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Physical Activity: Lack of Mitigation of Adverse Effect of Pro-Inflammatory Diet

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Physical Activity: Lack of Mitigation of Adverse Effect of Pro-Inflammatory Diet

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TABLE OF CONTENTS

ABSTRACT

BACKGROUND: To date, no studies have evaluated if moderate and/or vigorous PA physical activity (mv-PA) mitigates the adverse effect of a pro-inflammatory diet. **METHODS:** We conducted a cross-sectional analysis using data from the National Health and Nutrition Examination Survey (NHANES) and constructed the Dietary Inflammatory Index (DII) score. Expenditure of mv-PA was obtained from two sources. Multivariate Logistic Regression was performed to calculate Odds Ratios (OR) and 95% Confidence Intervals (CIs). **RESULTS:** Participants with a DII score in the top quartile were 33% more likely to exhibit elevated CRP than persons with a DII score in the lowest quartile (referent). This estimate did not vary appreciably when either mv-MET-mins/wk or mv-PA.Mnt.mins/wk were added to the model. When examining the independent effect of self-reported leisure-time mv-PA, those who expended the recommended 1000 or more mv-MET-mins/wk were less likely to have elevated CRP compared to the referent group of < 250 mv-MET-mins/wk. Likewise, with accelerometer-assessed PA, the topmost quartile of mv-PA minutes per week was associated with lower CRP compared to the referent quartile. These estimates did not vary appreciably when the DII score was added to the model. **CONCLUSIONS:** Both a pro-inflammatory diet and mv-PA appear to be independently associated with a chronic low-grade inflammatory state.

1.0 INTRODUCTION

Inflammation is part of a healthy immune response involving cells and physiological chemicals to heal injury and fight infection. However, when the system malfunctions or there is a continuous insult to tissues, a chronic low-grade state of inflammation can result. In turn, persistent inflammation can cause multiple diseases, including and not limited to cancer, diabetes, depression, heart disease, stroke, and Alzheimer's disease. Modifiable risk factors related to chronic inflammation consist of being overweight or obese, high consumption of red and/or processed meats, physical inactivity, moderate-to-heavy alcohol consumption, and current smoking (Huxley et al., 2009). Diet high in refined starches, sugar, and saturated and trans-fatty acids induce pro-inflammation (Giugliano et al., 2006). In contrast, there is much evidence that physical activity reduces inflammation as measured by various circulating biomarkers (Hopps et al., 2011). Chronic low-grade inflammation is associated with increased cancer risk (Coussens et al., 2002). This study investigates if regular moderate or vigorous physical activity can mitigate the impact of a proinflammatory diet. In the study herein, we use C-reactive protein (CRP) can serve as a surrogate biomarker of low-grade systemic inflammation (Pepys, 2005). The purpose of the present study is to investigate if regular moderate or vigorous physical activity can mitigate the impact of a proinflammatory diet.

2.0 BACKGROUND

2.1 Chronic Inflammation. The innate immune system responds, in an immediate fashion, to damage caused by either chemical or physical injury. Acute inflammation allows for healing with leukocytes infiltrating a damaged region, removing stimulus, and repairing tissue. Chronic inflammation, on the hand, involves prolonged, dysregulated, and maladaptive responses. The persistent inflammation can cause many chronic human conditions including, but not limited, to heart disease, cancer, diabetes, stroke, Alzheimer's disease, kidney disease, and chronic lower respiratory disease. Multiple factors such as mitochondrial dysfunction, hyperglycemia-driven advanced glycation end products due to elevated blood sugar levels, uric acid crystals, and oxidized lipoprotein can contribute to chronic inflammation. Risk factors promoting chronic inflammation include increasing age, obesity, high saturated fat intake, and high sugar intake can promote chronic inflammation.

A number of systemic biomarkers are useful surrogates of chronic low-grade inflammation. Elevated levels of inflammatory biomarkers – C-reactive protein (CRP), interleukin (IL) 6 and 18, fibrinogen, and adhesion molecules (e.g., E-selectin, intercellular adhesion molecule 1 [ICAM-1], and vascular cell adhesion protein 1 [VCAM-1]) – correlate with increased incidence of type 2 diabetes (DMT2), cardiovascular disease (CVD), and cancer (Pradhan et al., 2001; Thorand et al., 2005; Tsilidis et al., 2008). Conversely, levels of anti-inflammatory hormone adiponectin associate inversely with CVD, DMT2, and obesity-related cancer (Kelesidis et al., 2006; Li et al., 2009; Shibata et al., 2009).

2.2 Diet and Inflammation. From epidemiologic and clinical evidence, a typical "Western" diet (high in refined starches, sugar, and saturated and trans-fatty acids and poor in natural antioxidants and fiber from fruits, vegetables, whole grains, and omega-3-fatty acids) can activate the innate immune system in producing excessive production of pro-inflammatory cytokines and limiting anti-inflammatory cytokines, resulting in chronic low-grade inflammation

(Giugliano et al., 2006). The chronic low-grade inflammation induces repeated cellular injury, in turn, accelerates cellular proliferation, which creates opportunities for genetic mutations to occur and hasten the carcinogenic process (Heikkila et al., 2009). The Dietary Inflammatory Index (DII) was developed recently based on a large-scale literature review of studies of specific food components which found a link (pro- and anti-) to various surrogates of chronic inflammation (Shivappa et al., 2014).

2.3 Physical Activity and Inflammation. Physical activity (PA) is known to reduce biomarkers of inflammation by decreasing adipocytokine production and cytokine release from skeletal muscles, endothelial cells, and the immune system, and improving antioxidant status. A recent study shows that combined exercise of aerobic and resistance training can have significantly decrease in CRP, IL6, IL1β, tumor necrosis factor alpha (TNFα), leptin, and resistin and increase in anti-inflammatory cytokines such as IL4, IL10, and adiponectin (Hopps et al., 2011). More frequent PA independently associates with lower odds of an elevated CRP. Compared with those who participate in PA 0 to 3 times per month, the odds of having elevated CRP is reduced among those who engage in PA 4 to 21 times per month (Abramson et al., 2002).

Based on the evidence, the American College of Sports Medicine recommends exercising at least 150 minutes of moderate-intensity activity or 75 minutes of vigorous-intensity activity each week (ACSM, 2011).

