CVD Health Factors and CVD Risk Factors: State of the Science, Emerging Priorities Part 2: Obesity Prevention

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Abstract: This report outlines a course of action to prevent obesity and stall the obesity epidemic now underway in the United States and other parts of the world. While African Americans and Hispanics are most vulnerable to obesity, the etiology of obesity shows that both genetic and environmental factors are responsible for overweight and obesity. Although obesity is familial, genes may not be the main culprit; and, in fact, explain <20% of the obesity prevalence. Clearly, environmental factors (specifically those related to energy intake [diet] and energy output [physical activity]) are more often associated with obesity. Patients with multiple risk factors, including obesity, for cardiovascular disease need to be treated aggressively with lifestyle modifications and medications, when necessary, to affect positive cardiovascular health outcomes. However, a wiser, healthier approach to obesity is to prevent it from occurring in the first place. (*Ethn Dis*. 2012; 22[Suppl 1]:S1-36–S1-40)

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Obesity Prevalence

In 1985, little data had been collected on obesity prevalence throughout the United States; the Centers for Disease Control had data on only 21 states. Of those states, the highest levels were found among seven states where rates were reported to be between 10%–15% of the population.[1] Ten years later, in 1995, all states reported obesity prevalence rates; important to the Jackson Heart Study, Mississippi ranked among the four states with the highest levels of obesity (>25%). In contrast, Colorado distinguished itself with the lowest rate of obesity (<10%) and was the only state to report at that level.[2] By 2008, the prevalence of obesity among US adults had risen dramatically; yet, Mississippi and Colorado remained as polar opposites: Mississippi with >30% prevalence of obesity and Colorado with a 15%–19% obesity rate and again the only state at that lowest level.[3]

Obesity Prevalence by Race

According to the 2006–2008 BRFSS (behavior risk factor surveillance survey) data of nearly a million Whites, 85,000 Blacks and 64,000 Hispanics, Blacks had the highest prevalence of obesity at 35.7% vs 23.7% and 28.7% for Whites and Hispanics, respectively.[4] Alarmingly, the early onset of obesity in minority groups appears to be a national trend. Among US preschool children, Anderson and Whitaker found that the highest rates of obesity were among American Indian/Native Alaskan children (31.2%) followed by Hispanic children (22.0%), Black children (20.8%) and White children (15.9%).[5] While the United States is leading the trend in higher rates of obesity among children, nations around the world are experiencing similar increases in childhood obesity.[6]

Etiology of Obesity

Genetic Influences

Factors that cause obesity have been discussed and reported in the literature and include genetic (susceptibility genes, monogenic syndromes) and environmental factors (intrauterine, food intake, culture, physical activity).[7] Although heritability estimates range from 40–70%,[8] genetic factors may not contribute to obesity as much as one might like to think. Research has shown that, among families, genetics may explain no more than between 25% to 50% of the obesity cases and only 60%–80% of identical twins sharing similar BMIs. Moreover, using gene-wide association studies approaches, <20% of obesity is explained by gene variants.[9] Studies conducted with twins show that BMI and waist-to-hip ratios may be heritable traits, with genetics accounting for up to 70% of the variability.[10,11] Adipocyte number is a major determinant for the determination of fat mass in adults; yet, fat cell number is constant in adults whether they are lean or obese, indicating that the number of adipocytes is determined before adulthood, ie, during growth and development.[12]

Current research continues to explore how genetic factors affect obesity; much work focuses on adipocyte differentiation and complex genetic traits of oligogenes and polygenes. We do not yet completely understand the growth and proliferation of fat cells; knowledge in this area could inform therapies and interventions for weight gain. Research from Bouchard and colleagues at the Pennington

Biomedical Research Center has identified the effect size of the allele and have mapped Mendelian syndromes (eg, leptin deficiency, leptin receptor deficiency) relevant to human obesity to a genomic region; causal genes or strong candidates have been identified for most of these syndromes. Overall, more than 430 genes, markers and chromosomal regions have been linked with human obesity phenotypes.[13] Bouchard et al have also found that the effect size is greater for single gene traits but minimal for polygenic disorders. A number of candidate gene variants for oliogenic obesity have been identified and appear to disrupt pathways of energy balance: PPARs, POMC, MC4-R, and the FTO, a gene which appears to influence African Americans somewhat differently than as found in Caucasians. Overall, when genes play a role in obesity, it appears that common obesity will be polygenic involving complex gene-gene interactions and gene-environment interactions.[14]

