CONSTANCY OF THE RELATIONSHIP BETWEEN BMI AND ADIPOSITY BEFORE AND DURING THE CURRENT OBESITY EPIDEMIC

By

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ABSTRACT

Introduction. The prevalence of overweight and obesity has increased substantially over the past two decades, making monitoring of this epidemic a high priority both nationally and globally. Overweight and obesity are most commonly assessed using Body Mass Index (BMI). The correlation between BMI and various measures of adiposity has been shown to be strong and statistically significant, but the constancy of this relationship has not been assessed over time. Data suggest that a reduction in total physical activity has played a central role in the increase in the prevalence of overweight and obesity, making it likely that adiposity has increased even beyond that indicated by BMI. Therefore, it is possible that a given level of BMI represents a higher degree of adiposity in recent years as compared to two decades ago, which would have implications for the assessment of the severity of the obesity epidemic and for strategies for obesity prevention.

Methods. National Health and Nutrition Examination Survey (NHANES) II and III data were compared in order to ascertain whether the relationship between BMI and adiposity has changed over time in the U.S. adult population. Specifically, the statistical interaction between BMI and time in multivariate linear regression models predicting skinfold thickness were used to assess a change in the relationship. In addition, graphical methods illustrating the change in the distribution of BMI and skinfold thickness were used to assess the comparability of the two measures in describing trends in body weight and adiposity in the population.

Results and Conclusions. Overall, skinfold thickness relative to BMI remained relatively constant or declined slightly among women, but increased among normal to overweight men. While there are limitations to the measures used in the analysis, these data suggest that the severity of the overweight epidemic in particular is underestimated when relying solely

on BMI as the indicator of overweight and obesity. Data show that BMI has increased substantially over time, but these results indicate that adiposity may have increased to an even greater degree than body weight. Therefore, using a more direct measure of adiposity to supplement monitoring efforts using BMI may provide a more complete picture of trends in overweight and obesity. In addition, these data also suggest that the nature of weight gain over the past few decades and thus possibly the root causes behind the observed weight gain, vary by gender. Therefore, research, monitoring, and intervention that are sensitive to these potential differences may help to better understand and control the overweight and obesity epidemic.

I. INTRODUCTION

The Overweight and Obesity Epidemic in the United States

The current overweight and obesity epidemic in the United States is well recognized as a serious threat to the population's health due not only to the widespread and numerous health consequences of overweight and obesity but also to the sheer number of people affected (WHO 1997). Both the magnitude and the significance of the epidemic have been well documented by nationally representative surveys. Data from the Behavioral Risk Factor Surveillance System (BRFSS) (Galuska, Serdula et al. 1996; Mokdad, Serdula et al. 1999; Mokdad, Serdula et al. 2000) and the National Health and Nutrition Examination Survey (NHANES) (Flegal, Carroll et al. 1998) show substantial increases in the prevalence of overweight and obesity since the 1980's. NHANES 1999 data indicate that the prevalence of overweight and obesity are 34% and 27%, respectively (NCHS 2000). This means that almost two-thirds of the U.S. adult population are overweight or obese. Obesity prevalence has increased 86% since 1980 and more than doubled since 1962 (Flegal, Carroll et al. 1998; NCHS 2000). [1]

This increase in prevalence can be seen, in various degrees, in virtually all population subgroups, and increases in BMI have been observed not only among overweight and obese groups but also among those of normal weight (Flegal and Troiano 2000). It is also important to note that most of the increase took place since the late 1970s, or, alternatively, between the NHANES II and NHANES III data collection periods (Figure 1). One group of investigators have gone so far as to say that the infiltration of the epidemic among

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[1] These prevalence estimates relied on National Health Examination Survey (NHES, 1960) and NHANES I, II and III data. These data sources are valuable for monitoring trends in overweight and obesity because they contain measured height and weight. Most surveys collect self-reported height and weight, which are subject to reporting bias that becomes more pronounced as weight increases. (Palta, Prineas et al. 1982; Rowland 1990).

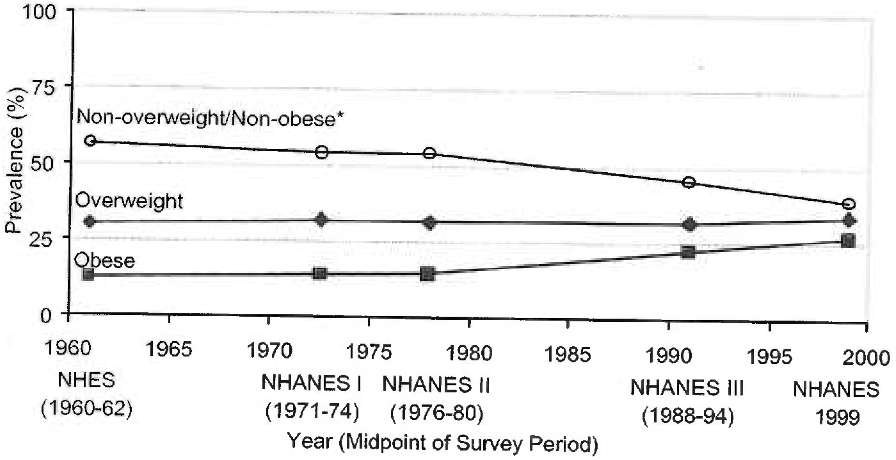

Figure 1. Overweight and obesity prevalence from 1960 to 1999. (Flegal, Carroll et al. 1998; NCHS 2000)
* Non-overweight/obese figures are calculated based on prevalence of overweight and obesity combined.

subpopulations and the rate of increase are more characteristic of an infectious disease epidemic than of a chronic disease epidemic (Mokdad, Serdula et al. 1999).

The increases in the prevalence of overweight and obesity in the U.S. appear to be just one portion of a growing epidemic occurring throughout the world. Parallel trends have been observed globally, particularly in developed countries including Canada (Katzmarzyk 2002; Tremblay, Katzmarzyk et al. 2002), Australia (Booth, Chey et al. 2002) and certain European nations (Prentice and Jebb 1995; Artalejo, Garcia et al. 2002; Visscher, Kromhout et al. 2002), but also in developing nations in which overweight and obesity occur concurrently with undernutrition (Popkin and Doak 1998; Seidell 1998; WHO 1998; Gardner and Halweil 2000). The expansiveness of this epidemic suggests that the root causes of weight gain in recent years are common across cultures and political boundaries. Therefore, trends observed in the U.S. are important for understanding and monitoring overweight and obesity both in the U.S. and other nations.

Individual and Societal Consequences

The health risks, economic costs, and social consequences of the current epidemic have also been explored extensively. It has been shown that obesity is associated with a wide range of diseases including diabetes, hypertension, hyperlipidemia, diabetes mellitus, cardiovascular disease (Jonsson, Hedblad et al. 2002; Paeratakul, Lovejoy et al. 2002), gallbladder disease, and osteoarthritis (Pi-Sunyer 1991; Must, Spadano et al. 1999), disability (Ferraro, Su et al. 2002), and sleep apnea and other respiratory problems (DHHS 1998). Associations have also been found between obesity and various forms of cancer (Pi-Sunyer 1991; Ford 1999). In sum, "obesity is just a first step, a gateway, to the rest of the chronic diseases." - Osman Galal (McLellan 2002)

Furthermore, obesity is associated with increased mortality, and the risk of mortality increases throughout the normal weight to obese and severely obese weight ranges[2] (Manson, Stampfer et al. 1987; Manson, Willett et al. 1995; Troiano, Frongillo et al. 1996; Bender, Trautner et al. 1998; Calle, Thun et al. 1999). The annual number of deaths directly or indirectly attributable to obesity in the United States has been estimated to be between 280,000 and 325,000 (Allison, Fontaine et al. 1999).

Direct and indirect costs related to obesity have been estimated to comprise 4.3% of all health care expenditures in the United States (Allison, Zannolli et al. 1999) and obesity has been shown to be associated with a larger increase in inpatient and outpatient spending and use of prescription medications than either smoking or drinking (Sturm 2002). Finally, the social consequences of obesity are complex and multidirectional, but discrimination,

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[2] The risk associated with underweight remains under debate. Some investigators have shown a U- or J-shaped mortality curve, suggesting that BMI at the lower end of the distribution brings with it increased risk of mortality, while others have demonstrated that these patterns are due to unintentional weight loss due to age and illness. It has also been suggested that the U- or J-shaped curve is the result of two overlapping, linear patterns: an increase in mortality with increased fat mass and with decreased fat-free mass. (Allison, Zhu et al. 2002; Calle, Thun at al. 1999; Manson, Stampfer et al. 1987; Troiano, Frongillo et al. 1996).

social isolation, and lower socioeconomic status (Gortmaker, Must et al. 1993; Stunkard and Sorenson 1993; Wolf and Colditz 1996; Ball, Mishra et al. 2002), especially among women (Laitinen, Power et al. 2002), are associated with obesity.

Causes of Obesity: The Energy Balance Debate

Given the evidence that overweight and obesity prevalence is increasing at an alarming rate and that the health consequences are both wide reaching and substantial, there is little question that the current growing epidemic poses a serious threat both to the health and well being of individuals and to the productivity and sustainability of health systems and society as a whole. It is important, then, to assess the cause of increasing body weight within the U.S. and throughout the world.

Despite the large body of research and considerable debate about the role of metabolic and genetic regulatory factors that may contribute and/or cause obesity, the issue always returns to energy balance. Alternative explanations have been suggested and explored, such as changes in diet quality (White, Porter et al. 2000), frequency of meals (Ruidavets, Bongard et al. 2002), or presence of infection (Dhurandhar 2002). The pervasiveness of the overweight and obesity epidemic in virtually all sub-populations and across cultures, however, suggest that an overriding, common factor or set of factors is responsible for the increase in weight over time. While alternative explanations may have contributed to this trend, it is likely that the contribution is small relative to changes in energy intake and expenditure.

In general, there are three factors considered to play a role in obesity: genetics, diet, and physical activity. While there is plenty of evidence that genetics plays a role in the development of obesity (Weinsier, Hunter et al. 1998; Comuzzie 2002; Segal and Allison 2002) it cannot account for the increase in obesity prevalence over the past couple of decades, since an alteration in the genetic makeup of the population is unlikely to have occurred in such a short period of time. To the contrary, it is likely that traits developed through the millennia that have helped humans survive in harsh environments – such as favoring of energy dense foods and the ability to store fat – have become a liability in modern times. The influence of genetics in the current epidemic most likely lies in individual differences in the ability to compensate (Hill and Melanson 1999) for the so-called "obesogenic environment" (Egger 1997); that is, the ability to control appetite in a culture pervasive with food, and to maintain a physically active lifestyle in a society that favors energy-saving conveniences. A discussion of the influence of energy intake and energy expenditure follows.

Trends in Energy Intake

It has been assumed by most that responsibility for the overweight and obesity epidemic lies with an increase in energy consumption and a decrease in energy expenditure. The placement of soda machines in schools, the "Super Sizing" of fast food meals, and growing restaurant food portions (Critser 2000; Gardner and Halweil 2000; Young and Nestle 2002; Critser 2003) take the brunt of the blame for the "Fattening of America" (Pi-Sunyer 1994). However, data sources vary in the degree to which this assumption is supported.

Sources indicating an increase in total caloric intake include USDA food supply data (Putnam and Allshouse 1999), even after adjustment for spoilage and waste (Putnam 1999), NHANES 24-hour recall data (McDowell, Briefel et al. 1994), and ecologic data on food consumption patterns and portion size. However, there are limitations to the estimates provided by each of these studies. To begin, spoilage and waste adjustment of food supply data likely does not fully account for changes in food consumption patterns, namely the increased waste associated with restaurant meals and deep fat frying of foods (Kantor, Lipton et al. 1997). A similar pattern, in which food supply data appears to increasingly overestimate food intake, has been noted in Japan and other countries, particularly those experiencing economic growth and, therefore, an increasingly complex food supply system (Crane, Lewis et al. 1992).

Likewise, NHANES 24-hour dietary recall data show an increase in calorie consumption over time. NHANES is a periodic survey that provides extensive, nationally representative health data from interviews, questionnaires, physical examinations, and 24-hour dietary recalls. However, comparison of NHANES 24-hour dietary recall data over time is flawed due to methodological changes that systematically biased food intake estimates from the NHANES II to NHANES III study periods. Possibly the most important change was a deliberate effort to obtain more complete 24-hour dietary recalls in the NHANES III interviews, including probing for more detailed information and using a list of frequently omitted foods. Other changes included a greater proportion of dietary recalls performed for weekend days and the use of an automated interview data collection system and a different, possibly more complete, food nutrient database (McDowell, Briefel et al. 1994).

More convincingly, ecologic data show increases in meals eaten away from home, particularly at fast food restaurants, and in the availability of convenience foods. There is also some evidence to suggest that restaurant portion size has increased (Harnack, Jeffery et al. 2000). While these findings in themselves do not necessarily demonstrate increased consumption, food served at restaurants tend to be calorie dense and high in fat (Harnack, Jeffery et al. 2000), and it has been shown that food intake increases in response to larger portion sizes (Rolls, Morris et al. 2002).

Contrary to the evidence cited above, several sources, including United States Department of Agriculture (USDA) survey data (Heini and Weinsier 1997), and Framingham Study data (Posner, Franz et al. 1995) show a decline in average total calories consumed. In addition, many sources show a decline in percent calories consumed from fat (Stephen and Wald 1990; Byers 1993; Heini and Weinsier 1997; Popkin, Siega-Riz et al. 2001), although it has been suggested that this may reflect a shift from visible to invisible fats rather than a true decline in fat intake (Popkin, Siega-Riz et al. 2001). Many sources also show decreases in consumption of high fat foods and alcohol (Breslow, Subar et al. 1997), and increases in fruit and vegetable consumption (Li, Serdula et al. 2000) and reduced-calorie and reduced-fat products (Harnack, Jeffery et al. 2000).

