Current Research

Beyond Energy Balance: There Is More to Obesity than Kilocalories

GEORGE A. BRAY, MD; CATHERINE M. CHAMPAGNE, PhD, RD, FADA

ABSTRACT

Using an epidemiologic model of the interactions between environmental agents and human hosts to explain obesity, we explored food, medications, physical inactivity, toxins, and viruses as environmental agents that interact with a genetically programmed host to disturb energy balance and cause obesity. Large portion sizes, high fat intakes, easy access to calorically sweetened beverages, and lack of any need to be physically active all play a role in the toxic environment that leads to obesity. The genetic and physiologic responses of a host determine whether or not this toxic environment will produce obesity. Reversing the current trends of obesity requires a new look at the limits of the energy balance concept, and a better understanding of how environmental factors acutely and chronically change the responses of susceptible hosts.


Obesity is a chronic, relapsing, stigmatized, neurochemical disease that is increasing in prevalence (1,2). During the early part of the 20th century the prevalence of obesity rose slowly, but around 1980 it began to rise more rapidly. Children are affected by obesity, with the prevalence rising from 5% in 1960 to 15% in 2000 (2). Associated with this rise in obesity rates was an increase in the prevalence of type 2 diabetes mellitus in children and adolescents (3). This presages a dire future for these children as complications of blindness, heart disease, renal failure, and amputation disable them during the next 20 years or so.

Obesity increases health risk and the cost of health care (4). Diabetes mellitus, gall bladder disease, heart disease, hypertension, osteoarthritis, and several types of cancer are all increased in persons with overweight. These risks can be reversed by modest weight loss. To tackle the hazards of obesity for children, adolescents, and adults, we need to adopt effective strategies for prevention and, where prevention fails, for treatment of obesity. Many children and adults with overweight are traumatized by the stigma of obesity. Children may be teased at school and labeled “fatty.” Adults experience prejudice in social and economic situations. Measures of quality of life show that persons with obesity score lower on many scales and that weight loss improves their quality of life.

BEYOND ENERGY BALANCE

There is no doubt that obesity results from energy imbalance, and that we can predict the magnitude of weight change over time if we know the net energy balance. However, it is what the energy balance concept does not tell us that is most important in dealing with obesity. The first law of thermodynamics, which describes the concept of energy balance, does not tell us anything about the regulation of food intake or the way in which genes are involved in this process. It does not help us to understand why men and women distribute fat in different places on their bodies, or to understand how fat distribution changes with age. The first law also doesn’t help us understand why some drugs produce weight gain and others weight loss, or why weight loss stops after a period of treatment with diet or medication (5). Understanding these mechanisms will allow us to tackle the epidemic of obesity.

Another problem with the concept of energy balance is that we are never in energy balance. To study energy balance, we housed healthy men in small rooms (respiration calorimeters) where we manipulated food intake and exercise to get as close as possible to zero energy balance; ie, when energy intake equals energy expenditure. In fact, we rarely got closer than 50 kcal/day, or about 2.5% out of an intake of 2,000 kcal/day. The values for energy imbalance in these healthy men ranged from 50 to 150 kcal/day. Had these differences been maintained for 1 year, these men would be expected to gain about 2.5 kg (5.5 lb) at the smaller error and 7.5 kg (16.5 lb) at the larger error. To keep from gaining weight we must correct energy intake or energy expenditure every few days to counterbalance the error that occurred on previous days. These corrective responses around a weight of relative stability make it look like there is weight regulation. For some persons, the oscillations around this balance point can keep weight stable for many years. For others, there is a slow upward drift in this regulatory point and weight is gained gradually. Persons fortunate enough to have robust corrective responses can maintain a stable weight over many years. If their weight is not stable, two other
strategies are available. One is conscious control, exhibited in some persons by a pattern of restrained eating. The second and perhaps best way to maintain weight over a long period is not counting kilocalories, but weighing oneself regularly at the same time of day on an accurate scale, and then decreasing food intake or increasing activity if weight has been gained. This can allow one to correct weight gain before it gets out of hand.

The consequences of energy imbalance are graphically illustrated in the movie by Morgan Spurlock, *Supersize Me* (2004, Hart Sharp Video, Roadside Attractions, and Samuel Goldwyn Films), in which the documentarian gained 25 lb in 1 month by eating all of his meals at McDonald's restaurants, and supersizing the portions if the clerk asked. Because we are never in energy balance, we need to view energy balance as an ideal—not a realistic goal to be obtained by counting kilocalories.

From the perspective of energy balance, the solution to obesity should be simple: Eat less and exercise more. The truth of this advice was shown by Kinsell and colleagues (6) for overweight persons in a metabolic ward who were provided with all of their food. During the course of several months, patients ate diets providing 1,200 kcal/day. After an initial rapid weight loss due to rebalancing body fluids, subsequent weight loss was linear and was not affected by wide variations in macronutrient content of the diet. More recent studies using foods that were tagged with a nonradioactive isotope (carbon-13) showed that the better the adherence to a diet, the greater the weight loss (7). Thus, it is adherence to diets, not diets themselves, that makes the difference (8).

Another limitation to the concept of energy balance as the cause of obesity is the implication that if one is getting fatter, it is one's own fault. One need only to control his or her energy intake and energy expenditure to control the problem. This implies that we should blame our children for their obesity. This seems grossly unfair. If obesity were easily controlled by moderating energy intake, the US military would not discharge up to 5,000 men and women yearly for failing to meet its weight standards. If loss of livelihood is not sufficient motivation to lose weight, then the problem must be more complex.

The cure of obesity in leptin-deficient human beings treated with leptin shows a genetic basis for one type of obesity, and that obesity is more than simply lack of willpower (9). Although simple in theory, applying the ideas of energy balance and counting kilocalories to body weight control has proven unsuccessful. More than 95% of persons using diet, behavior, and lifestyle approaches to lose weight regained it in less than 5 years (10).

**ENVIRONMENTAL AGENTS**

The current epidemic can be viewed from the perspective of an epidemiologic model, shown in Figure 1. Food, drugs, viruses, toxins, and low physical activity are the environmental agents that facilitate the development of obesity. One or more of these factors acting on a susceptible host can produce obesity. Using this model, we can approach the problem by manipulating either the environment or the host.

![Figure 1. Epidemiologic model of obesity. In this model, the agent that produces obesity is food or food-related products. If food is in limited supply, obesity does not develop. The food that is ingested interacts with the host. In a susceptible host, the toxic effects of food produce the disease of obesity.](image)

**Food**

As the spokesperson for the Grocery Manufacturers of America said in the movie *Supersize Me*, “The food industry is part of the problem.” Several components of our food supply may be important in determining whether or not obesity develops. The first of these is the portion size of packages and servings. There is convincing evidence that when larger portion sizes are provided, more food is eaten (11). Portion sizes have dramatically increased in the past 40 years (12) and now need reduction. Calorically sweetened beverages that contain 10% high-fructose corn syrup (HFCS), available in containers of 12, 20, or 32 oz, provide 150, 250, or 400 kcal if it is all consumed. Many foods list the kilocalories per serving, but the package often contains more than one serving.

Patterns of food consumption have changed during the past 30 years (13). The most striking change from 1970 to 2000 was in the rising consumption of HFCS (14). HFCS is now used as the caloric sweetener in almost all soft drinks as well as in reconstituted juice drinks and many solid foods. The rise in HFCS consumption occurred during the same time interval as the rapid rise in the prevalence of obesity (2,14). On one hand, this relationship may be strictly coincidental. But, on the other hand, it may not (Figure 2). Fructose is sweeter than glucose, or sucrose, a molecule that is a combination of fructose and glucose. In addition, HFCS is a solution of both fructose and glucose as separate molecules, and thus it differs in osmotic properties from a solution with the same concentration of sucrose.

The intake of calorically sweetened beverages can be related to the epidemic of obesity (14-17). Ludwig and colleagues (15) reported that the intake of soft drinks was a predictor of initial body mass index (BMI) in children in the Planet Health Study. They also showed that higher soft drink consumption predicted an increase in BMI during nearly 2 years of follow-up, those with the highest soft drink consumption at baseline having the highest increase in BMI. A Danish study (16) showed that persons consuming calorically sweetened beverages over 10 weeks gained weight, whereas subjects drinking the
same amount of artificially sweetened beverages lost weight. In children, a study focusing on reducing intake of carbonated beverages and replacing them with water showed slower weight gain than those not advised to reduce the intake of carbonated beverages (18). These studies strongly suggest that energy-containing soft drinks could play a role in the epidemic of obesity. If so, then their consumption should be curtailed, particularly for very young children in whom neuronal changes may reflect the response of insulin to these beverages, and for school children for whom beverages are a ready source of energy with few other nutrients.

Dietary fat is another component that may be related to the epidemic of obesity (19). Foods combining fat and sugar may be a particular problem because they are often very palatable and usually inexpensive (20). The Leeds Fat Study (21) showed that persons who were high fat consumers had increased prevalence of obesity. Providing palatable low-fat foods is important.

There are now several studies showing that when breastfeeding is the sole source of nutrition for more than 3 months, risk of obesity is significantly reduced at the time of entry into school and in adolescents when compared with infants who are not breastfed at all or for less than 3 months (22). This may be an example of infant imprinting. The composition of the breast milk may also be important. During the past 50 years, the proportion of n-6 fatty acids in human breast milk has increased, reflecting changes in dietary fat composition. The amount of n-3 fatty acids in breast milk has remained constant. A higher amount of n-6 fatty acids provides prostaglandin derivatives that stimulate fat cell proliferation in infants (23). This is a concept that needs additional evaluation.

The rate of weight gain between ages 2 and 12 years also predicts future obesity—those children who gain the most weight have the highest risk of becoming obese (24). Monitoring weight change early can be predictive of future obesity.

Calcium intake is another dietary factor that may be related to the development of obesity in children and adults. The level of calcium intake in population studies is inversely correlated with the risk of being overweight. In other epidemiologic studies and in feeding trials, higher dietary calcium is associated with reduced BMI or reduced incidence of insulin resistance (25).

Low Levels of Physical Activity

Epidemiologic data show that low levels of physical activity and watching more television predict higher body weight (26). Recent studies suggest that persons in US cities where they had to walk more than persons in other cities tended to weigh less. Low levels of physical activity also increase the risk of early mortality. Using normal weight, physically active women as the comparison group, Hu and colleagues (27) found that the relative risk of mortality increased to 1.55 in inactive lean women, to 1.92 in active obese women, and to 2.42 in women who are obese but physically inactive. It is thus better to be thin than fat and to be physically active rather than inactive.

Drugs and Chemicals that Produce Weight Gain

Several drugs can cause weight gain, including a variety of hormones and psychoactive agents (28). The degree of weight gain is generally not sufficient to cause substantial obesity, except occasionally in patients treated with high-dose corticosteroids, some psychoactive drugs, or valproate. These drugs can also increase the risk of future type 2 diabetes mellitus. Cessation of smoking is another environmental agent that will affect body fat stores. Partially mediated by nicotine withdrawal, a weight gain of 1 to 2 kg is seen in the first few weeks and is often followed by an additional 2- to 3-kg weight gain over the next 4 to 6 months, resulting in an average weight gain of 4 to 5 kg or more (29). The concept that increasing energy expenditure through drugs that act like physical activity is being tested in several ways, but as yet no effective agents have been identified.

Viruses

The injection of several viruses into the central nervous system produces obesity in mice. Recent findings of antibodies to one of the adenoviruses (AM-36) in larger amounts in obese human beings raises the possibility that viruses are involved in some cases (30). The adeno-viral syndrome can be replicated in nonhuman primates and is characterized by modest obesity and a low circulating cholesterol concentration. Further studies are needed to establish that a syndrome of obesity associated with low concentrations of cholesterol clearly exists in human beings. If so, this would enhance the value of the epidemiologic model.

Toxins

In experimental animals, exposure in the neonatal period to monosodium glutamate, a common flavoring ingredient in food, will produce obesity. A similar effect of reduction in glucose can also produce obesity, suggesting that the brains of growing animals, and possibly those of human beings, may respond with damage to the metabolic sensors that regulate food needs. In human beings, body fat stores many toxic chemicals that are mobilized with...
weight loss. The metabolic rate can be reduced by organochlorine molecules (31), and prolonged exposure to many chlorinated chemicals in our environment has conceivably affected metabolic pathways and energy metabolism. Food additives are another class of chemicals that are widely distributed and may be involved in the current epidemic of obesity.

THE HOST

Genetic Factors

Significant insight into the causes of obesity has come from the cloning of genes that produce obesity in animals. Extensive molecular and reverse genetic studies (mouse knockouts) have also helped establish critical pathways regulating body fat and food intake. Leptin, identified in 1994, is an important hormone produced in adipose tissue and secreted into the blood relative to the amount of body fat (32). Leptin-deficient persons are massively obese and when leptin is administered, food intake falls and body fat is mobilized until body weight is nearly normalized, indicating that important metabolic-genetic pathways exist that can control body fat. Similar deficiencies in food intake have been found with genetic changes in the amino acid sequence of a key regulator of food intake called the melanocortin-4 receptor (33). When this receptor is inactive, food intake is nearly as high as when leptin is deficient, but when partially preserved, the food intake is only modestly above control levels (34). These basic biological insights tell us that body fat has important regulation that is largely, if not completely, independent of will power.

Intrauterine Imprinting

Several intrauterine events may lead to obesity later in life, probably due to fetal imprinting as a result of early exposure that affects brain plasticity. The Dutch winter famine of 1945 showed that starvation of infants in utero could affect long-term postnatal weight status. Another example is the infants of mothers who smoked during pregnancy, who have an increased risk of becoming overweight during their first 3 decades of life when compared with infants of mothers who did not smoke during pregnancy (35). Similarly, infants of mothers with diabetes are at higher risk of developing obesity than infants born to mothers who did not have diabetes during pregnancy (36). Infants who are small for their gestational age are at higher risk of developing central adiposity and diabetes than normal-weight infants (24). Finally, experimental studies teach us that exposure to high levels of insulin during the period of brain plasticity can lead to obesity later in life.

Physiologic Control

To maintain a stable body weight over time, the body must correct daily errors in energy balance. A number of physiologic factors are known to disturb this correction. A high rate of carbohydrate oxidation, as measured by a high respiratory quotient predicts future weight gain (37). One explanation is that when carbohydrate oxidation is higher than carbohydrate intake, carbohydrate stores are depleted and we must eat to replace them. Persons with obesity who have lost weight are less effective in increasing fat oxidation in the presence of a high-fat meal than normal-weight persons, and this may be one reason why they are so susceptible to weight regain. Low metabolic rate may also predict future weight gain (38). Physical activity gradually declines with age, accounting for some increase in body fat. Recent studies suggest moderate exercise is beneficial in reducing risk of cardiovascular disease (39) and type 2 diabetes, and in facilitating the oxidation of fat in the diet (40).

Fat cells in our body serve two major functions. They store and release fatty acids ingested from food or from liver or fat cells and they secrete many important hormones and chemicals. The discovery of leptin catapulted the fat cell into the arena of endocrine cells (41). In addition to leptin, the fat cell secretes a variety of other peptides (lipoprotein lipase, adipsin [complement D], complement C, adiponectin, tumor necrosis factor-α, interleukin-6, plasminogen activator inhibitor-1, angiotensinogen, bradykinin, and resistin). The fat cell also releases other metabolites such as lactate, fatty acids, glycerol, and prostacyclin formed from arachidonic acid. Our understanding of fat cells as important endocrine cells continues to expand.

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Production of cortisol from inactive cortisone in fat cells by the enzyme 11-β-hydroxysteroid dehydrogenase type 1 may be important in determining the quantity of visceral adipose tissue (42). Changes in this enzyme may contribute to the risk for menopausal women of developing more visceral fat. High levels of this enzyme keep the quantity of cortisol in visceral fat high, providing a fertile environment for developing new fat cells.

Information about hunger and satiety comes from the gastrointestinal tract where several peptides signal the body to stop or start eating. Ghrelin (43) has received recent attention because, in contrast to other gastrointestinal hormones, it stimulates food intake. Levels of ghrelin are low in obesity, except in those with Prader-Willi syndrome, suggesting that it may play a role in the development of hyperphagia seen in these persons.

The brain is a receiver, transducer, and transmitter of information about hunger and satiety. Several neurotransmitter systems are involved in regulation of food intake (44). Receptors for serotonin modulate both the quantity of food eaten and macronutrient selection and their loss through genetic targeting produces obesity. Peptide neurotransmitters also play a very important role in the regulation of feeding. Sleep deprivation is one way to enhance the release of peptides that produce hunger (45). In young men allowed to sleep only 4 hours/night for 2 days, leptin decreased and ghrelin increased relative to the pattern seen with 10 hours of sleep on each of two
nights. Thus, our epidemic of obesity may reflect one response to less sleep.

**OBESITY IS A CHRONIC, RELAPSING, NEUROCHEMICAL DISEASE PRODUCED BY THE INTERACTION OF ENVIRONMENT AND HOST**

The epidemic of obesity occurs on a genetic background that has not changed significantly in the past 100 years and certainly not since the epidemic began 20 years ago. Nonetheless, it is clear that genetic factors play a critical role in the susceptibility of becoming obese in a “toxic environment” (46). One analogy is that genes load the gun and a permissive or toxic environment pulls the trigger. Modification of environmental factors acting on our ancient genes must be the strategy to prevent the disease. To believe that this can be done by a person alone is to miss the argument of how environmental factors, with major emphasis on the imprinting of the plastic brain of a growing child or adolescent, have acted on these genes to produce the current epidemic.

We argue that the first law of thermodynamics has lulled us into the uncomfortable place of believing that persons, through willpower, increased food choices, or more places to exercise, can overcome the current epidemic of obesity. Cognitive approaches relying on individual commitment and resolve have been unsuccessful in stemming obesity in the past, and nothing suggests that they will be more successful in the future.

