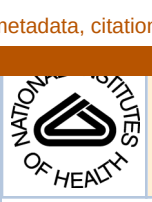

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Associations of dairy intake with CT lung density and lung function

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Abstract

Objective—Dairy products contain vitamin D and other nutrients that may be beneficial for lung function, but are also high in fats that may have mixed effects on lung function. However, the overall associations of dairy intake with lung density and lung function have not been studied.

Methods—We examined the cross-sectional relations between dairy intake and CT lung density and lung function in the Multi-Ethnic Study of Atherosclerosis (MESA). Total, low-fat and high-fat dairy intakes were quantified from food frequency questionnaire responses of men and women, aged 45–84 years, free of clinical cardiovascular disease. The MESA-Lung Study assessed CT lung density from cardiac CT imaging and prebronchodilator spirometry among 3,965 MESA participants.

Results—Total dairy intake was inversely associated with apical-basilar difference in percent emphysema and positively associated with FVC (the multivariate-adjusted mean difference between the highest and the lowest quintile of total dairy intake was −0.92 (p for trend=0.04) for apical-basilar difference in percent emphysema and 72.0 mL (p=0.01) for FVC). Greater low-fat dairy intake was associated with higher alpha (higher alpha values indicate less emphysema) and lower apical-basilar difference in percent emphysema (corresponding differences in alpha and apical-basilar difference in percent emphysema were 0.04 (p=0.02) and −0.98 (p=0.01) for low-fat dairy intake, respectively). High-fat dairy intake was not associated with lung density measures. Greater low- or high-fat dairy intake was not associated with higher FEV_1, FVC and FEV_1/FVC.

Conclusions—Higher low-fat dairy intake but not high-fat dairy intake was associated with moderately improved CT lung density.

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Keywords

dairy intake; lung density; emphysema; lung function; chronic obstructive pulmonary disease

INTRODUCTION

Chronic obstructive pulmonary disease (COPD), characterized by the presence of airflow limitation on spirometry that is not fully reversible, is currently the fourth leading cause of death in the United States and Europe [1–3]. It is projected that COPD will overtake stroke and become the third leading cause of death worldwide by 2020 [4]. Despite the growing importance of COPD, little is known about the preventable risk factors of this condition other than avoidance of cigarette smoking.

Genetic susceptibility studies have linked variants of vitamin D-binding protein gene to the development of COPD [5–8]. Black *et al.* demonstrated a significant positive relationship between serum levels of 25-hydroxy vitamin D and percent predicted values of forced expiratory volume in one second (FEV_1) in a national population-based sample of the United States [9]. Milk in the United States and some of European countries is fortified with vitamin D and other dairy products (cheese, ice cream, etc.) contain small amounts of vitamin D that is produced by the animal itself, which may be beneficial for lung function. Other components of dairy products such as vitamin A, magnesium and selenium may also be beneficial for lung function/COPD [10].

However dairy products are also high in fats. A high intake of n-3 fatty acids was associated with improved lung function and decreased risk of COPD whereas a high intake of n-6 fatty acids was associated with impaired lung function and increased COPD risk [11–12].

Although several constituents of dairy products have been associated with lung function, no published epidemiological studies have examined the overall association between intake of dairy products and lung function. To date, no large population-based epidemiological studies have measured CT lung density, which quantifies emphysema and represents an intermediary phenotype in COPD. We therefore examined the associations of total, low- and high-fat dairy intake with CT lung density and lung function in a large and well characterized population-based cohort.

SUBJECTS AND METHODS

Study Population

The Multi-Ethnic Study of Atherosclerosis (MESA) is a prospective multiethnic cohort study of the United States designed to investigate the prevalence, correlates and progression of subclinical cardiovascular disease in individuals without clinical cardiovascular disease. The protocol and recruitment has been previously described [13]. In brief, MESA enrolled 6,814 men and women aged 45–84 years old, free of clinical cardiovascular disease at baseline, who were recruited in 2000–2002 from six Field Centers: Baltimore MD; Chicago, IL; Forsyth County, NC; Los Angeles, CA; New York, NY; and St. Paul, MN. It included 38.5 percent Whites, 27.8 percent African-Americans, 21.9 percent Hispanics, and 11.8 percent Chinese American. The MESA protocol was approved by the Institutional Review Boards of all collaborating institutions and the National Heart Lung and Blood Institute (NHLBI).

