**Problematic relationship to eating and food and its association to body mass index, incident diabetes, metabolic syndrome, and diet in middle-aged adults: The Coronary Artery Risk Development in Young Adults (CARDIA) Study**

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## Abstract

**Background**: There is a high prevalence among adults of eating behaviors and attitudes that do not meet the threshold or fulfill the Diagnostic and Statistical Manual of Mental Disorders, 5th edition (DSM-V) criteria for eating disorders. Examples include overeating with or without the sense of loss of control or distress associated with overeating or sense of loss of control. These subclinical eating behaviors and attitudes may be called a 'Problematic Relationship to Eating and Food' (PREF) and may occur on a continuum. That is, unhealthy eating behaviors may vary by severity, ranging from normal eating, through unhealthy behaviors and attitudes that do not require psychiatric or medical treatment, to the most severe clinical eating disorders. However, while problematic eating behaviors have been studied in young people, little is known of the prevalence and long-term effects of problematic eating behaviors in generally healthy middle-aged adults enrolled in a prospective cohort. Thus this thesis adds to the field of eating disorders and eating behaviors by exploring the prevalence of a range of behaviors and attitudes related to eating and food among a large sample of generally healthy middle-aged adults who have been observed in 9 clinical examinations over 30 years in their adult life. Using this long-term follow-up, the objective of this thesis is to investigate the association of a PREF scale with BMI trajectories, risk of incident diabetes and metabolic syndrome, as well as energy intake, dietary patterns and diet quality in the Coronary Artery Risk Development in Young Adults (CARDIA) Study.

**Methods**: This dissertation includes three separate research projects which aimed to describe the prevalence of problematic behaviors and attitudes related to eating and food among generally healthy middle-aged adults. A Problematic Relationship to Eating and Food (PREF) score was defined as the sum of number of behavioral and attitudinal constructs endorsed by participants. The PREF score was assessed based on the Questionnaire on Eating and Weight Patterns-Revised (QEWP-R, originally created to gather data in support of the concept of Binge Eating Disorder), administered in the Coronary Artery Risk Development in Young Adults (CARDIA) study in its Year 10 examination when the community based sample of nearly 4000 participants was aged 27-41 years. PREF captures 8 behaviors and attitudes related to eating and food including anxiety around eating or food, endorsement of unhealthy compensatory behaviors intended to lose weight or to maintain weight loss, consumption of a large amount of food in a relatively short period of time, sense of loss of control when overeating in a relatively short period of time, distress associated with overeating, distress associated with sense of loss of control, preoccupation with dieting, and concern about personal weight and shape. The study then investigates how PREF is

prospectively associated, among generally healthy middle-aged adults, with 1) body mass index (BMI), 2) incident diabetes and metabolic syndrome, and 3) energy intake, dietary intake, pattern, and quality. The first project examined how PREF was associated with the trajectories of BMI throughout 15 years of follow-up (through CARDIA Year 25), using repeated measures regression. In addition, PREF associations with BMI classes were examined using multinomial logistic regression. The second project examined how the problematic eating behaviors were associated with incident diabetes and metabolic syndrome using proportional hazards regression, logistic regression and Kaplan-Meier curves. The last project, concerned the examination of associations between PREF and energy intake, dietary pattern, and diet quality (including an objective measure of diet quality, the sum of 4 serum carotenoids), used multiple linear regression.

**Results**: Results for the three research projects were as follows. We identified six categories of problematic relationships to eating and food by giving one point for each PREF construct endorsed. PREF 0 points (called normal eaters in this thesis) and participants with PREF (1, 2, 3, 4-5 points, and 6-8 points) were identified. Almost 60% of the participants endorsed at least one construct (therefore being assigned at least 1 PREF point). Moreover, even after the exclusion of 3.7% of the participants with PREF 6-8 points (i.e., who endorsed 6 to 8 constructs, which presumptively closely corresponds to a diagnosable eating disorders), 54.4% endorsed 1 to 5 constructs (PREF 1-5 points). Therefore, problematic eating attitudes and behaviors were prevalent in middle-aged adults. Greater BMI trajectories were observed in PREF $\geq$1 point compared to PREF 0 points. Among those with PREF 1-5 points, mean BMI was graded by the number of PREF constructs endorsed. The BMI trajectories further diverged throughout 25 years of follow-up, with approximately 0.6kg/$m^2$ greater BMI per PREF point in CARDIA Year 0, increasing to 1.0 kg/$m^2$ per PREF point in CARDIA Years 10 and 25. Participants had 1.2 times the hazard of diabetes per PREF point after 15 years of follow-up, adjusting for demographic and behaviors. Participants had 1.2 times hazard of metabolic syndrome per PREF point after 10 years of follow-up, adjusting for demographic characteristics and health behaviors. However, both associations were close to null after further adjustment for Year 10 body mass index, suggesting associations between problematic eating behaviors and attitudes were mediated through BMI. A less favorable diet in those with PREF $\geq$ 6 points was suggested by greater energy intake and greater consumption of artificially-sweetened beverages. However, a healthier *A Priori* Diet Quality Score among those with PREF $\geq$ 1 point (p=0.04 in a graded relationship across PREF points,1.9 *A Priori* Diet Quality Score points higher in PREF 6-8 points than in PREF 0 points)

suggested knowledge of and attention to diet composition in those with any PREF points, despite having substantial excess body weight. This finding of slightly better quality diet was supported by greater values of the objective measure, a sum of 4 serum carotenoids, which, after adjustment for BMI, were found in participants with PREF ≥1 point versus those with PREF 0 points. While some of the above associations were not significant among those with PREF 1-5 points when each such category was compared specifically to PREF 0 points, the statistically significant linear trend suggests that the associations of dietary patterns and intakes among PREF 1-5 points follows the general trend and thus are similar to those with presumptive eating disorders.

**Conclusions**: These results indicate that people in all PREF categories above 0 had greater BMI trajectories, were at greater risk of diabetes and metabolic syndrome, had greater energy intake, and consumed more artificially-sweetened beverages, all of which are of potential concern for public health. In contrast, they had greater *A Priori* Diet Quality Scores (healthier diet). A novel aspect of this study was our ability to examine the serum concentration of the sum of 4 carotenoids, which are not synthesized by humans and are only available through diet from plant foods (especially fruits and vegetables); and which empirically are lower in the presence of oxidative stress, for example when BMI is high. After adjustment for demographics, behavioral variables, and particularly for CARDIA Year 10 BMI, the sum of carotenoids was positively associated with PREF points. These associations with PREF were not seen to differ by race and sex. These findings illustrate the need for early identification and treatment of people with problematic relationships to eating and food, and the need to view unhealthy eating behaviors as a continuum and to investigate the full spectrum of eating behaviors. Obesity in those with PREF is consistent with their higher energy intake and this higher intake likely contributes to their excess BMI. However, the fact that those with PREF did not have worse diet quality suggests that they show interest in eating a healthy diet (by the fact that their diet score is higher, confirmed by their sum of 4 carotenoids). Despite their apparent interest in eating a good composition diet, this disconnect with their ongoing obesity may suggest a window for teaching better ways to relate to food both at the individual and policy levels. Further research is necessary to estimate the magnitude and effect of problematic relationship to eating and food in the US population, and whether interventions might help to reduce this problem.

**Table of Contents**

## LIST OF TABLES

## LIST OF FIGURES

# Chapter 1: Background, Overall Aims, and Objectives

## 1.1 Chapter overview

The overarching aim of this thesis is to fill in the current gaps in the literature concerning eating behaviors in middle age, with focus on unhealthy eating behaviors that do not meet the threshold of DSM-V eating disorders. Therefore, this thesis expresses problematic eating behaviors and attitudes from individual or aggregated constructs that are used to diagnose eating disorders, including overeating, sense of loss of control, and associated distresses. This thesis focuses on those who endorse at least one of the constructs as having a 'Problematic Relationship to Eating or Food' (PREF). Although problematic eating behaviors and attitudes are prevalent, there has been little longitudinal examination of these behaviors and their long-term effects in population-based cohort studies.

Therefore, the primary aim is to examine the prevalence of the problematic eating attitudes and behaviors in generally healthy middle-aged adults. The secondary aim is to investigate the long-term effects of PREF on body mass index (BMI), diabetes, and metabolic syndrome, and to assess aspects of dietary intake in people with PREF: energy intake, dietary pattern, and diet quality. This first chapter serves as a general overview of how we define PREF constructs, score and prevalence.

## 1.2 Background

We define the core characteristic of PREF as having a distorted relationship with food and weight. Clinically diagnosed Anorexia Nervosa (AN), Bulimia Nervosa (BN), and Binge Eating Disorder (BED) are regarded as the extreme and severe clinical manifestation of PREF. Nonetheless, the dimensions and constructs that are present in eating disorders have not been examined in combinations that do not constitute diagnosable eating disorders.

Although OSFED and more broadly, problematic aspects related to eating and food are more prevalent than the clinical AN, BN, or BED [1], less attention has been given to adults with PREF in longitudinal studies. Because most of the eating disorder research has been restricted to severe cases of AN or BN requiring clinical treatment or relying on registered patients with eating disorders, less is known about PREF in the general population or those residing in the community [2]. Further, while most studies have been conducted in adolescents [3-6] and young adults [7-8], less research has been conducted on adults using population based samples [1-2]. Therefore, understanding is incomplete of the occurrence of a whole range of problematic eating behaviors and attitudes in the general adult population, and the long-term associations with physical health

conditions including obesity and other consequences. The understanding of PREF behaviors and attitudes and their associated long-term risk for excess weight, diabetes, metabolic syndrome, and dietary pattern in the general population is important because of the high prevalence of the problematic eating behaviors in the adults [1]. Even if those with PREF do not progress to full-scale eating disorders, and most PREF are thought to be mild and self-limiting [9-10], it is possible that PREF may have harmful physical [11-13], psychological [14-15], and social consequences [16-17].Therefore, there is a need for greater understanding of the full spectrum of unhealthy eating behaviors in the general population that may or may not be captured under DSM-V diagnoses.

### 1.3 Objective

The overall objective of this thesis is to investigate the characteristics of PREF, examine the prevalence of PREF in middle-aged generally healthy adults including some who are often excluded from this line of research, namely males and blacks. Besides describing how PREF is defined in the epidemiological setting from a self-reported, self-administered questionnaire, and estimating the prevalence of PREF in a community-based sample of generally healthy adults, this thesis includes three separate research projects. With the three research projects, we aim to examine the associations between epidemiologically defined PREF in midlife and body mass index (BMI), diabetes, metabolic syndrome, and evaluate dietary intake (how much and what people with PREF are eating). We hypothesized that participants with higher PREF scores would have greater BMI compared to normal eaters; participants with PREF would be at greater risk of incident diabetes and metabolic syndrome compared to normal eaters and the association would be partially explained by BMI; and participants with PREF would have greater energy intake and worse diet quality compared to normal eaters. This thesis does not consider intervention to prevent or ameliorate PREF; it only describes empirical associations of PREF with several physical health outcomes. It is noted that the PREF identified in this thesis were likely present before ascertainment in the study population used for analyses [18-20].

Findings from this thesis will add to the limited literature examining longitudinal associations of problematic behaviors and attitudes related to eating with BMI, incident diabetes, metabolic syndrome, and dietary intake in a community-based sample of middle-aged adults.

### 1.4 Interim conclusion

Given that sub-threshold eating disorders are comorbid with other physical and psychiatric disorders [17], there is a need for further research on problematic aspects related to eating and food, beyond the people who are diagnosed with full eating disorders. Sub-threshold eating

disorders and related behaviors and attitudes indicated by PREF represent a significant public health concern and priority given that scant prior evidence suggests that subclinical behaviors are prevalent among adults [1] but little is known of the long-term risk on BMI, incident diabetes, incident metabolic syndrome, and dietary aspects among participants with PREF.

## Chapter 2

## Background on DSM-V Eating Disorders and Problematic Relationship to Eating and Food

### 2.1 Epidemiology of Eating Disorders and Disordered Eating Behaviors in middle-aged adults and older adults from the general population

The prevalence of disordered eating behaviors is difficult to estimate and likely varies considerably depending on the geographic location as well as the specific definitions and measures of behaviors used. Prior estimates of the prevalence of sub-threshold disordered eating behaviors in generally healthy adults have ranged from 0.6% of United States women having a sub-threshold binge eating disorder (defined strictly as 'binge eating episodes, occurring at least twice a week for at least 3 months, and not occurring solely during the course of anorexia nervosa, bulimia nervosa, or binge eating disorder') [17] to 11.8% with disordered eating behaviors in Norwegian young adults (<30 years old), assessed from the Eating Attitude Test, with focus on 'oral control' and 'bulimia and food preoccupation' [21]. These disordered eating behaviors in the general population are generally considered to be much more prevalent than AN or BN [17]. Although EDs are often considered to be disorders of adolescence, AN is most prevalent during that age period. Thus there are other eating disorders and disordered eating behaviors that are more common in adulthood [22-24]. Because problematic eating behaviors exist beyond adolescence, and the onset of bulimia nervosa and binge eating disorder is at a much older age than anorexia nervosa [22,24], more emphasis should be given to problematic eating behaviors beyond the period of adolescence and young adulthood. Nevertheless, most studies have been conducted among young people [25-26] or adolescents with clinical eating disorders [22,27]. Therefore there is a knowledge gap regarding the specific presentations of PREF and their associations with comorbidity in the general population in midlife and beyond.

### 2.2 Eating disorders and disordered eating behaviors among non-white ethnic and racial groups and among males

The majority of research in eating behaviors has been done with young White and European or North American women [28]. Although the number of studies of eating disorders and disordered eating behaviors conducted among other age, sex, race and ethnicities are growing, the focus on young Caucasian females leaves other ethnic groups, males, and older age groups largely unexplored [27]. There is a growing literature showing that men increasingly suffer from body image issues due to societal pressures, which further leads to greater rates of

disordered eating behaviors among men compared to past decades [29]. The literature suggests that ethnic minorities have a decreased risk of developing eating disorders due to lower social and cultural preference for thin figures [30-31]. However, with the increasing research on other race/ethnicities during the past decade, the rates of problematic eating behaviors in ethnic minorities remain inconclusive compared to White participants. Some studies have found that eating disorders equally affect both blacks and whites and males and females, while other studies find lower levels of bulimic symptoms among Black and Asian minorities [32], higher levels of purging behaviors in black minorities only [33], and higher prevalence of binge eating in ethnic minority women. While many studies suggest comparable rates of binge eating behavior across different ethnicities, it remains unclear whether the severity of other sub-threshold and problematic eating behaviors are also comparable across different ethnic groups. Therefore, knowledge of the characteristics and epidemiology of problematic eating behaviors among men and people of non-Caucasian race or ethnicity remains limited.

## Chapter 3. Published information about problematic eating behaviors in relation to obesity

### 3.1 Literature review of problematic eating behaviors in relation to obesity

Previously identified problematic eating behaviors linked to excessive weight gain, overweight and obesity include dieting, unhealthy weight control behaviors, binge eating, dietary restraint, disordered eating behaviors, and the speed of eating. Cross-sectional studies conducted among adolescents and young to middle-aged adults in South London [2] and Norway [34] and among adolescents in Minnesota [35] have shown that greater BMI is associated with disordered eating behaviors. While loss of control was associated with overweight (OR: 1.9, 95% CI: 1.2-2.8), the association with loss of control was stronger among those categorized as having obesity (OR: 3.2, 95% CI: 2.1-4.9) in a cross-sectional study conducted in South London [2]. More specifically among young adults (<30 years old), participants who were categorized as having obesity were at greater risk for bulimia and preoccupied with food (OR: 2.22, 95% CI: 1.35-3.66) [34]. Among middle-aged adults (≥30 years old), disordered eating behaviors (such as feeling guilty or sensing a need to follow a diet) were associated with obesity (OR: 12.0, 95%CI: 10.0-14.4) and extreme obesity (OR: 22.5, 95%CI: 18.37-27.55) in the cross-sectional study conducted in Norway [34]. While cross-sectional studies [2, 34] are unable to distinguish the temporality between disordered eating behaviors and BMI categories, Project EAT, a longitudinal study conducted among US adolescents reported that participants who endorsed dieting were at 1.8 times greater risk for overweight after 5 years of follow-up, and those who engaged in unhealthy weight control behaviors were at 3.1 times greater risk for overweight after 5 years of follow-up among male adolescents [35]. After 10 years of follow-up, Project EAT revealed that persistent dieters had greater mean BMI compared to participants who did not endorse any dieting at two time points (1998-1999 and 2003-2004), 1.95 $kg/m^2$ and 3.51$kg/m^2$ for females and males, respectively (both $p < 0.01$). Similarly, mean BMI was greater among participants who endorsed unhealthy weight control behaviors (2.34$kg/m^2$ and 1.77$kg/m^2$, for females and males, respectively, both $p<0.01$) compared to participants who did not endorse any unhealthy weight control behaviors [36]. Similar findings were reported from the Growing Up Today study (GUTS), which reported that participants with compensatory behaviors including self-induced vomiting or usage of laxatives were at greater risk for obesity onset over 4 years of follow-up [37]. Other community-based cohort studies also reported that frequent dieting was associated with greater weight gain compared to participants who did not endorse any dieting behaviors [38]. In Japan, cross-sectional and cohort studies with 7 years of follow-up have shown that those who eat rapidly were at 1.8 to 3.1 times greater risk for obesity compared to those who relatively eat slowly [39-40].

Beyond studies of individual features of disordered eating behaviors in relation to overweight, a longitudinal study carried out in Finland also examined aggregated features of disordered eating behaviors among young adults (22 to 27 years old) and the associations with BMI. The study reported individual and aggregated features of binge eating behaviors assessed with the questions, 'I stuff myself with food', 'I feel extremely guilty after overeating', 'I eat when I'm upset', 'I have gone on eating binges where I have felt that I could not stop', 'I eat moderately in front of others and stuff myself when they're gone', 'I think about bingeing (overeating)', 'I eat or drink in secrecy'. These individual and aggregate features were associated with greater BMI cross-sectionally and with BMI measured after 10 years of follow-up (31 to 37 years old) [41]. Besides these findings of aggregated constructs of binge eating [41], other studies examined the speed of eating in relation to BMI [42-43].

Nevertheless, despite the longitudinal study with 5 to 10 years of follow-up that examined individual and aggregated constructs of binge eating among adolescents and young adults [41], little is known of individual and aggregated eating disorder constructs and their association with BMI among black, white, male, and female middle-aged adults. Studies reviewed in this chapter are summarized in Table 3.1.

**Table 3.1 Summary of selected findings about problematic eating behaviors in relation to obesity**

| Reference # First Author | Study Design | Adolescents/ Adults | Independent | Dependent | Findings |
|---|---|---|---|---|---|
| 38 (Field, 2003) | Cohort | Adolescents (14,972) | Dieting<br>Binge eating | Weight gain | Among girls, weight gain from frequent dieters and infrequent dieters were greater compared to non-dieters (0.058 and 0.042 BMI z scores) after 3 years of follow-up<br><br>Among boys, weight gain from frequent and infrequent dieters was greater compared to non-dieters (0.073 BMI z scores) after 3 years of follow-up |
| 37 (Stice, 2005) | Cohort | Adolescents (n=496) | Binge Eating (from Eating Disorder Examination, EDE)<br><br>Dietary restraint (from the Dutch Restrained Eating Scale) | BMI | Participants with dietary restraints were at 3.39 times greater risk for obesity onset during the 4 year follow-up period (OR: 3.39, 95% CI: 1.92-5.99)<br><br>Participants with compensatory behaviors were at 5.17 times greater risk for obesity onset during the 4 year follow-up period (OR: 5.17, 95% CI: 1.77-15.13)<br><br>Binge eating did not predict did not predict obesity onset (OR: |

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| | | | Compensatory behaviors (from Eating Disorder Examination) | | |
| 35 Neumark-Sztainer (2007) | Cohort | Adolescents, followed for 5 years<br><br>N=2,516<br><br>(1,386 girls, 1,130 boys) | Social, personal, and behavioral factors | Overweight, binge-eating, and extreme weight control | Among girls, those reporting being teased about their weight were at 2.0 times greater risk for overweight after 5 years of follow up; 1.7 times greater risk for binge eating, and at 1.4 times greater risk for engagement in extreme weight control behaviors<br><br>Among boys, those who endorsed dieting were at 1.8 times greater risk for overweight and at 3.0 times greater risk for binge eating.<br><br>Endorsement of unhealthy weight control behaviors was associated with 3.1 times greater risk for overweight and at 6.1 times greater risk for binge eating, and 5.6 times greater risk for extreme weight control behaviors |
| 36 Neumark-Sztainer (2011) | Cohort | Adolescents (n=1902) | Dieting, Unhealthy weight control behaviors | BMI | Among females, participants with persistent dieting behavior had 4.33±0.26 increase of BMI compared to participants who did not diet (2.38±0.32)<br>Among females, participants who persistently endorsed unhealthy weight control behaviors had 4.63±0.25 increase of BMI compared to participants who did not endorse any unhealthy weight control behaviors (2.29±0.33) |

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| | | | | | Among males, participants with persistent dieting behavior had 6.96±0.41 increase of BMI compared to participants who did not diet (3.45±0.18)<br>Among males, participants who persistently endorsed unhealthy weight control behaviors had 5.42±0.33 increase of BMI compared to participants who did not endorse any unhealthy weight control behaviors (3.65±0.18) |
| 2 (Solmi, 2014) | Cross-sectional | 16-90 years old men and women, in South London N=1,698 individuals aged ≥16 years | Obesity<br>BMI<br>Overweight | Disordered Eating (SCOFF questionnaire) | People who were overweight had 1.9 times greater risk for loss of control (OR: 1.9, 95% CI 1.2-2.8)<br>People who were categorized as having obesity had 3.2 times greater risk for loss of control (OR: 3.2, 95% CI: 2.1-4.9)<br>People who were categorized as having obesity had 1.6 times greater risk for weight loss (OR: 1.6, 95% CI: 1.0-2.5)<br>People who were categorized as having obesity had 0.6 times the risk for preoccupation with food (OR: 0.6, 95% CI: 0.4-0.8) |
| 34 (Eik-Nes T, 2015) | Cross-sectional | Norwegian women 19-99 years old N=27,252 women | Disordered Eating Behaviors (EAT for <30 years old)<br><br>Eating Disturbance Scale (EDS-5 | BMI<br>Dieting and weight dissatisfaction<br><br>Symptoms of bulimia and | Among women <30 years old, those who were categorized as having obesity were at 2.2 times greater risk for bulimia and preoccupation on food compared to normal eaters (OR: 2.22, 95% CI: 1.35-3.66)<br><br>Among women ≥ 30 years old, those who were categorized as having obesity and those who were categorized as having extreme obesity were at 12.0 (OR: 12.0, 95% CI: 10.0-14.4) and 22.5 (OR: |

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|---|---|---|---|---|---|
| | | | for ≥ 30 years old) | preoccupation with food | 22.5, 95% CI: 18.37-27.55) times greater risk for disordered eating behaviors |
| 41 (Mustelin, 2017) | Cross-sectional and Cohort | FinnTwin16 cohort, age 22-27 old, followed for 10 years (age 31-37)<br>N=5,248 adults (2,423 men and 2,825 women) | Individual and aggregated components relevant to binge eating disorder | BMI | Binge eating components were associated with greater BMI cross-sectionally and 10 years later<br><br>Associations were graded by number of constructs endorsed |
| 39 (Shigeta, 2001) | Cross-sectional, Japanese study | Adults<br>N=453<br>(321 men and 131 women) | Time spent eating a meal<br>Regularity of meals | Obesity | Eating rapidly was associated with 1.8 times greater risk for obesity compared to normal eaters (OR: 1.78, 95% CI: 1.17-2.70)<br>Eating meals irregularly was associated with 2.2 times greater risk for obesity (OR: 2.18, 95% CI: 1.42-3.34) compared to eating meals regularly<br>People who skipped breakfast were at 2.2 times greater risk for obesity compared to those who ate eating breakfast (OR: 1.64, 95% CI: 1.08-2.50) |

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| 40 (Sakurai, 2012) | Cohort with 7 years follow-up, Japan | Male adults (metal products factory) N=2050 male employees of a metal products factor in Japan | Eating speed | Obesity | Obesity<br>Males who were fast eaters were at 3.1 times greater risk for obesity compared to participants who eat slowly after adjustment of age, history of diabetes, smoking, alcohol consumption, habitual exercise, and presence of hypertension, and hyperlipidemia at baseline. (RR: 3.07, 95% CI: 2.08-4.53) |

*Note studies are sorted in the order of participant age

### 3.1.1. Interim conclusion about problematic eating behaviors in relation to obesity

Cross-sectional and cohort studies have shown individual and aggregated symptoms of binge eating disorder predicts greater BMI 5 to 10 years later. Despite the findings, less is known of the prevalence of individual and aggregated constructs of disordered eating behaviors other than speed of eating among young to middle-aged adults (27 to 41 years old) and its association with BMI. Our hypothesis is developed based on a prospective study finding prospective association of number of constructs with greater mean BMI in young to middle-aged adults at age 22 to 27 years old [41]. In this thesis, middle-aged participants were hypothesized to have a greater BMI in the 15 years of follow-up and graded by the number of the constructs endorsed. With the assumption of persistence of disordered eating behaviors [36], we further hypothesized that a problematic relationship to eating and food would be associated with BMI in the earlier years before the PREF were assessed. Detailed finding of our study is reported in Chapter 7.

## Chapter 4. Published information about problematic eating behaviors in relation to diabetes and metabolic syndrome

### 4.1 Literature review of problematic eating behaviors in relation to diabetes

According to the Centers for Disease Control and Prevention's National Health and Nutrition Examination Survey in 2015, 30.3 million (9.4%) people in US had diabetes (mostly Type 2), which corresponds to 13.6% of adult men and 11.2% of adult women. Incidence rates of diabetes during 2012 were 3.6 per 1,000 person among those who were 20-44 years old, 12.0 per 1,000 person for 45-64 years old, and 11.5 per 1,000 person for 65 years or older [44]. Type 2 diabetes, which typically develops in midlife [45], is characterized by elevated blood sugar, resulting from insulin resistance, inadequate insulin secretion, and/or inappropriate secretion of glucagon [46]. Because overweight is positively correlated with Type 2 diabetes, weight reduction is considered one of the most effective approaches to manage Type 2 diabetes in the early stages.

Several eating behaviors and attitudes have been identified as being related to diabetes, although Type 1 has been most studied. These include anorexia nervosa, bulimia nervosa, binge eating disorder, restraint eating behaviors, excessive concerns of weight and shape, and the speed of eating, Studies report that more than 20% of those with Type 2 diabetes endorse overeating, binge eating or engaging in excessive energy intake [47]. Cross-sectional studies conducted among adults report that Bulimia Nervosa (BN), Binge Eating Disorders (BED) are associated with Type 2 diabetes (OR: 2.1, 95% CI: 1.3-3.4 and OR: 2.6, 95% CI: 1.7-4.0, respectively) after adjustments for age and sex [48]. Furthermore, among participants with type 2 diabetes, restraint eating behaviors were greater compared to participants without type 2 diabetes [49]. While temporality cannot be determined from these cross-sectional studies, a cohort study with 5 years of follow-up showed a positive association between binge eating disorders and incident type 2 diabetes. However the association was not significant after adjustment for age and sex [12], Another 16 year follow-up study has shown greater risk of type 2 diabetes among participants with BN and BED (OR: 1.7, 95% CI: 1.2-2.5 and OR: 6.5, 95% CI: 3.4-12.3, respectively) [50]. Furthermore, individual features of eating disorders including the speed of eating were found to be associated with greater insulin resistance among males, after adjustments for BMI among middle-age Japanese adults in a cross-sectional study (OR: 1.53, 95% CI: 1.05-2.23) [39,51]. Similarly, a 7 year follow-up study conducted in Japan reported males who ate fast were at 1.97 times greater risk for diabetes compared to participants eating slowly, after adjustments for age, family history of diabetes, smoking, alcohol intake, habitual exercise, and presence of

hypertension and hyperlipidemia (OR: 1.97, 95% CI: 1.10-3.55) [40]. Similar but stronger risk was reported in a case control study conducted in Kaunas, Lithuania. Those who were eating fast were at 2.5 times greater risk for type 2 diabetes compared to participants who were eating slowly (OR: 2.52, 95% CI: 1.56-4.06) after adjustment of family history, education, BMI, waist circumference, smoking, exercise, and plasma triglycerides [52]. Studies reviewed here are summarized in Table 4.1.