**At least three preventive strategies are available to deal with the epidemic: education, regulation, and modification of the food supply.**

We also argue that it is what the first law of thermodynamics does not tell us that is important. In this context, it is the unconscious host systems on which environmental factors operate to produce obesity. If the vending machines that now provide kickbacks to schools contained beverages with no added sugar or HFCS, available kilocalories would be reduced. We have argued that the exposure of young children to HFCS may produce detrimental imprinting of the brain, making obesity more likely and more difficult to control.

At least three preventive strategies are available to deal with the epidemic: education, regulation, and modification of the food supply. Education in school curricula about good nutrition and healthful weight would be beneficial in helping all children learn how to select appropriate foods and could be included in schools, with school breakfast and lunch programs designed to match these educational messages.

It is unwise to rely on educational strategies alone because they have not prevented the epidemic of obesity. Regulation is a second strategy. Regulating an improved food label is one good idea. Regulations on appropriate serving sizes might be part of the information provided by restaurants when requested.

Modification in some components of the food system is a third and most important strategy. Because the energy we eat comes from food, we need to modify this system to provide smaller portions and less energy density if we are to succeed in combating the epidemic of obesity.

**CONCLUSIONS**

Where do dietetics professionals fit into this picture? First, educated dietetic professionals need to be keenly aware of the complexity of the obesity problem. A dietetics professional obviously cannot alter a person’s genetic makeup, but he or she is able to address the environmental aspects that serve to exacerbate the situation. Simply handing out diet sheets is not enough and should be discouraged. Helping a patient with obesity requires attention to overall diet history, current eating habits, activity patterns, and behavioral obstacles that either cause problems or prevent change. While quick weight loss may be a patient’s immediate desire, the need for permanent lifestyle changes should be the primary objective. Tips for addressing this have been outlined previously by Bray and Champagne (47). Finally, dietetics professionals can be instruments of change by appealing to policymakers to modify environmental conditions, such as the school vending machines. We can think of no better professionals to craft this effective message to both lawmakers and school officials alike.

**FUTURE DIRECTIONS**

Our lives are constrained by the laws of nature—gravity, momentum, and thermodynamics. The strategies we employ to deal with the influence of these laws on our lives include education, regulation, and product design. Deaths resulting from the effects of the laws of momentum produced by automobile accidents provide a glimpse into the strategies we could use to minimize accidents just as the law of energy balance provides ideas about how we might minimize obesity. Although the laws of momentum or the laws of thermodynamics cannot be changed, their ability to produce automobile accidents and obesity can be mitigated. This can be done through better education about driving and about nutritional needs to prevent obesity. This can be complemented by regulations that, in the case of cars, include requiring seat belts, airbags, and other safety devices. In the case of obesity, it includes limiting access to large portion sizes and high-energy-density foods and having an environment in which physical activity is more difficult to avoid. Finally, product design can make cars safer, and modifying the types of foods that are available can provide strategies to combat the obesity epidemic by redesigning the food environment.

This research was supported in part by the US Department of Agriculture CSREES Special Grant No. 2003-34323-14010 to the Pennington Biomedical Research Center.

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Obesity has been steadily increasing in the United States for the past 3 decades. At present almost 65% of the population is overweight or obese, with the prevalence higher for minority populations. Obesity now is present in 31% of the population and overweight in 34% (1). Approximately 1% of the adult population is moving into the obese category (body mass index [BMI] > 30) every year. A similar increase is being seen among children and adolescents (2). This pattern is not confined to the United States, but is also occurring throughout the world, in both developed and less developed countries (3).

Obesity is associated with several risk factors and diseases. These include insulin resistance, glucose intolerance, type 2 diabetes mellitus, hypertension, dyslipidemia, coronary heart disease, stroke, heart failure, and certain kinds of cancer, as well as earlier mortality (4). This has led to increasing costs. Obesity has been reported to be responsible for 5.5% to 7.8% of all health care costs (5), to lead to a loss of productivity by days lost from work, and to cause a great number of disabilities (6). These disabilities are expensive both financially and with respect to quality of life.

The change in weight of the US population has occurred without changes in the gene pool, suggesting that the root cause of the epidemic is change in lifestyle and environment rather than a biological genetic change in the population. This does not imply that genes are not important. Between 30% and 40% of the variance of weight is genetic (7). There is clearly a gene-environment interaction, with some individuals being more sensitive than others to the “toxic” environment we now experience.

The environmental determinants of weight gain in the population are diet and physical activity. Individuals are eating more and exercising less, and this imbalance between energy intake and energy expenditure leads to a situation in which adults between 20 and 40 years of age in this country gain about 1.8 to 2.0 pounds per year (8).

What are the future directions in the field that could improve health outcomes? It is evident that much remains to be learned about all aspects of obesity, ranging from basic biology to effective intervention programs for prevention and treatment. We have learned a great deal over the years about many important aspects of obesity; nonetheless, we have not been able to translate it to better intervention for prevention and treatment. As mentioned earlier, there is still an alarming increase in overweight and obesity in all population groups.

We need to do everything we can to get people to understand that they are ingesting too many calories. We need to improve nutrition education. This will require a combined effort of nutrition professionals, physicians, health maintenance organizations, insurance companies, government, and industry. We need to alert people to avoid large portion sizes, energy-dense foods, indiscriminate snacking, high intake of caloric beverages, and empty calories. A better understanding of the basis of a sound diet that brings adequate micronutrients without extra calories is required.

We also need to encourage people to be more physically active. This will require public awareness campaigns by the government, the medical profession, voluntary health agencies, and private groups. In addition, we need to improve the environment to create the venues in which physical activity can take place. This includes safe streets and sidewalks, better and safer parks, more and open gymnasiums, and more bike paths and public swimming pools.

Studies to date have shown that relatively small decreases in weight and relatively small increases in exercise can have a profound effect on health. The Diabetes Prevention Program (9) and the Finnish Diabetes Prevention Study (10) have both reported this. A 6% to 7% decrease in weight and a 30-minute per-day increase in physical activity can decrease the conversion of impaired glucose tolerance to diabetes by more than 50%.

We need to get industry to undertake changes that can help to ameliorate the obesity problem. These include, both for food companies and for restaurants, better nutrition labeling, smaller portion sizes, lower energy density, and more low-calorie alternatives. Adolescent obesity tracks to adult obesity, so it is particularly important to attempt to stem the increase in obesity in this group. School-based initiatives should be created to try to develop efficacious and practical programs to prevent and
reverse obesity. More and better nutrition education and physical education are needed in the schools. We are deficient in this regard in the United States.

We have learned a great deal in the last decade about the biology of the regulation of food intake, but we need to know much more. More research funding is needed from the federal government. Research is necessary for understanding how important centers in the gut, the brain, and elsewhere control hunger, satiety, and thermogenesis. We need to understand more about which genes are important in turning food intake on and off and influencing energy expenditure. We need to identify the peptides and other molecules that are important, and we need to understand the mechanisms by which they work. We have to look seriously at the genetic underpinnings of behavior. Little work has been done in this area to date. The fat cell as an endocrine organ must be studied because it produces bioactive molecules that have an influence on inflammation, thrombosis, endothelial function, macro-nutrient disposal, and energy production. The role that ectopic fat plays in the development of diabetes and cardiovascular disease needs to be better defined and explained. How inflammatory stimuli abet the chronic diseases associated with obesity has to be further explored. The role of vascular reactivity and its relation to products released by excessive and ectopic fat must be defined.

We need to learn more about effective weight-loss diets/programs and how best to counsel patients. This will require more research that is designed to understand dietary patterns (including individual components of the diet) that result in the prevention of weight gain and successful treatment of obesity. This research will need to be in the form of intervention trials that actually test the role of nutrients and their effects. Simply doing observational longitudinal studies is not enough. Observational cross-sectional studies are worse than useless because they are often misleading.

Although our current tools for confronting the obesity epidemic are weak because our knowledge base is still small, we know enough now to make concerted efforts to begin to improve public health. This will require, as mentioned earlier, changes in people's consciousness about the problem, improved education about healthful diets and physical activity, an improved environment, and serious efforts by government and industry to help in the difficult task of turning this epidemic around.

Recent dietary guidelines have addressed the overweight and obesity problem in the United States. The 2005 Dietary Guidelines (11) have stressed for the first time the importance of physical activity. The recommendations take into consideration the growth of obesity in the United States and address the important issues. In addition to the guidelines themselves, an evidence-based report by the Dietary Guidelines Advisory Committee has also been published (12) and is available to all health professionals and the general public. Similarly, the American Heart Association Dietary Guidelines (13) recommend that the major emphasis for weight management should be on avoiding excess total energy intake and following a regular pattern of physical activity. These guidelines are written for the general population. Widespread implementation of these guidelines, though challenging, is necessary. Strategically, the dietetics community is confronted with what to do to lessen the burden of the obesity epidemic. Simply stated, this means developing and implementing effective strategies for treating overweight and obesity on an individual level and in large cohorts at the community, state, and national levels. The magnitude of the obesity epidemic is so serious that, to have a major impact on slowing (and even stopping) the rate of increase and ultimately dramatically reducing the incidence of obesity, dietetics professionals must identify new strategies to deal with this enormous health problem. Although some optimistic observers suggest that the incidence of obesity is plateauing, we see no such evidence to date. Hopefully, some of our remedial suggestions may help to bring this about. The role of the dietetics professional in practice has evolved in response to changing societal needs. When the American Dietetic Association (ADA) was founded in 1917, it was dedicated to helping the government conserve food and improve the public's health and nutrition during World War I. History shows that the early ADA provided valuable assistance to this cause. The nutrition and health needs of the US population are different today than in 1917, with diseases related to overconsumption assuming prominence in health care. In parallel, dietetics practice has changed markedly with the evolution of many different practice emphases (such as private practice, foodservice management, nutrition education, clinical nutrition, and many others) that relate to food behaviors. Thus, with the broad education and training required of dietetics professionals and the diversity of expertise in the ADA membership, the dietetics profession is in a strong position to develop innovative and effective obesity intervention programs.

Traditionally, a model that favors one-on-one counseling approaches has guided medical nutrition therapy. There is much information in the literature about guidelines for the treatment of overweight and obesity summarized in the National Institutes of Health Clinical Guidelines Report (14). The role of the dietetics professional in providing medical nutrition therapy involves assessing nutritional status and planning and recommending food behavior interventions (15). Medical nutrition therapy also involves identifying effective interviewing approaches, treatment plans that involve patients/clients, ideal documentation strategies, suitable follow-up timelines, and appropriate referrals when indicated.

Although there is little dispute that dietitians are experts at delivering medical nutrition therapy using this time-honored approach, the magnitude of the obesity problem argues that the profession must develop new ways to have a substantial impact on the obesity epidemic. The reality is that the health care profession is a long way from where it needs to be if it is to rein in the obesity epidemic. There is no question that innovative and bold new approaches must be developed for the prevention and treatment of obesity. The critically pressing question is: what are they? There is no simple solution. The dietetics profession confronts a complex and challenging problem (16).

What should dietetics practice look like in the future? It must go beyond the traditional in all areas of the profession. The future paradigm will involve population-based obesity interventions that will require the full cooperation of the entire health care community. Moreover, it
will require coordinated integration of the expertise represented by different health care disciplines with the diversity of skills to develop innovative ways to tackle the obesity problem. The magnitude of the problem is such that the food industry and government also must be active participants in planning and implementing solutions. Active cooperation of the health care community, the private sector, and policymakers is essential if we are to make marked progress.

The expertise and diversity of skills of the dietetics profession offers much for a bold initiative to battle obesity. A major effort will be required to meaningfully reduce the incidence of obesity in the population at large. First, new education efforts are needed to overcome the rampant public misunderstanding about what lifestyle strategies are effective for weight loss. The importance of a balanced diet for lifetime health has to be at the forefront of our effort. Given the public's perceptions about the efficacy of unbalanced diets, this will be a major challenge. Dietetics professionals are well positioned to lead this nutrition education effort. It is essential that dietetics professionals continue their legacy of implementing practice guidelines for the treatment of overweight and obesity. This will continue to make an impact at the individual level.

Dietetics professionals must emphasize sound weight-management approaches in all counseling sessions. Repeated messages about a healthful diet and physical activity patterns for achieving and maintaining a goal weight will reinforce important messages about preventing overweight and obesity, and even preventing small weight changes that occur slowly over time. A dietetics professional and patient partnership that defines reasonable changes and expectations is important to set the stage for smaller, permanent changes. By implementing state-of-the-art counseling skills, dietetics professionals will have a long-term impact on the weight-management efforts of individual clients. With advances in pharmacotherapy for obesity, it is important for dietetics professionals to work with physicians in implementing medication use within the context of lifestyle change.

On a grander scale, dietetics professionals should be encouraged to participate in nutrition advocacy at the local, state, and federal levels with policymakers and the private sector, and to encourage healthful eating and lifestyle behaviors, including developing public information campaigns (17). Importantly, they must spearhead nutrition efforts to promote healthful eating behaviors at the grassroots level. Collectively, the dietetics community must participate in the public and scientific discussions at all levels to identify solutions and sensible and effective government policies to catalyze a new framework that makes substantive strides in reducing obesity in the United States.

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Hanah N. Polotsky, M.D., F.A.C.P., and Alex J. Polotsky, M.D., F.A.C.O.G.

ABSTRACT

The incidence of metabolic syndrome increases substantially during perimenopause and early menopause. Postmenopausal women are at a higher risk of hypertension, proatherogenic lipid changes, diabetes, and severe cardiovascular disease as compared with their premenopausal counterparts. Whether or not menopause has a causative contribution to the deteriorating metabolic profile that is independent of chronological aging has been a subject of many studies. Menopause transition is associated with significant weight gain (2 to 2.5 kg over 3 years on average), which is not dissimilar to that in premenopausal women of like age. Concomitantly, there is an increase in abdominal adiposity and a decrease in energy expenditure, phenomena that have been postulated to explain the higher risk of metabolic syndrome and increases in cholesterol and triglycerides. Hypertension and diabetes become more prevalent with age and should be timely diagnosed and treated. Lifestyle changes including moderately decreased caloric intake and aerobic exercise could prevent proatherogenic changes and weight gain observed with aging. Accurate prediction of cardiovascular risk in midlife women is essential to help identify the subset of women who are likely to benefit from intensive management of metabolic risk factors. This review focuses on metabolic changes associated with menopausal transition, specifically alterations in weight, waist circumference, body fat distribution, energy expenditure, and circulating biomarkers including adipokines.

KEYWORDS: Menopause, obesity, metabolic syndrome, cardiovascular risk

Connection between body habitus and health had been contemplated since antiquity as illustrated by a treatise on “drawbacks of excessive obesity” written by Avicenna (980–1037) in his “Canon in Medicine.” For women, postmenopausal status has been traditionally regarded as a cardiovascular risk factor. Incidence of heart disease increases with age in both genders, yet it occurs a decade later in women, largely after menopause. Increase in heart disease risk was observed in women following surgical and natural menopause. Estrogen deficiency has been posited as a cause of this increase. However, trials of hormone therapy for primary and secondary prevention of cardiovascular disease (CVD) in postmenopausal women demonstrated an unexpected increase in CVD with estrogen supplementation. An increase in prevalence of heart disease at midlife could be related to a multitude of metabolic and hormonal changes occurring during the menopausal transition and early postmenopause. The effect of menopausal transition on anthropometric parameters, blood pressure, lipids, insulin sensitivity, and metabolic syndrome has been a subject of several recent studies. Postmenopausal heart disease may be related to an observed increase in the incidence of metabolic syndrome.
DEFINITION AND TERMINOLOGY OF MENOPAUSE

Menopause involves the transition from reproductive competence to postmenopause and is best thought of as a dynamic process that takes place over several years. It involves many hormonal and physiological changes including but not limited to increased follicle-stimulating hormone (FSH) production by the pituitary, changes in the length and regularity of menstrual cycles with eventual attainment of amenorrhea, decreases in hepatic sex hormone-binding globulin (SHBG) and serum levels of estradiol (E2), and minimal decline in circulating androgens. In contradistinction, alterations in nonreproductive hormones produced by thyroid, parathyroid, and pancreas that are noticeable postmenopause are thought to be related to chronological aging without a significant relationship to menopause. Knowledge and investigation of the menopausal physiology and timeline were greatly facilitated by the development of staging systems of reproductive aging. The following terminology, adopted from the Stages of Reproductive Aging Workshop, is used in this review:

- Menopause: A state after 12 months of amenorrhea following the final menstrual period (FMP); note the retrospective nature of this definition.
- Menopausal transition: Early (stage 2) or late (stage 1) includes changes in menstrual regularity and increases in FSH that culminates in the FMP.
- Perimenopause: Menopausal transition plus 1 year after FMP.
- Postmenopause: Early (stage +1) includes 5 years after FMP and late (stage +2) until death.

CHANGES IN PHENOTYPE, ENERGY EXPENDITURE, AND METABOLIC MILIEU WITH REPRODUCTIVE AGING

Obesity, as defined by World Health Organization (Table 1), is more prevalent in women than in men. The latest National Health and Nutrition Examination Survey data estimate that approximately two thirds of women 40 to 60 years of age are overweight or obese. Body weight increases with age, irrespective of the baseline weight in normal and obese individuals alike. Weight gain during menopausal transition has been scrutinized as a major contributing factor to midlife body weight. The Healthy Women Study demonstrated an average weight gain of 2.5 kg over a 3-year-period during the menopausal transition, a significant finding that was nonetheless similar to the observed change of control women who remained premenopausal during the study period. In contrast to the observational studies, weight gain appeared more pronounced in women on hormone therapy (HT). Yet the wide range of weight changes made it difficult to reach generalizable conclusions because some women gained up to 32 kg and others lost close to 15 kg. No baseline characteristics, including initial body mass index (BMI), were predictive of the degree of weight gain. Similarly, the Study of Women’s Health across the Nation (SWAN) demonstrated no difference in the BMI between premenopausal women and those who experienced natural menopause, with an average weight gain of 2.1 kg related to chronological aging but not to menopause per se. Likewise, in a longitudinal study from Scotland, women gained weight independent of their menopausal status or hormone replacement therapy use.