3.0 HYPOTHESIS and SPECIFIC AIMS

There is extensive evidence that a pro-inflammatory diet associates with a higher CRP level, which correlates with increased disease risk through an inflammation pathway. In contrast, physical activity (PA), particularly at a regular moderate and/or vigorous level, has been demonstrated to reduce the overall chronic low-grade inflammation. However, it remains unknown how pro-inflammatory diets and physical activity interact to influence the level of CRP. We hypothesize that, among persons who report consuming a pro-inflammatory diet as measured by the DII, those who regularly engage in moderate and/or vigorous physical activity will have a reduced likelihood of an elevated CRP compared to those who do not engage in less PA. Using data from 11,555 participants in the 2001-2006 National Health and Nutrition Examination Surveys (NHANES), this study aims to:

(1) describe the demographic and lifestyle characteristics of people with normal and elevated CRP;

(2) assess potential sampling bias by determining if our study sample reflects the well-known independent relationships between a pro-inflammatory diet and moderate and/or vigorous PA with an elevated CRP level.

(3) assess if CRP level is lower among those who report consuming a pro-inflammatory diet yet who also engage in moderate and/or moderate on a weekly basis. We anticipate that the impact of PA will present in a dose-response manner.

(4) determine if the associations above vary if moderate and/or vigorous PA assessed by a self-reported survey or accelerometer.

4.0 METHODS

4.1 Study Population. Data from 11,555 participants in the NHANES from 2001 to 2006 were analyzed. Included were individuals ≥20 years of age, of BMI > 18.5, and with a CRP level of <10 mg/dL (CRP ≥10 is indicative of an acute infection). NHANES is designed to assess the health and nutritional status of adults and children in the U.S. through in-home interviews, physical examinations, and laboratory assessments. The interview portion includes demographic, socioeconomic, dietary, and health-related questions. The physical examination component consists of medical, dental, physiological, anthropometric measurements, and laboratory tests. NHANES findings provide prevalence and incidence estimates of major diseases and their risk factors (CDC, 2013). To capture adequate numbers for analysis of important sub-groups, NHANES over-samples people 60 and older, African Americans, and Hispanics. A complete description of NHANES sampling design, recruitment and consenting process can be found elsewhere (Curtin et al., 2012).

4.2 Dietary Inflammatory Index (DII). The DII was calculated using data from the NHANES 24-recall protocol, which included serving sizes. The 48 food items in the DII represent carbohydrates, protein, fat, grams of alcohol, fiber, cholesterol, saturated, monosaturated, polyunsaturated fatty acids, omega3 and omega6 polyunsaturated fatty acids, niacin, vitamins (A, B1, B2, B6, B12, C, D, E), iron, magnesium, zinc, selenium, folic acid, beta carotene, and caffeine. The DII was designed from a meta-analysis review of 1943 peer-reviewed articles which identified 45 food parameters linked to one or more serum inflammatory markers including CRP. The calculations provide a “standard mean” for each food parameter. The z-score was created by subtracting "standard mean" from individual's estimate of intake, then dividing the result by its standard deviation, which was converted to percentile and centered by doubling value and subtracting 1 (Shivappa et al., 2014). The articles were weighted by study design. DII scores typically range from -5.0 to 5.0+ with scores above zero denoting a pro-inflammatory diet.

4.3 Physical Activity Variables. We analyzed data from two separate methods in the NHANES protocol that collected moderate and/or vigorous physical activity (mv-PA): (1) Self-Reported Survey completed by all participants, and (2) an ActiGraph Accelerometer Monitor worn by a subset of randomly selected participants. The self-report protocol consisted the Ainsworth Compendium (Ainsworth et al., 2000), an interviewer-guided survey of 17 items of leisure time activities from which participants provided the following information per: typical frequency (i.e., # of times in past 30 days), intensity (i.e., moderate or vigorous) and duration of episode (i.e., minutes). We converted monthly data to weekly to parallel national exercise guidelines (see below). Participants with a total time of 12 hours or more per day were excluded from analyses per CDC-NHANES guidelines (CDC, 2013).

To obtain an estimate of self-reported *total* mv-PA minutes per week, we performed the following calculations. First, the Metabolic Equivalent of Task (MET) weighting factor was applied to the number of minutes per week engaged in an activity (e.g., running at moderate intensity for 5 times per week @ 30 minutes per time). MET represents the ratio of one minute engaging in a specific activity at a specified intensity compared to the body at rest for one minute. Second, MET-weighted minutes were summed for all activities reported to obtain the total mv-MET-mins/wk. MET score is a standardized way to describe the intensity of different activities. Light PA is defined as ≤ 3 METs, moderate as 3-6 METs, and vigorous as ≥ 6 METs (Hojbjerre et al., 2011). Lastly, for analyses, a mv-PA Survey was used as a continuous value or categorized into four groups with cut-points of <250, 250 to <500, 500 to 999, and 1000+ MET-Mins per Week with the top two categories reflecting the American College of Sports Medicine (ACSM) target recommendations per week for adults. Specifically, ACSM guidelines call for at least 5 days per week of moderate intensity physical activity (PA) for 30 minutes or more, or at least 3 days per week of vigorous intensity PA for 20 minutes or more, or a combination of both (ACSM, 2013).

For the monitor derived mv-PA, a valid participant was defined by NHANES as one who wore the monitor for at least 10 hours per day for at least 4 days in a 7-day period. The mv-PA was recorded based on degree of acceleration per movement in one minute units. Values for each minute of wear time were summed using an NCI-NHANES SAS to obtain a total of mv-PA.Mnt.mins/wk. In analyses, mv-PA total minutes per week were used either as a continuous variable or categorized by quartiles (i.e., <3.0, 3.0 to <10.25, 10.25 to <25.0, and 25.0+) derived from the full sub-sample of adults who wore the monitor prior to the administration of exclusion criteria (e.g., missing CRP data).

4.4 Statistical Analyses. Descriptive analyses were performed for gender, race/ethnicity, education, age, smoking status, BMI, blood pressure, glucose, triglycerides, and waist circumference in relation to CRP, DII, physical activity with either survey or monitor using t-tests for continuous data and chi-square tests for proportions. We calculated univariate- and multivariate-adjusted Odds Ratios and 95% CIs using Logistic Regression with elevated CRP as the binary outcome. Results were considered statistically significant if $p<0.05$ and the confidence interval did not contain 1.0. Statistical analyses were performed with SPSS version 22.0.