It is possible that apparent declines in food consumption and fat intake are due to increasing reporting bias over time. Heitmann et al show an increase in under-reporting of total caloric intake and fat and/or carbohydrate intake after an intensive, diet-focused health education campaign in Denmark (Hietmann, Lissner et al. 2000). This finding suggests that people tend to under-report those foods that they believe to be unhealthy, a bias that is likely applicable to the U.S. population. In addition, obese individuals tend to under-report to a greater extent than other individuals (Black 1998), so an increase in obesity prevalence would increase the impact of this bias (Heini and Weinsier 1997).

Based on patterns related to food supply data seen in different countries and the biases discussed above, Crane et al indicate that survey data may more accurately reflect real trends than food supply data despite these potential flaws (Crane, Lewis et al. 1992). Trend data showing declines in food intake from the European Union provide additional evidence that a decline in caloric intake simultaneous to an increase in overweight and obesity prevalence is a reasonable finding, regardless of how counter-intuitive it may seem (Prentice and Jebb 1995).

Consideration of the more valid data sources discussed above – survey data showing declines in nutrient intake and ecologic indicators of food consumption showing increases in the purchase of high fat, calorie dense food – suggest that while energy intake has likely played a role in the increase in the prevalence of overweight and obesity, it is probably not the only responsible factor.

Trends in Physical Activity

Data suggest that sedentary lifestyle has decreased (Casperson, Christenson et al. 1986) and reported leisure time physical activity has either increased or remained constant (Brooks 1988; Jacobs, Hahn et al. 1991; CDC 2001) in the U.S. over the past few decades. Physical activity and inactivity are, unfortunately, tremendously difficult to measure in free-living individuals (Troiano, Macera et al. 2001). In addition, these self-reported data are subject to the same "social-desirability" biases (Brooks 1988) as food intake data but are even less quantifiable due to variations in the intensity and duration of physical activity. Moreover, the most easily measured type of physical activity is leisure-time physical activity (LTPA), which excludes both lifestyle physical activity and "incidental movement" (Egger 1997).

Indeed, the American lifestyle seems to take full advantage of technology's energy saving devices at home, at work, and elsewhere, and those modern conveniences can all contribute to decreased energy needs. In an economic analysis of technological change and the increase in obesity, one group found that 60% of the increase in weight between 1976 and 1994 in the U.S. is due to declining physical activity related to technological changes in home and market production (Lakdawalla and Philipson 2002). Data from the European

Union show that while energy intake has declined in recent decades, various indexes of physical inactivity – such as number of automobiles owned per household and hours of television viewing – correspond remarkably well with obesity trends (Prentice and Jebb 1995), providing further evidence that modernization may be a factor in population weight gain. One study in a developing country showed significantly higher levels of overweight and obesity and significantly lower levels of physical activity in urban areas when compared to rural areas (Sobngwi, Mbanya et al. 2002), suggesting that the modern conveniences in urban areas, particularly motorized transportation, may be the driving force behind the increase in overweight and obesity across cultures. While some continue to argue that data do not support the attribution of the obesity epidemic to the modern lifestyle (Sorenson 2000), others have noted that "becoming obese is a normal response to the American environment" (Critser 2000), and that reduction of calorie intake to the level of calorie expenditure may be futile given the "abnormally low" calorie use in modern society (Brown 2000).

In support of these ecologic and observational data, there are much data to suggest that low levels of physical activity are associated with weight gain and the development of obesity (Jebb and Moore 1999), and there is evidence that this association is relatively sensitive. That is, differential weight gain has been shown to be associated with very small differences in physical activity, even within the narrow range of physical activity observed among sedentary individuals (Weinsier, Hunter et al. 2002).

The limitations in the data, the strong association between physical activity and overweight and obesity, and the observations discussed above have led this investigator and many others to the conclusion that a decline in total physical activity is the primary driving force behind the overweight and obesity epidemic (Hill and Melanson 1999; Blair 2002).

Changes in Physical Activity and the Implications for Body Mass Index

Given that we have chosen, in Prentice and Jebb's words, "sloth" over "gluttony" as the primary determinant behind America's overweight and obesity epidemic (Prentice and Jebb 1995), the way in which we measure overweight and obesity becomes important. Most research and monitoring efforts use the World Health Organization's (WHO) definition of overweight and obesity: Body Mass Index (BMI)[3] of greater than or equal to 25 kg/m^2 is defined as overweight, and greater than or equal to 30 kg/m^2 is defined as obese (WHO 1997; WHO 1998). The obesity category is further broken down into three classes of severity: Obese Class I (30.0-34.9 kg/m^2), Class II (35.0-39.9 kg/m^2), and Class III ($\geq$40.0 kg/m^2).

The WHO has recommended the use of BMI as the primary standard measure of overweight and obesity (WHO 1998). The strengths of BMI include high correlation with more direct measures of adiposity, primarily skinfold thickness measurements (Micozzi, Albanes et al. 1986; Willett 1998; Ulijaszek and Kerr 1999). Moreover, contrary to the high inter- and intra-observer variability (Ulijaszek and Kerr 1999) and decline in reliability with increased measurements (Marks, Habicht et al. 1989) associated with skinfold thickness measurement, BMI is easily, reliably, and routinely measured in the field (WHO 1998).

However, BMI may be inadequate for monitoring overweight and obesity over time for at least two reasons: 1) it fails to detect overweight or obesity due to an increase in body fat without a commensurate amount of weight gain, and 2) it fails to detect improvements in overweight and obesity due to increased muscle mass without a commensurate amount of weight loss.

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[3] BMI is calculated as an individual's weight in kilograms divided by the square of their height in meters

First, with a decrease in physical activity, one may see increased adiposity[4] with under-representative weight gain and, therefore, little or no change in BMI. Analysis of fat-free mass index (FFMI) and fat mass index (FMI) at various ages illustrates that FMI increases substantially with age while BMI increases only slightly[5] (Schultz, Kyle et al. 2002). This phenomenon has also been shown in post-menopausal women, in whom abdominal adiposity tends to increase with no associated weight gain, suggesting that waist circumference is a better measure of adiposity in this population (Pelt, Evans et al. 2001). Likewise, BMI has been shown to underestimate obesity as compared to bioelectrical impedance measures (Frankenfield, Rowe et al. 2001) and waist circumference (Booth, Hunter et al. 2000).

Second, BMI may not be able to detect improvements in overweight and obesity trends due to an increase in physical activity. Public health efforts to curb the epidemic will likely emphasize physical activity even more than in the past, but if these efforts are successful, increased physical activity will likely lead to increased muscle mass but not necessarily to commensurate weight loss. While the effects of increased physical activity on body composition independent of body weight are likely to be relatively small, it is important to understand the nature of weight gain and weight loss in the population. Indeed, studies suggest that the benefits of physical activity are maintenance of body weight and increase in fat-free mass rather than a loss in body weight (Kyle, Genton et al. 2002), and that BMI is not related to physical activity (Fentem and Mockett 1998), making BMI inadequate for detecting improvements due to physical activity.

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[4] Adiposity refers to the degree of body fatness independent of body weight.

[5] FMI increased 55% in men and 62% in women; BMI increased 9% in males and 19% in females.

While BMI is strongly correlated with adiposity, the suspected decline in physical activity may have changed the relationship between BMI and adiposity over time. Specifically, one would expect a given BMI to predict higher levels of adiposity in recent years as compared to two decades ago. The goal of this study is to assess whether this expectation is true and to describe how the relationship between BMI and body composition has changed in the U.S. adult population.

SIGNIFICANCE

The ability to monitor overweight and obesity over time is critical for directing public health efforts to curb this epidemic. A measure of overweight and obesity that is consistent with health risks, reliable over time, and capable of measuring changes, is of primary importance in achieving adequate monitoring. BMI is used almost universally in this monitoring capacity but may not meet the third requirement above, so evaluation of the adequacy of BMI as a stable measure of body fatness is essential to research and surveillance in this area. To the investigator's knowledge, assessment of the consistency of the relationship between BMI and adiposity over time or, equivalently, the ability of BMI to show changes in adiposity has not been performed. Furthermore, BMI may underestimate already high estimates of overweight and obesity prevalence; confirmation of this suspicion may prompt a higher level of urgency in intervention efforts.

SPECIFIC AIMS

1) Ascertain whether the relationship between BMI and a Body Fat Index (BFI) composed of skinfold thickness measurements has changed over time in the U.S. adult population.
2) Assess the comparability of BMI and BFI in describing trends in body weight and adiposity over time.

II. MATERIALS AND METHODS

National Health and Nutrition Examination Survey (NHANES)

The National Health and Nutrition Examination Survey (NHANES) is a national survey conducted by the National Center for Health Statistics (NCHS) of the Centers for Disease Control and Prevention (CDC). It utilizes complex, multi-stage, stratified, clustered samples of the United States civilian, non-institutionalized population. The NHANES II sample was composed of 27,801 individuals aged 6 months to 74 years, representing a population of 203 million; NHANES III sampled 33,994 individuals 2 months and older, representing a population of 251 million. Data collected include questionnaire, interview, medical examination, dietary recall, and laboratory data. Household and family questionnaires and in some cases limited physical exams were administered in the home, while the remainder of the data were collected at the Mobile Examination Centers (MEC).

Excluding the NHANES survey currently in progress, three surveys have been conducted since 1970: NHANES I (1971-1975), NHANES II, (1976 to 1980), and NHANES III (1988-1994). Detailed documentation of the data collection and processing procedures involved with these surveys have been published elsewhere (NCHS 1981; NCHS 1992; NCHS 1994).

The current study used data from the NHANES II and NHANES III surveys. These collection periods were chosen because overweight and obesity trends suggest that the environmental and behavioral factors that have contributed to the current epidemic became active during this time period. As referenced earlier in this document, the most pronounced increase in overweight and obesity prevalence took place since the early 1980s, so analysis of NHANES I data would likely have added little to the analysis.

Data Management

NHANES II files were imported into DBMS Copy Version 7 and NHANES III files were imported into SAS Version 8.0 using the SAS script distributed with the data files. Data management was conducted using Microsoft (MS) Access 2000 and SPSS Version 11.0 statistical software. Records within each data file were linked with the subject identification number using MS Access. For both datasets – NHANES II and NHANES III – a single file was created containing the desired variables. Both data files were recoded into a uniform coding scheme and merged within MS Access. Variables to be included in the merged data files were determined based on the relevance to the current study and the comparability between surveys.[6] These files were exported from MS Access and imported into SPSS. Additional recoding, collapsing of categories, and other data management issues that came up during data analysis were performed using SPSS.

Study Design

Study Population. This analysis was limited to adults aged 20-74 years. This age range was based on both comparability between surveys and sampling strata. First, NHANES III sampled individuals older than 74 years but NHANES II did not, so older adults could not be included in this analysis. Second, the stratified sampling design used the young adult age groups of 12-19 years and 20-29 years. To be consistent with the survey sampling design, adult age was defined as 20 years and older rather than 18 years and older.

Second, only individuals examined in the MEC were included in analysis. In both surveys, anthropometric measurements were taken during the physical exam, most of which were performed at a MEC. The NHANES III protocol allowed for limited home

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[6] For a detailed discussion of the inclusion and exclusion of variables in the analysis, refer to sections on the primary independent variables, biologic control variables, and physical activity and nutrient intake variables later in this document.

examinations that included some anthropometric measurements, but these measurements did not include subscapular skinfold, one component of the primary dependent variables in this study.

Third, women with confirmed pregnancy at the time of interview or exam were excluded from this analysis. Women for whom pregnancy status was unknown were not excluded. 2% and 0.9% (un-weighted data) of females age 20-74 years had confirmed and unknown pregnancy status, respectively, so the proportion of women with unknown pregnancy status and who are actually pregnant to the extent that body weight would be affected was probably very small and was unlikely to affect the analysis.

Dependent Variable: Skinfolds Thickness. The dependent variable was a body fat index (BFI) composed of the sum of triceps and sub-scapular skin folds measured in millimeters. BFI was interpreted as an index for overall adiposity, and calculation of percent body fat from BFI was not attempted. It is important to note that the purpose of this study is not to develop models to predict skinfolds from BMI, but rather to assess the relationship between BMI and a presumably meaningful indicator of adiposity at two points in time.

Subsequent to the initial analysis, it was discovered that while body measurement procedures did not change substantially between the two study periods, Lange skinfold thickness calipers were used in NHANES II while Holtain calipers were used in NHANES III. One difference between these skinfold calipers is that the maximum skinfold thickness measurement is larger for Lange calipers than Holtain calipers. More problematic, due to differences in caliper-jaw surface area and spring tension, skinfold thickness measurements made with Holtain calipers tend to be smaller than those made with Lange calipers (Ulijaszek and Kerr 1999).

Due to the difference in skinfold caliper capacity, large skinfold thickness measurements were recoded for consistency. In NHANES III, skinfold thickness measurements of greater than 50 millimeters were coded as "too large for caliper," but NHANES II data contains measurements of up to 65 millimeters. NHANES III measurements coded as too large for the skinfold caliper were recoded as 50 millimeters; likewise, NHANES II measurements greater than 50 millimeters were recoded as 50 millimeters to be consistent with the NHANES III data. Among the study population defined in the previous section, the un-weighted proportions of triceps and subscapular skinfold thickness greater than 50 millimeters was 1.0% and 1.7% in the NHANES II data, respectively, and 2.0% and 2.6% in the NHANES III data, respectively. These differences are consistent with the overall increase in skinfold thickness. The truncation of these measurements at 50 millimeters did not have a substantial impact on the distribution of the outcome variable. These recoded measurements were used in both the original and caliper-adjusted analyses (described below).

Table 1. Multiplication factors used for adjusted skinfold thickness measurements

Gender	Skinfold	Multiplication Factor
Males	Triceps	1.117
	Subscapular	1.054
Females	Triceps	1.076
	Subscapular	1.046

Differences in caliper-jaw surface area and spring tension between the two types of skinfold calipers was addressed by adjusting NHANES III data to be more consistent with skinfold thickness measured with the Lange caliper. To adjust NHANES III skinfold thickness measurements, the recoded values described above were increased proportionally by multiplying by the constants listed in Table 1. Multiplication factors were based on gender specific mean differences in skinfold thickness measurements taken with Lange and Harpenden calipers as reported by Gruber et al (Gruber, Pollack et al. 1990). Harpenden calipers have been shown to be similar to Holtain calipers (Lohman, Pollack et al. 1984). All analyses were repeated using these adjusted values, referred to as "caliper-adjusted" throughout this thesis. The impact of this method of adjustment on the variability in skinfold thickness measurements and ultimately on statistical tests between NHANES II measurements and caliper-adjusted NHANES III measurements are recognized, so these adjusted analyses were used as a tool to estimate the impact of difference in skinfold calipers on the results.