Weight gain at midlife is partially attributed to the reduction in energy expenditure (EE). Lovejoy et al demonstrated a larger decrease in EE in women who underwent menopause compared with the premenopausal controls at 4-year follow-up. Several explanations were proposed to rationalize this observed decline in EE including a reduction in leisure time physical activity, loss of lean body mass causing basal EE decline as well as a loss of the luteal phase increases in EE described in the premenopausal years. Changes in waist circumference, visceral adipose tissue (VAT), and body fat distribution has been ascribed to both chronological aging and menopause. In SWAN, chronological aging was a contributing factor to the increase in weight and waist circumference, whereas menopausal status was not. Using computed tomography (CT), Lovejoy et al demonstrated an increase in subcutaneous adipose tissue with age, independent of menopausal status, whereas VAT and total body fat increased only in women who became postmenopausal during the
4 years of follow-up. This change in visceral adiposity was accompanied by a decrease in circulating estradiol and increase in FSH and was attributed by the authors to influences of estrogen on lipoprotein lipase activity and lipolysis. A smaller study by Franklin et al used magnetic resonance imaging to study total abdominal, visceral, and subcutaneous adiposity in eight healthy women before and after menopause; the authors demonstrated an overall increase in the absolute adiposity, without evidence of fat redistribution from the subcutaneous to visceral sites. Of note, BMI and waist circumference did not change in this study.

VAT is thought to play an important role in the production of inflammatory adipokines: monocyte-chemoattractant protein(MCP)-1, tissue plasminogen activator inhibitor (tPA), tumor necrosis factor-α, and interleukin-6. Patients with increased abdominal adiposity have been demonstrated to have higher levels of leptin and C-reactive protein (CRP) and lower levels of adiponectin. Associations between inflammatory cytokines and increased risk of postmenopausal coronary artery disease, metabolic syndrome, and diabetes have been reported. During menopausal transition Lee et al demonstrated a positive correlation between intraperitoneal fat and changes in leptin, tPA, MCP-1, and CRP; and a negative correlation with adiponectin.

**METABOLIC SYNDROME AND MENOPAUSE**

Metabolic syndrome (MetS) is a cluster of cardiovascular disease and diabetes risk factors (Table 2) that was recognized in the 1990s as a major risk factor for cardiovascular morbidity and mortality. Although the terminology and diagnostic criteria of MetS have been a subject of debate, controversy, most experts agree that each individual component of the purported syndrome constitutes an independent risk factor for CVD.

Recently, a joint statement of several international organizations published unified criteria of MetS with waist circumference measurements based on regional or national data (Table 2). By this definition, approximately a quarter of the U.S. population is affected by the metabolic syndrome at midlife. Menopause is associated with a 60% increased risk of MetS, a relationship that is described as being independent of age, BMI, and physical activity. Beyond the defined clinical features of MetS, (i.e., central adiposity and hypertension), a proatherogenic and a proinflammatory environment and insulin resistance describe the metabolic milieu of MetS. Further, a close relationship between abdominal adiposity and insulin resistance is recognized. Increased visceral adiposity during menopausal transition is thought to be associated with the worsening insulin resistance, elevated free fatty acid levels as well as decreased adiponectin. Low circulating SHBG levels were linked to MetS in postmenopausal women in the Women’s Health Study. In SWAN, prevalence of MetS prior to the FMP was 32.7% with an additional 13.7% of the cohort developing incident MetS at the time of FMP. The incidence of MetS had been demonstrated to increase progressively during the menopausal transition and in the 6 years following menopause. An increase in the bioavailable testosterone and a decrease in SHBG observed in SWAN were both associated with the development of MetS, whereas changes in estradiol and total testosterone were not. A relative excess of androgens rather than estrogen deficiency was found to be related to the risk of developing MetS in the SWAN cohort, independent of age or other cardiovascular risk factors.

Taken together, the studies suggest that prevalence of MetS increases substantially during menopausal transition and is independent of age, body mass, and physical activity. Changes in the androgens-to-estrogens ratio after menopause appears to be related to an
observed rise in the deposition of intra-abdominal fat mediating insulin resistance and detrimental lipid changes observed in the MetS.

### DIABETES RISK, DIABETES, AND MENOPAUSE

Approximately 10 million women live with diabetes in the United States based on the Centers for Disease Control and Prevention statistics. The risk of diabetes increases with age in women and men. A role of menopause as a risk factor for diabetes, independent of age and excess BMI, had been suggested but remains unproven. Impaired glucose tolerance (Table 3) has been observed in patients with increased abdominal adiposity. The incidence of MetS, but not type 2 diabetes, had been described to rise with menopausal transition. The increased free testosterone and decreased SHBG described in the context of menopause are implicated in the pathophysiology of the observed greater risk of type 2 diabetes and impaired fasting glucose in postmenopausal women. A cross-sectional study by Muscelli et al found no difference in insulin sensitivity, fasting glucose, or insulin levels between premenopausal and postmenopausal women matched for age and body mass. A 6-year longitudinal study from Australia by Sorgi et al failed to show an appreciable change in impaired glucose tolerance or type 2 diabetes in women during or after menopausal transition. In this study, the women progressively gained weight during follow-up, yet no changes in waist circumference, abdominal adiposity, or other cardiovascular risk parameters were observed. Of note, most studies of women treated with HT, including a secondary analysis of the Women’s Health Initiative, found a decreased incidence type 2 diabetes in women on HT. A combination therapy of estrogen and progesterone had a greater effect on type 2 diabetes incidence reduction than estrogen alone. These observational studies mostly used fasting glucose, and not 2-hour oral glucose tolerance testing, to diagnose diabetes. Some studies but not others demonstrated that women with diabetes, type 1 and type 2 alike, undergo menopausal transition at a younger age. Women with type 1 diabetes may be preferentially at a higher risk for ovarian failure based on a shared predisposition for autoimmune pathogenesis of both entities. The earlier time of menopause observed in women with type 2 diabetes may likely be related to obesity per se and not diabetes itself. Increased free androgens observed in diabetes are most likely related to lower levels of SHBG caused by hyperinsulinemia and not necessarily to menopausal status.

Unlike MetS, no independent increase in the risk for diabetes had been demonstrated in studies during menopausal transition or menopause. Patients treated with HT, however, had a significant decrease in the incidence of type 2 diabetes in some studies. Further research is needed to elucidate the precise relationship of reproductive hormone dynamics and diabetes risk during menopausal transition.

### LIPID CHANGES AND MENOPAUSE

Multiple studies demonstrated an association between postmenopausal status and increased levels of total cholesterol, low-density lipoprotein cholesterol (LDL-C), lipoprotein(a), and decreased levels of high-density lipoprotein-cholesterol (HDL-C). These lipid changes are attributed to an increase in abdominal adiposity, especially visceral (omentumal and mesenteric) adiposity occurring during menopausal transition, rather than to reproductive senescence per se. Androgen and estrogen receptors are found in adipocytes from subcutaneous fat with high density of androgen receptors isolated in the visceral fat. Higher amount of free fatty acids (FFA) produced by the VAT contributes to decreases in degradation of apolipoprotein B (apoB) in the liver that leads to increase production of small very low density lipoproteins particles and triglycerides. Increases in FFA lead to increased activity of the hepatic lipase with subsequent increases in production of smaller and denser LDL-C and HDL-C particles, which are more atherogenic. FFAs are also implicated in worsening insulin resistance, especially in the skeletal muscle, mediated through inhibition of glucose transport. In the SWAN population, proatherogenic lipid changes occurred during the late peri- and early postmenopausal period. On one hand, higher E2 levels of during the menopausal transition predicted lower levels of total cholesterol, LDL-C, and triglycerides, whereas on the other, women with higher FSH levels tended to have higher levels of HDL-C. Of interest is the relationship between HDL-C and reproductive stage that exhibited an inverted “U”-shaped relationship as HDL-C was observed to peak during perimenopause with a subsequent decline in postmenopause compared with premenopausal levels. Triglycerides increased progressively across the menopausal transition, and this change was independent of age. Women with the highest BMI demonstrated the
The smallest changes in total cholesterol and LDL-C, which was attributed to higher levels of E2 in this subgroup. Thinnest women experienced the greatest changes in lipids during the menopausal transition. In concert with these findings, an elegant study of premenopausal and postmenopausal twin pairs reported higher levels of total cholesterol, triglycerides, and apoB after menopause, independent of age. LDL-C levels increased by 10–20% with menopause. Density of LDL particles decreased significantly during the menopausal transition with more atherogenic small, dense LDL-C reported in postmenopause then prior to menopause. Women with a predominance of small dense LDL-C versus large LDL-C have been reported to have a threefold increase in cardiovascular risk and higher coronary calcium scores demonstrated by CT. Further, triglycerides increase significantly across the menopausal transition, peaking in the early postmenopausal period. Although the prevalence of triglyceridemia increases significantly at midlife in both genders, this finding appears to be more predictive of an increased risk of heart disease in women.

Preponderance of data thus demonstrate attainment of a more proatherogenic lipid profile comitant with reproductive aging. Of interest is the appreciation that increases in total cholesterol, triglycerides, and LDL-C, and a decrease in HDL-C with menopause were more pronounced in the thinnest women as compared with their overweight and obese counterparts. Increases in FFA with subsequent production of more atherogenic smaller and denser LDL-C and HDL-C particles could partially explain the increased incidence and severity of heart disease observed in postmenopausal women. These proatherogenic lipid changes appear to be independent of age and are likely related to a shift in body fat preferentially to intra-abdominal deposits during and following menopause.

**BLOOD PRESSURE AND MENOPAUSE**

Studies of the relationship between menopause and hypertension have produced mixed results. An increase in systolic and diastolic blood pressure has been associated with menopause independent of age and BMI in many cross-sectional and some prospective studies; other prospective studies, however, demonstrate no associated between menopause, blood pressure, and cardiovascular risk independent of age. A deteriorating cardiovascular risk profile is known to ensue within weeks of surgical menopause, in the absence of estrogen replacement; the latter phenomena appear to be independent of age. Differences in blood pressure may be underestimated because many more women are treated for hypertension postmenopausally compared with in premenopausal years. In some studies, the onset of menopause at a younger age and longer duration of postmenopause existence were associated with higher blood pressure levels. Menopause has been associated with a considerable decrease in estradiol and the estradiol-to-testosterone ratio, creating an androgen dominant milieu that is theorized to be of pathogenic significance in the causation of blood pressure elevation. Indeed, such a profile is well described in women diagnosed with polycystic ovarian syndrome (PCOS) who demonstrate a higher risk of hypertension and CVD. The effects of the hormonal changes seen in PCOS and menopause are difficult to differentiate from other cardiovascular risk factors contributing to hypertension including obesity, age, insulin resistance, inflammatory milieu, and dyslipidemia. Several mechanisms can contribute toward the development of hypertension in postmenopausal women. Certainly, endothelial dysfunction, inappropriate activation of the renin angiotensin and sympathetic systems, oxidative stress, dyslipidemia, and inflammatory mediators are all identified as contributory to postmenopausal blood pressure elevations. However, it remains uncertain whether these physiological changes are caused by menstrual transition or are related to chronological aging.

To date, few studies have evaluated the relationship between changes in blood pressure and menopause in a way that allowed researchers to study the independent effects of age, body composition, insulin resistance, and dyslipidemia on blood pressure. Women experiencing surgical menopause or premature ovarian failure may have a more pronounced effect of the estrogen-deficient state on blood pressure compared with those experiencing natural and age-appropriate menopause. The scientific evidence for the relationship between blood pressure and menopause thus remains scarce and requires further investigation.

**CARDIOVASCULAR DISEASE AND MENOPAUSE**

Although premenopausal women are at a lower risk of heart disease compared with men, a twofold increase in risk for CVD follows menopause. After surgical menopause without estrogen therapy, a significant increase in cardiovascular events risk is observed. This effect has been attributed to changes in estrogen levels occurring at and following menopause. The contributions of multiple cardiovascular risk factors observed in the context of menopause and aging render the relationship complex; a “cause-and-effect” relationship for the individual risks is difficult to tease apart from contributions of aging per se. Increase in hypertension observed with aging is closely related to the increased risk of cardiovascular events. Dyslipidemia, exacerbated by menopausal transition and related to an increased abdominal adiposity, is a modifiable risk factor. Increases in LDL-C and triglycerides and decreases in HDL-C are independent contributors to risk for cardiovascular morbidity and mortality.
Primary prevention studies using statins to lower LDL-C demonstrated considerable reductions in cardiovascular events.66 Prevalence of diabetes increases with age and the incidence of MetS increases with menopause independent of age, both exacerbating cardiovascular risk in aging women. Increase in abdominal visceral adiposity is a significant risk factor for heart disease in both men and women. Decrease in EE and leisurely physical activity observed following menopause, in addition to the progressive weight gain concomitant with aging, all contribute to a detrimental metabolic environment that is contributory to the observed higher CVD events in the postmenopausal population.67 A significant increase in total peripheral resistance and cardiac wall thickness with a concomitant decrease in cardiac index was reported after menopause; importantly this was independent of hypertension.68 The authors postulate a direct effect of estrogens on the myocardium, with low estrogen exerting a negative inotropic effect and hence resulting in impaired systolic function. Diurnal variations in blood pressure are described in the premenopausal years, and cyclic reduction in the blood pressure has been attributed to positive effects of estrogen on mediating arterial vasodilatation; blunting of this latter phenomenon is described after menopause and could contribute to the postmenopausal increase in blood pressure and worsening left ventricular strain. Increases in blood viscosity with decreases in circulating volume and left ventricular size are also mentioned in relation to menopause.68

In summary, menopause is associated with increased prevalence and severity of CVD. The androgenic hormonal milieu observed in menopause is associated with worsening of abdominal adiposity accompanied by proatherogenic lipid changes, increases in incidence of insulin resistance, and MetS that may contribute to heart disease. Further studies are warranted to investigate the independent effects of menopause on cardiac function and vasculature independent of weight, lipids, and insulin resistance.

CONCLUSIONS AND PUBLIC HEALTH PERSPECTIVE

Increases in BMI, in measures of central adiposity and a preferential increase in visceral fat, accompany the transgression of reproductive stages toward and into menopause. The incidence of MetS goes up considerably in the aging female population, and the metabolic profile becomes more proatherogenic and proinflammatory. Although the prevalence of hypertension increases with age, many hypertensive postmenopausal women remain undiagnosed and undertreated.60 Because CVD is the leading cause of death in women, it is critical from a public health standpoint to identify risk factors and implement strategies to minimize the metabolic detriment that accompanies the menopause transition and menopause.

Identification of risk factors and establishing overall cardiovascular risk in perimenopausal women would help timely implementation of strategies that can mitigate end organ damage and prevent cardiovascular morbidity and mortality in the future. Recognition and treatment of established CVD in perimenopausal and postmenopausal women are critical to the success of secondary preventive strategies.69 Until recently most of the global cardiovascular risk scores used in women were based on the Framingham study done 40 years ago that used age, hypertension, smoking, diabetes, and hyperlipidemia in calculation of the risk.69 Cardiovascular risk assessment scores specific for women would be more helpful because 20% of women experience coronary events even in the absence of classic coronary risk factors.70 Many women with high risk scores based on the Framingham study do not experience cardiovascular adverse events.70 The Reynolds Risk Score, a recently developed and validated assessment tool, incorporates measures of HDL-C and high-sensitivity CRP.71 Body composition and hormonal changes occurring during the menopausal transition may need to be included in future risk calculators to help account for biological differences in heart disease presentation between men and women. The menopause transition should be perceived as a time for more stringent routine health-care assessments, and women in menopausal transition should have regular medical visits with monitoring of BMI, waist circumference, lipid profile, fasting glucose, and blood pressure. Women diagnosed with MetS should be treated aggressively to improve individual metabolic risks in efforts to decrease the overall risk of CVD that is recognized as associated with a diagnosis of MetS.

Exercise has been shown to attenuate the deteriorating metabolic profile of menopause. Cuff et al demonstrated mitigation in insulin resistance and a decrease in abdominal adiposity in postmenopausal diabetic women with exercise.72 Bergström et al demonstrated a statistically significant decrease in waist circumference with moderate physical exercise program in postmenopausal women.73 Weight loss through dietary intervention and exercise should be a mainstay of management women across all reproductive stages, in those who manifest features of MetS or who exhibit a high CVD risk profile, as well as in healthy women going through menopause to minimize the metabolic detriment of menopause. The Women’s Healthy Lifestyle Project followed 535 healthy premenopausal women across the menopausal transition for 5 years. Half of the women were treated with a lifestyle intervention that included a 1300 kcal/day diet (25% total fat, 7% saturated fat, 100 mg dietary cholesterol) with a moderate increase in physical activity equivalent of brisk walking 10 to 15 miles per week and weight loss goal of
5 to 15 lb depending on the baseline BMI. Women in the intervention group maintained their weight compared with the control group that gained an average of 2.5 kg consistent with age-dependent weight gain observed in other studies. Lifestyle intervention significantly reduced increases in LDL-C, triglycerides, blood glucose, and insulin occurring during the menopausal transition that were observed in the control group. Likewise, the Diabetes Prevention Program Study demonstrated a significant decrease in the incidence of diabetes and MetS with a similar lifestyle intervention regimen. Medical treatment of elevated blood pressure, glucose, and hyperlipidemia in addition to lifestyle changes are needed to combat heart disease in at-risk perimenopausal and menopausal women. Educational efforts should focus on lifestyle changes including a healthy diet with moderately decreased calorie intake, regular moderate aerobic exercise, smoking cessation, and decreased alcohol consumption that decrease the weight gain, the central obesity, and the accompanying deterioration in metabolic profile observed during and beyond the menopausal transition. Weight maintenance and weight reduction would benefit overall health and likely decrease the cardiovascular morbidity and mortality observed in postmenopausal women.