5.0 RESULTS

5.1 Descriptive Analyses

Demographic and Lifestyle Factors. Characteristics of participants (n=11555) according to the CRP level (normal vs elevated) are shown in Table 1. There were more females than males in the elevated-CRP group (21.5% vs 11.8%, respectively, p=.001). There was variation in percentage of persons with elevated CRP across different ethnic groups (omnibus p=.001) with Non-Hispanic Blacks, Other Hispanics, and Mexican Americans having the highest (18.7%, 18.7%, and 18.4%, respectively) and Other Race and Multi-races and Non-Hispanic Whites having the lowest (13.2% and 15.3%, respectively) percentages. Individuals who completed at least college had the lowest proportion of persons with elevated CRP compared to those who completed 9-11th grade or less than 9th grade (12.7%, 19.4% and 18.3%, respectively, omnibus p=.01). In a dose-related association, participants with normal body mass index (BMI) were substantially less likely to have elevated CRP than those who were overweight, obese, and morbidly obese (8.4%, 13.9%, 23.1%, and 38.9%, respectively, omnibus p=.001). Similarly, individuals with a sex-specific elevated waist circumference were more likely to exhibit elevated-CRP (24.0% vs 8.2%, p=.001). CRP status did not differ by age, smoking status, and blood pressure.

Dietary Inflammatory Index. Table 2 illustrates participant characteristics according to dietary inflammatory index (DII) scores categorized into quartiles. DII score quartiles varied by sex with males tending to have a more pronounced anti-inflammatory diet compared to females (p=.001). Also, DII scores among females tended to be fairly evenly distributed among the quartiles (e.g., 27.6%, 25.5%, 24.4%, and 22.5%). The majority of each ethnicity was in the Q1 and Q2 DII quartiles; however, proportionately, there were more Non-Hispanic Blacks, other Hispanics, and Mexican Americans in the highest DII score quartile compared to other races and multi-races and Non-Hispanic White (21.4%, 20.8%, 17.6%, 15.4% and 14.8%, respectively, p=.001). Individuals who completed 9-11th grade and less than 9th grade were more likely to be in the highest DII quartile compared to those with college, some college, and high school degrees (21.0% and 25.4% vs 8.9%, 15.2%, and 18.4%, respectively, p=.001). There was marginal difference between participants with normal BMI and overweight and obese and morbidly obese in the highest DII quartile (16.4% and 15.5% vs 18.9% and 19.2% respectively, p=.001). Similarly, those with normal WC were less likely than those with elevated WC to be in the highest DII quartile (14.8% vs 18.6%, p=.001). Age, smoking status, blood pressure, glucose, and triglycerides was not significantly associated with DII quartiles.

Physical Activity Survey. Participant characteristics according to mv-PA Survey categorized by MET-Mins per Week are displayed by Table 3. Overall, for most variables listed, individuals were more likely to not have met the recommended range. For example, proportionately, there were more males than females in the highest PASR quartile (31.5% vs 23.0%, p=.001). Mexican Americans were the least likely to be in the highest quartile compared to Other Hispanics, Non-Hispanic Black, Non-Hispanic White, and Other races/Multiple Races (18.9%, 27.8%, 26.8%, 30.6%, and 27.4%, respectively, omnibus p=.001). There existed a correlation between higher level of education and more likelihood to be in the highest quartile with college graduate and above at 41.0%, some college graduate at 31.4%, high school graduate at 24.2%, 9-11th grade graduate at 19.7%, and less than 9th grade graduate at 11.6% (p=.001). As expected, correlation also existed between age and physical activity level; the youngest group with individuals between 20 and 29 year-olds were the most likely to be in the highest quartile compared to those above 80 year-olds (35.0% and 14.6%, p=.001). Participants who never smoked were most likely to be in the highest quartile compared to former and current smokers (29.1%, 27.5% and 22.5%, respectively, p=.001). Individuals with normal and overweight BMI were more likely than those with obese and morbidly obese BMI to be in the highest quartile (30.7%, 27.5%, 24.8% and 27.3%, respectively, p=.001). In the highest mv-PA Survey quartile, participants were more likely to have normal blood pressure (29.8% vs 24.9%, p=.001), glucose (28.8% vs 24.2%, p=.001), and triglycerides (29.4% vs 22.2%, p=.001). Similarly, individuals with normal WC were more likely than the ones with elevated BMI to be in the highest PASR quartile (32.9% vs 22.6%, p=.001).

Physical Activity Monitor. Table 4 depicts participant characteristics according to physical activity Mins per Week categorized by quartiles. More males compared to females were found in in the highest quartile (42.6% and 22.4%, p=.001). Mexican Americans and other Hispanics were more likely than Non-Hispanic Blacks, Non-Hispanic Whites, and other races and multi-races in the highest quartile (37.4%, 43.4%, 28.5%, 32.7%, and 24.7%, respectively, p=.001). Those who completed higher degrees were more likely to be in the highest mv-PA Monitor quartile with college graduate and above at 42.1%, some college graduate at 33.4%, high school graduate at 26.5%, 9-11th grade graduate at 31.7%, and less than 9th grade graduate at 28.6% (p=.001). As expected, variation also appeared across ages (p=.001). For example, 45.7% of 20-29 year-olds were found in the top quartile versus 4.2% of 80+ year-olds. Interestingly, there were somewhat more current smokers compared to former smokers in the highest quartile (34.4% and 29.0%, omnibus p=.001). Participants of normal or overweight BMI were more likely to have been in the highest quartile compared to those who were obese or morbidly obese BMI (37.6%, 36.5%, 27.4% and 17.4%, respectively, omnibus p=.001). In the highest PAM quartile, there were more individuals with normal glucose (37.4% and 28.5%, p=.001) and WC (44.6% and 22.4%, p=.001). Triglycerides did not significantly vary across mv-PA Monitor quartiles.

5.2 DII and mv-PA in Relation to Elevated CRP

Dietary Inflammatory Index. Crude, age-adjusted, and multivariate-adjusted without and with physical activity are shown in Table 5. A pro-inflammatory diet appears to be associated with elevated CRP level. Compared to the referent group of the lowest DII quartile, participants in consecutively higher quartiles exhibited a higher likelihood for elevated CRP in crude analyses (*Q2*: OR 1.413, 95% CI 1.238-1.614; *Q3*: OR 1.458, 95% CI 1.268-1.676; *Q4*: OR=1.742, 95% CI 1.507-2.014). Similar point estimates were seen in age-adjusted analysis yet ORs were attenuated in multivariate analyses using the basic model. Adjusted ORs did not change appreciably when controlling for mv-PA Survey compared to the basic multivariate model. For mv-PA Monitor, while point estimates were comparable to those observed in the mv-PA Survey multivariate model, the findings were not statistically significant.