The MESA-Lung Study enrolled 3,965 MESA participants of 4,484 selected who were sampled randomly among those who consented to genetic analyses, underwent baseline

measures of endothelial function, and attended an examination during the MESA-Lung recruitment period in 2004–2006. Chinese were over-sampled to improve the precision of estimates for this group.

For the present analysis, we excluded participants without information on dairy intake (n=327) and participants with extremely low (<600 kcal/day) or high (>6000 kcal/day) total energy intake (n=86). Because this analysis is related to obstructive lung disease, we further excluded participants with a restrictive pattern of spirometry (n=279), defined as a forced expiratory volume (FVC) less than the lower limit of normal [14] with a FEV_1/FVC ratio above 0.70. In a sensitivity analysis, we included those with a restrictive pattern of spirometry.

Dietary Assessment

A self-administered 120-item food frequency questionnaire (FFQ) was administered at the baseline examination (2000–2002). The FFQ asked participants how often, on average, they had consumed listed items during the previous year and the average serving size of items consumed. Low-fat dairy products included intakes of low-fat milk, low-fat dairy desserts (frozen yogurt, low-fat ice cream, ice milk, sherbert, and sweetened condensed milk), low-fat cheeses (cottage or ricotta cheese), yogurt, and pudding/custard/flan. High-fat dairy products included intakes of whole milk, high-fat cheeses (cheese, burritos, enchiladas, and pasta with cream/cheese sauce), ice cream, pizza (presuming substantial contribution to cheese intake), cream in coffee or tea, and cream soups. Total daily dairy intake was the sum of the daily intake for low-fat and high-fat dairy products.

The MESA FFQ was modified from the FFQ used in the Insulin Resistance Atherosclerosis Study (IRAS) to include unique Chinese foods and to collect supplemental information [13; 15]. It was validated against 24-hour dietary recalls in non-Hispanic white, black, and Hispanic persons in IRAS [16]. A recent validation study on dietary macronutrient intake and plasma lipids demonstrated criterion performance of the MESA FFQ [17].

Assessment of Lung Density and Lung Function

The MESA-Lung Study assessed lung density measures in the lung fields of MESA cardiac scans, which imaged approximately 70% of the lung volume from the carina to the base [18]. Cardiac CT scans were performed at full inspiration on multi-detector (MD) and electron-beam CT scanners in 2000–02 following a standardized protocol [19]. In our analyses, lung density measures were calculated by using a threshold of −910 Hounsfield Units (HU) to define emphysema-like lung. This threshold was picked based upon pathology comparisons [20] and the generally mild emphysema in the sample.

Alpha was defined as the negative of the slope of the log-log plot of hole size (x-axis) vs. percent of holes (y-axis) (lung holes were defined as connected voxels within a scanned slice falling below −910 HU). It was reasoned by Mishima *et al* that if the initial onset of emphysema was fractal in nature the slope would be linear and if once an initial set of holes were present in the lung, further destruction of the lung were to be dominated by small holes merging to form larger holes, the slope of the log-log relationship would decrease as emphysema progressed. Thus alpha would decrease as emphysema advances. Percent emphysema-like lung (also known as percent low attenuation area and hereafter we referred to as percent emphysema) was defined as the percentage of the total voxels in the lung which fell below −910 HU. The apical or basal lung was defined as the cephalad or caudal eighths of the lung divided among the z-axis scan coverage. The apical-basilar difference in percent emphysema was calculated as the difference between the percent emphysema in the apical and basal lung. We previously validated lung density measures from cardiac scans

against full-lung scans in MESA, suggesting that the lung imaging from paired cardiac CTs provides a valid quantitative assessment of emphysema [18].

All MESA-Lung study participants underwent uniform, standardized prebronchodilator spirometry in 2004–2006. Spirometry was conducted in accordance with the American Thoracic Society/European Respiratory Society guidelines [21]. Each participant performed at least three acceptable maneuvers on a dry-rolling seal spirometer (SensorMedics 1022; SensorMedics, Yorba Linda, CA). The highest values of FEV_1 and FVC from acceptable maneuvers were used in this analysis. All test sessions were reviewed at the Pulmonary Function Reading Center by a single quality control supervisor [22]. Participants with no acceptable curves were excluded from spirometry analyses. Average intraclass correlation coefficients between original measures and 10% quality control replicate tests were 0.985 for FEV_1 and 0.988 for FVC.

Assessment of Smoking and Other Covariates

Current smoking was defined as self-report of a cigarette in the prior 30 days or urinary cotinine level greater than 100 ng/mL on the day of CT exam. Cotinine was measured by immunoassay (Immulite 2000 Nicotine Metabolite Assay; Diagnostic Products Corp., Los Angeles, CA). Packyears of cigarette smoking was calculated as the number of years between the ages of starting and quitting (or current age if current cigarette smoker) × (cigarettes per day/20).