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Executive summary of the clinical guidelines on the identification, evaluation, and treatment of overweight and obesity in adults

THE NATIONAL HEART, LUNG, AND BLOOD INSTITUTE EXPERT PANEL ON THE IDENTIFICATION, EVALUATION, AND TREATMENT OF OVERWEIGHT AND OBESITY IN ADULTS

A n estimated 97 million adults in the United States are overweight or obese, a condition that substantially raises their risk of morbidity from hypertension, dyslipidemia, type 2 diabetes, coronary heart disease, stroke, gallbladder disease, osteoarthritis, sleep apnea and respiratory problems, and endometrial, breast, prostate, and colon cancers. Higher body weights are also associated with increases in all-cause mortality. Obese individuals may also suffer from social stigmatization and discrimination. As a major contributor to preventable death in the United States today, overweight and obesity pose a major public health challenge.

Overweight is here defined as a body mass index (BMI, calculated as kg/m²) of 25 to 29.9 and obesity as a BMI of ≥ 30. However, overweight and obesity are not mutually exclusive, since obese persons are also overweight. A BMI of 30 is about 30 lb overweight and equivalent to 221 lb in a 6’0” person and to 186 lb in one 5’6”. The number of overweight and obese men and women has risen since 1960; in the last decade the percentage of people in these categories has increased to 54.9% of adults age 20 years or older. Overweight and obesity are especially evident in some minority groups, as well as in those with lower incomes and less education.

Obesity is a complex multifactorial chronic disease that develops from an interaction of genotype and the environment. Our understanding of how and why obesity develops is incomplete, but involves the integration of social, behavioral, cultural, physiological, metabolic, and genetic factors.

While there is agreement about the health risks of overweight and obesity, there is less agreement about their management. Some have argued against treating obesity because of the difficulty in maintaining long-term weight loss and of potentially negative consequences of the frequently seen pattern of weight cycling in obese subjects. Others argue that the potential hazards of treatment do not outweigh the known hazards of being obese. The intent of these guidelines is to provide evidence for the effects of treatment on overweight and obesity. The guidelines focus on the role of the primary care practitioner in treating overweight and obesity.

EVIDENCE-BASED GUIDELINES

To evaluate published information and to determine the most appropriate treatment strategies that would constitute evidence-based clinical guidelines on overweight and obesity for physicians and associated health professionals in clinical practice, health care policy makers, and clinical investigators, the National Heart, Lung, and Blood Institute’s Obesity Education Initiative in cooperation with the National Institute of Diabetes and Digestive and Kidney Diseases convened the Expert Panel on the Identification, Evaluation, and Treatment of Overweight and Obesity in Adults in May 1995. The guidelines are based on a systematic review of the published scientific literature found in MEDLINE from January 1980 to September 1997 of topics identified by the panel as key to extrapolating the data related to the obesity evidence model. Evidence from approximately 394 randomized controlled trials (RCTs) was considered by the panel.

The panel is comprised of 24 members, 8 ex-officio members, and a methodologist consultant. Areas of expertise contributed to by panel members included primary care, epidemiology, clinical nutrition, exercise physiology, psychology, physiology, and pulmonary disease. There were 5 meetings of the full panel and 2 additional meetings of the executive committee comprised of the panel chair and 4 panel members.

The San Antonio Cochrane Center assisted the panel in the literature abstraction and in organizing the data into appropriate evidence tables. The center pretested and used a standardized 25-page form or “Critical Review Status Sheet” for the literature abstraction. Ultimately, 236 RCT articles were abstracted and the data were then compiled into individual evidence tables developed for each RCT. The data from these RCTs served as the basis for many of the recommendations contained in the guidelines.

1A complete list of the members of the Expert Panel is found at the end of this article.

Editor’s note: The Executive Summary was first published in the Archives of Internal Medicine, September 28, 1998. Reprinted with permission.
<table>
<thead>
<tr>
<th>Evidence category</th>
<th>Sources of evidence</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Randomized controlled trials (RCTs) (rich body of data)</td>
<td>Evidence is from endpoints of well-designed RCTs (or trials that depart only minimally from randomization) that provide a consistent pattern of findings in the population for which the recommendation is made. Category A therefore requires substantial numbers of studies involving substantial numbers of participants.</td>
</tr>
<tr>
<td>B</td>
<td>RCTs (limited body of data)</td>
<td>Evidence is from endpoints of intervention studies that include only a limited number of RCTs, post-hoc or subgroup analysis of RCTs, or meta-analysis of RCTs. In general, Category B pertains when few randomized trials exist, they are small in size, and the trial results are somewhat inconsistent, or the trials were undertaken in a population that differs from the target population of the recommendation.</td>
</tr>
<tr>
<td>C</td>
<td>Nonrandomized trials; observational studies</td>
<td>Evidence is from outcomes of uncontrolled or nonrandomized trials or from observational studies.</td>
</tr>
<tr>
<td>D</td>
<td>Panel consensus judgment</td>
<td>Expert judgment is based on the panel's synthesis of evidence from experimental research described in the literature and/or derived from the consensus of panel members based on clinical experience or knowledge that does not meet the above-listed criteria. This category is used only in cases where the provision of some guidance was deemed valuable but an adequately compelling clinical literature addressing the subject of the recommendation was deemed insufficient to justify placement in one of the other categories (A through C).</td>
</tr>
</tbody>
</table>

The panel determined the criteria for deciding on the appropriateness of an article. At a minimum, studies had to have a time frame from start to finish of at least 4 months. The only exceptions were a few 3-month studies related to dietary therapy and pharmacotherapy. To consider the question of long-term maintenance, studies with outcome data provided at approximately 1 year or longer were examined. Excluded were studies in which self-reported weights by subjects were the only indicators used to measure weight loss. No exclusions of studies were made by study size. The panel weighed the evidence based on a thorough examination of the threshold or magnitude of the treatment effect. Each evidence statement (other than those with no available evidence) and each recommendation is categorized by a level of evidence which ranges from A to D. Table 1 summarizes the categories of evidence by their source and provides a definition for each category.

- **Who is at risk?** All overweight and obese adults (age 18 years of age or older) with a BMI of $\geq 25$ are considered at risk for developing associated morbidities or diseases such as hypertension, high blood cholesterol, type 2 diabetes, coronary heart disease, and other diseases. Individuals with a BMI of 25 to 29.9 are considered overweight, while individuals with a BMI $\geq 30$ are considered obese. Treatment of overweight is recommended only when patients have 2 or more risk factors. It should focus on altering dietary and physical activity patterns to prevent development of obesity and to produce moderate weight loss. Treatment of obesity should focus on producing substantial weight loss over a prolonged period. The presence of comorbidities in overweight and obese patients should be considered when deciding on treatment options.

- **Why treat overweight and obesity?** Obesity is clearly associated with increased morbidity and mortality. There is strong evidence that weight loss in overweight and obese individuals reduces risk factors for diabetes and cardiovascular disease (CVD). Strong evidence exists that weight loss reduces blood pressure in both overweight hypertensive and nonhypertensive individuals; reduces serum triglycerides and increases high-density lipoprotein (HDL)-cholesterol; and generally produces some reduction in total serum cholesterol and low-density lipoprotein (LDL)-cholesterol. Weight loss reduces blood glucose levels in overweight and obese persons without diabetes; and weight loss also reduces blood glucose levels and HbA1c in some patients with type 2 diabetes. Although there have been no prospective trials to show changes in mortality with weight loss in obese patients, reductions in risk factors would suggest that development of type 2 diabetes and CVD would be reduced with weight loss.

- **What treatments are effective?** A variety of effective options exist for the management of overweight and obese patients, including dietary therapy approaches such as low-calorie diets and lower-fat diets; altering physical activity patterns; behavior therapy techniques; pharmacotherapy$^3$; surgery; and combinations of these techniques.

**CLINICAL GUIDELINES**

Treatment of the overweight or obese patient is a 2-step process: assessment and treatment management. Assessment requires determination of the degree of overweight and overall risk status. Management includes both reducing excess body weight and instituting other measures to control accompanying risk factors.

**Assessment**

When assessing a patient for risk status and as a candidate for weight loss therapy, consider the patient’s BMI, waist circumference, and overall risk status. Consideration also needs to be given to the patient’s motivation to lose weight.

$^3$As of September 1997, the Food and Drug Administration (FDA) requested the voluntary withdrawal from the market of dexfenfluramine and fenfluramine due to a reported association between valvular heart disease and the use of dexfenfluramine or fenfluramine alone or combined with phentermine. The use of these drugs for weight reduction, therefore, is not recommended in this report. Sibutramine is approved by FDA for long-term use. It has limited but definite effects on weight loss and can facilitate weight loss maintenance. (Note: FDA approval for orlistat is pending a resolution of labeling issues and results of Phase III trials.)
Table 2
Classification of overweight and obesity by body mass index (BMI)

<table>
<thead>
<tr>
<th>Obesity class</th>
<th>BMI</th>
</tr>
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<tbody>
<tr>
<td>Underweight</td>
<td>&lt; 18.5</td>
</tr>
<tr>
<td>Normal</td>
<td>18.5-24.9</td>
</tr>
<tr>
<td>Overweight</td>
<td>25.0-29.9</td>
</tr>
<tr>
<td>Obesity I</td>
<td>30.0-34.9</td>
</tr>
<tr>
<td>Obesity II</td>
<td>35.0-39.9</td>
</tr>
<tr>
<td>Extreme obesity</td>
<td>≥40</td>
</tr>
</tbody>
</table>

*Calculated as kg/m².

Body mass index: The BMI, which describes relative weight for height, is significantly correlated with total body fat content. The BMI should be used to assess overweight and obesity and to monitor changes in body weight. In addition, measurements of body weight alone can be used to determine efficacy of weight loss therapy. BMI is calculated as weight (kg)/height squared (m²). To estimate BMI using pounds and inches, use: [weight (pounds)/height (inches)²] × 703. Weight classifications by BMI, selected for use in this report, are shown in Table 2. A conversion table of heights and weights resulting in selected BMI units is provided in Table 3.

Waist circumference: The presence of excess fat in the abdomen out of proportion to total body fat is an independent predictor of risk factors and morbidity. Waist circumference is positively correlated with abdominal fat content. It provides a clinically acceptable measurement for assessing a patient's abdominal fat content before and during weight loss treatment. The following sex-specific cutoffs can be used to identify increased relative risk for the development of obesity-associated risk factors in most adults with a BMI of 25 to 34.9:

**High Risk**
- Men > 102 cm ( > 40 in)
- Women > 88 cm ( > 35 in)

These waist circumference cutoffs lose their incremental predictive power in patients with a BMI ≥35 because these patients will exceed the cutoffs noted above. Table 4 adds the disease risk of increased abdominal fat to the disease risk of BMI. These categories denote relative risk, not absolute risk; that is, relative to risk at normal weight. They should not be equated with absolute risk, which is determined by a summation of risk factors. They relate to the need to institute weight loss therapy and do not directly define the required intensity of modification of risk factors associated with obesity.

Risk Status: Assessment of a patient's absolute risk status requires examination for the presence of:

Disease conditions: established coronary heart disease (CHD), other atherosclerotic diseases, type 2 diabetes, and sleep apnea; patients with these conditions are classified as being at very high risk for disease complications and mortality.

Other obesity-associated diseases: gynecological abnormalities, osteoarthritis, gallstones and their complications, and stress incontinence.

Cardiovascular risk factors: cigarette smoking, hypertension (systolic blood pressure ≥140 mm Hg or diastolic blood pressure ≥90 mm Hg, or the patient is taking antihypertensive agents), high-risk LDL-cholesterol (≥160 mg/dL), low HDL-cholesterol (< 35 mg/dL), impaired fasting glucose (fasting plasma glucose of 110 to 125 mg/dL), family history of premature CHD (definite myocardial infarction or sudden death at or before 55 years of age in father or other male first-degree relative, or at or before 65 years of age in mother or other female first-degree relative), and age (men ≥45 years and women ≥55 years or postmenopausal). Patients can be classified as being at high absolute risk if they have 3 of the aforementioned risk factors. Patients at high absolute risk usually require clinical management of risk factors to reduce risk.

Patients who are overweight or obese often have other cardiovascular risk factors. Methods for estimating absolute risk status for developing cardiovascular disease based on these risk factors are described in detail in the National Cholesterol Education Program's Second Report of the Expert Panel on the Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (NCEP's ATP II) and the Sixth Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC VI). The intensity of intervention for cholesterol disorders or hypertension is adjusted according to the absolute risk status estimated from multiple risk correlates. These include both the risk factors listed above and evidence of end-organ damage present in hypertensive patients. Approaches to therapy for cholesterol disorders and hypertension are described in ATP II and JNC VI, respectively. In overweight patients, control of cardiovascular risk factors deserves equal emphasis as weight reduction therapy. Reduction of risk factors will reduce the risk for CVD whether or not efforts at weight loss are successful.

Other risk factors: physical inactivity and high serum triglycerides (> 200 mg/dL). When these factors are present, patients can be considered to have incremental absolute risk above that estimated from the preceding risk factors. Quantitative risk contribution is not available for these risk factors, but their presence heightens the need for weight reduction in obese persons.

Patient Motivation: When assessing the patient's motivation to enter weight loss therapy, the following factors should be evaluated: reasons and motivation for weight reduction; previous history of successful and unsuccessful weight loss attempts; family, friends, and worksite support; the patient's understanding of the causes of obesity and how obesity contributes to several diseases; attitude toward physical activity; capacity to engage in physical activity; time availability for weight loss intervention; and financial considerations. In addition to considering these issues, the health care practitioner needs to heighten a patient's motivation for weight loss and prepare the patient for treatment. This can be done by enumerating the dangers accompanying persistent obesity and by describing the strategy for clinically assisted weight reduction.

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2To convert mmol/L cholesterol to mg/dL, multiply mmol/L by 38.7. To convert mg/dL cholesterol to mmol/L, multiply mg/dL by 0.026. Cholesterol of 5.00 mmol/L = 193 mg/dL.

3To convert mmol/L glucose to mg/dL, multiply mmol/L by 18.0. To convert mg/dL glucose to mmol/L, multiply mg/dL by 0.0555. Glucose of 6.0 mmol/L = 108 mg/dL.

4To convert mmol/L triglyceride to mg/dL, multiply mmol/L by 88.6. To convert mg/dL triglyceride to mmol/L, multiply mg/dL by 0.0113. Triglyceride of 1.80 mmol/L = 159 mg/dL.
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*Metric conversion formula for BMI=weight (kg)/height (m)². For example, a person who weighs 78.93 kg and is 177-cm tall has a BMI of 25: weight (78.93 kg)/height (1.77 m)²=25.

Nonmetric conversion formula for BMI=weight (lb)/height (in)²×703. For example, a person who weighs 164 lb and is 68 in (or 5 ft 8 in) tall has a BMI of 25: weight (164 lb)/height (68 in)²×703=25.
Reviewing the patients’ past attempts at weight loss and explaining how the new treatment plan will be different can encourage patients and provide hope for successful weight loss.

**Evaluation and Treatment**

The general goals of weight loss and management are: (1) at a minimum, to prevent further weight gain; (2) to reduce body weight; and (3) to maintain a lower body weight over the long term. The overall strategy for the evaluation and treatment of overweight and obese patients is presented in the Treatment Algorithm (see the Figure). This algorithm applies only to the assessment for overweight and obesity and subsequent decisions based on that assessment. It does not include any initial overall assessment for cardiovascular risk factors or diseases that are indicated. Each step (designated by a box) in this process is described.

**Box 1: Patient Encounter** A patient encounter is defined as any interaction between a health care practitioner (generally a physician, nurse practitioner or physician's assistant) that provides the opportunity to assess a patient's weight status and provide advice, counseling, or treatment.

**Box 2: History of Overweight or Recorded BMI ≥ 25** The practitioner must seek to determine whether the patient has ever been overweight. While a technical definition is provided, a simple question such as "Have you ever been overweight?" will accomplish the same goal. Questions directed towards weight history, dietary habits, physical activities, and medications may provide useful information about the origins of obesity in particular patients.

**Box 3: BMI Measured in Past 2 Years** For those who have not been overweight, a 2-year interval is appropriate for the reassessment of BMI. While this time span is not evidence-based, it is believed to be a reasonable compromise between the need to identify weight gain at an early stage and the need to limit the time, effort, and cost of repeated measurements.

**Box 4: Measure Weight, Height, Waist Circumference; Calculate BMI** Weight must be measured so that the BMI can be calculated. Most charts are based on weights obtained with the patient wearing undergarments and no shoes. BMI can be manually calculated (kg/height in meters$^2$), but is more easily obtained from a nomogram. Waist circumference is important because evidence suggests that abdominal fat is a particularly strong determinant of cardiovascular risk in those with a BMI of 25 to 34.9. Increased waist circumference can also be a marker of increased risk even in persons of normal weight. A nutrition assessment will also help to assess the diet and physical activity habits of overweight patients.