The sum of triceps and subscapular skinfolds (both original and caliper-adjusted) was transformed to meet normality assumptions as closely as possible and then scaled to facilitate interpretation of regression coefficients and variability. Natural log, square root, and inverse transformations were considered, but the natural log transformation achieved a distribution that most closely approximated the normal distribution. However, this transformation condensed the distribution substantially, making it difficult to interpret the values of coefficient estimates, so it was multiplied by a factor of ten. BFI, therefore is defined as

$$\text{BFI} = 10^{*}\ln(\text{triceps skinfold} + \text{subscapular skinfold}).$$

Other investigators have used summed skinfold measurements in general and triceps and subscapular skinfolds in particular as indicators of adiposity. The sum of five or six skinfolds has been used as an indicator of overall subcutaneous adiposity (Katzmarzyk, Malina et al. 1999; Ball, Owen et al. 2001; Fortier, Katzmarzyk et al. 2002; Katzmarzyk, Craig et al. 2002), but unfortunately triceps and subscapular skinfolds are the only two skinfold measurements in common between the NHANES II and NHANES III examination protocols. However, some early body composition studies relied on the sum of only two skinfold measurements (Willett 1998), and other investigators have more recently used these two particular skinfold measurements exclusively in their studies of body composition. For example, Allison et al used the sum of the z-scores of triceps and subscapular skinfold measurement as an indicator of fat mass (Allison, Zhu et al. 2002), and Gillum et al used triceps skinfold as an index for peripheral adiposity and sub-scapular skinfold as an index for truncal adiposity (Gillum, Mussolino et al. 2001). Aghdassi et al calculated percent body fat using the logarithm of the sum of triceps and subscapular skinfold thicknesses (Aghdassi, Tam et al. 2001).

BFI was assigned as the dependent variable due to the high variability and low reliability associated with skinfold thickness measurements. Since variability is built into statistical modeling methods, the reliability of skinfold thickness measurements appears to be adequate for multivariate analysis (Marks, Habicht et al. 1989). In addition, intra-observer reliability is greatly improved by using the mean of two duplicate measurements, as NHANES does (Marks, Habicht et al. 1989).

In addition to the difference in skinfold calipers, other limitations of skinfold thickness measurements specific to this study involve other potential sources of bias between the two studies. The first source of potential bias between studies results from the high degree of inter-observer variability, particularly between studies conducted almost a decade apart from the other (Marks, Habicht et al. 1989). Other sources of between-study bias are slight differences in the protocols used to collect skinfold thickness measurements during the two study periods. Differences include the following: 1) skinfold thickness was measured to the nearest 0.5mm in NHANES II, 0.1mm in NHANES III, 2) error tolerance between replicate measurements was set at 1mm in NHANES II and 2mm for every 10mm measured in NHANES III, and 3) replicate measurements were taken by the same technician in NHANES II but could be taken by the same or a different technician in NHANES III (NCHS 1976; NCHS 1988). These issues are likely to affect the variability of the measurements but there is no reason to believe that they would lead to biased estimates.

Primary Independent Variables. The primary independent variables were BMI, defined as weight in kilograms divided by the square of height in meters (kg/m^2), and NHANES survey period (II or III). BMI was computed to the accuracy allowed in SPSS and analyzed as a continuous variable. Survey period was analyzed as a categorical variable as an indicator of time. NHANES II was conducted in one phase, and NHANES III was conducted in two phases, the first from 1988-1991 and the second from 1991-1994. However, the two NHANES III survey phases do not comprise two independent samples, so conventional methods cannot be used for statistically comparing the two phases. Therefore, NHANES III data were treated as one time point and, combined with NHANES II data, a total of two time points were used for comparison.

Biologic Control Variables. Body fat distribution and body density and, therefore, the relationship between BMI and other measures of adiposity have been shown to vary with certain biologic factors. Body composition and body fat distribution differ greatly by gender (Deurenberg, Weststrate et al. 1991; Ley, Lees et al. 1992; Gallagher, Visser et al. 1996; Gallagher, Heymsfield et al. 2000; Jackson, Stanforth et al. 2002; Perissinotto, Pisent et al. 2002), so all analyses were conducted separately for males and females.

In addition, adiposity and body fat distribution change with age (Deurenberg, Weststrate et al. 1991; Ley, Lees et al. 1992; Gallagher, Visser et al. 1996; Jackson, Stanforth et al. 2002; Perissinotto, Pisent et al. 2002), and vary by race (Deurenberg, Yap et al. 1998; Gallagher, Heymsfield et al. 2000; Okosun, Tedders et al. 2000; Fernandez, Heo et al. 2002; Jackson, Stanforth et al. 2002), particularly for various Asian groups (Lin, Lee et al. 2002) and African Americans (Zillikens and Conway 1990), so age and race were considered the primary control variables.

Age was analyzed as a continuous variable, but selected analyses present data using age categories. Categorization of age followed the recommendations made in the NHANES analytical and reporting guidelines, using the age groups 20-29, 30-39, 40-49, 50-59, and over 60 years of age (NCHS 1996). As a result, isolation of older age groups (i.e., 70-74 years) was not possible despite the special considerations required for examination of body composition among the elderly population.

The racial and ethnic categories used in NHANES II and III were not comparable, so examination of racial categories more detailed than white, black, and other was not possible. Further, NHANES documentation recommends that analysis using this race variable be limited to comparisons of white versus black race or white versus other race (including black race) due to insufficient cell sizes in the "other" race category (NCHS 1996), so this analysis used the coarse breakdown of white versus non-white race.

Physical Activity and Nutrient Intake. As described above, physical activity likely impacts the relationship between BMI and adiposity in any setting, so looking at the effects of physical activity in this analysis was considered to be important. Unfortunately, physical activity assessment questions were not comparable across surveys. However, a limited set of social indicators were considered to control for differences in physical activity to the extent possible. Race, age, education, and income have been shown to be related to physical activity or sedentary lifestyle in most studies (Casperson, Christenson et al. 1986; CDC 1993; Casperson and Merritt 1995; CDC 2000; Schoenborn and Barnes 2002). Others have found marital status and degree of urbanicity (Schoenborn and Barnes 2002) and health status and smoking status (Norman, Bellocco et al. 2002) to also be important predictors of physical activity.

Therefore, in addition to the biologic variables described above, the social indicators used in the present study included education level, poverty status, health status, and marital status[7]. Poverty status was the only income variable appropriate for trend analysis because it is "relatively" standardized for inflation and other factors (NCHS 1996). Current tobacco use and current and past cigarette use[8] were assessed because of their association with physical activity and their effects on overweight and obesity (Williamson, Madans et al. 1991; Flegal, Troiano et al. 1995; Manson, Willett et al. 1995) through behavioral differences (Williamson, Madans et al. 1991) and increase in metabolic rate caused by nicotine (Hofstetter, Schultz et al. 1986; Perkins, Epstein et al. 1989).

As noted previously, nutrient intake data are not comparable between NHANES II and NHANES III data due to changes in the dietary recall procedures that likely contributed to the apparent increase in caloric intake (McDowell, Briefel et al. 1994). However, nutrient intake data can be analyzed as a covariate because changes in procedure are controlled for by including survey period in the model. Therefore, total caloric intake, and percent calories from fat and protein were potential control variables in the analysis.

Statistical Software and Sample Design Specifications

As noted above, both surveys use a complex sampling scheme. In order to account for the sampling design, all statistical analyses were conducted using SUDAAN for Windows version 8.0. Appropriate weights were applied in order to correct for unequal sampling probabilities and non-response bias and to post-stratify estimates to U.S. population estimates. Since this study was limited to individuals examined in the Mobile Examination

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[7] Employment status was not included in analysis because it was not available for individuals under 25 years of age in the NHANES II data set. Urban versus rural residence was not included in this analysis because the NHANES II and NHANES III used different definitions.

[8] Categorization of pipe and cigar smoking into current, former, and never groups was not possible due to the structure of the NHANES II question sequence.

Center (MEC), sample weights specific to this subgroup within each survey were used in analysis. Combining data from two surveys did not require any modification of the sample weights.

However, strata and Primary Sampling Unit (PSU) codes were duplicated after merging the two data sets. Strata and PSU codes were de-duplicated by adding the largest value from NHANES II to each NHANES III strata code and PSU code, respectively. These two de-duplicated codes were specified in the SUDAAN NEST statement. Validation of this method was performed by calculating 1) the BMI mean for each survey in SPSS, 2) the BMI mean and standard error for each survey separately in SUDAAN using the original strata and PSU codes, and 3) the BMI mean and standard error in SUDAAN using the de-duplicated strata and PSU codes and stratifying by survey number. The point estimates matched for all three methods and the standard errors matched for the second two methods, as expected.

Predicted values and their variance were calculated by performing matrix multiplication of SUDAAN-generated coefficient and variance-covariance matrices in S-Plus Student Version 4.5. These values were used to calculate ratios of predicted values and 95% predicted intervals of the ratios.

Statistical Analysis

Due to the biologic differences between men and women, the relationship between BMI and BFI was assessed specific to each gender. That is, all analyses were performed separately for males and females, consistent with many other investigators (Micozzi, Albanes et al. 1986; Deurenberg, Weststrate et al. 1991; Gallagher, Visser et al. 1996; Deurenberg, Yap et al. 1998; Frankenfield, Rowe et al. 2001; Jackson, Stanforth et al. 2002; Perissinotto, Pisent et al. 2002). Preliminary analysis included exploration of relationships between the dependent and independent variables using t-tests, chi-square, and any other appropriate statistical tests.

Linear Regression Modeling. To assess whether the relationship between BMI and BFI has changed over time, linear regression was used to model BFI as a function of BMI and survey phase. Statistical significance of the interaction between BMI and survey phase was used to indicate if the relationship between BMI and BFI has changed over time. For main effects, statistical significance was set at $p<0.05$; significance for interactions was set at $p<0.10$. Diagnostics included the creation and assessment of residual plots for residual distribution, curvilinear relationships, and outliers, and remedial measures included transformation of variables and exclusion of outlying cases that impacted parameter estimates. Square root, natural log, and inverse transformations were considered for continuous independent variables; the most appropriate choice was selected based on residual plots, R^2 values, and existing literature, if available. A case was considered to impact parameter estimates if its removal resulted in a change of more than 2% in one or more coefficient estimates. Unadjusted R^2 was the primary measurement of goodness of fit for the regression model.

Linear regression modeling was performed in two steps. First, "biologic" models were built, containing only survey period, BMI, race, age, and any significant interactions. All possible interactions were considered in these models, and the BMI*survey period interaction term was forced into the model. Appropriate diagnostic and remedial measures were performed at this point; therefore, the biologic models can be treated as final models that control for biologic variation in the relationship between BMI and adiposity due to gender, age, and race. Transformations, interactions, and excluded cases established for the biologic models were carried over to the expanded model.

Expanded models were developed with the remaining variables – social indicators, tobacco use, and dietary intake variables – as potential candidates to be added to each biologic model. Each candidate variable was added one at a time to the biologic model; grouping of categorical candidate variables was assessed and modified at this time. All variables with Wald significance in the multivariate regression model of $p<0.0001$ were then added to the biologic model; variables were removed if they became non-significant. Next, all variables with Wald significance of $0.0001=p<0.05$ were added to the model, then removed if they became non-significant. Transformations of continuous variables were based on residual plots. Interactions of each new covariate with survey period and with BMI were attempted. Diagnostics and remedial measures were then performed for a final time.

Biologic and expanded models were developed for males and females first using BFI, then using the caliper-adjusted BFI (BFI$_a$). Caliper-adjusted analyses were guided by results from the original models, but the significance levels and scaling of covariates were verified, and diagnostics and remedial measures were applied to the caliper-adjusted models.

Descriptive Analysis. Additional analyses were descriptive graphical comparisons of increased adiposity and weight as determined from skinfolds and BMI, respectively, over time. These analyses were important for assessing how comparable the two measures are at the population level and provided additional information about the nature of the increase in body weight between the two time periods.

Flegal and Troiano conducted an analysis of the change in distribution of BMI between the NHANES II and III study periods using Tukey mean-difference plots. A description of mean-difference plots in general and Flegal and Troiano's methods in specific are discussed in their findings (Flegal and Troiano 2000).

Briefly, mean-difference plots are a way to display differences between two distributions, much like an observed distribution is compared to an expected normal distribution in a normality plot. In a mean-difference plot, each data point is defined by the mean and the difference between a given percentile from the two distributions: the x-value is the mean value calculated from a given percentile from the two distributions, and the y-value is the difference between the two percentile values. For example, if the 90th percentile is 100 in one distribution and 110 in the other, the corresponding (x,y) data point will be (105,10), with 105 calculated from the mean of 100 and 110, and 10 calculated from the difference between 110 and 100. A shift from one distribution to the other is indicated by data points above or below the x-axis, and a change in the shape of the distribution is indicated by variation in the distance from the x-axis.

In Flegal and Troiano's study and the current analysis, the two distributions compared are body measurement data from NHANES II and III. This study replicates their analysis of the change in the distribution of BMI and compares the results to mean-difference plots generated from skinfold thickness measurements. Even percentiles were calculated from untransformed, weighted data using SUDAAN. Skinfold measurements recoded as described earlier in this section were used in this component of the study.

III. RESULTS

Descriptive Characteristics

The study population was comprised of 26,180 participants that met the inclusion criteria[9]: 12,479 males (5604 from NHANES II, 6875 from NHANES III) and 13,701 females (6161 from NHANES II, 7540 from NHANES III). Of those, 95.8% of males and 95.4% of females had complete data for height, weight, and triceps and subscapular skinfold thickness.