Environment Influences

Diet

Despite the fact that genetics contribute to body weight, body composition and body fat distribution, the obesity epidemic, developed in the last two decades, clearly cannot be explained by genetic factors alone. Instead, this genetic predisposition may be the building block for obesity to occur in individuals as weight is influenced by certain behavioral, cultural, social and environmental factors. Part of the answer to the obesity epidemic is as simple as: if you eat more calories (food intake) than you burn (physical activity), you will gain weight. Yet, taking all environmental and biological factors into account, predicting weight gain or excess fat gain in humans becomes more complex. Metabolic flexibility, which allows the body to cope with major discontinuities in both the supply of, and demand for, energy, is required for the body to utilize lipid and carbohydrate fuels and to transition between them. For example, skeletal muscle tissue requires oxidative phosphorylation for energy production but obesity inhibits the metabolic flexibility in the oxidation of carbohydrate and lipid fuels. This dysregulation appears to lead to impairment of the skeletal muscle mitochondria contributing to body weight dysregulation.[15]

In a recent study, we explored the effect of a high-carbohydrate vs a high-fat diet on the stability of body weight and composition over a four-year interval.[16] In this crossover design study, we followed 23 normal-weight, 8 overweight and 8 obese men and women aged 25–36 years. Among the study participants, there was little or no difference in rates of fasting respiratory quotient (RQ) or fasting glucose. Resting metabolic rate, an important consideration associated with maintenance of body weight, increased from 1,629 kcal/d to 2,138 kcal/d between the normal and obese weight groups. More details on the study design and procedures are published elsewhere.[16] Each participant was randomized for diet order and followed either a 15-day isocaloric high-fat diet, followed by a 4–6 week washout period, or a 15-day high-carbohydrate diet. Weight and body composition were measured annually for four years; outcomes for fat mass, percentage body fat, and weight were also measured. We found that, on a high-carbohydrate diet, study participants who had a higher positive carbohydrate balance on day 15, while they were inactive in the whole room calorimeter, gained less fat mass during the four-year period. In other words, when excess carbohydrate is stored rather than burned when physically inactive, there was less fat storage over the longterm.[16] So it's not fat or carbohydrate but how you handle the excess carbohydrates during periods of inactivity.

Metabolic Syndrome

Researchers also take into account factors that influence obesity, such as various population and cardiometabolic function differences among groups. The metabolic syndrome is a paradigm that accounts for lifestyle factors that relate to diabetes and cardiovascular disease risk. Since 1998, researchers have defined metabolic syndrome using various parameters; the global definition used today was accepted in 2009 by representatives of leading cardiovascular, diabetes and obesity associations. Metabolic syndrome occurs when three of five of the following are present within a patient: increased abdominal circumference (national and regional cut points vary); triglycerides $>$150 mg/dL; high density lipoprotein (HDL) cholesterol $<$40 mg/dL for men and $<$50 mg/dL for women; blood pressure $>$130/85 mm Hg; fasting plasma glucose $>$100 mg/dL.[17]

The prevalence of metabolic syndrome differs among ethnic groups. An analysis by Ford et al was conducted using data on 8,814 men and women aged $\geq$20 years from the Third NHANES to estimate the prevalence of metabolic syndrome in the United States, as defined by the Adult Treatment Panel (ATP) III report. When considering metabolic syndrome by ethnicity, Hispanic men and women had the highest age-adjusted prevalence of the metabolic syndrome (31.9%) (Figure 1).[18] Hispanic women had an approximately 26% higher prevalence than Hispanic men. Conversely, African American women had a prevalence of 27%, an approximately 57% higher prevalence than African American men 17%). The results of this study, which used 2000 census data, showed that about 47 million US residents have metabolic syndrome as defined by the ATP III report. The study concluded that metabolic syndrome is highly prevalent in US adults, which may have important implications for the health care sector. The relative lower