**Box 5: BMI ≥ 25, OR Waist Circumference > 88 (F) or > 102 cm (M)** These cutpoints divide overweight from normal weight and are consistent with other national and international guidelines. The relation between weight and mortality is J-shaped, and evidence suggests that the right side of the “J” begins to rise at a BMI of 25. Waist circumference is incorporated as an “or” factor because some patients with BMI lower than 25 will have disproportionate abdominal fat, and this increases their cardiovascular risk despite their low BMI. These abdominal circumference values are not necessary for patients with a BMI ≥ 25.

**Box 6: Assess Risk Factors** Risk assessment for CVD and diabetes in a person with evident obesity will include special considerations for the history, physical examination, and laboratory examination. Of greatest urgency is the need to detect existing CVD or end-organ damage. Since the major risk of obesity is indirect (obesity elicits or aggravates hypertension, dyslipidemias, and diabetes, which cause cardiovascular complications), the management of obesity should be implemented in the context of these other risk factors. While there is no direct evidence demonstrating that addressing risk factors increases weight loss, treating the risk factors through weight loss is a recommended strategy.

**Box 7: BMI ≥ 30, OR (BMI 25 to 29.9 OR Waist Circumference > 88 or > 102 cm) AND ≥ 2 risk factors** The panel recommends that all patients meeting these criteria attempt to lose weight. However, it is important to ask the patient whether or not they want to lose weight. Those with BMIs between 25 and 29.9 who have one or no risk factors should work on maintaining their current weight rather than embark on a weight reduction program. The panel recognizes that the decision to lose weight must be made in the context of other risk factors (eg, quitting smoking is more important than losing weight) and patient preferences.

**Box 8: Clinician and Patient Devise Goals** The decision to lose weight must be made jointly between the clinician and patient. Patient involvement and investment is crucial to success. The patient may choose not to lose weight but rather to...
Treatment Algorithm. Note: The algorithm applies only to the assessment for overweight and obesity and subsequent decisions based on that assessment. It does not include any initial overall assessment for cardiovascular risk factors or diseases that are indicated.
prevent further weight gain as a goal. The panel recommends a
initial goal of the loss of 10% of baseline weight, to be lost
at a rate of 1 to 2 lb/week, establishing an energy deficit of 500
to 1,000 kcal/day. For individuals who are overweight, a deficit
of 300 to 500 kcal/day may be more appropriate, providing a
weight loss of about ½ lb/week. Also, there is evidence that an
average of 8% of weight can be lost in a 6-month period. Since
the observed average 8% weight loss includes people who do
not lose weight, an individual goal of 10% is reasonable. After
6 months, most patients will equilibrate (caloric intake balancing
energy expenditure) and will require adjustment of energy
balance if they are to lose more weight.

The 3 major components of weight loss therapy are dietary
therapy, increased physical activity, and behavior therapy.
Lifestyle therapy should be tried for at least 6 months before
considering pharmacotherapy. In addition, pharmacotherapy
should be considered as an adjunct to lifestyle therapy in
patients with a BMI ≥ 30 with no concomitant obesity-related
risk factors or diseases, or for patients with a BMI ≥ 27 with
concomitant obesity-related risk factors or diseases. The risk
factors or diseases considered important enough to warrant
pharmacotherapy at a BMI of 27 to 29.9 are hypertension,
dyslipidemia, CHD, type 2 diabetes, and sleep apnea. However,
sibutramine, the only FDA-approved drug for long-term use,
should not be used in patients with a history of hypertension,
CHD, congestive heart failure, arrhythmias, or history of stroke.
Certain patients may be candidates for weight loss surgery.
Each component of weight loss therapy can be introduced
briefly. The selection of weight loss methods should be made
in the context of patient preferences, analysis of past failed
attempts, and consideration of the available resources.

Box 9: Progress Being Made/Goal Achieved During the
acute weight loss period and at 6-month and 1-year follow-up
visits, the patients should be weighed, BMI calculated, and
progress assessed. If at any time it appears that the program is
failing, a reassessment should take place to determine the
reasons (see Box 10). If pharmacotherapy is being used,
appropriate monitoring for side effects is recommended. If a
patient can achieve the recommended 10% reduction in body
weight in 6 months to 1 year, this change in weight can be
considered good progress. The patient can then enter the
phase of weight maintenance and long-term monitoring. It is
important for the practitioner to recognize that some persons
are more apt to lose or gain weight on a given regimen and that
this phenomenon cannot always be attributed to degree of
compliance. However, if significant obesity remains and abso-
lute risk from obesity-associated risk factors remains high, at
some point an effort should be made to reinstitute weight loss
therapy to achieve further weight reduction. Once a limit of
weight loss has been obtained, the practitioner is responsible
for long-term monitoring of risk factors and for encouraging
the patient to maintain a reduced weight level.

Box 10: Assess Reasons for Failure to Lose Weight If a
patient fails to achieve the recommended 10% reduction in
body weight in 6 months or 1 year, a reevaluation is required.
A critical question is whether the level of motivation is high
enough to continue clinical therapy. If motivation is high,
revise the goals and strategies (see Box 8). If motivation is not
high, clinical therapy should be discontinued, but the patient
should be encouraged to embark on efforts to lose weight or to
at least avoid further weight gain. Even if weight loss therapy
is stopped, risk factor management must be continued.
Failure to achieve weight loss should prompt the practitio-
nor to investigate energy intake (dietary recall including alco-
hol intake, daily intake logs), energy expenditure (physical
activity diary), attendance at behavior therapy group meet-
tings, recent negative life events, family and societal pressures,
or evidence of detrimental psychiatric problems (depression,
binge eating disorder). If attempts to lose weight have failed,
and the BMI is ≥ 40, surgical therapy should be considered.

Box 11: Maintenance Counseling Evidence suggests that
over 80% of persons who lose weight will gradually regain it.
Patients who continue on weight maintenance programs have
a greater chance of keeping weight off. Maintenance consists of
continued contact with the health care practitioner for con-
tinued education, support, and medical monitoring.

Box 12: Does the Patient Want to Lose Weight? All
patients who are overweight (BMI 25 to 28.9), or do not have
a high waist circumference, and have few (0 to 1) cardiovas-
cular risk factors and do not want to lose weight, should be
counseled regarding the need to keep their weight at or below
its present level. Patients who wish to lose weight should be
guided per Boxes 8 and 9. The justification for offering these
overweight patients the option of maintaining (rather than
losing) weight is that their health risk, while higher than that
of persons with a BMI < 25, is only moderately increased.

Box 13: Advise to Maintain Weight/Address Other Risk
Factors Those who have a history of overweight and are now
at appropriate weight, and those who are overweight and not
obese but wish to focus on maintenance of their current
weight, should be provided with counseling and advice so that
their weight does not increase. An increase in weight increases
their health risk and should be prevented. The physician
should actively promote prevention strategies including en-
hanced attention by the patient to diet, physical activity,
and behavior therapy. For addressing other risk factors, see Box 6,
because even if weight loss cannot be addressed, other risk
factors should be covered.

Box 14: History of BMI ≥ 25 This box differentiates those
who are not overweight now and never have been from those
with a history of overweight; see Box 2.

Box 15: Brief Reinforcement Those who are not overweight
and never have been should be advised of the importance of
staying in this category.

Box 16: Periodic Weight, BMI, and Waist Circumference
Check Patients should receive periodic monitoring of their
weight, BMI, and waist circumference. Patients who are not
overweight or have no history of overweight should be screened
for weight gain every 2 years. This time span is a reasonable
compromise between the need to identify weight gain at an
early stage and the need to limit the time, effort, and the cost
of repeated measurements.

GOALS OF WEIGHT LOSS AND MANAGEMENT
The initial goal of weight loss therapy is to reduce body
weight by approximately 10% from baseline. If this goal is
achieved, further weight loss can be attempted, if indicated
through further evaluation.
A reasonable time frame for a 10% reduction in body weight
is 6 months of therapy. For overweight patients with BMIs in
the typical range of 27 to 35, a decrease of 300 to 500 kcal/day
will result in weight losses of about ½ to 1 lb/week and a 10% loss
in 6 months. For more severely obese patients with BMIs > 35,
deficits of up to 500 to 1,000 kcal/day will lead to weight
losses of about 1 to 2 lb/week and a 10% weight loss in 6 months. Weight loss at the rate of 1 to 2 lb/week (caloric deficit of 500 to 1,000 kcal/day) occurs safely for up to 6 months. After 6 months, the rate of weight loss usually declines and weight plateau because of a lesser energy expenditure at the lower weight.

Experience reveals that lost weight usually will be regained unless a weight maintenance program consisting of dietary therapy, physical activity, and behavior therapy is continued indefinitely.

After 6 months of weight loss treatment, efforts to maintain weight loss should be put in place. If more weight loss is needed, another attempt at weight reduction can be made. This will require further adjustment of the diet and physical activity prescriptions.

For patients unable to achieve significant weight reduction, prevention of further weight gain is an important goal; such patients may also need to participate in a weight management program.

STRATEGIES FOR WEIGHT LOSS AND WEIGHT MAINTENANCE

Dietary Therapy
A diet that is individually planned and takes into account the patient's overweight status in order to help create a deficit of 500 to 1,000 kcal/day should be an integral part of any weight loss program. A patient may choose a diet of 1,000 to 1,200 kcal/day for women and 1,200 to 1,500 kcal/day for men. Depending on the patient's risk status, the low-calorie diet (LCD) recommended should be consistent with the NCEP's Step I or Step II Diet. Besides decreasing saturated fat, total fats should be 30% or less of total calories. Reducing the percentage of dietary fat alone will not produce weight loss unless total calories are also reduced. Isocaloric replacement of fat with carbohydrates will reduce the percentage of calories from fat, but will not cause weight loss. Reducing dietary fat, along with reducing dietary carbohydrates, usually will be needed to produce the caloric deficit needed for an acceptable weight loss. When fat intake is reduced, priority should be given to reducing saturated fat to enhance lowering of LDL-cholesterol levels. Frequent contacts with the practitioner during dietary therapy help to promote weight loss and weight maintenance at a lower weight.

Physical Activity
An increase in physical activity is an important component of weight loss therapy, although it will not lead to substantially greater weight loss over 6 months. Most weight loss occurs because of decreased caloric intake. Sustained physical activity is most helpful in the prevention of weight regain. In addition, it has a benefit in reducing cardiovascular and dia-

Pharmaceutical Therapy
In carefully selected patients, appropriate drugs can augment LCDs, physical activity, and behavior therapy in weight loss. Weight loss drugs that have been approved by the FDA for long-term use can be useful adjuncts to dietary therapy and physical activity for some patients with a BMI of ≥ 30 with no concomitant risk factors or diseases, and for patients with a BMI of ≥ 27 with concomitant risk factors or diseases. The risk factors and diseases considered important enough to warrant pharmacotherapy at a BMI of 27 to 29.9 are hypertension, dyslipidemia, CHD, type 2 diabetes, and sleep apnea. Continual assessment by the physician of drug therapy for efficacy and safety is necessary.

At the present time, sibutramine is available for long-term use. (Note: FDA approval of orlistat is pending a resolution of labeling issues and results of Phase III trials.) It enhances weight loss modestly and can help facilitate weight loss maintenance. Potential side effects with drugs, nonetheless, must be kept in mind. With sibutramine, increases in blood pressure and heart rate may occur. Sibutramine should not be used in patients with a history of hypertension, CHD, congestive heart failure, arrhythmias, or history of stroke. With orlistat, fat soluble vitamins may require replacement because of partial malabsorption. All patients should be carefully monitored for these side effects.

Weight Loss Surgery
Weight loss surgery is one option for weight reduction in a limited number of patients with clinically severe obesity, ie, BMIs ≥ 40 or ≥ 35 with comorbid conditions. Weight loss surgery should be reserved for patients in whom efforts at medical therapy have failed and who are suffering from the complications of extreme obesity. Gastrointestinal surgery (gastric restriction [Vertical gastric banding] or gastric bypass [Roux-en Y]) is an intervention weight loss option for motivated subjects with acceptable operative risks. An integrated program must be in place to provide guidance on diet, physical activity, and behavioral and social support both prior to and after the surgery.

ADAPT WEIGHT LOSS PROGRAMS TO MEET THE NEEDS OF DIVERSE PATIENTS
Standard treatment approaches for overweight and obesity must be tailored to the needs of various patients or patient
groups. Large individual variation exists within any social or cultural group; furthermore, substantial overlap among subcultures occurs within the larger society. There is, therefore, no “cookbook” or standardized set of rules to optimize weight reduction with a given type of patient. However, to be more culturally sensitive and to incorporate patient characteristics in obesity treatment programs: consider and adapt the setting and staffing for the program; consider how the obesity treatment program integrates into other aspects of patient healthcare and self-care; and expect and allow for program modifications based on patient responses and preferences.

The issues of weight reduction after age 65 involve such questions as: does weight loss reduce risk factors in older adults; are there risks associated with obesity treatment that are unique to older adults; and does weight reduction prolong the lives of older adults? Although there is less certainty about the importance of treating overweight at older ages than at younger ages, a clinical decision to forego obesity treatment in older adults should be guided by an evaluation of the potential benefit of weight reduction and the reduction of risk for future cardiovascular events. In the obese patient who smokes, smoking cessation is a major goal of risk factor management. Many well-documented health benefits accompany smoking cessation, but a major obstacle to cessation has been the attendant weight gain observed in about 80% of quitters. This weight gain averages 4.5 to 7 lb, but in 15% of women and 10% of men, weight gain exceeds 28 lb. Weight gain that accompanies smoking cessation has been quite resistant to most dietary, behavioral, or physical activity interventions. The weight gained with smoking cessation is less likely to produce negative health consequences than would continued smoking. For this reason, smoking cessation should be strongly advocated regardless of baseline weight. Prevention of weight gain through diet and physical activity should be stressed. For practical reasons, it may be prudent to avoid initiating smoking cessation and weight loss therapy simultaneously. If weight gain ensues after smoking cessation, it should be managed vigorously according to the guidelines outlined in this report. Although short-term weight gain is a common side effect of smoking cessation, this gain does not rule out the possibility of long-term weight control.

**SUMMARY OF EVIDENCE-BASED RECOMMENDATIONS**

**Advantages of Weight Loss**

The recommendation to treat overweight and obesity is based not only on evidence that relates obesity to increased mortality but also on RCT evidence that weight loss reduces risk factors for disease. Thus, weight loss may not only help control diseases worsened by obesity, it may also help decrease the likelihood of developing these diseases. The panel reviewed RCT evidence to determine the effect of weight loss on blood pressure and hypertension, serum/plasma lipid concentrations, and fasting blood glucose and fasting insulin. Recommendations focusing on these conditions underscore the advantages of weight loss.

**Blood Pressure**

To evaluate the effect of weight loss on blood pressure and hypertension, 76 articles reporting RCTs were considered for inclusion in these guidelines. Of the 45 accepted articles, 35 were lifestyle trials and 10 were pharmacotherapy trials. There is strong and consistent evidence from these lifestyle trials in both overweight hypertensive and nonhypertensive patients that weight loss produced by lifestyle modifications reduces blood pressure levels. Limited evidence exists that decreases in abdominal fat will reduce blood pressure in overweight nonhypertensive individuals, although not independent of weight loss, and there is considerable evidence that increased aerobic activity to increase cardiorespiratory fitness reduces blood pressure (independent of weight loss). There is also suggestive evidence from randomized trials that weight loss produced by most weight loss medications, except for sibutramine, in combination with adjuvant lifestyle modifications will be accompanied by reductions in blood pressure. Based on a review of the evidence from the 45 RCT blood pressure articles, the panel makes the following recommendation:

Weight loss is recommended to lower elevated blood pressure in overweight and obese persons with high blood pressure. Evidence Category A.

**Serum/plasma lipids**

Sixty-five RCT articles were evaluated for the effect of weight loss on serum/plasma concentrations of total cholesterol, LDL-cholesterol, very low-density lipoprotein (VLDL)-cholesterol, triglycerides, and HDL-cholesterol. Studies were conducted on individuals over a range of obesity and lipid levels. Of the 22 articles accepted for inclusion in these guidelines, 14 RCT articles examined lifestyle trials while the remaining 8 articles reviewed pharmacotherapy trials. There is strong evidence from the 14 lifestyle trials that weight loss produced by lifestyle modifications in overweight individuals is accompanied by reductions in serum triglycerides and by increases in HDL-cholesterol. Weight loss generally produces some reductions in serum total cholesterol and LDL-cholesterol. Limited evidence exists that a decrease in abdominal fat correlates with improvement in lipids, although the effect may not be independent of weight loss, and there is strong evidence that increased aerobic activity to increase cardiorespiratory fitness favorably affects blood lipids, particularly if accompanied by weight loss. There is suggestive evidence from the 8 randomized pharmacotherapy trials that weight loss produced by weight loss medications and adjuvant lifestyle modifications, including caloric restriction and physical activity, does not result in consistent effects on blood lipids. The following recommendation is based on the review of the data in these 22 RCT articles:

Weight loss is recommended to lower elevated levels of total cholesterol, LDL-cholesterol, and triglycerides, and to raise low levels of HDL-cholesterol in overweight and obese persons with dyslipidemia. Evidence Category A.