Age, gender, race/ethnicity, educational attainment, family income, and medical history were self-reported. Height and weight was measured using standard techniques. Body mass index (BMI) was calculated as weight (kg)/height $(m)^2$. Occupational exposures (to vapors or gas, dust, and fumes) were assessed by the American Thoracic Society-Division of Lung Disease (ATS-DLD) standardized questionnaire [23].

Levels of total cholesterol and high density lipoprotein cholesterol were measured at the Collaborative Studies Clinical Laboratory at Fairview-University Medical Center (Minneapolis, Minnesota).

Statistical Analysis

We modeled the associations between dairy intake and CT lung density and lung function using generalized additive models. All lung outcome measures were normally distributed except percent emphysema, for which square root transformation was used to make the originally skewed distribution more symmetric. Models were adjusted for potential confounders, including age, gender, race/ethnicity, smoking status, pack-years, urinary cotinine, second-hand tobacco exposure, study site (as a surrogate for sun exposure, a significant source of vitamin D), education, family income, BMI, physician-diagnosed asthma (<45 yrs), family history of COPD, beta-blocker use, occupational exposure (only exposure to dust was included in the analyses, as adding exposure vapors or gas, or dust resulted in little change to the model), total/HDL ratio, supplement use, and several dietary variables. Lung density analyses were additionally adjusted for weight (>220lb) and CT scanner type. Lung function analyses were additionally adjusted for height. Loess smoothing functions for all the continuous covariates were used to allow for the flexible specification of relationships and to minimize residual confounding. We conducted tests for trend by using the median values of the categories of dairy intake to form continuous variables. We also used restricted cubic spline regressions with four knots to plot and model the associations flexibly. Nonlinearity was tested in nested models using a −2 log-likelihood test.

We further conducted stratified analyses to examine whether the associations between dairy intake and lung density and lung function were modified by smoking status and race/ethnicity. Interaction terms for interaction between dairy intake and smoking status (or race/ethnicity) were entered into the models, and chi-square tests for models with and without the interaction terms were used to evaluate the significance of the interaction terms.

Analyses were performed using SAS 9.1 (SAS Institute, Cary, NC) and the gam function in R 2.6 (R Foundation, Vienna, Austria).

RESULTS

Apart from Chinese which we oversampled in the MESA-Lung subcohort, baseline demographic characteristics were not very much different between MESA subjects in our study and MESA subjects not included in the study. Comparing the 3,271 individuals in our study and 3,542 MESA subjects not included in the study, the respective mean age was 61.6 years and 62.6; proportion of female was 50.3% and 55.2%; proportion of current smoker was 11.6% and 14.5%, proportion of past smoker was 35.9% and 37.3%, and proportion of never smoker was 52.5% and 48.3%.

The baseline characteristics of the study participants, stratified by the first and fifth quintile of total dairy, low-fat and high-fat dairy intake, are shown in Table 1. Participants in the highest quintile of total dairy intake were more likely to be current smokers, to have a higher BMI, and to have a report of asthma at age 45, family history of COPD, and occupational exposure, and were less likely to use beta-blocker, compared with those in the lowest quintile. In addition, participants with higher total dairy intake had lower intake of fruits, vegetables, fish, but higher intake of calories. The distributions of characteristics for high-fat dairy intake were similar to that for total dairy intake. Participants in the highest quintile of high-fat dairy intake were also less likely to have higher education levels. In contrast, participants in the highest quintile of low-fat dairy intake were less likely to be current smokers and to have a history of asthma at age 45, were more likely to have higher education levels than those in the lowest quintile.

Dairy Intake and Lung Density

Total dairy intake was inversely associated with apical-basilar difference in percent emphysema (Table 2). The multivariate-adjusted mean differences in apical-basilar difference in percent emphysema between the highest and the lowest quintile of total dairy intake were −0.92 (p for trend = 0.04). Additionally adjustment for waist-to-hip ratio did not change the results appreciably (mean difference = −0.94; p for trend = 0.04).

