The Consequences of Childhood Overweight and Obesity

Stephen R. Daniels

Summary

Researchers are only gradually becoming aware of the gravity of the risk that overweight and obesity pose for children's health. In this article Stephen Daniels documents the heavy toll that the obesity epidemic is taking on the health of the nation's children. He discusses both the immediate risks associated with childhood obesity and the longer-term risk that obese children and adolescents will become obese adults and suffer other health problems as a result.

Daniels notes that many obesity-related health conditions once thought applicable only to adults are now being seen in children and with increasing frequency. Examples include high blood pressure, early symptoms of hardening of the arteries, type 2 diabetes, nonalcoholic fatty liver disease, polycystic ovary disorder, and disordered breathing during sleep.

He systematically surveys the body's systems, showing how obesity in adulthood can damage each and how childhood obesity exacerbates the damage. He explains that obesity can harm the cardiovascular system and that being overweight during childhood can accelerate the development of heart disease. The processes that lead to a heart attack or stroke start in childhood and often take decades to progress to the point of overt disease. Obesity in childhood, adolescence, and young adulthood may accelerate these processes. Daniels shows how much the same generalization applies to other obesity-related disorders—metabolic, digestive, respiratory, skeletal, and psychosocial—that are appearing in children either for the first time or with greater severity or prevalence.

Daniels notes that the possibility has even been raised that the increasing prevalence and severity of childhood obesity may reverse the modern era's steady increase in life expectancy, with today's youth on average living less healthy and ultimately shorter lives than their parents—the first such reversal in lifespan in modern history. Such a possibility, he concludes, makes obesity in children an issue of utmost public health concern.

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Health professionals have long known that being overweight carries many serious health risks for adults. Medical researchers have also investigated how obesity affects the health of children and adolescents, but work in this area has advanced more slowly. The epidemic of overweight and obesity in children and adolescents, however, has intensified the pace of research. In the face of this new epidemic, researchers are raising the question of whether children face the same set of health risks as adults—or whether their risks are unique. The answer, to a certain extent, is both. Many health conditions once thought applicable only to adults are now being seen in children and with increasing frequency. Even if the conditions do not appear as symptoms until adulthood, they may appear earlier than usual in a person's lifetime if the person had weight problems in childhood. Further, children are also more vulnerable to a unique set of obesity-related health problems because their bodies are growing and developing.

In this article, I will discuss both the adverse outcomes associated with childhood obesity and the risk that obese children and adolescents will become obese adults and be exposed to other health problems.

The obesity epidemic is taking a heavy toll on the nation's children. Some obesity-related conditions are having an immediate adverse effect on their health; others will have more chronic long-term effects. Because of overweight and obesity, today's young people may, on average, live less healthy and ultimately shorter lives than their parents. The epidemic is an issue of urgent public health concern.

Adverse Health Outcomes in Children

As the prevalence and severity of childhood obesity increase, concern about adverse health outcomes in childhood and adolescence is rising. Table 1 shows the prevalence in children and adolescents of various health problems associated with obesity. In what follows, I will provide details on how obesity affects various important body systems. Obesity can cause great damage to the cardiovascular system, for example, and being overweight or obese during childhood can accelerate the development of obesity-related cardiovascular disease. Likewise, obesity is linked with many disorders of the metabolic system. Such disorders, heretofore seen primarily in adulthood, are now appearing in children. Even when the disorders do not present themselves in childhood, childhood obesity or overweight increases the risk of their developing in adulthood. Much the same generalization applies to the obesity-related disorders in the other bodily systems.

Cardiovascular Problems

In the cardiovascular system, the heart pumps blood, which is carried back and forth between the heart and the body by blood vessels. Arteries, which move blood from the heart to the rest of the body, are not just simple tubes, but a dynamic series of conduits that control blood flow. They are vulnerable to many diseases that can ultimately lead, in the case of coronary arteries, to a heart attack or, in the case of cerebral arteries, to a stroke. The heart muscle is also vulnerable to processes that thicken it and diminish its function. The critical risk factors for heart attack or stroke—diabetes, high blood pressure, high blood cholesterol, and cigarette smoking—are well known.

Table 1. Disorders Related to Childhood Obesity, by Body System

System and disorder	Explanation	Estimated prevalence in pediatric populations
Cardiovascular		
Hypertension	High blood pressure	2–4%
Left ventricular hypertrophy	Increased thickness of the heart's main pumping chamber	Unknown
Atherosclerosis	Hardening of the arteries	50% (fatty streaks) 8% (fibrous plaques) 4% (>40 in those with stenosis)
Metabolic		
Insulin resistance	The process in which the action of insulin is retarded	Unknown
Dyslipidemia	Abnormal changes in cholesterol and triglycerides (fats) in the blood	5-10%
Metabolic syndrome	Constellation of risk factors including increased waist circumference, elevated blood pressure, increased triglyceride and decreased HDL-cholesterol concentrations, and raised plasma glucose	4% overall, 30% in obese
Type 2 diabetes	A condition in which the body either makes too little insulin or cannot properly use the insulin it makes, leading to elevated blood glucose	1–15 persons per 100,000 overall, almost all in obese
Pulmonary		
Asthma	A chronic inflammatory pulmonary disorder characterized by reversible obstruction of the airways	7–9%
Obstructive sleep apnea	A breathing disorder characterized by interruptions of breathing during sleep	1–5% overall, approx. 25% in obese
Gastrointestinal		
Nonalcoholic fatty liver disease	Fatty inflammation of the liver not caused by excessive alcohol use	3–8% overall, 50% in obese
Gastroesophageal reflux	Backward flow of stomach contents into the esophagus	2–20%
Skeletal		
Tibia vara (Blount disease)	Bowing of children's legs caused by a growth disturbance in the proximal tibial epiphysis	Uncommon
Slipped capital-femoral epiphysis	A disorder of the hip's growth plate	1–8 persons per 100,000
Psychosocial		
Depression	A mood disorder characterized by sadness and loss of interest in usually satisfying activities	1–2% in children, 3–5% in adolescents
Other		
Polycystic ovary syndrome	A constellation of abnormalities including abnormal menses, clinical manifestations of such androgen excess as acne and excessive growth of hair, elevated levels of circulatory androgens, and polycystic ovaries on ultrasound evaluation	Unknown in adolescents, 5–10% in adult women
Pseudotumor cerebri	Raised intracranial pressure	Rare

Source: Author's estimates based on various sources.

Until recently, most medical concerns about children's hearts involved birth defects. But as advances in noninvasive testing have made it possible to evaluate children's hearts and blood vessels, health professionals have discovered that some disease processes, such as hardening of the arteries, once thought to be predominantly adult health concerns can in fact begin in childhood.

One major risk factor for heart attack and stroke in adults is hypertension, or high blood pressure.[1] And obesity is an important contributor to developing high blood pressure not

only in adults, but also in children and adolescents.[2] B. Rosner and several colleagues have demonstrated that the odds of elevated blood pressure are significantly higher for children whose body mass index (BMI) is at or above the 90th percentile than for those with BMI at or below the 10th percentile. The risk of elevated blood pressure ranges from 2.5 to 3.7 times higher for the overweight children, depending on their race and sex.[3]

Recent national epidemiological studies have suggested that today's children and adolescents have higher blood pressure than did their counterparts in past decades.