**Table 4.1 Summary of selected findings about problematic eating behaviors in relation to diabetes**

| Reference # | Study Design | Adolescents/ Adults | Independent Variable | Dependent Variable | Findings |
|---|---|---|---|---|---|
| 48 (de Jonge, 2014) | Nationwide cross-sectional; 19 countries | Adults ≥18 N=52,095 community-dwelling adults in 19 countries | Eating disorders | Type 2 diabetes | People with Bulimia Nervosa were at 2.1 times greater risk of diabetes (OR 2.1, 95% CI 1.3-3.4 ) after adjustment for age, sex, country<br><br>People with Binge Eating Disorder were at 2.6 times greater risk of diabetes (OR: 2.6, 95% CI 1.7-4.0) after adjustment for age, sex, country |
| 49 (Mannucci , 2002) | Cross-sectional | Adults N=396 adults (118 male and 278 female) | Type 2 diabetes | Disordered eating behaviors (Eating Disorder Examination) Restraint eating, Eating concern, Weight concern, and Shape concern | Among males with diabetes, the score of restraint eating behaviors were 2.0 points greater;<br><br>Among females with diabetes, the score of restraint eating behaviors were 1.5 points greater ($p<0.05$) |
| 12 (Hudson, 2010) | Cohort with 5 yrs follow-up | Adults≥ 18 | Binge eating disorder | Type 2 diabetes | Incidence of type 2 diabetes was greater among participants categorized having obesity with binge eating disorder compared |

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| | | N=268 adults (134 individuals with binge eating disorder, 134 individuals with no history of eating disorders) | | | to participants categorized having obesity without binge eating disorder, however this was nonsignificant after adjustment<br><br>(HR: 1.6, 95% CI: 0.67, 3.90) after adjustments of age, sex, and BMI. |
| 50 (Raevuori, 2015) | Cohort with16 years of follow-up | Adults<br>N=11,710 | AN BN BED seeking treatment | Type 2 diabetes | People with Binge Eating Disorder had greater risk for incident type 2 diabetes<br>(RR: 6.5, 95% CI: 3.4-12.3)<br><br>People with Bulimia Nervosa had greater risk for incident type 2 diabetes<br>(RR: 1.7, 95% CI: 1.2-2.5) |
| 51 (Otsuka, 2008) | Cross-sectional , Japanese study | Adults (35-69 years old)<br>N=3,465 adults (2704 male and 761 female) | Speed of eating | HOMA-IR | Speed of eating (eating fast) was associated with HOMA-IR in middle-age men after adjustment for BMI |
| 39 (Shigeta, 2001) | Cross-sectional, Japanese study | Adults<br>N=453 adults (321 men and 131 women) | Time spent eating a meal<br>Regularity of meals | Obesity<br>Insulin resistance (HOMA IR) | Rapid eaters were at 1.5 times greater risk for insulin resistance (HOMA-IR ≥2.0) compared to HOMA-IR <2.0 (OR: 1.53, 95% CI: 1.05-2.23) |

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| | | | | | Eating meals irregularly was assoiciated with 1.6 times greater risk for insulin resistance (HOMA-IR ≥2.0 )<br>(OR: 1.60, 95% CI: 1.08-2.38) compared to eating meals regularly<br><br>People who skipped breakfast were at 2.2 times greater risk for insulin resistance (HOMA-IR≥2.0 ) compared to breakfast eaters<br>(OR: 1.75, 95% CI: 1.04-2.96) |
| 40 (Sakurai, 2012) | Cohort with 7 years follow-up, Japan | Male adults (metal products factory)<br>N=2050 male employees of a metal products factor in Japan | Eating speed | Incidence of diabetes | Fast eaters were at 1.97 times greater risk for incidence diabetes compared to participants eating slowly after adjustments for age, family history of diabetes, smoking, alcohol intake, habitual exercise, and presence of hypertension and hyperlipidemia).<br>(OR: 1.97, 95% CI: 1.10-3.55) |
| 52 (Radzevičienė , 2013) | Case control, Lithuania study | Adults (35-85 years old)<br>N=702 adults (234 cases and 468 controls) | Speed of eating | Type 2 diabetes | Fast eaters were at 2.3 times greater risk for type 2 diabetes compared to participants who eat slowly after adjustment for family history, education, BMI, and waist circumference<br>(OR: 2.26, 95% CI: 1.44, 3.55). |

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| | | | | | Risk of type 2 diabetes were even greater among those who eat faster compared to those eat slowly after further adjustment of smoking, exercise, and plasma TG (OR: 2.52, 95% CI: 1.56, 4.06) |

*Note: studies are sorted by independent variable

### 4.1.1 Interim conclusion about problematic eating behaviors in relation to diabetes

The findings regarding the association of disordered eating behaviors with risk of diabetes generally suggest excess risk of diabetes associated with diagnosed eating disorders and some related behaviors. However because the majority of the studies focus on clinical populations with clinical eating disorders, less is known of the risk of incident diabetes among participants with less severe disordered eating behaviors among middle age adults. Suggestive evidence for association of disordered eating behaviors with the development of incident diabetes comes from Japanese cross-sectional studies and Lithuanian case control study. The Japanese cross-sectional studies examined the speed of eating and insulin resistance and found greater insulin resistance among males after adjustment for BMI [39, 51] and the Lithuanian case control study reporting greater risk for type 2 diabetes among those eat fast [52]. Thus this literature is the basis for our hypothesis that in addition to the clinical eating disorders, participants with subclinical disordered eating behaviors are at greater risk for type 2 diabetes.

## 4.2 Literature review of problematic eating behaviors in relation to metabolic syndrome

Metabolic syndrome is a constellation of physiologically and statistically interrelated metabolic risk factors including insulin resistance, obesity, dyslipidemia, and hypertension. Along with the estimation that 24% of the US population has metabolic syndrome [53], the rate is much higher among those who are categorized as having obesity, reaching nearly 50% of the women and 60% of the men [54]. Therefore, obesity is a central feature of metabolic syndrome. For example, a large cross-sectional study conducted in Italy reported that obesity is associated with individual and aggregated components of metabolic syndrome [55]. More than 99% of those who were categorized as having obesity met at least 1 criterion of metabolic syndrome besides elevated waist circumference; more than 53% of those who were categorized as having obesity participants met 3 or more of the metabolic syndrome components [55]. Furthermore the prevalence of metabolic syndrome is graded by the degree of obesity, ranging from 43.6% in class I obesity to 51.1% in class II obesity, and 65.5% in class III obesity [55].

In addition to the increasing prevalence of metabolic syndrome with the increasing rates of obesity [53], metabolic syndrome is of concern because the interrelated metabolic risk factors that are involved in metabolic syndrome promote the development of atherosclerotic cardiovascular disease, type 2 diabetes, and all-cause mortality [56]. Metabolic syndrome is an economic health-care burden in the United States [57]. Therefore, public health strategies to

reduce its prevalence and prevent resulting complications are a high priority and determination of etiological factors for metabolic syndrome is an important step toward this goal.

Growing evidence from both observational and interventional studies suggests that eating behaviors and weight are associated with metabolic syndrome [12,58-59]. For example, a test meal study among those who were categorized as having severe obesity found that the speed of eating is positively correlated with triglycerides (r=0.42), Waist to Hip Ratio (r=0.46), and liver fat (from biopsy (r=0.55), which are components of metabolic syndrome [59]. Besides the speed of eating, other studies report many other disordered eating behaviors and attitudes including binge eating [41] associate with greater BMI and type 2 diabetes [40,42-43, 51-52, 58, 61]. A cross-sectional study conducted in Korea reported that the speed of eating was associated with several components of metabolic syndrome in both males and females [58]. Greater speed of eating was associated with greater weight and BMI were greater and with lower High Density Lipoprotein-Cholesterol was among males after adjustment for age, smoking, alcohol intake, and physical activity. Among females, the speed of eating was associated with greater weight, BMI, blood pressure, and Low Density Lipoprotein- Cholesterol after adjustment for age, smoking, alcohol intake, and physical activity [58].

Additionally, a study with 5 year follow-up reported 2.2 times greater hazard of incident dyslipidemia among those with binge eating disorders (HR: 2.2, 95% CI: 1.1-4.2). The same cohort study reported 1.7 times greater hazard of having at least one component of metabolic syndrome among those with binge eating disorders (HR: 1.7, 95% CI: 1.1-2.6) versus those without; the hazard of having at least two components of metabolic syndrome was 2.4 times greater among those with binge eating disorder (HR: 2.4, 95% CI: 1.1-5.7) [12].

Thus, we conclude that problematic eating behaviors may confer added risk for metabolic syndrome, in addition to the known risk factors, such as elevated blood triglycerides and insulin.

**Table 4.2 Summary of selected findings about problematic eating behaviors in relation to metabolic syndrome**

| Reference # | Study Design | Adolescents/ Adults | Independent Variable | Dependent Variable | Findings |
|---|---|---|---|---|---|
| 59 (Kral, 2001) | Laboratory feeding study | Women who were categorized as having severe obesity, aged 19-52<br><br>Men who were categorized as having severe obesity, aged 18-53<br>N=46 | Eating rates | WHR, serum triglycerides, | Eating rate was correlated with serum trigylcerides ($r=0.42$, $p<0.05$)<br>Eating rate was correlated with WHR ($r=0.46$, $p<0.01$)<br>Eating rate was correlated with liver fat ($r=0.55$, $p<0.01$) |
| 58 (Lee, 2013) | Cross-sectional, Korea | Adults (20-80 yr)<br>N=8,775 | Eating rates | Cardiometabolic risk factors | Among males, weight and BMI were greater among rapid eaters<br>HDL-C was lower among rapid eaters after adjustment for age, smoking, alcohol intake, and physical activity.<br><br>Among females, weight, BMI, diastolic blood pressure, and LDL-C were greater among rapid eaters;<br>HDL-C was lower among rapid eaters after adjustment for age, smoking, alcohol intake, and physical activity. |

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| 12 (Hudson, 2010) | Cohort with 5 yrs follow-up | Adults≥ 18<br>N=268<br>(134 individuals with binge eating disorder, 134 individuals with no history of eating disorders) | Binge eating disorder | Metabolic syndrome | Incidence of type 2 diabetes was greater among those who were categorized as having severe obesity with binge eating disorder compared to participants without binge eating disorder<br>(HR: 1.6, 95% CI: 0.67, 3.90) after adjustment for age, sex, and BMI.<br><br>The hazard of dyslipidemia was 2.2 times greater among those with binge eating disorder (HR: 2.2, 95% CI: 1.1-4.2)<br><br>The hazard of any metabolic syndrome component was 1.7 times greater among those with binge eating disorder (HR: 1.7, 95% CI: 1.1-2.6)<br><br>The hazard of two or more metabolic syndrome components was 2.4 times greater among those with binge eating disorder (HR: 2.4, 95% CI: 1.1, 5.7) |

*Note: studies are ordered by independent variable

### 4.2.1 Interim conclusion about problematic eating behaviors in relation to metabolic syndrome

Only a handful of studies have examined the association of disordered eating behaviors with metabolic syndrome, with most of these focused on the speed of eating or binge eating. From these studies, it appears that individual eating behaviors including binge eating and speed of eating were associated with individual components of metabolic syndrome and adverse metabolic profiles. However, more research is needed to explore the association between disordered eating disorders beyond speed of eating and binge eating, and metabolic syndrome among middle-aged adults. Because the speed of eating and binge eating are central features of disordered eating behaviors, we hypothesize that middle-age adults with individual and aggregated components that define disordered eating behaviors are at greater risk of metabolic syndrome. Details of the risk of diabetes and metabolic syndrome among those with problematic relationship to eating and food are reported in Chapter 8.

# Chapter 5. Published information about problematic eating behaviors in relation to dietary aspects

## 5.1 Literature review of problematic eating behaviors in relation to aspects of dietary quality and quantity

### 5.1.1 Problematic eating behaviors in relation to energy intake

The hallmark of problematic eating is the inability to maintain a healthy, stable relationship with food. Characteristics of problematic eating often include fasting or skipping meals; restrictive dieting; unbalanced eating; and binge eating [62-64]. A summary of articles relevant to problematic eating and energy intake is given in Table 6.1. Extensive laboratory feeding studies of BN and BED have explored food intake and food preference when instructed to binge eat in a laboratory setting [65-69]. All laboratory feeding studies of participants with BED report greater energy compared to non-BED participants when participants were instructed to binge eating with BED intake ranging from 1515 kcal to 2963kcal versus non-BED intake of 1115 to 2017 kcal (Participants were presented with a multiple item array of foods, including their personalized binge tray and a standard hospital dinner, and were instructed to 'Let yourself go and eat as much as you like' [65]. Differences in fat intake by BED are inconsistent between studies, where some laboratory feeding studies report greater fat intake either measured in grams [65] or % [66], while other studies report no difference of fat intake [67]. Protein intake was also inconsistent among studies [65-66, 68]. When specific food items were examined, people with BED had greater consumption of cake, potato chips, rice, and butter [66] compared to those without BED ($p< 0.02$). Findings were similar among participants with BN in the aspect of greater energy intake [67]. However among BN, the proportion of carbohydrate, protein, and fats did not differ between BN and controls [67].

The majority of the existing studies on eating disorders and energy intake are laboratory feeding studies. One exception was a case control study restricted to participants with eating disorders, which reported greater intake of dairy products and soft drinks, but lower proportions of protein and complex carbohydrates among BN and BED compared to controls [69]. Less is known about energy intake in participants with subtle problematic eating behaviors, although a cross-sectional study examined energy and nutrient intake between habitual dieters compared to nondieters [70] and a longitudinal study examined the energy intake among adolescents who engaged in unhealthy weight control behaviors [71]. Because laboratory feeding studies instruct the participants when to binge or not, it is questionable whether feeding studies are capable of capturing the disordered eating episodes, or can assess the overall general intake that occurs in a

natural setting outside of overeating episodes. Furthermore, because most food items in the feeding studies are preselected by the researchers and often patients were allowed to state their preference of snack and allowance was made for extra servings, it is questionable whether the food items and the amount consumed represent the participants' food choice and energy intake. Finally, participants' food selection may have been influenced by the patients knowing that they are involved in an experiment or a research study.

Thus, from the feeding studies or case control studies, it is difficult to understand the typical energy intake beyond the days when the feeding study was conducted or beyond the past 7 days when the food diary was recorded. The non-significant findings of intakes of food groups in feeding studies may be due to the small sample sizes. Thus there is a need for longitudinal studies with greater sample sizes which examine the typical energy intake and dietary patterns in a non-experimental and non-laboratory setting among participants with problematic eating behaviors and attitudes.

**Table 5.1 Summary of selected findings about problematic eating behaviors in relation to energy intake**

| Reference # | Study Design | Adolescents/ Adults | Independent Variable | Dependent Variable | Findings |
|---|---|---|---|---|---|
| 65 (Raymond, 2007) | Laboratory feeding study | Women<br>N=20 women<br>(12 BED, 8 BMI and aged matched controls) | BED | Food intake | People with Binge Eating Disorder consumed more energy intake (2151±430kcal vs 1608±700kcal compared to non-BED participants who were categorized as having obesity<br><br>Fat intake was greater among people with Binge Eating Disorder compared to non-BED participants who were categorized as having obesity (922±259kcal from fat vs 623±298kcal from fat, respectively)<br><br>Consumption of dairy products was greater among people with Binge Eating Disorder compared to non-BED participants who were categorized as having obesity (1.33±0.65 vs 0.50±0.54 servings of dairy products, respectively<0.05) |
| 66 (Yanovski,1992) | Laboratory feeding study | Females who were categorized as having obesity with BED | BED | Selection | Energy intake was greater among women with BED (2963kcal, 2017kcal, p <0.01) compared to women without BED when instructed to binge eat |

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| | | N=19 women<br>(10 women with Binge Eating Disorder, 9 women without Binge Eating Disorder) | | | Proportion of kcal from fat was greater among women with BED compared to women without BED (38.9% vs 33.5%) when instructed to binge eat<br><br>Protein intake was less among women with Binge Eating Disorder compared to women without Binge Eating Disorder (11.4% vs 15.4%, $p<0.01$) when instructed to binge eat<br><br>The intake of cake, potato chips (desserts and snack), rice (bread and cereal), and butter (condiments) were greater among women with Binge Eating Disorder compared to women without Binge Eating Disorder ($p<0.02$) when instructed to binge eat |
| 68 (Cooke, 1996) | Laboratory feeding study | Adults<br><br>N=20 women who were categorized as having obesity<br><br>(10 women who were categorized as | BED | Food selection | Greater energy intake among women who were categorized as having obesity with Binge Eating Disorder compared to women who were categorized as having obesity women without Binge Eating Disorder<br>(1515 ±392kcal vs 1115±317kcal)<br><br>Among four categories of food: desserts, meats, vegetables, and carbohydrates, greater consumption of |

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| | | having obesity women with Binge Eating Disorder, 10 women who were categorized as having obesity without Binge Eating Disorder) | | | meat was observed among women who were categorized as having obesity with Binge Eating Disorder compared to women who were categorized as having obesity without Binge Eating Disorder (200±59 vs 136±89, p <0.04)<br><br>No difference were seen in total amount consumed from dessert, vegetable, and carbohydrates between women who were categorized as having obesity women with Binge Eating Disorder and women who were categorized as having obesity women without Binge Eating Disorder<br><br>Protein intake was greater among women who were categorized as having obesity women with Binge Eating Disorder compared to women who were categorized as having obesity women without Binge Eating Disorder (200g vs 136g, respectively ) |
| 67 (Kaye, 1992) | Laboratory feeding study | BN with normal weight<br>N=32 women | BN | Energy intake | Energy intake was greater among normal weight women with Bulimia Nervosa compared to healthy women without Bulimia Nervosa<br>(7101±9546 kcals per day compared to 1844±518 kcals per day, respectively) |

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| | | (21 normal weight women with bulimia nervosa, 11 healthy volunteer women) | | | The proportion of carbohydrates, protein, and fats did not differ between normal weight women with Bulimia Nervosa compared to healthy women without Bulimia Nervosa |
| 69 (Segura-Garcia, 2014) | Case control | Female adults with AN-R, AN-BP, BN, BED<br><br>N=144<br>(124 females with eating disorder, 20 female adults without eating disorders) | AN-R, AN-BP, BN, and BED | Food choice (from daily dietary record for 7 days)<br><br>Macronutrient intake | People with Bulimia Nervosa had greater proportion of energy intake from dairy products and soft drinks compared to females without Bulimia Nervosa (15.8% vs 8.1%, and 7.9% vs 2.3%, respectively)<br><br>Alcohol and coffee consumption were less in people with Bulimia Nervosa compared to females without Bulimia Nervosa (0.5% vs 4.6% and 2.0% vs 7.8%, respectively)<br><br>People with Bulimia Nervosa and Binge Eating Disorder had greater % of less animal proteins compared to females without Bulimia Nervosa or Binge Eating Disorder (5.1%, 6.4%, and 10.2%, respectively); less lacto proteins (3.1%, 3.1%, and 4.4%, respectively) |

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| | | | | | People with Bulimia Nervosa had less complex carbohydrates compared to females without Bulimia Nervosa (30.7% vs 44.5%, respectively) |
| 70 (Neumark-Sztainer, 1996) | Cross-sectional | Healthy women<br>N=999<br><br>(180 regular dieters, 816 non-dieters) | Regular dieters and non-dieters | Total energy intake,<br>% energy from fat<br>% energy from protein<br>% energy from carbohydrate<br>Saturated fat (g)<br>Cholesterol (mg)<br>Iron (mg)<br>Calcium (mg)<br>Vitamin A (IU)<br>Vitamin C (mg)<br>Dietary fiber (g)<br>% energy from sweets<br>Vegetables (servings/day)<br>Fruit (servings/day) | Energy intake did not differ between female dieters and female non-dieters<br><br>Less % of fat, less saturated fat, less cholesterol, greater fruits and vegetables were consumed among female dieters compared to non-dieters |
| 71 (Larson, 2009) | Longitudinal | Adolescents and young adults | Unhealthy weight control behaviors | Meal frequency / week, energy and nutrient intake/day, | Less energy intake among female adolescents who endorsed unhealthy weight control behaviors compared to participants who did not engage in unhealthy weight control behaviors |

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| | | (1242 females and 1007 males) | | and food and beverage intake/ day | (1771kcal vs 1904kcal, respectively).<br><br>Energy intake did not differ between male participants who engaged in unhealthy weight control behaviors compared to male participants who did not engage in unhealthy weight control behaviors<br>(2142 kcal vs 2123 kcal, respectively). |

*Note: studies are sorted by the study design followed by the independent variable

#### 5.1.1.1. Interim conclusion about problematic eating behaviors in relation to energy intake

Most studies that explored the energy intake among participants with disordered eating behaviors were feeding studies[65-69], restricted to those with a small number of participants with eating disorders, in which test meals were presented. It is widely accepted from feeding studies that when participants with eating disorders are instructed to binge eat, their energy intake is greater compared to the controls. In addition to the feeding studies, a cross-sectional study of adults who were habitual dieters reported no difference of energy intake compared to adults who did not engage in any dieting behavior [70]. Similarly, a longitudinal study conducted among young female adolescents who engaged in unhealthy weight control behaviors reported less energy intake compared to the participants who did not engage in unhealthy weight control behaviors [71]. Considering the inconsistent results about energy intake across studies, little is known of the typical energy intake among middle-aged adults with disordered eating behaviors. However, because participants who endorse problematic eating behaviors and attitudes in this thesis may endorse multiple of the behaviors, closely resembling eating disorders, participants with a problematic relationship to eating and food were hypothesized to have greater energy intake compared to the normal eaters. This hypothesis concerning whether problematic eating behaviors and their association with energy intake measured 10 years later in CARDIA is further discussed in chapter 9.

### 5.1.2. Problematic eating behaviors in relation to diet quality

Laboratory feeding studies consistently report that energy intake is greater among participants with binge eating and bulimia nervosa [65-69], while the preference for specific food items and the proportionate consumption of food groups among those with eating disorders remain inconclusive [65-69]. Despite the important role of dietary intake and quality of diet in reducing the progression of chronic diseases, few studies have looked at dietary patterns or the quality of food habitually consumed in people with problematic eating behaviors [72-74]. Among many of the indices that measure diet quality, *A Priori* Diet Quality Score has been used in CARDIA to assess dietary pattern and diet quality among generally healthy adults [75-77].

In CARDIA studies, the *A Priori* Diet Quality Score was inversely associated with oxidative stress and concentration of circulating cellular adhesion molecules, which indicates healthier vascular function [75-76]. Furthermore, higher *A Priori* Diet Quality Score was inversely associated with total deaths and with death related to CVD or to inflammation (and to a lesser extent to cancer deaths) in older women living in Iowa [77]. Therefore, higher *A Priori* Diet Quality Scores suggest a healthier dietary patterns and generally healthy lifestyle. While the *A Priori* Diet Quality Score is known as an indicator of healthier dietary patterns and generally

healthy lifestyle, the association between *A Priori* Diet Quality Score and disordered eating behaviors in generally healthy adults has not been studied.

In addition to the *A Priori* Diet Quality Score, there are some other indices that reflect dietary guidelines and that are used to assess diet quality in research settings, including the Healthy Eating Index and the Mediterranean Diet Scores [72, 78-79]. There are relatively few well controlled longitudinal studies [80] that test differences in diet quality using Healthy Eating Index, Mediterranean Diet Score among participants with disordered eating behaviors compared to cross-sectional studies [73-74, 78]. Table 6.2 summarizes studies in the literature review reported here. The Healthy Eating Index (HEI) score is derived from 12 foods components where higher scores implies greater adherence to Dietary Guidelines for America [78].

A cross-sectional study [74] of 47 adolescents with diagnosed eating disorders examined the association between the eating disorders (atypical anorexia nervosa, anorexia nervosa, bulimia nervosa, and avoidant restrictive food intake disorders) and diet quality measured by Healthy Eating Index-2010 (HEI). The study reported no significant difference of diet quality score among those with atypical anorexia nervosa, anorexia nervosa, bulimia nervosa, and avoidant restrictive food intake disorders. However all 4 subtypes of eating disorders had a mean HEI score ranging between 51 to 80 points, leading the authors to suggest that they, like others, need improvement in compliance to the Dietary Guidelines for Americans. However some authors have questioned whether HEI is appropriate to assess diet quality among those with eating disorders or disordered eating behaviors; for example, HEI may be unable to accurately assess diet quality when energy intake is less than 1600kcal [81].

Similar to HEI scores, Mediterranean Diet Index (MDI) is an index that assesses the diet quality by the compliance to Mediterranean diet. Because Mediterranean diet is rich in olive oils, vegetables, fruits, wine, legumes, fish/seafood, and nuts, greater score of MDI indicates better diet quality and healthier dietary pattern [79]. A cross-sectional study of 1472 people aged 18-90 (mean age 45 yr) seeking treatment for weight loss or weight maintenance in an Italian clinic examined whether adherence to Mediterranean diet assessed by Mediterranean Diet Index is associated with binge eating disorder. The cross-sectional study reported adherence to Mediterranean diet (MED-score $\geq$9 points) was associated with lower risk of BED, based on a score of at least 17 on the binge eating scale questionnaire (BES), after adjustments for age, gender, nutritional status, education, and physical activity (OR: 0.54, 95% CI: 0.19-0.97) [72] . Thus the inverse association between those with BED and MED-score suggests those with BED have a lower diet quality [72]. However, due to the cross-sectional study design, the temporality cannot be established.

**Table 5.2 Summary of selected findings about problematic eating behaviors in relation to diet quality dietary aspects**

| Reference # | Study Design | Participants | Independent | Dependent | Findings |
|---|---|---|---|---|---|
| 74 (Santiago, 2017) | Cross-sectional | Adolescents with diagnosed eating disorders (12-20yr) N=46 | atypical anorexia nervosa, anorexia nervosa, bulimia nervosa, and avoidant restrictive food intake disorders | Diet quality measured by Healthy Eating Index-2010 (HEI). | No difference in diet quality score among people with different eating disorder diagnoses |
| 73 (Tse, 2012) | Cross-sectional | Adolescents with Type 1 Diabetes (13-18 yr) N=151 | At risk for eating disorder (n=22) vs not at risk (n=122)<br><br>At risk defined by Diabetes Eating Problem Survey (DEPS) | 3 day diet record, HEI-2005 | At risk people had lower diet quality but similar energy intake |
| 72 (Bertoli, 2015) | Cross-sectional, Italy | Middle aged adults who were categorized as having overweight or obesity (mean age 45 yr) seeking treatment in a clinic for weight problems) with and without | BED on the binge eating scale questionnaire (BES)<br><br>BED scores ≥ 27 indicates presence of severe binge eating<br><br>BED scores 17-27 indicates moderate binge<br><br>BED scores < 17 indicates absence of binge eating | Adherence to Mediterranean diet (from a 14 item questionnaire)<br><br>Mediterranean diet score (MED-score) ≥ 9 points indicate compliant with Mediterranean diet | MED-score ≥ 9 points were at lower risk of BED after adjustments for age, gender, nutritional status, education, and physical activity (OR: 0.54, 95% CI: 0.19-0.97) |

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| | | questionnaire-diagnosed BED N=1472 | | | |
| 75 (Meyer, 2013) | Cohort | Adults N=2736 | *A Priori* Diet Quality Score | Oxidative stress | Greater *A Priori* Diet Quality Score is associated with less oxidative stress |
| 76 (Sijtsma, 2014) | Cohort | Adults N=3,818 adults | *A Priori* Diet Quality Score | Circulating cellular adhesion molecules | *A Priori* Diet Quality Score is associated with lower concentration of circulating cellular adhesion molecules (P-selectin, ICAM-1, VCAM) |
| 77 (Mursu, 2013) | Cohort | Women in Iowa (aged 55-69 yr, N~ 30,000) followed for 26 years | *A Priori* Diet Quality Score | Total and CVD and inflammation-related death | *A Priori* Diet Quality Score inversely associated with total death, CVD deaths and deaths related to inflammation |

Note: studies are sorted by the study design

#### 5.1.2.1. Interim conclusion about problematic eating behaviors in relation to diet quality

Healthy Eating Index and Mediterranean Diet Scores are commonly used to assess diet quality in research settings. Research has shown various eating disorders including binge eating and bulimia nervosa are likely to have low scores of HEI suggesting a need for improvement in diet quality [73-74]. Binge eating has been shown to be inversely associated with adherence to Mediterranean diet score [72], suggesting that binge eating is associated with a low diet quality. In addition to those diet quality indexes, *A Priori* Diet Quality Scores is often used in research, particularly within the CARDIA study which is the data source for this thesis. Vascular health, oxidative stress [75], and mortality has been associated with lower *A Priori* Diet Quality Score [77]. However, it has not been studied whether participants with disordered eating behaviors have lower *A Priori* Diet Quality Scores Therefore, based on the cross-sectional findings of disordered eating behaviors associated with worse diet quality measured by HEI [73-74] and Mediterranean diet scores [72]. We hypothesize that a problematic relationship to eating and food is associated with a lower *A Priori* Diet Quality Scores suggesting worse diet quality scores among middle-age adults in CARDIA. Full examinations of the association are discussed in Chapter 9.

### 5.1.3 Problematic eating behaviors in relation to carotenoids

Studies have shown that people with binge eating disorder consume a large amount of energy compared to those without eating disorders [75-79] and prefer palatable foods, including sugar, sweets, and fat [65-66]. In addition to the greater energy intake and preference of sugar, sweets, and fat, most studies which examined the diet quality of the food intakes were based on self-report [72-74] rather than an objective indicator to measure the quality of their dietary intake. Furthermore, little is known of how problematic eating behaviors relate to dietary patterns including diets rich in carotenoids such as fruits and vegetables. In research settings, self-reported history of dietary intake is commonly used to assess general dietary intake and dietary pattern [82-84]. Reports on the general dietary intake of fruits and vegetables, plant-based dietary patterns, and lifestyles assessed by an objective indicator among people with disordered eating behaviors are limited. Three cross-sectional studies examined the association between individual constructs of eating behaviors and their associations with the consumption of fruits and vegetables assessed through self-report [82-84]. Two of these cross-sectional studies found a positive association between dieting and restrained eating behaviors with greater consumption of fruits and vegetables [82-83]. In contrast the third cross-sectional study found a negative association between binge eating behaviors and consumption of fruits and vegetables [84].

Furthermore, cross-sectional studies of African American and Hispanics reported binge eating, assessed from The Binge Eating Scale was negatively associated with intakes of fruits and vegetables ($r=-0.21$, $p<0.01$) [84].

However, under- or over-reports of their actual intake are often noted as limitations of self-reported dietary intake questionnaires. To overcome the limitations of self-reported dietary questionnaires and food frequency questionnaires, objective markers are necessary for accurate assessment of dietary intake and dietary patterns. Serum carotenoids (α-carotene, β-carotene, cryptoxanthine, zeaxanthin/lutein) are frequently used as an objective marker to assess fruits and vegetables based dietary patterns without the concern of under- or over-reporting their dietary intake [85-87]. Because fruits and vegetables are high in carotenoids [72, 88-90], greater circulating serum carotenoids concentrations are assumed to represent a healthier diet pattern. In addition to the serum carotenoids being an indicator of healthier plant-based dietary pattern, serum carotenoids have been observed to be an objective marker of healthier, active lifestyles including greater physical activity, and lower BMI [91] and are a marker of healthier vascular health evidenced by lower oxidative stress and inflammation [91-94]. Thus in addition to being a marker of foods high in carotenoids, the marker additionally suggests whether the diet is rich in antioxidants and low in oxidation causing foods.

Nevertheless, most studies that examine the association between fruits and vegetables intake among participants with disordered eating behaviors are cross-sectional studies with subjective food frequency questionnaires and diet history. Furthermore, because a greater sum of serum carotenoids are more likely to suggest a healthier dietary pattern, there is a need to replicate the self-reported cross-sectional studies [83-84] with a longitudinal study to assess the association between disordered eating behaviors and the serum carotenoids.