**Blood Glucose**

To evaluate the effect of weight loss on fasting blood glucose and fasting insulin levels, 49 RCT articles were reviewed for inclusion in these guidelines. Of the 17 RCT articles accepted, 9 RCT articles examined lifestyle therapy trials and 8 RCT articles considered the effects of pharmacotherapy on weight loss and subsequent changes in blood glucose. There is strong evidence from the 9 lifestyle therapy trials that weight loss produced by lifestyle modification reduces blood glucose levels in overweight and obese persons without diabetes, and weight loss reduces blood glucose levels and HbA1c in some patients with type 2 diabetes. There is
suggestive evidence that decreases in abdominal fat will improve glucose tolerance in overweight individuals with impaired glucose tolerance, although not independent of weight loss; and there is limited evidence that increased cardiorespiratory fitness improves glucose tolerance in overweight individuals with impaired glucose tolerance or diabetes, although not independent of weight loss. In addition, there is suggestive evidence from randomized trials that weight loss induced by weight loss medications does not appear to improve blood glucose levels any better than weight loss through lifestyle therapy in overweight persons both with and without type 2 diabetes. Based on a full review of the data in these 17 RCT articles, the panel makes the following recommendation:

**Measurement of Degree of Overweight and Obesity**

Patients should have their BMI and levels of abdominal fat measured not only for the initial assessment of the degree of overweight and obesity, but also as a guide to the efficacy of weight loss treatment. Although there are no RCTs that review measurements of overweight and obesity, the panel determined that this aspect of patient care warranted further consideration and that this guidance was deemed valuable. Therefore, the following four recommendations that are included in the Treatment Guidelines were based on nonrandomized studies as well as clinical experience.

**BMI to assess overweight and obesity**

There are a number of accurate methods to assess body fat (eg, total body water, total body potassium, bioelectrical impedance, and dual-energy X-ray absorptiometry), but no trial data exist to indicate that one measure of fatness is better than any other for following overweight and obese patients during treatment. Since measuring body fat by these techniques is often expensive and is not readily available, a more practical approach for the clinical setting is the measurement of BMI; epidemiological and observational studies have shown that BMI provides an acceptable approximation of total body fat for the majority of patients. Because there are no published studies that compare the effectiveness of different measures for evaluating changes in body fat during weight reduction, the panel bases its recommendation on expert judgment from clinical experience:

Practitioners should use the BMI to assess overweight and obesity. Body weight alone can be used to follow weight loss, and to determine efficacy of therapy. Evidence Category C.

**BMI to estimate relative risk**

In epidemiological studies, BMI is the favored measure of excess weight to estimate relative risk of disease. BMI correlates both with morbidity and mortality; the relative risk for CVD risk factors and CVD incidence increases in a graded fashion with increasing BMI in all population groups. Moreover, calculating BMI is simple, rapid, and inexpensive, and can be applied generally to adults. The panel, therefore, makes this recommendation:

The BMI should be used to classify overweight and obesity and to estimate relative risk of disease compared to normal weight. Evidence Category C.

**Assessing abdominal fat**

For the most effective technique for assessing abdominal fat content, the panel considered measures of waist circumference, waist-to-hip ratio (WHR), magnetic resonance imaging (MRI), and computed tomography. Evidence from epidemiological studies shows waist circumference to be a better marker of abdominal fat content than WHR, and that it is the most practical anthropometric measurement for assessing a patient's abdominal fat content before and during weight loss treatment. Computed tomography and MRI are both more accurate but impractical for routine clinical use. Based on evidence that waist circumference is a better marker than WHR—and taking into account that the MRI and computed tomography techniques are expensive and not readily available for clinical practice—the panel makes the following recommendation:

The waist circumference should be used to assess abdominal fat content. Evidence Category C.

**Sex-specific measurements**

Evidence from epidemiological studies indicates that a high waist circumference is associated with an increased risk for type 2 diabetes, dyslipidemia, hypertension, and CVD. Therefore, the panel judged that sex-specific cutoffs for waist circumference can be used to identify increased risk associated with abdominal fat in adults with a BMI in the range of 25 to 34.9. These cutpoints can be applied to all adult ethnic or racial groups. On the other hand, if a patient is very short, or has a BMI above the 25 to 34.9 range, waist cutpoints used for the general population may not be applicable. Based on the evidence from nonrandomized studies, the panel makes this recommendation:

For adult patients with a BMI of 25 to 34.9, sex-specific waist circumference cutoffs should be used in conjunction with BMI to identify increased disease risks. Evidence Category C.

**Goals for Weight Loss**

The general goals of weight loss and management are to reduce body weight, to maintain a lower body weight over the long term, and to prevent further weight gain. Evidence indicates that a moderate weight loss can be maintained over time if some form of therapy continues. It is better to maintain a moderate weight loss over a prolonged period than to regain from a marked weight loss.

**Initial Goal of Weight Loss from Baseline**

There is strong and consistent evidence from randomized trials that overweight and obese patients in well-designed programs can achieve a weight loss of as much as 10% of baseline weight. In the diet trials, an average of 8% of baseline weight was lost. Since this average includes persons who did not lose weight, an individualized goal of 10% is reasonable. The panel, therefore, recommends that:
The initial goal of weight loss therapy should be to reduce body weight by approximately 10% from baseline. With success, further weight loss can be attempted if indicated through further assessment. Evidence Category A.

**Amount of weight loss** Randomized trials suggest that weight loss at the rate of 1 to 2 lb/week (calorie deficit of 500 to 1,000 kcal/day) commonly occurs for up to 6 months.

Weight loss should be about 1 to 2 lb/week for a period of 6 months, with the subsequent strategy based on the amount of weight lost. Evidence Category B.

**How to Achieve Weight Loss**

The panel reviewed relevant treatment strategies designed for weight loss that can also be used to foster long-term weight control and prevention of weight gain. The consequent recommendations emphasize the potential effectiveness of weight control using multiple interventions and strategies, including dietary therapy, physical activity, behavior therapy, pharmacotherapy, and surgery, as well as combinations of these strategies.

**Dietary therapy** The panel reviewed 86 RCT articles to determine the effectiveness of diets on weight loss (including LCDs, very low-calorie diets [VLCDS], vegetarian diets, American Heart Association dietary guidelines, the NCEP’s Step 1 diet with caloric restriction, and other low-fat regimens with varying combinations of macronutrients). Of the 86 articles reviewed, 48 were accepted for inclusion in these guidelines. These RCTs indicate strong and consistent evidence that an average weight loss of 8% of initial body weight can be obtained over 3 to 12 months with an LCD and that this weight loss effects a decrease in abdominal fat; and, although lower-fat diets without targeted caloric reduction help promote weight loss by producing a reduced caloric intake, lower-fat diets with targeted caloric reduction promote greater weight loss than lower-fat diets alone. Further, VLCDs produce greater initial weight losses than LCDs (over the long term of >1 year, weight loss is not different than that of the LCDs). In addition, randomized trials suggest that no improvement in cardiorespiratory fitness as measured by VO₂ max appears to occur in obese adults who lose weight on LCDs alone without physical activity. The following recommendations are based on the evidence extracted from the 48 accepted articles:

LCDs are recommended for weight loss in overweight and obese persons. Evidence Category A. Reducing fat as part of an LCD is a practical way to reduce calories. Evidence Category A.

Reducing dietary fat alone without reducing calories is not sufficient for weight loss. However, reducing dietary fat, along with reducing dietary carbohydrates, can facilitate caloric reduction. Evidence Category A.

A diet that is individually planned to help create a deficit of 500 to 1,000 kcal/day should be an integral part of any program aimed at achieving a weight loss of 1 to 2 lb/week. Evidence Category A.

**Physical Activity**

**Effects of physical activity on weight loss** Twenty-three RCT articles were reviewed to determine the effect of physical activity on weight loss, abdominal fat (measured by waist circumference), and changes in cardiorespiratory fitness (VO₂ max). Thirteen of these articles were accepted for inclusion in these guidelines. A review of these articles reveals strong evidence that physical activity alone, ie, aerobic exercise, in obese adults results in modest weight loss and that physical activity in overweight and obese adults increases cardiorespiratory fitness, independent of weight loss. Randomized trials suggest that increased physical activity in overweight and obese adults reduces abdominal fat only modestly or not at all, and that regular physical activity independently reduces the risk for CVD. The panel’s recommendation on physical activity is based on the evidence from these 13 articles:

Physical activity is recommended as part of a comprehensive weight loss therapy and weight control program because it: (1) modestly contributes to weight loss in overweight and obese adults (Evidence Category A), (2) may decrease abdominal fat (Evidence Category B), (3) increases cardiorespiratory fitness (Evidence Category A), and (4) may help with maintenance of weight loss (Evidence Category C).

Physical activity should be an integral part of weight loss therapy and weight maintenance. Initially, moderate levels of physical activity for 30 to 45 minutes, 3 to 5 days a week, should be encouraged. All adults should set a long-term goal to accumulate at least 30 minutes or more of moderate-intensity physical activity on most, and preferably all, days of the week. Evidence Category B.

**Effects of Physical Activity and Diet on Weight Loss** (Combined Therapy) Twenty-three RCT articles were reviewed to determine the effects on body weight of a combination of a reduced-calorie diet with increased physical activity. Fifteen of these articles were accepted for inclusion in the guidelines. These articles contain strong evidence that the combination of a reduced-calorie diet and increased physical activity produces greater weight loss than diet alone or physical activity alone, and that the combination of diet and physical activity improves cardiorespiratory fitness as measured by VO₂ max in overweight and obese adults when compared to diet alone. The combined effect of a reduced-calorie diet and increased physical activity seemingly produced modestly greater reductions in abdominal fat than either diet alone or physical activity alone, although it has not been shown to be independent of weight loss. The panel’s following recommendations are based on the evidence from these articles:
The combination of a reduced calorie diet and increased physical activity is recommended since it produces weight loss that may also result in decreases in abdominal fat and increases in cardiorespiratory fitness. Evidence Category A.

Behavior Therapy
Thirty-six RCTs were reviewed to evaluate whether behavior therapy provides additional benefit beyond other weight loss approaches, as well as to compare various behavioral techniques. Of the 36 RCTs reviewed, 22 were accepted. These RCTs strongly indicate that behavioral strategies to reinforce changes in diet and physical activity in obese adults produce weight loss in the range of 10% over 4 months to 1 year. In addition, no one behavior therapy appeared superior to any other in its effect on weight loss; multimodal strategies appear to work best and those interventions with the greatest intensity appear to be associated with the greatest weight loss. Long-term follow-up of patients undergoing behavior therapy shows a return to baseline weight for the great majority of subjects in the absence of continued behavior intervention. Randomized trials suggest that behavior therapy, when used in combination with other weight loss approaches, provides additional benefits in assisting patients to lose weight short-term, ie, 1 year (no additional benefits are found at 3 to 5 years). The panel found little evidence on the effect of behavior therapy on cardiorespiratory fitness. Evidence from these articles provided the basis for the following recommendation:

Behavior therapy is a useful adjunct when incorporated into treatment for weight loss and weight maintenance.
Evidence Category B.

There is also suggestive evidence that patient motivation is a key component for success in a weight loss program. The panel, therefore, makes the following recommendation:

Practitioners need to assess the patient’s motivation to enter weight loss therapy, assess the readiness of the patient to implement the plan and then take appropriate steps to motivate the patient for treatment.
Evidence Category D.

Summary of Lifestyle Therapy
There is strong evidence that combined interventions of an LCD, increased physical activity, and behavior therapy provide the most successful therapy for weight loss and weight maintenance. The panel makes the following recommendation:

Weight loss and weight maintenance therapy should employ the combination of LCDs, increased physical activity, and behavior therapy.
Evidence Category A.

Pharmacotherapy
A review of 44 pharmacotherapy RCT articles provides strong evidence that pharmacological therapy (which has generally been studied along with lifestyle modification, including diet and physical activity) using dexfenfluramine, sibutramine, orlistat, or phentermine/fenfluramine results in weight loss in obese adults when used for 6 months to 1 year. Strong evidence also indicates that appropriate weight loss drugs can augment diet, physical activity, and behavior therapy in weight loss. Adverse side effects from the use of weight loss drugs have been observed in patients. As a result of the observed association of valvular heart disease in patients taking fenfluramine and dexfenfluramine alone or in combination, these drugs have been withdrawn from the market. Weight loss drugs approved by the FDA for long-term use may be useful as an adjunct to diet and physical activity for patients with a BMI of ≥30 with no concomitant obesity-related risk factors or diseases, as well as for patients with a BMI of ≥27 with concomitant risk factors or diseases; moreover, using weight loss drugs singly (not in combination) and starting with the lowest effective doses can decrease the likelihood of adverse effects. Based on this evidence, the panel makes the following recommendation:

Weight loss drugs approved by the FDA may be used as part of a comprehensive weight loss program, including dietary therapy and physical activity for patients with a BMI of ≥30 with no concomitant obesity-related risk factors or diseases, and for patients with a BMI of ≥27 with concomitant obesity-related risk factors or diseases. Weight loss drugs should never be used without concomitant lifestyle modifications. Continuing assessment of drug therapy for efficacy and safety is necessary. If the drug is efficacious in helping the patient to lose and/or maintain weight loss and there are no serious adverse effects, it can be continued. If not, it should be discontinued. Evidence Category B.

Weight Loss Surgery
The panel reviewed 14 RCTs that examined the effect of surgical procedures on weight loss; 8 were deemed appropriate. All of the studies included individuals who had a BMI of 40 or above, or a BMI of 35 to 40 with comorbidity. These trials provide strong evidence that surgical interventions in adults with clinically severe obesity, ie, BMIs ≥40 or ≥35 with comorbid conditions, result in substantial weight loss, and suggestive evidence that lifelong medical surveillance after surgery is necessary. Therefore, the panel makes the following recommendation:

Weight loss surgery is an option for carefully selected patients with clinically severe obesity (BMIs ≥40 or ≥35 with comorbid conditions) when less invasive methods of weight loss have failed and the patient is at high risk for obesity-associated morbidity or mortality. Evidence Category B.

GOALS FOR WEIGHT LOSS MAINTENANCE
Once the goals of weight loss have been successfully achieved, maintenance of a lower body weight becomes the challenge. Whereas studies have shown that weight loss is achievable, it
is difficult to maintain over a long period of time (3 to 5 years). In fact, the majority of persons who lose weight, once dismissed from clinical therapy, frequently regain it—so the challenge to the patient and the practitioner is to maintain the weight loss. Successful weight reduction thus depends on continuing a maintenance program on a long-term basis. In the past, obtaining the goal of weight loss has been considered the end of weight loss therapy. Observation, monitoring, and encouragement of patients who have successfully lost weight should be continued long-term. The panel’s recommendations on weight loss maintenance are derived from RCT evidence as well as nonrandomized and observational studies.

Weight Maintenance Phase

RCTs from the Behavior Therapy section above suggest that lost weight usually will be regained unless a weight maintenance program consisting of dietary therapy, physical activity, and behavior therapy is continued indefinitely. Drug therapy in addition may be helpful during the weight maintenance phase. The panel also reviewed RCT evidence that considered the rate of weight loss and the role of weight maintenance. These RCTs suggest that, after 6 months of weight loss treatment, efforts to maintain weight loss are important. Therefore, the panel recommends the following:

- After successful weight loss, the likelihood of weight loss maintenance is enhanced by a program consisting of dietary therapy, physical activity, and behavior therapy, which should be continued indefinitely. Drug therapy can also be used. However, drug safety and efficacy beyond 1 year of total treatment have not been established. Evidence Category B.

A weight maintenance program should be a priority after the initial 6 months of weight loss therapy. Evidence Category B.

Strong evidence indicates that better weight loss results are achieved with dietary therapy when the duration of the intervention is at least 6 months. Suggestive evidence also indicates that during dietary therapy, frequent contacts between professional counselors and patients promote weight loss and maintenance. Therefore, the panel recommends the following:

The literature suggests that weight loss and weight maintenance therapies that provide a greater frequency of contacts between the patient and the practitioner and are provided over the long term should be utilized whenever possible. This can lead to more successful weight loss and weight maintenance. Evidence Category C.

SPECIAL TREATMENT GROUPS

The needs of special patient groups must be addressed when considering treatment options for overweight and obesity. The guidelines focus on three such groups including smokers, older adults, and diverse patient populations.

Smokers

Cigarette smoking is a major risk factor for cardiopulmonary disease. Because of its attendant high risk, smoking cessation is a major goal of risk-factor management. This aim is especially important in the overweight or obese patient, who usually carries excess risk from obesity-associated risk factors. Thus, smoking cessation in these patients becomes a high priority for risk reduction. Smoking and obesity together apparently compound cardiovascular risk, but fear of weight gain upon smoking cessation is an obstacle for many patients. Therefore, the panel recommends that:

All smokers, regardless of their weight status, should quit smoking. Evidence Category A. Prevention of weight gain should be encouraged and if weight gain does occur, it should be treated through dietary therapy, physical activity, and behavior therapy, maintaining the primary emphasis on the importance of abstinence from smoking. Evidence Category C.

Older Adults

The general nutritional safety of weight reduction at older ages is of concern because restrictions on overall food intake due to dieting could result in inadequate intake of protein or essential vitamins or minerals. In addition, involuntary weight loss indicative of occult disease might be mistaken for success in voluntary weight reduction. These concerns can be alleviated by providing proper nutritional counseling and regular body weight monitoring in older persons for whom weight reduction is prescribed. A review of several studies indicates that age alone should not preclude treatment for obesity in adult men and women. In fact, there is evidence from RCTs that weight reduction has similar effects in improving cardiovascular disease risk factors in older and younger adults. Therefore, in the panel’s judgment:

A clinical decision to forego obesity treatment in older adults should be guided by an evaluation of the potential benefits of weight reduction for day-to-day functioning and reduction of the risk of future cardiovascular events, as well as the patient’s motivation for weight reduction. Care must be taken to ensure that any weight reduction program minimizes the likelihood of adverse effects on bone health or other aspects of nutritional status. Evidence Category D.