Recent national epidemiological studies have suggested that today's children and adolescents have higher blood pressure than did their counterparts in past decades.[4] P. Muntner and several colleagues have also found that a portion of this increase in blood pressure is due to population trends for increased overweight.[5] As children on average have become more overweight, their blood pressure on average has gone up. BMI during childhood and, to an even greater extent, the increase in BMI from childhood to adulthood have been linked significantly with blood pressure in adulthood.[6] Overweight and obese children and those who become even more overweight in adulthood are more likely than others to have high blood pressure as adults.

Left ventricular hypertrophy, or increased thickness of the heart's main pumping chamber, is an independent risk factor for cardiovascular disease in adults. Adults with high blood pressure and with a left ventricular mass index greater than 51 g/m have a fourfold increase in adverse cardiovascular outcomes.[7] Left ventricular hypertrophy has been associated with obesity and high blood pressure in adults.

As with high blood pressure, left ventricular hypertrophy has also been linked with increased BMI in children and adolescents.[8] The most important aspect of body composition that affects left ventricular mass is lean body mass, probably because the heart's development matches the development of the body's muscles to which it must supply blood.[9] This appears to be a physiologic—that is, normal—relationship. But fat mass and systolic blood pressure also have a significant relationship with left ventricular mass.[10] These more pathologic, or abnormal, relationships could lead to the increased heart thickness that raises the risk of a heart attack. In addition, among children with essential hypertension (the most common form of high blood pressure), increased BMI is linked with more severe left ventricular hypertrophy.[11] Left ventricular hypertrophy may thus be another important pathway by which obesity can increase the future risk of cardiovascular disease in children.

Ultimately the most important process for developing cardiovascular disease is hardening of the arteries, or atherosclerosis, which begins as a fatty streak on the artery's inner lining and progresses into a fibrous plaque (a raised lesion) that ultimately causes a heart attack or a stroke by blocking blood flow to the heart or to the brain. The well-known risk factors for this progression in adults include cigarette smoking, high blood pressure, elevated cholesterol, and diabetes.

Whether obesity directly influences the progression of atherosclerosis in adults is not clear.

Obesity's role in the earliest stages of atherosclerosis during childhood has been even less clear, in part because researchers lack noninvasive tools to evaluate the early atherosclerotic lesions. Two pathology studies, however, have helped to clarify these relationships. The Pathobiologic Determinants of Atherosclerosis in Youth (PDAY) and the Bogalusa studies used autopsy data on adolescents and young adults who died of accidental causes.[12] Pathologists working on these autopsies were able to observe directly the fatty streaks and fibrous plaques in these young people's arteries and to evaluate whether the presence of these lesions was related to the known risk factors for heart attack and stroke. In both studies, measures of adiposity (or fat) were significantly related to the presence of atherosclerotic lesions. In the Bogalusa study, an increase in the number of risk factors, including overweight, high blood pressure, and high cholesterol, was associated with a dramatically increased risk of atherosclerosis.[13] In another study L. T. Mahoney and several colleagues used electron beam computed tomography (EBCT) to evaluate calcium's presence in the coronary arteries of young adults.[14] Calcium deposits provide an important indication of the progression of the atherosclerotic process. Mahoney's team found coronary calcium in approximately 30 percent of healthy young adult males and approximately 10 percent of young adult females in a normal sample (that is, the sample did not consist only of overweight young people). They also found that increased weight during childhood and a high body mass index in young adulthood were linked with an increased risk of coronary artery calcium deposits in young adults.

All these studies provide important evidence that obesity is detrimental to the heart and blood vessels even in very young children. Doctors know that the processes that lead to a heart attack or stroke often take decades to progress to overt disease. It now appears, however, that these processes may be starting earlier than once thought and that becoming obese in childhood, adolescence, and young adulthood may accelerate them. The current generation of children may thus suffer the adverse effects of cardiovascular disease at a younger age than did previous generations, despite the advent of new drugs to treat such problems as high blood pressure and abnormal blood cholesterol.

Metabolic Disorders

The metabolic system is a complex set of interrelated processes that control how the body uses and stores energy. It includes the gastrointestinal tract, which governs absorption of nutrients and energy; the liver, which is the body's major metabolic organ; and a variety of hormonal systems that govern the ebb and flow of nutrients and energy. The system involves many overlapping components, each of which can, to some extent, compensate for an abnormality in another. But this compensation may often come at a price of an increased risk for other adverse health consequences.

Many metabolic disorders—among them insulin resistance, the metabolic syndrome, dyslipidemia (abnormal levels of fat in the blood), and type 2 diabetes mellitus—have been linked with obesity in adulthood.[15] In fact, many were long considered diseases of adulthood. Type 2 diabetes had even been called adult-onset diabetes. In the past fifteen years, however, much has changed in this field as the prevalence and severity of overweight have increased in children and adoles-

cents, with type 2 diabetes now appearing in children as young as eight years old. Insulin resistance, for example, or the process in which the action of insulin is retarded, is a relatively new concern in the pediatric age range. The precise mechanism for insulin resistance is unknown, but it often occurs in the context of obesity and results in increased insulin secretion by the pancreas and increased circulating levels of insulin. The increased insulin helps keep the blood sugar in the normal range but may cause other problems. J. Steinberger and several colleagues have shown that obesity in children is associated with decreased insulin sensitivity and increased circulating insulin and that these abnormalities persist into young adulthood.[16] Increased circulating insulin may in turn raise blood pressure and cholesterol levels.

The metabolic syndrome is likely associated with an increased risk of cardiovascular disease and diabetes even in young people.

The metabolic syndrome is a constellation of risk factors, including increased waist circumference, elevated blood pressure, increased triglyceride and decreased HDL-cholesterol concentrations, and raised blood sugar levels.[17] The underlying risk factors for the metabolic syndrome are abdominal obesity and insulin resistance. The metabolic syndrome is an important risk factor for cardiovascular disease and for the development of type 2 diabetes in adults.[18] It may also be associated with other abnormalities, including fatty liver disease, polycystic ovary disease, and obstructive sleep apnea.