Descriptive characteristics are shown by gender and survey period in Table 2. Among males and females, the NHANES III populations had higher BMI and were more educated, less likely to be married or smoke tobacco products, and more likely to report Good or Very Good health status than the corresponding NHANES II population ($p<0.0001$). There was no difference in average age, but it should be noted that the age distribution was truncated at 74 years as a result of the sample design for NHANES II and of exclusion of individuals older than 74 years in analysis for NHANES III. Average total calories consumed increased by approximately 235 and 275 calories in males and females, respectively ($p<0.0001$). Average percent calories consumed from fat and protein decreased by approximately 2.6-2.7 percentage points and 0.6 percentage points, respectively, in both males and females ($p<0.0001$). These trends in nutrient intake are consistent with the change in nutrient recall procedures discussed earlier.

Average subscapular skinfold thickness increased by 7.8% in males ($p<0.0001$) and average triceps skinfold decreased by 3.5% in females ($p=0.0091$); there was no significant change in average triceps skinfold thickness among males or average subscapular skinfold thickness among females ($p>0.10$). The sum of the two skinfold thickness measurements

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[9] These figures are reported from unweighted data representing approximately 295,480,471 individuals.

Table 2. Characteristics of NHANES II and III adult survey populations[a] by gender and survey

	MALE			FEMALE		
	(Mean ± SE) or %			(Mean ± SE) or %		
	NHANES II	NHANES III	p[b]	NHANES II	NHANES III	p[b]
Age	42.03 ± 0.33	41.81 ± 0.38	0.6738	42.98 ± 0.32	43.01 ± 0.41	0.9452
Race (White)	87.73%	84.71%	0.145	86.82%	83.31%	0.0473
Triceps[c] (mm)	13.16 ± 0.14	13.31 ± 0.15	0.4556	25.33 ± 0.25	24.43 ± 0.22	0.0091
Subscapular[c] (mm)	17.90 ± 0.18	19.30 ±0.17	<0.0001	21.61 ± 0.29	22.31 ± 0.33	0.1174
Skinfold Sum[c] (mm)	31.05 ± 0.30	32.28 ± 0.25	0.0022	46.94 ± 0.53	46.39 ± 0.53	0.4563
BFI[cd]	33.25 ± 0.09	33.95 ± 0.08	<0.0001	37.49 ± 0.11	37.54 ± 0.12	0.7367
Triceps[c] (mm) – Adj[e]	13.16 ± 0.14	14.86 ± 0.17	<0.0001	25.33 ± 0.25	26.28 ± 0.24	0.0085
Subscapular[c] (mm) – Adj[e]	17.90 ± 0.18	20.34 ±0.18	<0.0001	21.61 ± 0.29	23.33 ± 0.34	0.0003
Skinfold Sum[c] (mm) – Adj[e]	31.05 ± 0.30	34.85 ± 0.27	<0.0001	46.94 ± 0.53	46.24 ± 0.56	0.0037
BFI[cd] - Adj[e]	33.25 ± 0.09	34.72 ± 0.08	<0.0001	37.49 ± 0.11	38.14 ± 0.12	0.0001
Height (cm)	175.46 ±0.16	175.84 ±0.15	0.0905	161.72 ± 0.11	162.25 ±0.14	0.0046
Weight (kg)	78.52 ± 0.20	82.54 ±0.38	<0.0001	65.72 ± 0.29	69.72 ±0.41	<0.0001
BMI (kg/m^2)	25.48 ± 0.07	26.63 ± 0.11	<0.0001	25.16 ± 0.11	26.49 ± 0.16	<0.0001
Total Calories	2457.84 ± 26.23	2693.02 ± 28.01	<0.0001	1515.45 ± 12.40	1790.70 ± 16.06	<0.0001
% Calories from Fat	36.67 ± 0.19	33.91 ± 0.29	<0.0001	35.94 ± 0.17	33.31 ± 0.24	<0.0001
% Calories from Protein	16.04 ± 0.10	15.37 ± 0.11	<0.0001	16.00 ± 0.09	15.39 ± 0.10	<0.0001
Poverty (Pov Indx >=1.0)	8.61%	10.63%	0.0393	12.86%	14.07%	0.2763
Education			0.0001			<0.0001
<HS	30.81%	24.02%		32.06%	22.26%	
HS	29.21%	31.37%		37.04%	37.20%	
>HS	39.98%	44.61%		30.90%	40.54%	
Marital Status			0.0003			<0.0001
Married/Living as Married	74.11%	70.67%		65.26%	63.85%	
Previously Married	7.90%	9.72%		21.90%	21.55%	
Never Married	17.91%	19.61%		12.84%	14.60%	
Health			<0.0001			<0.0001
Excellent	29.80%	22.19%		24.56%	19.73%	
Very Good	27.11%	32.34%		27.35%	30.76%	
Good	26.81%	32.56%		29.14%	32.96%	
Fair	11.05%	10.45%		14.03%	13.74%	
Poor	5.23%	2.47%		4.92%	2.80%	
Smoke Tobacco	49.20%	36.05%	<0.0001	33.46%	26.93%	<0.0001
Smoke Cigarettes	40.95%	33.19%	<0.0001	33.35%	26.87%	<0.0001

[a] Populations included males and non-pregnant females age 20-74 years who completed a physical examination in the Mobile Examination Center (MEC).

[b] p-values indicate differences between NHANES II and NHANES III populations within each gender as determined by the independent t-test for continuous variables and Chi-Square test for homogeneity for categorical variables.

[c] Skinfold measurements were recoded for consistency: measurements over 50mm were recoded as 50mm.

[d] BFI=10*ln(triceps skinfold + subscapular skinfold)

[e] "Adj" indicates NHANES III skinfold measurements adjusted for differences in skinfold calipers. NHANES II values were not caliper-adjusted, so these values are identical to the corresponding non-adjusted skinfold measurements.

increased among males (p=0.0022) but not among females. In contrast, all mean caliper-adjusted skinfold measurements increased from the NHANES II to NHANES III study periods in both males and females (p<=0.01). The sum of two caliper-adjusted skinfold measurements increased by 12.2% in males (p<0.0001) and 1.5% in females (p=0.0037).

Regression Models – Males

Biologic Model. For both males and females, the biologic models served to assess the differential relationship between BMI and BFI with survey period after controlling for race and age, both of which have been shown to be important factors in the prediction of body composition. This differential relationship was assessed based on the magnitude and significance of the interaction between BMI and survey period.

Table 3. Biologic Model (Outcome=BFI) – **Males**

Variable	Coeff (b)	SE(b)	p-value
Intercept	59.6890	0.7484	<0.0001
1/BMI	-658.5188	18.1278	<0.0001
Survey (Ref: NHANES II)	-4.0098	0.4616	<0.0001
1/BMI*Survey	90.5713	10.0421	<0.0001
Age	-0.0576	0.0143	0.0001
Age*1/BMI	1.4598	0.3513	0.0001
Race (Ref: White)	1.4285	0.4595	0.0026
Race*1/BMI	-35.3343	11.8261	0.0037
Age*Survey	0.01115	0.0041	0.0069

Notes: $R^2 = 0.6171$; Excludes 3 cases based on regression diagnostics

Table 4. Caliper Adjusted Biologic Model (Outcome=BFI_a) - **Males**

Variable	Coeff (b)	SE(b)	p-value
Intercept	59.7430	0.7455	<0.0001
1/BMI	-659.8904	18.0202	<0.0001
Survey (Ref: NHANES II)	-3.2928	0.4656	<0.0001
1/BMI*Survey	92.1673	10.0612	<0.0001
Age	-0.0580	0.0145	0.0001
Age*1/BMI	1.4680	0.3561	0.0001
Race (Ref: White)	1.4567	0.455	0.0020
Race*1/BMI	-36.4071	11.5832	0.0023
Age*Survey	0.0112	0.0042	0.0089

Notes: $R^2 = 0.6262$; Excludes 5 cases based on regression diagnostics

Parameter estimates for the biologic model for males are presented in Table 3. BMI, survey period, age, and race were all significant in this biologic model, and there were significant interactions between BMI and survey, BMI and age, BMI and race, and age and survey. Three-way interactions were attempted but were not significant. Results from the caliper-adjusted biologic model for males are presented in Table 4 and are discussed in the following section.

A curvilinear relationship between BMI and BFI was found in models for both males and females (results for females are presented in the next section); the inverse transformation of BMI was used, which is consistent with the findings from Gallagher et al regarding prediction of body fat from BMI (Gallagher, Heymsfield et al. 2000). Age effects were linear in both models.

It is important to note that the coefficients related to BMI in all models for males and females are estimates based on the inverse of BMI. For example, $b_{1/BMI} = -658.52$ in Table 3 indicates that higher values of 1/BMI predict lower values of BFI. However, large values of BMI correspond with small values of 1/BMI. Therefore, the reduction in BFI associated with higher levels of 1/BMI is equivalent to the elevation of BFI with higher levels of BMI. Likewise, a positive interaction term involving BMI such as $b_{survey*1/BMI} =$ 90.57 in Table 3 indicates that for the NHANES III population, the slope of the BFI vs. *1/BMI* curve is *larger* than the same curve for the NHANES II population. This is equivalent to stating that the slope of the BFI vs. *BMI* curve is *smaller* for the NHANES III population as compared to the NHANES II population.

Figure 2 plots predicted skinfolds sum against BMI (both transformed back to their original scaling), illustrating this interaction of BMI with survey period. Over the majority of the BMI distribution, the predicted skinfold sum for a given BMI is lower for NHANES III than NHANES II, and the magnitude of this difference is proportional to BMI. For lower levels of BMI, predicted skinfold thickness are slightly higher for NHANES III than

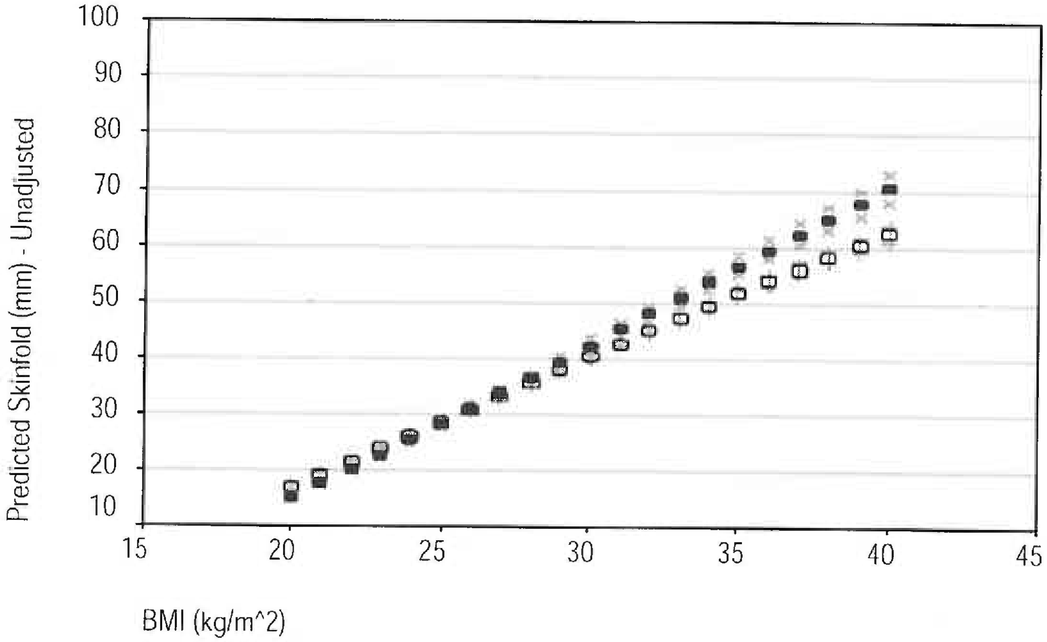

Figure 2. Predicted skinfold sum at select levels of BMI - **Males**.
Based on the model presented in Table 3. BMI and BFI were transformed back to their original scaling of kg/m² and mm, respectively. Age set to an approximate mean (45 years); race set to 0.5.
●=Predicted value for NHANES II, ×=95% prediction interval for NHANES II
○=Predicted value for NHANES III, +=95% prediction interval for NHANES III

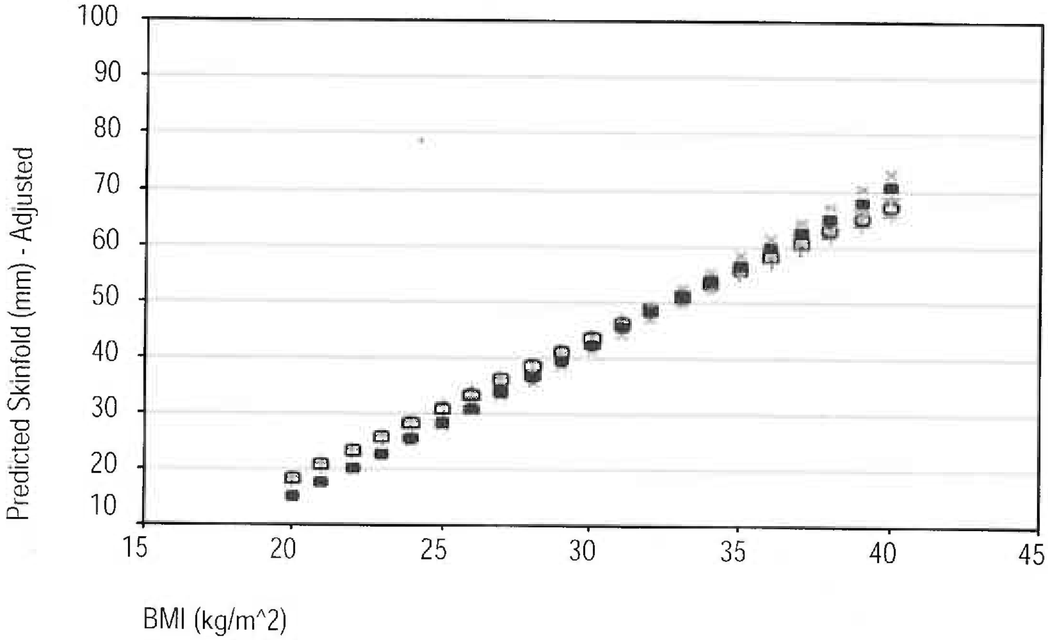

Figure 3. **Caliper Adjusted** Predicted skinfold sum at select levels of BMI - **Males**.
Based on the model presented in Table 4. BMI and BFI were transformed back to their original scaling of kg/m² and mm, respectively. Age set to an approximate mean (45 years); race set to 0.5.
●=Predicted value for NHANES II, ×=95% prediction interval for NHANES II
○=Predicted value for NHANES III, +=95% prediction interval for NHANES III

NHANES II. The BMI at which predicted skinfold thickness measurements for NHANES II become smaller than those for NHANES III (the intersection of the two curves) is 25.8 kg/m^2 at age 45, though this value varies with age, as shown in the expanded model.