Diverse Patient Populations

Standard obesity treatment approaches should be tailored to the needs of various patients or patient groups. It is, however, difficult to determine from the literature how often this occurs, how specific programs and outcomes are influenced by tailoring, and whether it makes weight loss programs more effective. After reviewing 2 RCTs, 4 cross-sectional studies, and 4 intervention studies, as well as additional published literature on treatment approaches with diverse patient populations, the panel recommends the following:

The possibility that a standard approach to weight loss will work differently in diverse patient populations must be considered when setting expectations about treatment outcomes. Evidence Category B.
CLOSING

The clinical guidelines evidence report was reviewed by 115 health experts at major medical and professional societies. It has been endorsed by members of the coordinating committees of the National Cholesterol Education Program and the National High Blood Pressure Education Program, the North American Association for the Study of Obesity, and the National Institute of Diabetes and Digestive and Kidney Diseases National Task Force on the Prevention and Treatment of Obesity. These groups represent 54 professional societies, government agencies, and consumer organizations. An abbreviated practical guide based on the evidence report will be distributed to primary care physicians in the United States as well as to other interested health care practitioners. The Clinical Guidelines on the Identification, Evaluation, and Treatment of Overweight and Obesity in Adults: Evidence Report is published as the September 1998 supplement to the Journal of Obesity Research and is available on the NHLBI website—at http://www.nhlbi.nih.gov/nhlbi/nhlbi.htm or by writing to the NHLBI Information Center, PO Box 30105, Bethesda, MD 20824-0105.

The following persons served on the National Heart, Lung, and Blood Institute Expert Panel on the Identification, Evaluation, and Treatment of Overweight and Obesity in Adults.

Expert Panel members: F. Xavier Pi-Sunyer, MD, MPH, Chair of the Expert Panel; chair of Endocrinology, Diabetes, and Nutrition, and director of the obesity Research Center, St Luke's/Roosevelt Hospital Center, and professor of Medicine, Columbia University College of Physicians and Surgeons, New York, NY; Diane M. Becker, ScD, MPH, director of the Center for Health Promotion and associate professor of the Department of Medicine, The Johns Hopkins University, Baltimore, Md; Claude Bouchard, PhD, professor of Exercise Physiology, Physical Activity Sciences Laboratory, Laval University, Sainte-Foy, Quebec, Canada; Richard A. Carleton, MD, professor of Medicine with the Brown University School of Medicine, Providence, RI; Graham A. Colditz, MD, DrPH, associate professor of Medicine with the Harvard Medical School, Channing Laboratory, Boston, Mass; William H. Dietz, MD, PhD, director of the Division of Nutrition and Physical Activity, National Center for Chronic Disease Prevention and Health Promotion, Centers for Disease Control and Prevention, Atlanta, Ga; John P. Foreyt, PhD, professor of Medicine and director of the Nutrition Research Clinic, Baylor College of Medicine, Houston, Tex; Robert J. Garrison, PhD, associate professor with the Department of Preventive Medicine, University of Tennessee, Memphis; Scott M. Grundy, MD, PhD, director of the Center for Human Nutrition, University of Texas, Southwestern Medical Center at Dallas; Barbara C. Hansen, PhD, professor of Physiology and director of the Obesity and Diabetes Research Center, University of Maryland School of Medicine, Baltimore; Milton Higgins, MD, Department of Epidemiology, School of Public Health, University of Michigan, Ann Arbor; James O. Hill, PhD, associate director of Research for the Center for Human Nutrition, University of Colorado Health Sciences Center, Denver; Barbara V. Howard, PhD, president of Mediatric Research Institute, Washington, DC; Robert J. Kuczmarski, DrPH, RD, nutrition analyst with the National Center for Health Statistics, Centers for Disease Control and Prevention, Hyattsville, Md; Shiriki Kumanyika, PhD, RD, MPH, professor and head, Department of Human Nutrition and Dietetics, The University of Illinois at Chicago; R. Dee Legako, MD, Prime Care Family Park Family Physicians, Inc., Edmond, Okla; T. Elaine Preuitt, DrPH, RD, assistant professor, Department of Preventive Medicine and Epidemiology, Loyola University Medical Center, Maywood, Ill; Albert P. Rocchini, MD, chief of Cardiology, University of Michigan Medical Center, Ann Arbor; Philip L. Smith, MD, professor of Medicine, Division of Pulmonary and Critical Care Medicine, The Johns Hopkins Asthma and Allergy Center, Baltimore, Md; Linda G. Snetkael, PhD, RD, associate professor and head of Preventive Nutrition Education, Department of Preventive Medicine, University of Iowa, Iowa City; James R. Sowers, MD, professor of Medicine and Physiology and director of the Division of Endocrinology, Metabolism, and Hypertension, Wayne State University School of Medicine, University Health Center, Detroit, Mich; Michael Werntz, MD, director of the Office of Drug Evaluation, Food and Drug Administration, Rockville, Md; David F. Williamson, PhD, MS, epidemiologist, Division of Diabetes Translation (K-10), Centers for Disease Control and Prevention, Atlanta, Ga; G. Terence Wilson, PhD, Oscar K. Baros Professor of Psychology and director of the Rutgers Eating Disorders Clinic, Piscataway, NJ.

Ex-officio members: Clarence D. Brown, MS, project manager, CODA Research, Inc, Silver Spring, Md; Karen A. Donato, MS, RD, executive director of Expert Panel and coordinator of the NHLBI Obesity Education Initiative, National Heart, Lung, and Blood Institute, National Institutes of Health, Bethesda, Md; Nancy Ernst, PhD, RD, nutrition coordinator, Office of the Director, Division of Epidemiology and Clinical Applications, National Heart, Lung, and Blood Institute, National Institutes of Health, Bethesda, Md, D. Robin Hill, PhD, social science analyst, Behavioral Medicine Branch, Division of Epidemiology and Clinical Applications, National Heart, Lung, and Blood Institute, National Institutes of Health, Bethesda, Md; Michael J. Horan, MD, ScM, director of the NIH Division of Heart and Vascular Diseases, National Heart, Lung, and Blood Institute, National Institutes of Health, Bethesda, Md; Vass V. Hubbard, MD, PhD, director of the NIH Division of Nutrition Research Coordination, and chief of the Nutritional Sciences Branch, National Institute of Diabetes and Digestive and Kidney Diseases, Bethesda, Md; James P. Kiley, PhD, director of the Airway Biology and Disease Program, Division of Lung Diseases, National Heart, Lung, and Blood Institute, National Institutes of Health, Bethesda, Md; Eva Obrazcanek, PhD, RD, MPH, research nutritionist, Prevention Scientific Research Group, Division of Epidemiology and Clinical Applications, National Heart, Lung, and Blood Institute, National Institutes of Health, Bethesda, Md.

Consultant: David Schriger, MD, MPH, FACEP, associate professor, UCLA Emergency Medicine Center, University of California at Los Angeles, School of Medicine, Los Angeles, Calif.

San Antonio Cochrane Center: Elaine Chiquette, PharmD, V.A. Cochrane Center at San Antonio, Audie L. Murphy Memorial Veterans Hospital, San Antonio, Tex.

*Member of the National Heart, Lung and Blood Institute (NHLBI) Obesity Initiative Task Force.
Effects of Lifestyle Intervention on Health Care Costs: Improving Control with Activity and Nutrition (ICAN)

ANNE M. WOLF, MS, RD; MIR SIADATY, MD; BEVERLY YAEGER, MS, RN; MARK R. CONAWAY, PhD; JAYNE Q. CROWTHER, MS, RN; JERRY L. NADLER, MD; VIKTOR E. BOVBJERG, PhD, MPH

ABSTRACT
Objective To evaluate program and health care costs of a lifestyle intervention in a high-risk obese population.
Design Twelve-month randomized controlled trial comparing lifestyle case management to usual care.
Subjects/setting Health plan members (n=147) with obesity (body mass index ≥27) and type 2 diabetes.
Intervention Lifestyle case management entailed individual and group education, support, and referrals by registered dietitians. Those in the usual-care group received educational material.
Main outcome measures Medical and pharmaceutical health care costs reimbursed by the participant’s primary insurance company.
Statistical analysis Total costs were modeled using the four-equation model using previous year cost as a predictor.
Results Net cost of the intervention was $328 per person per year. After incorporating program costs, mean health plan costs were $3,586 (95% confidence interval [CI]: $8,036, $25, P<0.05) lower in case management compared to usual care. The difference was driven by group differences in medical (−$3,316, 95% CI: −$7,829 to −$320, P<0.05) but not pharmaceutical costs (−$239, 95% CI: −$870 to $280, not statistically significant), with fewer inpatient admissions and costs among case management compared with usual care (admission prevalence: 2.8% vs 22.5% respectively, P<0.001).
Conclusion Addition of a modest-cost, registered dietitian-led lifestyle case-management intervention to usual medical care did not increase health care costs and suggested modest cost savings among obese patients with type 2 diabetes. Larger trials are needed to determine whether these results can be replicated in a broader population. The findings can be judiciously applied to support that the addition of a registered dietitian-led lifestyle case-management program to medical care does not increase health care costs.

The direct cost of diabetes in the United States was $91.8 billion in 2002 (1). The cost of overweight and obesity was equally high (2). As prevalence of both diabetes and obesity in the United States increases (3), so does the human and financial burden of these conditions. An estimated 38% of the increase in the cost of diabetes between 1987 and 2001 was due to increases in the prevalence of obesity as well as increased medical spending on care of obese individuals (4). This suggests that treating obesity in the context of diabetes management may improve both health and economic outcomes.

Lifestyle treatment (diet and physical activity) is the cornerstone of treatment for both type 2 diabetes and obesity. Modest weight loss improves insulin sensitivity (5) and improves glycemic control, blood pressure, and lipid profiles in people with existing type 2 diabetes (6-9). Independent of weight loss, lifestyle treatment is an effective means of improving glycemic control (10), blood pressure (11,12), and lipid levels (13-15). Moreover, lifestyle treatment with modest weight loss has been shown to be an effective (19-21) and a more cost-effective means...
to prevent diabetes than metformin or usual care in patients at high risk of developing diabetes (22,23). Registered dietitians (RDs) could play a vital role in the delivery of lifestyle treatment considering their training in food and nutritional sciences, health, and behavior change. In addition, many RDs have advanced certification in diabetes and weight management.

Despite this, health systems have generally not integrated lifestyle treatment into clinical practice or systematically reimbursed for nutrition services. The resource burden of some lifestyle treatments demonstrated in efficacy trials may be too great for patients, clinicians, and health care systems to sustain. During the 3 years of the Diabetes Prevention Project, the cost for lifestyle treatment, from a health system’s perspective, was $2,780 per person (24). Translation of lifestyle efficacy trials into lower-intensity, cost effective interventions is one approach to maximize their applicability and long-term maintenance for obese individuals with type 2 diabetes (25,26).

We have previously reported that a modestly priced, RD-led case management approach to lifestyle modification was more effective than usual medical care for improving clinical and health-related quality of life outcomes and decreasing self-reported prescription medication use of patients with obesity and type 2 diabetes (27). The purpose of this analysis is to evaluate the within-trial program costs and economic outcomes associated with a 1-year lifestyle intervention led by an RD lifestyle case manager.

METHODS AND PROCEDURES

The Improving Control with Activity and Nutrition (ICAN) study was a randomized controlled trial (RCT) conducted from 2001 to 2003. The University of Virginia Institutional Review Board approved the study. It is in compliance with Health Insurance Portability and Accountability Act of 1996, and all patients gave written informed consent.

Study Design

The purpose of the ICAN pilot project was to evaluate the differences in clinical, humanistic, and economic outcomes of a nutrition intervention involving lifestyle case management and medical nutrition therapy by an RD compared with usual medical care for obese individuals with type 2 diabetes. The intervention is aimed at moderate weight loss (5% to 10%), improvement in diet quality, and an increase in physical activity. In addition, we wanted to obtain effect sizes of the intervention and gather necessary data critical to planning a larger randomized trial.

Eligibility criteria were: type 2 diabetes (ICD-9 [International Classification of Diseases-9th edition] code 250.XX, 357.2 362.0, 362.02, or 366.41, and confirmed by physician), diabetes medication use, body mass index (calculated as kg/m²) of 27 or more, age 20 years or older, ability to comprehend English, and membership in Southern Health Services health plan as primary health insurance. Exclusion criteria were: pregnancy, cognitive limitations, or medical reasons precluding dietary and physical activity modifications.

Eligible participants were randomly assigned to either case management or usual care using random permuted blocks with randomly chosen block sizes of 2 or 4. Study personnel were blinded to allocation schedule until assignment.

Intervention—Lifestyle Case Management by a Registered Dietitian

One RD case manager met with participants individually, in groups, and by phone for assessment, goal setting, education, and referrals to community resources. The RD measured weight and waist circumference, reviewed laboratory results, and discussed patient-care issues with physicians when appropriate. Individual sessions occurred six times throughout the year, totaling 4 hours. Individual sessions were similar to an outpatient nutrition visit during which the participant’s lifestyle was assessed and patient-centered goals were developed. Goals were tailored but based on national dietary recommendations for people with type 2 diabetes and obesity (28,29). Follow-up visits reassessed whether participants met their goals and, if not, discussed ways to overcome barriers; goals were reset to more achievable levels. Participants also attended six, 1-hour small group (10 or more people per group) sessions developed to provide the majority of education regarding diet and physical activity for improved glucose control and weight loss. Brief monthly phone contacts provided support. Participants were given the LEARN (Lifestyle, Exercise, Attitudes, Relationships, Nutrition) manual (30).

Control Group—Usual Care

Usual care participants received written educational material including the LEARN manual (30). Usual care patients were seen by a research associate every 3 months for weight measurements and to complete questionnaires. The research associate was allowed to answer questions but did not assess, set goals, or have an ongoing dialogue about a participant’s diet or physical activity level.

Outcome Measures

The primary outcome measures were health care utilization and health plan costs during the year of the trial. Utilization is defined as the number of claims during the year, except for inpatient and pharmaceutical use. Utilization within the inpatient analysis represents the number of unique hospital admissions. Length of stay was defined by Southern Health Services and represents the number of nights in the hospital. Utilization in the pharmacy analysis represents the 12-month change in self-reported number of prescription medications taken daily. Cost is defined as the dollar amount paid by the health insurance company. We also explored other perspectives of health care cost, including costs to patients (medical costs + copay) and charges, but focused on costs paid by the insurer. Direct nonmedical costs (out-of-pocket costs for exercise equipment and diet food) were not included in this analysis.

The health plan variable “place of service” was aggregated from 11 potential place of service categories. Inpa-
tient services included all paid claims for care in hospitals. Outpatient included all paid claims for services occurring in physician offices and other clinical practices, outpatient hospital services, and independent laboratories outside physician offices. Emergency room included all paid claims originating from emergency departments and ambulance use. Procedures included all paid claims generated by ambulatory surgical centers. Pharmaceutical was generated from the pharmacy database and represents claims and payment for insurance-covered prescription medications. Other types of services (ie, nursing home and rehabilitative facilities) were not included due to low occurrence. The outcomes were defined as the sum of claims and cost for a person from the initial visit to 365 days after that visit. There were 23 participants who completed the trial whose pharmaceutical claims did not cover a full 365 days (three with fewer than 3 months of data; six with fewer than 6 months; five with fewer than 9 months; and nine with fewer than 12 months). All available data within that timeframe were used.

Program Costs
Program costs were calculated by applying standard unit costs to the resources used. Resource use included educational materials and patient care unit time. Unit costs were actual costs of educational material. Salary and overhead were based on published costs from the Diabetes Prevention Project (24). All costs were adjusted to 2002 US dollars using the medical component of the consumer price index (in accordance with the intervention year and the direct medical costs). Net program costs subtract usual-care program costs from the case management intervention program costs. Although both groups were allowed to join other weight management or diabetes care programs outside the ICAN program, these program costs were minimal and are not included in the analysis. We excluded the costs of the research component including resources used for recruitment, data collection and surveillance of complications and outcomes. Laboratory costs incurred as part of the study were not included in the cost of the intervention. Clinical lab tests ordered by participants’ physicians as part of their usual medical care are included as part of their direct medical expenses. This avoids double-counting laboratory costs.

Direct Medical Costs
Direct medical costs typically represent expenditures for medical services and products that are usually paid for by health systems and include costs of hospitalization, urgent care, outpatient care, laboratory tests, and procedures. The cost variables within this analysis represent the dollar amount that the health insurance plans paid for the practice or provider (physician, pharmacy, hospital). Health plan administrative data were linked to research databases by participant number. The health plans used two internal databases to document payments: the pharmaceutical and the medical care databases. The pharmaceutical database included outpatient prescription pharmaceutical claims and costs. The medical care database included all medical claims (except outpatient pharmaceuticals); inpatient pharmaceuticals, procedures and care; outpatient visits; ambulatory procedures and diagnostic testing; and urgent care. Claim and cost data were carefully evaluated for validity. Absolute cost differences between groups are reported for the year of the trial because participants were all members of Southern Health Services. Relative cost differences between groups are reported when comparing the year preceding the year of the trial due to an administrative change in insurance companies between these years.

Study and Analysis Group
One hundred forty-seven participants were randomly assigned to usual care (n=74) or case management (n=73). Three patients withdrew before baseline assessment, so the intention-to-treat analysis population was comprised of 72 usual-care participants and 72 case-management participants.

For health care cost data in the year preceding the trial, there were five participants without medical claims data (ie, they were not health plan members before the study) and 14 participants without pharmaceutical claims data (non—health plan members or lack of pharmaceutical benefits within their Southern Health Services medical care coverage). For health care cost data during the intervention (primary analysis), there were 11 people with missing pharmaceutical claims data (8 people without pharmacy benefits and 3 people who: [a] didn’t have pharmacy benefits, [b] had no claims data during the intervention period, or [c] changed health insurance companies at the beginning of the trial). The final sample size for pharmaceutical cost was 133 (65 in usual care and 68 in case management). For medical claims data, there were two participants with missing claims data for the entire year due to changing health insurance companies during the trial. Hence, the final sample size for medical claims cost was 142 (71 in usual care and 71 in case management).