Defining the metabolic syndrome has been controversial in adults, so its definition has been even more complicated in pediatric populations. S. Cook and several colleagues evaluated the prevalence of the metabolic syndrome in children and adolescents using an adaptation of one adult definition. They found the metabolic syndrome in only 4 percent of all children but in 30 percent of children who are obese.[19] R. Weiss and colleagues reported that each half-unit increase in the BMI z score (equivalent to an increase of half a standard deviation in BMI) resulted in a roughly 50 percent increase in the risk of the metabolic syndrome among overweight children and adolescents.[20]

The metabolic syndrome is likely associated with an increased risk of cardiovascular disease and diabetes even in young people. The Bogalusa study noted above showed that young victims of accidental death who had a number of metabolic syndrome factors had increased atherosclerotic lesions. Such findings suggest that the risk associated with the metabolic syndrome begins early in life.[21]

Obesity is associated with cholesterol abnormalities, often referred to as atherogenic dyslipidemia, that involve abnormal changes in cholesterol and triglycerides (or fats) in the blood.[22] These abnormalities, which appear to accelerate atherosclerosis, also occur in obese children and adolescents.[23]

The prevalence of type 2 diabetes mellitus has increased dramatically in adolescents—in parallel with the increasing incidence and severity of obesity.[24] Type 2 diabetes is related to insulin resistance. Although the beta

cells of the pancreas compensate for insulin resistance by making more insulin, they may not be able to keep up insulin production. When that happens, blood sugar starts to increase, first in response to meals and then ultimately even in the fasting state. At that point diabetes is present. In Cincinnati the prevalence of type 2 diabetes in adolescents increased tenfold between 1982 and 1994.[25] In the Bogalusa study 2.4 percent of overweight adolescents developed type 2 diabetes by age thirty while none of the lean adolescents did.[26] An American Diabetes Association review has suggested that as many as 45 percent of newly diagnosed cases of diabetes in children and adolescents are now type 2 diabetes.[27]

The increased prevalence of type 2 diabetes raises concern about cardiovascular disease risk. The National Cholesterol Education Program has identified diabetes as a coronary artery disease risk equivalent, meaning that patients with diabetes face a similar risk for a future adverse cardiovascular event as patients who have already had a heart attack or a stroke caused by an arterial blockage.[28] That finding suggests doctors should aggressively manage cardiovascular risk factors, such as high blood pressure and cholesterol in adults with diabetes, to prevent future illnesses and deaths from cardiovascular disease. If adolescents with type 2 diabetes have this same advanced risk, they may be more likely to have heart attacks, strokes, or heart failure at a very young age, perhaps even in their twenties and thirties. More research is needed to determine the likelihood of this happening and, if so, how best to prevent it.

Pulmonary Complications

The pulmonary system includes the lungs and associated blood vessels. The lungs take in air and exchange oxygen for carbon dioxide in the blood. The right side of the heart pumps blood through the pulmonary arteries to small capillaries in the lungs where this exchange occurs. The oxygenated blood then returns to the left side of the heart through the pulmonary veins to be pumped by the left ventricle to the body. Air is brought to the lungs by the trachea, which is connected to smaller and smaller airway branches, ultimately ending in the bronchioles where gas exchange occurs.

In asthma, one of the most common respiratory diseases of childhood, the airways in the lungs are constricted, either because inflammation causes the airways' lining to swell or because tightening of the smooth muscles that surround the airways can reduce their diameter. Asthma is generally thought to involve an allergic reaction, but much remains to be learned about the specific genetic and environmental factors that trigger the reaction. The prevalence and severity of childhood asthma have increased in the past two decades, again in parallel with the increasing prevalence and severity of childhood obesity.

Cross-sectional studies have demonstrated a link between overweight and asthma in children, though the link may be complicated by socioeconomic status, cigarette smoking, or other variables.[29] M. A. Rodriguez and colleagues found that children with a BMI above the 85th percentile had an increased risk of asthma independent of age, sex, ethnicity, socioeconomic status, and exposure to tobacco smoke. Their study also found socioeconomic status and cigarette smoking to be independent predictors of asthma.[30]

It is not clear why obesity may increase the risk of asthma. On the one hand, obesity has been associated with increased inflammation,

which could contribute to asthma. On the other hand, children with asthma may have only limited physical activity and may be treated with corticosteroids, which may promote obesity development. Increased adipose mass could have a physical effect on lung function. And an excess of abdominal fat can alter lung function both through increasing the weight on the wall of muscle and bone that surrounds the lungs and through limiting the motion of the diaphragm. Studies in adults with asthma have shown that weight loss can improve pulmonary function, but such studies have not yet been done in children.[31]

Sleep-disordered breathing may be one of the most important but also most under-recognized medical complications in overweight children and adolescents.

Obesity and obstructive sleep apnea are clearly related, both in adults and in children. Obstructive sleep apnea, or an abnormal collapse of the airway during sleep, results in snoring, irregular breathing, and disrupted sleep patterns. Sleep disruption can lead to excessive daytime sleepiness, which may itself decrease physical activity and heighten the risk of further obesity. Daytime sleepiness may also harm school performance. Obstructive sleep apnea has also been associated with learning disabilities and memory defects.[32] G. B. Mallory and colleagues found that one-third of young severely overweight patients had symptoms associated with obstructive sleep apnea and 5 percent had severe obstructive sleep apnea.[33]

Obstructive sleep apnea can also have long-term adverse cardiovascular consequences. In the short term, episodes of low oxygen levels in the blood cause temporary increases in blood pressure in the pulmonary artery and decrease blood flow in areas in the heart.[34] Over the longer term, obstructive sleep apnea can lead to daytime elevated blood pressure, increased left ventricular mass, and diastolic dysfunction (or an inability of the heart to relax and fill with blood appropriately) of the left ventricle.[35] Treating obstructive sleep apnea improves left ventricular hypertrophy and cardiac function.[36] Sleep-disordered breathing may be one of the most important but also most under-recognized medical complications in overweight children and adolescents.

Gastrointestinal Disorders

The gastrointestinal (GI) system includes the mouth, esophagus, stomach, small and large intestines, and the anus. Often the liver is also considered part of the GI system. Although it has always been obvious that the GI system is involved in obesity because of its role in food intake, it has not always been clear that obesity can also affect the GI system. Recent research has verified that obesity can contribute to liver disease and gastroesophageal reflux disease, which causes the stomach's contents to flow back into the esophagus.

Nonalcoholic fatty liver disease (or fat deposition in the liver) and nonalcoholic steatohepatitis (or an inflammation of the liver related to fat deposits) are recognized as complications of obesity in adults. As obesity develops, fat can be deposited in the liver. In their early stages, the fat deposits are thought

to be relatively innocuous, but the deposits lead to steatohepatitis, which can then progress to fibrosis, cirrhosis, and even to end-stage liver disease and liver failure, ultimately requiring a liver transplant.[37] No one knows why obesity-related nonalcoholic fatty liver disease progresses more rapidly to its more severe form in some people than in others.

Researchers now recognize that this same process of fat deposit and inflammation can afflict children and adolescents. The prevalence of nonalcoholic fatty liver disease is difficult to determine because it has no symptoms and requires a liver biopsy for confirmation. Some studies have attempted to estimate the prevalence, with one calculating that as many as 50 percent of obese children may have fat deposits in their livers while some 3 percent of obese children have the more advanced nonalcoholic steatohepatitis.[38] Another study has found that nonalcoholic fatty liver disease is the most common form of liver disease in children and adolescents.[39] Epidemiologic studies have shown that males and people of Hispanic ethnicity are at the highest risk for nonalcoholic fatty liver disease.[40] Most patients with nonalcoholic fatty liver disease also have insulin resistance. The degree of insulin resistance is associated with the severity of liver disease.[41] In adults with diabetes, the prevalence of fat deposits in the liver is high; approximately 50 percent have steatohepatitis and 19 percent have cirrhosis.[42] In adults, weight loss improves obesity-related fatty liver disease.[43] This and other potential treatments of nonalcoholic fatty liver disease have not been extensively studied in young patients.