Greater low-fat dairy intake was associated with statistically significant higher alpha and lower apical-basilar difference in percent emphysema (Table 2). The multivariate-adjusted mean differences between the highest and the lowest quintile of low-fat dairy intake was 0.04 (p for trend = 0.02) for alpha and −0.98 (p for trend = 0.01) for apical-basilar difference in percent emphysema. Greater low-fat dairy intake was also associated with lower percent emphysema but the test for trend did not reach statistical significance (p = 0.08). High-fat dairy intake was not associated with lung density measures. Regression splines demonstrated consistent inverse relations of total and low-fat dairy intake with apical-basilar difference in percent emphysema (Figure 1). Nonlinear functions did not improve model fit in comparison with linear functions.

Analyses of individual food or food groups showed that the associations of low-fat dairy intake with alpha and apical-basilar difference in percent emphysema were primarily limited to low-fat milk (Table 4).

There was no evidence that the relations between dairy intake and lung density measures were modified by smoking status or race/ethnicity (p for interaction >0.05, data not shown).

Dairy Intake and Lung Function

Total dairy intake was not associated with FEV_1 and FEV_1/FVC (Table 3). However, total dairy intake was positively associated with FVC (Table 3). Compared with participants in the lowest quintile, the multivariate-adjusted mean difference in FVC for those in the highest quintile of total dairy intake was 72.0 mL (p for trend = 0.01).

We also examined the associations of lung function measures with each low-fat and high-fat dairy intakes (Table 3). Low-fat dairy intake was associated, although not statistically significant, with higher FEV_1, FVC and FEV_1/FVC. In contrast, high-fat dairy intake was significantly inversely associated with FEV_1/FVC (p for trend = 0.04). High-fat dairy intake was not associated with either FEV_1 or FVC.

Analyses of individual foods or food groups showed that the inverse association between high-fat dairy intake and FEV_1/FVC was primarily limited to whole milk and cream in coffee or tea (data not shown).

We found no apparent modification of the relationships between dairy intake and lung function measures by smoking status or race/ethnicity (p for interaction >0.05, data not shown).

Sensitivity Analyses

We performed sensitivity analyses by including the participants with a restrictive pattern of spirometry. The associations of dairy intake with lung density measures were similar to the associations in the main analyses. The associations with lung function measures were slightly attenuated. In this sample, high-fat dairy intake was not significantly associated with FEV_1/FVC.

DISCUSSION

In this large population-based cohort, we found an inverse association between total dairy intake and apical-basilar difference in percent emphysema and a positive association between total dairy intake with FVC. These associations were observed mainly for low-fat dairy intake. Greater low-fat dairy intake was also associated with higher alpha, FEV_1, FEV_1/FVC and lower percent emphysema, but the associations with FEV_1, FEV_1/FVC and percent emphysema did not reach statistical significance. In contrast, we found a statistically significant inverse association between high-fat dairy intake and FEV_1/FVC after adjustment for potential confounders. In general, greater high-fat dairy intake was not associated with better lung function and lung density measures.

Several constituents of dairy products may explain the potential benefits of low-fat dairy intake. Vitamin D has been suggested to play an important role in lung development and function in animal models and in human fetal lung in vitro studies. The vitamin D metabolite, $1\alpha,25(OH)_2$ vitamin D, has been reported to stimulate lung maturity, alveolar type II cell differentiation and pulmonary surfactant synthesis in rat lung [24–26]. Phokela *et al* found that vitamin D regulates surfactant protein gene expression in human lung and type II cells [27]. Rehan *et al* showed that $1\alpha,25(OH)_2$-3-epi-vitamin D3, a natural intermediary metabolite of $1\alpha,25(OH)_2$ Vitamin D3, possesses significant activity in stimulating surfactant synthesis in alveolar type II cells [28]. These data, together with the data from genetic susceptibility studies [5–9], suggest vitamin D intake may have beneficial effects on lung function and COPD risk. The MESA diet group is currently working on the assessment

of vitamin D intake in this cohort and we will be examining the associations with vitamin D intake when it is available to use. Other components of dairy intake such as vitamin A, magnesium and selenium have a potential protective role in the oxidative stress and inflammatory responses, which may protect against lung damage [10].

It is unclear why the potential benefits of dairy intake on lung density and lung function were observed for low-fat dairy intake, but not for high-fat dairy intake. Similar findings were also observed in several other studies for coronary heart disease [29] type 2 diabetes [30] and hypertension [31]. It is possible that n-6 fatty acids and saturated fatty acids in high-fat dairy products may mitigate the potential benefits of other components of dairy intake because of the proinflammatory properties of n-6 fatty acids and saturated fatty acids [12]. Also, the processing and preparation of low fat milk and whole milk may lead to a change in nutrition composition of the milk [30; 31]. In addition, a pooled analysis of 12 cohort studies showed that low-fat milk intake had a much higher correlation with dietary vitamin D intake (r=0.68) than whole milk (r=0.13) [32].