The biologic model accounted for approximately 61.7% of the variability in BFI ($R^2 = 0.6171$), as compared to 60.7% for the model containing only BMI and intercept, 60.7% for the model containing BMI, survey, and intercept, and 61.0% for the model containing BMI, survey, BMI*survey, and intercept. These results indicate that BMI explains most, if not all, of the variability in BFI, and the remaining variables such as age and race contribute little to the R^2 value in this model.

Caliper-Adjusted Biologic Model. In order to estimate the trends that might have been observed if the same skinfold caliper was used for both the NHANES II and NHANES III study periods, NHANES III skinfold thickness values were adjusted upward to account for the smaller measurements expected with the Holtain skinfold caliper. Caliper-adjusted BFI (BFI_a) was calculated based on these adjusted measurements.

The biologic model for males based on BFI_a (Tabnle 4) was identical to that based on BFI (Table 3). The fitted values were also similar, except that the estimated coefficient for survey period was still negative but closer to zero and the estimated coefficient for the survey period*BMI interaction was smaller than that based on BFI. These two differences magnified slightly the increase in predicted skinfold from NHANES II to NHANES III through the lower portion of the BMI distribution and diminished the decrease in skinfold through the upper portion of the BMI distribution. Compared to the original biologic model, the intersection of the two curves occurs at a larger BMI, from 25.8 kg/m^2 in the original model (Figure 2) to 33.0 kg/m^2 in the caliper-adjusted model (Figure 3) among males 45 years of age. Further, the decreases in predicted skinfold thickness became non-significant in the caliper-adjusted model.

Table 5. Expanded Model (Outcome=BFI) - **Males**

Variable	Coeff (b)	SE(b)	p-value
Intercept	60.9502	0.8147	<0.0001
1/BMI	-659.3242	18.5395	<0.0001
Survey (Ref: NHANES II)	-3.8694	0.4592	<0.0001
1/BMI*Survey	90.6770	10.0826	<0.0001
Age	-0.0649	0.0149	<0.0001
Age*1/BMI	1.6126	0.3602	<0.0001
Race (Ref: White)	1.4158	0.4552	0.0026
Race*1/BMI	-34.1130	11.6316	0.0044
Age*Survey	0.0082	0.0041	0.0499
SQRT(Total Calories)	-0.0241	0.0035	<0.0001
% Calories from Fat	0.0085	0.0039	0.0314
Current Cigarette Smoker	-0.3595	0.0713	<0.0001
Education (Ref: >=HS)	-0.5794	0.0981	<0.0001

Notes: $R^2 = 0.6243$; Excludes 3 cases based on regression diagnostics

Table 6. Caliper Adjusted Expanded Model (Outcome=BFI_a) - **Males**

Variable	Coeff (b)	SE(b)	p-value
Intercept	60.9980	0.8087	<0.0001
1/BMI	-660.0920	18.3653	<0.0001
Survey (Ref: NHANES II)	-3.1753	0.4657	<0.0001
1/BMI*Survey	92.8607	10.1468	<0.0001
Age	-0.0639	0.0148	<0.0001
Age*1/BMI	1.5861	0.3603	<0.0001
Race (Ref: White)	1.4320	0.4515	0.0021
Race*1/BMI	-34.8728	11.4011	0.0030
Age*Survey	0.0079	0.0041	0.0613
SQRT(Total Calories)	-0.0242	0.0035	<0.0001
% Calories from Fat	0.0082	0.0039	0.0411
Current Cigarette Smoker	-0.3510	0.0712	<0.0001
Education (Ref: >=HS)	-0.5882	0.0959	<0.0001

Notes: $R^2 = 0.6334$; Excludes 5 cases based on regression diagnostics

Expanded Model. Expanded models were developed in order to assess the impact of nutrient intake and some social factors on the parameters of interest (b_{BMI}, b_{survey}, and $b_{BMI*survey}$). These social factors are included because they may help to control for differences in physical activity between the two study periods.

The expanded model for males is described in Table 5. In addition to the variables included in the biologic model, total calories consumed, percent calories consumed from fat, current cigarette use, and education were significantly associated with BFI. Poverty, health, and marital status were not statistically significant so they were excluded from the model. Results from the caliper-adjusted expanded model for males are presented in Table 6 and discussed in the next section.

Total calories consumed were better modeled as the square root. Interactions between BMI and survey with the additional covariates were considered but were not significant. These additional variables did not explain much more variability than the biologic model ($R^2 = 0.6243$ versus 0.6171)[10], and controlling for them did not substantially impact the magnitude or significance of any of the estimates in the biologic model.

Impacts of nutrient intake and social variables on BFI were small. After controlling for BMI, higher total calories consumed predicted lower BFI, while higher percent calories consumed from fat predicted higher BFI. Current cigarette use and less than high school education was associated with lower BFI. Predicted skinfold thickness by race and survey for selected ages and values of BMI (skinfold thickness and BMI are transformed back to the original scaling in mm and kg/m^2, respectively) is presented in Table 7. Also presented are ratios of the predicted skinfold thickness from NHANES II and NHANES III and 95% prediction intervals for that ratio. Because skinfold thickness was modeled as the natural log of the skinfold sum, differences in the skinfold thickness transformed back to the original scaling in millimeters must be assessed using the ratio of the two predicted values. Ratios less than one indicate a decrease, and ratios greater than one indicate an increase in the predicted skinfold thickness (mm). Statistically significant differences are indicated if the prediction interval for the ratio does not cross the value one. Overall, significant increases in predicted skinfold thickness are observed in normal weight males (BMI approximately 20-25 kg/m^2), and significant decreases in predicted skinfold thickness are observed in obese (BMI > 30 kg/m^2) males, although the patterns vary somewhat with age.

The age, age*survey, and age*BMI coefficient estimates and the predicted skinfold thickness values presented in Table 7 indicate that the BMI at which predicted skinfold

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[10] This small increase in R^2 is expected due to the increase in the number of estimated parameters.

Table 7. Predicted[a] skinfold sum at select levels of BMI by survey period, age group and race: **Males.**

		White Race				Non-White Race			
Age	BMI	NHANES II	NHANES III	Ratio[b]	95% PI[c]	NHANES II	NHANES III	Ratio[b]	95% PI[c]
25	20	14.9	16.2	1.09	(1.05, 1.13)	14.5	15.8	1.09	(1.03, 1.16)
	25	27.6	27.5	1.00	(0.98, 1.02)	27.8	27.7	1.00	(0.96, 1.04)
	30	41.8	39.2	0.94	(0.91, 0.97)	42.9	40.3	0.94	(0.90, 0.98)
	35	56.1	50.4	0.90	(0.86, 0.93)	58.6	52.6	0.90	(0.85, 0.95)
35	20	15.1	16.6	1.10	(1.07, 1.13)	14.7	16.1	1.10	(1.05, 1.16)
	25	27.6	27.7	1.00	(0.99, 1.02)	27.8	27.9	1.00	(0.97, 1.04)
	30	41.3	39.0	0.95	(0.92, 0.97)	42.5	40.1	0.95	(0.91, 0.98)
	35	55.0	49.8	0.91	(0.88, 0.94)	57.5	52.1	0.91	(0.86, 0.95)
45	20	15.4	17.0	1.11	(1.08, 1.13)	14.9	16.5	1.11	(1.06, 1.16)
	25	27.6	28.0	1.01	(1.00, 1.03)	27.8	28.1	1.01	(0.98, 1.05)
	30	40.8	38.9	0.95	(0.93, 0.97)	42.0	40.0	0.95	(0.92, 0.99)
	35	54.0	49.3	0.91	(0.89, 0.94)	56.4	51.5	0.91	(0.87, 0.96)
55	20	15.6	17.4	1.12	(1.09, 1.15)	15.2	16.9	1.12	(1.07, 1.17)
	25	27.6	28.2	1.02	(1.00, 1.04)	27.7	28.3	1.02	(0.99, 1.06)
	30	40.4	38.8	0.96	(0.94, 0.98)	41.5	39.9	0.96	(0.92, 1.00)
	35	53.0	48.8	0.92	(0.89, 0.95)	55.4	51.0	0.92	(0.88, 0.97)
65	20	15.8	17.9	1.13	(1.09, 1.17)	15.4	17.4	1.13	(1.07, 1.19)
	25	27.6	28.4	1.03	(1.01, 1.05)	27.7	28.5	1.03	(0.99, 1.07)
	30	39.9	38.7	0.97	(0.94, 1.00)	41.1	39.8	0.97	(0.93, 1.01)
	35	52.0	48.3	0.93	(0.89, 0.97)	54.3	50.4	0.93	(0.88, 0.98)

[a] Based on the model presented in Table 5. BMI and BFI were transformed back to their original scaling of kg/m^2 and mm, respectively. Remaining continuous variables set to an approximate mean (total calories = 2500, % calories from fat = 35); remaining categorical variables set to 0.5.

[b] Ratio of predicted skinfold thickness from NHANES II and III survey periods.

[c] 95% Prediction Interval for the ratio between survey period predicted skinfold thickness.

thickness for NHANES II becomes larger than that for NHANES III (the intersection of the two curves) increases with age, from just 24.7 at age 25 to 27.2 at age 65. Since there was no significant interaction between survey and race, the general patterns observed with respect to survey phase, BMI, and age were similar for white and non-white race. The effect of race was to magnify the relationship between BMI and skinfold thickness; that is, predicted BFI was lower in non-whites for BMI less than approximately 25 kg/m^2 and higher in non-whites for BMI greater than 25 kg/m^2.

Table 8. Caliper Adjusted predicted[a] skinfold sum at select levels of BMI by survey period, age group and race: **Males.**

		White Race				Non-White Race			
Age	BMI	NHANES II	NHANES III	Ratio[b]	95% PI[c]	NHANES II	NHANES III	Ratio[b]	95% PI[c]
25	20	14.9	17.6	1.18	(1.14, 1.23)	14.4	17.0	1.18	(1.11, 1.25)
	25	27.6	29.7	1.08	(1.05, 1.11)	27.7	29.9	1.08	(1.03, 1.12)
	30	41.8	42.3	1.01	(0.98, 1.05)	42.9	43.4	1.01	(0.97, 1.06)
	35	56.2	54.4	0.97	(0.93, 1.01)	58.7	56.8	0.97	(0.92, 1.02)
35	20	15.1	18.0	1.19	(1.15, 1.23)	14.6	17.4	1.19	(1.13, 1.26)
	25	27.6	30.0	1.08	(1.06, 1.11)	27.7	30.1	1.08	(1.04, 1.13)
	30	41.3	42.2	1.02	(0.99, 1.05)	42.5	43.3	1.02	(0.98, 1.06)
	35	55.1	53.8	0.98	(0.94, 1.01)	57.6	56.2	0.98	(0.93, 1.03)
45	20	15.3	18.4	1.20	(1.16, 1.24)	14.9	17.8	1.20	(1.14, 1.26)
	25	27.6	30.2	1.09	(1.07, 1.12)	27.7	30.3	1.09	(1.05, 1.14)
	30	40.9	42.0	1.03	(1.00, 1.06)	42.0	43.2	1.03	(0.98, 1.07)
	35	54.1	53.2	0.98	(0.95, 1.02)	56.5	55.6	0.98	(0.93, 1.04)
55	20	15.6	18.8	1.21	(1.17, 1.25)	15.1	18.2	1.21	(1.15, 1.28)
	25	27.6	30.4	1.10	(1.07, 1.13)	27.7	30.5	1.10	(1.06, 1.15)
	30	40.4	41.9	1.04	(1.00, 1.07)	41.5	43.0	1.04	(0.99, 1.08)
	35	53.1	52.6	0.99	(0.95, 1.03)	55.5	55.0	0.99	(0.94, 1.05)
65	20	15.8	19.3	1.22	(1.16, 1.28)	15.3	18.7	1.22	(1.15, 1.29)
	25	27.6	30.6	1.11	(1.07, 1.15)	27.7	30.8	1.11	(1.06, 1.16)
	30	40.0	41.8	1.04	(1.00, 1.09)	41.1	42.9	1.04	(0.99, 1.10)
	35	52.1	52.1	1.00	(0.95, 1.05)	54.5	54.4	1.00	(0.94, 1.06)

[a] Based on the model presented in Table 6. BMI and BFI were transformed back to their original scaling of kg/m^2 and mm, respectively. Remaining continuous variables set to an approximate mean (total calories = 2500, % calories from fat = 35); remaining categorical variables set to 0.5.

[b] Ratio of predicted skinfold thickness from NHANES II and III survey periods.

[c] 95% Prediction Interval for the ratio between survey period predicted skinfold thickness.

Caliper-Adjusted Expanded Model. There were no changes to the best fit model based on the BFI$_a$ (Table 6) as compared to BFI (Table 5). The most substantial change in coefficient estimates occurred for survey period and survey period*BMI interaction terms, as seen for the biologic model. Table 8 presents predicted caliper-adjusted skinfold thickness at selected ages and levels of BMI. The same general trends described in the original models are observed in the caliper-adjusted models with the exception of the differences noted about the caliper-adjusted biologic model. That is, nutrient intake and social indicator variables did not substantially impact the relationship among BFI, BMI, and survey period, and the additional variability explained by these additional variables was negligible. As observed for the caliper-adjusted biologic model, the caliper-adjusted expanded model resulted in a more pronounced increase in skinfold at the lower portion of the BMI distribution and smaller decreases in skinfold at the upper portion of the BMI distribution. Significant increase in predicted skinfold thickness occurred in the approximately lower half of the BMI distribution for all age groups and, additionally, among Class I obese males in older age groups.