**Table 5.3 Summary of selected findings about problematic eating behaviors in relation to carotenoids**

| Reference # | Study Design | Adolescents/ Adults | Independent | Dependent | Findings |
|---|---|---|---|---|---|
| 82 (Bas, 2007) | Cross-sectional | Adolescents N=600 | Excessive dieting Endorsement of weight control behaviors<br><br>(EAT-26) | Consumption of fruits and vegetables<br><br>Fruit, juice, and vegetable consumption were assessed with two questions:<br><br>In a typical day, how many servings of fruit do you eat<br><br>In a typical day, how many servings of vegetables do you eat<br><br>Daily consumptions were estimated on a 5 point scales (0 servings/day to 4+servings/day) | Among males, consumption of vegetables were greater with dieting ($p<0.04$); in females dieting was associated with greater fruits and vegetables intake ($p <0.01$) |
| 83 (Elfhag, 2008) | Cross-sectional | Adults N=1,441 | Restrained eating (the<br><br>Dutch Eating Behaviour Questionnaire and | Intake of fruits and vegetables | Fruits and vegetables were associated with restrained eating (more restrained eating implies healthier food choices) |

| | | | | | |
|---|---|---|---|---|---|
| | | | Food Frequency Questionnaire) | | Positive correlation between restrained eating and fruits (0.18 for women, 0.15 for men) and vegetables intakes (0.14 for women and men) |
| 84 (Wilson, 2012) | Cross-sectional | African American, Hispanics adults N=283 | Binge Eating (The Binge Eating Scale BES): Higher score indicates greater severity of binge eating symptoms<br><br>BES <18: non-binge eaters<br>BES 18-26: moderate binge eaters<br>BES ≥26: severe binge eaters | Fruits and vegetables consumption (National Cancer Institute's Fruit and Vegetable Screener and Fat Screener)<br><br>Fruit and vegetable consumption: frequency and amount consumed over last month | Significant negative correlation between BES scores and fruits and vegetables consumption n ($r=-0.219$, $p<0.01$) |

*Note: studies are ordered by participant age

#### 5.1.3.1. Interim conclusion about problematic eating behaviors in relation to carotenoids

Studies that examined associations between problematic eating behaviors and energy intake have been mostly laboratory feeding studies and case control studies that were restricted to participants with clinically diagnosed eating disorders. The approach of the feeding studies or case control studies done among clinical eating disorders are less relevant to the thesis where our interest are those without clinically diagnosed eating disorders. Most studies that examine the association between dietary pattern and individual constructs of disordered eating behaviors are cross-sectional [82-84] and assess dietary patterns via self-report. Because participants may under- or over-report their actual intake of fruits and vegetables in self-reported diet history or diet questionnaires, there is a need for an objective marker to assess dietary patterns. The sum of serum carotenoids not only indicates a generally healthy diet given the greater concentration of carotenoids and antioxidants that are found in a plant based diet, but also indicates a healthier lifestyle as carotenoids correlate with healthier lifestyles including less smoking, lower BMI, more physical activity, in addition to less oxidative stress and physiological stress which uses those carotenoids up. Thus overall the marker of greater serum carotenoids serves as an objective marker of healthy lifestyles, with a strong correlation with diet rich in carotenoids. With the mixed findings of individual constructs of disordered eating behaviors and the consumption of fruits and vegetables, it is helpful to examine the findings using a longitudinal study design with serum carotenoids as a marker of plant-based diet and healthier lifestyle. Given the known association of BED with greater weight and adverse metabolic profiles and lower Mediterranean diet score and BED [72], we hypothesize that aggregated components of disordered eating behaviors are associated with lower serum concentrations of carotenoids. Detailed findings of the association between problematic behaviors and attitudes and its association with serum carotenoids are reported in Chapter 9.

### 5.1.4. Problematic eating behaviors in relation to sugar-sweetened and artificially-sweetened beverages

Among participants with eating disorders including binge eating disorder, studies report that large proportion of energy intake comes from dietary fats, simple sugars, and sugar-sweetened beverages, and that there is high consumption of artificially-sweetened beverages and sweeteners [66, 69, 95-96]. Liquid forms of sugar including sugar-sweetened beverages and their substitute- artificially-sweetened beverages may lead to less satiety due to rapid transit of liquids through the stomach and intestines which leads to reduced stimulation of satiety signals and

hunger cues, leading to have adverse effects on appetite control [97-103]. Therefore, the sense of lack of satiety from excessive amount of sweetened and artificial beverages may lead to overeating, which is a core characteristic of many disordered eating behaviors. Despite the fact that studies have shown that excessive consumption of sugar and artificially-sweetened beverage is paradoxically associated with weight gain [104-106] and incident obesity [102], short-term randomized studies report no weight change [107-108]. Thus associations between excessive consumption of artificially-sweetened beverage and weight gain are inconsistent across studies [102, 104-108]. Furthermore, excessive consumption of artificially-sweetened beverages is associated with weight-related disease, such as diabetes [109-111], and metabolic syndrome [102, 109-114]. Considering the inconsistent associations, among generally healthy adults, cross-sectional studies examined and reported disordered eating behaviors were correlated with sugar-sweetened beverages and artificially-sweetened beverages [115-117]. A cross-sectional study reported that in adults, greater consumption of sugar-sweetened beverage was inversely associated with those who restrict their energy intake (restraint eaters: $r=-0.22$ and $r=-0.12$ among women and men respectively, $p<0.01$) while the consumption of sugar-sweetened beverage is greater among participants who are more sensitive to external food cues including sight, smell, and taste of food (external eaters, $r=0.07$, $p<0.01$), and those who eat in response to their emotions ($r=0.1$, $r=0.7$, $p<0.05$ for women and men respectively) [115]. Likewise, artificially-sweetened beverages intake were greater among participants who restrict their diet (restrained eaters) ($r=0.16$ and $r=0.19$ for women and men respectively, $p < 0.01$) and emotional eaters who eat in response to their emotions, $r=0.09$ and $r=0.13$, $p < 0.01$) [115]. A similar cross-sectional study reported habitual consumption of artificially sweetened beverages was associated with greater scores of restrained eating, dieting, drive for thinness, and body dissatisfaction compared to those who do not use artificial sweetened beverage [116-117].

The temporality between disordered eating behaviors and sugar-sweetened and artificially-sweetened beverages cannot be drawn from cross-sectional studies. However, these studies suggest that those with subtle subclinical eating behaviors including behaviors such as restricting their diet or eating in response to their emotion tend to have greater consumption of both sugar-sweetened and artificially-sweetened beverages. Little is known of disordered eating behaviors other than external eaters (participants who are sensitive to external stimuli such as smell and visuals), restrained eating, and emotional eating behaviors [118-120]. Thus longitudinal studies are warranted to determine the association between excessive consumption of sugar-sweetened beverages and artificially-sweetened beverages consumption among adults with disordered eating behaviors.

**Table 5.4 Summary of selected findings about problematic eating behaviors in relation to sugar-sweetened and artificially-sweetened beverages**

| Reference # | Study Design | Adolescents/ Adults | Independent | Dependent | Findings |
|---|---|---|---|---|---|
| 118 (Elfhag, 2007) | Cross-sectional | Children and adults (Parental Influences on their Children's Health), Sweden N=3265 men and women and their 12-year old children | External eating (eating more in response to external food cues such as sight, smell, and taste of food)<br><br>Restrained eating (conscious determination and efforts to restrict food intake and calories in order to control body weight)<br><br>Emotional eating (inclination to eat in response to disagreeable emotions such as depression, disappointments, and feelings of loneliness)<br><br>Dutch Eating Behaviour Questionnaire (DEBQ) | Sugar-sweetened beverage<br><br>Artificially-sweetened beverage | People with restrained eating was inversely associated with sugar-sweetened beverages; External eaters were associated with sugar-sweetened soft drinks<br><br>Artificially-sweetened beverages were greater among people with restrained eaters and emotional eaters<br><br>People with restrained eating and sugar-sweetened (r =-0.22, -0.12, $p<0.01$ for women and men)<br>People with restrained eating and artificially-sweetened (r =0.16, 0.19, $p<0.01$)<br><br>People with emotional eating and sugar-sweetened<br>(r =0.1, 0.7 $p<0.05$) |

| | | | | | |
|---|---|---|---|---|---|
| | | | | | People with emotional eating and artificially-sweetened (r =0.09, 0.13, p<0.01)<br><br>People with external eating and sugar-sweetened (r =0.07, 0.11, p<0.01) |
| 119 (Bragg, 2013) | Cross-sectional | Adults (mean age 34.4 yr)<br>N=2,077 | Binge eating<br>Overeating<br>Purging<br><br>Eating Disorder Examination Questionnaire | Sugar-sweetened beverages<br><br>Artificially-sweetened beverages<br><br>What type of soda do you usually drink?<br>'Diet' 'Regular'<br><br>How many sodas do you drink per day<br>'12 oz' '20 oz' '2L' | Artificial sugar-sweetened beverage consumption were associated with binge eating, purging behaviors, restraint eating behaviors, and weight and shape concern |
| 120 (Appleton, 2001) | Cross-sectional | Adults<br>N=120 | Habitual heavy users of artificially sweetened beverages | Dutch Eating Behaviors Questionnaire (DEBQ) | Habitual heavy users of artificially sweetened beverages had higher scores of restrained eating 30.1±9.5 vs |

| | | | | | |
|---|---|---|---|---|---|
| | | | Habitual non-users of artificially sweetened beverages | Yale Eating Patterns Questionnaire (YEPQ)<br><br>Eating Disorder Inventory (EDI) | 19.5±7.4), dieting (6.1±13.3 vs 4.4±16.6), drive for thinness (6.6±6.5 vs 0.9±2.4), body dissatisfaction (14.5±9.3 vs 5.6±6.0) compared to non-users of artificially sweetened beverages |
| 96 (Klein, 2006) | Retrospective | Women adults<br>N=62<br>(30 women with Anorexia Nervosa, 32 healthy controls) | Eating Disorders<br><br>Anorexia Nervosa with restricting<br>Anorexia Nervosa with binge/purge subtypes<br>Bulimia Nervosa<br>Control | Artificially Sweetened products<br><br>Chewing gum<br>Artificially sweetened low-calorie beverages<br>Packets of artificially sweetener | Females with Bulimia Nervosa had greater consumption of artificially-sweetened beverage intakes |

*Note: studies are sorted by study design

#### 5.1.4.1. Interim conclusion about problematic eating behaviors in relation to sugar-sweetened and artificially-sweetened beverages

Greater consumption of sugar-sweetened and artificially-sweetened beverage may be associated with excessive weight gain and greater risk of diet-related disease [102, 104-106, 109-114]. However the reverse association may occur where people categorized as having obesity or diabetes may consume more artificially-sweetened beverages. Cross-sectional studies report inverse associations between sugar-sweetened beverage intake and restrained eating behaviors, but positive associations between emotional eating and external eating behaviors with sugar-sweetened beverage intake [118-120]. From cross-sectional studies, greater consumption of artificially sweetened beverage was reported to associate with restrained eating and emotional eating [118-120]. Additional studies [119-120] report that artificially sweetened beverage consumption is associated with individual constructs related to disordered eating behaviors including weight and shape concern. However because less is known of the individual and aggregated constructs of disordered eating behaviors other than restrained, and emotional eating behaviors, a longitudinal study is necessary to examine the association of individual and aggregated constructs of disordered eating behaviors with sugar-sweetened and artificially-sweetened beverage consumption. From previous studies reporting that restrained eaters or emotional eaters, and excessive dieting were associated with greater artificially sweetened beverages but less sugar-sweetened beverages, in the longitudinal CARDIA study we hypothesized that individual and aggregated disordered eating behaviors would associate with less sugar-sweetened beverages, but greater artificially-sweetened beverages. Full details are provided in Chapter 9.

## Chapter 6: The Coronary Artery Risk Development in Young Adults (CARDIA) Study

### 6.1 Overview and description of CARDIA

Data analyzed in this thesis were collected in the Coronary Artery Risk Development in Young Adults (CARDIA) Study, a longitudinal cohort followed over 25 years since 1985-1986, funded primarily as a contract with the National Heart, Lung, and Blood Institute. This chapter describes those aspects of CARDIA that are most pertinent to the thesis (see Figure 6.1 for a summary and timeline). CARDIA has focused on evolution of cardiovascular risk factors and risk among black and white young adults who were 18 to 30 years old in 1985-1986 [121-123]. CARDIA initially recruited 5115 participants at random from 4 centers: Birmingham, Alabama; Chicago, Illinois; Oakland, California, and Minneapolis, Minnesota. The proportions of participants were balanced in each center on race (52% African American and 48% Caucasians) and sex (46% men, 54% women), as well as on age and educational attainment. There have been 7 follow-up data collection waves since 1985-1986 (in 1987-88, 1990-91, 1992-93, 1995-96, 2000-01, 2005-06, and 2010-11) with follow-up rates of 91, 86, 79, 74, 72, and 72% of the survivors respectively [124]. (A year 30 examination was conducted in 2015-16 with 71% response rate, but those data are not included in this thesis.) Each CARDIA exam cycle was approximately 1 calendar year in duration and is referred to as years since baseline, that is, as CARDIA Year 0 (or just 'Year 0'), Year 2, Year 5, Year 7, Year 10, Year 15, Year 20, and Year 25.

### 6.2 Questionnaire on Eating and Weight Patterns-Revised (QEWP-R)

The QEWP-R was administered at CARDIA Year 10 when participants were 27-41 years old to assess their eating behaviors. The QEWP-R, reproduced as Figure 6.2, includes questions concerning anxiety associated with eating or food, the endorsement of episodic overeating, the sense of loss of control when overeating, the use of compensatory behavior to avoid weight gain, distress related to episodic overeating, distress related to the sense of loss of control when overeating, weight and shape concern, and the time spent on dieting [125]. Verbatim questions of QEWP-R how they related to the 8 constructs used to define PREF are shown in Table 6.1

### 6.3 Validity and Reliability of QEWP-R

CARDIA administered the QEWP-R only once at CARDIA Year 10, thus has no internal data on reliability. Previous studies have tested the stability, validity, and reliability of the QEWP-R and rated these aspects as good [126-128]. Findings from the QEWP-R related to binge

eating frequency as well as other criteria for the diagnosis of BED have been compared with clinical interviews based on the criteria for BED in the DSM-IV. Comparing the results between self-administered QEWP-R and a clinical interview based on the same measure, a kappa of 0.60 was reported, which reflects a moderate agreement. When the QEWP-R was compared to a modified structured clinical interview for DSM-III-R, 77% of the individuals with BED (sensitivity) and 80% of the individuals without BED (specificity) were correctly identified [128]. While no internal reliability and validity of QEWP-R is reported in CARDIA, Project EAT reported that several PREF constructs including binge eating, dieting and compensatory behaviors were persistent over time [18-20]. Thus we assumed the behavior of dieting, which was assessed at multiple time points independent of the QEWP-R, would be persistent over time in CARDIA and thus expected an agreement across two time periods, Year 0 and Year 10. In CARDIA, the construct 'dieting' as measured by the QEWP-R in Year 10 had a substantial internal agreement when compared with earlier years of history of dieting in Year 0, which suggests that QEWP-R would be partially reliable.

### 6.4 Assessment of Problematic Relationship to Eating and Food (PREF)

The QEWP-R includes questions (Table 3.1) about a wide range of potential problematic behaviors and attitudes toward eating and food [126]. Closely following the corresponding DSM-V eating disorders element and its diagnostic criteria, a participant was considered to have 'endorsed a construct' if he or she answered affirmatively to the construct question or question set, as follows. The following abbreviated terminology is used only in this thesis for convenient reference to the 8 specific constructs which are the focus of this thesis. The terminology is not generally used in the field of eating behaviors. Anx: anxiety surrounding food and eating (endorsement means answered 'yes' to 3 or more out of 5 questions); Com: compensation to avoid gaining weight (endorsed any of 6 compensatory behaviors at a frequency of 1/wk or more); Epieat: episodic overeating (endorsed eating a large amount of food in a short period of time at any frequency); and LoC: endorsed a sense of loss of control after episodic overeating with the frequency of at least once a week (contingent on Epieat); Overeat: upset over episodic overeating (endorsed moderately or more upset); Control: upset over loss of control when overeating (endorsed moderately or more upset); Shape: shape and weight concerns (endorsed weight and shape are main things concerned about); and Diet: proportion of time spent on dieting (endorsed spending at least half of the time dieting as an adult). Eight constructs to were counted to represent a composite summary of low to high individual involvement with these characteristics. The PREF point scale was formed by assigning a point for each construct

endorsed. PREF ranged from 0 to 8 points. PREF 0 points are classified as normal eaters. As most constructs defined in QEWP-R are used for defining DSM-V eating disorders and endorsement of 6-8 points indicates presumptive eating disorders.

### 6.5 Assessment of Body Mass Index

Weight and height were measured at each examination with participants wearing light clothes and no shoes. Body weight was measured to the nearest 0.2 kg using a balance beam scale and height using a centimeter ruler to the nearest 0.5 cm [121]. Body mass index (BMI) was calculated as weight (kg)/height $(m)^2$.

Using the National Heart, Lung, and Blood Institute classification, we classified BMI into 6 groups: (1) BMI less than 18.5, underweight; (2) BMI 18.5 to less than 25, normal (3) BMI 25 to less than 30, having overweight, (4) BMI 30 to less than 35, having obesity (class I) (5) BMI 35 to less than 40, having obesity (class II) (6) BMI 40 or higher, having extreme obesity (class III)[129].

### 6.6 Assessment of Diabetes

Fasting blood glucose concentrations were quantified in a venous blood sample using the hexokinase method and standard radioimmunoassay (RIA) [130]; subsequently glucose and insulin were calibrated for comparability across examinations. At all CARDIA exams, diabetes was defined as either1) self-reported use of diabetes medication or 2) fasting glucose ≥126 mg/dl. In addition to those 2 measures, 2 hour post-challenge glucose ≥ 200mg/dl was included at Years 10, 20, and 25 and glycated hemoglobin (HbA1c) ≥ 6.5% was added in Years 20 and 25. It is strongly believed that most diabetes identified in CARDIA is Type 2, and CARDIA did not attempt to distinguish Type 1 from Type 2 diabetes, and the general term 'diabetes' is used.

### 6.7 Assessment of Metabolic Syndrome

At all CARDIA exams, metabolic syndrome was defined based on the National Cholesterol Education Program Adult Treatment Panel III (ATP III) guidelines [131]. Those with at least three of the following five criteria were considered to have metabolic syndrome: 1) *Waist circumference* ≥ 88 cm for women or ≥102 cm for men where waist circumference was measured to the nearest 0.5 cm around the maximal abdominal girth. 2) *Elevated systolic blood pressure ≥ 130mmHg or diastolic blood pressure ≥ 85 mmHg, respectively, or use of antihypertensive medication*. Through Year 15, after a participant had been sitting in a quiet room for 5 minutes, blood pressure was measured three times at 1-minute intervals using a Hawksley random zero

mercury sphygmomanometer (WA Baum, Inc). Subsequently, in Years 20-25, an oscillometer (Omron model HEM907XL; Omron, Mannheim, Germany) calibrated to the random zero values was used to measure blood pressure. At each visit, blood pressure was measured 3 times, where the average of the second and third measurement was used in the analyses. 3) *Elevated fasting triglyceride level ≥150 mg/dL*. Plasma lipids were measured enzymatically by Northwest Lipids Research Laboratory at the University of Washington (Seattle, WA) [132]. 4) *High density lipoprotein (HDL)-cholesterol < 50 mg/dL in women or <40 mg/dL in men*. Low density lipoprotein (LDL)-containing lipoproteins were precipitated with dextran sulphate/magnesium chloride before determining HDL concentrations [133]. 5) *Fasting blood glucose ≥ 100 mg/dL or meeting diabetes criteria*. Details concerning assessment of fasting glucose are found under assessment of diabetes.

**6.8 Assessment of Energy Intake**

Energy intake was assessed at Year 0, 7, and 20 using the interviewer-administered CARDIA diet history [134]. The CARDIA diet history questionnaire's reliability and validity have previously been reported with a correlation of 0.3 to 0.8 across energy intake and several nutrients for reliability and comparative validity (compared to 7 randomly time 24 hour recalls) indicating moderate agreement [135]. The diet history questionnaire involved assessment of general dietary intake of various food groups within the past month was asked by the interviewers. Quantity of food intake was expressed as servings per day, while nutrients are expressed as grams or as kcal of the nutrient per day. We excluded participants with very high and very low energy intakes, including men reporting intake of less than 800 kcal/day or greater than 8,000kcal/day (n=60) and women consuming less than 600kcal/day or greater than 6,000 kcal (n=34). The energy intake and daily nutrient intakes from the diet history questionnaire had a high correlation with the corresponding variable determined by 7 repeated 24 hour recalls (comparative validity): r=0.5 to 0.8 for whites and r =0.3 to 0.7 for blacks [135]. In CARDIA participants followed over many years, the tracking correlation of energy intake was 0.60 between Years 0 and 7; 0.46 between Years 0 and 20; and 0.54 between Years 7 and 20, which suggests that relative ranking of energy intake in participants is linear and is strongly correlated over many years (after adjustment for age, race, and sex and restriction to the 2652 people who completed all 3 measures with energy intake estimated to be between 800-8000 kcal/day in men and 600-6000 kcal/day in women).

**6.9 Assessment of *A Priori* Diet Quality Score**

Participants' *A Priori* Diet Quality Score was assessed at Years 0, 7, and 20 from the interviewer administered CARDIA Diet History [134]. Foods were assigned to one of the 166 food groups using the food grouping system devised by the University of Minnesota Nutrition Coordinating Center (NCC). The 166 food groups were further grouped into 46 food groups based on their nutrient characteristics. *A Priori* Diet Quality Score further categorized these 46 food groups into 3 groups (beneficial, neutral, and adverse), based on the hypothesized health effects [75-76]. Beneficial food groups include fruit, vegetables, legumes, low fat dairy products, fish, poultry, coffee, tea, and moderate amount of alcoholic drinks. Adverse food groups include fried foods, high fat meat, salty snacks, desserts, high fat dairy products, and soft drinks. The *A Priori* Diet Quality Score was the sum of category scores 0–4 for the beneficial food groups plus scores in reversed order (4–0) for adverse food groups (neutral food groups scored 0). (For each food group the 0-4 points relate either to quintiles of intake or to a nonconsumer category and quartiles among consumers). Thus higher score indicates better diet quality and healthier dietary pattern (maximum 132 points)[76]. This *A Priori* Diet Quality Score measured in Year 0, 7, and 20 has a high tracking correlation, ranging between 0.60 and 0.65. Additionally, the *A Priori* Diet Quality Score represents a diet pattern that has been inversely related to oxidative stress, and positively associated with better cognitive function in the CARDIA study [77, 136]. Similarly, higher scores of *A Priori* Diet Quality Score predicted lower total, cardiovascular, cancer, and other inflammatory related mortality in the Iowa Women's Health Study [137].

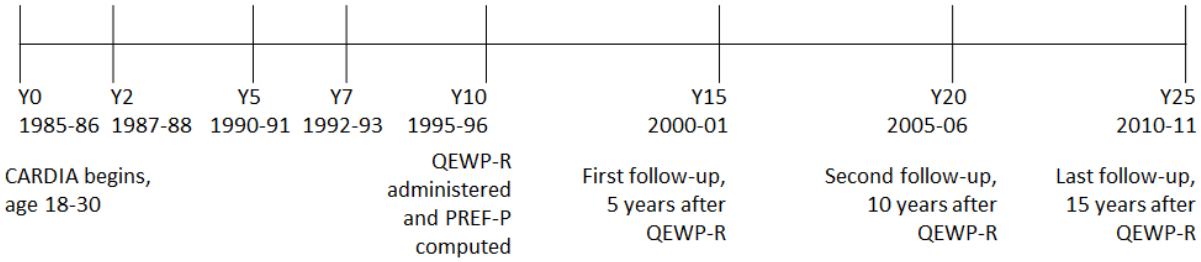
**6.10 Assessment of Carotenoids**

Five carotenoids were assessed: α-carotene, β-carotene, β-cryptoxanthine, lutein/ zeaxanthin, and lycopene. These carotenoids were assessed from blood samples from CARDIA participants using a modified high-performance liquid chromatography [138]. Samples from which serum carotenoids were derived were stored at −70°C until shipped on dry ice to a central laboratory [88]. A higher sum of the four serum carotenoids (α-carotene, β-carotene, β-cryptoxanthine, and lutein/ zeaxanthin) are indicative of greater dietary consumption of carotenoid-rich fruit and vegetables [89-91]. Epidemiologically this sum correlates strongly with many aspects of lifestyle, including nonsmoking, physical activity, and thinness [91]. Lycopene correlates primarily with tomato products, is not closely related to the other 4 carotenoids, and its epidemiologic profile did not conform to a healthier lifestyle. Therefore it was excluded from the sum of carotenoids.

**6.11 Assessment of sugar-sweetened and artificially-sweetened beverages**

Information about sugar-sweetened and artificially-sweetened beverages were obtained from the CARDIA diet history [134]. Sugar-sweetened beverages and artificially-sweetened beverages were measured as servings per day (rather than in calories) for comparability to each other because artificially-sweetened beverages have very few calories. Five specific beverages were used to define sugar-sweetened beverages: non-alcoholic beer, non-alcoholic light beer, sweetened fruit drinks, sugar sweetened beverages, and sweetened water. Four beverages were used to define artificially-sweetened beverages: artificially sweetened fruit drinks, artificially sweetened water, artificially sweetened soft drinks, and unsweetened soft drinks.

**Figure 6.1 Flow chart of CARDIA timeline**




* BMI measured at each CARDIA exam year
* Diabetes and Metabolic Syndrome evaluated at CARDIA year 0,7,10,15,20,25
* Energy intake, *A Priori diet quality score,* sugar sweetened and diet beverages were measured in CARDIA years 0,7,20
* Sum of 4 serum carotenoid (α-carotene, β-carotene, β-cryptoxanthine, lutein/zeaxanthin) were assessed in CARDIA year 0, 7, 15,20

* Y: CARDIA exam year
* QEWP-R=Questionnaire on Eating and Weight Patterns-Revised
* PREF-P=Problematic relationship to eating and food points

**Figure 6.2. Questionnaire on Eating and Weight Patterns-Revised (copied from the CARDIA public use website, https://www.cardia.dopm.uab.edu/)**

Form 50
Page 1 of 11

**CARDIA V**

__ /__ /__
exam date

Please ~~circle~~ mark the appropriate number or response, or write in information where asked. You may skip any question you do not understand or do not wish to answer.

1. During the past **six** months, did you often eat within any two-hour period what most people would regard as an unusually large amount of food?

   1 ☐ No ——> (GO TO QUESTION 3)

   2 ☐ Yes

2. During the times when you ate this way, did you often feel you couldn't stop eating or control what or how much you were eating?

   1 ☐ No ——> (ANSWER QUESTION 3, THEN GO TO QUESTION 7)

   2 ☐ Yes ——> (GO TO QUESTION 4)

3. During the past **six** months, did you have any of the following experiences?

| No | Yes | |
|---|---|---|
| 1 ☐ | 2 ☐ | a. Eating much more rapidly than usual? |
| 1 ☐ | 2 ☐ | b. Eating until you felt uncomfortably full? |
| 1 ☐ | 2 ☐ | c. Eating large amounts of food when you didn't feel physically hungry? |
| 1 ☐ | 2 ☐ | d. Eating alone because you were embarrassed by how much you were eating? |
| 1 ☐ | 2 ☐ | e. Feeling disgusted with yourself, depressed, or feeling very guilty after overeating? |

(GO TO QUESTION 7)

4. During the past six months, how often, on average, did you have times when you ate this way - that is, large amounts of food **plus** the feeling that your eating was out of control? (There may have been some weeks when it was not present - just average those in.)

1 ☐ Less than one day a week

2 ☐ One day a week

3 ☐ Two or three days a week

4 ☐ Four or five days a week

5 ☐ Nearly every day

5. Did you **usually** have any of the following experiences during these occasions?

| No | Yes | |
|---|---|---|
| 1 ☐ | 2 ☐ | a. Eating much more rapidly than usual? |
| 1 ☐ | 2 ☐ | b. Eating until you felt uncomfortably full? |
| 1 ☐ | 2 ☐ | c. Eating large amounts of food when you didn't feel physically hungry? |
| 1 ☐ | 2 ☐ | d. Eating alone because you were embarrassed by how much you were eating? |
| 1 ☐ | 2 ☐ | e. Feeling disgusted with yourself, depressed, or feeling very guilty after overeating? |

6. Think about a typical time when you ate this way; that is, large amounts of food **plus** the feeling that your eating was out of control.

6.A. What time of day did the episode start?

1 ☐ Morning (8 AM to 12 Noon)

2 ☐ Early afternoon (12 Noon to 4 PM)

3 ☐ Late afternoon (4 PM to 7 PM)

4 ☐ Evening (7 PM to 10 PM)

5 ☐ Night (After 10 PM)

6.B. Approximately how long did this episode of eating last, from the time you started to eat to when you stopped and didn't eat again for at least two hours?

_____hours _____minutes

6.C. At the time this episode started, how long had it been since you had previously finished eating a meal or snack?

_____hours _____minutes

7. In general, during the past **six** months, how upset were you by overeating (eating more than you think is best for you)?

1 ☐ Not at all

2 ☐ Slightly

3 ☐ Moderately

4 ☐ Greatly

5 ☐ Extremely

8. In general, during the past **six** months, how upset were you by the feeling that you couldn't stop eating or control what or how much you were eating?

1 ☐ Not at all

2 ☐ Slightly

3 ☐ Moderately

4 ☐ Greatly

5 ☐ Extremely

9. During the past **six** months, how important has your weight or shape been in how you feel about or evaluate yourself as a person - as compared to other aspects of your life, such as how you do at work, as a parent, or how you get along with other people?

   1 ☐ Weight and shape were **not very important**

   2 ☐ Weight and shape **played a part** in how you felt about yourself

   3 ☐ Weight and shape **were among the main things** that affected how you felt about yourself

   4 ☐ Weight and shape **were the most important things** that affected how you felt about yourself

10. During the past **three** months, did you ever make yourself vomit in order to avoid gaining weight or to lose weight?

   1 ☐ No

   2 ☐ Yes ——>

   How often, **on average,** was that?

   1 ☐ Less than one day a week

   2 ☐ Once a week

   3 ☐ Two or three times a week

   4 ☐ Four or five times a week

   5 ☐ More than five times a week

11. During the past **three** months, did you ever take more than twice the recommended dose of laxatives in order to avoid gaining weight or to lose weight?

1 ☐ No

2 ☐ Yes ——>

How often, **on average,** was that?

1 ☐ Less than once day a week

2 ☐ Once a week

3 ☐ Two or three times a week

4 ☐ Four or five times a week

5 ☐ More than five times a week

12. During the past **three** months, did you ever take more than twice the recommended dose of diuretics (water pills) in order to avoid gaining weight or to lose weight?

1 ☐ No

2 ☐ Yes ——>

How often, **on average,** was that?

1 ☐ Less than once a week

2 ☐ Once a week

3 ☐ Two or three times a week

4 ☐ Four or five times a week

5 ☐ More than five times a week

13. During the past **three** months, did you ever fast (not eat anything at all for at least 24 hours) in order to avoid gaining weight or to lose weight?

1 ☐ No
2 ☐ Yes →

How often, **on average,** was that?
1 ☐ Less than once a week
2 ☐ Once a week
3 ☐ Two or three times a week
4 ☐ Four or five times a week
5 ☐ Nearly every day

14. During the past **three** months, did you ever exercise for more than an hour **specifically** in order to avoid gaining weight or to lose weight?

1 ☐ No
2 ☐ Yes →

How often, **on average,** was that?
1 ☐ Less than once a week
2 ☐ Once a week
3 ☐ Two or three times a week
4 ☐ Four or five times a week
5 ☐ More than five times a week

15. During the past **three** months, did you use diet pills, such as Acu-Trim, Dexatrim, to avoid gaining weight or to lose weight?