Physical Activity Survey. Table 6A reports the crude, age-adjusted, multivariate-adjusted without and with DII score for mv-PA survey data. Compared to referent group (< 250 MET-minutes per week), individuals who were more active were less likely to have had elevated CRP as depicted in the crude Logistic Regressions particularly so in the highest strata (*250-499:* OR .741, 95% CI .617-.891; *500-999:* OR .748, 95% CI .640-.875; and, *1000+*: OR, .552 95% CI .487-.626). Similar point estimates were observed in age-adjusted and multivariate analyses as well as when the DII score was added to the model. Of note, however, point estimates for the top strata (1000+) in the crude and age-adjusted analyses (i.e., .552 and .553, respectively) were attenuated somewhat after adjustment by the basic model and when DII was added (i.e., 709 and .726, respectively) with little overlap in 95% CIs between the two pairs of findings.

Physical Activity Monitor. Table 6B shows crude, age-adjusted, multivariate-adjusted findings without and with DII score added. Participants in the highest quartile of mv-PA (25.0 minutes per week) compared to the referent quartile (< 3 minutes per week) exhibited a reduced likelihood for elevated CRP in crude analyses (OR .416, 95% CI=.301-.574). Similar estimates were observed in age-adjusted analyses as well for results from the basic model and model plus DII. Point estimates calculated in the mv-PA Monitor analyses tended to be lower than ORs calculated in the mv-PA survey analyses.

Sensitivity Analyses. Multivariate Logistic Regressions simultaneously including DII and the two mv-PA measures were repeated by adding hypertension, glucose, and triglycerides as covariates in separate analyses (Table 7). Resultant ORs for DII score in relation to elevated CRP were somewhat attenuated when glucose and triglycerides were added to the full multivariate model but were comparable to prior analyses when hypertension was added to the model. For example, when adding hypertension to the model including mv-PA Survey, participants in the top DII Score quartile were still more likely to have an elevated CRP level (Adj. OR 1.347, 95% CI 1.111-1.634) to a similar degree found in analyses without hypertension (see Table 5).

6.0 DISCUSSION

6.1 DII, mv-PA and elevated CRP level. Our findings were not supportive of our primary hypothesis that engaging in high levels of moderate and vigorous activity would mitigate the adverse impact of a pro-inflammatory diet. Further, this finding held when measuring mv-PA either from self-report survey of leisure time activities or via an accelerometer monitor worn continuously during waking hours for several days. We observed, however, that both a pro-inflammatory diet and mv-PA appear to be independently associated with CRP level when simultaneously controlling for these variables in the same multivariate model. While both measures of mv-PA were inversely related to CRP, data from the monitor appears to be more precise estimator of effect, as evidenced by lower point estimates and marginally overlapping 95% CIs than self-report of leisure time activity only. The differences between results from the survey and monitor is most likely resulted from the accelerator capturing all volitional activity during the course of a day rather than only energy expenditure during leisure.

Our study is the first to simultaneously examine DII, mv-PA and CRP. Our findings, however, are largely consistent with results reported by Kantor et al. (2013) when examining the association between CRP and individual pro- or anti-inflammatory dietary components among 9,895 adults in 1999-2004 NHANES dataset. For example, Kantor et al. (2013) reported that that increasing percent of energy intake from saturated fat was significantly associated with increasing CRP, while increasing fiber intake was inversely associated with CRP. These relationships also held when accounting for leisure time physical activity. Kasapis et al. (2005) did a widespread search on PubMed for articles published between 1975 through 2004 and related to physical activity and CRP, which revealed 19 articles on acute inflammatory response to exercise, 18 on cross-sectional comparisons of subjects by activity levels, and 5 examining the effects of exercise on inflammatory process. The results showed exercise produced a short-time, inflammatory response, whereas both cross-sectional comparisons and longitudinal exercise training studies demonstrated a long-term "anti-inflammatory" effect.

6.2 Descriptive Associations. Findings from our study sample that that elevated CRP level by sex, race/ethnicity, education, BMI, glucose, triglycerides, and waist circumference. Similar findings have been reported in a study by Rethorst et al. (2014) who demonstrated that individuals with elevated CRP levels had significantly higher body weight, waist circumference, and BMI. Similar to our results, Rethorst et al. also did not find an association between elevated inflammation and age yet, unlike our study, they did not observe a link with gender and race. Regarding associations with DII, individuals in the highest quartile differed from those in the lowest quartile in terms of sex, race/ethnicity, education, waist circumference, BMI. DII score did not vary by age, smoking status, blood pressure, glucose, and triglycerides. These findings had similarities and differences compared to other studies. For example, a study by Esmaillzadeh et al. (2006) showed individuals with the most fruit and vegetable intake, which was equivalent to lowest DII score, were slightly younger and less likely to be obese and a lower prevalence of metabolic syndrome. Regarding associations with mv-PA assessed from survey data, we observed variation by sex, race/ethnicity, education, age, smoking status, BMI, blood pressure, glucose, triglycerides, and WC. These covariates, except triglycerides, also varied in association in relation to mv-PA detected by the monitor. Berkemeyer et al. (2016) reported physical activity volume was significantly lower across increasing age and BMI and across decreasing strata for education, in both men and women.

6.3 Causal Pathway. The exact protective mechanism linking physical activity to decreased CRP level remains to be elucidated. Increased exercise training may alter redox balance that involves reactive oxygen species (ROS) and antioxidants in favor of the latter. ROS can react with and remove electrons from structural and functioning proteins leading to increased inflammation marked with elevated CRP. On the contrary, antioxidants have the ability to donate their electrons enabling them to neutralize ROS and inhibit its production (Parker et al., 2014). Given the results of our study of a lack of a mitigating effect from mv-PA on a pro-inflammatory diet, however, the potential anti-inflammatory effects from PA appear to not a level to combat the pro-inflammatory impact of certain dietary

6.4 Study Strengths and Limitations. A major asset of our study is the use of NHANES datatsets consisting of validated and repeatable data from a large, national resource with data collected by highly-trained personnel. At the same time, there are several limitations to consider. Foremost, all measurements took place at only one time point. Future, prospective studies could benefit from longitudinal data collection of CRP along with diet and PA. An additional shortcoming is that accelerometers do not differentiate among activities making it difficult to develop specific activity recommendations. In addition, accelerometers are known to not be sensitive to detect upper body movements including biking or swimming, which could lead to underestimating of physical activity. Although we have adjusted for a wide range of potential confounding variables, unmeasured or unknown factors may have partly contributed to the reported associations. Also, even though sensitivity analyses were conducted to illuminate the possible impact of chronic health conditions, we did not conduct a comprehensive assessment.