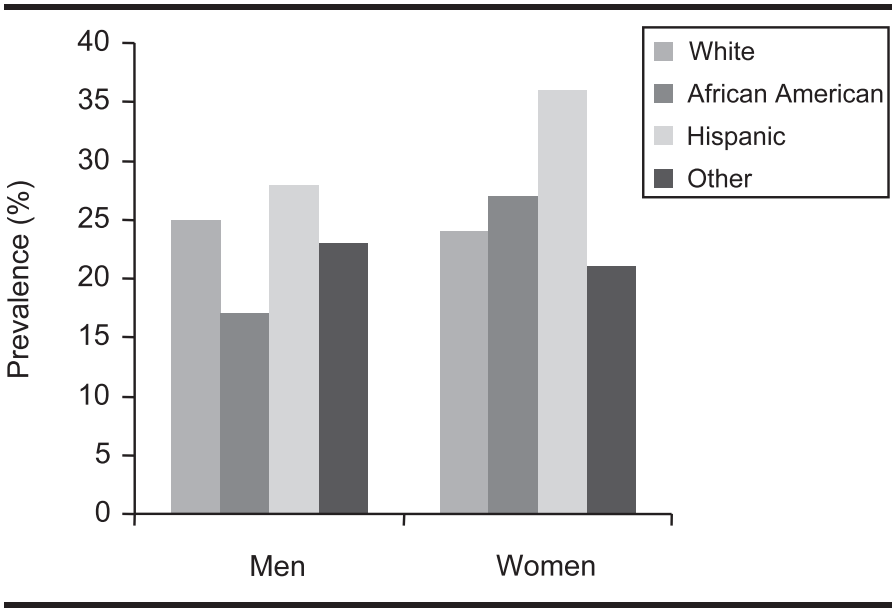

Fig 1. Prevalence of metabolic syndrome by ethnicity, NHANES, 2002. (*N*= 8814)[18]

prevalence of the metabolic syndrome among African American men, and less so in women, may be influenced by the lower rates of triglycerides, as reported by Sumner and colleagues.[19] The relatively higher prevalence of metabolic syndrome among African American (AA) women may be explained by the fact that, while AA women have lower triglycerides, hypertension and waist circumference may be greater.[18] Waist circumference among African Americans may be driven by more subcutaneous adipose tissue and relatively less visceral adipose tissue.[20]

Lifestyle interventions that improve the quality of diet, increase physical activity and produce weight reduction have been shown to improve metabolic syndrome markers. Patients successful in achieving these lifestyle changes will likely see an improvement in the metabolic syndrome markers: a reduction in waist circumference, triglycerides, blood pressure, glucose and inflammatory markers and an increase in HDL cholesterol.[21]

Preventing Weight Gain

In the absence of disorders such as heart failure, liver disease and/or kidney disease, those who burn more energy than the calories they eat will lose weight and, conversely, those who eat more calories than they burn will gain weight. The impact of this energy imbalance on weight gain can be estimated by the following example. If one assumes a weight of 164 lb and a BMI of 25.0 kg/m^2 at age 25 and a 20 lb weight gain over the next 20 years (an average weight gain seen in the USA over that interval),[22] the resultant BMI would be 28 kg/m^2. This amount of caloric imbalance calculates at 8 kcal/day excess. While we do not have instruments sensitive enough to measure that caloric difference, the fact points to a need for increasing biotechnology to try to get to the basis of this important metabolic issue.

In addition to weight gain among the adult population, childhood obesity is one of the biggest health problems in the United States today. Programs like the Alliance for a Healthier Generation have been designed to reduce both childhood and adult obesity. Yet, because biologically driven pathways that relate to the resumption of the obese state make it difficult to maintain weight loss,[23] preventing obesity in the first place should be the nation's primary goal.

One question that remains unanswered is whether an individual has a set or settling point for body weight. That is, do individuals have a genetically defined set point that determines their ideal weight? If this were the case, the obesity epidemic seen over the last two decades would not have occurred. Instead, individuals are more likely to have a *settling* point that relates to environmental influences, such as diet and physical activity, that result in *settling* into a new ideal weight point.

In our current research as part of the Colorado Obesity Research Initiative headed by Dr. Jim Hill at the University of Anschutz Medical Campus, we have been exploring the concept of body weight regulation in much more detail. From this research, we hope to identify interventions successful in long-term weight management and answers to the following questions: What settings are the most conducive to weight management interventions? What are the types and intensity of successful primary or secondary interventions? Preliminary data suggest that interventions at worksites are more successful than those conducted at clinics or community-based locations. We are investigating primary interventions (eg, weight tracking, calorie counting, physical activity, incentives) and secondary interventions (eg, educational materials, weight maintenance and lifestyle classes/counseling).