Gastroesophageal reflux is a relatively common problem in adults that can cause acute symptoms of heartburn, long-term damage of the esophageal lining, and ultimately esophageal cancer. Several studies in adults have linked obesity with increased symptoms of gastroesophageal reflux. In a study of more than 10,000 adults aged twenty to fifty-nine in the United Kingdom, L. Murray and colleagues found that being above normal weight increased the likelihood of heartburn and acid regurgitation. Obese adults were almost three times as likely to have such symptoms as normal-weight individuals.[44] M. Nilsson and colleagues found a similar association, which was stronger among women, especially premenopausal women.[45] V. Di Francesco and colleagues reported that a vertical banded gastroplasty, an operation to decrease the stomach's size to produce weight loss, successfully reduced weight but not gastroesophageal acid reflux.[46] The disorder has not been studied extensively in obese children and adolescents, so researchers do not know whether it is linked with overweight in young people.

Skeletal Abnormalities

The skeletal system includes the bones and joints. In obesity, skeletal abnormalities, often referred to as orthopedic problems, can affect the lower extremities. Hip problems and abnormal growth of the tibia, or the main bone of the lower leg below the knee, are most common.

Some complications of obesity are physical—the effect of excess body weight—rather than metabolic, or the effect of increased adipose tissue. One such complication in adults is osteoarthritis, where excess weight results in wear and erosion of weight-bearing joints. Orthopedic problems also afflict obese children. Tibia vara, or Blount disease, is a mechanical deficiency in the medial tibial growth plate in adolescents that results in bowing of the tibia, a bowed appearance of

the lower leg, and an abnormal gait. Adolescent tibia vara is not common but most often affects boys older than age nine who are overweight.[47]

Another orthopedic problem related to overweight in young patients is slipped capital femoral epiphysis, a disorder of the hip's growth plate that occurs around the age of skeletal maturity. In this disorder the femur (the bone in the upper leg and hip) is rotated externally from under the growth plate, causing pain, making it impossible to walk, and requiring surgical repair. The pathophysiology is not completely known, but it seems to involve both mechanical and biological factors. The increased stress, which is mechanical, often results from excess weight. The bone's covering at this age, usually during the growth spurt, is thin and unable to resist the shearing forces. The abnormality is more common in overweight males and in African Americans. In about one-third to one-quarter of afflicted children, both legs are affected. Avoiding abnormal weight gain can prevent such orthopedic problems.[48]

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Psychosocial Issues

Psychosocial issues involve psychological health and the ability to relate to family members and peers. Such issues may have many determinants, some of which are genetic and some, socioeconomic. Childhood obesity is also linked with various psychosocial problems, the best studied of which is depression.

Depression is a common mental health problem in adolescents.[49] Adolescent-onset depression is often persistent and may be related to longer-term adverse mental health and health outcomes.[50] Although risk factors for depression in adolescents are not well known, one that has been studied, particularly in girls, is body dissatisfaction. In a long-term study, E. Stice and several colleagues found that body dissatisfaction, dietary restraint, and symptoms of bulimia are linked to depression.[51] Weight issues often cause body dissatisfaction, but they may affect girls of various ethnic groups differently. J. Siegel, for example, found that African American girls have a more positive body image than white, Hispanic, and Asian girls and that weight affects body image and satisfaction less in African American girls than in others.[52] The sample size in this study was small, however, so it is not conclusive.

Other studies have documented that obese adolescents seeking treatment for their obesity have more depressive symptoms than community-based obese or non-obese control groups.[53] In general, researchers have been unable to determine whether differences in depressive symptoms are based on the severity of obesity. Published studies have been based on relatively small samples, raising questions about the conclusions' validity. Nevertheless in a study by S. Erermis and several colleagues, more than half of their sample of obese adolescents had a clinically important diagnosis, often involving major depressive disorder.[54]

To discern the direction of the relationship between obesity and depression is difficult.

Depression itself is often associated with abnormal patterns of eating and physical activity that could result in future obesity; however, obesity may also result in psychosocial problems that can produce depression. Evidence supports both hypotheses. On the one hand, youths with depression are at greater risk to develop an increased body mass index.[55] E. Goodman and R. C. Whitaker found that increased BMI was associated with increased depression at a one-year follow-up, with depression scores highest among adolescents who had the greatest increase in body mass index.[56] On the other hand, in elementary school girls, higher BMI was linked with increasing symptoms of depression.[57] And overweight adolescents who had been teased by peers or family members were found to have increased suicidal thoughts and attempts.[58]

It appears that obese children and adolescents have difficulties with peer relationships. Overweight children, for example, tend to have few friends.[59] Mapping childhood social networks demonstrates that normal-weight children have more social relationships with a central network of children, while overweight children have more peripheral and isolated relationships in the network. In a contrary finding, however, a study of nine-year-old girls in the United Kingdom did not demonstrate that overweight girls were less popular and had fewer friends.[60]

An important psychosocial issue for overweight children and adolescents is quality of life. Research on this issue has not been extensive, and existing studies have focused on overall measures of quality of life rather than obesity-specific measures. J. S. Schwimmer and colleagues found that obese children and adolescents reported significantly lower health-related quality of life than their normal-weight counterparts, and they were five times more likely to have impaired quality of life.[61] In fact, the health-related quality of life for obese children and adolescents was similar to that of children diagnosed with cancer. And obese children and adolescents with obstructive sleep apnea reported even lower quality of life than those without it did, perhaps because of their increased daytime sleepiness. Ongoing research seeks to confirm the findings of Schwimmer's team and to refine the understanding of how, specifically, obesity affects children's quality of life.

Other Adverse Health Effects

Polycystic ovary syndrome consists of a constellation of abnormalities, including abnormal menses, such clinical manifestations of androgen excess as acne and excessive hair growth, elevated levels of circulatory androgens, and polycystic ovaries on ultrasound evaluation.[62] Among women with polycystic ovary syndrome, a substantial share is overweight or obese.[63] Although obesity is generally not considered the cause of the syndrome, it can exacerbate the associated metabolic derangements, including insulin resistance. The onset of polycystic ovary syndrome is often around the time of menarche, but it can occur after puberty, particularly after excess weight gain. The syndrome is one of the most common female hormonal disorders, with a reported prevalence of 5 to 10 percent.[64]

Women who suffer from polycystic ovary syndrome are at risk for infertility. Perhaps even more important, they are at substantial risk for type 2 diabetes and cardiovascular disease, as are those with metabolic syndrome.[65] Obesity is present in at least 35 percent of cases of polycystic ovary syndrome, with the share sometimes as high as 75 percent.[66] Weight loss or pharmacologic treatment im-

proves insulin resistance and often improves metabolic abnormalities.[67]

Another important complication of obesity is pseudotumor cerebri, a condition in which increased intracranial pressure often results in headache and sometimes in vomiting or blurred vision.[68] Pseudotumor cerebri may have multiple causes, including obesity, though the precise relationship between obesity and increased intracranial pressure remains unknown. Pseudotumor cerebri may be difficult to treat and can call for aggressive weight-loss therapy, including bariatric surgery. The problem is uncommon in children and adolescents but may be more common in adults.