1 ☐ No (GO TO QUESTION 17)

2 ☐ Yes →

How often, **on average,** was that?

1 ☐ Less than once a week
2 ☐ Once a week
3 ☐ Two or three times a week
4 ☐ Four or five times a week
5 ☐ More than five times a week

16. During the past **three** months, did you ever take more than twice the recommended dose of a diet pill in order to avoid gaining weight or to lose weight?

1 ☐ No

2 ☐ Yes →

How often, **on average,** was that?

1 ☐ Less than once a week
2 ☐ Once a week
3 ☐ Two or three times a week
4 ☐ Four or five times a week
5 ☐ More than five times a week

17. During the past **three** months, did you use any dietary products, such as Slim-Fast, fiber bars or protein powders, for meal replacement to avoid gaining weight or to lose weight?

1 ☐ No

2 ☐ Yes ——> How often, **on average,** was that?

1 ☐ Less than once a week

2 ☐ Once a week

3 ☐ Two or three times a week

4 ☐ Four or five times a week

5 ☐ More than five times a week

18. During the past **six** months, did you go to any meetings of an organized weight control program (e.g., Weight Watcher, Optifast, Nutrisystem) or a self-help (e.g., TOPS, Overeaters Anonymous)?

1 ☐ No

2 ☐ Yes ——> Name of program _____

19. Since you have been an adult (18 years old) how much of the time have you been on a diet, been trying to follow a diet, or in some way been limiting how much you were eating in order to lose weight or keep from regaining weight you had lost? Would you say...?

1 ☐ None or hardly any of the time

2 ☐ About a quarter of the time

3 ☐ About half of the time

4 ☐ About three-quarters of the time

5 ☐ Nearly all the time

20. **(SKIP THIS QUESTION IF YOU NEVER LOST AT LEAST 10 LBS BY DIETING.)** How old were you the first time you lost at least 10 lbs by dieting, or in some way limiting how much you ate? If you are not sure, what is your best guess?

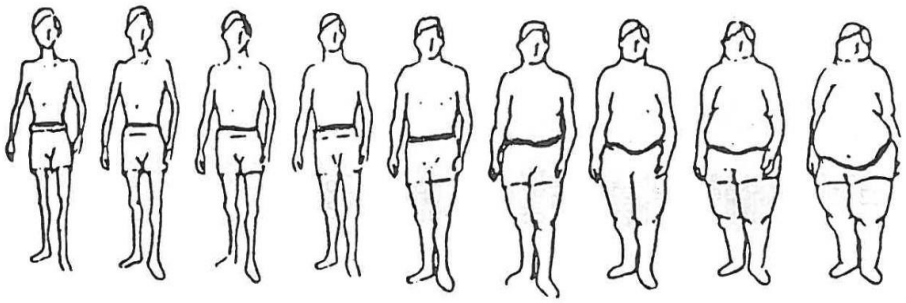
_____ years

21. **(SKIP THIS QUESTION IF YOU'VE NEVER HAD EPISODES OF EATING UNUSUALLY LARGE AMOUNTS OF FOOD ALONG WITH THE SENSE OF LOSS OF CONTROL.)** How old were you when you first had times when you ate large amounts of food and felt that your eating was out of control? If you are not sure, what is your best guess?

_____ years

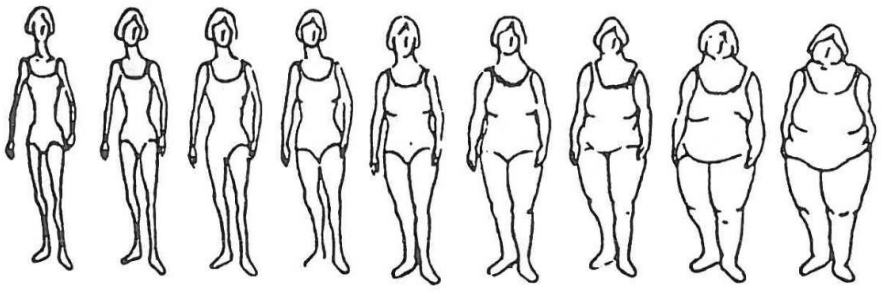
22. Please take a look at these silhouettes. Put a circle around the silhouettes that most resemble the body build of your natural father and mother **at their heaviest.** If you have no knowledge of your biological father and/or mother, don't circle anything for that parent.

22.A. Your Father



1 2 3 4 5 6 7 8 9

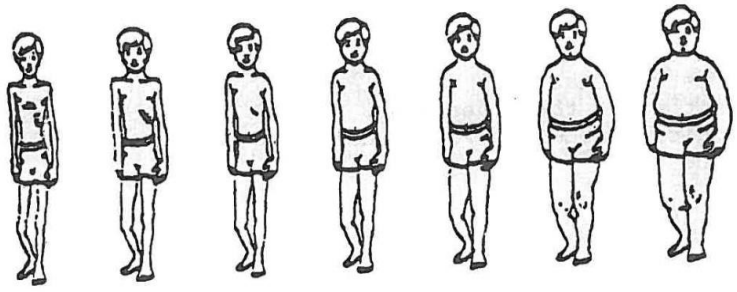
22.B. Your Mother



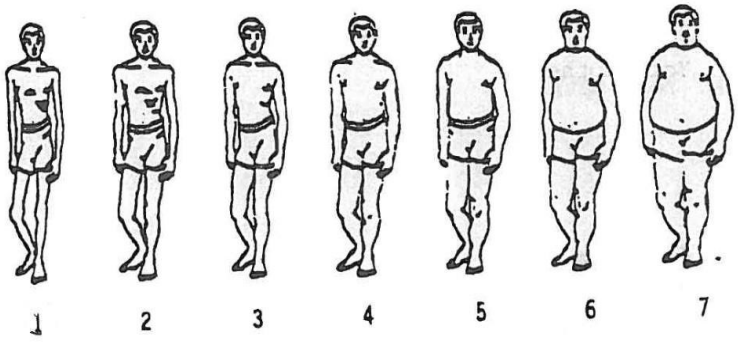
1 2 3 4 5 6 7 8 9

23. **MEN**

23.A. Choose the picture that most closely resembles the way you looked when you were 9 to 10 years old.

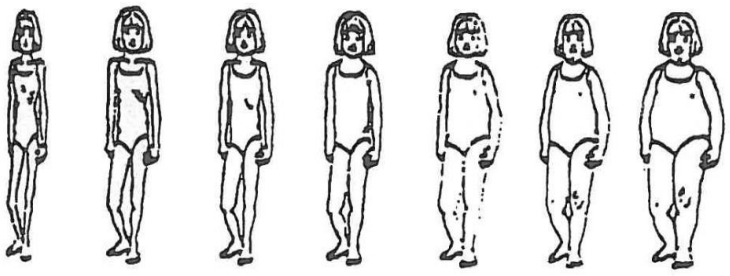



23.B. Choose the picture that most closely resembles the way you looke when you were 14 or 15 years old.

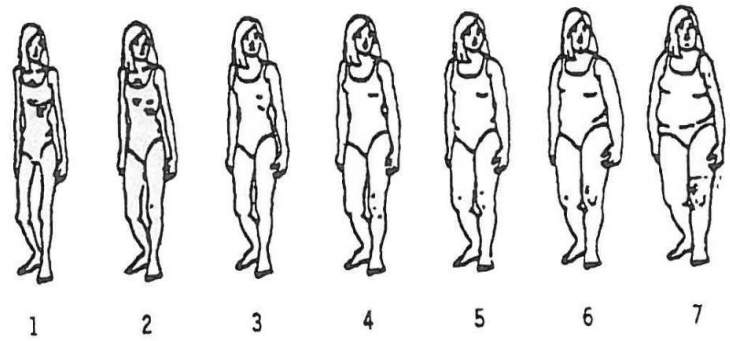


23. **WOMEN**

23.A. Choose the picture that most closely resembles the way you looked when you were 9 or 10 years old.




23.B. Choose the picture that most closely resembles the way you looked when you were 14 or 15 years old.




___ ___ ___ INTERVIEWER ID

**Table 6.1**. **Verbatim QEWP-R questions and PREF construct algorithms**

| Constructs | Verbatim Questions from QEWP-R | QEWP-R response options | Points assigned in study |
|---|---|---|---|
| Anxiety surrounding food and eating (Anx) | In the past 6 months, did you have any of the following experiences:<br>1) Eating much more rapidly than usual?<br>2) Eating until you felt uncomfortably full?<br>3) Eating large amounts of food when you didn't feel physically hungry?<br>4) Eating alone because you were embarrassed by how much you were eating?<br>5) Feeling disgusted with yourself, depressed, or feeling very guilty after overeating? | Yes or no to each of 5 items | 0: answered 'yes' to less than 3 questions out of 5 questions<br>1: answered 'yes' to 3 or more questions out of 5 questions |
| Use of compensatory behavior to avoid weight gain (Com) | In the past 3 months, did you ever:<br>1) Make yourself vomit in order to avoid gaining weight or to lose weight?<br>2) Take more than twice the recommended dose of laxatives in | Yes or no to each of 6 items | 0: answered no or less than once a week to all of the compensatory behavior questions<br>1: answered yes to 1 or more of the |

| | | | |
|---|---|---|---|
| | order to avoid gaining weight or to lose weight?<br>3) Take more than twice the recommended dose of diuretics (water pills) in order to avoid gaining weight or to lose weight?<br>4) Take more than twice the recommended dose of a diet pill in order to avoid gaining weight or to lose weight?<br>5) Fast (not eat anything at all for at least 24 hours) in order to avoid gaining weight or to lose weight<br>6) Exercise for more than an hour specifically in order to avoid gaining weight or to lose weight?<br>During the past three months, how often did you endorse the above compensatory behaviors?<br>1) Less than once a week<br>2) Once a week<br>3) Two or three times a week | | compensatory behavior questions with a frequency of at least once a week |

| | | | |
|---|---|---|---|
| | 4) Four or five times a week<br>5) More than five times a week | | |
| Episodic overeating without loss of control (Epieat) | During the past six months, did you often eat within any two-hour period what most people would regard as an unusually large amount of food? | 0: no<br>1: yes | 0: no<br>1: yes |
| Episodic overeating with a sense of loss of control (asked only when episodic overeating was affirmative) (LoC) | During the times when you ate this way, did you often feel you couldn't stop eating or control what or how much you were eating?<br><br>During the past six months, how often, on average, did you have times when you ate this way<br>1) Less than one day a week<br>2) One day a week<br>3) Two or three days a week<br>4) Four or five days a week<br>5) Nearly every day | 0: no<br>1: yes | 0: no<br>1: yes with a frequency of at least one day a week |
| Distress about overeating (Overeat) | In general, during the past six months, how upset were you by overeating (eating more than you think is best for you)? | 0: not at all<br>1: slightly<br>2: moderately | 0: not at all or slightly<br>1: moderately or more |

| | | | |
|---|---|---|---|
| | | 3: greatly<br>4: extremely | |
| Distress about sense of loss of control (Control) | In general, during the past six months, how upset were you by the feeling that you couldn't stop eating or control what or how much you were eating? | 0: not at all<br>1: slightly<br>2: moderately<br>3: greatly<br>4: extremely | 0: not at all or slightly<br>1: moderately or more |
| Weight and shape concerns (Shape) | During the past six months, how important has your weight or shape been in how you feel about or evaluate yourself as compared to other aspects of your life, such as how you do at work, as a parent, or how you get along with other people? | 1: not very important<br>2: played a part<br>3: were among the main things<br>4: were the most important things | 0: not very important or played a part<br>1: a main thing or more |
| Proportion of time spent on dieting to lose weight or prevent weight gain (Diet) | Since you have been an adult (18 years old) how much of the time have you been on a diet, been trying to follow a diet, or in some way been limiting how much you were eating in order to lose weight or keep from regaining weight you had lost? Would you say…? | 0: none or hardly any of the time<br>1: about a quarter of the time<br>2: about half of the time<br>3: about three-quarters of the time<br>4: nearly all the time | 0: none or hardly any of the time or about a quarter of the time<br>1: about or more than half of the time |

## Chapter 7. Problematic relationship to eating and food and 25 year trajectories of body mass index: The Coronary Artery Risk Development in Young Adults (CARDIA) Study

### 7.1 INTRODUCTION

The current Diagnostic and Statistical Manual of Mental Disorders (DSM-V) dichotomously classifies eating disorders into either present or absent [139], based on the severity of symptoms. This current 'all or none' approach does not address individual and aggregated eating behaviors and attitudes that do not fulfill the strict DSM-V defined eating disorders criteria. In the US, the prevalence of individual problematic behaviors and attitudes related to eating and food in young adults (18-35 years) has been found to range from 3.1 to 29.6% in women and 1.5 to 26.0% in men [140]. In Finland, the prevalence of individual components relevant to binge eating disorders varied from 7.4 to 44.7% in women and 2.5 to 48.9% in men [41]. Thus the prevalence of individual and aggregated components of disordered eating patterns were substantially higher [41] compared to the prevalence of subclinical eating disorders among middle-aged women, which is less than 5% [141-142]. Several studies considered the association of constructs relevant to binge eating disorders with weight status among young adults [36, 41, 143]. However, this type of analysis has not typically been done within large studies that focus on obesity and cardiovascular disease. The database of the large Coronary Artery Risk Development in Young Adults (CARDIA) offers an opportunity to examine individual and aggregated eating behaviors starting in middle-age, across 25 years of follow-up. Subclinical eating behaviors and attitudes in middle-age are important as they may be linked with adverse emotional [144] and physical health [145] and are problematic as they may progress to full-blown eating disorders. In aggregate, these subclinical eating behaviors and attitudes may reflect a problematic relationship to eating and food. These problematic behaviors and attitudes toward food are likely to occur along a continuum of severity, ranging from normal eating, through behaviors and attitudes that do not rise to the level of a psychiatric condition, to clinically diagnosable eating disorders.

The Questionnaire on Eating and Weight Patterns-Revised (QEWP-R) was self-administered in CARDIA when participants were aged 27-41 years old assesses a range of potential problematic behaviors and attitudes related to eating and food that are likely associated with obesity, even among those whose behaviors fall short of full-blown eating disorders [146].

Using these data, characteristics and prevalences of problematic behaviors and attitudes were explored in a non-clinical population. Eight individual QEWP-R constructs were used to create a new scale by assigning a point for each construct endorsed (Problematic Relationship to Eating and Food (PREF) points). Our second aim is to study the reliability of PREF in the aspect of dieting, given that the psychometric characteristics of the QEWP-R have not been thoroughly assessed. Our third aim is to examine the association of PREF with BMI trajectories and categories of BMI ranging from underweight to class III obesity. Higher PREF assessed in CARDIA Year 10 (1995-1996) was hypothesized to associate with greater BMI up to 15 years later. Further, we hypothesize that behaviors and attitudes measured by PREF are likely long-standing and thus there is an association of PREF with BMI in the earlier years of CARDIA. Because people with multiple problematic behaviors (6 to 8 points) may have diagnosable eating disorders that have already been more extensively researched, our primary interest is in those with subclinical behaviors, i.e. those in the range of 1-5 PREF points.

## 7.2 METHODS

### Study Sample

CARDIA is a prospective cohort in Birmingham AL, Chicago IL, Minneapolis MN, and Oakland CA. The study recruited 5,115 black and white adults aged between 18 to 30 years old at CARDIA baseline (designated Year 0) in 1985 and 1986 [121]. The follow up rates for the 7 follow up examinations (Year 2, 5, 7, 10, 15, 20, and 25) were 91%, 86%, 81%, 79%, 74%, 72%, and 72% of survivors, respectively. At each study center, the Institutional Review Board approved the study and each participant signed written informed consent. Eligible participants were those who answered the QEWP-R at Year 10 (CARDIA form 50, downloadable from http://www.cardia.dopm.uab.edu) and had measured or reliably imputable BMI (n=3,892 at Year 10). The study flow and timing important design elements are also displayed in Figure 7.1.

### Measurements

Weight and height were measured at each examination with participants wearing light clothes and no shoes. Body weight was measured to the nearest 0.2 kg using a balance beam scale and height using a centimeter ruler to the nearest 0.5 cm [121]. Body mass index (BMI) was calculated as weight (kg)/height $(m)^2$.

Standard structured questionnaires were used to obtain age, race, sex, educational attainment, smoking, alcohol drinking, and physical activity [147] among CARDIA participants at each examination (documented at http://cardia.dopm.uab.edu).

**Questions Related To A Problematic Relationship to Eating and Food**

The QEWP-R is a standard self-administered questionnaire [126-127] developed by Spitzer et al [126] which was administered only once at CARDIA Year 10 (participant ages 27-41years). The QEWP-R includes questions about a range of potential problematic behaviors and attitudes toward food. Paralleling the DSM-V eating disorders diagnostic criteria, we say that the participant 'endorsed a construct' if he or she answered affirmatively to the construct question or question set, as follows: **Anx**: anxiety surrounding food and eating (affirmative answer to 3 or more of 5 anxiety questions was counted as Anx=1); **Com**: compensation to avoid gaining weight (compensatory behaviors at a frequency of 1/wk or more, assessed using 6 questions, was counted as Com=1); **Epieat**: episodic overeating (1 question, 'yes' was counted as Epieat=1); **LoC**: sense of loss of control after overeating with the frequency of at least 1/week (1 question asked of those who endorsed Epieat, 'yes' was counted as LoC=1); **Overeat**: upset over overeating (those reporting being moderately or more upset about overeating were counted as having Overeat=1); **Control**: upset over loss of control when overeating (those reporting being moderately or more upset over loss of control were counted as having Control=1); **Shape**: shape and weight concerns (those reporting shape and weight were a main concern or the most important concern were counted as having Shape=1); and **Diet**: proportion of time spent on dieting (those reporting they spent at least half of the time dieting as an adult were counted as having Diet=1). Verbatim questions and application of the above criteria are provided in Table 6.1. One point was assigned for each construct endorsed to form the PREF scale. PREF ranges from 0 to 8 points. We call those who had 0 points 'normal eaters'. An overview of the problematic relationship to eating and food constructs and categories is provided in Figure 7.2.

**Repeated measures of history of dieting for reliability of QEWP-R dieting construct**

History of past and current dieting (i.e., 'Have you been on a weight reducing diet?' and 'Are you on such a diet now?') was asked at each of Years 0, 2, 7, 10, 15, 20, and 25. Based on the responses at each exam, participants were categorized into three categories 'no history of dieting', 'history of ever dieting, but not currently dieting', and 'currently dieting'.

**Statistical Analysis**

The prevalences of each construct and participant characteristics were assessed. Descriptive statistics were presented as mean ± SD or % frequency. In many cases, the PREF scale was summarized into 6 categories: 0 points, 1 point, 2 points, 3 points, 4 or 5 points, and 6 to 8 points. Preliminary analyses indicated that BMI was similar between 4 and 5 points; 6-8 points were collapsed to maintain adequate numbers of participants.

Reliability of PREF was assessed in the dimension of dieting. The proportion of time spent on dieting reported on the QEWP-R at CARDIA Year 10 ('Diet' construct in PREF) was compared to the history of past and current dieting reported at each CARDIA examination. Concurrent reliability was assessed using diet history asked at Year 10. We assessed the association of QEWP-R Year 10 dieting with early adulthood dieting reported at Year 0. Problematic eating behaviors and attitudes were assumed to exist before they were queried at Year 10, that is, that answers to QEWP-R hold to some degree for years before QEWP-R was assessed. Therefore, BMI trajectories were examined as a function of PREF using repeated measures regression across the 8 CARDIA examinations (Toeplitz or banded correlation structure assumed) in three time points: cross-sectionally (BMI Year 10), prospectively (BMI measured in Year 15 to 25), and retrospectively (BMI measured in Year 0 to 7) in relation to PREF. For a more specific examination of the relationship of within-person change in BMI with the PREF categories, a change was computed for each examination relative to Year 10. We differenced so that an increase in BMI was a positive number: BMI at Year 10- BMI at each specific examination year (for Years 0, 2, 5, and 7) and BMI at each specific examination Year- BMI at Year 10 (for Years 15, 20, and 25). These changes in relation to the PREF categories were examined.

BMI was further examined in 6 BMI categories (underweight, normal weight, having overweight, having obesity (class I), having obesity (class II), and having obesity (class III) [129]. Associations were examined between PREF and BMI categories at Year 0 (young adulthood, the earliest CARDIA examination in the BMI trajectory), Year 10 (time of QEWP-R self-administration), and Year 25 using multinomial logistic regression.
Statistical tests were two sided with a type 1 error rate of 0.05. Statistical analyses were conducted using SAS 9.4 (SAS Institute Inc., Cary, NC).

## 7.3 RESULTS

The study sample included 794 black men, 1,094 black women, 944 white men, and 1,060 white women. The mean age at PREF assessment was 35 years (range 27-41 years). Mean educational attainment was 14.6 years. Average BMI in the sample was 27.5 $kg/m^2$; 25.6% were

classified as having obesity, 25.4% were current smokers, and the sample had mean physical activity of 331 exercise units (which equates approximately to 30 minutes of moderate intensity activity 5 days a week [148]. Twenty-six percent of men were heavier alcohol consumers (consumed at least 14 alcoholic drinks per week), and 20.0% of women were heavier alcohol consumers (consumed at least 7 drinks per week) (Table 7.1).

**Individual problematic relationship to eating and food constructs and their associations with BMI**

The independent BMI differences at time of PREF assessment were 0.1 $kg/m^2$ for Anx compared to those not endorsing Anx, and correspondingly 1.4 for Com, 1.3 for Epieat, 0.2 for LoC, 1.5 for Overeat, 2.5 for Control, -0.3 for Shape, and 2.6 $kg/m^2$ for Diet compared to those not endorsing the respective construct (Table 7.2). Proportion of time spent on dieting (the PREF Diet construct) had the strongest association with BMI consistently throughout the 25 years. Concern about weight or appearance (Shape) was the only construct that had a negative association with BMI (Table 7.2); Shape was rarely the only PREF construct endorsed.

**Prevalence of PREF and distribution across participant characteristics**

Of the 3,892 participants, 59% had PREF ≥1 points, 25%had 1 point, 12.6% had 2 points, 7.5% had 3 points, 9.0% had 4-5 points, and 3.7% had 6-8 points (Table 7.1). Women and whites had disproportionately greater prevalence of PREF ≥3 compared to men and blacks. Age and educational attainment varied little across PREF. Some other health-related behaviors correlated with PREF. Mean physical activity was lower among those with PREF ≥2 points compared to those with 0 points.

Prevalences of individual constructs among the full sample of 3892 people who filled out the QEWP-R at Year 10 ranged from 28.9% for Shape and 26.1% for Epieat through intermediate values for Anx, Overeat, Control, and Diet, to low values for LoC (5.4%) and Com (3.6%), as shown in Table 7.3. Most people who endorsed PREF 1 point had Shape (36.3%) or Epieat (31.9%), the remainder expressing anxiety or distress (16.8%) or taking some action (Diet 12.3%and Com 2.7%). Endorsement of Com was over 10% of participants only in those with PREF 6-8 points. LoC was also rarely endorsed in those with PREF 2-4 points.

**Reliability and Internal consistency of the proportion of time spent dieting as reported on the QEWP-R**

To examine the reliability of QEWP-R in the dimension of time spent on dieting as an adult, the PREF construct 'Diet' was compared to the early years (Year 0) of history of dieting 'Have you ever been on a weight reducing diet' with a contingent question asking 'If yes, are you on such a diet now'. Responses to these questions in Year 0 were either 'yes' 'or 'no' Those who reported no past-year dieting at Year 0 also reported very low levels of dieting on the QEWP-R assessed 10 years later, suggesting consistency in this behavior over time. Among 2,455 participants who reported never having been on a diet in Year 0, in the QEWP-R, 6.4% said they dieted half or more of the time. This compares to 50.3% endorsing half or more of the time dieting among the 306 who were currently on a diet at Year 0.

**PREF and BMI**

Across the 8 examinations, trajectories of mean BMI over the 25 years were graded by PREF points (Figure 7.3). The difference between BMI in PREF 4 points and PREF 5 points was generally small. The association of mean BMI with the number of PREF points strengthened over the 25 years of follow-up. Mean BMI was about 4.5 $kg/m^2$ higher for 6-8 vs 0 points at Year 0, increasing to about 7.0 $kg/m^2$ at Year 25. The trajectories of mean BMI did not change much after adjustments for demographic and behavioral variables, including smoking or alcohol consumption. Mean BMI was generally ordered with black women having the highest BMI, followed by black men, white men, and white women. However, there were no significant race-sex interactions in BMI trajectories between PREF point categories ($p>0.8$).

**Year 0 Diet History and BMI**

Similar to PREF, history of dieting in CARDIA Year 0 was associated with greater BMI (data not tabulated). Throughout 25 years, the BMI trajectory among those who were never on a diet was lower compared to those who had previously ever dieted,, but were not currently dieting (4.0kg/m2 cross-sectionally, 4.0 to 4.2kg/m2 prospectively, and 3.7 to 4.0kg/m2 retrospectively) and compared to those who were dieting (6.4kg/m2 cross-sectionally, 5.8 to 6.5kg/m2 prospectively, and 4.8 to 6.3kg/m2 retrospectively).

In addition to the trajectories of mean BMI, we examined BMI categories. In Year 0 (young adulthood), grades 2 and 3 obesity were infrequent (about 4.9% of the Year 0 sample), but the proportion was higher in those with higher PREF (from 1.3% in the PREF 0 points to 7.5% in the PREF 6 to 8 points, Figure 7.4). Similarly in Year 10, prevalence of grades 2 and 3 obesity were higher over the PREF scale (from 5.5% in 0 points to 35.0% in 6 to 8 points). Underweight was rare in all exam years; most underweight persons had 0 PREF points.

## 7.4 DISCUSSION

In a community sample of middle-aged adults, problematic behaviors and attitudes toward food were highly prevalent. About 60% of CARDIA participants endorsed one or more of the problematic behaviors and attitudes toward food, with 55% endorsing 1 to 5 PREF points. The prevalence of nearly 60% who endorsed problematic relationship to eating and food is much higher compared to an earlier CARDIA report which found only 1.5% of the participants meeting the criteria of binge eating disorder [149]. Additionally, BMI trajectories increased over time across all PREF points, from 3 to 10 years before these eating behaviors were assessed to 15 years of follow-up, which may reflect the fact that these eating behaviors and attitudes may have been longstanding. The shape of these trajectories across all PREF categories mirrors the recent CARDIA finding that the overall mean weight increase throughout the first 15 years was followed by a relatively flat mean weight trajectory [150]. Most importantly, greater mean BMI and greater adiposity was strongly graded across PREF points, including PREF 1-5 points. For example, those who had PREF 1 point had a mean BMI about 1.1 $kg/m^2$ greater than normal eaters (PREF 0 points) in Year 10, while those with PREF 4-5 points had BMI 5.6$kg/m^2$ greater than normal eaters.

Furthermore, 7 of the 8 problematic eating/attitude constructs were associated with higher BMI. Therefore it is consistent with our hypothesis that individual eating behavior constructs can be used to form an efficient epidemiological definition of minimal to severe problematic relationship to eating and food that has potential consequences for weight-related health.

Given their high prevalences, these behaviors may be seen as normative in middle-aged adults, a finding that echoes prior work. Similar to the highly prevalent PREF behaviors in our study, a longitudinal study conducted in Finland that assessed 7 components relevant to binge eating disorders from the Eating Disorder Inventory-2 (corresponding approximately to the Epieat, LoC, and Anx constructs in this report) found that 67% of young women endorsed at least one binge eating disorder construct, and 19% and 3.9% endorsed 3-5 components, and 6-7 components, respectively [41].

Our findings regarding the association between PREF and BMI are also consistent with prior studies. Several additional studies have looked at whether problematic eating behaviors and attitudes align with adiposity trajectories [36-38, 41,143, 145, 151-152]. Among adolescents and young adults participating in Project EAT, dieting and unhealthy weight control behaviors were associated with greater BMI increase over 5 years [36, 143] and 10 years [36]. In the young adults in the FinnTwin16 cohort study, the individual and aggregated binge eating disorder

components endorsed were cross-sectionally and prospectively associated with greater BMI assessed 10 years later [41]. Our findings of greater and graded BMI trajectories across the PREF points among middle aged adults extends the current literature and implies that middle aged adults are also at a greater risk for greater BMI and adiposity if they have problematic attitudes and behaviors toward food. Coupled with these findings, our results suggest that endorsement of 1-5 PREF points captures problematic issues that are important for individuals and for public health. Importantly, most of these behaviors would not rise to the level of psychiatric attention and thus may not typically receive medical or public health attention.

Strengths of our study include employing a large population-based sample of generally healthy men and women, including black and white Americans, enhancing generalizability of the results. Our study participants were middle aged (27 to 41 years old) when the QEWP-R was administered, whereas most other studies focused on adolescence or college-age [2,19-20, 35-38, 143-144, 151-155].

We note several limitations of our study. First, not having a full study of the internal reliability of PREF is a limitation of our study. However the reliability of QEWP-R was assessed in the dimension of 'Diet'. The substantial agreement of the response to 'time spent on dieting' in the QEWP-R with responses to questions in prior years about 'no history or hardly dieting', 'history of ever dieting, but not currently dieting', and 'currently dieting' indicates the QEWP-R measure of dieting has good reliability. Other studies have found moderate concordance between QEWP (original version) and interview-based measures including the Structured Clinical Interview (SCI) for DSM-IV and the Eating Disorder Examination (EDE) (kappa 0.57) [144]. Furthermore, QEWP-R has been recommended for screening binge-eating disorder, because it has greater sensitivity (although lower specificity) compared to SCI and EDE [127]. Second, the temporality between weight and PREF cannot be determined solely from the single administration of the QEWP-R data available in the current study. However, several other studies have found that binge eating, which closely corresponds to the PREF construct of Epieat, LoC in our study [19, 150], binge eating disorder (BED), which closely corresponds to the PREF construct of Epieat, LoC, and Overeat in our study [153], and the usage of diet pill and laxative, which corresponds to the PREF construct of Com [20] were stable between adolescence and young adulthood, suggesting that the PREF here captures long-standing behaviors. Nonetheless, future research with QEWP-R administered at multiple time points would be desirable to confirm the stability of the problematic behaviors and attitudes over time in CARDIA and confirm temporal relationships with BMI. Third, because the QEWP-R in CARDIA is not a clinical diagnosis and CARDIA has no record of diagnosed eating disorders, there was no intention to

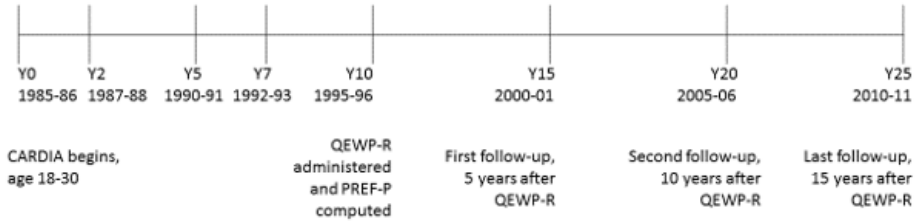
identify people with clinical eating disorders. However, it is plausible to presume that those with PREF 6-8 points in CARDIA have eating disorders, given that they meet several elements' of DSM-V eating disorder diagnostic criteria. Because our study looks at the full spectrum of eating behaviors, including both extreme ends of eating behaviors and less extreme eating behaviors, our finding may differ from studies that strictly look at participants at the most extreme ends. Finally, as in all observational epidemiological studies, our study is limited by potential confounding from unmeasured or unknown confounders.