Regression Models – Females

Table 9. Biologic Model (Outcome=BFI)- **Females**

Variable	Coeff (b)	SE(b)	p-value
Intercept	61.4580	0.4451	<0.0001
1/BMI	-569.0357	10.0311	<0.0001
Survey (Ref: NHANES II)	-2.5739	0.3301	<0.0001
1/BMI*Survey	47.9365	8.1872	<0.0001
Age	-0.0865	0.0085	<0.0001
Age*1/BMI	1.9095	0.2080	<0.0001

Notes: $R^2 = 0.7313$; Excludes 2 cases based on regression diagnostics

Table 10. **Caliper Adjusted** Biologic Model (Outcome=BFI_a) - **Females**

Variable	Coeff (b)	SE(b)	p-value
Intercept	61.4528	0.4452	<0.0001
1/BMI	-568.9500	10.0334	<0.0001
Survey (Ref: NHANES II)	-1.9988	0.3300	<0.0001
1/BMI*Survey	48.5579	8.1861	<0.0001
Age	-0.0864	0.0085	<0.0001
Age*1/BMI	1.9079	0.2080	<0.0001

Notes: $R^2 = 0.7327$; Excludes 2 cases based on regression diagnostics

Biologic Model. Parameter estimates for the biologic model for females are displayed in Table 9. BMI, survey period, and age were all highly significant; race was not statistically significant so it was eliminated from the model. There were significant interactions between BMI and survey period and BMI and age. As noted previously, the inverse of BMI best accounted for the curvilinear relationship between BMI and BFI. Age was linear, and three-way interactions were considered but were not statistically significant. Overall, this model accounted for 73.1% of the variability of BFI ($R^2 = 0.7313$), compared to 71.9% for the model containing intercept and BMI, 72.4% for the model containing BMI, intercept, and survey period, and 72.5% for the model containing intercept, BMI, survey period, and BMI*survey period interaction. These R^2 values are substantially higher than those observed for the corresponding models for males.

Figure 4 illustrates the differential relationship between BMI and BFI with survey period. Predicted skinfolds sum is lower for NHANES III than NHANES II across the entire distribution of BMI. As seen in the biologic model for males, the magnitude of this difference becomes larger proportional to BMI.

Caliper-Adjusted Biologic Model. As observed for males, modeling BFI_a rather than BFI did not change the resulting models; the same variables were significant in both models and the scaling of those variables were also identical (Table 10). Parameter estimates were very similar to the original biologic model except, as seen in the models for males, the survey period coefficient was still negative but closer to zero and the BMI*survey period interaction was slightly smaller. These changes had a net effect of decreasing the distance between the curves for NHANES II and III survey periods (Figure 5). Despite the significant BMI*Survey interaction, the overlapping prediction intervals in Figure 5 suggest that the two curves are statistically indistinguishable for normal to overweight females.

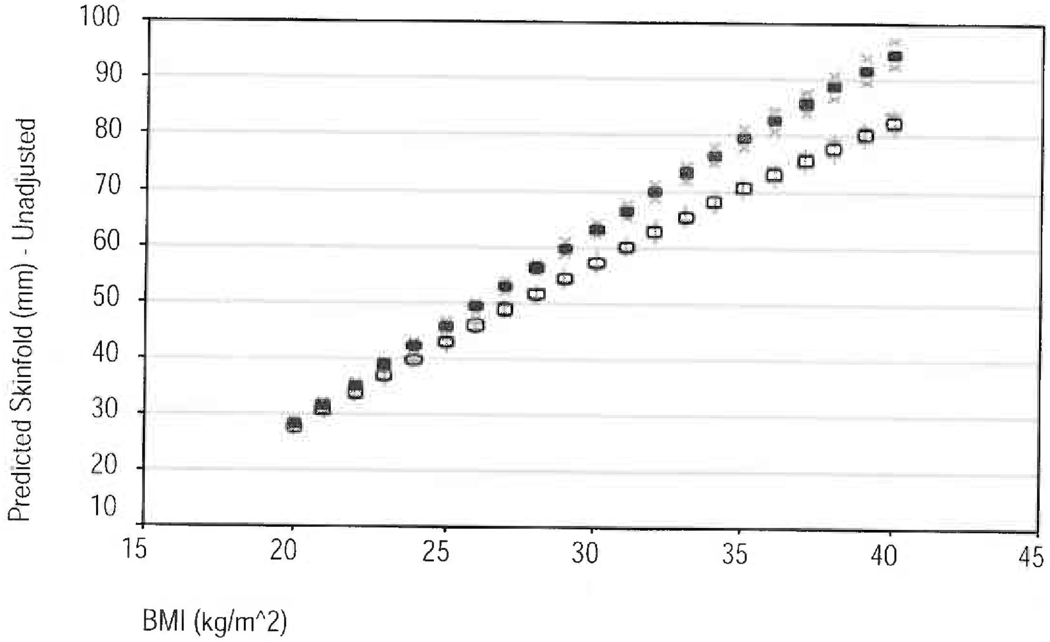

Figure 4. Predicted skinfold sum at select levels of BMI: **Females**.
Based on the model presented in Table 9. BMI and BFI were transformed back to their original scaling of kg/m² and mm, respectively. Age set to an approximate mean (45 years).
●=Predicted value for NHANES II, ×=95% prediction interval for NHANES II
○=Predicted value for NHANES III, +=95% prediction interval for NHANES III

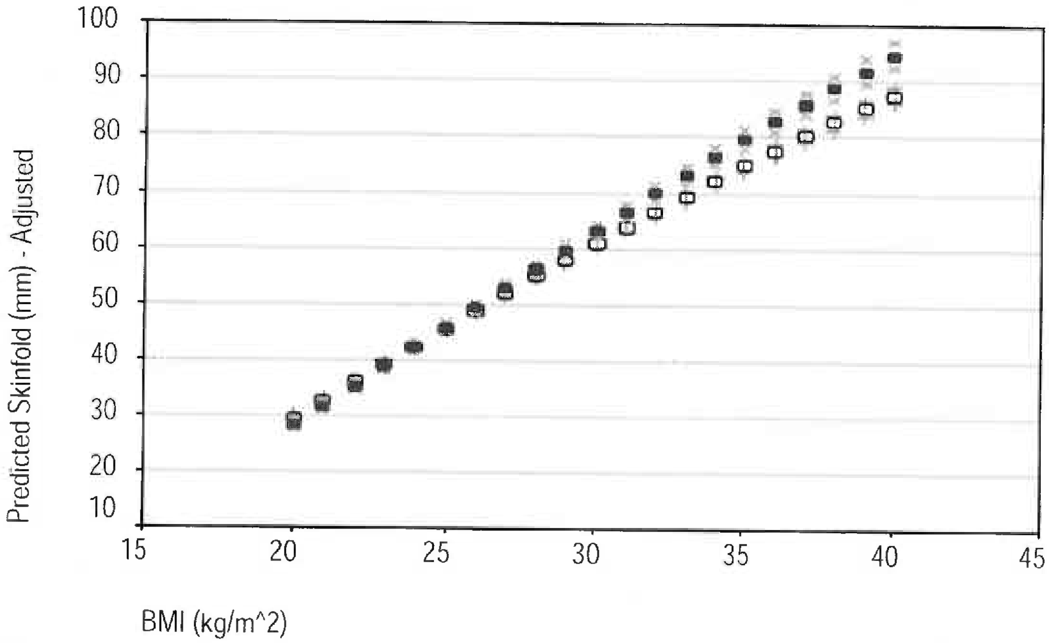

Figure 5. **Caliper Adjusted** predicted skinfold sum at select levels of BMI: **Females**.
Based on the model presented in Table 10. BMI and BFI were transformed back to their original scaling of kg/m² and mm, respectively. Age set to an approximate mean (45 years).
●=Predicted value for NHANES II, ×=95% prediction interval for NHANES II
○=Predicted value for NHANES III, +=95% prediction interval for NHANES III

Expanded Model. Results from the expanded model for females are displayed in Table 11. Additional significant variables in this expanded model included total calories consumed, percent calories consumed from fat, current cigarette use, education, and marital status. There were also significant interactions between BMI and current cigarette use and BMI and education. Poverty and health status were not statistically significant so they were excluded from the model. There was a curvilinear relationship between total calories consumed and BFI that was best modeled using the square root transformation on total calories consumed. As observed in the expanded model for males, addition of nutrient intake, tobacco use, and social indicators did not explain much more variability in BFI (R^2 = 0.7424 versus 0.7313)[11], and they did not impact the magnitude or

Table 11. Expanded Model (Outcome=BFI) – **Females**

Variable	Coeff (b)	SE(b)	p-value
Intercept	60.9600	0.4955	<0.0001
1/BMI	-553.2138	9.8585	<0.0001
Survey (Ref: NHANES II)	-2.4772	0.3200	<0.0001
1/BMI*Survey	45.6965	7.8790	<0.0001
Age	-0.0907	0.0085	<0.0001
Age*1/BMI	2.0004	0.2075	<0.0001
SQRT(Total Calories)	-0.0076	0.0032	0.0194
% Calories from Fat	0.0066	0.0032	0.0423
Current Cigarette Use	0.7813	0.2324	0.0012
Education (Ref: >=HS)	0.5226	0.2314	0.0266
Currently married	0.2739	0.0523	<0.0001
Current Cigarette Use*1/BMI	-33.0170	6.0458	<0.0001
Education*1/BMI	-18.4275	5.9838	0.0028

Notes: R^2 = 0.7424; Excludes 8 cases based on regression diagnostics

Table 12. Caliper Adjusted Expanded Model (Outcome=BFI_a) – **Females**

Variable	Coeff (b)	SE(b)	p-value
Intercept	60.9512	0.4956	<0.0001
1/BMI	-553.1110	9.8583	<0.0001
Survey (Ref: NHANES II)	-1.9025	0.3199	<0.0001
1/BMI*Survey	46.3269	7.8816	<0.0001
Age	-0.0906	0.0085	<0.0001
Age*1/BMI	1.9985	0.2075	<0.0001
SQRT(Total Calories)	-0.0075	0.0032	0.0199
% Calories from Fat	0.0066	0.0032	0.0413
Current Cigarette Use	0.7210	0.2325	0.0012
Education (Ref: >=HS)	0.5227	0.2314	0.0266
Currently married	0.2747	0.0522	<0.0001
Current Cigarette Use*1/BMI	-33.0335	6.0485	<0.0001
Education*1/BMI	-18.4810	5.9832	0.0028

Notes: R^2 = 0.7439; Excludes 8 cases based on regression diagnostics

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[11] This small increase in R^2 is expected due to the increase in the number of estimated parameters.

significance of the parameters of interest.

The effects of nutrient intake variables on BFI were similar to those seen in the expanded models for males. Higher total calories consumed was associated with lower predicted skinfold sum, and higher percent calories consumed from fat was associated with higher predicted skinfold sum. Current cigarette use, less than a high school education, and being currently married were positively associated with predicted skinfold thickness. However, the elevation in predicted skinfold thickness due to cigarette use and lower education status was more pronounced at higher levels of BMI.

Predicted skinfold thickness are displayed in Table 13. With the exception of the lowest levels of BMI, NHANES III predicted values are significantly smaller than NHANES II within all age groups.

Caliper-Adjusted Expanded Model. Also parallel with the regression models for males, modeling BFI_a did not change the final expanded model, and the effects of nutrient intake and social variables remained similar to that seen in the original expanded model (Table 12). The changes in parameter estimates for survey period and survey period*BMI interaction were consistent with those observed in the caliper-adjusted versus original biologic models predicting BFI versus BFI_a. Predicted skinfold thickness values are displayed in Table 14. NHANES III predicted skinfold thickness is significantly higher in the lower-normal weight females and are significantly lower in obese females as compared to NHANES II.

Table 13. Predicted[a] skinfold sum at select levels of BMI by survey period, age group and race – **Females.**

Age	BMI	NHANES II	NHANES III	Ratio[b]	95% PI[c]
25	20	27.0	26.5	0.98	(0.95, 1.01)
	25	45.8	42.9	0.94	(0.91, 0.96)
	30	65.2	59.2	0.91	(0.88, 0.93)
	35	83.8	74.6	0.89	(0.86, 0.92)
	40	101.3	88.6	0.88	(0.84, 0.91)
35	20	27.2	26.7	0.98	(0.95, 1.01)
	25	45.3	42.5	0.94	(0.92, 0.96)
	30	63.6	57.8	0.91	(0.89, 0.93)
	35	81.1	72.1	0.89	(0.86, 0.92)
	40	97.2	85.1	0.88	(0.85, 0.90)
45	20	27.5	27.0	0.98	(0.95, 1.01)
	25	44.8	42.0	0.94	(0.92, 0.96)
	30	62.1	56.5	0.91	(0.89, 0.93)
	35	78.4	69.7	0.89	(0.86, 0.91)
	40	93.4	81.7	0.88	(0.85, 0.90)
55	20	27.8	27.2	0.98	(0.95, 1.01)
	25	44.4	41.6	0.94	(0.91, 0.96)
	30	60.6	55.1	0.91	(0.89, 0.93)
	35	75.8	67.4	0.89	(0.86, 0.92)
	40	89.6	78.4	0.88	(0.85, 0.90)
65	20	28.0	27.5	0.98	(0.95, 1.02)
	25	43.9	41.1	0.94	(0.91, 0.96)
	30	59.2	53.8	0.91	(0.88, 0.93)
	35	73.3	65.2	0.89	(0.86, 0.92)
	40	86.1	75.3	0.88	(0.84, 0.91)

[a] Based on the model presented in Table 11. BMI and BFI were transformed back to their original scaling of kg/m^2 and mm, respectively. Remaining continuous variables set to an approximate mean (total calories = 1600, % calories from fat = 34); remaining categorical variables set to 0.5.

[b] Ratio of predicted skinfold thickness from NHANES II and III survey periods.

[c] 95% Prediction Interval for the ratio between survey period predicted skinfold thickness.