6.5 Conclusions and Future Directions. We that found that although engaging in moderate and/or physical activity was linked independently to lower CRP level, particularly at high PA levels, it appears that a pro-inflammatory diet is still a countervailing influence. Future studies utilizing longitudinal design are needed to better understand the strength of observed association. Another careful consideration for future direction is to minimize potential effects of confounding variables. Although different covariates are included in present study, there is possibility that unmeasured confounders may still be present. The impact upon disease risk in the simultaneous context of exercise and diet is a complex question to answer, and more research is needed to refine estimates. It would be valuable to prepare dot plots of these two factors, together, and in relation to CRP level, to gain insight into variability of the correlations among these continuous variables. Also of important would be to examine if the relationships we uncovered in this study held for both men and women, and across race/ethnic groups. The American College of Sports Medicine (ACSM) currently recommends a regular leisure-time exercise program consisting of a minimum of 150 minutes of moderate PA per week and/or 75 minutes of vigorous PA per week for maintaining cardiorespiratory health (ACSM, 2011). Our study findings support the premise that both an anti-inflammatory diet and exercise independently reduce the risk for medical conditions and diseases that are linked to chronic low-grade inflammation.

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8.0 FIGURES and TABLES

Figure 1 Formation of Study Sample Size

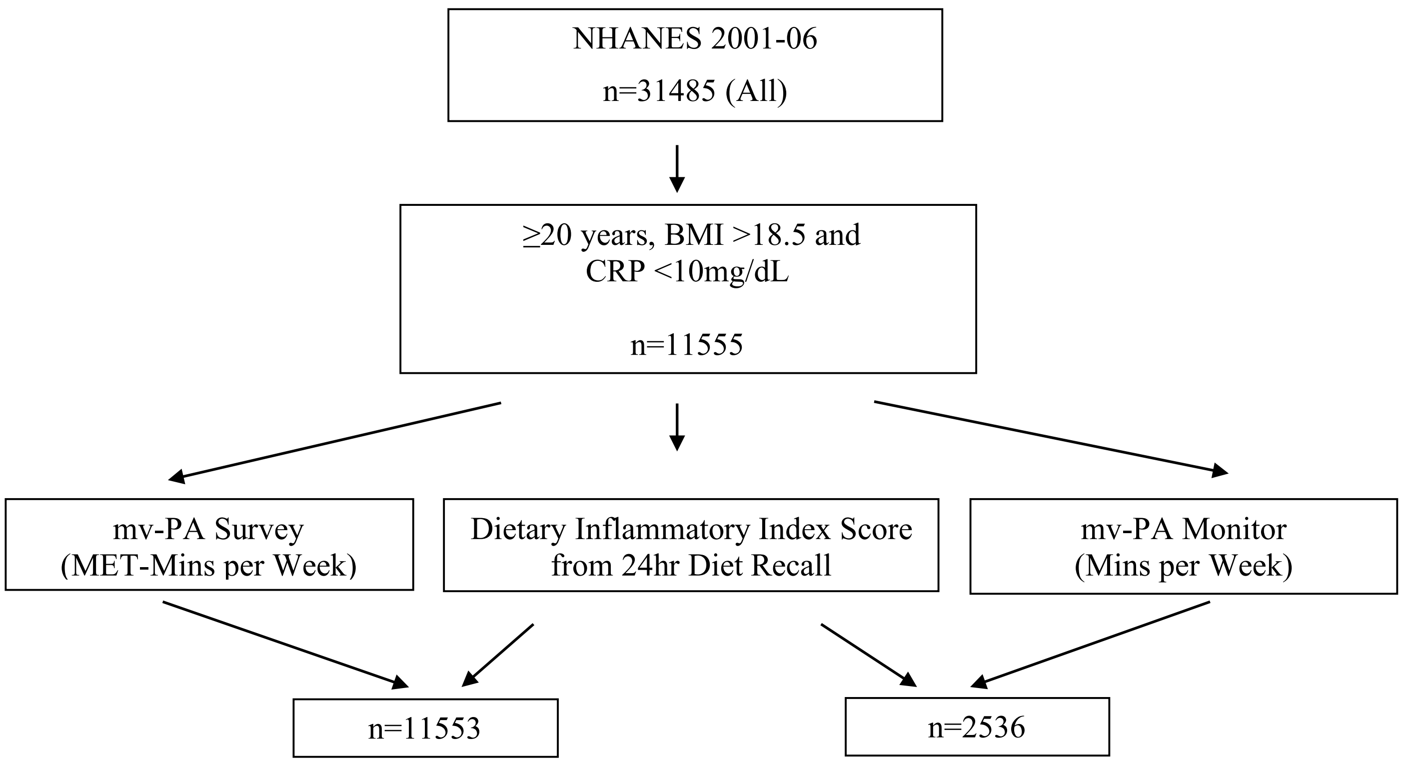

Table 1 Participant Characteristics according to C-Reactive Protein Level

	C-Reactive Protein		Chi-sq[2]	p-Value
	Normal <3mg/dL	Elevated ≥3mg/dL to <10mg/dL		
Sex				
Male	5144 (88.2)[1]	689 (11.8)	195.585	.001
Female	4492 (78.5)	1230 (21.5)		
Race/Ethnicity				
Non-Hispanic Black	1759 (81.3)	405 (18.7)	24.979	.001
Other Hispanics	331 (81.3)	75 (18.7)		
Mexican American	1962 (81.6)	441 (18.4)		
Other Race and Multi-races	396 (86.8)	60 (13.2)		
Non-Hispanic White	5188 (84.7)	937 (15.3)		
Education				
College Graduate and above	2072 (87.3)	302 (12.7)	39.151	.001
Some College	2644 (83.2)	534 (16.8)		
High School Graduate	2292 (82.9)	473 (17.1)		
9-11th Grade	1352 (80.6)	326 (19.4)		
Less than 9th Grade	1267 (81.7)	283 (18.3)		
Age				
20-29	1864 (83.6)	365 (16.4)	20.298	.002
30-39	1696 (84.8)	303 (15.2)		
40-49	1708 (83.8)	331 (16.2)		
50-59	1263 (83.0)	258 (17.0)		
60-69	1315 (79.9)	330 (20.1)		
70-79	1045 (83.6)	205 (16.4)		
80+	745 (85.4)	127 (14.6)		
Smoking Status				
Never	4966 (83.5)	979 (16.5)	.859	.651
Former	2570 (83.6)	505 (16.4)		
Current	2090 (82.8)	435 (17.2)		
Body Mass Index				
Normal (18.5-24.9)	3385 (91.6)	312 (8.4)	715.982	.001
Overweight (25.0-29.9)	3774 (86.1)	607 (13.9)		
Obese (30.0-34.9)	1718 (76.9)	517 (23.1)		
Morbidly Obese (35+)	759 (61.1)	483 (38.9)		
Blood Pressure				
Normal (<80/120)	2863 (85.0)	506 (15.0)	6.471	.011