Economic Issues

Of all the economic issues related to obesity, perhaps the most important is the cost of its associated health problems. In an analysis of people younger than sixty-five, R. Sturm estimated that obese adults' medical expenses are 36 percent higher than those of their non-obese peers.[69] In preparing their estimate of obesity's medical costs, A. M. Wolf and G. A. Colditz began with the relative risk of disease for obese and non-obese adults for such conditions as type 2 diabetes, coronary heart disease, hypertension, and some types of cancer.[70] Based on estimates of disease costs, they projected spending on obesity to be about 6 percent of national health spending in 1995. Because their estimate is somewhat dated and because they used cost estimates from the 1980s, it likely underestimates current obesity-related health spending.

Using a nationally representative data set and complex statistical analysis to evaluate U.S. medical spending on overweight or obesity in 1998, E. A. Finkelstein and colleagues found that spending on obesity accounted for 5.3 percent of national health spending.[71] Spending on overweight and obesity together accounted for 9.1 percent of total annual U.S. medical spending, a total rivaling even the estimated medical costs attributable to smoking.[72] Also important, Medicaid and Medicare cover approximately half of these increased costs, so that increases in obesity will place further demands on public health care spending.

Evaluating the costs of overweight and obesity in childhood and adolescents is difficult because of a paucity of data. G. Wang and W. H. Dietz used hospital discharge diagnoses from 1997 through 1999 to estimate the cost of obesity-related disorders in childhood.[73] They used the most frequent principal diagnoses where obesity was listed as a secondary diagnosis and then compared hospital diagnosis figures with those in 1979–81 for children aged six to seventeen. Not surprisingly, they found increases in obesity-related diagnoses. Asthma associated with obesity increased from 6 to 8 percent; diabetes associated with obesity, from 1.4 to 2.4 percent. They also found that time spent as an inpatient was longer for children with obesity and estimated that obesity-related inpatient costs were about 1.7 percent of total annual U.S. hospital costs. Better understanding of childhood obesity's costs will help the health care system determine the best approach to preventing and treating childhood obesity. For example, A. M. Tershakovec and several colleagues estimated that payers covered only some 11 percent of costs in a pediatric weight-management program.[74]

Other obesity-related economic issues may begin in childhood and carry over into adulthood. Overweight people are stigmatized in many cultures, including the United States, where they are often characterized as lazy,

sloppy, ugly, or stupid.[75] The degree of negative stereotyping increases with age and appears to affect girls more than it does boys.[76]

The implications of negative stereotyping in childhood carry into the experience of obese individuals as they enter adulthood. Women who are obese as adolescents become adults with less education, lower earning power, a higher likelihood of poverty, and a lower likelihood of marriage.[77] (These issues are substantially less pronounced for overweight adolescent males.) Obese individuals have more difficulty gaining admission to college.[78] Obese adults may also experience discrimination in renting apartments and houses.[79]

The indirect economic costs of adult obesity—reductions in economic opportunity or productivity—have been estimated at $23 billion a year in the United States.[80] One study of Swedish adult women estimated that 10 percent of all costs of sick leave and disability are obesity related.[81] The indirect costs of childhood obesity remain unknown. But if childhood obesity is causing an increased burden of disease, those costs may include time lost from work and day care costs for parents as well as time lost from school for the child.

Tracking Overweight and Obesity into Adulthood

With overweight and obesity such serious health risks for adults, an important question is whether overweight in children and adolescents predicts overweight in adulthood—in other words, whether children retain their relative ranking related to their peers as they age and become adults. That concept is known as "tracking."

Many studies have shown that overweight children are more likely than their normal-weight peers to become overweight adults. S. S. Guo and several colleagues evaluated how well BMI during childhood predicted overweight or obesity at age thirty-five in the Fels Longitudinal Study.[82] They found that for children and adolescents with BMI above the 95th percentile at any age during childhood, the probability of being obese at age thirty-five years ranged from 15 to 99 percent. The probability rises the older a child is when he or she becomes obese. Obese children, in other words, are more likely to become obese adults the older they are obese as children.

The link between parental overweight and childhood obesity is likely to be both genetic and environmental, and untangling the two is often difficult.

Robert C. Whitaker and several colleagues investigated the relationship between obesity at various times during childhood and obesity in young adults aged twenty-one to twenty-nine.[83] Obesity in very young children (aged one to two) was not associated with adult obesity, but for obese children older than two and for obese adolescents, the odds of becoming an obese adult were higher. Those odds increased the higher their BMI was, and the older they were when they became obese as children. Finally, having obese parents made it more likely that an obese child would continue to be obese into adulthood. The probability that an obese child aged three to five would remain obese as a young adult was 24 percent if neither parent was

obese at the time, but it rose to 62 percent if one parent was obese. The link between parental overweight and childhood obesity is likely to be both genetic and environmental, and untangling the two is often difficult. Researchers do not know which genes cause obesity to develop in children, though it is likely that many genes act together. And parents clearly create important aspects of the child's environment, including which foods are available and what opportunities the child has for physical activity or sedentary time. All of these factors may contribute to the tracking that makes it more likely that an obese child will become an obese adult.

Illness and Death Related to Obesity in Adults

Obesity in adulthood has long been associated with both increased illness and a greater chance of death. The Metropolitan Life Insurance Company's relative weight measure has been used for more than seventy-five years to assess mortality risks.[84] The most common adverse effects of adulthood obesity are cardiovascular disease and diabetes. Endometrial, colon, kidney, and postmenopausal breast cancer have also been associated with obesity. The Framingham Heart Study's consistent finding of a link between obesity and cardiovascular disease led the American Heart Association to recognize the emergence of obesity as one of the most important risk factors for heart disease and stroke in both men and women.[85] In the Nurses' Health Study, the heaviest subjects had fatal and nonfatal heart attacks three times more frequently than did the lightest subjects.[86] In addition to overweight and obesity in general, studies of adults have focused on the distribution of fat. For example in the Honolulu Heart Study, the risk of developing coronary artery disease was higher in men whose fat was concentrated around their abdomens, even after controlling for other risk factors.[87] The Framingham Heart Study found the same relationship for women.[88]

In adults obesity has been linked with cholesterol abnormalities, in particular lower HDL cholesterol (note that HDL is the "good" cholesterol, and higher values are better), elevation of triglycerides (fats), and high blood pressure.[89] In a review of population-based epidemiologic studies, B. N. Chiang and several colleagues reported increases in both systolic and diastolic blood pressure related to increasing weight.[90] Although these relationships between obesity and illness and death have long been well known in adults, relatively fewer data exist on the adverse health consequences of obesity in children and adolescents. Understanding these relationships in young people has become more urgent as the prevalence of overweight and obesity has increased in their age group.[91]

The cumulative effects of obesity-related diseases may be to cut short the lifespan of those affected. The question of how many people die because of obesity has been controversial. In 2004, A. H. Mokdad, of the Centers for Disease Control and Prevention (CDC), published a paper with several of his colleagues in the *Journal of the American Medical Association* that set the annual death toll at 400,000, an estimate that rivaled the toll of cigarette smoking.[92] Subsequent discussion led Mokdad's team to revise their estimate downward to 365,000.[93] A still later publication in the same journal used more recent data sets and lowered the estimated annual obesity-related death toll much further, to 112,000.[94] Part of the difficulty in estimating the obesity death toll is calculating a precise and valid estimate of obesity-related mortality. Each approach includes assump-

tions that are subject to question. For example, the analyses differed both in how they defined the normal weight used in the comparative calculations and in how they incorporated age into the analysis. That the analysis including more recent data sets found a lower overall obesity-related mortality is of interest. It seems counterintuitive because of obesity's increasing prevalence in recent years. But all heart disease risk factors except diabetes appear less likely to be present in overweight individuals in the more recent data, perhaps because of the medical profession's improved ability to treat these risk factors and heart disease. Unfortunately, the controversy over precisely what the death toll is has overshadowed the fact that both studies find obesity to be a major health threat. The focus on the death rate has also diverted attention from the illness and disability related to obesity.