Table 14. Caliper Adjusted predicted[a] skinfold sum at select levels of BMI by survey period, age group and race – **Females.**

Age	BMI	NHANES II	NHANES III	Ratio[b]	95% PI[c]
25	20	27.0	28.1	1.04	(1.01, 1.08)
	25	45.8	45.6	1.00	(0.97, 1.02)
	30	65.2	62.9	0.96	(0.94, 0.99)
	35	83.8	79.1	0.94	(0.91, 0.98)
	40	101.3	94.0	0.93	(0.89, 0.96)
35	20	27.2	28.4	1.04	(1.01, 1.07)
	25	45.3	45.1	1.00	(0.97, 1.02)
	30	63.6	61.4	0.96	(0.94, 0.99)
	35	81.1	76.5	0.94	(0.92, 0.97)
	40	97.2	90.3	0.93	(0.90, 0.96)
45	20	27.5	28.7	1.04	(1.01, 1.07)
	25	44.8	44.6	1.00	(0.97, 1.02)
	30	62.1	59.9	0.96	(0.94, 0.99)
	35	78.4	74.0	0.94	(0.92, 0.97)
	40	93.4	86.7	0.93	(0.90, 0.96)
55	20	27.8	28.9	1.04	(1.01, 1.08)
	25	44.4	44.1	1.00	(0.97, 1.02)
	30	60.6	58.5	0.96	(0.94, 0.99)
	35	75.8	71.6	0.94	(0.92, 0.97)
	40	89.6	83.2	0.93	(0.90, 0.96)
65	20	28.0	29.2	1.04	(1.01, 1.08)
	25	43.9	43.7	1.00	(0.97, 1.02)
	30	59.2	57.1	0.96	(0.94, 0.99)
	35	73.3	69.2	0.94	(0.91, 0.97)
	40	86.1	79.9	0.93	(0.89, 0.96)

[a] Based on the model presented in Table 12. BMI and BFI were transformed back to their original scaling of kg/m^2 and mm, respectively. Remaining continuous variables set to an approximate mean (total calories = 1600, % calories from fat = 34); remaining categorical variables set to 0.5.

[b] Ratio of predicted skinfold thickness from NHANES II and III survey periods.

[c] 95% Prediction Interval for the ratio between survey period predicted skinfold thickness.

Descriptive Trends

Mean-difference plots were developed in order to illustrate that descriptive trends may look quite different depending on the indicator used. In this case, changes in adiposity as determined by two indicators – BMI and skinfold thickness – are compared using a graphical representation of the change in distribution throughout the population.

To review, the mean-difference plots utilized in this study display the change in BMI and skinfold thickness over time relative to the magnitude of BMI and skinfold thickness. Data points above or below the x-axis represent an increase or decrease from NHANES II to NHANES III, respectively. Variation in the distance from the x-axis indicates a change in the shape of the distribution. For example, the upward slope seen in each of the BMI mean-difference plots in Figure 6 and Figure 7 indicate that the magnitude of the increase in BMI was proportional to the mean BMI; in other words, the greatest increases in BMI occurred in the upper end of the BMI distribution, or alternatively, among the "heaviest" groups.

BMI Mean-Difference Plots. BMI mean-difference plots are displayed in the first column of Figure 6 for males and Figure 7 for females. Findings are identical to those found by Flegal and Troiano (Flegal and Troiano 2000). For both males and females in all adult age groups, BMI mean-difference plots illustrate increased skewness and an increase in BMI from NHANES II to NHANES III throughout the most of the BMI distribution.

Among males, the BMI difference remained relatively small and more constant through the majority of the BMI distribution and increased sharply at approximately 30 kg/m^2. That is, the distribution became more right skewed. With increasing age, this pattern became less distinct; in older age groups the BMI difference was slightly larger throughout the lower portion of the distribution and the increase in the obese range was less pronounced and smaller in magnitude.

Among females, the BMI difference increased more constantly across the lower portion of the BMI distribution and then plateaued in the obese BMI range. Again, this pattern became less pronounced among older age groups in which the BMI difference was smaller and increased more slowly with mean BMI.

Skinfold Mean-Difference Plots. In contrast, caliper-adjusted skinfold mean-difference plots show an increase in skinfold sum from NHANES II to NHANES III at the lower end of the distribution and a decrease in skinfold sum at the upper end of the distribution for both males and females. Due to the nature of the caliper-adjustment procedure, there were predictable changes in the shape of the caliper-adjusted skinfold thickness mean-difference plots, namely a general shift upward and attenuation of the decrease in skinfold thickness at the upper end of the distribution. Because of these similarities, the descriptive nature of these analyses that does not involve the estimation of variance for hypothesis testing, and evidence that caliper-adjusted measurements probably better reflect changes in skinfold thickness, only caliper-adjusted skinfold thickness mean-difference plots are presented.

In the caliper-adjusted skinfold mean-difference plots for males, skinfold sum increased throughout the skinfold sum distribution with exceptions in the upper percentiles. The skinfold difference was larger in the lower portion of the distribution, and the decline in skinfold difference with increased skinfold mean was more gradual. The 30-39, 40-49, and 60-74 year age groups showed in an initial increase in skinfold difference through 20-25mm, then a consistent decrease. Note that this pattern is opposite to that seen in the BMI mean-difference plots.

Female caliper-adjusted skinfold mean-difference plots display distributions that are right-skewed but more evenly distributed than observed for males. That is, the upper portion of the distribution is more spread out than the lower portion, but to a lesser extent than that observed in the caliper-adjusted mean-difference plots for males. The majority of the distribution experienced an increase in skinfold measurement, but overall a greater proportion of the distribution displayed negative skinfold differences than was observed for males. Among all age groups the rate of decrease in difference increased with mean skinfold sum at the upper portion of the distribution. The point at which the difference became negative decreased with age. In the lower half of the distribution for most age groups, the magnitude of the difference in skinfold thickness becomes larger or stays relatively constant as the mean value becomes larger, which is more consistent with the pattern seen in BMI mean-difference plots for females.

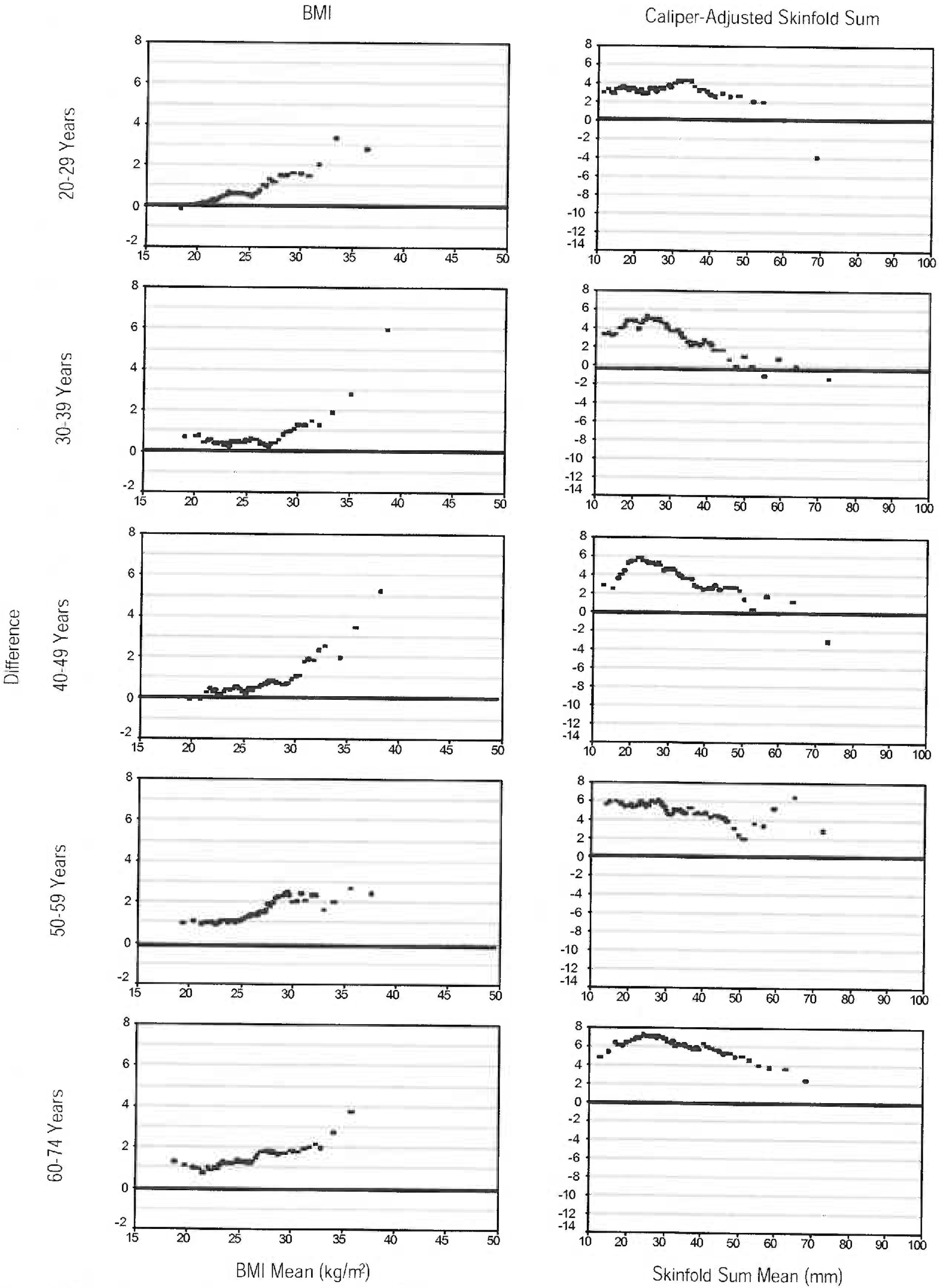

Figure 6. Mean-difference plots for the distribution of BMI and caliper-adjusted skinfold sum from NHANES II to NHANES III – **Males**.

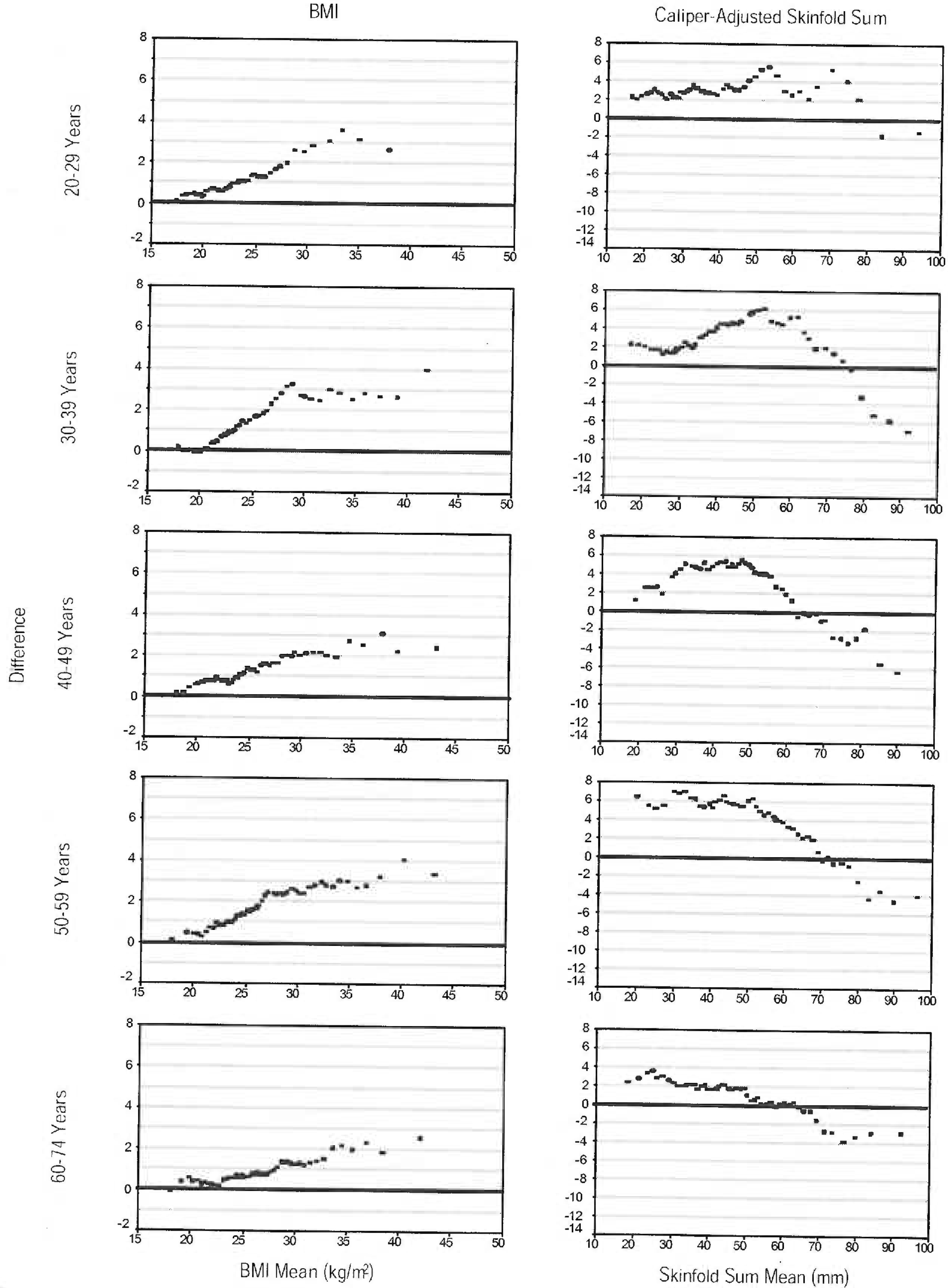

Figure 7. Mean-difference plots for the distribution of BMI and caliper-adjusted skinfold sum from NHANES II to NHANES III – **Females**.

IV. DISCUSSION

The prevalence of overweight and obesity is currently at epidemic levels and has been increasing at an accelerating rate since the 1970s. The scope and severity of the epidemic warrant public health action and with that, the development and maintenance of effective means to monitor the status of the epidemic. Effective monitoring and surveillance of disease prevalence requires reliable measures of disease status that are consistent over time. While BMI has been recommended by WHO and NIH and accepted by most researchers as the standard indicator of adiposity, there is reason to believe that BMI may correspond with different levels of adiposity at various points in time. That is, changes in food consumption and physical activity over time that resulted in weight gain may have also resulted in changes in body composition and, therefore, the meaning of BMI as a measure of adiposity.