## 7.5 CONCLUSION

PREF is a highly prevalent public health issue in mid-adulthood that is associated with elevated weight. Although those with problematic eating behaviors related to eating and food that fall short of clinically diagnosable eating disorders (PREF between 1-5 points) may not suffer the same degree of severe morbidity and mortality common in eating disorders [36, 142-143, 156-164], the problematic relationship to eating and food in middle aged adults is nonetheless of concern, given the potential impact on quality of life. Findings from the current study showing that long-term associations with BMI suggests a need to support the need for public health interventions aimed at reducing problematic eating attitudes and behaviors. Unfortunately, messages and interventions to reduce obesity may inadvertently lead to increases in these problematic eating attitudes and behaviors, which may, in turn lead to further increases in BMI. Our study supports the idea that the spectrum of disordered eating should be conceptualized as a matter of degree or severity (from 'healthy eating practices' to 'problematic relationship to eating and food' to 'subthreshold eating syndrome' and to 'the more severe clinical eating disorders'). The full spectrum of eating behaviors should be addressed within public health interventions.

*__Note:__ Nov, 22, 2017: This manuscript has been accepted in a slightly modified form for publication in IJED

**Figure 7.1 Flow chart showing CARDIA exam years and sample for the analyses**




* BMI measured at each CARDIA exam year
* Y: CARDIA exam year
* QEWP-R=Questionnaire on Eating and Weight Patterns-Revised
* PREF-P=Problematic relationship to eating and food points

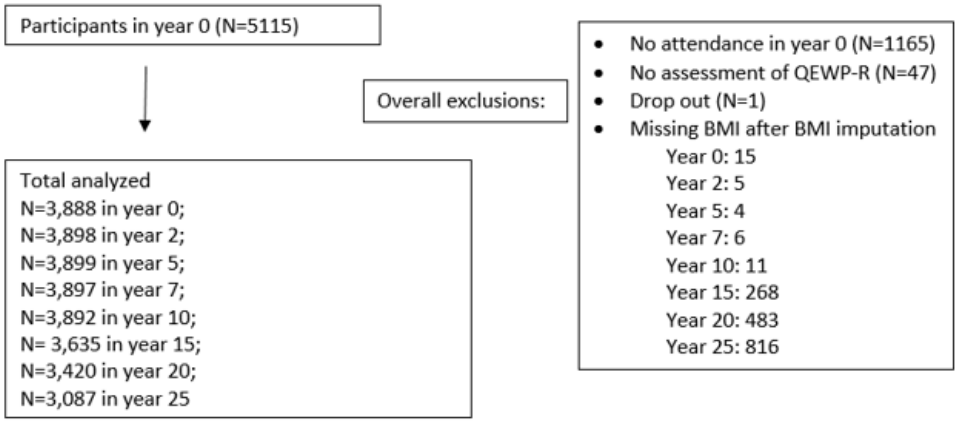


**Figure 7.2 Overview of the Problematic Relationship to Eating and Food concept and its points and categories**

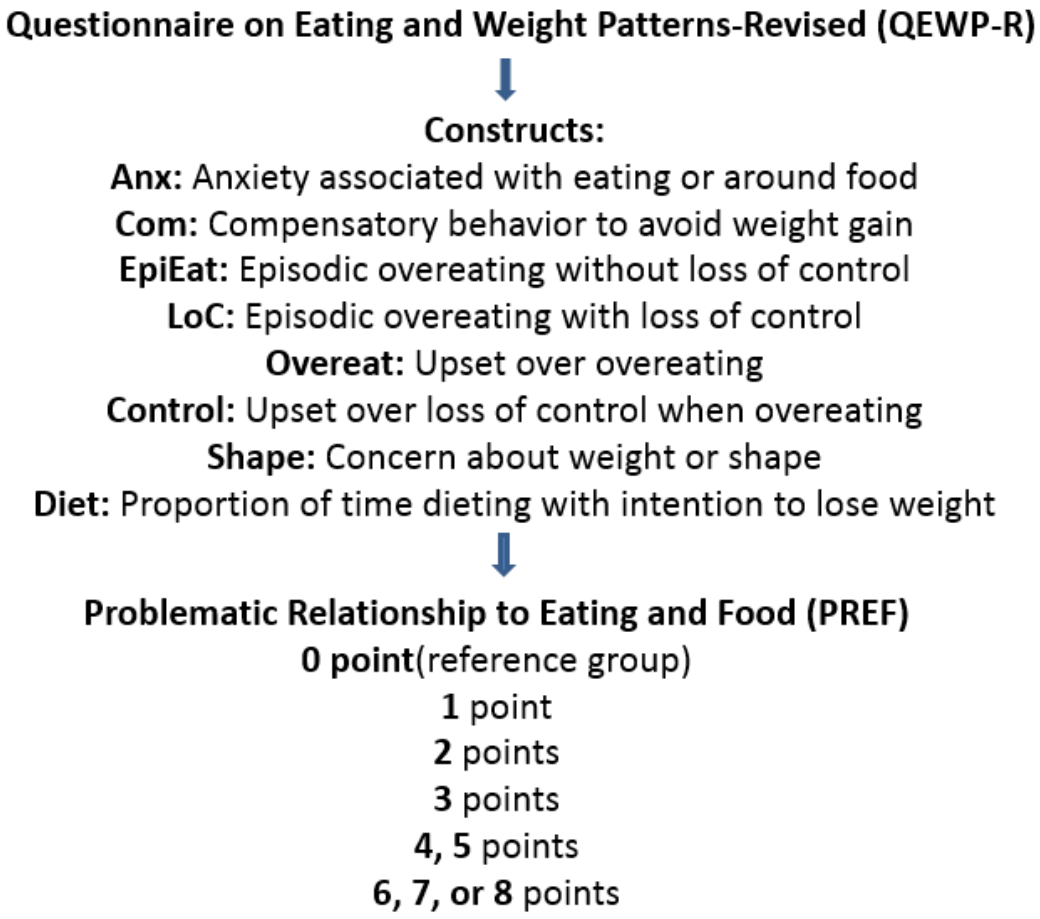
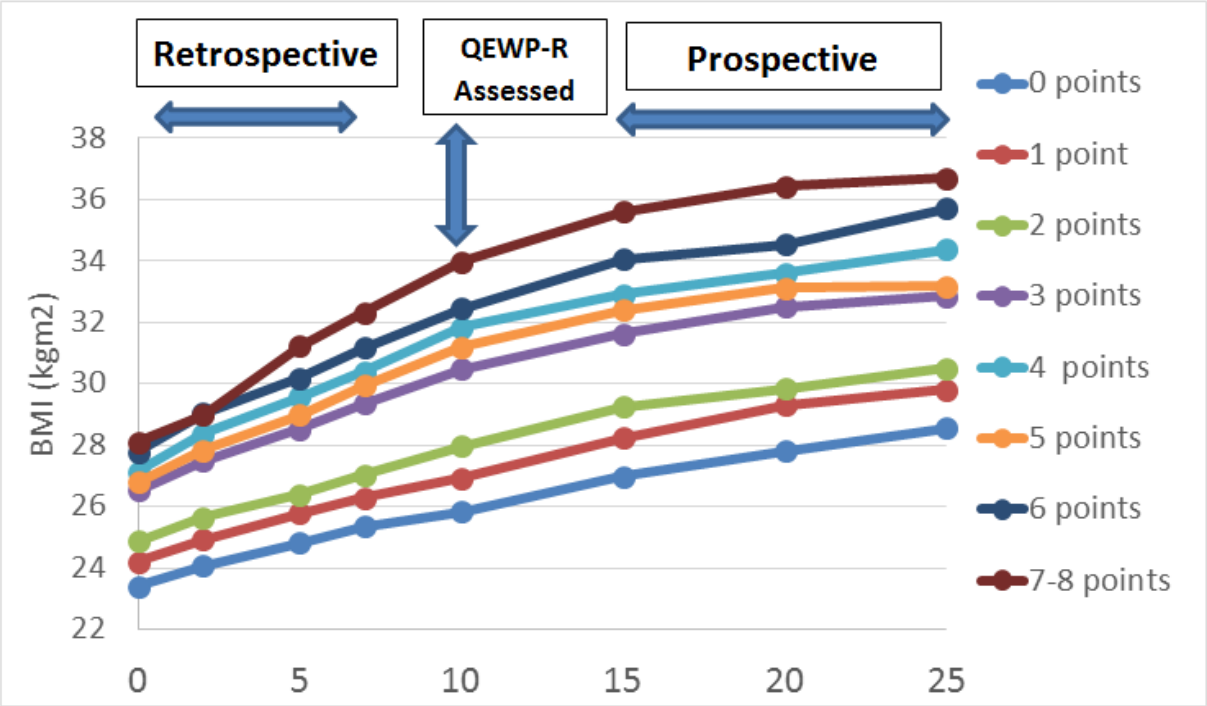


**Figure 7.3. BMI trajectory by 8 PREF points and 5 point categories. Part 1: Mean BMI observed at each time by PREF (Problematic Relationship to Eating and Food Points). Part 2: BMI change from Year 10 per 5 year interval**




Sample size:

0 points n=1637, 1 point n=989, 2 points n=492, 3 points n=293, 4 points n=198, 5 points n=151, 6 points n=81, 7-8 points n=62. QEWP-R assessed in CARDIA Year 10, Year 0 to 7 is retrospective, Year 10 is cross-sectional, and Year 15 to 25 is prospective. PREF 7 and 8 points were collapsed for the small sample size.

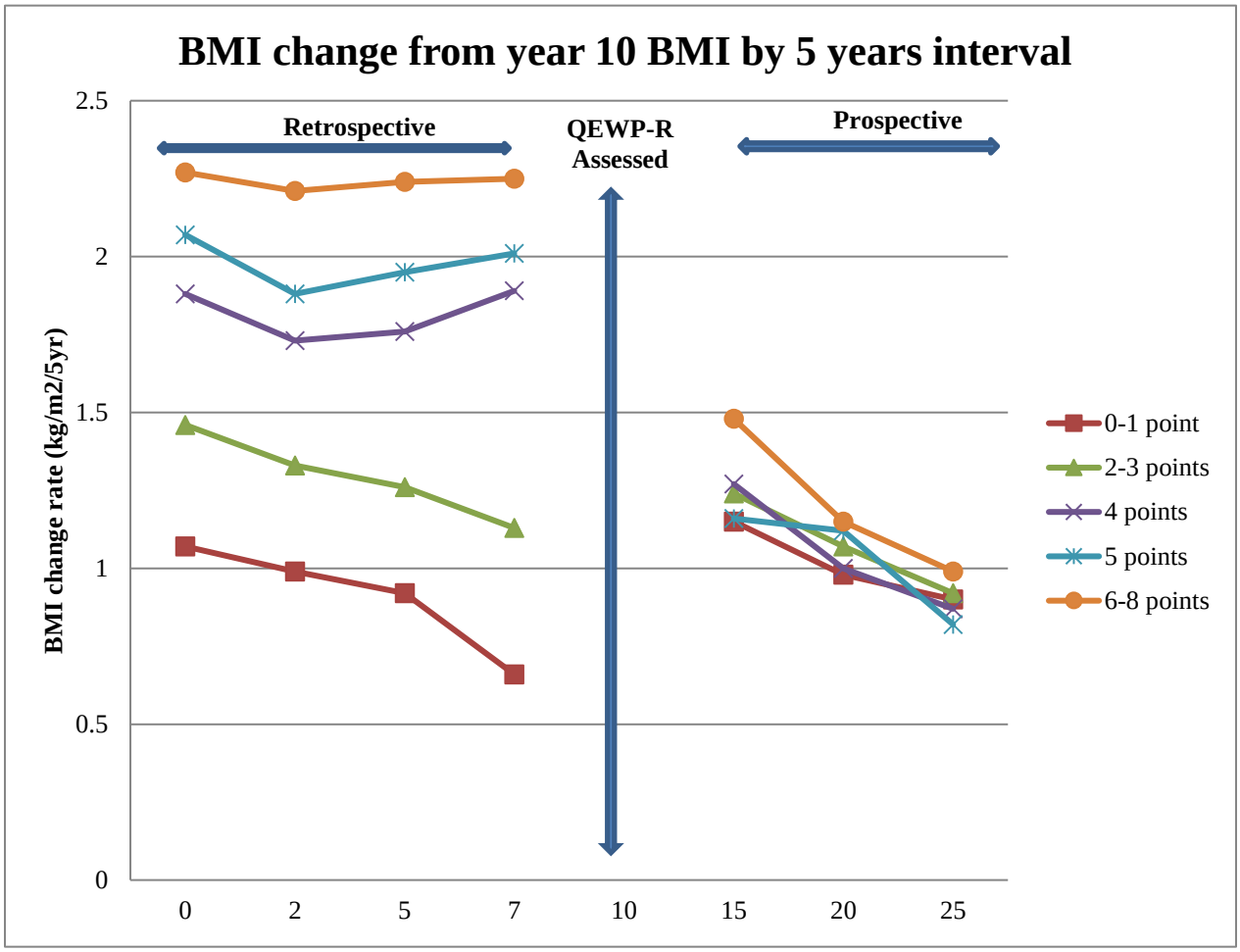
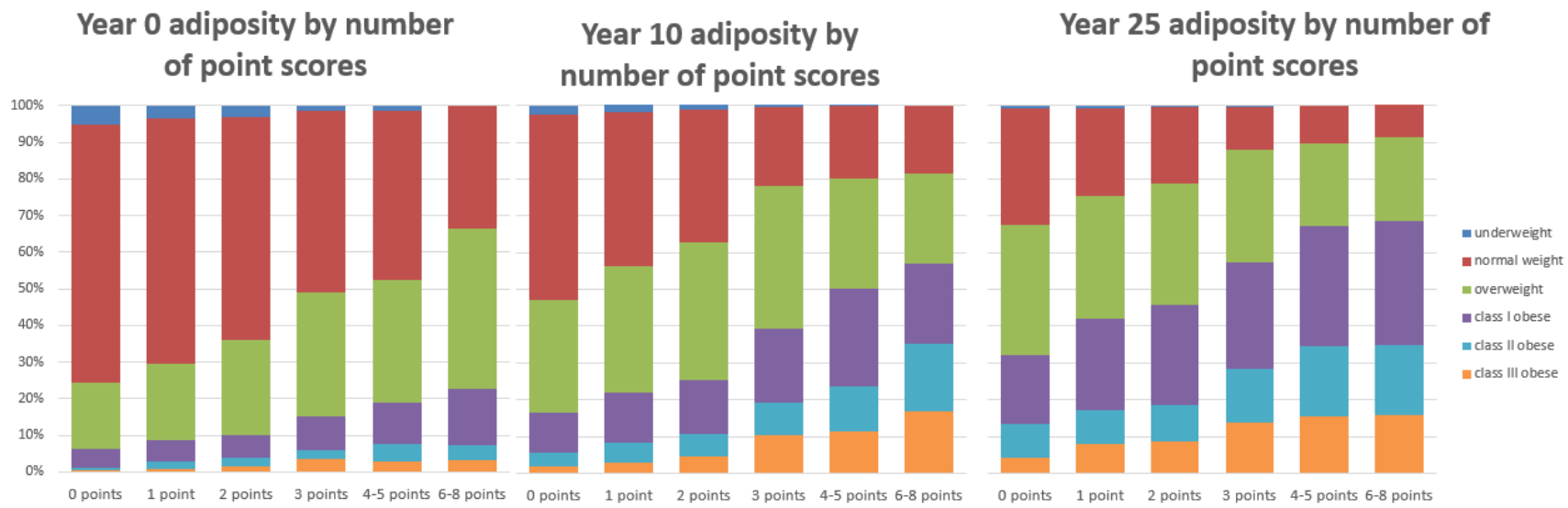

BMI change from year 10 BMI by 5 years interval
Retrospective
QEWP-R Assessed
Prospective
BMI change rate (kg/m2/5yr)
2.5
2
1.5
1
0.5
0
0
2
5
7
10
15
20
25
0-1 point
2-3 points
4 points
5 points
6-8 points

**Figure 7.4 Prevalences of adiposity categories according to the cumulative counts of points of Problematic Relationship to Eating and Food (PREF) points at Years 0, 10, and 25**




Note: age, race, sex, educational attainment, and study center adjusted. Most adipose categories (having obesity, class III) are plotted on the bottom of each column.

**Table 7.1 Characteristics of participants with Problematic Relationship to Eating and Food measured in 1995-1996 (CARDIA Year 10): Coronary Artery Risk Development in Young Adults (n=3,892)**

| | **Problematic relationship to food and eating categories N (%)** | | | | | | |
|---|---|---|---|---|---|---|---|
| | **0 points 1,630 (41.9)** | **1 point 986 (25.3)** | **2 points 491 (12.6)** | **3 points 293 (7.5)** | **4-5 points 349 (9.0)** | **6-8 points 143 (3.7%)** | **Total (n=3,892)** |
| Black Men | 373 (47.0) | 225 (28.3) | 101 (12.7) | 58 (7.3) | 28 (3.5) | 9 (1.1) | 794 |
| Black Women | 442 (40.4) | 235 (21.5) | 141 (12.9) | 91 (8.3) | 128 (11.7) | 57 (5.2) | 1094 |
| White Men | 444 (47.0) | 259 (27.4) | 126 (13.3) | 49 (5.2) | 45 (4.8) | 21 (2.2) | 944 |
| White Women | 371 (35.0) | 267 (28.3) | 123 (12.4) | 95 (9.0) | 148 (14.0) | 56 (5.3) | 1060 |
| | | | | | | | |
| Age (SD), years | 35.2 (3.6) | 34.9 (3.7) | 34.8 (3.7) | 34.8 (3.6) | 35.1 (3.7) | 34.8 (3.7) | 35.0 (3.7) |
| Education (SD), years | 14.6 (2.6) | 14.6 (2.5) | 14.7 (2.7) | 14.5 (2.4) | 14.5 (2.5) | 14.9 (2.6) | 14.6 (2.6) |
| Weight (cm) | 168.4 (39.7) | 174.8 (9.4) | 181.0 (45.1) | 193.9 (49.2) | 195.0 (50.9) | 206.4 (56.8) | 177.3 (44.7) |
| Height (lb) | 171.3 (9.4) | 171.6 (9.5) | 171.1 (9.7) | 169.9 (9.3) | 167.6 (8.3) | 168.0 (8.2) | 170.8 (9.4) |
| BMI (SD), $kg/m^2$ | 25.9 (5.4) | 26.9 (5.9) | 28.0 (6.5) | 30.6 (7.8) | 31.5 (7.6) | 32.9 (8.0) | 27.5 (6.5) |
| % categorized as having obesity (BMI $\geq 30.0$ $kg/m^2$) | 18.2 | 22.7 | 26.7 | 41.6 | 51.3 | 57.3 | 26.6 |
| | | | | | | | |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Physical activity (SD), exercise units | | 323.7 (268.0) | 357.4 (277.0) | 318.5 (280.2) | 318.5 (280.2) | 267.0 (221.0) | 284.3 (252.2) | 331.4 (275.3) |
| Current smokers (%) | | 24.9 | 29.1 | 23.3 | 24.5 | 21.8 | 24.7 | 25.4 |
| Heavier alcohol consumption (%) | ≥14 drinks/ wk for men | 25.8 | 27.5 | 27.6 | 25.8 | 14.9 | 17.7 | 26.0 |
| | ≥7 drinks /wk for women | 23.2 | 16.4 | 14.6 | 19.8 | 24.6 | 8.4 | 20.0 |

Note: 0 points n= 1630, 1 point n=986, 2 points n=491, 3 points n=293, 4-5 points n=349, 6-8 points n=143

**Table 7.2 Predicted BMI difference (kg/m$^2$) from each of 8 Problematic Relationship to Eating and Food constructs**

| CARDIA Year | Anx | Com | Epieat | LoC | Overeat | Control | Shape | Diet |
|---|---|---|---|---|---|---|---|---|
| 10 | 0.1±0.31 | 1.4±0.54 | 1.3±0.25 | 0.2±0.50 | 1.5±0.35 | 2.5±0.29 | -0.3±0.23 | 2.6±0.29 |

Regression coefficient ±SEM are presented. The regression coefficient is the BMI difference (kg/m$^2$) for those with vs without each construct. All 8 constructs were included in a single model. The dichotomous constructs are defined in Methods with full details in Chapter 6 and Table 6.1.

Anx = anxiety surrounding food and eating, Com = use of compensatory behaviors intended to avoid gain, Epieat = episodic overeating without loss of control, LoC = episodic overeating with loss of control, Overeat= upset over overeating, Control= upset over loss of control when overeating, Shape=weight or shape concern, Diet=frequent dieting intended to avoid weight gain

**Table 7.3 Prevalence of Problematic Relationship to Eating and Food constructs and prevalence of constructs by PREF points in CARDIA**

| Constructs | Epieat | LoC | Com | Anx | Overeat | Control | Diet | Shape |
|---|---|---|---|---|---|---|---|---|
| N endorsing construct (% of 3892) | 1020 (26.1) | 211 (5.4) | 140 (3.6) | 679 (17.4) | 888 (22.8) | 633 (16.2) | 625 (16.1) | 1128 (28.9) |
| PREF points | | | | | | | | |
| 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 1 | 223 (31.9) | 0 | 19 (2.7) | 50 (7.1) | 57 (8.1) | 11 (1.6) | 86 (12.3) | 254 (36.3) |
| 2 | 147 (43.5) | 14 (4.1) | 19 (5.6) | 84 (24.9) | 106 (31.4) | 46 (13.6) | 95 (28.1) | 165 (48.8) |
| 3 | 90(44.6) | 15 (7.4) | 17 (8.4) | 81 (40.1) | 139 (68.8) | 101 (50.0) | 61 (30.2) | 102 (50.5) |
| 4 | 73 (50.0) | 12 (8.2) | 14 (9.6) | 91 (62.3) | 131 (89.7) | 106 (72.6) | 65 (44.5) | 92 (63.0) |
| 5 | 77 (72.6) | 28 (26.4) | 7 (6.6) | 88 (83.0) | 102 (96.2) | 87 (82.1) | 62 (58.5) | 79 (74.5) |
| 6 | 52 (92.8) | 34 (60.7) | 7 (12.5) | 53 (94.6) | 55 (98.2) | 52 (92.9) | 33 (58.9) | 50 (89.3) |
| 7 | 41 (100) | 36 (87.8) | 9 (22.0) | 41 (100) | 41 (100) | 40 (97.6) | 39 (95.1) | 40 (97.6) |
| 8 | 5 (100) | 5 (100) | 5 (100) | 5 (100) | 5 (100) | 5 (100) | 5 (100) | 5 (100) |

# Chapter 8. Problematic relationship to eating and food and incident diabetes and metabolic syndrome: The Coronary Artery Risk Development in Young Adults (CARDIA) Study

## 8.1 INTRODUCTION

Metabolic syndrome, which precedes type 2 diabetes, shares a strong relationship with obesity and insulin resistance. Diabetes and metabolic syndrome represent a major health challenge for the upcoming decade and a growing burden in the United States [57]. However, studies investigating the association between diabetes [50], metabolic syndrome [165], and eating behaviors are focused on those with eating disorders. Therefore in order to reduce the risk of insulin resistance and the consequent development of type 2 diabetes, there is an unmet need to understand problematic eating behaviors and attitudes that lead to overweight, obesity, metabolic syndrome and the development of type 2 diabetes.

The Coronary Artery Risk Development in Young Adults (CARDIA) Study, a community-based cohort of white and black adults, characterized a wide range of eating behaviors and attitudes in midlife that are likely associated with obesity, using the self-administered Questionnaire on Eating and Weight Patterns-Revised (QEWP-R) . These eating behaviors and attitudes are defined here as 'problematic relationships to eating and food' (PREF), and range from normal behaviors and attitudes toward food to diagnosable eating disorders. In chapter 7 and a previous publication [166], a PREF score was defined as the count of 8 constructs that were used to define DSM-V eating disorders from QEWP-R (anxiety surrounding food and eating; compensatory behaviors with the intention to lose weight, or avoid weight gain; episodic overeating; loss of control; distress about overeating; distress about sense of loss of control; weight and shape concern; and proportion of time spent on dieting to lose weight or to prevent weight gain). In chapter 7, PREF was found to strongly associate with greater BMI [166]. Because it is well established that type 2 diabetes and metabolic syndrome are more prevalent among those who are categorized as having either overweight or obesity [167-170], PREF may be associated with development of these conditions via its association with BMI. Expanding on chapter 7 and on previous studies [166-170], the overall purpose of this study was to examine the full spectrum of problematic eating behaviors among middle-aged adults and its association with on metabolic health. Therefore the aim of this paper was to explore the prospective association between PREF and diabetes and metabolic syndrome over 15 years of follow-up (CARDIA Year 10 to 25) in CARDIA. A higher PREF score was hypothesized to associate with greater risk of incident diabetes and metabolic syndrome and be partially explained by Year 10 BMI. Because

people with multiple problematic eating behaviors, reflected as PREF 6 to 8 points, are presumed to have presumptive eating disorders that have already been extensively researched, our primary interest was in those within the range of PREF 1-5 points.

## 8.2 STUDY POPULATION AND METHODS

### Study Sample

CARDIA is a prospective cohort based in 4 field centers: Birmingham AL, Chicago IL, Minneapolis MN, and Oakland CA. CARDIA was initiated with 5,115 black and white participants aged between 18 to 30 years old in 1985 to 1986 [121]. The response rates for the follow-ups in CARDIA Year 2, 5, 7, 10, 15, 20, and 25 were 91, 86, 81, 79, 74, 72, and 72% of survivors respectively. At each study center, the Institutional Review Board approved the study and written informed consent and was obtained from each participant. Excluded from the analyses were those who did not attend the examination in Year 10 (n=1,165) and those who did not answer QEWP-R (n=48). For the association between problematic eating behaviors and diabetes, those with prevalent diabetes in Year 10 (n=114) were further excluded. For metabolic syndrome, those with prevalent metabolic syndrome in Year 10 (n=567) were excluded. Therefore, the risks of incident diabetes and metabolic syndrome through Year 25 as a function of Year 10 PREF were analyzed among 3,788 and 3,307 participants, respectively. The study flow and timing of important design elements are displayed in Figure 8.1.

## MEASUREMENTS

### Assessment of Problematic Relationship to Eating and Food (PREF)

PREF was defined based on a single administration of the QEWP-R at Year 10, including 8 constructs concerned with problematic relationship to eating and food. The verbatim questions underlying the constructs, defined *a priori*, are described in detail in Table 6.1 and Chapter 7. Following the diagnostic criteria of DSM-V eating disorders, we consider a participant to have 'endorsed a construct' if he or she answered affirmatively to the construct question or question set, as follows. Anx: anxiety surrounding food and eating (a composite of 5 questions, affirmative is 3 or more of the questions answered yes); Com: compensation to avoid gaining weight (a composite of 6 questions, any endorsed at a frequency of 1/wk or more); Epieat: episodic overeating (1 question); and LoC: sense of loss of control after overeating with the frequency of

at least once a week (1 question contingent on Epieat); Overeat: upset over overeating (1 question, moderately or more upset); Control: upset over loss of control when overeating (1 question, moderately or more upset); Shape: shape and weight concerns (1 question, main or most things concerned about); and Diet: proportion of time spent on dieting (1 question, spent at least half of the time dieting as an adult). We count 8 constructs to represent a composite summary of low to high individual involvement with these characteristics. One point was given for each endorsement of a construct and a maximum of 8 points was possible when participants endorsed all 8 constructs. Participants with PREF ≥1 point had greater cross-sectional BMI in CARDIA compared to PREF 0 points, and graded across the 8 points [166]. PREF 4-5 points were collapsed for similar CARDIA Year 10 BMI; 6-8 points were collapsed to maintain adequate cell sizes. Thus we created 6 PREF categories ranging from normal eaters (PREF 0 points) to categories that meet several criteria of DSM-V eating disorders, suggesting presumptive eating disorder (PREF 6-8 points).

**Diabetes Classification**

Fasting blood glucose concentrations were quantified in a venous blood sample using the hexokinase method and standard radioimmunoassay (RIA) [130]. At all CARDIA exams, diabetes was defined as 1) self-reported use of diabetes medication or 2) fasting glucose ≥126 mg/dl. In addition to those 2 criteria, 2 hour post-challenge glucose ≥ 200mg/dl was included at Years 10, 20, and 25 and glycated hemoglobin (HbA1c) ≥ 6.5% was added in Years 20 and 25 [121].

**Metabolic Syndrome Classification**

At all CARDIA exams, metabolic syndrome was defined based on the National Cholesterol Education Program Adult Treatment Panel III (ATP III) guidelines [171]. Those with at least three of the following five criteria were considered to have metabolic syndrome: 1) *Waist circumference* ≥ 88 cm for women or ≥102 cm for men where waist circumference was measured to the nearest 0.5 cm around the maximal abdominal girth. 2) *Elevated systolic blood pressure ≥ 130mmHg or diastolic blood pressure ≥ 85 mmHg, respectively, or use of antihypertensive medication*. Through Year 15, after a participant had been sitting in a quiet room for 5 minutes, blood pressure was measured three times at 1-minute intervals using a Hawksley random zero mercury sphygmomanometer (WA Baum, Inc). Subsequently, in Years 20-25, an oscillometer

(Omron model HEM907XL; Omron, Mannheim, Germany) calibrated to the random zero values was used to measure blood pressure. At each visit, blood pressure was measured 3 times, where the average of the second and third measurement was used in the analyses. 3) *Elevated fasting triglyceride level ≥150 mg/dL*. Plasma lipids were measured enzymatically by Northwest Lipids Research Laboratory at the University of Washington (Seattle, WA) [132]. 4) *Low high density lipoprotein (HDL)-cholesterol < 50 mg/dL in women or <40 mg/dL in men*. Low density lipoprotein (LDL)-containing lipoproteins were precipitated with dextran sulphate/magnesium chloride before determining HDL concentrations [133]. 5) Fasting blood glucose ≥ 100 mg/dL or meeting diabetes criteria. Fasting blood glucose concentrations were quantified using the hexokinase methods and standard RIA [130].