Preventing obesity[24] follows many of the same four prevention principles used for cancer, diabetes and cardiovascular disease[25]: smoking cessation, screen for early detection of disease, improve nutrition, and increase physical activity. While maintaining a healthy eating pattern relates to cardiovascular disease health, it also relates to weight. People who consume more fiber, fruits and vegetables tend to gain less weight than people whose diet is lacking in these food groups. The American Heart Association[26](AHA) recommends a

Table 1. Benefits of physical activity on cardiovascular health

CV Health Factor	Effect
Anti-atherosclerotic	
	Improved lipids
	Lower blood pressure
	Reduced adiposity
	↑ Insulin sensitivity
	↓ Inflammation
Anti-thrombotic	
	↓ Platelet adhesiveness
	↑ Fibrinolysis
	↓ Fibrinogen
	↓ Blood viscosity
Anti-ischemic	
	↓ Myocardial O_2 demand
	↑ Coronary flow
	↓ Endothelial dysfunction
Anti-arrhythmic	
	↑ Vagal tone
	↓ Adrenergic activity
	↑ HR variability

four-point nutrition guideline that encourages Americans to: 1) eat an overall balanced diet; 2) maintain a healthy body weight by matching caloric intake to physical activity; 3) maintain a desirable lipoprotein profile; 4) maintain a normal blood pressure. Of these, physical activity should be emphasized as an extremely important component in lifestyle choices; it, or more precisely lack of physical activity, plays a central role as an independent risk factor for heart disease and will be emphasized in updates to existing NHLBI guidelines on cardiovascular health. Data have repeatedly shown the benefits of physical activity on cardiovascular health as shown in Table 1.[27]

In a recent study on therapeutic lifestyle and drug therapy interventions to reduce cardiovascular disease, Ardern et al assessed the interventions' effects on cardiovascular disease risk and mortality.[28] Following a group of >19,000 men aged 20–79 years during 1979–1995, Ardern and colleagues study found that, among those with LDL-C levels at goal, those who needed lifestyle modification vs those who needed medications to manage LDL-C levels, were more likely to have improved outcomes. The researchers also found that, even among those obese or at-risk of obesity, if the individual was considered physically fit, mortality rates were lower than those in the unfit group.

For women, less is known about the impact of physical activity on cardiovascular health. Researchers of one meta-analysis published in 2004 found a dose-response relationship between levels of physical activity and risk of stroke, myocardial infarction or other cardiovascular disease. The authors concluded that inactive women would benefit by even a slightly increased amount of physical activity.[29]

It becomes clear that America needs to embrace a campaign to prevent an unhealthy weight gain; meeting the needs of obesity treatment and management is more expensive and much more complicated. As mentioned earlier, the Alliance for a Healthier Generation is one such campaign designed to reduce childhood obesity and is a joint venture begun in 2005 between the Clinton Foundation and the AHA. The program's mission is to reduce the nationwide prevalence of childhood obesity by 2015 and to empower children nationwide to make healthy lifestyle choices. This long-term commitment will allow the two organizations to work together during the next 10 years to address the issues that contribute to childhood obesity and influence children's lifestyles. The alliance will create solutions that inspire all young Americans to develop life-long healthy habits.

The AHA and the Clinton Foundation share common priorities and interests in reaching children and other stakeholders with messages on preventing childhood obesity and creating a healthier generation of children. This initiative is not just about helping children who are already obese, but ensuring that all children have the information and motivation they need to adopt heart-healthy habits, such as: looking at food options and making healthy choices, regardless of weight; incorporating physical activity into daily routines to keep weight in check and blood pressure and cholesterol at healthy levels.

The program encompasses four pillars of activity, including industry, schools, children and health care. In industry, one successful effort has been to address the types of foods allowed from the vending machine industry; to date, data show an 88% reduction in total beverage calories being consumed in American schools. In schools, the Robert Wood Johnson Foundation teamed up with the Alliance to enroll schools (12,000 schools representing 5 million children to date) to work toward criteria to earn designation as a "healthy school." For kids, Nickelodeon, a division of Viacom International, a US-based media company, partnered with the Alliance and gave a $30 million grant to develop *empowerMe*, a program that has encouraged 2.3 million children to adapt a healthy lifestyle. In health care, the Alliance works with professional associations and other health care groups to create tools and continuing medical education (CME) programs that help to enhance the knowledge and skills of primary health care providers in better recognizing, preventing and treating obesity in children.

CONCLUSION

In summary, the obesity epidemic is upon us and the environment is largely to blame for this health risk linked to cardiovascular disease, diabetes and other conditions. Once a person becomes obese, weight loss is hard work; but, it is possible by lifestyle changes alone and, for some, by surgical or pharmacological treatment approaches to achieve and maintain weight reduction and reduced risk for cardiovascular disease and diabetes. If weight loss does not occur, research

shows that getting physically fit can still have some benefits. Patients with multiple risk factors, including obesity, for cardiovascular disease need to be treated aggressively to effect positive health outcomes. However, a wiser, healthier approach to obesity is to prevent it from occurring in the first place. To achieve obesity prevention, it will take a global effort, starting with the individual, and including the family, the health care professionals, the community and the nation.

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