A recent article in the *New England Journal of Medicine* raised the alarming possibility that the increasing prevalence of severe obesity in children may reverse the modern era's steady increase in life expectancy, with the youth of today on average living less healthy and ultimately shorter lives than their parents.[95] That claim too has been the subject of criticism. In an accompanying editorial in the same journal, S. H. Preston urged caution in accepting the claim, because many other factors continue to increase life expectancy in this and coming generations of children.[96] Methodological issues have also arisen regarding the calculations used to predict future longevity. Nevertheless, these data raise the possibility that the current generation of children could suffer greater illness or experience a shorter lifespan than that of their parents—the first such reversal in lifespan in modern history. That possibility makes childhood obesity an issue of utmost public health concern.

With the increasing prevalence of overweight and obesity in children and adolescents and the important tracking of overweight from childhood to adulthood, this generation of children could well have an even higher prevalence of obesity and adverse health consequences in adulthood than do their parents. Preventing childhood obesity is thus of urgent importance.

Notes

1. A. V. Chobanian and others, "The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure: The JNC 7 Report," *Journal of the American Medical Association* 289 (2003): 2560–72.

2. B. Falkner and S. R. Daniels, "Summary of the Fourth Report on the Diagnosis, Evaluation, and Treatment of High Blood Pressure in Children and Adolescents," *Hypertension* 44 (2004): 387–88.

3. B. Rosner and others, "Blood Pressure Differences between Blacks and Whites in Relation to Body Size among U.S. Children and Adolescents," *American Journal of Epidemiology* 151 (2000): 1007–19.

4. P. Muntner and others, "Trends in Blood Pressure among Children and Adolescents," *Journal of the American Medical Association* 291 (2004): 2107–13.

5. Ibid.

6. R. M. Lauer and W. R. Clarke, "Childhood Risk Factors for High Adult Blood Pressure: The Muscatine Study," *Pediatrics* 84 (1989): 633–41.

7. G. de Simone and others, "Effect of Growth on Variability of Left Ventricular Mass: Assessment of Allometric Signals in Adults and Children and Their Capacity to Predict Cardiovascular Risk," *Journal of American College of Cardiology* 25 (1995): 1056–62.

8. M. Yoshinaga and others, "Effect of Total Adipose Weight and Systemic Hypertension on Left Ventricular Mass in Children," *American Journal of Cardiology* 76 (1995): 785–87.

9. S. R. Daniels and others, "Effect of Lean Body Mass, Fat Mass, Blood Pressure, and Sexual Maturation on Left Ventricular Mass in Children and Adolescents: Statistical, Biological, and Clinical Significance," *Circulation* 92 (1995): 3249–54.

10. Systolic blood pressure is the pressure that occurs each time the heart pushes blood into the vessels; diastolic pressure is pressure that occurs when the heart rests.

11. S. R. Daniels and others, "Left Ventricular Geometry and Severe Left Ventricular Hypertrophy in Children and Adolescents with Essential Hypertension," *Circulation* 97 (1998): 1907–11.

12. H. C. McGill Jr. and others, "Effects of Nonlipid Risk Factors on Atherosclerosis in Youth with a Favorable Lipoprotein Profile," *Circulation* 103 (2001): 1546–50; G. S. Berenson and others, "Association between Multiple Cardiovascular Risk Factors and Atherosclerosis in Children and Young Adults: The Bogalusa Heart Study," *New England Journal of Medicine* 338 (1998): 1650–56.

13. Berenson and others, "Association between Multiple Cardiovascular Risk Factors and Atherosclerosis" (see note 12).

14. L. T. Mahoney and others, "Coronary Risk Factors Measured in Childhood and Young Adult Life Are Associated with Coronary Artery Calcification in Young Adults: The Muscatine Study," *Journal of the American College of Cardiology* 27 (1996): 277–84.

15. S. Klein and others, "Clinical Implications of Obesity with Specific Focus on Cardiovascular Disease: A Statement for Professionals from the American Heart Association Council on Nutrition, Physical Activity, and Metabolism," *Circulation* 110 (2004): 2952–67.

16. J. Steinberger and others, "Adiposity in Childhood Predicts Obesity and Insulin Resistance in Young Adulthood," *Journal of Pediatrics* 138 (2001): 469–73.

17. "Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III), Final Report," *Circulation* 106 (2002): 3143–421.

18. S. M. Grundy and others, "Diagnosis and Management of the Metabolic Syndrome: An American Heart Association/National Heart, Lung, and Blood Institute Scientific Statement," *Circulation* 112 (2005): 2735–52; A. J. Hanley and others, "Metabolic and Inflammation Variable Clusters and Prediction of Type 2 Diabetes: Factor Analysis Using Directly Measured Insulin Sensitivity," *Diabetes* 53 (2004): 1773–81.

19. S. Cook and others, "Prevalence of a Metabolic Syndrome Phenotype in Adolescents: Findings from the Third National Health and Nutrition Examination Survey, 1988–1994," *Archives of Pediatric and Adolescent Medicine* 157 (2003): 821–27.

20. R. Weiss and others, "Obesity and the Metabolic Syndrome in Children and Adolescents," *New England Journal of Medicine* 350 (2004): 2362–74.

21. Berenson and others, "Association between Multiple Cardiovascular Risk Factors and Atherosclerosis" (see note 12).

22. Atherogenic dyslipidemia includes an aggregation of lipid and lipoprotein abnormalities including an elevation of triglycerides and apolipoprotein B, a reduced level of HDL-cholesterol (the good cholesterol), and increased small LDL particles (a form of the bad cholesterol that predisposes to hardening of the arteries).

23. "Third Report of the National Cholesterol Education Program" (see note 17).

24. O. Pinhas-Hamiel, "Increased Incidence of Non-Insulin-Dependent Diabetes Mellitus among Adolescents," *Journal of Pediatrics* 128 (1996): 608–15.

25. Ibid.

26. S. R. Srinivasan and others, "Adolescent Overweight Is Associated with Adult Overweight and Related Multiple Cardiovascular Risk Factors: The Bogalusa Heart Study," *Metabolism* 45 (1996): 235–40.