**Covariates**

CARDIA follow-up examinations after Year 0 included a medical history, anthropometric measurements, and a questionnaire regarding lifestyle behaviors. Body weight and height were measured with no shoes and excess clothing removed on the same calibrated scale [121]. Body weight was measured to the nearest 0.2 kg on a beam scale. Height was measured with a vertical ruler to the nearest 0.5 cm. BMI was calculated as the body weight (kg) divided by the square of the height ($m^2$). The Homeostasis Model Assessment of Insulin Resistance (HOMA-IR), an indicator of insulin resistance, was calculated as glucose (mmol/L)*insulin (mU/L)/22.5 [172]. Educational status was quantified as the self-reported maximum number of years of school attained. Information on lifestyle factors, including smoking, drinking alcohol, physical activity, and medical history of taking antihypertensive medication or taking lipid-lowering medication, or taking anti-diabetic medication were obtained by self-administered questionnaire. Smoking status was self-reported and classified as never, former, or current smokers. Alcohol intake was quantified from an alcohol use questionnaire. A physical activity score was derived from the CARDIA physical activity history [173]. Physical activity was obtained by the frequency of participation in moderate and vigorous physical activity. Total physical activity was calculated by multiplying the months of physical activity endorsed and the level of physical activity intensity, where approximately 300 exercise units were equivalent to the recommended amount of physical activity for adults [173]. *A Priori* Diet Quality Score was derived from the CARDIA diet history [76]. The *A Priori* Diet Quality Score

reflects the dietary intake in the previous month, with greater score indicating better diet quality [76].

**Statistical Analysis**

Person-years were calculated as the sum of individual follow-up times until the occurrence of diabetes or metabolic syndrome, censoring, or the end of the Year 25 examination in 2010-2011. Incidence densities of diabetes and of metabolic syndrome were presented by number of PREF points. The analysis of association between diabetes and PREF was further examined by proportional hazards models, adjusted in Model 1 for age, race, sex, study center, educational attainment, adding behaviors smoking, alcohol intake, physical activity, and *A Priori* Diet Quality Score in Model 2. Model 3 further adjusted for Year 10 BMI in addition to variables in Model 2, and Model 4 adjusted for HOMA-IR, fasting glucose, blood pressure, HDL-C, LDL-C, triglycerides, and blood pressure medications in addition to Model 3. Logistic regression over disjoint follow-up periods was used for the association of metabolic syndrome and PREF. We also calculated the excess cases of diabetes and metabolic syndrome associated with PREF, using Model 2 hazard ratios (HR) for categories of PREF with ≥1 points. The sum of each PREF category-specific number of cases multiplied by the hazard ratio-1 computes the number of cases beyond what would be predicted if the HR for all PREF categories were 1. Additional analysis was performed restricting PREF to 1-5 points vs 6-8 points. Statistical analysis was two sided with a type 1 error rate of 0.05. Statistical analyses were conducted using SAS 9.4 (SAS Institute Inc., Cary, NC).

**8.3 RESULTS**

**Participant characteristics and change with follow up years**

Among the 3,788 participants free of diabetes in CARDIA Year 10, the mean age was 35.0 years, education attainment was 15.3 years, and mean BMI was 27.3 kg/m$^2$ (25.8 to 32.7kg/m$^2$ across PREF categories in Table 1). Approximately half (55%) were females (50.3 to 79.9% across PREF categories) and 52% were whites (50.1 to 55.8% across PREF categories). Participants with PREF≥1 point had a greater *A Priori* Diet Quality Score, suggesting a healthier diet compared to normal eaters. As previously reported [166], mean BMI showed a graded

increase over PREF groups. Findings were similar in the 3307 participants free of metabolic syndrome in Year 10.

**Association between individual problematic relationship to eating and food constructs on Diabetes and Metabolic Syndrome**

The independent risk of diabetes in CARDIA Year 10 for those endorsing Anx was 1.68 (OR: 1.68, 95% CI: 1.02, 2.78) times the risk those not endorsing Anx, and correspondingly 1.80 (OR: 1.80, 95% CI: 0.72, 4.51) for Com, 1.27 (OR: 1.27, 95% CI: 0.79, 2.04) for Epieat, 1.68 (OR: 1.68, 95% CI: 0.76, 3.69) for LoC, 1.62 (OR: 1.62, 95% CI: 1.01, 2.60) for Overeat, 1.83 (OR: 1.83, 95% CI: 1.11, 3.04) for Control, 0.55 (OR: 0.55, 95% CI: 0.32, 0.97) for Shape, and 1.74 (OR: 1.74, 95% CI: 1.04, 2.90) for Diet compared to those not endorsing the respective construct. Upsetness over sense of loss of control when overeating (the QEWP-R 'control' construct) was most strongly associated with diabetes. Parallel analysis was done for metabolic syndrome. Independent risk of metabolic syndrome by each component was similar to diabetes, but proportion of time spent on dieting (the QEWP-R diet construct) had the strongest association with metabolic syndrome. Concern about weight or appearance (Shape) was the only construct that had an inverse association with diabetes and metabolic syndrome (Table 8.2).

**Association between problematic relationship to eating and food score and incident diabetes**

Incidence densities per 10,000 person-years at year 25 were graded across PREF categories (Table 8.3), with a hazard ratio of 1.20 (95% CI 1.12, 1.28) per PREF point after adjustment for demographics (Table 8.3, model 1). After further adjustments for behaviors (model 2), the hazard ratio attenuated when BMI and other variables were added in other models (models 3 and 4). In Kaplan-Meier testing and proportional hazards model for individual PREF point categories, the risk of incident diabetes were greater in PREF ≥3 points relative to PREF of 0 points ($p<0.01$) (Figure 8.2) and remained significant after adjustment of demographics (Table 8.3 model 1). Associations were attenuated when further adjusted for behaviors, BMI, and other variables (Table 8.3 models 2, 3, and 4).

Among the 379 total incident cases of diabetes (252 of which occurred in people with PREF≥1 points, we utilized model 2 HRs, which was adjusted for sociodemographic and behavioral variables as the standard in Table 3 to estimate that there were 77 excess cases of diabetes across the 15 years of follow-up among participants with PREF≥1 points. Among the 77

excess cases, 63 occurred in people with PREF 1-5 points, compared to 14 excess cases of diabetes among PREF 6-8 points.

**Year 0 Diet History and Diabetes**

Because we previously found that history of dieting at CARDIA Year 0 is strongly correlated with PREF assessed in Year 10 in chapter 7, we assume history of dieting is a reasonable proxy for Year 0 PREF. Participants who reported previous but no current dieting at CARDIA Year 0 (CARDIA Year 0 past-dieters) or current dieting (CARDIA Year 0 current dieters) had hazard ratios that estimated 1.97 times (95% CI: 1.55-2.51) and 2.17 times (95% CI: 1.54-3.07) greater risk for diabetes over 25 years of follow-up, respectively, compared to participants who reported that they were never on a diet at CARDIA Year 0, after adjustment for demographic variables (data not tabulated). The hazard ratio was close to null after adjustment for CARDIA Year 0 BMI, suggesting the association occurred from having a higher BMI.

**Association between problematic relationship to eating and food and incident metabolic syndrome**

Findings for incident metabolic syndrome paralleled those for diabetes: incidence densities per 10,000 person-years in Years 10 to 15 and Years 15 to 20 were graded across PREF categories (Table 8.4), with hazard ratio 1.30 (95% CI 1.20, 1.39) and 1.18 (95% CI 1.09, 1.28) per PREF point respectively. Findings were not substantially changed after adjustment of demographics and behaviors (HR 1.27, 95% CI 1.17, 1.37 and HR 1.18 95% CI 1.09, 1.29 respectively) but were attenuated when BMI and other variables were added in other models (models 3 and 4). In Kaplan-Meier testing and proportional hazards models for individual PREF point categories, risk for metabolic syndrome was greater in PREF ≥3 points compared to PREF 0 points. This persisted after adjustment for demographics in Years 10 to 15 (Table 8. 4, model 1). The association was attenuated after further adjustment of behaviors, BMI, and other variables (model 2, 3, and 4). The association was not significant for incident metabolic syndrome during Years 20 to 25 (Table 8.4).

Among the 279 total incident cases of metabolic syndrome (193 of which occurred in people with PREF≥1 points) at Year 15, using model 2 HRs adjusted for sociodemographic and behavioral variables in Table 8.4 we estimated that there were 85 excess cases of metabolic after 5 years of follow-up among participants with PREF≥1 points. Among the 85 excess cases, 69

excess cases of incident metabolic syndrome occurred in people with PREF 1-5 points. Similar results, but with fewer excess cases, were observed in Years 20 and 25 (data not tabulated).

## 8.4 DISCUSSION

In this study participants with a problematic relationship to eating and food at average age 35 years were at subsequent greater risk for both diabetes and metabolic syndrome compared to normal eaters. The risks for diabetes and metabolic syndrome were greater among PREF ≥1 point than PREF 0 points, although the association with metabolic syndrome was less robust and attenuated after 10 years of follow-up. The associations between PREF and diabetes and metabolic syndrome were attenuated by CARDIA Year 10 BMI, as hypothesized.

Our finding that PREF behaviors and attitudes were associated with greater risk of diabetes and metabolic syndrome among middle age adults is consistent with other, conceptually narrower cross-sectional [174] and cohort studies [40] conducted in Japan and with the Framingham cohort studies [175], which explored speed of eating and binge eating. The prevalence of rapid eating in Japan (43.4%) and subjective binge eating (7.1%) in Framingham study were lower than the prevalence of PREF≥1 in our study. The much greater prevalence of problematic behaviors related to eating and food in our study is likely due to the broader and more comprehensive definition of problematic relationship to eating and food. In the Japanese longitudinal study, participants who ate rapidly were at 1.97 times the risk for type 2 diabetes compared to those who did not eat rapidly after adjustment for age, family history of diabetes, smoking, alcohol drinking, habitual exercise, hypertension, and hyperlipidemia [40]. In agreement with our findings, the association was attenuated to 1.47 times the risk when further adjusted for BMI [40]. Similarly, in the Framingham Heart Study and Third Generation and Omni 2 cohorts, participants who engaged in binge eating were at 2.9 times the risk for type 2 diabetes and at 3.2 times the risk for insulin resistance compared to non-binge eating participants. Both associations were attenuated after adjustment for BMI [175].

In terms of metabolic syndrome, the cross-sectional study conducted in Japan reported the rapid eaters were at 1.27 to 1.61 times the risk for metabolic syndrome compared to normal eaters [174]. As in our study, with further adjustment for BMI, the association was attenuated closer to null [174]. Similar to the speed of eating, binge eaters had 2.8 times greater risk for metabolic syndrome compared to non-binge eaters in Framingham Heart Study Third Generation and Omni 2 cohort studies after adjustment for age and sex. [175]. Similar to our findings, the association was attenuated after adjustment for BMI [175].

Our study adds to the existing literature suggesting that middle-aged adults who endorse problematic behaviors or attitudes but do not meet the DSM-V eating disorder criteria (PREF 1 to 5 points) are at greater risk of diabetes and metabolic syndrome. These risks were graded across PREF points, achieving statistical significance in individual categories for PREF ≥3 points, after adjustment for demographics; the hazards for PREF 1 and 2 points followed the general association of greater risk of diabetes and metabolic among participants with PREF. Furthermore, our study suggests that, if this relationship is causal, 20.3% of the incident diabetes cases and 17.1% of the incident metabolic syndrome cases could be attributed to the excess risks of PREF≥1. Much of this impact of PREF arose from the large number of participants with PREF 1 to 5 points (16.8% and 14.0% of the excess risk for incident diabetes and metabolic syndrome).

Although the exact mechanisms linking problematic eating behaviors and weight-related metabolic health consequences are not clear, several hypotheses exist to explain why unhealthy problematic behaviors related to eating and food may play a role in development of obesity, which leads to the development of type 2 diabetes and/or metabolic syndrome. Binge eating, that is, eating a large amount of food in a relatively short period of time, may induce less satiation [42-176] leading to excessive energy intake [177-178], which further leads to hyperinsulinemia and insulin resistance [51], which further mediates progression to diabetes [38, 40, 51-52, 179-180] and metabolic syndrome [181-182]. Our finding that adjustment for BMI attenuates the PREF–Type 2 diabetes and PREF–metabolic syndrome associations lends support to this hypothesis. Another possibility is that binge eating may disrupt the level of adipocytokines [183], which mediates the production of glucose and fatty acid oxidation [183-184], which may sustain peaks of glucose and insulin [183].

One strength of the present investigation is that it is a cohort study with 15 year follow-up, allowing us to clarify the temporal association from PREF to the incidence of diabetes or metabolic syndrome in middle age adults. Furthermore, our finding shows that participants with PREF 1 to 5 points, who are less likely to have diagnosable eating disorders, are at greater risk for diabetes and metabolic syndrome compared to normal eaters (PREF 0 points). In addition, our study includes community-based samples of both black and whites males and females, which differs from other studies with samples of adolescents and those receiving treatment for their clinically diagnosed eating disorders. Therefore, this improves the generalizability of the findings. However, several limitations of the study warrant mention. Because QEWP-R was only administered once in CARDIA Year 10, the internal validity and reliability is unknown. However

as we have previously reported in chapter 7, we find that QEWP-R is reliable in the dimension of dieting behavior measured in CARDIA Year 0. Those who reported on the Year 10 QEWP-R that they spent more than half of their time dieting as an adult (that is, when they were 28-41 years old) strongly tended to report at Year 0 (when they were 18 to 30 years old) that they were on a diet or had been on a diet. Additionally, because QEWP-R is not a clinical diagnostic tool and CARDIA does not collect any medical records of diagnosed eating disorders, and did not do any in-depth psychological testing, the overlap of clinically diagnosable eating disorders with PREF categories is not known.

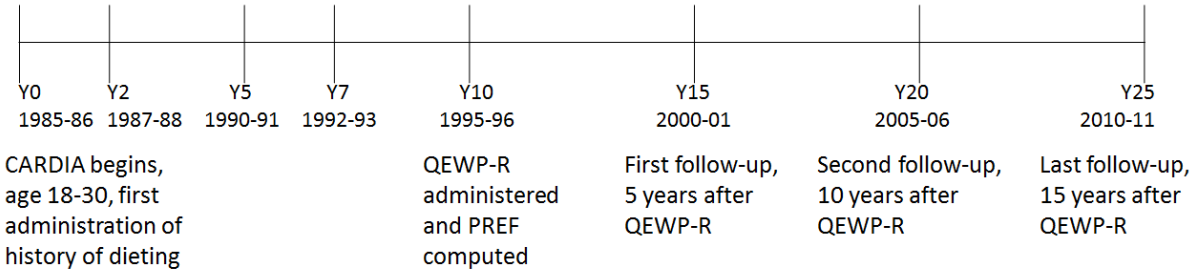
However, this point may also be viewed as a strength, as our research raises the question whether it might be generally useful to know about more modest disturbances in eating behaviors, corresponding to PREF 1-5 points. The QEWP-R appears to be a sensible tool to quantify disturbed eating behaviors in individuals. As in the case of all observational epidemiologic studies, our study is susceptible to potential residual confounding from unmeasured or unknown confounders. Lastly, although it is strongly believed that most diabetes identified in CARDIA is Type 2, CARDIA did not attempt to distinguish Type 1 from Type 2 diabetes.

**8.5 CONCLUSION**

In our study, having a problematic relationship to eating and food (PREF) at average age 35 years was associated with greater risk of incident diabetes measured 15 years later and metabolic syndrome in follow-up of 10 years. Furthermore, the risk of diabetes and metabolic syndrome were graded by PREF points. The association between problematic eating behaviors and diabetes or metabolic syndrome in this sample from the general population suggests that individuals without eating disorders, yet who have problematic relationship with eating and food, are at greater risk for weight-related adverse metabolic outcomes and contribute to a substantial proportion of diabetes and metabolic syndrome cases. However it is important to note that the associations appeared to be at least partially mediated by CARDIA Year 10 BMI.

Understanding and intervening on problematic eating behaviors and attitudes related to food may be important to address the risk of the harmful behaviors and to control the epidemic of metabolic disorders.

**Figure 8.1 Flow chart: CARDIA exam Years and sample for the analyses**




* Diabetes and Metabolic Syndrome evaluated at CARDIA year 0,7,10,15,20,25
* Y: CARDIA exam year
* QEWP-R=Questionnaire on Eating and Weight Patterns-Revised
* PREF =Problematic relationship to eating and food points

Participants in year 0 (N=5115)

Overall exclusions:

Total analyzed in year 25:
- 3788 for diabetes
- 3307 for metabolic syndrome

Diabetes:
- No attendance in year 10 (N=1165)
- No assessment of QEWP-R (N=48)
- Prevalent cases of diabetes at year 10 (N=114)

Metabolic Syndrome:
- No attendance in year 10 (N=1165)
- No assessment of QEWP-R (N=48)
- No assessment of metabolic syndrome (N=28)
- Prevalent cases of metabolic syndrome at year 10 (N=567)

**Figure 8.2 Kaplan-Meier Curve of Diabetes by PREF categories**

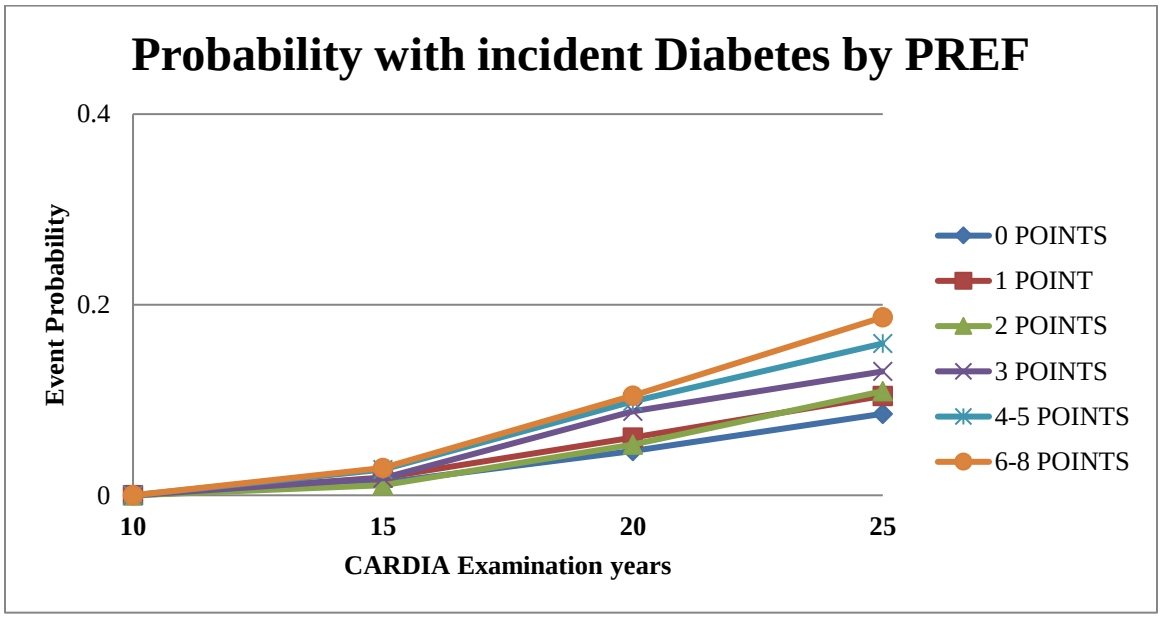


**Figure 8.3 Kaplan-Meier Curve of Metabolic Syndrome by PREF categories**

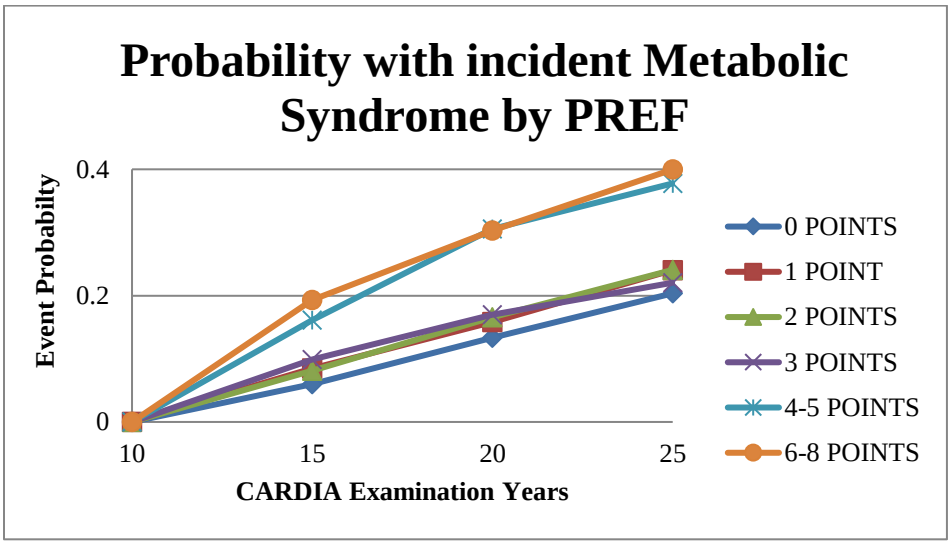


**Table 8.1 Characteristics of CARDIA study participants free of diabetes at Year 10 by PREF at Year 10**

| | | 0 points (n=1593) | 1 point (n=965) | 2 points (n=476) | 3 points (n=280) | 4-5 points (n=335) | 6-8 points (n=139) | Total (3,788) | P for trend |
|---|---|---|---|---|---|---|---|---|---|
| Age (years) | | 35.2±3.6 | 34.9±3.7 | 34.8±3.7 | 34.8±3.8 | 35.0±3.7 | 34.8±3.7 | 35.0±3.7 | 0.14 |
| Female (%) | | 50.3 | 50.8 | 53.8 | 63.2 | 78.8 | 79.9 | 55.4 | <0.01 |
| White (%) | | 50.1 | 53.4 | 51.9 | 50.4 | 55.8 | 54.7 | 51.9 | 0.09 |
| Education (years) | | 15.3±2.6 | 15.3±2.6 | 15.5±2.6 | 15.2±2.5 | 15.4±2.5 | 15.6±2.6 | 15.3±2.6 | 0.38 |
| Physical activity (exercise units) | | 322.6±266.2 | 360.0±275.0 | 371.2±314.9 | 323.3±281.6 | 267.5±223.8 | 284.3±252.4 | 332.0±273.8 | 0.01 |
| Current smokers (%) | | 24.9 | 29.0 | 23.0 | 24.6 | 21.8 | 23.9 | 25.4 | 0.83 |
| Alcohol intake (ml) | | 11.5±22.2 | 11.7±23.2 | 12.5±27.3 | 9.4±15.6 | 7.1±12.7 | 8.7±22.1 | 11.0±22.1 | <0.01 |
| Heavier alcohol | ≥ 14 drinks /wk for men | 16.1 | 18.1 | 18.6 | 15.7 | 9.9 | 10.7 | 16.6 | 0.88 |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| consumption (%) | ≥7 drinks/wk for women | 10.3 | 7.6 | 6.7 | 9.7 | 10.2 | 8.1 | 9.0 | 0.72 |
| *A Priori* Diet Quality Score (y7) | | 66.5±12.3 | 67.3±12.0 | 67.0±12.5 | 66.6±12.1 | 68.3±12.3 | 69.2±11.8 | 67.0±12.2 | <0.01 |
| BMI (kg/m$^2$) | | 25.8±5.3 | 26.8±5.8 | 27.8±6.5 | 30.0±7.4 | 31.1±7.4 | 32.7±7.9 | 27.3±6.4 | <0.01 |
| WC (cm) | | 82.9±12.9 | 84.9±13.4 | 86.4±14.1 | 89.7±14.8 | 90.8±16.4 | 93.7±17.1 | 85.4±14.1 | <0.01 |
| SBP (mmHg) | | 109.6±12.3 | 109.7±12.4 | 110.5±13.4 | 111.2±13.3 | 109.0±12.9 | 108.2±12.2 | 109.8±12.6 | 0.87 |
| DBP (mmHg) | | 72.0±9.9 | 72.1±10.1 | 72.4±10.5 | 73.7±10.8 | 71.9±9.6 | 72.7±9.9 | 72.2±10.1 | 0.21 |
| Plasma TG (mg/dL) | | 88.9±71.1 | 88.3±57.0 | 89.5±57.1 | 88.0±59.4 | 101.0±96.1 | 89.3±51.1 | 89.8±67.4 | 0.07 |
| Plasma HDL-C (mg/dL) | | 51.3±14.0 | 49.9±13.2 | 50.2±14.8 | 50.2±14.9 | 49.2±13.6 | 50.1±14.6 | 50.4±14.0 | 0.03 |
| Plasma LDL-C (mg/dL) | | 107.0±31.0 | 111.1±33.9 | 107.7±31.3 | 111.0±29.6 | 110.5±30.5 | 111.8±32.9 | 108.9±31.7 | 0.02 |
| Fasting glucose (mg/dL) | | 85.5±9.1 | 86.4±8.7 | 86.1±8.6 | 86.6±7.9 | 85.9±8.7 | 85.7±7.8 | 85.9±8.8 | 0.23 |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Normal glucose (%) | 94.5 | 93.4 | 92.9 | 94.6 | 94.9 | 94.2 | 94.1 | 0.92 |
| Prediabetes (%) | 5.3 | 6.6 | 7.1 | 5.4 | 5.1 | 5.8 | 5.9 | 0.92 |
| Blood pressure medication use (%) | 3.1 | 2.5 | 2.3 | 4.3 | 3.0 | 2.9 | 2.9 | 0.85 |
| Lipid medication use (%) | 0.25 | 0.31 | 0.63 | 0.36 | 0.30 | 0.72 | 0.34 | 0.15 |

Abbreviations:

BMI: Body Mass Index

WC: Waist Circumference

SBP: Systolic Blood Pressure

DBP: Diastolic Blood Pressure

TG: Triacylglycerols

HDL-C: High Density Lipoprotein-Cholesterol

LDL-C: Low Density Lipoprotein-Cholesterol

**Table 8.2 Unadjusted associations of diabetes and metabolic syndrome at Year 10 with each of the 8 constructs that form Problematic**

| **Odds Ratio of Diabetes at Year 10** | | | | | | | |
|---|---|---|---|---|---|---|---|
| **Anx** (n=3899) | **Com** (n=3902) | **Epieat** (n=3902) | **LoC** (n=3902) | **Overeat** (n=3900) | **Control** (n=3899) | **Shape** (n=3902) | **Diet** (n=3894) |
| 1.68 (1.02, 2.78) | 1.80 (0.72, 4.51) | 1.27 (0.79, 2.04) | 1.68 (0.76, 3.69) | 1.62 (1.01, 2.60) | 1.83 (1.11, 3.04) | 0.55 (0.32, 0.97) | 1.74 (1.04, 2.90) |
| **Odds Ratio of Metabolic Syndrome at Year 10** | | | | | | | |
| **Anx** (n=3871) | **Com** (n=3874) | **Epieat** (n=3874) | **LoC** (n=3874) | **Overeat** (n=3872) | **Control** (n=3871) | **Shape** (n=3874) | **Diet** (n=3866) |
| 1.58 (1.24, 2.02) | 1.67 (1.06, 2.65) | 1.48 (1.19, 1.84) | 1.41 (0.94, 2.10) | 1.67 (1.34, 2.08) | 1.79 (1.41, 2.28) | 0.89 (0.70, 1.11) | 1.74 (1.36, 2.22) |

**Relationship to Eating and Food score**

**Table 8.3 Incidence density of diabetes per 10,000 person-years through Year 25 and Hazard ratio (95% CI) of incident diabetes from Year 10 by PREF**

| | PREF HR (95% CI) | | | | | | PREF (continuous, per point) |
|---|---|---|---|---|---|---|---|
| | 0 points | 1 point | 2 points | 3 points | 4-5 points | 6-8 points | |
| Incident diabetes | 127 | 94 | 48 | 35 | 51 | 24 | |
| N at risk | 1593 | 965 | 476 | 280 | 335 | 139 | |
| Person years | 26385 | 15920 | 7895 | 4790 | 5625 | 2225 | |
| Incidence density | 48 | 59 | 61 | 73 | 91 | 108 | |
| Model 1 | 1.00 (reference) | 1.27 (0.97, 1.66) | 1.33 (0.95, 1.85) | 1.60 (1.10, 2.33) | 2.11 (1.51, 2.93) | 2.64 (1.70, 4.11) | 1.20 (1.12, 1.28) |
| Model 2 | 1.00 (reference) | 1.26 (0.95, 1.68) | 1.32 (0.93, 1.88) | 1.42 (0.92, 2.17) | 2.07 (1.45, 2.95) | 2.22 (1.34, 3.68) | 1.17 (1.09, 1.26) |
| Model 3 | 1.00 (reference) | 1.10 (0.83, 1.47) | 1.09 (0.76, 1.56) | 0.85 (0.55, 1.33) | 1.21 (0.84, 1.75) | 1.01 (0.59, 1.73) | 1.02 (0.94, 1.09) |
| Model 4 | 1.00 (reference) | 1.04 (0.77, 1.40) | 1.12 (0.77, 1.61) | 0.95 (0.61, 1.49) | 1.26 (0.86, 1.86) | 1.28 (0.74, 2.25) | 1.05 (0.97, 1.13) |

Model 1: adjusted for age, race, sex, education, and center
Model 2: model 1+ Year 10 smoking, alcohol, physical activity, and Year 7 *A Priori* diet score

Model 3: model 2+Year 10 BMI
Model 4: model 3+ HOMA, fasting glucose, blood pressure, HDL-C, LDL-C, triglycerides, and blood pressure medications

**Table 8.4 Hazard ratio (95% CI) of incident metabolic syndrome from Year 10 by PREF years with disjoint follow-up periods**

| | | PREF score at Year 10 | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | 0 points | 1 point | 2 points | 3 points | 4-5 points | 6-8 points | | continuous, per point |
| Year 10-15 | N at risk | 1435 | 852 | 406 | 233 | 267 | 114 | | |
| Model 1 | HR | 1.00 (ref) | 1.45 (1.06, 1.98) | 1.37 (0.92, 2.06) | 1.73 (1.09, 2.74) | 3.16 (2.17, 4.61) | 3.92 (2.43, 6.31) | | 1.30 (1.20, 1.39) |
| Model 2 | HR | 1.00 (ref) | 1.48 (1.06, 2.06) | 1.37 (0.89, 2.12) | 1.63 (0.97, 2.73) | 2.97 (1.98, 4.46) | 3.38 (2.01, 5.69) | | 1.27 (1.17, 1.37) |
| Model 3 | HR | 1.00 (ref) | 1.27 (0.91, 1.77) | 1.13 (0.73, 1.75) | 1.03 (0.61, 1.73) | 1.53 (0.99, 2.35) | 1.41 (0.81, 2.44) | | 1.07 (0.98, 1.17) |
| Model 4 | HR | 1.00 (ref) | 1.24 (0.88, 1.74) | 1.08 (0.69, 1.69) | 0.93 (0.54, 1.60) | 1.39 (0.89, 2.18) | 1.45 (0.82, 2.57) | | 1.06 (0.97, 1.16) |
| | | | | | | | | | |
| Year 15-20 | N at risk | 1363 | 787 | 377 | 211 | 225 | 92 | | |
| Model 1 | HR | 1.00 (ref) | 1.06 (0.77, 1.46) | 1.24 (0.83, 1.84) | 1.04 (0.61, 1.77) | 2.49 (1.69, 3.67) | 1.99 (1.08, 3.64) | | 1.18 (1.09, 1.28) |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Model 2 | HR | 1.00 (ref) | 1.03 (0.73, 1.45) | 1.38 (0.92, 2.08) | 1.16 (0.67, 2.01) | 2.39 (1.59, 3.59) | 1.96 (1.07, 3.60) | | 1.18 (1.09, 1.29) |
| Model 3 | HR | 1.00 (ref) | 0.95 (0.67, 1.33) | 1.23 (0.82, 1.85) | 0.83 (0.47, 1.44) | 1.48 (0.96, 2.27) | 1.08 (0.57, 2.02) | | 1.05 (0.96, 1.15) |
| Model 4 | HR | 1.00 (ref) | 0.98 (0.69, 1.38) | 1.26 (0.83, 1.90) | 0.86 (0.48, 1.53) | 1.39 (0.89, 2.15) | 1.19 (0.63, 2.25) | | 1.06 (0.97, 1.16) |
| | | | | | | | | | |
| Year 20-25 | N at risk | 1261 | 728 | 345 | 95 | 187 | 80 | | |
| Model 1 | HR | 1.00 (ref) | 1.22 (0.88, 1.68) | 1.10 (0.72, 1.69) | 0.76 (0.41, 1.42) | 1.34 (0.88, 2.24) | 1.89 (0.98, 3.66) | | 1.06 (0.97, 1.17) |
| Model 2 | HR | 1.00 (ref) | 1.29 (0.92, 1.80) | 0.92 (0.56, 1.50) | 0.67 (0.32, 1.39) | 1.22 (0.69, 2.14) | 1.95 (1.00, 3.78) | | 1.04 (0.94, 1.15) |
| Model 3 | HR | 1.00 (ref) | 1.19 (0.85, 1.67) | 0.82 (0.50, 1.35) | 0.46 (0.22, 0.96) | 0.71 (0.39, 1.27) | 1.00 (0.50, 2.00) | | 0.92 (0.83, 1.03) |
| Model 4 | HR | 1.00 (ref) | 1.27 (0.90, 1.79) | 0.91 (0.55, 1.50) | 0.56 (0.27, 1.18) | 0.81 (0.45, 1.47) | 1.24 (0.62, 2.49) | | 0.96 (0.86, 1.07) |

Model 1 adjusted for age, race, sex, education, and center
Model 2: model 1+ Year 10 smoking, alcohol, physical activity, and Year 7 *a priori* diet score
Model 3: model 2+Year 10 BMI
Model 4: model 3+ HOMA, fasting glucose, blood pressure, HDL-C, LDL-C, triglycerides, and blood pressure medications

## Chapter 9. Problematic relationship to eating and food and energy intake and diet quality: The Coronary Artery Risk Development in Young Adults (CARDIA) Study

### 9.1 Introduction

Problematic eating behaviors, including binge eating and excessive dieting are prevalent in adolescents [185-186] and middle-age adults [166]. Children and adolescents [187-188] who express characteristics of anorexia nervosa or bulimia nervosa are known to consume less energy. However little is known about how problematic eating behaviors are associated with the intake of energy, dietary patterns, and diet quality in middle-aged adults. Additionally, most research on this topic has focused on food consumption when instructed to binge eat or overeat in a laboratory setting [65-66]. Little is known about the association of problematic eating behaviors in middle age with usual energy intake or diet patterns and quality, beyond the time when the episodes occurred.