The inverse association between high-fat dairy intake and FEV_1/FVC deserves further examination. In this study, high-fat dairy intake was not statistically significantly associated with other lung function and lung density measures except for FEV_1/FVC in multivariate analyses. No statistically significant inverse associations with high-fat dairy intake were observed in any of the studies mentioned above. Because of multiple tests and comparisons were performed, the observed association between high-fat dairy intake and FEV_1/FVC could be due to chance.

A major concern of this study is that participants' lifestyle characteristics may have confounded the observed associations because participants who frequently consumed low-fat dairy products had a healthier lifestyle in general than those who rarely consumed low-fat dairy foods. To overcome possible confounding by lifestyle characteristics, we adjusted for participants' social economic status, smoking history, and several dietary variables considered to be related to a healthy diet in our multivariate analyses. To minimize residual confounding due to cigarette smoking, we adjusted not only for smoking status, smoking pack-years, but also for urinary cotinine, a reliable marker of smoking status. In addition, we used spline terms for each of the continuous variables in the analyses to reduce residual confounding by the use of categories for the continuous covariates. Other concerns also warrant consideration. Dietary intake was self-reported in this study; therefore, there was inevitable measurement error, which, if nondifferential, may have led to underestimation of the true associations. The CT lung density measures were based on partial lung scans; however, we have validated the CT measures from partial lung scans against full lung scans [18]. Because only pre-bronchodilator spirometry was measured in this study, we can't be sure that airflow limitation was the results of COPD. Also, a cross-sectional study design can not discern temporal relationships between dairy intake and lung function or lung density. Finally, we did not have enough power to examine the interactions between dairy consumption and race/ethnicity, given the four ethnic groups in this population and the limited range of dairy intake.

CONCLUSION

Greater low-fat dairy intake was associated with moderately improved lung density. The inverse association between high-fat dairy intake and FEV_1/FVC needs to be further confirmed.

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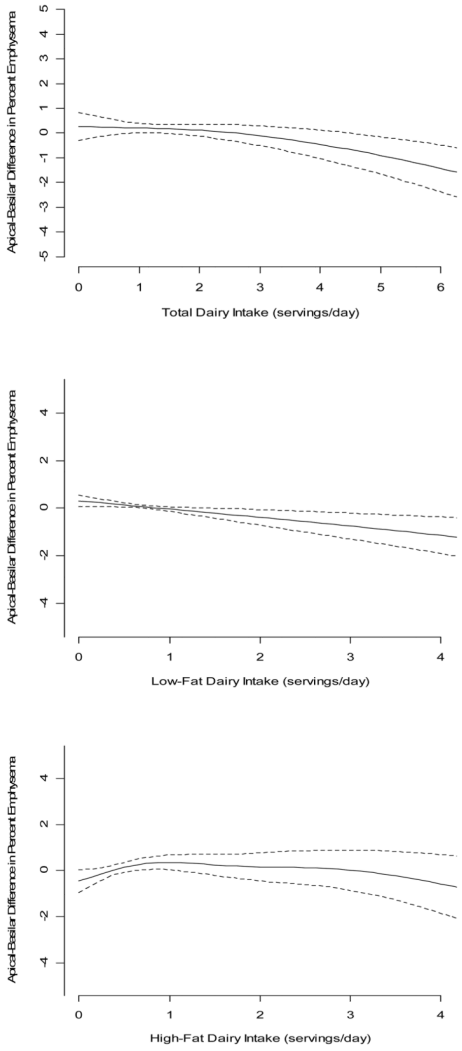

Figure 1.

Apical-basilar difference in percent emphysema according to total, low- and high-fat dairy intake. The results, obtained from spline regression models, were adjusted age, gender, race/ethnicity, height, smoking status, pack-years, urine cotinine, and second-hand tobacco exposure, study site, education, family income, BMI, physician-diagnosed asthma (<45 yrs), family history of COPD, beta-blocker use, occupational exposure, total/HDL ratio, supplement use, and dietary intake of vegetables, fruits, fish, cured meats and total energy. Dashed lines, 95% confidence interval.