Elevated (>80/120)	3369 (82.8)	700 (17.2)		
Glucose				
Normal (<100mg/dL)	2801 (83.8)	541 (16.2)	8.133	.004
Elevated (>100mg/dL)	1835 (80.9)	434 (19.1)		
Triglycerides				
Normal (<150mg/dL)	3112 (85.4)	530 (14.6)	57.137	.001
Elevated (>150mg/dL)	1504 (77.4)	439 (22.6)		
Waist Circumference (sex-specific)[2]	4954 (91.8)	411 (8.2)	512.923	.001
Normal	4496 (76.0)	1418 (24.0)		
Elevated				

[1] *n(%)*

[2] *High waist circumference is defined as males >40in (102cm) and females >35in (88cm).*

Table 2 Participant Characteristics according to Dietary Inflammatory Index Score

	Dietary Inflammatory Index Score Quartiles				Chi-sq	p-Value
	Q1 <-.82	Q2 -.82 to <.32	Q3 .32 to <1.25	Q4 1.25+		
Sex						
Male	2410 (43.1)[1]	1518 (27.1)	1036 (18.5)	631 (11.3)	443.678	.001
Female	1510 (27.6)	1396 (25.5)	1337 (24.4)	1234 (22.5)		
Race/Ethnicity						
Non-Hispanic Black	598 (29.4)	521 (25.6)	482 (23.7)	436 (21.4)	117.807	.001
Other Hispanics	109 (27.7)	116 (29.4)	87 (22.1)	82 (20.8)		
Mexican American	741 (32.2)	631 (27.4)	525 (22.8)	404 (17.6)		
Other Race/Multi	174 (41.2)	102 (24.2)	81 (19.2)	65 (15.4)		
Non-His. White	2298 (38.8)	1544 (26.1)	1198 (20.2)	878 (14.8)		
Education						
College Grad.	1112 (48.3)	586 (25.4)	399 (17.3)	206 (8.9)	388.283	.001
Some College	1094 (35.8)	838 (27.4)	658 (21.6)	463 (15.2)		
High School Grad.	905 (34.1)	684 (25.7)	580 (21.8)	488 (18.4)		
9-11th Grade	451 (28.2)	437 (27.3)	337 (21.0)	337 (21.0)		
Less than 9th Grade	355 (24.5)	367 (25.3)	368 (25.4)	368 (25.4)		
Age						
20-29	717 (33.6)	567 (26.6)	495 (23.2)	353 (16.6)	72.920	.001
30-39	752 (39.6)	500 (26.3)	382 (20.1)	266 (14.0)		
40-49	753 (38.6)	517 (26.5)	395 (20.3)	284 (14.6)		
50-59	516 (35.3)	399 (27.3)	301 (20.6)	247 (16.9)		
60-69	540 (33.7)	417 (26.0)	338 (21.1)	306 (19.1)		
70-79	399 (32.9)	303 (25.0)	280 (23.1)	232 (19.1)		
80+	243 (29.9)	211 (26.0)	182 (22.4)	177 (21.8)		
Smoking Status						
Never	1998 (35.2)	1491 (26.3)	1228 (21.6)	963 (17.0)	24.622	.001
Former	1131 (38.1)	781 (26.3)	609 (20.5)	445 (15.0)		
Current	789 (32.6)	641 (26.5)	533 (22.1)	454 (18.8)		
Body Mass Index						
Normal (18.5-24.9)	1301 (37.0)	878 (25.0)	758 (21.6)	575 (16.4)	39.594	.001
Overw. (25.0-29.9)	1538 (36.6)	1155 (27.5)	858 (20.4)	652 (15.5)		
Obese (30.0-34.9)	704 (32.7)	573 (26.6)	467 (21.7)	407 (18.9)		
Morb. Obese (35+)	377 (31.3)	308 (25.5)	290 (24.0)	231 (19.2)		
Blood Pressure						
Normal (<80/120)	1183 (36.3)	851 (26.1)	680 (20.8)	549 (16.8)	7.332	.062
Elevated (>80/120)	1308 (33.3)	1052 (26.8)	855 (21.8)	713 (18.2)		
Glucose						
Nl (<100mg/dL)	1112 (34.6)	887 (27.6)	680 (21.1)	538 (16.7)	3.757	.289
Ele. (>100mg/dL)	801 (36.7)	557 (25.5)	457 (20.9)	368 (16.9)		
Triglycerides						
Nl (<150mg/dL)	1258 (35.9)	895 (25.6)	741 (21.2)	606 (17.3)	7.756	.051
Ele. (>150mg/dL)	654 (34.8)	542 (28.9)	390 (20.8)	292 (15.5)		
Waist Circumference						
Normal	2005 (38.7)	1353 (26.1)	1061 (20.5)	768 (14.8)	55.505	.001
Sex-Specific Elevated[2]	1867 (32.6)	1516 (26.5)	1275 (22.3)	1064 (18.6)		

[1] *n(%)*

[2] *High waist circumference is defined as males >40in (102cm) and females >35in (88cm).*