Based on trends in physical activity from other data sources, it was hypothesized that body fat may have increased to an even greater extent than BMI in the past few decades. Specifically, it was predicted that in later time periods, any given value of BMI would correspond with higher body fat, as indicated in this case by an index derived from skinfold thickness measurements. NHANES data were analyzed to test this hypothesis; NHANES II (1976-80) and NHANES III (1988-94) study periods defined the two time points.

Overall, these results suggest that among women, the relationship between BMI and adiposity has declined slightly or remained constant, but among men, a given BMI predicts a higher skinfold thickness in NHANES III versus NHANES II. In other words, while there has been an increase in BMI and skinfold thickness throughout the population from the NHANES II to NHANES III study periods, there has been an even larger increase in adiposity, particularly among normal to overweight males (BMI approximately 20-30 kg/m^2). These findings are consistent with the hypothesized increase in adiposity due to decreases in total physical activity and/or other behavior trends.

Constancy of the BMI-Adiposity Relationship

The initial results of regression analysis of BFI were, for the most part, directly contrary to this hypothesis. Among obese men and all women, predicted skinfold thickness was higher in NHANES II than NHANES III at any given BMI. Results for normal weight men were consistent with the hypothesized pattern of higher predicted skinfold thickness in the NHANES III study period relative to the NHANES II study period. These observations remained true after controlling for selected nutrient intake and social variables.

BMI explained the majority of the variability in BFI. The remainder of the variables included in the models, while statistically significant, increased the percent of explained variance by only a few percentage points. This result is expected, because the correlation between BMI and skinfold thickness has been shown to be high and, in fact, BMI was assessed and validated on the basis of its ability to predict some measure of body fatness. R^2 values were substantially higher in models for females ($R^2 \cong 0.74$) as compared to models for males ($R^2 \cong 0.62$), which is consistent with findings from other studies in which the correlation between BMI and percent body fat was higher in women than in men (Deurenberg, Weststrate et al. 1991; Gallagher, Visser et al. 1996)

In order to address the possible bias introduced by the change in skinfold caliper type between study periods, analyses were repeated using BFI adjusted to account for the expected differences in calipers. While the methods used to adjust BFI have not been validated and may not perfectly reflect the relationship between measurements obtained from Lange versus Holtain calipers, they are based on empirical data and should provide a rough approximation of trends that would have been observed if the same calipers had been used in both survey periods. It should also be noted that by design, analyses of BFI_a yielded predictable changes in the effects of survey period from the original analyses, since adjusting the NHANES III skinfold measurements simply shifted the NHANES III skinfold distribution upward proportional to the magnitude of skinfold thickness. Nevertheless, these adjusted values provided valuable information to aid in the interpretation of the results in this study.

Indeed, caliper-adjusted models for both males and females suggest that much of the observed decrease in skinfold thickness, given constant BMI, could be explained by the smaller measurements expected from the Holtain skinfold caliper. In the caliper-adjusted model, the increase in skinfold among normal to overweight males was accentuated, and the decrease in skinfold among obese males and all females was substantially diminished.

These findings are further supported by BMI and skinfold mean-difference plots. BMI mean-difference plots for both males and females indicate that while there was an increase in BMI throughout the population, the magnitude of this increase became larger among heavier groups. Skinfolds also increased throughout the majority of the population. Among males, however, the magnitude of this increase declined with higher skinfold thickness. Taken together, mean-difference plots suggest that despite small increases in BMI between survey periods among normal weight and overweight males, there was a substantial increase in adiposity. Among females, the patterns of increase in BMI and skinfold mean-difference plots were more consistent, suggesting that the relationship between BMI and adiposity has remained more constant over time. These observations are consistent with the results from regression analysis.

Due to a number of factors, interpretation of results for extremely obese populations should be performed with caution. First, the reliability of skinfold thickness measurement declines as skinfold thickness becomes larger (Marks, Habicht et al. 1989; Himes 2001). Second, the upper limits of the Lange caliper is 65mm while the upper limit of the Holtain caliper is 50mm. Recoding skinfold measurements above 65mm to 50mm likely removed much of this bias, but measurements of near 50mm taken with the Holtain caliper approach the upper limits of the caliper while the same measurements taken with the Lange caliper may be more reliable because they are well within the capacity of the caliper. Therefore, the reliability in the upper ranges of skinfold measurement was likely not constant between the two survey periods. Finally, because, as observed in mean-difference plots, the frequency of individuals in the upper portion of the skinfold distribution was relatively small, estimates in that region are probably less reliable than those with smaller skinfold thickness.

The attenuation of the decrease in predicted skinfold for high BMI's in the caliper-adjusted regression models and in the caliper-adjusted mean-difference plots in combination with the above limitations of using skinfold thickness measurements in obese populations suggest that the observed decreases in skinfold thickness in the upper portion of the BMI and skinfold distributions may be a result of measurement bias.

In sum, these data provide evidence that the relationship between BMI and BFI is not constant among normal to overweight men, but has remained relatively stable among normal to overweight women. Specifically, for normal to overweight men, predicted BFI (adiposity) is higher at any given BMI in the NHANES III population as compared to the NHANES II population, and this effect increases with age. For 25 year-old males with a BMI of 20, the predicted skinfold sum is 18.1% higher for the NHANES III than the

NHANES II study period, and for a 65 year-old male with a BMI of 20, this percent increase is 22.2%.

Gender Differences and their Connection to Behavioral Trends

This difference in trends in adiposity between males and females may be indicative of differences in behavior trends. Dietary trends indicate that fat consumption patterns are similar, while trends in fruit and vegetable consumption and total caloric intake differ between males and females. Fat consumption patterns observed from National Health Interview Survey (NHIS) (Breslow, Subar et al. 1997), USDA National Food Consumption Survey (NFCS) (Heini and Weinsier 1997; Popkin, Siega-Riz et al. 2001), and multi-study compiled data (Stephen and Wald 1990) are similar for men and women. Women have exhibited more positive improvements in fruit and vegetable consumption (Breslow, Subar et al. 1997; Li, Serdula et al. 2000), but the impact of these differential trends on body composition are unclear. Unfortunately, the primary sources of total caloric intake data are food disappearance data, which are measured at the population level and cannot be stratified by gender, and NHANES dietary recall data, which for the reasons discussed in earlier sections should not be used for trend analysis. Assuming that the bias due to survey methods is comparable for males and females, though, there was a differential increase in total calories from NHANES II to NHANES III: total calories increased by 18.1% among females and 9.6% among males included in the current study population.

Another possible explanation for differential trends in adiposity between males and females is a difference in improvement in physical activity. Trends in physical activity are, as discussed earlier, limited primarily to leisure time physical activity (LTPA), but LTPA data are still valuable for comparing trends. From the early to late 1980's, there was a greater increase in moderate and heavy LTPA among women (Jacobs, Hahn et al. 1991), and from

1986-1990 the prevalence of physically inactive lifestyles decreased among both men and women, but prevalence of regularly active, intensive lifestyles increased only among women (Casperson and Merritt 1995). Physical activity data were not comparable in the NHANES II and NHANES III survey data, but NHANES III data indicates that, among the current study population, a greater proportion of females than males (17.5% versus 12.9%) reported being more active at the time of the NHANES interview as compared to ten years previous (X^2 $p<0.0001$). Taken together, these trend data and retrospective reporting suggest that LTPA has increased more in women relative to men during the time frame relevant to the NHANES II and III study periods. In addition, energy expended in household chores is thought to be a substantial component in energy expenditure among women (Jacobs, Hahn et al. 1991) and this is likely to have remained relatively constant with time. These points support the speculation that increases in physical activity and maintenance of lifestyle physical activity may have enabled women to maintain similar or lower levels of lean body mass proportional to total body mass as compared to men.

Because changes in adiposity over time are likely a result of the combined effect of changes in diet and physical activity, these differential trends in diet, physical activity, and adiposity by gender suggest that the nature of weight gain in the past 20-30 years may differ between males and females. They are also consistent with the hypothesis that the change in adiposity relative to BMI over time may be due, at least partially, to declines in physical activity. Further, it may be beneficial to maintain monitoring efforts specific to gender and develop interventions that address barriers and supports to healthy behaviors that may be gender specific.

Impact of Other Demographic, Nutrient Intake, and Social Variables

Demographic, nutrient intake, and social variables were included in the models primarily as control variables, but their impact on predicted skinfold thickness deserves some attention. For both males and females, older age was associated with higher predicted skinfold thickness for lower levels of BMI and lower predicted skinfold thickness for higher levels of BMI, but this decrease was more pronounced among females. Non-white race was associated with slightly lower skinfold thickness among normal weight males but higher skinfold thickness for overweight and obese males. Racial category was not significant in the female models which, given the extensive evidence that body composition varies by race, is surprising. However, the coarse categorization of race in this study likely masked differences between more specific racial categories such as Asian/Pacific Islander and Black race.

Also unexpected was that higher total calories consumed was associated with smaller skinfold thickness in both males and females and in both the original and caliper-adjusted models, though this association was not as strong for females. It is possible that total caloric intake may be a better indicator of energy expenditure rather than diet quality. In other words, high energy intake may be indicative of high energy needs rather than excess calories. More consistent with expectations, higher percent calories consumed from fat was predictive of larger skinfold thickness. Percent calories consumed from protein was not significantly associated with skinfold thickness after controlling for BMI among males or females.

Current cigarette use was associated with lower skinfold thickness among both males and females, though this relationship was more pronounced for females. This finding is consistent with evidence that nicotine increases metabolic rate. Lower education attainment predicted smaller skinfold thickness among males and females, and this decline was more pronounced among females with lower BMI. Currently married females tended to have higher skinfold thickness than females who were not married, but marital status was not significantly associated with skinfold thickness among males.

In addition, poverty and health status were not significant in any of the models. Poverty was highly correlated with many of the other covariates, including race, education level, marital status, health status, and smoking of tobacco products ($p<0.0001$, data not shown), so in the absence of race and/or education, poverty would have been an important control variable. Likewise, health status is also correlated with several variables, so its exclusion from the regression models is probably due to its strong relationship with covariates included in the model.

Study Limitations

As discussed above, a primary limitation of this study is the imperfect method used to adjust for the difference in skinfold calipers. The method was based on empirical data, using the percent difference in mean values between calipers. It was assumed that the percent difference between calipers would remain the same throughout the skinfold distribution, but it is possible that due to the difference in capacity and other considerations, the percent difference may increase in the upper measurement ranges. The two calipers upon which the data were based were the Lange, used in NHANES II, and the Harpenden caliper, which is thought to be similar to the Holtain caliper used in NHANES III based on a study performed in female athletes (Lohman, Pollack et al. 1984). While this latter study cannot be generalized to the general adult population for some purposes, assessment of the similarity of the two calipers is probably less likely to be impacted by these factors than estimation of the magnitude of the measurement difference. In any case, the resulting adjustments were, as stated above, based on existing literature and were very useful for estimating the effect of the caliper difference on the primary analysis. Moreover, the increase in adiposity among normal and overweight males was observed even in the unadjusted analysis, so if the adjustment performed in this study underestimated the bias, the increase adiposity would have been even larger than reported in this study.

Second, the decreased reliability of skinfold thickness measurement as those measurements become larger, and decreased confidence in the adjustment methods discussed above limit our ability to assess to constancy of the BMI-adiposity relationship in the severely obese subpopulation. An alternative indicator of adiposity would have improved utility of the analysis overall but particularly in the obese subpopulation, but the necessary data were not available. However, the importance of this issue to public health monitoring and policy is limited, since an increase or decrease in adiposity among the severely obese is irrelevant given the high risk of morbidity and mortality at very high BMI regardless of these relatively small changes in adiposity.

A third limitation is the absence of comparable data on physical activity. The study hypothesis was developed based on trends in physical activity and it would have been informative to relate the results to physical activity level. However, social variables that have been demonstrated to be associated with physical activity were included in the models, so at least a portion of the impact of changes in physical activity were controlled for in regression analysis.

Despite these limitations, the methods used in this study are derived from empirical evidence and are, for the most part, consistent with methods used by other investigators. They provided effective means for assessing the study hypothesis, especially among normal weight and overweight males and females.

Sufficiency of BMI as an Indicator of Overweight and Obesity

BMI is an easy and reliable method for indicating overweight and obesity at the population level. These findings do not contradict the benefits of BMI as a measure of obesity convincingly outlined by the WHO and NIH (DHHS 1998; WHO 1998), and the limitations of alternative measures such skinfold thickness, waist circumference, and Bioelectrical Impedance Analysis (BIA) still remain. Skinfold thickness measurements in particular are problematic due to all of the issues discussed in this thesis, including high inter-observer variability, especially in large studies in which many technicians perform the measurements (Ulijaszek and Kerr 1999); high intra-observer variability (Ulijaszek and Kerr 1999); variability due to differences in caliper types (Burgert and Anderson 1979; Gruber, Pollack et al. 1990); and the upper limits at which skinfold thickness become impractical, especially in an increasingly obese population (Himes 2001).

However, the WHO suggested that BMI be used in conjunction with other measures of adiposity, though this recommendation is often overlooked. These findings support this recommendation, suggesting that relying solely on BMI to monitor overweight and obesity in the population may not be sufficient for detecting important changes in the nature of weight gain or loss. Changes in the distribution of skinfold thickness and in the relationship between BMI and skinfold thickness among healthy to overweight men indicate that the severity of the overweight epidemic in particular may be underestimated by even the shockingly high overweight prevalence figures based on BMI. Additionally, BMI alone could not have detected the change in the nature of the increase in overweight and obesity prevalence and how it may differ between males and females.

Conclusions and Future Research

In conclusion, these findings provide evidence that adiposity has increased independent of BMI among normal weight and overweight males but not among females, and that there are gender specific differences in body composition trends that may warrant development of public health policy that addresses gender specific issues.

Opportunities for future research include further examination of the constancy of the BMI-adiposity relationship with additional time points as they become available and using alternative indicators of adiposity, such as BIA, waist circumference, or waist-to-hip ratio; and investigation of possible environmental and behavioral factors that can help explain the observed gender differences.

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