Table 1

Baseline characteristics according to the first and fifth quintile of total dairy, low-fat and high-fat dairy intake

	Dairy intake					
Characteristics[a]	**Total dairy**		**Low-fat dairy**		**high-fat dairy**	
	Quintile 1 (<0.58 servings/day)	**Quintile 5 (>2.75 servings/day)**	**Quintile 1 (<0.08 servings/day)**	**Quintile 5 (>1.30 servings/day)**	**Quintile 1 (<0.16 servings/day)**	**Quintile 5 (>1.46 servings/day)**
Age, years	61.5 (9.6)	61.4 (10.1)	60.6 (9.7)	62.9 (10.1)	64.3 (9.6)	59.9 (9.7)
Male, %	49.9	48.8	56.8	46.8	43.3	52.6
Race/ethnicity, %						
Caucasian	20.6	51.0	19.8	51.3	23.0	41.9
Black	28.6	15.8	26.0	14.3	20.9	24.5
Hispanic	13.6	26.7	25.4	23.9	12.2	29.4
Chinese	37.2	6.5	28.9	10.4	43.9	4.2
Height, cm	165 (9.8)	168 (10.1)	166 (10.3)	167 (9.7)	164 (9.5)	168 (10.3)
Smoking status, %						
Never	53.6	45.2	47.4	49.3	61.0	38.0
Past	36.6	39.2	35.6	40.9	31.4	40.5
Current	9.8	15.6	17.0	9.8	7.5	21.5
Pack-years	21.5 (23.5)	25.0 (27.1)	23.4 (23.5)	21.6 (25.4)	21.5 (23.4)	25.6 (27.2)
Second-hand smoker, %	31.6	36.7	28.9	35.8	26.9	38.5
Family income, %						
<25K	31.5	25.4	35.7	28.4	37.2	25.4
25K-<50K	27.8	30.9	28.0	30.5	27.9	31.8
≥50K	40.7	43.8	36.3	41.1	34.9	42.7
Education, %						
<High school degree	17.1	14.5	23.4	14.5	19.5	18.0
High school degree	18.1	17.9	18.7	16.3	15.9	17.6
Some college	26.2	30.0	26.3	26.8	23.2	32.0
College degree	19.2	18.6	16.9	19.4	21.2	16.5
>Bachelor’s degree	19.4	19.0	14.7	23.0	20.1	15.9

	Dairy intake					
Characteristics[a]	**Total dairy**		**Low-fat dairy**		**high-fat dairy**	
	Quintile 1 (<0.58 servings/day)	**Quintile 5 (>2.75 servings/day)**	**Quintile 1 (<0.08 servings/day)**	**Quintile 5 (>1.30 servings/day)**	**Quintile 1 (<0.16 servings/day)**	**Quintile 5 (>1.46 servings/day)**
BMI, kg/m^2	26.8 (5.22)	28.4 (4.95)	27.2 (5.5)	27.9 (4.9)	25.9 (4.7)	28.8 (5.1)
Asthma at 45 y, %	6.2	8.4	7.3	6.8	6.5	8.8
Family history of COPD, %	11.2	15.6	11.5	14.8	9.9	15.1
Beta-blocker use, %	11.6	8.7	9.4	9.8	10.4	8.2
Occupational exposure, %	30.1	38.1	35.9	34.7	25.3	44.6
Total/HDL ratio	0.27 (0.08)	0.26 (0.08)	0.26 (0.08)	0.27 (0.08)	0.28 (0.08)	0.26 (0.08)
Diet						
Vegetables, servings/day[b]	1.68 (1.16)	0.88 (0.60)	1.31 (1.10)	1.02 (0.71)	1.86 (1.17)	0.86 (0.60)
Fruits, servings/day[b]	1.51 (1.28)	0.97 (0.87)	1.11 (1.13)	1.15 (0.89)	1.74 (1.38)	0.89 (0.86)
Fish, servings/day[b]	0.26 (0.24)	0.15 (0.15)	0.21 (0.22)	0.17 (0.17)	0.27 (0.25)	0.15 (0.15)
Cured meats, servings/day[b]	0.02 (0.06)	0.03 (0.06)	0.03 (0.07)	0.03 (0.05)	0.01 (0.04)	0.04 (0.07)
Total calories, kcal	1202 (452)	2288 (915)	1510 (681)	2055 (863)	1234 (449)	2299 (943)
Supplement use, %	62.6	60.4	61.4	61.3	61.5	61.1

[a] Values are means ± standard deviation or %.

[b] per 1000 kcal.