Table 3 Participant Characteristics according to mv-PA Survey

	Total MET-Minutes per Week				Chi-sq[2]	p-Value
	<250	250 to 499	500 to 999	1000+		
Sex						
Male	2809 (48.2)[1]	465 (8.0)	723 (12.4)	1835 (31.5)	110.672	.001
Female	3163 (55.3)	534 (9.3)	709 (12.4)	1315 (23.0)		
Race/Ethnicity						
Non-Hispanic Black	1192 (55.1)	173 (8.0)	219 (10.1)	580 (26.8)	220.501	.001
Other Hispanics	223 (54.9)	27 (6.7)	43 (10.6)	113 (27.8)		
Mexican American	1502 (62.5)	196 (8.2)	250 (10.4)	455 (18.9)		
Other Race/Multi	216 (47.4)	48 (10.5)	67 (14.7)	125 (27.4)		
Non-His. White	2839 (46.4)	555 (9.1)	853 (13.9)	1877 (30.6)		
Education						
College Grad.	749 (31.6)	238 (10.0)	414 (17.4)	972 (41.0)	909.632	.001
Some College	1455 (45.8)	318 (10.0)	407 (12.8)	998 (31.4)		
High School Grad.	1531 (55.4)	217 (7.8)	349 (12.6)	668 (24.2)		
9-11th Grade	1077 (64.2)	125 (7.5)	145 (8.6)	330 (19.7)		
Less than 9th Grade	1152 (74.3)	101 (6.5)	117 (7.5)	180 (11.6)		
Age						
20-29	992 (44.5)	186 (8.3)	271 (12.2)	779 (35.0)	230.993	.001
30-39	960 (48.0)	192 (9.6)	262 (13.1)	585 (29.3)		
40-49	1007 (49.4)	189 (9.3)	253 (12.4)	589 (28.9)		
50-59	774 (50.9)	138 (9.1)	199 (13.1)	410 (27.0)		
60-69	912 (55.4)	148 (9.0)	211 (12.8)	374 (22.7)		
70-79	741 (59.3)	83 (6.6)	140 (11.2)	286 (22.9)		
80+	586 (67.2)	63 (7.2)	96 (11.0)	127 (14.6)		
Smoking Status						
Never	2901 (48.8)	556 (9.4)	754 (12.7)	1732 (29.1)	88.529	.001
Former	1563 (50.8)	246 (8.0)	419 (13.6)	847 (27.5)		
Current	1501 (59.4)	196 (7.8)	259 (10.3)	569 (22.5)		
Body Mass Index						
Normal (18.5-24.9)	1771 (47.9)	314 (8.5)	478 (12.9)	1134 (30.7)	85.883	.001
Ovrwgt. (25.0-29.9)	2212 (50.5)	405 (9.2)	557 (12.7)	1206 (27.5)		
Obese (30.0-34.9)	1242 (55.6)	172 (7.7)	266 (11.9)	555 (24.8)		
Morb. Obese (35+)	747 (60.2)	108 (8.7)	131 (10.6)	3150 (27.3)		
Blood Pressure						
Nl (<80/120)	1612 (47.8)	328 (9.7)	425 (12.6)	1004 (29.8)	40.848	.001
Elev. (>80/120)	2232 (54.9)	322 (7.9)	500 (12.3)	1014 (24.9)		
Glucose						
Nl (<100mg/dL)	1648 (49.3)	305 (9.1)	426 (12.8)	962 (28.8)	18.063	.001
Elev. (>100mg/dL)	1237 (54.5)	196 (8.6)	287 (12.6)	549 (24.2)		
Triglycerides						
Nl (<150mg/dL)	1774 (48.7)	328 (9.0)	469 (12.9)	1070 (29.4)	39.181	.001
Elev. (>150mg/dL)	1096 (56.4)	173 (8.9)	243 (12.5)	431 (22.2)		
Waist Circumference						
Normal	2477 (45.9)	453 (8.4)	690 (12.8)	1774 (32.9)	169.481	.001
Sex-Specific Elevated[2]	3325 (56.2)	532 (9.0)	721 (12.2)	1335 (22.6)		

[1] *n(%)*
[2] *High waist circumference is defined as males >40in (102cm) and females >35in (88cm).*

Table 4 Participant Characteristics according to mv-PA Monitor

	Total Minutes per Week				Chi-Sq	p-Value
	<3.0	3.0 to <10.25	10.25 to <25.0	25.0+		
Sex						
Male	169 (12.9)[1]	231 (17.6)	355 (27.0)	560 (42.6)	132.435	.001
Female	246 (20.1)	345 (28.3)	357 (29.2)	273 (22.4)		
Race/Ethnicity						
Non-Hispanic Black	90 (17.4)	131 (25.4)	148 (28.7)	147 (28.5)	63.172	.001
Other Hispanics	5 (6.6)	11 (14.5)	27 (35.5)	33 (43.4)		
Mexican American	49 (9.2)	120 (22.4)	166 (31.0)	200 (37.4)		
Other Race/Multi	8 (8.2)	30 (30.9)	35 (36.1)	24 (24.7)		
Non-His. White	263 (20.0)	284 (21.6)	336 (25.6)	429 (32.7)		
Education						
College Grad.	50 (9.1)	97 (17.6)	172 (31.2)	232 (42.1)	80.284	.001
Some College	103 (13.9)	170 (23.0)	220 (29.7)	247 (33.4)		
High School Grad.	117 (19.8)	156 (26.4)	162 (27.4)	157 (26.5)		
9-11th Grade	80 (23.7)	75 (22.2)	76 (22.5)	107 (31.7)		
Less than 9th Grade	65 (20.6)	78 (24.8)	82 (26.0)	90 (28.6)		
Age						
20-29	14 (3.7)	71 (18.6)	122 (32.0)	174 (45.7)	907.226	.001
30-39	13 (3.1)	76 (17.8)	150 (35.2)	187 (43.9)		
40-49	12 (2.6)	81 (17.2)	145 (30.9)	232 (49.2)		
50-59	33 (8.8)	89 (23.7)	124 (33.0)	130 (34.6)		
60-69	96 (23.2)	128 (30.9)	110 (26.6)	80 (19.3)		
70-79	111 (40.1)	97 (35.0)	47 (17.0)	22 (7.9)		
80+	136 (70.8)	34 (17.7)	14 (7.3)	8 (4.2)		
Smoking Status						
Never	208 (15.4)	273 (20.3)	404 (30.0)	462 (34.3)	28.889	.001
Former	145 (20.4)	186 (26.2)	173 (24.4)	206 (29.0)		
Current	62 (12.9)	117 (24.4)	135 (28.2)	165 (34.4)		
Body Mass Index						
Normal (18.5-24.9)	125 (16.0)	159 (20.4)	203 (26.0)	293 (37.6)	74.961	.001
Overw. (25.0-29.9)	142 (14.8)	188 (19.6)	278 (29.0)	350 (36.5)		
Obese (30.0-34.9)	84 (16.4)	126 (24.7)	161 (31.5)	140 (27.4)		
Morb. Obese (35+)	64 (22.3)	103 (35.9)	79 (24.4)	50 (17.4)		
Glucose						
Nl (<100mg/dL)	78 (12.4)	128 (20.3)	188 (29.9)	235 (37.4)	31.197	.001
Elev. (>100mg/dL)	127 (23.1)	132 (24.0)	134 (24.4)	157 (28.5)		
Triglycerides						
Nl (<150mg/dL)	127 (16.3)	166 (21.3)	206 (26.4)	281 (36.0)	7.796	.050
Elev. (>150mg/dL)	77 (19.4)	93 (23.5)	115 (29.0)	111 (28.0)		
Waist Circumference						
Normal	123 (10.4)	208 (17.7)	322 (27.3)	525 (44.6)	164.769	.001
Sex-Specific Elevated[2]	280 (21.1)	363 (27.4)	385 (29.1)	296 (22.4)		

