairy Consumption Categories

	Dairy Consumption Categories*							
	Low		Moderate		High		_	
	Consumption		Consumption		Consumption			
	n = 67		n = 138		n = 67		-	
HOMA: Variable Controlled	Mean	SD	Mean	SD	Mean	SD	F	P
None	0.19 <sup>a</sup>	0.58	0.22 <sup>a</sup>	0.55	0.41 <sup>b</sup>	0.53	6.90	0.0091
Age (years)	$0.19^{a}$		$0.22^{a}$		$0.41^{b}$		6.77	0.0098
Weight (kg)	0.21 <sup>a</sup>		0.21 <sup>a</sup>		$0.43^{b}$		9.18	0.0027
Body fat (%)	$0.18^{a}$		$0.23^{a}$		$0.40^{b}$		7.67	0.0060
Energy intake (kcal/day)	$0.22^{a_{**}}$		$0.22^{a}$		0.39 <sup>b</sup>		4.68	0.0315
Total PA (counts/week)	$0.19^{a}$		$0.22^{a}$		$0.42^{b}$		7.47	0.0067
Education	$0.18^a$		0.21 <sup>a</sup>		$0.40^{b}$		6.48	0.0114
kcal from CHO (%)	$0.17^{a}$		$0.23^{a}$		$0.42^{b}$		7.84	0.0055
kcal from PRO (%)	$0.19^{a}$		$0.23^{a}$		$0.41^{b}$		5.87	0.0160
kcal from FAT (%)	$0.17^{a}$		$0.23^{a}$		0.43 <sup>b</sup>		8.40	0.0041
Insoluble fiber (g/1000 kcal)	$0.19^{a}$		$0.22^{a}$		$0.42^{b}$		7.45	0.0068
Soluble fiber (g/1000 kcal)	$0.19^{a}$		$0.22^{a}$		$0.42^{b}$		7.69	0.0059
All covariates***	0.17 <sup>a</sup> **		0.19 <sup>a</sup>		0.34 <sup>b</sup>		4.71	0.0309

HOMA, log-transformed value of homeostasis model assessment of insulin resistance.

Means on the same row with different superscripts were significantly different (p < 0.05).



\*Low consumption included women with dairy intake at or below the  $25^{th}$  percentile. Moderate consumption included those whose dairy intake was between the  $25^{th}$  and  $75^{th}$  percentiles. High consumption included those with dairy intake at or above the  $75^{th}$  percentile. Mean dairy consumptions for the low, moderate, and high consumption categories were  $0.2 \pm 0.2$ ,  $1.0 \pm 0.4$ , and  $2.4 \pm 0.9$  servings per day, respectively.

\*\*Significant at the trend level (0.05 .

\*\*\*All of the following variables were statistically controlled simultaneously: age, weight, body fat, energy intake, total PA, education, kcal from PRO, kcal from FAT, insoluble fiber, and soluble fiber.