Table 2

Mean difference in lung density according to quintile of total dairy, low-fat and high-fat dairy intake

	Total dairy intake					
	Quintile 1	**Quintile 2**	**Quintile 3**	**Quintile 4**	**Quintile 5**	**P for trend**
Alpha, mean difference (SE)[a]	0 (ref)	7.31×10^{-3} (1.39×10^{-2})	-5.86×10^{-3} (1.43×10^{-2})	$8{,}27\times10^{-6}$ (1.51×10^{-2})	-2.65×10^{-4} (1.66×10^{-2})	0.88
Percent emphysema (in square root), mean difference (SE)[a]	0 (ref)	−0.04 (0.08)	−0.01 (0.08)	0.04 (0.08)	0.007 (0.09)	0.69
AB difference in percent emphysema[b], mean difference (SE)[a]	0 (ref)	−0.26 (0.40)	−0.03 (0.41)	−0.24 (0.43)	−0.92 (0.47) *	0.04
	Low-fat dairy intake					
	Quintile 1	Quintile 2	Quintile 3	Quintile 4	Quintile 5	P for trend
Alpha, mean difference (SE)[a]	0 (ref)	0.02 (0.01)	0.01 (0.01)	0.01 (0.01)	0.04 (0.01) **	**0.02**
Percent emphysema (in square root), mean difference (SE)[a]	0 (ref)	−0.06 (0.08)	−0.07 (0.08)	0.02 (0.08)	−0.17 (0.08) *	0.08
AB difference in percent emphysema[b], mean difference (SE)[a]	0 (ref)	0.16 (0.40)	−0.55 (0.40)	0.07 (0.40)	−0.98 (0.42) *	**0.01**
	High-fat dairy intake					
	Quintile 1	Quintile 2	Quintile 3	Quintile 4	Quintile 5	P for trend
Alpha, mean difference (SE)[a]	0 (ref)	−0.01 (0.01)	−0.01 (0.01)	−0.02 (0.02)	−0.03 (0.02)	0.06
Percent emphysema (in square root), mean difference (SE)[a]	0 (ref)	−0.02 (0.08)	0.01 (0.08)	0.04 (0.08)	0.09 (0.09)	0.17
AB difference in percent emphysema[b], mean difference (SE)[a]	0 (ref)	0.14 (0.41)	0.71 (0.42)	0.83 (0.43)	0.22 (0.47)	0.88

Abbreviations: SE, standard error.

*0.01≤p<0.05;

**p<0.01.

[a]Results were adjusted for age, gender, race/ethnicity, smoking status, pack-years, urinary cotinine, second-hand tobacco exposure, study site, family income, education, BMI, physician-diagnosed asthma (<45 yrs), family history of COPD, beta-blocker use, occupational exposure, total/HDL ratio, supplement use, dietary intake of vegetables, fruits, fish, cured meats and total energy, CT scanner type and weight (>220lbs).

[b]Apical-basilar difference in percent emphysema.

Table 3

Mean difference in lung function according to quintile of total dairy, low-fat and high-fat dairy intake

	Total dairy intake					
	Quintile 1	**Quintile 2**	**Quintile 3**	**Quintile 4**	**Quintile 5**	**P for trend**
FEV_1 (ml), mean difference (SE)[a]	0 (ref)	13.8 (22.6)	12.3 (23.1)	9.42 (24.4)	33.1 (26.9)	0.27
FVC (ml), mean difference (SE)[a]	0 (ref)	20.8 (25.9)	18.3 (26.6)	48.0 (28.1)	72.0 (30.9) *	**0.01**
FEV_1/FVC (%), mean difference (SE)[a]	0 (ref)	0.04 (0.42)	−0.26 (0.43)	−0.94 (0.46) *	−0.59 (0.51)	0.13
	Low-fat dairy intake					
	Quintile 1	Quintile 2	Quintile 3	Quintile 4	Quintile 5	P for trend
FEV_1 (ml), mean difference (SE)[a]	0 (ref)	34.5 (22.6)	42.7 (22.7)	34.2 (22.9)	39.0 (24.2)	0.32
FVC (ml), mean difference (SE)[a]	0 (ref)	3.35 (26.0)	39.2 (26.0)	32.4 (26.4)	40.5 (27.9)	0.14
FEV_1/FVC (%), mean difference (SE)[a]	0 (ref)	1.00 (0.43) *	0.40 (0.43)	0.21 (0.43)	0.38 (0.46)	0.84
	High-fat dairy intake					
	Quintile 1	Quintile 2	Quintile 3	Quintile 4	Quintile 5	P for trend
FEV_1 (ml), mean difference (SE)[a]	0 (ref)	5.05 (23.2)	−26.7 (23.6)	9.09 (24.6)	−2.40 (26.9)	0.87
FVC (ml), mean difference (SE)[a]	0 (ref)	−13.0 (26.6)	−21.9 (27.1)	15.1 (28.3)	25.2 (30.9)	0.15
FEV_1/FVC (%), mean difference (SE)[a]	0 (ref)	0.67 (0.44)	−0.42 (0.44)	−0.33 (0.46)	−0.66 (0.50)	**0.04**

Abbreviations: SE, standard error.