Statistical Analysis
Administrative data were extracted and transferred by Microsoft Access (version 5.0, 2002, Microsoft, Redmond, WA). Data preparation and quality assurance was implemented in SPSS (version 11, 2001, SPSS, Chicago, IL) (31). Estimation of descriptive statistics, significance tests, and fitting of models has been done in both R (R version 2.0, 2004, Vienna, Austria) (32) and SPSS.

The “four equation model” of Duan and colleagues (33) was used to model total costs. This approach was developed by authors of the RAND Health Insurance Experiment (34) to account for the wide variability observed due to inpatient health care costs and is now commonly applied to medical cost data. This method was applied only to medical costs and cannot be applied to the pharmaceutical database or to categories of health care (ie, outpatient care) that do not include inpatient hospitalizations. Previous year cost was a predictor in the equations. Logit link and bias corrected and accelerated nonparametric bootstrap (35) was used for obtaining standard errors.

RESULTS
Baseline Characteristics
Groups were similar in all demographic and clinical measures at baseline (Table 1). Study participants, on aver-
age, were in class 2 (body mass index = 35 to 39.9) obesity and had a high-risk waist circumference, suggesting very high-risk obesity (36). Participants reported a mean (± standard deviation) of 2.6 ± 1.6 “health problems” (eg, hypertension) in addition to diabetes; this was similar between groups. For the year preceding the trial, there were no significant differences between usual-care and case-management participants in medical (P = 0.65) or pharmaceutical costs (P = 0.39).

Program Costs
The direct cost of the intervention and usual care (per person per year) are presented in Table 2. Net program costs were approximately $325 per person per year.

Mean Annual Health Care Costs During Intervention
There were 5,329 pharmaceutical and 6,921 medical claims for all participants during the 1-year intervention period. Total health care costs (sum of medical and pharmaceutical costs) paid by the health plan during the 1 year of intervention were $3,911 per person per year less among those receiving lifestyle case management compared with usual care (95% confidence interval [CI]): $-8,374 to $-353, P < 0.05) (Table 3). There was a significant difference in medical care costs (eg, inpatient, outpatient, procedures) (95% CI for the mean difference in cost: $-7,829 to $-320, P < 0.05). Mean and median costs and utilization for prescription medications was not statistically significant (95% CI for the mean difference in cost: $-870 to $280, P = 0.28). Evaluating “cost” from the perspectives such as medical charges or adding patient co-pay onto medical costs were not statistically significant (95% CI charges: $-14,391 to $640, not significant; medical costs + co-pay: $-7,617 to $69, not significant). Comparing health care costs from the year preceding to the year of the trial, there was a relative increase in health care costs among both groups; 84% in usual care and 41% in case management.

Health Care Costs by Place of Service
Mean and median cost and mean utilization data by place of service are presented in Table 3. Group differences by place of service are provided for descriptive purposes only because the Duan and colleagues method is applied only
to services that include inpatient utilization. Overall, across all places of services, there were no significant differences in mean and median costs by types of service by groups.

Inpatient Admissions

Post hoc analyses indicated that there were 18 inpatient admissions during the intervention. The usual-care group had significantly more admissions during the intervention period (n=16, 22.5% of usual-care group) compared with the case-management group (n=2, 2.8% of case-management group) (P<0.001). Among the usual-care group, one person had five admissions and another had two admissions during the intervention. The remaining admissions were person-specific. There was a significant difference between the groups for the number of people with at least one hospital admission (usual care: n=11, 15.5% of usual-care group vs case management: n=2, 2.8% of case-management group, P=0.008).

Table 4 provides detailed information about the cost and diagnoses of the inpatient admissions during the trial. The mean (±standard deviation) length of stay among the usual-care group was 4.7±5.0 days compared with 1.0±0.0 day in the case-management group. All but four hospitalizations were for conditions often related to obesity and diabetes (ie, heart disease, stroke, osteoarthritis), and nine admissions in usual care and two admissions in case management were related to cardiovascular disease. The four admissions unrelated to obesity/diabetes/cardiovascular disease cost less than most of the cardiovascular- and diabetes-related admissions. Two admissions in usual care (C and I) had less-than-expected costs considering the number and type of claims. Further inquiry revealed that these claims were denied for a variety of reasons; this underreporting of total inpatient costs was observed only in the usual-care group.

### Total Health Care Costs Including Intervention Program Costs

Including the cost of the lifestyle program (Table 2) in the direct cost of health care during the year of intervention (Table 3), mean net total costs were $3,586 per person per year less among case management compared with usual care (95% CI: −$8,046, −$25, P<0.05).

### DISCUSSION

Our analysis found that the addition of a clinically feasible, modest-cost lifestyle intervention, involving an RD as a lifestyle case management for a high-risk obese population at best saved $8,046 per person per year and at worst did not increase health care costs (saved $25 per person per year) compared with usual medical care (P<0.05). We remain cautious in declaring a cost saving within this pilot project because of the relatively small sample size for an economic evaluation coupled with large confidence intervals. Larger trials are needed to verify our results.

There is growing evidence from large efficacy trials that lifestyle interventions among higher risk populations are cost-effective (22,23,37). Larger health systems are beginning to offer lifestyle treatment options for their patient populations. There is less evidence that translating findings from efficacy trials to more typical clinical settings will demonstrate cost effectiveness. In a health care environment in which spending outpaces inflation and wage growth (38), payers of health care are looking for cost-effective programs (39).

In 2000, the Institute of Medicine recommended coverage of nutrition services for the Medicare population based on “limited but consistent” evidence supporting the medical efficacy of nutrition services in improving outcomes and increasing quality of life, but stopped short of saying there was enough evidence to support the cost effectiveness of such treatment (40). A recent systematic review of the cost effectiveness of outpatient nutrition

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**Table 2. ICAN within-trial direct program costs by study group**

<table>
<thead>
<tr>
<th>Item</th>
<th>Provider</th>
<th>Units</th>
<th>Time (h)</th>
<th>Unit cost ($)</th>
<th>Total cost ($)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Lifestyle group</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Curriculum</td>
<td>RD&lt;sup&gt;p&lt;/sup&gt;</td>
<td></td>
<td>0.55</td>
<td>25.39</td>
<td>13.96</td>
</tr>
<tr>
<td>Materials</td>
<td>LEARN&lt;sup&gt;c&lt;/sup&gt;</td>
<td>1</td>
<td></td>
<td>16.17</td>
<td>16.17</td>
</tr>
<tr>
<td>In-person visits</td>
<td>RD</td>
<td>4</td>
<td>1</td>
<td>25.39</td>
<td>101.55</td>
</tr>
<tr>
<td>Group sessions</td>
<td>RD</td>
<td>0.10</td>
<td>9</td>
<td>25.39</td>
<td>26.36</td>
</tr>
<tr>
<td>Phone calls</td>
<td>RD</td>
<td>12</td>
<td>0.25</td>
<td>25.39</td>
<td>76.16</td>
</tr>
<tr>
<td>Reminder phone calls</td>
<td>RD</td>
<td>6</td>
<td>0.16</td>
<td>25.39</td>
<td>24.37</td>
</tr>
<tr>
<td>Overhead (48% of personnel)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Total annual cost: case management</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>374.57</td>
</tr>
<tr>
<td><strong>Usual-care group</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Materials</td>
<td>LEARN</td>
<td>1</td>
<td></td>
<td>16.17</td>
<td>16.17</td>
</tr>
<tr>
<td>Reminder phone calls</td>
<td>RN&lt;sup&gt;d&lt;/sup&gt;</td>
<td>5</td>
<td>0.16</td>
<td>25.39</td>
<td>20.31</td>
</tr>
<tr>
<td>Overhead</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>9.75</td>
</tr>
<tr>
<td><strong>Total annual cost: usual care</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>46.23</td>
</tr>
</tbody>
</table>

<sup>a</sup>ICAN=Improving Control with Activity and Nutrition study.
<sup>b</sup>RD=registered dietitian.
<sup>c</sup>LEARN=Lifestyle, Exercise, Attitudes, Relationships, Nutrition.
<sup>d</sup>RN=registered nurse.
services supports the Institute of Medicine findings (41). Five RCTs evaluated the cost effectiveness of nutrition services for patients with obesity and/or diabetes and supported the medical efficacy of these services (42-46). However, all of these studies took the provider perspective (evaluating only program costs) and therefore did not report medical utilization and cost during the intervention. In general, program cost without medical expense data offers limited information to health plan decision makers. On the other hand, medical care expenses among Kaiser Permanente Northwest members, who attended a behavioral weight-loss program and lost 5% or more of their initial weight, were significantly less the year after attending the program compared with age- and sex-matched control subjects ($2,935 vs $3,354, P < 0.05) (48), so we could evaluate economic outcomes. Baseline lipid levels indicated that many participants had not reached the Third National Cholesterol Education Program’s Adult Treatment Panel targets (49) for high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, and triglycerides; 64% of participants were on cardiovascular medications; 76% were on anti-hypertensive agents. Baseline body mass index and waist circumference placed them at very high risk (36). Eisenstein and colleagues reported that among patients with acute coronary syndrome, obesity was related to more inpatient utilization and costs (50). In general, obesity is associated with greater inpatient utilization in the US population (51) and in US managed care population (52). We did not evaluate diabetes-specific costs only because the study’s population had both diabetes and obesity. Because obesity is related to many comorbid conditions, and both obesity and diabetes influence outcomes in many other conditions, evaluating hospitalizations based on obesity or diabetes-specific diagnoses has the potential to introduce bias. Table 4 provides the diagnoses related to hospitalizations.
The main limitations of ICAN include its small sample size for economic evaluation, restriction to insured participants, the short follow-up, and the inherent limitations of administrative claims data. As with all studies, there is a possibility that our significant findings were due to chance. Because inpatient visits are rare but often expensive, there is wide variation in cost data, and in a study the size of ours typically results in broad confidence intervals. Despite this, the results using costs are consistent with the data for the number of hospitalizations by group. Furthermore, the control and treatment groups did not differ in their pretrial economic outcomes or the duration of being diagnosed with diabetes.

Regarding the study population, most participants (80%) were white and employed. Although we saw no substantial differences by race, study results may not be generalizable to multiethnic or uninsured populations. As with all clinical trials, volunteer participants may be healthier and more motivated to change behavior compared with eligible nonvolunteers. On the other hand, lifestyle interventions are always voluntary in practice, and likely to be attractive to more motivated patients. Our findings of decreased health care costs should also not be generalized across different types of lifestyle interventions, settings, or conditions.

Although use of administrative data is essential to

### Table 4. Inpatient utilization and costs during ICAN intervention year

<table>
<thead>
<tr>
<th>Participant</th>
<th>Primary diagnosis for hospitalization</th>
<th>Primary procedures</th>
<th>Length of stay (days)</th>
<th>Cost of hospitalization ($)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Usual-care group hospitalizations</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A</td>
<td>Osteoarthritis of the hip</td>
<td>Total hip joint replacement</td>
<td>5</td>
<td>24,441</td>
</tr>
<tr>
<td>B</td>
<td>Congestive heart failure</td>
<td>Cardiac diagnosis and treatment: Cardiac catheterization, ECHO, stress test</td>
<td>5</td>
<td>8,078</td>
</tr>
<tr>
<td>B</td>
<td>CVA&lt;sup&gt;c&lt;/sup&gt;</td>
<td>Cerebral vascular diagnosis and treatment: ECHO, stress test</td>
<td>2</td>
<td>5,450</td>
</tr>
<tr>
<td>B</td>
<td>CVA-related</td>
<td>Cerebral vascular diagnosis and treatment</td>
<td>2</td>
<td>3,707</td>
</tr>
<tr>
<td>B</td>
<td>CVA-related</td>
<td>MRI&lt;sup&gt;d&lt;/sup&gt;-brain, other diagnosis tests and treatment</td>
<td>4</td>
<td>7,242</td>
</tr>
<tr>
<td>B</td>
<td>CVA-related</td>
<td>CVA diagnosis and treatment: MRI, angiography</td>
<td>21</td>
<td>16,793</td>
</tr>
<tr>
<td>C</td>
<td>Intestinal vascular insufficiency</td>
<td>Diagnosis tests and treatment: Colonoscopy, abdominal operation, management of complications</td>
<td>4</td>
<td>1,664&lt;sup&gt;e&lt;/sup&gt;</td>
</tr>
<tr>
<td>C</td>
<td>Ischemic heart disease</td>
<td>Stress test</td>
<td>1</td>
<td>136</td>
</tr>
<tr>
<td>E</td>
<td>Bacterial pneumonia</td>
<td>Diagnosis and treatment of pneumonia</td>
<td>2</td>
<td>4522</td>
</tr>
<tr>
<td>F</td>
<td>ACS&lt;sup&gt;f&lt;/sup&gt;</td>
<td>Diagnosis and treatment of ACS</td>
<td>2</td>
<td>3,990</td>
</tr>
<tr>
<td>G</td>
<td>ACS with sepsis and pneumonia</td>
<td>Cardiac catheterization, CT&lt;sup&gt;g&lt;/sup&gt; scan, ECHO</td>
<td>10</td>
<td>14,279</td>
</tr>
<tr>
<td>H</td>
<td>Lumbar spinal stenosis</td>
<td>Pro laminectomy</td>
<td>5</td>
<td>14,597</td>
</tr>
<tr>
<td>I</td>
<td>Severe myositis</td>
<td>Diagnosis and treatment of myositis</td>
<td>6</td>
<td>6,341</td>
</tr>
<tr>
<td>I</td>
<td>Chest pain</td>
<td>Diagnostic services (stress test, CT scan) and intermediate ICU&lt;sup&gt;h&lt;/sup&gt;</td>
<td>3</td>
<td>4,039&lt;sup&gt;i&lt;/sup&gt;</td>
</tr>
<tr>
<td>J</td>
<td>Malignant neoplasm of brain</td>
<td>Brain biopsy</td>
<td>1</td>
<td>100</td>
</tr>
<tr>
<td>K</td>
<td>Trimalleolar fracture</td>
<td>Diagnosis and treatment</td>
<td>2</td>
<td>7,029</td>
</tr>
<tr>
<td>Mean ± SD&lt;sup&gt;j&lt;/sup&gt;</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Case-managed group hospitalizations</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>L</td>
<td>COPD&lt;sup&gt;j&lt;/sup&gt; with exacerbation</td>
<td>Observation</td>
<td>1</td>
<td>500</td>
</tr>
<tr>
<td>M</td>
<td>Congestive heart failure</td>
<td>Diagnostic tests (nuclear stress test, CT scan)</td>
<td>1</td>
<td>7814</td>
</tr>
<tr>
<td>Mean ± SD&lt;sup&gt;j&lt;/sup&gt;</td>
<td></td>
<td></td>
<td></td>
<td>1.0 ± 0</td>
</tr>
</tbody>
</table>

<sup>a</sup>ICAN = Improving Control with Activity and Nutrition study.
<sup>b</sup>ECHO = echocardiogram.
<sup>c</sup>CVA = cerebral vascular accident.
<sup>d</sup>MRI = magnetic resonance imaging.
<sup>e</sup>Admission had many denied paid claims.
<sup>f</sup>ACS = acute coronary syndrome.
<sup>g</sup>CT = computed tomography.
<sup>h</sup>ICU = intensive care unit.
<sup>i</sup>SD = standard deviation.
<sup>j</sup>COPD = chronic obstructive pulmonary disease.
capture costs from a payer’s perspective, there can be imprecision and change. A major administrative change in Southern Health Services is one example of this and underscores the importance of including longitudinal comparison groups (eg, in RCT or cohorts) when working with commercial health plans. Throughout the trial, the ICAN research team collaborated with health plan counterparts to minimize the imprecision and bridge the data gap between clinical research, clinical care, and business. The finding that inpatient costs among usual care were underreported due to our definition of cost being limited to costs reimbursed by the primary insurer is one such example. In addition, the increase in health care costs from the year previous to the year of the trial is another example. Brown and colleagues report that health care costs for people with diabetes varies little over time, but that costs, especially inpatient costs begin to increase in the seventh and eight year after diagnosis (53). The ICAN participants were a mean of 7.3 years from the time of diagnosis. The annual increase in health care cost as diabetes progresses, however, cannot explain the large increase we observed. A further explanation may be the accounting practice differences between Southern Health Services and Qual Choice, the health system acquired by Southern Health Services; hence, we report relative changes over time. The strength of the RCT design was critical to distribute inaccuracies randomly, resulting in groups with data of comparable accuracy.

CONCLUSIONS

In 1999-2000, only 52% of third-party payers (54) and 45% of Fortune 100 firms (55) covered outpatient nutrition services. Health plans, insurers, and employers may need business cases to support the decision to provide lifestyle behavior modification by an RD. The ICAN project provides preliminary evidence that moderate-intensity lifestyle intervention using an RD as a lifestyle case management reduces risk, improves quality of life (27), and does so without increasing health care costs. Given the growing prevalence of both diabetes and obesity and the substantial burden of health care costs to patients, employers, and society, effective interventions that are at least cost-neutral should be welcome additions to comprehensive medical care. Food and nutrition professionals can use these results to judiciously support the cost neutrality and effectiveness (27) of their services as an integral component of medical care.

This protocol was funded by grants from the American Dietetic Association, National Institute of Diabetes and Digestive and Kidney Diseases (R18 DK062942) and a grant to the University of Virginia General Clinical Research Center, MO1 RR00847.

The authors thank Kristen Yonkers-Hazen, the ICAN RD case manager, for her commitment and dedication, and to ICAN study participants for their dedication to diabetes and obesity treatment.

Any opinions, results, or conclusions set forth in this article are those of the authors and do not necessarily reflect the policies or opinions of Southern Health or any subsidiaries or affiliate companies.

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