[1] *n(%)*

[2] *High waist circumference is defined as males >40in (102cm) and females >35in (88cm).*

Table 5 Crude, Age-adjusted, and Multivariate-adjusted ORs and 95% CIs for Dietary Inflammatory Index Score in relation to Elevated CRP Level

	Crude	Age-Adjusted	Basic Model[1]	Model plus mv-PA Survey	Model plus mv-PA Monitor
DII Quartiles					
Q1 (<-.82)	1.00	1.00	1.00	1.00	1.00
Q2 (-.82 to <.32)	1.413 (1.238-1.614)*	1.412 (1.237-1.613)*	1.262 (1.098-1.450)*	1.247 (1.084-1.433)*	1.258 (.940-1.683)
Q3 (.32 to <1.25)	1.458 (1.268-1.676)*	1.456 (1.266-1.674)*	1.197 (1.032-1.387)*	1.188 (1.025-1.378)*	1.264 (.931-1.717)
Q4 (1.25+)	1.742 (1.507-2.014)*	1.735 (1.501-2.006)*	1.325 (1.133-1.549)*	1.306 (1.116-1.528)*	1.324 (.932-1.879)

[1] *Adjusted for age, sex, education, smoking status, and body mass index.*

Table 6 Crude, Age-adjusted, and Multivariate-adjusted ORs and 95% CIs for Physical Activity in relation to Elevated CRP Level

		Crude	Age-Adjusted	Basic Model[1]	Basic Model plus DII
A	**mv-PA Survey (MET-Mins per Wk)**				
	<250	1.00	1.00	1.00	1.00
	>250 to 499	.741 (.617-.891)*	.742 (.617-.891)*	.799 (.659-.970)*	.806 (.662-.981)*
	>500 to 999	.748 (.640-.875)*	.748 (.640-.876)*	.876 (.742-1.034)	.903 (.764-1.068)
	>1000+	.552 (.487-.626)*	.553 (.487-.627)*	.709 (.619-.812)*	.726 (.632-.834)*
B	**mv-PA Monitor (Mins per Wk)**				
	<3.0	1.00	1.00	1.00	1.00
	3.0 to <10.25	1.021 (.753-1.386)	.909 (.657-1.258)	.916 (.650-1.293)	.907 (.639-1.285)
	10.25 to <25.0	.747 (.551-1.012)	.630 (.447-.888)	.808 (.560-1.165)	.784 (.540-1.138)
	25.0 +	.416 (.301-.574)*	.341 (.235-.495)*	.543 (.363-.812)*	.539 (.358-.810)*

[1] *Adjusted for age, sex, education, smoking status, and body mass index.*

Table 7 Sensitivity Analyses[3] for ORs and 95% CIs for DII Score and mv-PA

	Model plus Hypertension	Model plus Glucose	Model plus Triglycerides
MODEL 1[1]			
DII Score Quartiles			
Q1 (<-.82)	1.00	1.00	1.00
Q2 (-.82 to <.32)	1.202 (1.008-1.433)*	1.179 (.971-1.432)	1.164 (.958-1.414)
Q3 (.32 to <1.25)	1.103 (.914-1.331)	1.103 (.895-1.359)	1.100 (.892-1.357)
Q4 (1.25+)	1.347 (1.111-1.634)*	1.136 (.908-1.420)	1.148 (.917-1.436)
mv-PA Survey (MET-Mins/Wk)			
<250	1.00[7]	1.00	1.00
250 to <500	.777 (.606-.995)*	.915 (.702-1.192)	.911 (.698-1.190)
500 to 999	.895 (.726-1.103)	.949 (.754-1.193)	.955 (.759-1.203)
1000+	.693 (.581-.825)*	.686 (.564-.836)*	.704 (.780-.858)*
MODEL 2[2]			
DII Score Quartiles			
Q1 (<-.82)		1.00	1.00
Q2 (-.82 to <.32)	§	1.099 (.732-1.649)	1.099 (.732-1.650)
Q3 (.32 to <1.25)		1.014 (.653-1.574)	1.025 (.660-1.590)
Q4 (1.25+)		.876 (.520-1.474)	.872 (.525-1.477)
mv-PA Monitor (Mins/Wk)			
<3.0		1.00	1.00
3.0 to <10.25		1.122 (.685-1.838)	1.189 (.722-1.955)
10.25 to <25.0	§	1.078 (.642-1.811)	1.146 (.680-1.931)
25.0 +		.519 (.291-.926)*	.568 (.317-1.017)

[1] Adjusted for DII, mv-PA Survey (categorical), age, sex, education, smoking status, BMI.
[2] Adjusted for DII, mv-PA Monitor (categorical), age, sex, education, smoking status, BMI.
[3] Hypertension, glucose, triglycerides added separately to multivariate models.
§ Values cannot be obtained due to empty cells