*0.01≤p<0.05;

**p<0.01.

[a]Results were adjusted for age, gender, race/ethnicity, height, smoking status, pack-years, urinary cotinine, and second-hand tobacco exposure, study site, family income, education, BMI, physician-diagnosed asthma (<45 yrs), family history of COPD, beta-blocker use, occupational exposure, total/HDL ratio, supplement use, and dietary intake of vegetables, fruits, fish, cured meats and total energy.

Table 4

Mean difference in alpha and apical-basilar difference in percent emphysema according to categories of intake of individual low-fat dairy foods/food groups

	Categories of intake of individual low-fat dairy foods/food groups					
Alpha						**P for trend**
Low-fat milk	1/month	1/month – 1/week	2–4/week	5/week–1/day	≥2/day	
No. of obs	810	761	690	710	301	
Mean difference (SE)[a]	0 (ref)	0.01 (0.01)	0.02 (0.01)	0.02 (0.01)	0.02 (0.02)	0.17
Low-fat dairy dessert	1/month	1/month – 3/month	1–2/week	≥3/week		
No. of obs	2189	665	227	191		
Mean difference (SE)[a]	0 (ref)	−0.01 (0.01)	0.01 (0.02)	0.01 (0.02)		0.51
Low-fat cheeses	1/month	1/month – 3/month	1–2/week	≥3/week		
No. of obs	2747	355	116	54		
Mean difference (SE)[a]	0 (ref)	−0.03 (0.01)	−0.002 (0.02)	−0.02 (0.03)		0.42
Yogurt	1/month	1/month – 3/month	1–2/week	≥3/week		
No. of obs	2834	270	120	48		
Mean difference (SE)[a]	0 (ref)	0.01 (0.02)	−0.01 (0.02)	−0.02 (0.04)		0.57
Pudding/custard/flan	1/month	1/month – 3/month	1–2/week	≥3/week		
No. of obs	2841	352	51	28		
Mean difference (SE)[a]	0 (ref)	0.01 (0.01)	0.05 (0.04)	0.03 (0.05)		0.16
AB difference in percent emphysema[b]						
Low-fat milk	1/month	1/month – 1/week	2–4/week	5/week–1/day	≥2/day	
No. of obs	810	761	690	710	301	
Mean difference (SE)[a]	0 (ref)	−0.13 (0.37)	−0.28 (0.38)	−0.21 (0.37)	−1.23 (0.50)*	**0.02**
Low-fat dairy dessert	1/month	1/month – 3/month	1–2/week	≥3/week		
No. of obs	2189	665	227	191		
Mean difference (SE)[a]	0 (ref)	0.16 (0.32)	0.56 (0.50)	−0.12 (0.55)		0.78
Low-fat cheeses	1/month	1/month – 3/month	1–2/week	≥3/week		
No. of obs	2747	355	116	54		

	Categories of intake of individual low-fat dairy foods/food groups					
Alpha						**P for trend**
Mean difference (SE)[a]	0 (ref)	0.19 (0.42)	0.08 (0.68)	0.23 (0.98)	0.75	
Yogurt	1/month	1/month – 3/month	1–2/week	≥3/week		
No. of obs	2834	270	120	48		
Mean difference (SE)[a]	0 (ref)	−0.13 (0.46)	−0.37 (0.67)	−0.60 (1.05)	0.42	
Pudding/custard/flan	1/month	1/month – 3/month	1–2/week	≥3/week		
No. of obs	2841	352	51	28		
Mean difference (SE)[a]	0 (ref)	0.08 (0.41)	−1.20 (1.01)	−1.07 (1.39)	0.27	

Abbreviations: SE, standard error.

*0.01≤p<0.05;

**p<0.01.

[a]Results were adjusted for age, gender, race/ethnicity, smoking status, pack-years, urinary cotinine, second-hand tobacco exposure, study site, family income, education, BMI, physician-diagnosed asthma (<45 yrs), family history of COPD, beta-blocker use, occupational exposure, total/HDL ratio, supplement use, and dietary intake of vegetables, fruits, fish, cured meats and total energy, CT scanner type, and weight (>220lbs).

[b]Apical-basilar difference in percent emphysema.