27. American Diabetes Association, "Type 2 Diabetes in Children and Adolescents," *Diabetes Care* 23 (2000): 381–89.

28. Ibid.

29. E. Luder, T. A. Melnik, and M. DiMaio, "Association of Being Overweight with Greater Asthma Symptoms in Inner-City Black and Hispanic Children," *Journal of Pediatrics* 132 (1998): 699–703.

30. M. A. Rodriguez and others, "Identification of Population Subgroups of Children and Adolescents with High Asthma Prevalence: Findings from the Third National Health and Nutrition Examination Survey," *Archives of Pediatric and Adolescent Medicine* 156 (2002): 269–75.

31. B. Stenius-Aarniala and others, "Immediate and Long-Term Effects of Weight Reduction in Obese People with Asthma: Randomised Controlled Study," *British Medical Journal* 320 (2000): 827–32.

32. S. K. Rhodes and others, "Neurocognitive Deficits in Morbidly Obese Children with Obstructive Sleep Apnea," *Journal of Pediatrics* 127 (1995): 741–44.

33. G. B. Mallory Jr., D. H. Fiser, and R. Jackson, "Sleep-Associated Breathing Disorders in Morbidly Obese Children and Adolescents," *Journal of Pediatrics* 115 (1989): 892–97.

34. A. Orea-Tejeda and others, "SPECT Myocardial Perfusion Imaging during Periods of Obstructive Sleep Apnea in Morbidly Obese Patients without Known Heart Disease," *Rev Invest Clin.* 55 (2003): 18–25.

35. R. S. Amin and others, "Twenty-Four-Hour Ambulatory Blood Pressure in Children with Sleep-Disordered Breathing," *American Journal of Respiratory Critical Care Medicine* 169 (2004): 950–56; R. S. Amin and others, "Left Ventricular Hypertrophy and Abnormal Ventricular Geometry in Children and Adolescents with Obstructive Sleep Apnea," *American Journal of Respiratory Critical Care Medicine* 165 (2002): 1395–99; R. S. Amin and others, "Left Ventricular Function in Children with Sleep-Disordered Breathing," *American Journal of Cardiology* 95 (2005): 801–04.

36. Amin and others, "Left Ventricular Function" (see note 35); R. D. Ross and others, "Sleep Apnea-Associated Hypertension and Reversible Left Ventricular Hypertrophy," *Journal of Pediatrics* 111 (1987): 253–55.

37. B. A. Neuschwander-Tetri and S. H. Caldwell, "Nonalcoholic Steatohepatitis: Summary of an AASLD Single Topic Conference," *Hepatology* 37 (2003): 1202–19.

38. A. Kinugasa and others, "Fatty Liver and Its Fibrous Changes Found in Simple Obesity of Children," *Journal of Pediatric Gastroenterology and Nutrition* 3 (1984): 408–14.

39. J. E. Lavine and J. B. Schwimmer, "Nonalcoholic Fatty Liver Disease in the Pediatric Population," *Clinical Liver Disease* 8 (2004): viii–ix, 549–58.

40. J. B. Schwimmer and others, "Obesity, Insulin Resistance, and Other Clinicopathological Correlates of Pediatric Nonalcoholic Fatty Liver Disease," *Journal of Pediatrics* 142 (2003): 500–05.

41. Ibid.

42. J. F. Silverman, W. J. Pories, and J. F. Caro, "Liver Pathology in Diabetes Mellitus and Morbid Obesity: Clinical, Pathological, and Biochemical Considerations," *Pathology Annual* 24, pt. 1 (1989): 275–302.

43. M. L. Frelut and others, "Uneven Occurrence of Fatty Liver in Morbidly Obese Children: Impact of Weight Loss," *International Journal of Obesity* 22 (1995): 43.

44. L. Murray and others, "Relationship between Body Mass and Gastro-Esophageal Reflux Symptoms: The Bristol Helicobacter Project," *International Journal of Epidemiology* 32 (2003): 645–50.

45. M. Nilsson and others, "Obesity and Estrogen as Risk Factors for Gastroesophageal Reflux Symptoms," *Journal of the American Medical Association* 290 (2003): 66–72.

46. V. Di Francesco and others, "Obesity and Gastro-Esophageal Acid Reflux: Physiopathological Mechanisms and Role of Gastric Bariatric Surgery," *Obesity Surgery* 14 (2004): 1095–102.

47. T. F. Kling Jr. and R. N. Hensinger, "Angular and Torsional Deformities of the Lower Limbs in Children," *Clinical Orthopaedics and Related Research* (1983): 136–47.

48. R. T. Loder and others, "Acute Slipped Capital Femoral Epiphysis: The Importance of Physeal Stability," *Journal of Bone and Joint Surgery* 75 (1993): 1134–40.

49. R. G. Wight and others, "A Multilevel Analysis of Ethnic Variation in Depressive Symptoms among Adolescents in the United States," *Social Science and Medicine* 60 (2005): 2073–84.

50. B. Brimaher, C. Arbelaez, and D. Brent, "Course and Outcome of Child and Adolescent Major Depressive Disorder," *Journal of the American Academy of Child and Adolescent Psychiatry* 11 (2002): x, 619–37.

51. E. Stice and others, "Body Image and Eating Disturbances Predict Onset of Depression among Female Adolescents: A Longitudinal Study," *Journal of Abnormal Psychology* 109 (2000): 438–44.

52. J. Siegel, "Body Image Change and Adolescent Depressive Symptoms," *Journal of Adolescent Research* 17 (2002): 27–41.

53. B. Britz and others, "Rates of Psychiatric Disorders in a Clinical Study Group of Adolescents with Extreme Obesity and in Obese Adolescents Ascertained via a Population-Based Study," *International Journal of Obesity and Related Metabolic Disorders* 24 (2000): 1707–14; S. Erermis and others, "Is Obesity a Risk Factor for Psychopathology among Adolescents?" *Pediatrics International* 46 (2004): 296–301.

54. Ibid.

55. D. S. Pine and others, "The Association between Childhood Depression and Adulthood Body Mass Index," *Pediatrics* 107 (2001): 1049–56.

56. E. Goodman and R. C. Whitaker, "A Prospective Study of the Role of Depression in the Development and Persistence of Adolescent Obesity," *Pediatrics* 110 (2002): 497–504.

57. S. J. Erickson and others, "Are Overweight Children Unhappy? Body Mass Index, Depressive Symptoms, and Overweight Concerns in Elementary School Children," *Archives of Pediatrics and Adolescent Medicine* 154 (2000): 931–35.

58. M. E. Eisenberg, D. Neumark-Sztainer, and M. Story, "Associations of Weight-Based Teasing and Emotional Well-Being among Adolescents," *Archives of Pediatrics and Adolescent Medicine* 157 (2003): 733–38.

59. R. S. Strauss and H. A. Pollack, "Social Marginalization of Overweight Children," *Archives of Pediatrics and Adolescent Medicine* 157 (2003): 746–52.

60. R. G. Phillips and J. J. Hill, "Fat, Plain, but Not Friendless: Self-Esteem and Peer Acceptance of Obese Preadolescent Girls," *International Journal of Obesity and Related Metabolic Disorders* 22 (1998): 287–93.

61. J. S. Schwimmer, T. M. Burwinkle, and J. W. Varni, "Health-Related Quality of Life of Severely Obese Children and Adolescents," *Journal of the American Medical Association* 289 (2003): 1813–19.