In the Coronary Artery Risk Development in Young Adults (CARDIA) study, the Questionnaire on Eating and Weight Patterns-Revised (QEWP-R) was self-administered once (at the Year 10 examination, ages 27-41 years). QEWP-R measures a set of constructs that are used to characterize subtle eating behaviors that range from problematic but common eating behaviors and attitudes toward food to presumptively severe eating disorders. From the QEWP-R, an 8 point scale of problematic relationship to eating and food was created [166]. A problematic relationship to eating and food (PREF), defined as endorsement of one or more problematic eating behavior constructs, was found in over half these CARDIA participants.

The primary objective of this report is to assess the association of severity of problematic relationship to food with subsequent dietary pattern 10 years later. Energy intake, diet quality, *A Priori* Diet Quality Score, and consumption of sugar-sweetened and artificially-sweetened beverages were assessed by diet history [135]. A plant-based dietary pattern, less oxidative stress, and healthful behaviors were assessed by an objective measure, the sum of 4 serum carotenoids (α-carotene, β-carotene, β-cryptoxanthin, zeaxanthin/lutein). Because of the previous study which showed positive association with body mass index [166], and with greater risk for diet related chronic diseases, diabetes and metabolic syndrome [189], participants with PREF were hypothesized to have greater energy intake, lower *A Priori* Diet Quality Score, less sugar-sweetened beverage intake, greater artificially-sweetened beverages intake, and lower serum

concentration of carotenoids. Because of the known different concentration of serum carotenoids by weight status [92], a sub analysis was conducted to investigate whether the associations between PREF and dietary patterns and eating behaviors differed by weight status. Stronger diet associations with PREF in participants with BMI $\geq 25 kg/m^2$ than in thinner participants were hypothesized. Additional studies have shown concentration of serum carotenoids and diet quality differs by smoking status [93,120]. Therefore, a parallel analysis was conducted to investigate whether the associations between PREF and dietary patterns and eating behaviors are modified by smoking status. Stronger diet associations with PREF in non-smokers were hypothesized compared to current smokers.

## 9.2 SUBJECTS AND METHODS

CARDIA is a prospective cohort based in 4 field centers, including Birmingham AL, Chicago IL, Minneapolis MN, and Oakland CA. CARDIA was initiated with 5,115 black and white participants aged between 18 to 30 years old in 1985 to 1986 [190]. The follow up rate for CARDIA examinations in Years 2, 5, 7, 10, 15, 20, and 25 were 91, 86, 81, 79, 74, 72, and 72% of survivors respectively. At each study center, the Institutional Review Board approved the study and written informed consent was obtained from each participant. For this study, eligible participants (Figure 9.1) were those who attended Year 10 and answered the 'Questionnaire on Eating and Weight Patterns-Revised (QEWP-R)'. Excluded from the analyses were those who did not attend the examination in Year 10 (n=1,165), had no assessment of QEWP-R (n=47), were missing covariates in Year 10 (N=77 for energy intake), did not attend Year 20 (N=699), or had a report of extreme energy intake in Year 20 (N=388). The same participants were analyzed for *A Priori* diet quality score, sugar-sweetened and artificially-sweetened beverages. Among those who attended Year 10 and had assessment of QEWP-R, for analyses of the sum of 4 carotenoids, those who did not have covariates assessed in Year 10 (N=154), no attendance in Year 20 (N=675), and no assessment of carotenoids (N=663) were further excluded. Therefore 2,739 participants for energy intake, *A Priori* diet quality score, sugar-sweetened beverages, artificially-sweetened beverages, and 2,411 participants for the sum of 4 serum carotenoids in Year 20 according to PREF categories were analyzed.

## Measurements

### Assessment of Problematic Relationship to Eating and Food (PREF)

A problematic relationship to eating and food is defined from the QEWP-R, measured in CARDIA at Year 10. The QEWP-R is a standard self-administered questionnaire, developed by Spitzer [126] to define binge eating disorder in DSM-IV. QEWP-R includes binge eating (referred to here as 'Epieat'), binge eating with loss of control ('LoC'), and related behaviors and psychological states, including anxiety around eating or food ('Anx'), upsetness over overeating ('Overeat'), upsetness over sense of loss of control ('Control'), compensatory behaviors ('Com'), weight history ('Diet'), and other eating-disordered behaviors including shape and weight concern ('Shape'). From the 8 constructs, the constructs are dichotomized to either 'yes' or 'no' in the following manner. If three or more of the five anxiety questions related to eating and food answered 'yes', 'Anx' was confirmed. A frequency of at least once a week was used as a qualifier for 'Com' and 'LoC'. Moderately or more upset was used as a cut off for general distress 'Overeat' and 'Control'. Those with weight and shape being a main or most important concern were classified positive for 'Shape' and those who have been on a diet for more than half of the time as an adult were classified as 'Diet'. Detailed cut-offs and verbatim questions are provided in Chapter 3, Table 3.1. A point for each construct endorsed was assigned to define problematic relationship to eating and food point scale (PREF). The sum of the 8 constructs represents a composite summary of low to high individual involvement with these characteristics. Therefore from these 8 QEWP-R constructs, a wide range of eating behaviors are assessable, ranging from subtle individual problematic behaviors and attitudes to combinations of problematic eating behaviors and attitudes which suggest clinical eating disorders. PREF 0 points was defined as normal eaters. Those with PREF 4-5 points were collapsed, because PREF 4 and 5 points had similar cross-sectional BMI in CARDIA Year 10 when PREF was assessed. PREF 6, 7, and 8 points were collapsed to maintain an adequate number of participants [166]. Thus 6 PREF categories were created ranging from PREF 0 points (normal eaters), 1, 2, 3, 4-5 points, and 6-8 points (presumptive eating disorders). QEWP-R's stability, validity, and reliability have been reported to be good in populations of those who were categorized as having obesity or self-referred as binge eaters [127].

### Energy Intake

Energy intake was assessed at Year 0, 7, and 20 using the interviewer-administered CARDIA diet history [191]. The CARDIA diet history questionnaire's reliability and validity

have previously been reported with a correlation of 0.3 to 0.8 indicating moderate agreement [135]. A general dietary intake of various food groups within the past month was asked from the interviewers, who asked 100 general questions such as, 'Do you eat meat?', followed by recording of open-ended food intake responses. Energy intake was computed (kcal/day). Participants were further excluded if they had implausibly high and low energy intakes, including men reporting intake of less than 800 kcal/day or greater than 8,000kcal/day (N=60) and women with energy intake of less than 600kcal/day or greater than 6,000 kcal (N=34).

***A Priori* Diet Quality Score**

*A Priori* Diet Quality Score was assessed at Years 0, 7, and 20 from CARDIA Diet History [191]. The *A Priori* Diet Quality Score was developed by categorizing 46 food groups [76, 135, 191-192] into 3 groups (beneficial, neutral, or adverse), by the hypothesized health effects. Food groups considered as either beneficial (n=20, fruit, vegetables, legumes, low fat dairy products, fish, poultry, coffee, tea, and moderate amount of alcoholic drinks) or adverse (n=13, fried foods, high fat meat, salty snacks, desserts, high fat dairy products, and soft drinks) were further categorized into quintiles or to a nonconsumer group and quartiles among consumers. The sum of category scores 0–4 for the beneficial food groups plus scores in reversed order (4–0) for adverse food groups (neutral food groups scored 0) constituted the A *Priori* Diet Quality Score. Thus higher score indicates better diet quality (maximum points of 132)[135].

**Sugar-Sweetened and Diet Beverages**

Sugar-sweetened and artificially-sweetened beverages were obtained from the CARDIA diet history [191]. Because artificially-sweetened beverages contain nearly zero calories, intake of artificially-sweetened beverages cannot be expressed in calories. Artificially-sweetened beverages are expressed as servings per day. Thus the intakes of sugar-sweetened beverages are also expressed as servings per day for compatibility with artificially-sweetened beverages. Five specific beverages were used to define sugar-sweetened beverages: non-alcoholic beer, non-alcoholic light beer, sweetened fruit drinks, sugar-sweetened beverages, and sweetened water. Four beverages were used to define artificially-sweetened beverages: artificially-sweetened fruit drinks, artificially-sweetened water, artificially-sweetened soft drinks, and unsweetened soft drinks.

**Carotenoids**

Five serum carotenoids α-carotene, β-carotene, β-cryptoxanthin, lutein/zeaxanthin, and lycopene were assayed in a venous sample drawn from CARDIA participants using modified

high-performance liquid chromatography [193]. Serum samples were stored at −70°C until shipped on dry ice to a central laboratory [138]. Because lycopene does not share the epidemiological characteristics of the other 4 carotenoids, it was excluded from the sum of the 4 carotenoids; thus α-carotene, β-carotene, β-cryptoxanthin, and lutein/zeaxanthin were summed to create the score used here. A higher sum of 4 serum carotenoids is a marker of higher quality diet because it indicates greater consumption of diets high in carotenoid-rich fruits and vegetables [89-90, 195] and is empirically related to a healthier diet pattern which tends to reduce oxidative stress, to nonsmoking, and to lower BMI [91-92,94].

**Smoking**

Smoking status was assessed at CARDIA Years 0, 2, 5, 7, 10, 15, 20, and 25 by answering an interviewer-administered tobacco use questionnaire. The tobacco use questionnaire asked 'Have you ever smoked cigarettes regularly for at least 3 months? By regularly, we mean at least 5 cigarettes per week, almost every week?' Those who responded 'no' to this question were classified as 'never smokers', those who answered 'yes' to the questionnaire were asked whether they currently smoke and accordingly classified as 'current smokers' or 'former smokers'.

**Weight Status**

Weight and height were measured without shoes and excessive clothing on a calibrated scale. BMI was calculated as the body weight (kg) divided by the square of the height ($m^2$) [121]. Following the National Heart, Lung, and Blood Institute classification of overweight and obesity by BMI [129], participants with BMI $\geq$30 kg/$m^2$ were classified as 'having obesity', and those with BMI <30kg/$m^2$ as 'not having obesity'.

**Other Measurements**

Standard structured interview and self-administered questionnaires were used to obtain demographic and behavioral information at each examination. Educational status was quantified as number of maximum years completed through Year 25. Information on physical activity, as well as medical history was obtained by self-administered questionnaire at the baseline and follow-up. A physical activity score was derived from the CARDIA physical activity history [173].

**Statistical Analysis**

Descriptive statistics of characteristics are described as mean ± SD or % for frequencies. The analysis of the longitudinal association of PREF with energy intake was conducted using

linear regression, adjusted for age, race, sex, smoking, physical activity, and study center. Parallel analyses were done for the prospective association between PREF and *A Priori* Diet Quality Score, intake of sugar-sweetened and artificially-sweetened beverages, and serum carotenoid concentration. Sub-analyses were conducted to determine modification of the associations by smoking status and weight status including tests for interaction. Statistical analysis was two sided with a type 1 error rate of 0.05. Statistical analyses were conducted using SAS 9.4 (SAS Institute Inc., Cary, NC).

## 9.3 RESULTS

### Sample characteristics of PREF

The analytic sample comprised 2,739 participants who were 55.3% female and 53.0% whites. The mean age at PREF assessment was 35 years (range 27–41 years), average educational attainment was 15.7 years, and mean BMI was 27.3kg/$m^2$. About 25% were current smokers, and the sample had mean physical activity of 270 exercise units, where 300 exercise units is equivalent to 30 minutes of moderate intensity activity 5 days a week [173] (Table 9.1). The proportion of 8 constructs endorsed in each PREF points are described in chapter 7. Among those with PREF 1 points, weight and shape concern was the most prevalent type of the single PREF behavior endorsed (36%), followed by overeating in a short period of time (Epieat, 32%), and dieting more than half of the time (Diet, 12%), with other constructs ranging from 0 to 8%.

### Energy intake and Diet quality score among PREF

Table 9.2 shows associations between PREF categories and greater energy intake after 10 years of follow-up. PREF 1, 2, and 6-8 points had greater energy intake compared to PREF 0 points (115, 126, and 312 kcal greater, respectively) after adjustment for age, race, sex, education attainment, center, smoking, and physical activity (model 3). While the greater energy intake in PREF 3, 4-5 points were not statistically greater compared to PREF 0 points, the greater energy intake in those categories follows the overall increasing energy intake across PREF categories. Little to no difference in these associations was observed before and after Year 10 BMI was adjusted (model 4).

While no specific PREF groups had statistically significant different diet quality scores compared to PREF 0 points, the *A Priori* Diet Quality Score generally increased per PREF points

after adjustments for demographic and behavioral variables (Table 9.3, model 3, linear trend, p=0.04). With additional adjustment for Year 10 BMI, PREF 2 points and PREF ≥ 4 points had greater *A Priori* Diet Quality Scores compared to PREF 0 points (1.5, 1.5, and 2.7 additional diet quality points, respectively, Table 9.3, model 4). The *A Priori* Diet Quality Score in PREF 1 and 3 points did not statistically significantly differ compared to PREF 0 points, but followed the generally increasing diet quality scores, suggesting a healthier diet. With further adjustment for Year 20 energy intake, there was little to no change of *A Priori* Diet Quality Score across PREF categories. The associations were not modified by smoking or weight status, tested by introducing corresponding product terms.

**Sugar-Sweetened and Artificially-Sweetened beverage consumption among PREF categories**

After 10 years of follow-up, in CARDIA Year 20, no significant association was observed between PREF categories and sugar-sweetened beverages after adjustment for demographics and behavioral variables (linear trend p= 0.32, Table 9.4, model 3). No significant changes were seen after further adjustment of Year 10 BMI. In the full model adjusted for Year 20 energy intake, the association between PREF categories and sugar-sweetened beverages were inversely associated (linear trend p=0.05) with a significantly less sugar-sweetened beverage intake observed among PREF 6-8 points compared to PREF 0 points (0.46 vs 0.89 additional servings per day).

In contrast to the sugar-sweetened beverages, greater artificially-sweetened beverage (servings per day) were observed with PREF ≥3 points (0.63, 0.48, 1.19 additional servings/day for PREF 3 points, PREF 4 to 5 points and PREF 6 to 8 points, respectively). Table 9.5 shows positive association between PREF categories and consumption of artificially-sweetened beverages (linear trend, p <0.01) after adjustment for demographics and behavioral variables (Table 9.5, model 3). The consumption of artificially-sweetened beverages in PREF 1 and 2 points did not differ from PREF 0 points, but followed the linear trend. Little to no changes in these estimates was seen after further adjustment of Year 10 BMI and Year 20 BMI (Table 9.5, model 5). Neither the associations of PREF with sugar-sweetened nor artificially-sweetened beverages intake differed by smoking status or weight status.

**Carotenoids among PREF categories**

In Year 20, no association was seen among PREF categories and sum of 4 serum carotenoids after adjustment for demographics and behavioral variables (p trend 0.11, Table 9.6, model 3), which agrees with the finding of no association between PREF and *A Priori* Diet Quality Scores in table 9.3, model 3. However after further adjustment for Year 10 BMI, a positive association was seen across PREF categories (p trend < 0.01) and greater concentration of the sum of 4 carotenoids were seen in PREF ≥1 points compared to PREF 0 points (3.4, 4.1, 4.7, 4.8, and 8.8 µg/dL, respectively, Table 9.6, model 4.

The positive association between PREF and sum of 4 carotenoids agrees with the findings from greater *A Priori* Diet Quality Score in PREF 2, 4-5, and 6-8 points (Table 9.3) after adjustment for Year 10 BMI, likely reflecting the significant correlation between *A Priori* Diet Quality Score and sum of 4 carotenoids ($\gamma$=0.43 to 0.57 across PREF categories) . The association between PREF and sum of 4 carotenoids did not differ by smoking or weight status.

## 9.4 DISCUSSION

In this study, we found that a problematic relationship to eating and food, PREF was associated with greater energy intake, greater intake of artificially-sweetened beverages after adjustment for sociodemographic and behavioral variables. The *A Priori* Diet Quality Score increased with PREF points, somewhat more strongly with further adjustment for Year 10 BMI. The association between PREF and sum of 4 carotenoids emerged after adjusting for BMI (which is one factor that is known to cause substantial reduction in circulating carotenoids), supporting that slightly greater diet quality was found with increasing PREF points.

Although greater energy intake, *A Priori* Diet Quality Scores and servings of artificially-sweetened beverages were not seen in all PREF categories compared to PREF 0 points, most associations followed positive linear trends across PREF categories. While studies report smoking status [96, 190] and weight status [92] modify dietary pattern and carotenoid concentrations, there was no modification by either smoking or weight status for any of the associations of the 5 diet related variables with PREF.

The finding of greater energy intake across PREF categories parallels laboratory feeding studies reporting greater energy intake during the episodes of binge eating [65-66], yet differs from other cross-sectional studies reporting less energy intake among children and adolescents

with disturbed eating behaviors [187-188]. Furthermore, a longitudinal study reported less or no difference in energy intake among female and male adolescents who engaged in unhealthy weight control compared to participants who did not engage in unhealthy weight control behaviors [71]. The different findings may originate from different age groups, type of disordered eating behaviors examined, and instruments used to assess and define problematic eating behaviors. Our findings further extend the finding to the non-clinical participants with subtle problematic eating behaviors and their general food intake beyond the episodes.

While it is unknown whether CARDIA participants with PREF are preoccupied with their food choices compared to normal eaters (PREF 0 points), our finding of greater *A Priori* Diet Quality Score per PREF point may suggest greater diet quality associated with PREF. However, despite the linear trend, none of the individual PREF categories had greater diet quality scores when compared to PREF 0 points. The linear association strengthened with adjustment for year 10, but we interpret this strengthening cautiously because BMI in some plausible scenarios is a collider variable (resulting both from higher PREF score and greater food consumption). Our finding differs from cross-sectional studies, which report lower diet quality score measured by Canadian Healthy Eating Index (HEI-C) among adolescents concerned with their body weight compared to adolescents not concerned about their body weight [196]. These differences might occur from our study participants over reporting or providing socially desirable answers on the diet history, given that the CARDIA diet history questionnaire was self-administered. Furthermore, the difference may arise from the fact that our study focuses on participants' usual and typical dietary intakes, and dietary patterns, not the exact time when the problematic eating behaviors occurred.

The non-significant association of sugar-sweetened beverages intakes but greater consumption of artificially-sweetened beverages among PREF compared to normal eaters is consistent with the finding from other clinical disordered eating behavior studies with sugar-sweetened soda intake [96,197]. However, the clinical studies [96,197] focused exclusively on soda, whereas our study enhanced the definition of sugar-sweetened beverages by including fruit drinks, water, sugar-sweetened beverages, beers, and light beers. The finding of greater consumption of artificially-sweetened beverage among PREF category further suggests participants with problematic relationship to eating and food, may tend to view artificially-sweetened beverages as an alternative way to restrict their energy intake as an attempt to lose excess weight.

In addition to the greater *A Priori* Diet Quality Score and intake of artificially-sweetened beverage, sum of concentrations of 4 carotenoids did not differ across PREF categories after adjustment for demographics, behavioral variables. Further adjustment of CARDIA Year 10 BMI was performed based on the concept that oxidative stress secondary to obesity causes a direct loss of circulating carotenoids as reflected in intervention studies reporting that changes in weight, fat mass, and % fat negatively correlated with changes in total serum carotenoids concentrations [198-199]. The correlation of the sum of 4 carotenoids with the *A Priori* Diet Quality Score is substantial, over 0.4. However, we interpret the association of PREF with serum carotenoids cautiously. The adjustment for BMI as a linear term may not perfectly correct for the extent to which obesity mediated oxidative stress reduces carotenoid concentrations. Further, from a purely epidemiologic perspective, both problematic eating behaviors and consumption of carotenoid containing foods could affect BMI, so the adjustment of BMI might result in a biased association between problematic eating behaviors and serum carotenoids [200]. The concordance of patterns of association of PREF with *A Priori* Diet Quality Score and with higher concentrations of sum of 4 carotenoids, the later after accounting for BMI, may indicate an awareness of the value of plant-based dietary patterns among participants with PREF. In agreement with our studies, other studies of adolescents report that excessive dieting is associated with greater fruit and vegetable intake [82, 201]. One study reported that frequency of dieting was associated with inadequate fruit consumption, but did not show any difference of vegetable intake [202]. Similar to our studies of at most small differences in dietary patterns indicated by *A Priori* Diet Quality Scores or sum of 4 carotenoids among participants with problematic eating behaviors and attitudes, a study conducted among African Americans and Hispanics who endorsed binge eating did not report greater fruit and vegetable consumption [203].

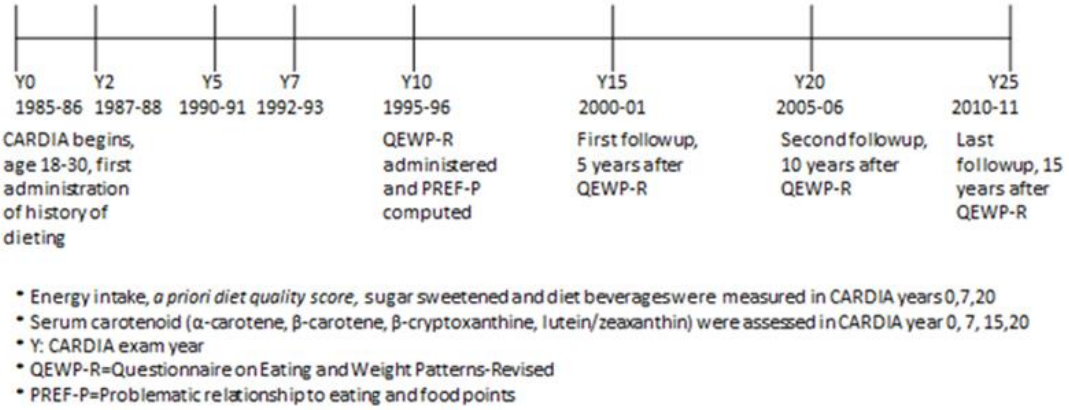
Strengths of our study include employing a large population-based sample of generally healthy men and women, including Black and White Americans, enhancing generalizability of the results. Our study participants were middle aged (27 to 41 years old) when the QEWP-R was administered, whereas other studies focused on adolescence or college-age at baseline [82, 187-188, 196, 201-202]. With less emphasis in the literature on participants with problematic eating behaviors compared to binge eating, our study adds to the literature by showing the positive association of energy intake, greater *A Priori* Diet Quality Scores, greater consumption of artificially-sweetened beverages, and sum of carotenoids among subtle problematic eating behaviors.

Several limitations warrant consideration. First that the QEWP-R is not administered in any other CARDIA exam except a single measure at Year 10 is a limitation, as the reliability of QEWP-R in CARDIA cannot be measured. Second, because QEWP-R in CARDIA is not a tool used to make clinical diagnosis and we did not intend to identify people with clinical eating disorders, we cannot confirm whether the PREF 6-8 points would be classified with clinically diagnosable eating disorders on further evaluation in an eating disorder clinic. Nevertheless, those with PREF 6-8 points share many constructs used to define bulimia nervosa and binge eating disorder. Thus we suggest PREF 6-8 points may have presumptive eating disorders. Third, no specific macro or micro nutrient intake was investigated among participants thus we did not report on their nutrient intake. Fourth, diet history was self-reported, thus there is a possible under-reporting of their behaviors and intake. Finally, as in all observational epidemiologic studies, potential residual confounding may exist from unmeasured or unknown confounders.

## 9.5 CONCLUSION

Among middle-aged adults, PREF categories were associated with greater energy intake and greater consumption of artificially-sweetened beverages, which can be interpreted as adverse behaviors which may lead to greater BMI (chapter 7) and future risk for diabetes and metabolic syndrome (chapter 8). PREF was associated with slightly greater *A Priori* Diet Quality Score and with the objectively measured sum of 4 carotenoids (α-carotene, β-carotene, β-cryptoxanthin, and zeaxanthin/lutein) after correction for the greater adiposity (which is an oxidative stressor) found in people with PREF ≥1 point. Along with habitual attempts at dieting to lose weight coupled with greater energy intake, this small difference in diet quality scores and dietary pattern may suggest that participants with PREF are at least not inferior in their diet quality to normal eaters with PREF 0 points. The slightly greater *A Priori* Diet Quality Score and preference for artificially-sweetened beverages among participants with PREF suggests that they are attempting unsuccessfully to lose weight. Thus the finding illustrates a lack of understanding on the part of participants about how their eating behaviors pertain to their body weight. Unlike in many studies [92-93, 190], the diet-related variables and associations with PREF categories did not differ by smoking status or weight status. Future studies are necessary for confirmation of dietary patterns and quality using objective markers of dietary intake.