62. "Revised 2003 Consensus on Diagnostic Criteria and Long-Term Health Risks Related to Polycystic Ovary Syndrome," *Fertility and Sterility* 81 (2004): 19–25.

63. D. A. Ehrmann and others, "Prevalence of Impaired Glucose Tolerance and Diabetes in Women with Polycystic Ovary Syndrome," *Diabetes Care* 22 (1999): 141–46.

64. M. Asuncion and others, "A Prospective Study of the Prevalence of the Polycystic Ovary Syndrome in Unselected Caucasian Women from Spain," *Journal of Clinical Endocrinology and Metabolism* 85 (2000): 2434–38.

65. C. J. Glueck and others, "Incidence and Treatment of Metabolic Syndrome in Newly Referred Women with Confirmed Polycystic Ovarian Syndrome," *Metabolism* 52 (2003): 908–15.

66. R. Azziz and others, "Troglitazone Improves Ovulation and Hirsutism in the Polycystic Ovary Syndrome: A Multicenter, Double Blind, Placebo-Controlled Trial," *Journal of Clinical Endocrinology and Metabolism* 86 (2001): 1626–32.

67. D. A. Ehrmann, "Polycystic Ovary Syndrome," *New England Journal of Medicine* 352 (2005): 1223–36.

68. S. D. Silberstein and J. Marcelis, "Headache Associated with Changes in Intracranial Pressure," *Headache* 32 (1992): 84–94.

69. R. Sturm, "The Effects of Obesity, Smoking, and Drinking on Medical Problems and Costs: Obesity Outranks Both Smoking and Drinking in Its Deleterious Effects on Health and Health Costs," *Health Affairs (Millwood)* 21 (2002): 245–53.

70. A. M. Wolf and G. A. Colditz, "Current Estimates of the Economic Cost of Obesity in the United States," *Obesity Research* 6 (1998): 97–106.

71. E. A. Finkelstein, I. C. Fiebelkorn, and G. Wang, "National Medical Spending Attributable to Overweight and Obesity: How Much, and Who's Paying?" *Health Affairs (Millwood)* Suppl. Web Exclusive (2003): W3-219-26. (http://content.healthaffairs.org/cgi/content/full/hlthaff.w3.219v1/DC1 [December 8, 2005]).

72. K. E. Warner, T. A. Hodgson, and C. E. Carroll, "Medical Costs of Smoking in the United States: Estimates, Their Validity, and Their Implications," *Tobacco Control* 8 (1999): 290–300.

73. G. Wang and W. H. Dietz, "Economic Burden of Obesity in Youths Aged 6 to 17 Years: 1979–1999," *Pediatrics* 109 (2002): e81.

74. A. M. Tershakovec and others, "Insurance Reimbursement for the Treatment of Obesity in Children," *Journal of Pediatrics* 134 (1999): 573–78.

75. J. R. Staffieri, "A Study of Social Stereotype of Body Image in Children," *Journal of Personality and Social Psychology* 7 (1967): 101–04.

76. J. A. Brylinsky and J. C. Moore, "The Identification of Body Build Stereotype in Young Children," *Journal of Research in Personality* 8 (1994): 170–181; N. H. Falkner and others, "Social, Educational, and Psychological Correlates of Weight Status in Adolescents," *Obesity Research* 9 (2001): 32–42.

77. S. L. Gortmaker and others, "Social and Economic Consequences of Overweight in Adolescence and Young Adulthood," *New England Journal of Medicine* 329 (1993): 1008–12.

78. H. Canning and J. Mayer, "Obesity: Its Possible Effect on College Acceptance," *New England Journal of Medicine* 275 (1966): 1172–74.

79. L. Karris, "Prejudice against Obese Renters," *Journal of Social Psychology* 101 (1977): 159–60.

80. "Obesity: Preventing and Managing the Global Epidemic—Report of a WHO Consultation," *World Health Organization Technical Report Series* 894 (2000): 1–253.

81. K. Narbro and others, "Economic Consequences of Sick Leave and Early Retirement in Obese Swedish Women," *International Journal of Obesity and Related Metabolic Disorders* 20 (1996): 895–903.

82. S. S. Guo and others, "Predicting Overweight and Obesity in Adulthood from Body Mass Index Values in Childhood and Adolescence," *American Journal of Clinical Nutrition* 76 (2002): 653–58.

83. Robert C. Whitaker and others, "Predicting Obesity in Young Adulthood from Childhood and Parental Obesity," *New England Journal of Medicine* 337 (1997): 869–73.

84. Metropolitan Life Insurance Company, "New Weight Standards for Men and Women" *Statistical Bulletin* 40 (1959): 1–4. The Metropolitan Life Insurance Company tables also take height into account.

85. H. B. Hubert and others, "Obesity as an Independent Risk Factor for Cardiovascular Disease: A 26-Year Follow-up of Participants in the Framingham Heart Study," *Circulation* 67 (1983): 968–77; R. H. Eckel and R. M. Krauss, "American Heart Association Call to Action: Obesity as a Major Risk Factor for Coronary Heart Disease—AHA Nutrition Committee," *Circulation* 97 (1998): 2099–100.

86. J. E. Manson and others, "A Prospective Study of Obesity and Risk of Coronary Heart Disease in Women," *New England Journal of Medicine* 322 (1990): 882–89.

87. R. P. Donahue and R. D. Abbott, "Central Obesity and Coronary Heart Disease in Men," *Lancet* 2 (1987): 1215.

88. W. B. Kannel, "Metabolic Risk Factors for Coronary Heart Disease in Women: Perspective from the Framingham Study," *American Heart Journal* 114 (1987): 413–19.

89. M. A. Berns, J. H. de Vries, and M. B. Katan, "Increase in Body Fatness as a Major Determinant of Changes in Serum Total Cholesterol and High-Density Lipoprotein Cholesterol in Young Men over a 10-Year Period," *American Journal of Epidemiology* 130 (1989): 1109–22.

90. B. N. Chiang, L. V. Perlman, and F. H. Epstein, "Overweight and Hypertension: A Review," *Circulation* 39 (1969): 403–21.

91. A. A. Hedley and others, "Prevalence of Overweight and Obesity among U.S. Children, Adolescents, and Adults, 1999–2002," *Journal of the American Medical Association* 291 (2004): 2847–50.

92. A. H. Mokdad and others, "Actual Causes of Death in the United States, 2000," *Journal of the American Medical Association* 291 (2004): 1238–45.

93. A. H. Mokdad, "Correction: Actual Causes of Death in the United States, 2000," *Journal of the American Medical Association* 293 (2005): 293–94.

94. K. M. Flegal and others, "Excess Deaths Associated with Underweight, Overweight, and Obesity," *Journal of the American Medical Association* 293 (2005): 1861–67.

95. S. J. Olshansky and others, "A Potential Decline in Life Expectancy in the United States in the 21st Century," *New England Journal of Medicine* 352 (2005): 1135–37.

96. S. H. Preston, "Deadweight? The Influence of Obesity on Longevity," *New England Journal of Medicine* 352 (2005): 1135-37.