**Figure 9.1 Flow chart: sample for the analyses**




Exclusions are in hierarchical in the order listed

**Table 9.1. Demographic and clinical characteristics of the sample of people with Problematic Relationship to Eating and Food in CARDIA Year 10 (N=2,739)**

| | 0 points (n=1,137, 41.5%) | 1 point (n=704, 25.7%) | 2 points (n=341, 12.5%) | 3 points (n=203, 7.4%) | 4-5 points (n=252, 9.2%) | 6-8 points (n=102, 3.7%) | Total (n=2,739) |
|---|---|---|---|---|---|---|---|
| Age (years) | 35.2±3.6 | 35.0±3.7 | 35.2±3.6 | 35.1±3.6 | 35.2±3.7 | 34.8±3.6 | 35.1±3.6 |
| Female (%) | 50.8 | 52.4 | 54.8 | 64.5 | 78.2 | 80.4 | 55.3 |
| White (%) | 53.5 | 57.2 | 54.3 | 52.2 | 59.1 | 56.9 | 53.0 |
| Current Smokers (%) | 20.8 | 24.9 | 19.7 | 19.7 | 20.6 | 20.6 | 21.6 |
| Education attainment (years) | 15.7±2.6 | 15.8±2.5 | 15.8±2.6 | 15.7±2.5 | 15.6±2.5 | 16.1±2.6 | 15.7±2.6 |
| BMI ($kg/m^2$) | 25.7±5.3 | 26.7±5.6 | 27.7±6.1 | 30.0±6.7 | 31.3±7.4 | 32.5±8.0 | 27.3±6.3 |
| Physical activity (units) | 261 (129, 458) | 311 (149, 521) | 316 (156, 552) | 266 (105, 436) | 206 (87, 394) | 217 (106, 392) | 270 (128, 475) |

**Table 9.2 CARDIA Year 20 energy intake in relation to Year 10 Problematic Relationship to Eating and Food categories**

| | Year 20 | | | | | | P trend |
|---|---|---|---|---|---|---|---|
| | 0 points (n=1,137, 41.5%) | 1 point (n=704, 25.7%) | 2 points (n=341, 12.5%) | 3 points (n=203, 7.4%) | 4-5 points (n=252, 9.2%) | 6-8 points (n=102, 3.7%) | |
| Model 1 | 2286 ± 30.5 | 2420 ± 38.8** | 2403 ± 55.8 | 2189 ± 72.3 | 2204 ±64.9 | 2393±102.0 | 0.55 |
| Model 2 | 2249 ± 28.7 | 2387 ± 36.4** | 2395 ± 52.2* | 2243 ± 67.7 | 2359 ±61.3 | 2570±95.8** | <0.01 |
| Model 3 | 2257±28.4 | 2372±36.0* | 2383±51.7* | 2248±67.0 | 2375±60.8 | 2569±94.8** | <0.01 |
| Model 4 | 2254±29.0 | 2371±36.1* | 2384±51.8* | 2253±67.6 | 2383±62.3 | 2581±96.5** | <0.01 |

Mean±se (kcal/day)

Model 1: crude model

Model 2: adjusted for age, race, sex, education, and center

Model 3: adjusted for model 2+ Year 10 smoking, physical activity

Model 4: adjusted for model 3 and Year 10 BMI

*significantly different from normal eaters ($p<0.05$)

**significantly different form normal eaters ( $p<0.01$)

**Table 9.3 CARDIA Year 20 *A Priori* Diet Quality Score in relation to Year 10 Problematic Relationship to Eating and Food categories**

| | Year 20 | | | | | | |
|---|---|---|---|---|---|---|---|
| | 0 points (n=1,137, 41.5%) | 1 point (n=704, 25.7%) | 2 points (n=341, 12.5%) | 3 points (n=203, 7.4%) | 4-5 points (n=252, 9.2%) | 6-8 points (n=102, 3.7%) | P trend |
| Model 1 | 69.8±0.38 | 70.8±0.48 | 71.7±0.69* | 70.8±0.89 | 71.5±0.80 | 72.8±1.25* | <0.01 |
| Model 2 | 70.0±0.32 | 70.8±0.41 | 71.6±0.58* | 71.0±0.75 | 70.7±0.68 | 71.9±1.07 | 0.04 |
| Model 3 | 70.1±0.31 | 70.8±0.40 | 71.3±0.57 | 70.9±0.74 | 70.9±0.67 | 71.9±1.05 | 0.04 |
| Model 4 | 69.9±0.32 | 70.7±0.40 | 71.3±0.57* | 71.3 ±0.75 | 71.4±0.69* | 72.6±1.07* | <0.01 |
| Model 5 | 69.9±0.32 | 70.7±0.40 | 71.3±0.57* | 71.3±0.75 | 71.4±0.68* | 72.6±1.07* | <0.01 |

Data are mean±se (points, 1 point is a difference of 1 higher category of a beneficial food group or 1 lower category of an adverse food group)

Model 1: crude model
Model 2: adjusted for age, race, sex, education, and center
Model 3: adjusted for model 2+ Year 10 smoking, and physical activity
Model 4: adjusted for model 2 and Year 10 BMI
Model 5: adjusted for model 3 and Year 20 energy intake
*significantly different from normal eaters ($p<0.05$)
**significantly different from normal eaters ($p<0.01$)

**Table 9.4 CARDIA Year 20 Sugar-Sweetened Beverages in relation to Year 10 Problematic Relationship to Eating and Food categories**

| | Year 20 | | | | | | |
|---|---|---|---|---|---|---|---|
| | 0 points (n=1,137, 41.5%) | 1 point (n=704, 25.7%) | 2 points (n=341, 12.5%) | 3 points (n=203, 7.4%) | 4-5 points (n=252, 9.2%) | 6-8 points (n=102, 3.7%) | P trend |
| Model 1 | 0.87 ± 0.04 | 0.99 ± 0.06 | 0.86 ± 0.08 | 0.73 ±0.11 | 0.84 ± 0.09 | 0.48 ±0.15* | 0.04 |
| Model 2 | 0.85 ± 0.04 | 0.98 ± 0.05 | 0.87 ± 0.08 | 0.73 ±0.10 | 0.92 ± 0.09 | 0.59 ±0.14 | 0.34 |
| Model 3 | 0.85 ± 0.04 | 0.97 ± 0.05 | 0.88 ± 0.08 | 0.74 ± 0.10 | 0.91 ± 0.09 | 0.58 ±0.14 | 0.32 |
| Model 4 | 0.86±0.04 | 0.97±0.05 | 0.88±0.08 | 0.73±0.10 | 0.90±0.09 | 0.57±0.14 | 0.27 |
| Model 5 | 0.89±0.04 | 0.95±0.05 | 0.86±0.07 | 0.77±0.10 | 0.88±0.09 | 0.46±0.14** | 0.05 |

Data are mean±se (servings/day)

Model 1: crude model

Model 2: adjusted for age, race, sex, education, and center

Model 3: adjusted for model 2+ Year 10 smoking and physical activity

Model 4: adjusted for model 3 and Year 10 BMI

Model 5: adjusted for model 4 and Year 20 energy intake

*significantly different from normal eaters ($p<0.05$)

**Table 9.5 CARDIA Year 20 artificially-sweetened Beverages in relation to Year 10 Problematic Relationship to Eating and Food categories**

| | Year 20 | | | | | | |
|---|---|---|---|---|---|---|---|
| | 0 points (n=1,137, 41.5%) | 1 point (n=704, 25.7%) | 2 points (n=341, 12.5%) | 3 points (n=203, 7.4%) | 4-5 points (n=252, 9.2%) | 6-8 points (n=102, 3.7%) | P trend |
| Model 1 | 0.43 ± 0.05 | 0.61 ± 0.06 * | 0.59 ± 0.09 | 1.07 ± 0.12 ** | 0.93 ± 0.10 ** | 1.64 ± 0.16** | <0.01 |
| Model 2 | 0.45 ± 0.05 | 0.59 ± 0.06 | 0.60 ± 0.09 | 1.08 ± 0.11 ** | 0.93 ± 0.10 ** | 1.63 ± 0.16** | <0.01 |
| Model 3 | 0.45 ± 0.05 | 0.59 ± 0.06 | 0.60 ± 0.09 | 1.08 ± 0.11 ** | 0.93 ± 0.10 * | 1.64 ± 0.16** | <0.01 |
| Model 4 | 0.50±0.05 | 0.60±0.06 | 0.59±0.09 | 1.00±0.11** | 0.80±0.10* | 1.46±0.16** | <0.01 |
| Model 5 | 0.50±0.05 | 0.60±0.06 | 0.59±0.09 | 1.00±0.11** | 0.80±0.10** | 1.47±0.16** | <0.01 |

Data are mean±se (servings/day)

Model 1: crude model
Model 2: adjusted for age, race, sex, education, and center
Model 3: adjusted for model 2+ Year 10 smoking and physical activity
Model 4: adjusted for model 3 and Year 10 BMI
Model 5: adjusted for model 4 and Year 20 energy intake

*significantly different from normal eaters ($p<0.05$)
**significantly different from normal eaters ($p<0.01$)

**Table 9.6 CARDIA Year 20 Sum of 4 Carotenoids (µg/dl) in relation to Year 10 Problematic Relationship to Eating and Food categories**

| | Year 20 | | | | | | P trend |
|---|---|---|---|---|---|---|---|
| | 0 points (n=1000, 41.5%) | 1 point (n=614, 25.5%) | 2 points (n=302, 12.5%) | 3 points (n= 185, 7.7%) | 4-5 points (n=219, 9.1%) | 6-8 points (n=91, 3.8%) | |
| Model 1 | 49.9 ± 0.97 | 50.3 ± 1.24 | 51.9 ±1.77 | 47.5 ±2.26 | 47.8 ± 2.07 | 51.2 ±3.22 | 0.61 |
| Model 2 | 50.1± 0.90 | 50.9 ± 1.14 | 51.3 ±1.63 | 48.3 ±2.08 | 46.5 ± 1.93 | 48.3 ±2.99 | 0.11 |
| Model 3 | 50.1±0.88 | 51.2±1.13 | 50.6±1.60 | 48.3±2.04 | 46.4±1.90 | 48.4±2.93 | 0.11 |
| Model 4 | 47.4± 0.86 | 50.8± 1.07* | 51.5± 1.53* | 52.1± 1.96* | 52.2± 1.84* | 56.2± 2.84** | <0.01 |
| Model 5 | 47.2±0.94 | 50.7±1.20* | 52.6±1.77* | 53.0±2.31* | 52.5±2.07* | 53.5±3.25 | <0.01 |
| Model 6 | 47.0±0.98 | 50.5±1.25* | 52.4±1.88* | 53.5±2.45* | 51.9±2.17* | 55.6±3.42* | <0.01 |

Data are mean±se
Model 1: crude model
Model 2: adjusted for age, race, sex, education, and center
Model 3: adjusted for model 2+ Year 10 smoking, physical activity
Model 4: adjusted for model 3+ Year 10 BMI
Model 5: adjusted for model 4+lipids
Model 6: adjusted for model 5+ Year 20 energy intake
*significantly different from normal eaters ($p<0.05$)

# Chapter 10 Summary

## 10.1 Summary of Study Findings

This thesis aimed to explore problematic eating behaviors and attitudes among middle-aged adults, which is a concern due to the high prevalence among adolescents and young adults and the implications of such behaviors and attitudes for health and well-being. In this thesis, problematic relationship to eating and food (PREF) was assessed by the Questionnaire on Eating and Weight Patterns-Revised (QEWP-R). PREF was defined based on constructs of behaviors and attitudes that are often involved in bulimia nervosa and binge eating disorder. Among participants with PREF, this thesis examined the association with 25 years of BMI trajectories and the risks for incident diabetes and metabolic syndrome. Energy intake, diet quality, and beverage consumption from diet history was further examined to characterize the dietary pattern of participants who endorsed PREF constructs.

In the first manuscript where we explored the association between PREF and BMI, as hypothesized, greater PREF scores were associated with greater BMI throughout 15 years of follow-up. Throughout the thesis, problematic behaviors and attitudes was hypothesized to persist years before PREF was assessed in CARDIA, given other longitudinal studies have shown individual disordered eating behaviors, including binge eating and compensatory behaviors persist from adolescents to young adulthood. Thus, when PREF scores were examined with earlier years of BMI in CARDIA, PREF scores were associated with greater BMI and graded by the number of PREF endorsed. The greater mean BMI among participants with PREF throughout 15 years of follow up followed the overall pattern from an earlier CARDIA study which indicated limited weight gain after CARDIA years 15 to 20 [150] and findings from another prospective study which reported a monotonic increase of BMI among participants who endorsed individual and aggregated disordered eating behaviors [41]. Similarly, the proportions of participants who were overweight or obese was greater among participants with PREF $\geq$1 point compared to normal eaters (PREF 0 points). The greater mean BMI graded by the number of constructs endorsed illustrates that problematic behaviors and attitudes should be considered in the design of interventions that aim to prevent overweight and obesity among middle-aged adults. The finding of mean BMI leveling off later in CARDIA years suggests it may be a general pattern that occurs over time, or that CARDIA participants, both those with and without PREF, may have changed

their behaviors and attitudes related to diet and physical activity later in life to slow down their personal BMI trajectory. However, the eight constructs that were used to define PREF in our study only show that PREF in middle-aged adults was associated with greater BMI over 15 years of follow-up. This thesis does not explain what may have triggered greater BMI and why the mean BMI (Figure 7.3, Part 1) and the association of PREF with BMI (Figure 7.3, Part 2) leveled off after 10 years of follow-up. Thus there is a need to explore etiological factors including events and transitions relevant to life stages, especially in middle-age which may trigger problematic eating behaviors and explain why middle-aged adults with PREF have greater BMI in short term follow-up but that this phenomenon slows down in the long-term. However if the problematic eating behaviors persist, and existed in the earlier years (Year 0) prior to when PREF was assessed, the greater BMI seen in CARDIA year 15, may have continued for a maximum of 15 years.

In the second manuscript, the CARDIA study also documented that risks for diabetes and metabolic syndrome were greater among participants with PREF throughout 10 to 15 years of follow-up. The risk profile for metabolic syndrome indicates that this effect of PREF waned over 5, then 10, then 15 years of follow-up. Associations of PREF with diabetes and metabolic syndrome were almost completely attenuated after adjustment for Year 10 BMI, which suggests that participants with PREF may be prone to overweight and obesity, and the excessive BMI expose them to at greater risk for diabetes and metabolic syndrome.

In the third manuscript, our findings were partially in agreement with the hypothesis. Energy intake was greater among participants with PREF. The finding of greater energy intake and greater BMI among participants with PREF suggests that the participants' greater energy intakes may have contributed to their greater BMI. In addition to greater energy intake, consumption of artificially-sweetened beverages was greater among participants with higher PREF score, which implies that participants with PREF may attempt to counteract their greater energy intake and greater BMI through artificially-sweetened beverage consumption. However, as our data has partially described, excessive consumption of artificially-sweetened beverage may eventually lead to greater BMI, which agrees with prospective cohort studies [204-205]. In contrast to our hypothesis of worse diet quality and worse dietary pattern to associate with PREF, the *A Priori* Diet Quality Score showed indications of being greater in those with more PREF points. Our study employed an objective marker which correlated substantially with the *A Priori* Diet Quality Score, namely the sum of serum concentrations of 4 carotenoids. The carotenoids are

introduced to the body only by carotenoid containing food, and are oxidized in the body when they encounter reactive species such as free radicals, which arise from consuming some less healthy foods (processed meats, animal products, oxidized fats, and fast foods that cause oxidative stress) and which are abundant in obesity [91, 94]. The sum of carotenoids is also reflective of nonsmoking, physical activity, and a generally healthy lifestyle, all of which correlate with better diet. However, the sum of carotenoids did not differ across PREF categories after adjustments for demographic and behavioral variables, without accounting for the substantial adiposity in people with PREF. After correction for BMI, the sum of carotenoids was positively associated with PREF, in parallel with the slight positive association of PREF with the *A Priori* Diet Quality Score. This finding suggests the diet quality among PREF was at least not inferior to that of normal eaters, and may have been slightly superior. Thus the BMI adjusted trend in sum of 4 serum concentrations across PREF categories further supports the finding that participants with PREF are at least not inferior in their dietary pattern compared to normal eaters, and also do not differ in general lifestyles. However, from a purely epidemiologic perspective, this healthier dietary pattern and lifestyle among participants with PREF may suffer to some extent from collider bias due to adjustment for Year 10 BMI, as PREF and dietary variables may both affect BMI. Taken together, the greater energy intake, BMI, and artificially-sweetened beverage intake among participants with PREF, contrasts with lack of evidence of poor diet quality, which indicates that there is a need for more research to better understand the dietary patterns and their dietary intake among participants with PREF. A summary of the key findings from this dissertation is included in Table 10.1.

**Table 10.1 Summary of Main Findings**

**BMI trajectories over 25 years**

Cross-sectional (CARDIA Year 10)

- Greater mean BMI in CARDIA Year 10 among PREF ≥1 point compared to PREF 0 points
- Mean BMI graded by PREF points

Retrospective (CARDIA Years 0-7)

- Greater mean BMI in CARDIA in Years 0, 2, 5, and 7 among PREF ≥1 point compared to PREF 0 points
- Mean BMI graded by PREF points
- BMI change relative to Year 10 BMI graded by PREF points

Prospective (CARDIA Year 15-25)

- Greater mean BMI in CARDIA in Years 15, 20, and 25 among PREF ≥1 point compared to PREF 0 points
- Mean BMI graded by PREF points
- Relatively flat course of mean BMI after CARDIA Year 20
- BMI change relative to Year 10 BMI not graded by PREF points

**Risk for Diabetes**

CARDIA Year 25

- After 15 years of follow-up (CARDIA Year 25), hazard risk for diabetes was greater among PREF ≥3 points compared to PREF 0 points after adjustment for demographics (HR: 1.60, 2.11, and 2.64, respectively).
- In a continuous model, participants with PREF were at 1.2 times greater risk for diabetes per PREF point after adjustment for demographics
- Associations were mediated by CARDIA Year 10 BMI

**Risk for Metabolic Syndrome**

CARDIA Years 10-15

- After 5 years of follow-up (CARDIA Years 10-15), hazard risk for metabolic syndrome was greater among PREF ≥3 points compared to PREF 0 points after adjustments for demographics (HR: 1.73, 3.16, 3.92, respectively)
- In a continuous model, participants with PREF were at 1.3 times greater risk for metabolic syndrome per PREF point after adjustment for demographics
- Association was mediated by CARDIA Year 10 BMI

CARDIA Years 15-20

- After 5 to 10 years of follow-up (CARDIA Years 15-20), hazard risk for metabolic syndrome was greater among ≥ 4 points compared to PREF 0 points after adjustments for demographics (HR: 2.49, 1.99, respectively)
- In a continuous model, participants with PREF were at 1.2 times greater risk for metabolic syndrome per PREF point after adjustment for demographics
- Association was mediated by CARDIA Year 10 BMI

CARDIA Years 20-25

- After 10 to 15 years of follow-up (CARDIA Years 20-25), the risk for metabolic syndrome was no longer statistically significant among participants with PREF≥1 point compared to PREF 0 points

**Dietary variables**

Energy Intake

- Greater energy intake after 10 years of follow-up among participants with PREF 1, 2, and 6-8 points compared to PREF 0 points after adjustment for demographic, behaviors variables
- Energy intake increased per PREF points suggesting PREF 3 and 4-5 points followed the trend of greater energy intake per PREF point

*A Priori* Diet Quality Score

CARDIA Year 0 and 7

- Higher diet quality scores among participants with PREF 1, 2, 4-5 and 6-8 points compared to PREF 0 points after adjustment for demographics, behavioral variables

- In continuous model, higher diet quality scores per PREF point, suggesting a healthier dietary pattern across all PREF categories

CARDIA Year 20

- After 10 years of follow-up, diet quality scores had a slight positive association with PREF points after adjustment for demographics, behavioral variables
- In a continuous model, higher diet quality scores per PREF point, suggesting a healthier dietary pattern across all PREF categories

Sugar-sweetened beverages

- No difference of sugar-sweetened beverages intakes between participants with PREF ≥1 point compared to PREF 0 points after adjustments for demographics, behavioral variables

Artificially-sweetened beverages

- After 10 years of follow-up, greater intake of artificially-sweetened beverage among participants with PREF ≥3 points compared to PREF 0 points
- Greater intake of artificially-sweetened beverage intake per PREF points, suggesting the intake in PREF 1 and 2 points follows the generally increasing pattern across all PREF categories

Sum of 4 serum carotenoids

- After 10 years of follow-up, concentration of sum of 4 serum carotenoids had a positive association with PREF points after correction for the higher BMI typical of people with PREF
- This objective measure has a substantial correlation (over 0.4) with the A Priori Diet Quality Score as well as with other aspects of healthy lifestyle

### 10.2 Strengths and Limitations of the Study

This thesis possesses several strengths which extend previous research on disordered eating behaviors. First, the inclusion of equally balanced race (blacks and whites) and gender (males and females) allows the study results to be generalizable to blacks and males who are often excluded in many studies of disordered eating behaviors [29, 206-207]. Second, the 8 constructs embedded

in QEWP-R, allowed the PREF scale to view unhealthy eating behaviors on a continuum ranging from normal eaters to unhealthy eating behaviors, to presumptively diagnosable eating disorders. On the PREF scale, participants with PREF 1-5 points were assumed to reflect participants with problematic eating behaviors and attitudes that fall short of clinical eating disorders, whereas PREF 6-8 points suggests presumably diagnosable eating disorders. Third, over 25 years of follow-up with over 2400 participants in CARDIA in all analyses allowed examination of BMI trajectories and of the risk of incident diabetes and metabolic syndrome up to 15 years after PREF was assessed. The history of dietary intake, which was assessed 10 years after PREF was assessed allowed examination of the effect of PREF on energy intake and diet quality. The sum of 4 carotenoids measured 10 years after the PREF was assessed allowed looking at the long-term association of problematic eating behaviors with dietary patterns using an objective biomarker. Lastly, the assessment of disordered eating behaviors among participants who were 27 to 41 years old in CARDIA study is a strength, given that many studies examined eating behaviors among adolescents and young adults [1-2, 12, 34-40, 48, 50-52, 58-59, 72, 74, 82-83, 96, 118-120, 203, 208-210]. Examination of an older age group adds to the research about disordered eating that these problematic eating behaviors exist in middle-aged adults and predicts greater risk of adverse metabolic health conditions, mediated by excess weight.

In addition to the strengths of our study, study limitations should also be taken into account in interpreting the findings. First, in CARDIA, the QEWP-R assessment of problematic eating behaviors and attitudes was administered only once in CARDIA Year 10 among middle-aged adults. Thus, it cannot be determined whether CARDIA participants endorsed problematic eating behaviors and attitudes prior to or after CARDIA Year 10. However, similar behaviors and attitudes relevant to PREF assessed in Project EAT among adolescents suggest that binge eating and compensatory behaviors are persistent after 5 and 10 years of follow-up [35-36]. This finding from Project EAT suggests that some of PREF constructs in CARDIA could be present in earlier years, although this cannot be confirmed. The internal reliability of PREF was assessed in the dimension of 'dieting'. In earlier years of CARDIA, participants were asked about their history of dieting to lose weight or to retain weight loss (never dieting, formerly dieting, and currently dieting). History of dieting, assessed in Year 0 was associated with the PREF dieting construct assessed in CARDIA Year 10. Thus, while we do not know whether all components of problematic eating behaviors existed in the earlier years, the data about history of dieting in CARDIA Year 0 and the findings from Project EAT suggest that participants with PREF in Year

10 may have endorsed problematic eating behaviors and attitudes in earlier years and carried their PREF score into and past Year 10. Thus this implies the need for future longitudinal studies which examine whether the problematic eating behaviors persist when participants transit from young adulthood to middle-aged adult, and to older adults. More studies should be carried out concerning whether people change their eating behaviors, and if so, why and what causes and triggers the change.

Second, in CARDIA, type 1 and type 2 diabetes were not distinguished, although it is assumed most diabetes in CARDIA was type 2. Third, given the large number of CARDIA participants, most of the diet related variables were based on self-reports. This self-report of dietary intake often results in the possibility of underreporting usual energy intake or overreporting 'socially acceptable' foods, thus improving diet quality. Although the use of the objective carotenoid marker partially mitigates these issues, the possibility of underreporting energy intake and overreporting diet quality must be taken into account when interpreting the results of self-reported dietary variables. Finally, as with all other epidemiological studies, there may be additional confounders or residual confounders which may not have been taken into account.

### 10.3 Findings and Implications for Future Interventions

This thesis explored problematic relationship to eating and food among middle-aged adults, examined whether middle-aged adults with problematic eating behaviors and attitudes had elevated BMI were at greater risk of diabetes and metabolic syndrome, and had worse dietary patterns during 15 years of follow-up. The prevalent disordered eating behaviors and associations among middle-aged adults have several implications. First, the finding that about 60% of the participants endorsed problematic eating behaviors and attitudes (PREF $\geq$1) indicates the public health significance of these behaviors and attitudes and the importance of examining in future studies and intervening for prevention and treatment. The highly prevalent problematic eating behaviors during middle-age imply that researchers should focus on a full spectrum of eating behaviors while medical health professionals need to be sensitive and not overlook those disordered eating behaviors and constructs when screening their patients who are admitted to the hospital for weight related health conditions [211]. Additionally middle-age adults themselves may feel shame in admitting to these problematic eating behaviors or attitudes when seeing a professional and may benefit from support groups or may be in denial about them. These support

groups may help participants to alleviate a certain amount of psychological distress related to eating and food. The lack of accountability and support from family members or close friends can enhance a sense of isolation, which may lead to greater risk of disordered eating behaviors [212]. This lack of social support and isolation might be more strongly associated with participants' eating alone because of shame and stigma accompanied with their eating behavior [213]. While the finding of PREF was shown to be highly prevalent among middle-aged adults, it is important to consider the fact that many of the participants may be actively involved in the workforce. Thus more convenient and readily available and tailored treatments should be considered to meet the unique needs of this population. Thus treatments and interventions for obesity, diabetes, and metabolic syndrome should consider participants, who cannot easily leave their families or their work to attend such interventions. Family and group therapies, support groups, at educational settings, healthcare settings, workplaces, churches, and even at health clubs [211] should be considered, which may promote healthy eating behaviors in our society. Support and education for healthy eating behavior will not only benefit the people with PREF, but may in the long term also create a healthier home environment and society and set a role model for their children or grandchildren.

Second, most of the individual 8 constructs were positively associated with greater BMI and were at greater risk of diabetes and metabolic syndrome. When each individual construct was coupled with other PREF constructs, participants with 2 or more of the aggregated constructs were at greater risk compared to risk associated with any individual construct and was graded by the number of constructs endorsed. The dose-response association between PREF and BMI, risk of diabetes and metabolic syndrome implies that health and well-being related to excess weight among participants with problematic relationship to eating and food are also threatened compared to those who do not endorse any of the disordered eating behaviors. The finding that greater risk of diabetes and metabolic syndrome and were mediated by BMI supports that there is a need to prevent obesity and weight-related health outcomes among participants with PREF. This finding suggests an area where clinicians could intervene, as most self-management programs for diabetes are focused on meal planning and restricting the intake of carbohydrates and do not address the issues related to eating behaviors and attitudes or weight management. Thus it suggests that more emphasis and practical instruction should be given on healthy weight loss and healthy weight gain when people with problematic eating behavior develop diabetes or metabolic syndrome, as we found the risk for diabetes and metabolic syndrome were mainly consequences

of carrying excess weight (presumably largely excess adipose tissue). In addition with greater BMI and greater energy intake, greater consumption of artificially-sweetened beverage illustrates the need of more concrete and actionable ideas and education required for participants with PREF. For example, there should be more research about how artificially-sweetened beverages may lead to greater weight gain in long-term and how artificially-sweetened beverages should not be thought as a substitute for sugar-sweetened beverages. The scientific issues concerning risks and benefits of artificial sweeteners are not all resolved and it is possible that an artificial sweetener does exist which is good for health.

Third, an open question remains between the temporality of problematic relationship to eating and food and BMI. When the change in BMI relative to Year 10 BMI in relation to PREF at Year 10 was examined, such change was greater and graded by PREF score starting in earlier years (CARDIA Year 0 to 7) than in later years, and the association with PREF score was lost in later years (CARDIA Year 15-25). While this analysis may seem to support that 'greater BMI causes PREF', it is reasonable to suppose that PREF and BMI would exist in a feedback loop, with unknown problematic psychosocial issues leading to overeating, which leads to higher BMI, which then leads to increased psychosocial concern and worsening of PREF score. For example, our epidemiologic analysis internal to CARDIA could not discern a situation in which aspects of PREF started in early adolescence or young adulthood, led to substantial weight gain then, followed by mitigation of the effects of PREF by actions that the person took around the time that CARDIA asked about PREF. Although we cannot confirm the origin of these problematic eating behaviors and attitudes within this thesis, this implies that regardless of the origin of the problematic behaviors, a feedback loop may operate between PREF and BMI in middle-aged adults. Thus psychosocial factors must be further investigated to examine whether it drives the loop or mitigates the loop. For example, at in individual level, one's lack of coping skills should be examined whether it is used as a way to relief stress or to feel as if they are in control of their life, which may further trigger problematic eating behaviors and attitudes [214]. Additionally, given that middle adulthood is a stage of life where participants are challenged by unforeseen life transitions in their life (including among many others divorce or other relationship difficulties, employment changes, and issues faced by their children), or may face modern society stressors which may all trigger problematic eating behaviors. Challenges and transitions that middle-aged adults may go through may differ from what adolescents or young adults experience, which may have a different impact on their eating behaviors. Thus, future work should examine whether life

stage related stressors including relationships prior to-or during marriage, divorce, separation, aging body, pregnancy, childbirth, parenting troubles, stress in work or schooling, career difficulties, work environment, work-life balance, retirement, financial strain, parental death, empty-nest, caregiving for their parents or their spouse, emotional and physiological changes brought by menopause, and fears associated with aging, and desire to look younger and slimmer than their age are psychological triggers that may initiate or exacerbate the disordered eating behaviors in middle-aged and older adults [215]. In addition to life-stage related stressors, there is a need to explore whether modern society stressors including competition and fast pace work environments may also trigger or exacerbate the onset of endorsement of problematic eating behaviors and attitudes in middle-aged adults.

Fourth, even though there was an overall increasing risk of developing incident diabetes and metabolic syndrome across PREF categories, it was only those with PREF $\geq$3 points that were significantly at greater risk for diabetes and metabolic syndrome compared to normal eaters. Thus, if there is excess risk in those with PREF 1 or 2 points, it is a lower risk than in those with more PREF points. However, it is an open question whether those with PREF 1 or 2 points tend to progress to a higher PREF score. This finding may imply that although PREF is a risk behavior that places people at greater risk, middle-aged participants who endorse 1 or 2 of the problematic eating behaviors should be the target to intervene and prevent excess weight gain and to prevent from developing diabetes and metabolic syndrome. The finding that PREF affected metabolic syndrome only for 5 to 10 years indicates that there should be more effort focused on young to middle-aged adults, with intervention on their eating behaviors, because diabetes and metabolic syndrome onset is most likely to develop during middle-age.

### 10.4 Directions for Future Studies

Future studies are needed to build on the findings in this thesis. First, with BMI as an indicator of excess weight, participants with PREF had greater BMI compared to normal eaters. However, the location of the excess weight on the body was not identified. Therefore, the finding suggests that future work should include where the excess weight is located at among participants with PREF. If participants with PREF have excess adipose tissue which is located in or around the viscera (visceral adipose tissue) or heart (pericardial adipose tissue), it may further suggest that participants with PREF are at greater risk of inflammation and cardiovascular diseases. Similarly, additional analyses should be conducted with a subset of surgical and natural postmenopausal women, as menopause is a period where metabolism changes and less estrogen is

produced, causing shifts and redistribution of fat that can result in greater abdominal fat [216-217].

Second, there is a need to examine whether the problematic eating behaviors persist in older adults. While many studies of disordered eating behaviors and their associations with weight or general health have been carried out in adolescents [35-38, 74, 82, 209-210] and young adults [2, 12, 34, 39-40, 48, 50-52,58-59, 83, 96, 118-120,150, 72, 203,208], our study adds to the limited number of studies that explore individual and aggregated disordered eating behaviors in middle-aged adults [150,36]. From Project EAT, it is well known that certain disordered eating behaviors persist from young adolescence to young adulthood [35-36]. However, less is known about whether disordered eating behaviors persist between middle-aged adults and older adults or whether the behavior changes accordingly with life course transitions. Therefore, there is a need for future longitudinal studies that are extended to look at problematic behaviors and attitudes in other age groups including older adults. In this regard there is a need to re-administer QEWP-R in CARDIA Year 35 and beyond in order to understand the prevalence of PREF in older years (52-66 yrs) and its association with physical and psychosocial health. Also of interest would be detailed interviews with CARDIA participants who endorsed PREF at Year 10 to better understand whether and how PREF had influenced their lives and perhaps continue to do so. Continuing follow-up, conceivably with physical measures in a clinic, in population based studies of younger adults is also supported by this thesis. Because we do not know whether the problematic eating behavior persists in older adults, or whether the behaviors change over time, longitudinal studies are required to track the change of the behaviors, and if the behaviors change over time, there is a need to know what personal, behavioral, social, and environmental factor drives the changes.

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